

Metal-Free Direct Oxidative Intermolecular Diarylation of Anilides at Ambient Temperature Assisted by Cascade Selective Formation of C-C and C-N Bonds

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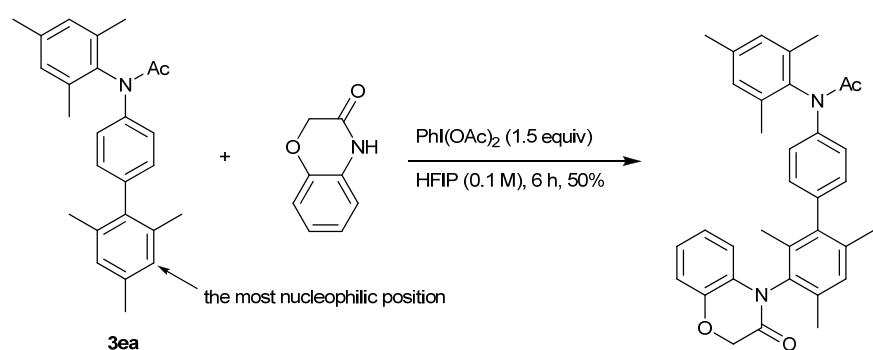
E-mail: andrey.antonchick@mpi-dortmund.mpg.de

Supporting Information:

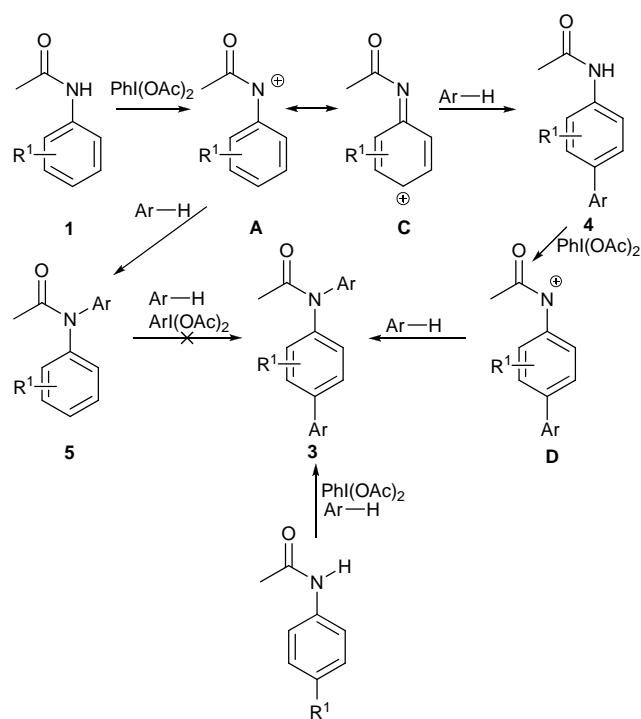
General:

Unless otherwise noted, all commercially available compounds were used as provided without further purification. Solvents for chromatography were technical grade. Petroleum ether 40-60 °C was used for column chromatography and thin layer chromatography. Dry solvents were purified by the Solvent Purification System M-BRAUN Glovebox Technology SPS-800. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel aluminium plates with F-254 indicator, visualised by irradiation with UV light. Column chromatography was performed using silica gel Merck 60 (particle size 0.040-0.063 mm). Solvent mixtures are understood as volume/volume.

¹H-NMR and ¹³C-NMR were recorded on Bruker DRX400 (400 MHz), DRX500 (500 MHz), INOVA500 (500 MHz) and INOVA600 (600 MHz) spectrometers in CDCl₃. Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet); coupling constants (J) are given in Hertz (Hz). Mass spectra were recorded on gas chromatograph (HP 6890) with mass detector (HP 5973), coupled to a J & W's fused silica GC column (GC column: stationary phase DB-5ms, 25 m × 0.202 mm × 0.33 μm, program: acquisition time delay: 3 min, initial temperature: 50 °C, initial time: 1 min, rate of temperature increasing: 40 °C/min, final temperature: 300 °C, final time: 15 min) or on a HPLC-MS HP Agilent 1100 series system equipped with a reversed-phase column (CC250/4 Nucleosil 120-5 C4 by Macherey-Nagel, flow 1.0 mL/min, from 90% A to 100% B over 15 min; A = 0.1% HCOOH in H₂O, B = 0.1% HCOOH in CH₃CN). High resolution mass spectra were recorded on a LTQ Orbitrap mass spectrometer coupled to an Accela HPLC-System (HPLC column: Hypersyl GOLD, 50 mm × 1 mm × 1.9 μm). Fourier transform infrared spectroscopy (FT-IR) spectra were obtained with a Bruker Tensor 27 spectrometer (ATR, neat) and are reported in terms of frequency of absorption (cm⁻¹). Chemical yields refer to pure isolated substances.

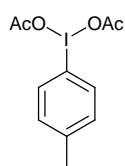


Scheme 1. Metal-free amination of derivative **3ea**.



Scheme 2. Proposed mechanism of the diarylation.

Preparation of 1-(Diacetoxyiodo)-4-methylbenzene¹



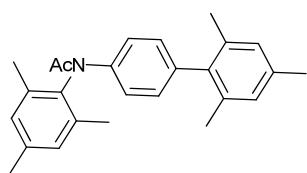
Sodium perborate tetrahydrate (100 mmol) was slowly added in portions during 20 min to a stirred solution of 4-iodotoluene (2.188 g, 10 mmol) in glacial acetic acid (90 mL) with CF₃SO₃H (60 mmol) at 40-45 °C, and the mixture was stirred at this temperature until TLC analysis indicated completion of reaction. Reaction time needed: 12 h. The solution was then concentrated to half its volume by evaporation of acetic acid under reduced pressure, and water (100 mL) was added. The solid separated was collected by filtration, washed with water, and dried in air. A second crop of product was obtained by extraction of the filtrate with dichloromethane (3 × 100 mL) followed by drying of the combined extracts (anhydrous Na₂SO₄), filtration, and removal of the solvent by evaporation under reduced pressure. The combined yield of the product was 77% (2.600 g, 7.7 mmol). The analytical data was identical to the data reported in literature ¹. White amorphous solid, ¹H NMR (400 MHz, CDCl₃) δ 7.97 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 2.44 (s, 3H), 2.00 ppm (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 176.49, 142.79, 135.09, 131.86, 118.44, 21.66, 20.50 ppm.

General Experimental Procedure for the Synthesis of Diarylated Anilides:

Acetanilide (**1**, 0.2 mmol) was dissolved in a 4 mL screw-capped vial with 1 mL of 1,1,1,3,3,3-hexafluoro-2-propanol. Then arene (**2**, 0.6-2.0 mmol) followed by *para*-tolylodonium diacetate (0.44-0.8 mmol) was added to the stirred solution at room temperature. The reaction mixture was stirred for 24-96 h. After completion of the reaction, it was quenched with saturated Na₂S₂O₃ solution and extracted with dichloromethane, washed with water, brine and dried over anhydrous MgSO₄. Then the organic extract was concentrated under reduced pressure and purified by silica gel column chromatography with 10-15% mixture of EtOAc in petroleum ether eluent.

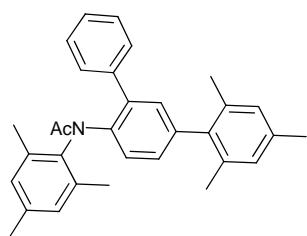
¹ M. D. Hossain and T. Kitamura, *J. Org. Chem.* 2005, **70**, 6984.

Physical data of Diarylated anilides:



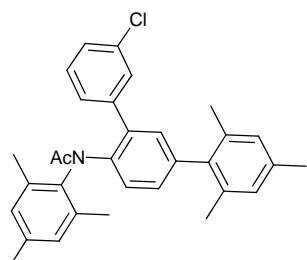
N-Mesityl-N-(2',4',6'-trimethylbiphenyl-4-yl)acetamide (3ea)

White amorphous solid; $R_f = 0.55$ (35% EtOAc in Petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.33 (d, $J = 8.5$ Hz, 2H), 7.04 (d, $J = 8.5$ Hz, 2H), 7.01 (s, 2H), 6.92 (s, 2H), 2.35 (s, 3H), 2.32 (s, 3H), 2.21 (s, 6H), 1.99 (s, 6H), 1.93 ppm (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 170.77, 139.36, 138.60, 138.48, 138.21, 137.31, 136.67, 136.39, 136.34, 130.11, 129.49, 128.10, 123.18, 24.04, 21.19, 21.14, 20.90, 18.20 ppm; FT-IR: $\tilde{\nu} = 2954, 2920, 2858, 1669, 1511, 1482, 1438, 1368, 1297, 1254, 1033 \text{ cm}^{-1}$; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{26}\text{H}_{30}\text{ON}$: 372.23219 found: 372.23257.



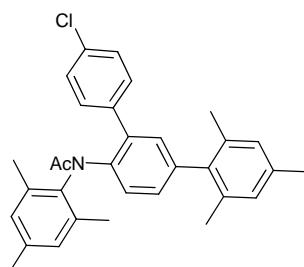
N-Mesityl-N-(2-phenyl-2',4',6'-trimethylbiphenyl-4-yl)acetamide (3ma)

White amorphous solid; $R_f = 0.50$ (35% EtOAc in Petroleum ether); ^1H NMR (500 MHz, CDCl_3) δ 7.39 (d, $J = 7.1$ Hz, 2H), 7.34-7.28 (m, 2H), 7.04 (d, $J = 1.7$ Hz, 1H), 7.00 (dd, $J = 8.4, 1.7$ Hz, 1H), 6.95 (d, $J = 8.4$ Hz, 2H), 6.91 (s, 2H), 6.90 (s, 2H), 2.31 (s, 3H), 2.30 (s, 3H), 2.14 (s, 6H), 2.05 (s, 6H), 1.74 ppm (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 172.08, 142.08, 138.71, 138.30, 138.23, 137.95, 137.32, 136.72, 136.21, 133.49, 130.29, 128.96, 128.74, 128.58, 128.28, 128.18, 127.90, 126.77, 125.04, 23.68, 21.13, 21.02, 21.00, 19.43 ppm; FT-IR: $\tilde{\nu} = 2922, 2856, 1738, 1676, 1476, 1365, 1294, 1242, 1037, 1012 \text{ cm}^{-1}$; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{32}\text{H}_{34}\text{ON}$: 448.26349 found: 448.26309.



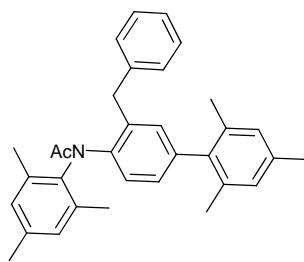
N-Mesityl-N-(3-chlorophenyl-2-yl-2',4',6'-trimethylbiphenyl-4-yl)acetamide (3na)

White amorphous solid; $R_f = 0.50$ (35% EtOAc in Petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.30 (s, 1H), 7.29–7.23 (m, 3H), 7.08 – 7.03 (m, 2H), 7.01 (s, 1H), 6.94 (s, 2H), 6.92 (s, 2H), 2.33 (s, 3H), 2.32 (s, 3H), 2.14 (s, 6H), 2.06 (s, 6H), 1.81 ppm (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.09, 143.56, 138.34, 138.31, 138.18, 137.91, 137.25, 136.83, 136.49, 136.35, 136.13, 135.75, 133.48, 133.06, 130.33, 129.33, 129.17, 128.19, 126.91, 126.81, 125.39, 23.70, 21.12, 21.02, 21.00, 19.39 ppm; FT-IR: $\tilde{\nu} = 2921, 2855, 1691, 1564, 1466, 1363, 1292, 1244, 1014 \text{ cm}^{-1}$; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{32}\text{H}_{33}\text{ON}^{35}\text{Cl}$: 482.22452 found: 482.22412; $[\text{M}+\text{H}]^+$ $\text{C}_{32}\text{H}_{33}\text{ON}^{37}\text{Cl}$: 484.22157 found: 484.22179.



N-Mesityl-N-(4-chlorophenyl-2',4',6'-trimethylbiphenyl-4-yl)acetamide (3oa)

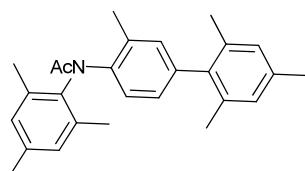
White amorphous solid; $R_f = 0.55$ (35% EtOAc in Petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.36 (d, $J = 8.5 \text{ Hz}$, 2H), 7.30 (d, $J = 8.5 \text{ Hz}$, 2H), 7.04 – 7.00 (m, 2H), 6.97–6.90 (m, 5H), 2.33 (s, 3H), 2.32 (s, 3H), 2.17 (s, 6H), 2.05 (s, 6H), 1.76 ppm (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 171.99, 140.59, 138.47, 138.40, 138.18, 137.96, 137.13, 136.93, 136.83, 136.58, 136.14, 133.22, 132.71, 130.37, 129.87, 129.12, 128.20, 128.11, 124.76, 23.71, 21.12, 21.01 (2C), 19.44 ppm; FT-IR: $\tilde{\nu} = 2925, 2860, 1680, 1479, 1369, 1297, 1272, 1249, 1094, 1017 \text{ cm}^{-1}$; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{32}\text{H}_{33}\text{ON}^{35}\text{Cl}$: 482.22452 found: 482.22399; $[\text{M}+\text{H}]^+$ $\text{C}_{32}\text{H}_{33}\text{ON}^{37}\text{Cl}$: 484.22157 found: 484.22178.



N-(3-Benzyl-2',4',6'-trimethylbiphenyl-4-yl)-N-mesitylacetamide (3ia)

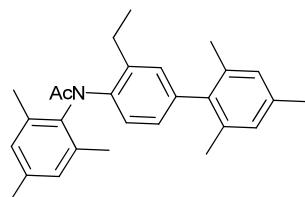
Light yellow oil; $R_f = 0.55$ (35% EtOAc in Petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.32 – 7.17 (m, 5H), 7.03 (s, 2H), 6.87 – 6.82 (m, 3H), 6.79 (d, $J = 8.2 \text{ Hz}$, 1H), 6.73 (d, $J = 1.5 \text{ Hz}$, 1H), 4.02 (s, 2H), 2.36 (s, 3H), 2.34 (s, 6H), 2.27 (s, 3H), 2.04 (s, 3H), 1.90 ppm (s, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 170.70, 140.87, 139.35, 138.57, 138.35, 138.18, 138.10, 137.56, 136.58,

136.25 (2C), 131.63, 130.27, 130.13, 128.54, 128.02, 127.43, 126.26, 123.77, 38.40, 23.44, 21.12, 21.06, 20.91, 18.78 ppm; FT-IR: $\tilde{\nu}$ = 2922, 2855, 1720, 1675, 1478, 1367, 1305, 1250, 1099, 1017 cm⁻¹; HRMS: calc. for [M+H]⁺ C₃₃H₃₆ON: 462.27914 found: 462.27866.



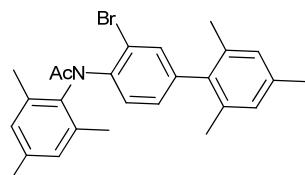
N-Mesityl-N-(2',3,4',6'-tetramethylbiphenyl-4-yl)acetamide (3fa)

White amorphous solid; R_f = 0.45 (35% EtOAc in Petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 7.02 (d, J = 1.3 Hz, 1H), 6.99 (s, 2H), 6.92 (s, 2H), 6.80 (dd, J = 8.2, 1.3 Hz, 1H), 6.73 (d, J = 8.2 Hz, 1H), 2.34 (s, 6H), 2.32 (s, 3H), 2.23 (s, 6H), 1.99 (s, 6H), 1.98 ppm (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 170.10, 139.48, 138.60, 138.58, 138.00, 137.84, 136.61, 136.27, 136.24, 134.84, 132.09, 130.18, 128.07, 127.22, 124.19, 23.34, 21.13, 21.10, 20.96, 20.36, 18.55 ppm; FT-IR: $\tilde{\nu}$ = 2971, 2921, 2856, 1668, 1484, 1366, 1310, 1250, 1034 cm⁻¹; HRMS: calc. for [M+H]⁺ C₂₇H₃₂ON: 386.24784 found: 386.24845.



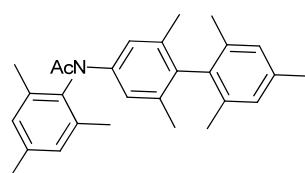
N-(3-Ethyl-2',4',6'-trimethylbiphenyl-4-yl)-N-mesitylacetamide (3ga)

Light yellow oil; R_f = 0.50 (35% EtOAc in Petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 7.15 (d, J = 1.6 Hz, 1H), 6.98 (s, 2H), 6.93 (s, 2H), 6.81 (dd, J = 8.2, 1.6 Hz, 1H), 6.73 (d, J = 8.2 Hz, 1H), 2.65 (q, J = 7.4 Hz, 2H), 2.33 (s, 3H), 2.32 (s, 3H), 2.23 (s, 6H), 2.02-1.97 (m, 9H), 1.31 ppm (t, J = 7.4 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 170.76, 140.16, 139.56, 138.88, 138.69, 137.95, 137.17, 136.66, 136.31, 130.19, 129.41, 128.12 (2C), 127.00, 124.17, 24.59, 23.30, 21.14, 21.09, 20.98, 18.56, 13.47 ppm; FT-IR: $\tilde{\nu}$ = 2971, 2921, 2856, 1668, 1484, 1366, 1310, 1250, 1034 cm⁻¹; HRMS: calc. for [M+H]⁺ C₂₈H₃₄ON: 400.26349 found: 400.26276.



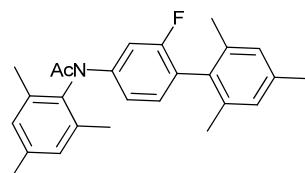
N-(3-Bromo-2',4',6'-trimethylbiphenyl-4-yl)-N-mesitylacetamide (3ha)

White amorphous solid; $R_f = 0.50$ (35% EtOAc in Petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.46 (d, $J = 1.8$ Hz, 1H), 6.99 (s, 2H), 6.96 (dd, $J = 8.2, 1.8$ Hz, 1H), 6.92 (s, 2H), 6.84 (d, $J = 8.2$ Hz, 1H), 2.33 (s, 3H), 2.31 (s, 3H), 2.29 (s, 6H), 2.00 ppm (s, 9H); ^{13}C NMR (101 MHz, CDCl_3) δ 170.54, 140.23, 138.78, 138.37, 138.31, 137.21, 137.01, 136.65, 136.14, 134.76, 130.22, 129.12, 128.22, 126.40, 121.90, 23.42, 21.14, 21.10, 20.93, 18.88 ppm ; FT-IR: $\tilde{\nu} = 2957, 2920, 2854, 1681, 1483, 1466, 1366, 1302, 1268, 1244, 1030 \text{ cm}^{-1}$; HRMS: calc. for $[\text{M}+\text{H}]^+ \text{C}_{26}\text{H}_{29}\text{ON}^{79}\text{Br}$: 450.14270 found: 450.14276; $[\text{M}+\text{H}]^+ \text{C}_{26}\text{H}_{29}\text{ON}^{81}\text{Br}$: 452.14066 found: 452.14025.



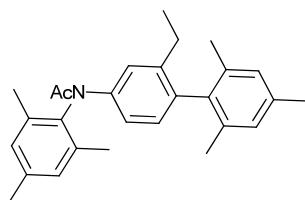
N-Mesityl-N-(2,2',4',6,6'-pentamethylbiphenyl-4-yl)acetamide (3la)

Light yellow oil; $R_f = 0.50$ (35% EtOAc in Petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.02 (s, 2H), 6.98 (s, 2H), 6.91 (s, 2H), 2.34 (s, 3H), 2.31 (s, 3H), 2.20 (s, 6H), 1.89 (s, 3H), 1.83 (s, 6H), 1.81 ppm (s, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 170.75, 139.31, 138.47, 138.20, 136.71, 136.66, 136.39, 136.23, 135.94, 135.66, 130.03, 128.28, 122.33, 24.13, 21.25, 21.20, 20.36, 19.89, 18.30 ppm; FT-IR: $\tilde{\nu} = 2920, 2856, 1666, 1601, 1469, 1369, 1318, 1282, 1033 \text{ cm}^{-1}$; HRMS: calc. for $[\text{M}+\text{H}]^+ \text{C}_{28}\text{H}_{34}\text{ON}$: 400.26349 found: 400.26302.



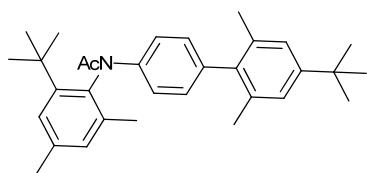
N-(2-Fluoro-2',4',6'-trimethylbiphenyl-4-yl)-N-mesitylacetamide (3ja)

White amorphous solid; $R_f = 0.60$ (35% EtOAc in Petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.20 (d, $J = 11.7$ Hz, 1H), 7.12 (d, $J = 11.7$ Hz, 1H), 7.05 – 6.98 (m, 3H), 6.94 (s, 2H), 2.35 (s, 3H), 2.31 (s, 3H), 2.18 (s, 6H), 2.01 (s, 6H), 1.91 ppm (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 170.92, 159.35 (d, $J = 243.1$ Hz), 141.43 (d, $J = 9.5$ Hz), 138.86, 137.64, 137.50, 136.95, 136.33, 132.03, 131.20 (d, $J = 5.3$ Hz), 130.27, 128.19 (2C), 118.31 (d, $J = 1.6$ Hz), 110.43 (d, $J = 27.0$ Hz), 24.25, 21.22, 21.20, 20.55, 18.09 ppm; FT-IR: $\tilde{\nu} = 2920, 2855, 1675, 1619, 1476, 1369, 1311, 1273, 1243, 1224, 1119, 1030 \text{ cm}^{-1}$; HRMS: calc. for $[\text{M}+\text{H}]^+ \text{C}_{26}\text{H}_{29}\text{ONF}$: 390.22277 found: 390.22361.



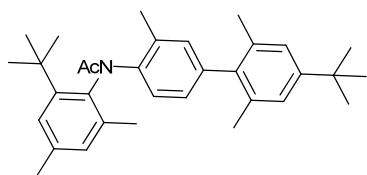
N-(2-Ethyl-2',4',6'-trimethylbiphenyl-4-yl)-N-mesitylacetamide (3ka)

Colourless oil; $R_f = 0.60$ (35% EtOAc in Petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.39 (d, $J = 1.9$ Hz, 1H), 7.03–6.96 (m, 3H), 6.91 (s, 2H), 6.85 (d, $J = 8.3$ Hz, 1H), 2.34 (s, 3H), 2.31 (s, 3H), 2.25 – 2.16 (m, 8H), 1.91 (s, 3H), 1.90 (s, 6H), 0.97 ppm (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 170.75, 142.05, 139.86, 138.37, 138.33, 137.73, 136.44, 136.38, 136.35, 136.29, 130.06, 129.47, 128.04, 123.28, 120.70, 26.08, 24.09, 21.21 (2C), 20.63, 18.22, 14.68 ppm; FT-IR: $\tilde{\nu} = 2970, 2921, 2858, 1672, 1605, 1477, 1367, 1298, 1032 \text{ cm}^{-1}$; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{28}\text{H}_{34}\text{ON}$: 400.26349 found: 400.26284.



N-(4'-tert-Butyl-2',6'-dimethylbiphenyl-4-yl)-N-(2-tert-butyl-4,6-dimethylphenyl)acetamide (3ei)

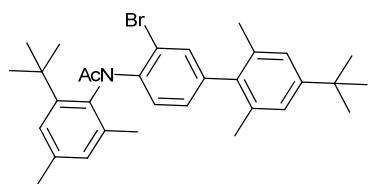
Light yellow oil; $R_f = 0.70$ (35% EtOAc in Petroleum ether); ^1H NMR (500 MHz, CDCl_3) δ 7.37 (d, $J = 8.4$ Hz, 2H), 7.28 (s, 1H), 7.09 (s, 2H), 7.07 (s, 1H), 7.05 (d, $J = 8.4$ Hz, 2H), 2.38 (s, 3H), 2.22 (s, 3H), 2.01 (s, 6H), 1.97 (s, 3H), 1.34 (s, 9H), 1.23 ppm (s, 9H); ^{13}C NMR (126 MHz, CDCl_3) δ 171.55, 149.78, 146.53, 140.58, 138.59, 138.40, 137.05, 136.96, 135.83, 130.44, 129.45, 128.93, 124.33, 122.61, 36.41, 34.43, 31.92, 31.56, 25.17, 21.53, 21.21, 18.59 ppm; FT-IR: $\tilde{\nu} = 2960, 2925, 2868, 1666, 1511, 1480, 1366, 1322, 1293, 1004 \text{ cm}^{-1}$; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{32}\text{H}_{42}\text{ON}$: 456.32609 found: 456.32561.



N-(4'-tert-Butyl-2',3,6'-trimethylbiphenyl-4-yl)-N-(2-tert-butyl-4,6-dimethylphenyl)acetamide (3fi)

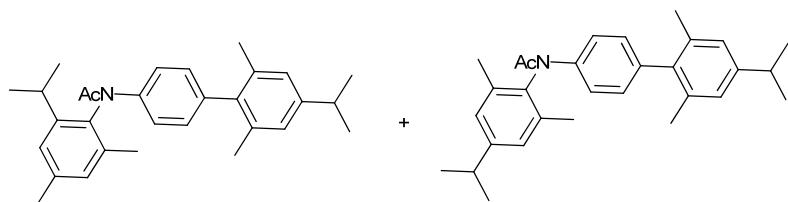
Colourless oil, $R_f = 0.60$ (20% EtOAc in Petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.26 (s, 1H), 7.10 (s, 1H), 7.08 (s, 2H), 7.05 (d, $J = 1.5$ Hz, 1H), 6.80 (d, $J = 8.1$ Hz, 1H), 6.64 (s, 1H),

2.38 (s, 3H), 2.37 (s, 3H), 2.28 (brs, 3H), 2.09 (s, 3H), 2.02 (s, 3H), 1.93 (s, 3H), 1.34 (s, 9H), 1.27 ppm (brs, 9H); ^{13}C NMR (101 MHz, CDCl_3) δ 149.68, 138.55, 138.06, 138.01, 135.84, 135.73, 134.39, 132.98, 130.71, 126.88, 124.29, 124.24, 34.40, 31.55, 24.71, 23.99, 22.10, 21.46, 21.07, 19.37 ppm; FT-IR: $\tilde{\nu}$ = 2961, 2868, 1678, 1480, 1363, 1288, 1263, cm^{-1} ; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{33}\text{H}_{44}\text{ON}$: 470.34174 found: 470.34096.



N-(3-Bromo-4'-tert-butyl-2',6'-dimethylbiphenyl-4-yl)-N-(2-tert-butyl-4,6-dimethylphenyl)acetamide (3hi)

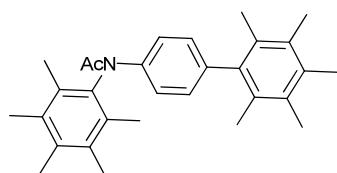
Colourless oil, R_f = 0.60 (20% EtOAc in Petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.49 (d, J = 1.7 Hz, 1H), 7.24 (s, 1H), 7.10 (s, 2H), 7.07 (s, 1H), 6.93 (d, J = 8.4 Hz, 1H), 6.68 (d, J = 8.4 Hz, 1H), 2.38 (s, 3H), 2.33 (s, 3H), 2.11 (s, 3H), 2.03 (s, 3H), 1.89 (s, 3H), 1.33 (s, 9H), 1.27 ppm (s, 9H); ^{13}C NMR (101 MHz, CDCl_3) δ 171.73, 150.30, 146.99, 140.23, 140.09, 139.47, 138.55, 137.81, 137.03, 135.83, 135.63, 130.75, 128.65, 128.06, 124.87, 124.47, 124.40, 121.47, 35.87, 34.46, 31.51, 31.10, 24.61, 23.98, 21.50, 20.93, 19.45 ppm; FT-IR: $\tilde{\nu}$ = 2961, 2869, 1688, 1476, 1367, 1279, 1234 cm^{-1} ; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{32}\text{H}_{41}\text{ON}^{79}\text{Br}$: 534.23660 found: 534.23622; $[\text{M}+\text{H}]^+$ $\text{C}_{32}\text{H}_{41}\text{ON}^{81}\text{Br}$: 536.23456 found: 536.23423.



N-(4'-Isopropyl-2',6'-dimethylbiphenyl-4-yl)-N-(2-isopropyl-4,6-dimethylphenyl)acetamide
N-(4'-Isopropyl-2',6'-dimethylbiphenyl-4-yl)-N-(4-isopropyl-2,6-dimethylphenyl)acetamide (3ej)

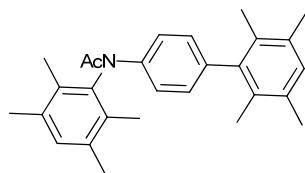
(Mixture of two regioisomers in 1: 1.2 ratio), Colourless oil; R_f = 0.60 (20% EtOAc in Petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.27 (m, 3H), 7.12-6.88 (m, 11H), 3.08 (m, 1.7H), 2.87 (m, 1H), 2.68 (m, 0.8H), 2.46-2.20 (m, 15H), 2.01-1.89 (m, 12H), 1.27 (d, J = 6.9 Hz, 6H), 1.25 – 1.19 (m, 6H), 1.07 – 1.00 (m, 4H), 0.75 ppm (t, J = 7.1 Hz, 4H); ^{13}C NMR

(101 MHz, CDCl₃) δ 171.04, 147.58, 147.12, 146.32, 146.28, 140.48, 140.40, 138.88, 138.85, 137.52, 137.41, 137.09, 137.00, 136.85, 136.47, 136.44, 136.25, 136.19, 129.70, 129.65, 129.48, 128.00, 127.42, 126.18, 125.43, 123.30, 123.21, 33.85, 28.01, 24.31, 24.29, 24.23, 24.16, 24.09, 23.98, 23.95, 23.83, 23.76, 23.74, 21.50, 21.47, 21.18, 21.04, 18.42 ppm; FT-IR: $\tilde{\nu}$ = 2961, 2925, 2868, 1677, 1478, 1366, 1321, 1297, cm⁻¹; HRMS: calc. for [M+H]⁺ C₃₀H₃₈ON: 428.29479 found: 428.29431.



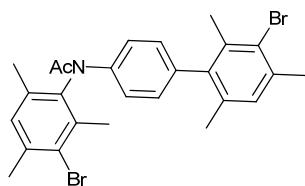
N-(2',3',4',5',6'-Pentamethylbiphenyl-4-yl)-N-(2,3,4,5,6-pentamethylphenyl)acetamide (3ee)

White amorphous solid; R_f = 0.55 (35% EtOAc in Petroleum ether); ¹H NMR (500 MHz, CDCl₃) δ 7.33 (d, J = 8.4 Hz, 2H), 7.01 (d, J = 8.4 Hz, 2H), 2.30 (s, 6H), 2.28 (s, 6H), 2.25 (s, 6H), 2.20 (s, 6H), 1.93 (s, 6H), 1.89 ppm (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 171.16, 139.72, 139.51, 139.17, 138.42, 135.66, 134.26, 134.08, 132.41, 132.05, 131.96, 129.66, 123.20, 24.28, 18.57, 17.08, 16.96, 16.91, 16.72, 15.56 ppm; FT-IR: $\tilde{\nu}$ = 2989, 2923, 1665, 1506, 1455, 1366, 1299, 1258, 1216, 1065, 1019 cm⁻¹; HRMS: calc. for [M+H]⁺ C₃₀H₃₈ON: 428.29479 found: 428.29440.



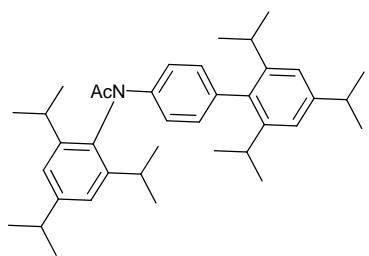
N-(2',3',5',6'-Tetramethylbiphenyl-4-yl)-N-(2,3,5,6-tetramethylphenyl)acetamide (3ed)

White amorphous solid; R_f = 0.55 (35% EtOAc in Petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 7.32 (d, J = 8.5 Hz, 2H), 7.06 (s, 1H), 7.01 (d, J = 8.5 Hz, 2H), 6.98 (s, 1H), 2.29 (s, 6H), 2.25 (s, 6H), 2.14 (s, 6H), 1.89 (s, 3H), 1.87 ppm (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 170.95, 141.66, 140.59, 139.47, 138.58, 135.55, 133.61, 132.44, 132.38, 131.75, 130.49, 129.48, 123.23, 24.21, 20.32, 20.29, 17.43, 14.65 ppm; FT-IR: $\tilde{\nu}$ = 2919, 1673, 1506, 1458, 1366, 1306, 1236, 1010 cm⁻¹; HRMS: calc. for [M+H]⁺ C₂₈H₃₄ON: 400.26349 found: 400.26273.



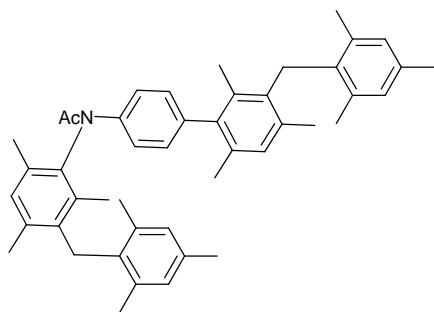
N-(3'-Bromo-2',4',6'-trimethylbiphenyl-4-yl)-N-(3-bromo-2,4,6-trimethylphenyl)acetamide (3eb)

Colourless oil; $R_f = 0.55$ (35% EtOAc in Petroleum ether); ^1H NMR (500 MHz, CDCl_3) δ 7.34–7.28 (m, 2H), 7.12 (s, 1H), 7.01 (s, 1H), 6.99 (s, 2H), 2.45 (s, 3H), 2.41 (s, 3H), 2.39 (s, 3H), 2.16 (s, 3H), 2.11 (s, 3H), 1.92 (s, 3H), 1.91 ppm (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 170.57, 140.31, 139.43, 139.21, 139.07, 137.78, 137.23, 137.14, 135.42, 135.13, 131.04, 129.52, 129.49, 126.26, 125.50, 123.35, 123.30, 24.11, 24.10 (2C), 22.19, 20.76, 19.44, 18.16 ppm; FT-IR: $\tilde{\nu} = 2957, 2925, 2856, 1675, 1453, 1370, 1242, 1097, 1017 \text{ cm}^{-1}$; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{26}\text{H}_{28}\text{ON}^{79}\text{Br}_2$: 528.05322 found: 528.05299; $[\text{M}+\text{H}]^+$ $\text{C}_{26}\text{H}_{28}\text{ON}^{79}\text{Br}^{81}\text{Br}$: 530.05117 found: 530.05061; $\text{C}_{26}\text{H}_{28}\text{ON}^{81}\text{Br}_2$: 532.04912 found: 532.04855.



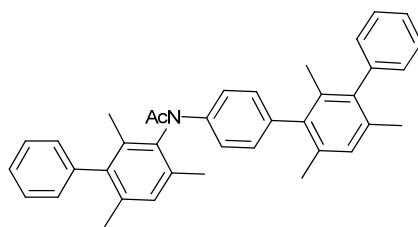
N-(2',4',6'-Triisopropylbiphenyl-4-yl)-N-(2,4,6-triisopropylphenyl)acetamide (3ef)

White amorphous solid; $R_f = 0.70$ (20% EtOAc in Petroleum ether); ^1H NMR (500 MHz, CDCl_3) δ 7.35 (d, $J = 8.3 \text{ Hz}$, 2H), 7.11 (s, 2H), 7.06 (d, $J = 8.3 \text{ Hz}$, 2H), 7.02 (s, 2H), 3.18–3.09 (m, 2H), 3.01 – 2.88 (m, 2H), 2.67–2.57 (m, 2H), 1.96 (s, 3H), 1.32 (s, 3H), 1.30 (s, 6H), 1.29 (s, 3H), 1.27 (s, 3H), 1.25 (s, 3H), 1.04 (s, 6H), 1.03 (s, 6H), 0.99 (s, 3H), 0.97 ppm (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 171.62, 150.02, 147.93, 146.81, 146.31, 141.27, 136.88, 136.76, 135.45, 129.93, 123.08, 122.95, 120.53, 34.38, 34.28, 30.29, 28.32, 24.75, 24.62, 24.26, 24.20, 24.14, 24.04 ppm; FT-IR: $\tilde{\nu} = 2960, 1676, 1510, 1467, 1364, 1318, 1295 \text{ cm}^{-1}$; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{38}\text{H}_{54}\text{ON}$: 540.41999 found: 540.41936.



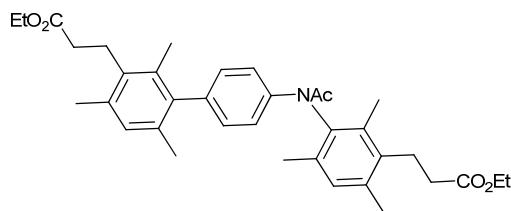
***N*-(2',4',6'-Trimethyl-3'-(2,4,6-trimethylbenzyl)biphenyl-4-yl)-*N*-(2,4,6-trimethylbenzyl)phenyl)acetamide (3eg)**

White amorphous solid; $R_f = 0.60$ (35% EtOAc in Petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.32 – 7.24 (m, 2H), 6.98 (s, 2H), 6.96 (s, 1H), 6.89 (s, 1H), 6.79 (s, 4H), 4.08 (s, 2H), 4.06 (s, 2H), 2.25 (s, 6H), 2.19 (s, 3H), 2.17 (s, 6H), 2.10 (s, 6H), 2.07 (s, 6H), 2.01 (s, 3H), 1.95 (s, 3H), 1.90 (s, 3H), 1.77 ppm (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 170.76, 139.98, 139.42, 139.17, 138.36, 138.25, 137.51, 136.70, 136.44, 135.71, 135.68, 135.59, 135.35, 135.28, 134.94, 134.85, 134.11, 133.64, 133.61, 131.40, 129.67, 129.53, 129.51, 123.15, 123.09, 31.93, 31.80, 24.12, 21.07, 21.01, 20.91, 20.82, 18.35, 18.15, 15.35 ppm; FT-IR: $\tilde{\nu} = 2919, 1675, 1509, 1477, 1452, 1365, 1320, 1295, 1012 \text{ cm}^{-1}$; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{46}\text{H}_{54}\text{ON}$: 636.41999 found: 636.41967.



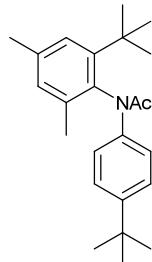
***N*-(3'-Phenyl-2',4',6'-trimethylbiphenyl-4-yl)-*N*-(3-phenyl-2,4,6-trimethylphenyl)acetamide (3ec)**

Light yellow oil; $R_f = 0.50$ (35% EtOAc in Petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.49 – 7.30 (m, 8H), 7.21-7.14 (m, 4H), 7.14-7.09 (m, 3H), 7.06 (s, 1H), 2.23 (s, 3H), 2.07-2.02 (m, 9H), 1.98 (s, 3H), 1.95 (s, 3H), 1.70 ppm (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 170.86, 141.84, 141.65, 140.63, 139.81, 139.37, 139.30, 138.55, 137.86, 136.79, 135.34, 135.16, 135.09, 134.96, 134.54, 130.52, 129.56, 129.42, 129.23, 129.20, 128.77, 128.75, 128.61, 128.54, 127.12, 126.61, 123.34, 123.31, 24.17, 21.04, 21.01, 20.98, 19.22, 18.31, 16.37 ppm; FT-IR: $\tilde{\nu} = 2925, 1668, 1454, 1371, 1302, 1017, \text{cm}^{-1}$; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{38}\text{H}_{38}\text{ON}$: 524.29479 found: 524.29431.



Ethyl 3-(3-(*N*-(3'-(3-ethoxy-3-oxopropyl)-2',4',6'-trimethylbiphenyl-4-yl)acetamido)-2,4,6-trimethylphenyl)propanoate (3ei)

Light yellow oil; $R_f = 0.30$ (35% EtOAc in Petroleum ether); ^1H NMR (500 MHz, CDCl_3) δ 7.34 - .29 (m, 2H), 7.03 - 6.98 (m, 3H), 6.93 (s, 1H), 4.19 – 4.14 (m, 4H), 3.05 – 2.95 (m, 4H), 2.50 – 2.41 (m, 4H), 2.37 (s, 3H), 2.35 (s, 3H), 2.25 (s, 3H), 2.15 (s, 3H), 1.98 (s, 3H), 1.93 (s, 3H), 1.88 (s, 3H), 1.27 ppm (td, $J = 7.1, 2.9$ Hz, 6H); ^{13}C NMR (126 MHz, cdcl_3) δ 173.29, 172.86, 170.79, 140.01, 139.41, 139.06, 138.09, 137.05, 136.90, 135.17, 134.96, 134.80, 134.63, 134.37, 134.29, 131.32, 129.50, 129.45, 123.14, 123.12, 60.74, 60.60, 33.77, 25.67, 25.53, 24.10, 20.89, 19.96, 19.91, 18.17, 17.33, 14.48, 14.38, 14.37 ppm; FT-IR: $\tilde{\nu} = 2981, 2923, 1733, 1676, 1511, 1449, 1370, 1297, 1253, 1181, 1156 \text{ cm}^{-1}$; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{36}\text{H}_{46}\text{O}_5\text{N}$: 572.33705 found: 572.33675.

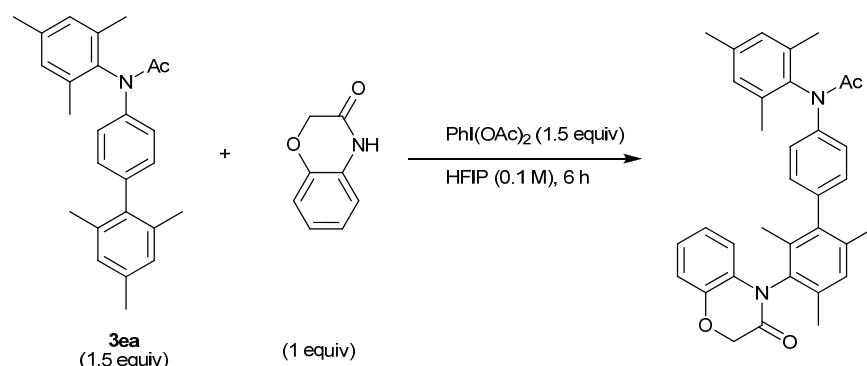


***N*-(2-*tert*-Butyl-4,6-dimethylphenyl)-*N*-(4-*tert*-butylphenyl)acetamide**

4-*tert*-Butylacetanilide (0.15 mmol) was dissolved in a 4 mL screw-capped vial with 1 mL of 1,1,1,3,3,3-hexafluoro-2-propanol. Then arene (0.45 mmol) followed by $\text{Phl}(\text{OAc})_2$ (0.22 mmol) was added to the stirred solution at room temperature. The reaction mixture was stirred for 4 h. After completion of the reaction, it was quenched with saturated $\text{Na}_2\text{S}_2\text{O}_3$ solution and extracted with dichloromethane, washed with water, brine and dried over anhydrous MgSO_4 . Then the organic extract was concentrated under reduced pressure and purified by silica gel column chromatography with 10-15% mixture of EtOAc in petroleum ether eluent in 63% yield as light yellow oil; $R_f = 0.70$ (25% EtOAc in Petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 7.25-7.23 (m, 5H), 7.02 (s, 1H), 2.36 (s, 3H), 2.12 (s, 3H), 1.92 (s,

3H), 1.26 (s, 9H), 1.22 ppm (s, 9H); ^{13}C NMR (101 MHz, CDCl_3) δ 171.44, 146.90, 146.57, 139.32, 138.30, 138.20, 136.70, 130.36, 128.95, 125.26, 122.09, 36.46, 34.36, 32.12, 31.45, 25.18, 21.50, 18.56 ppm; FT-IR: $\tilde{\nu}$ = 2958, 1669, 1506, 1499, 1369, 1289 cm^{-1} ; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{24}\text{H}_{34}\text{ON}$: 352.26349 found: 352.26389.

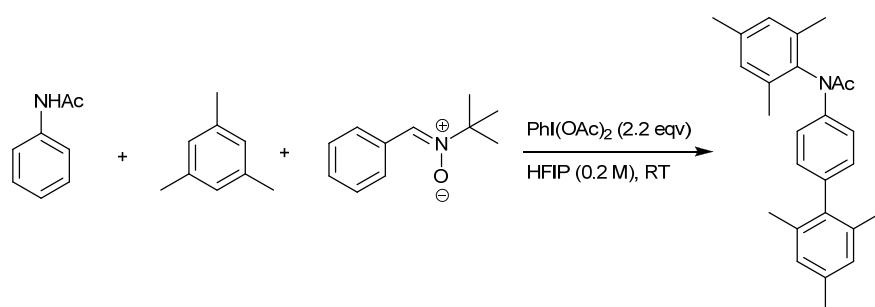
N-Mesityl-N-(2',4',6'-trimethyl-3'-(3-oxo-2*H*-benzo[*b*][1,4]oxazin-4(3*H*)-yl)biphenyl-4-yl)acetamide



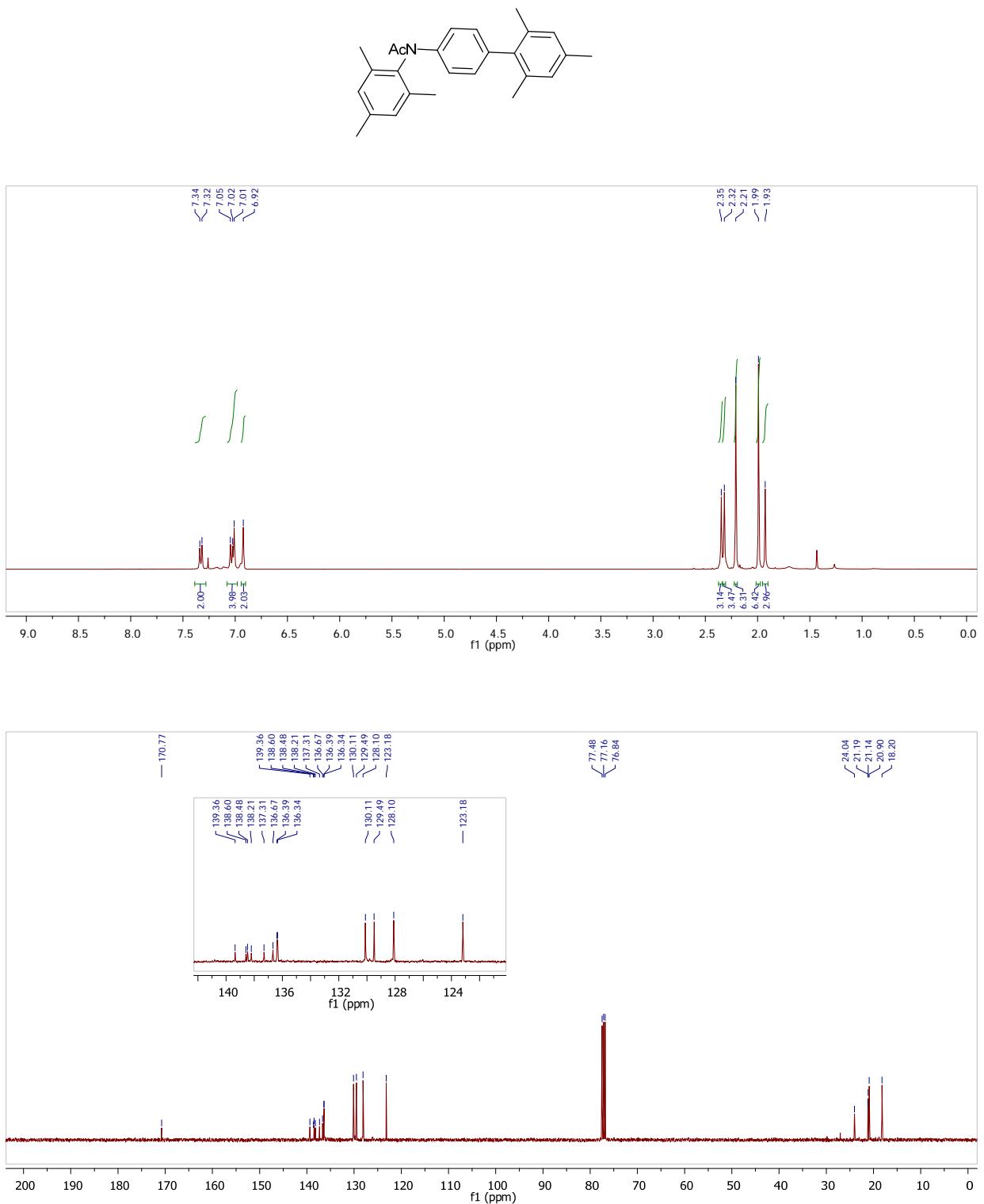
To a solution of compound **3ea** (0.15 mmol) and 2*H*-1,4-benzoxazin-3(4*H*)-one (0.1 mmol) in 1,1,1,3,3,3-hexafluoropropan-2-ol (1.0 mL), $\text{PhI}(\text{OAc})_2$ (0.15 mmol) was added at room temperature. The reaction mixture was stirred at this temperature for 6 h. The reaction mixture was quenched with saturated $\text{Na}_2\text{S}_2\text{O}_3$ solution and taken up in dichloromethane, washed with water, brine and dried over anhydrous MgSO_4 . The organic extracts were filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel (35% EtOAc in Pet. Ether) afforded the pure product in 50% yield.

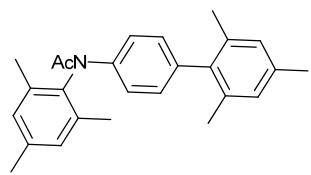
Light yellow oil, R_f = 0.35 (50% EtOAc in Petroleum ether); ^1H NMR (500 MHz, CDCl_3) δ 7.44 (d, J = 8.1 Hz, 1H), 7.23 (d, J = 8.4 Hz, 1H), 7.13 – 6.96 (m, 7H), 6.86 (t, J = 7.7 Hz, 1H), 6.35 – 6.32 (m, 1H), 4.78 (s, 2H), 2.34 (s, 3H), 2.18 (s, 6H), 2.09 (s, 3H), 2.03 (s, 3H), 1.91 (s, 3H), 1.74 ppm (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 170.83, 163.58, 145.07, 140.86, 139.77, 138.57, 138.13, 137.68, 136.75, 136.40, 135.12, 134.91, 131.23, 130.24, 130.16, 129.64, 129.41, 129.08, 124.21, 123.41, 123.09, 123.04, 117.09, 115.82, 68.12, 24.04, 21.18, 21.11, 18.17, 17.66, 15.69 ppm; FT-IR: $\tilde{\nu}$ = 2921, 1692, 1673, 1605, 1496, 1478, 1462, 1367, 1296, 1277 cm^{-1} ; HRMS: calc. for $[\text{M}+\text{H}]^+$ $\text{C}_{34}\text{H}_{35}\text{O}_3\text{N}_2$: 519.26422 found: 519.26362.

Radical Inhibition Study:

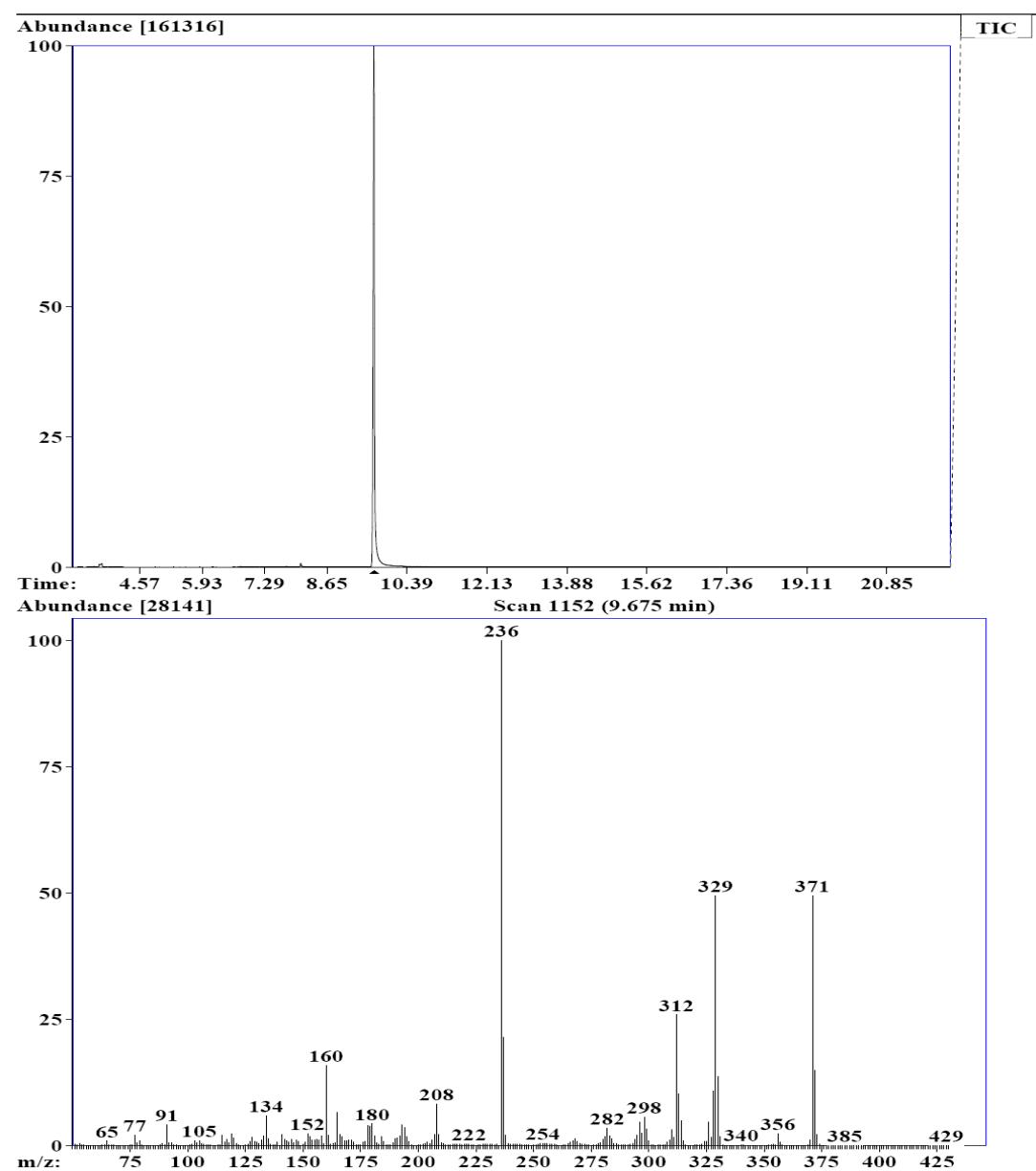


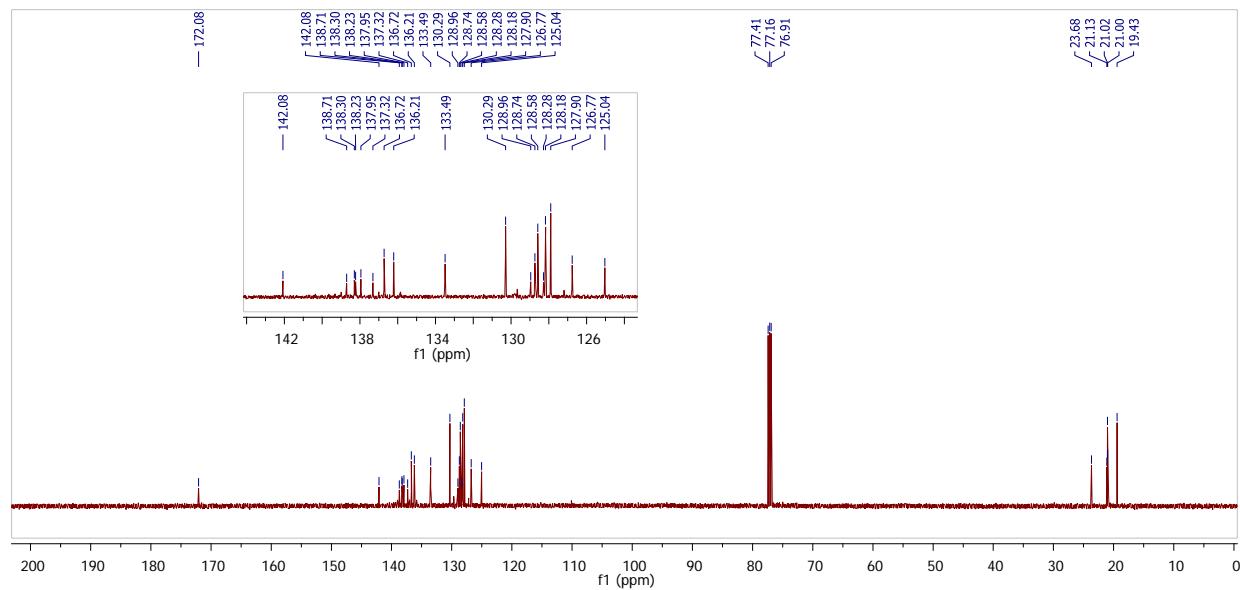
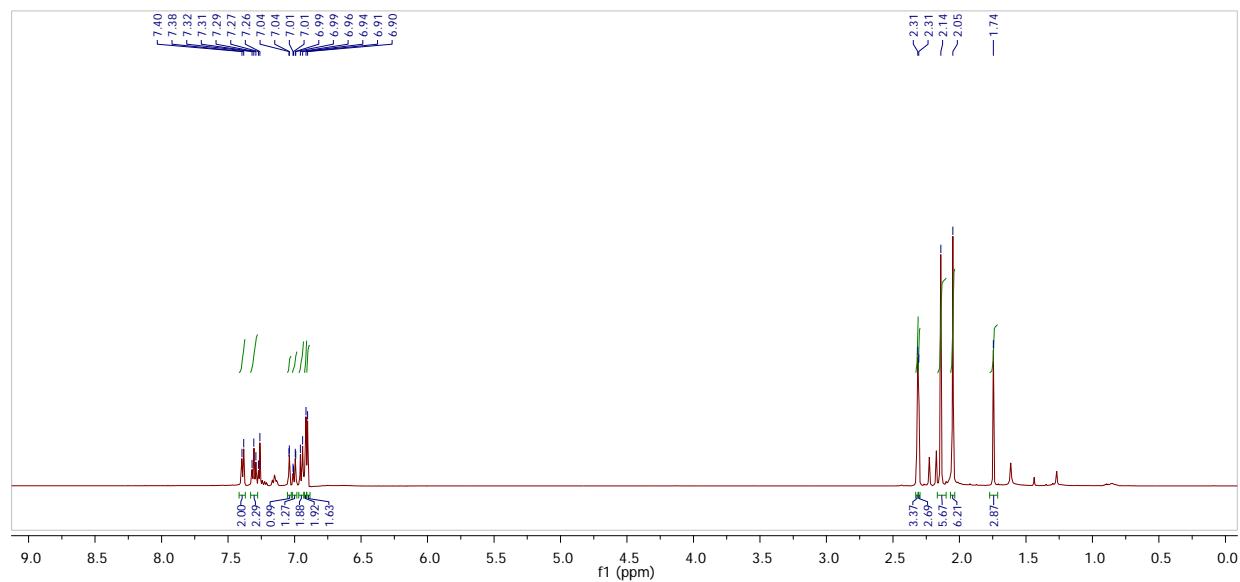
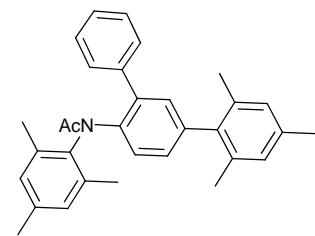
Acetanilide (0.1 mmol) was dissolved in a 4 mL screw-capped vial with 0.5 mL of 1,1,1,3,3,3-hexafluoro-2-propanol. Then mesitylene (0.5 mmol) followed by *N*-*tert*-Butyl-alpha-phenylnitrone (0.2 mmol) and PhI(OAc)_2 (0.22 mmol) were added to the stirred solution at room temperature. The reaction mixture was stirred for 16 h. After completion of the reaction, it was quenched with saturated $\text{Na}_2\text{S}_2\text{O}_3$ solution and extracted with dichloromethane, washed with water, brine and dried over anhydrous MgSO_4 . Then the organic extract was concentrated under reduced pressure and purified by silica gel column chromatography with 10-12% mixture of EtOAc in petroleum ether eluent in 60% yield.

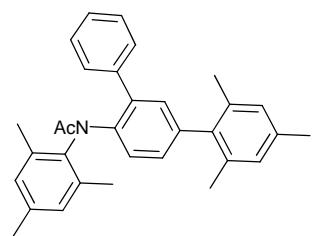




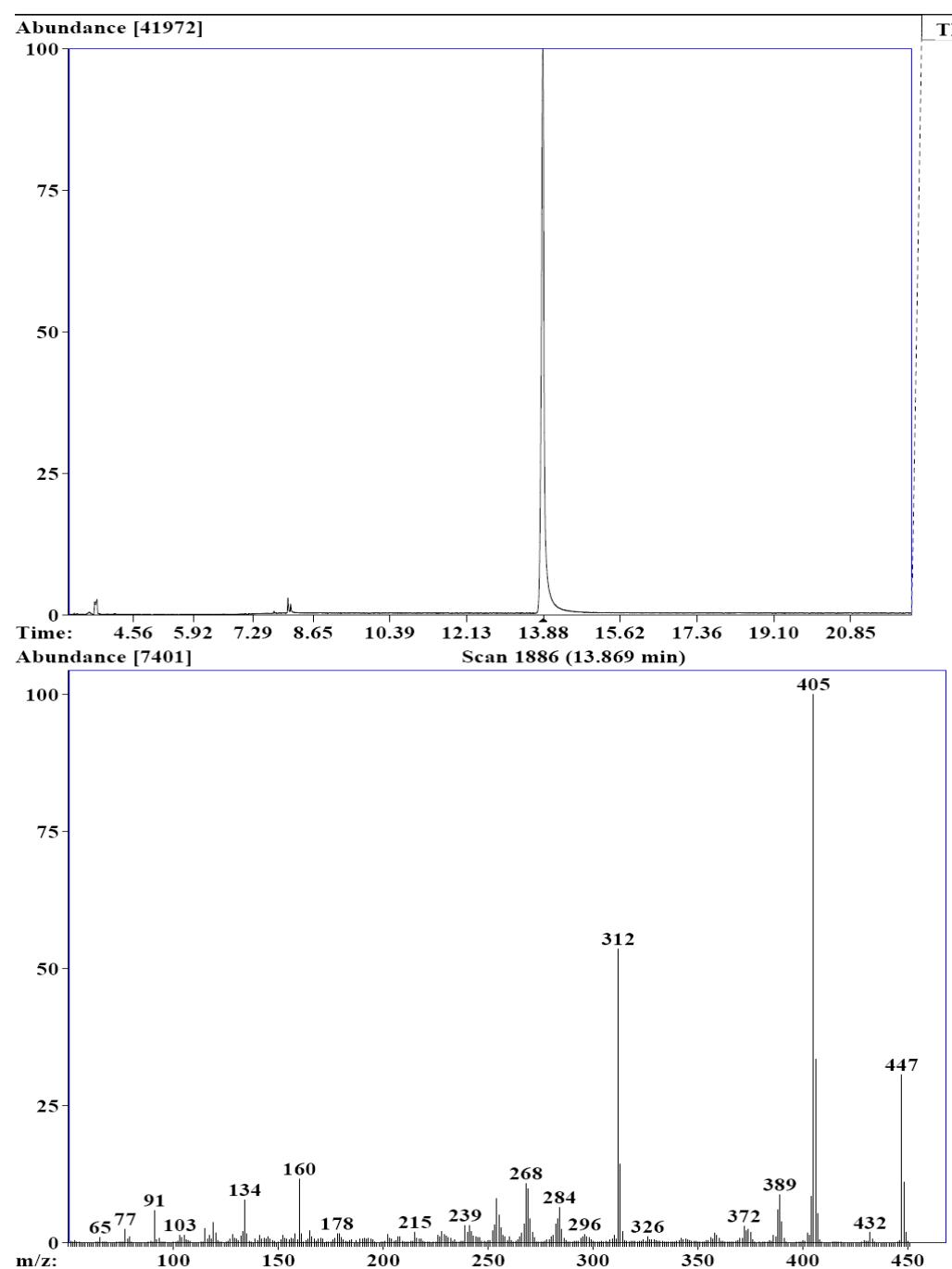
GC-MS

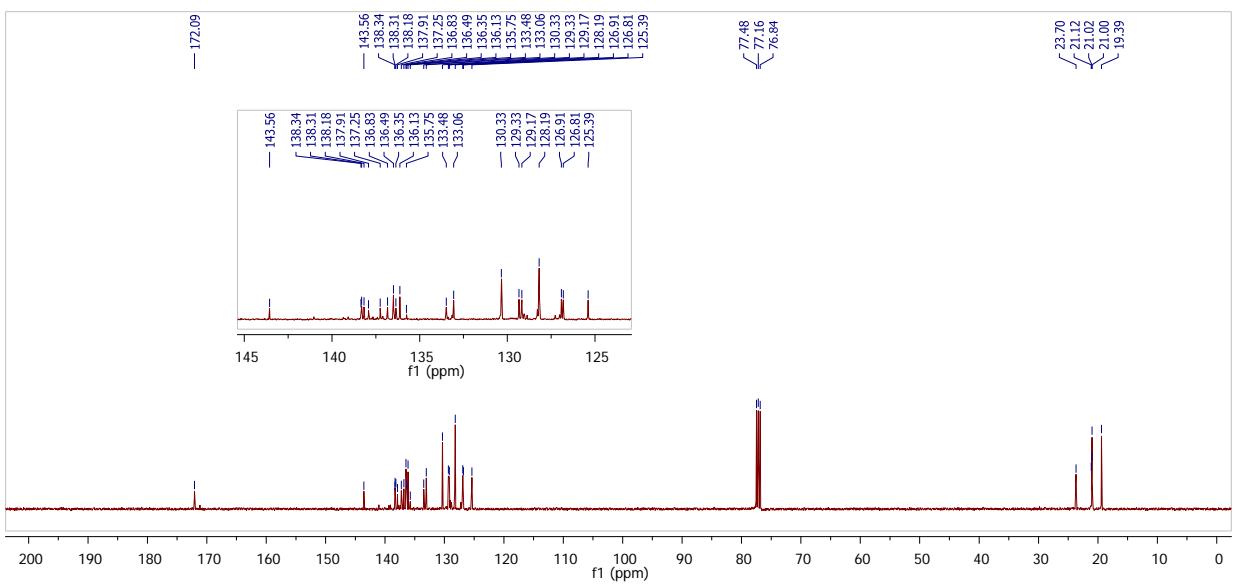
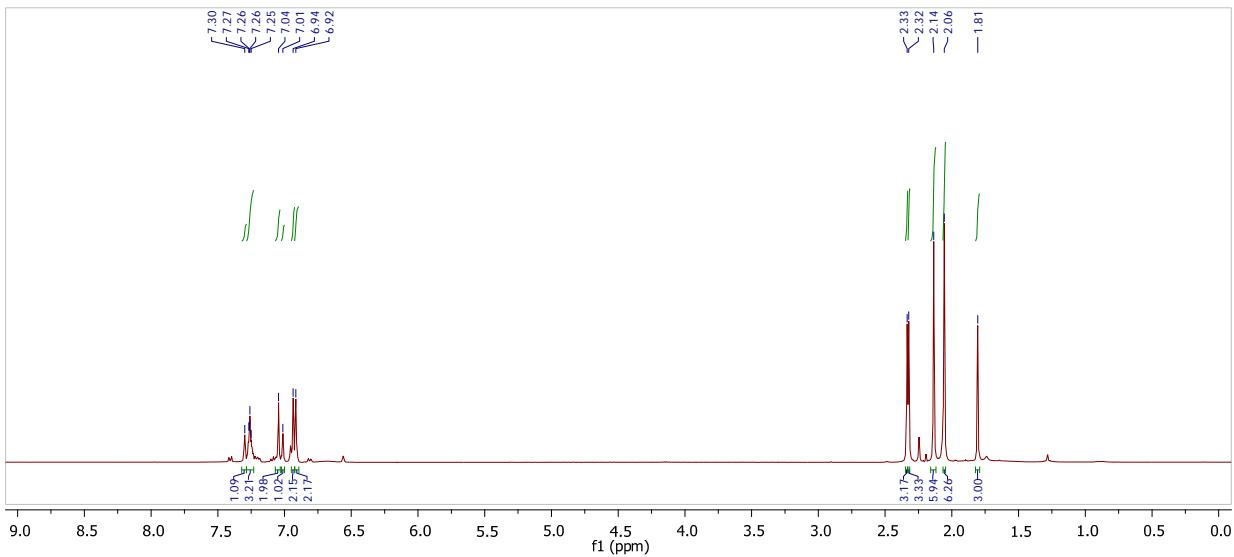
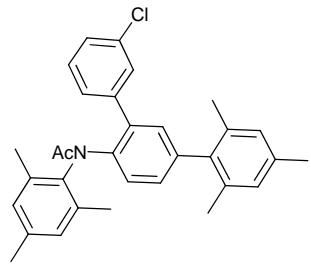


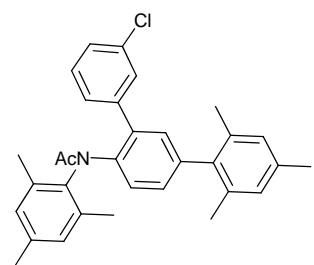




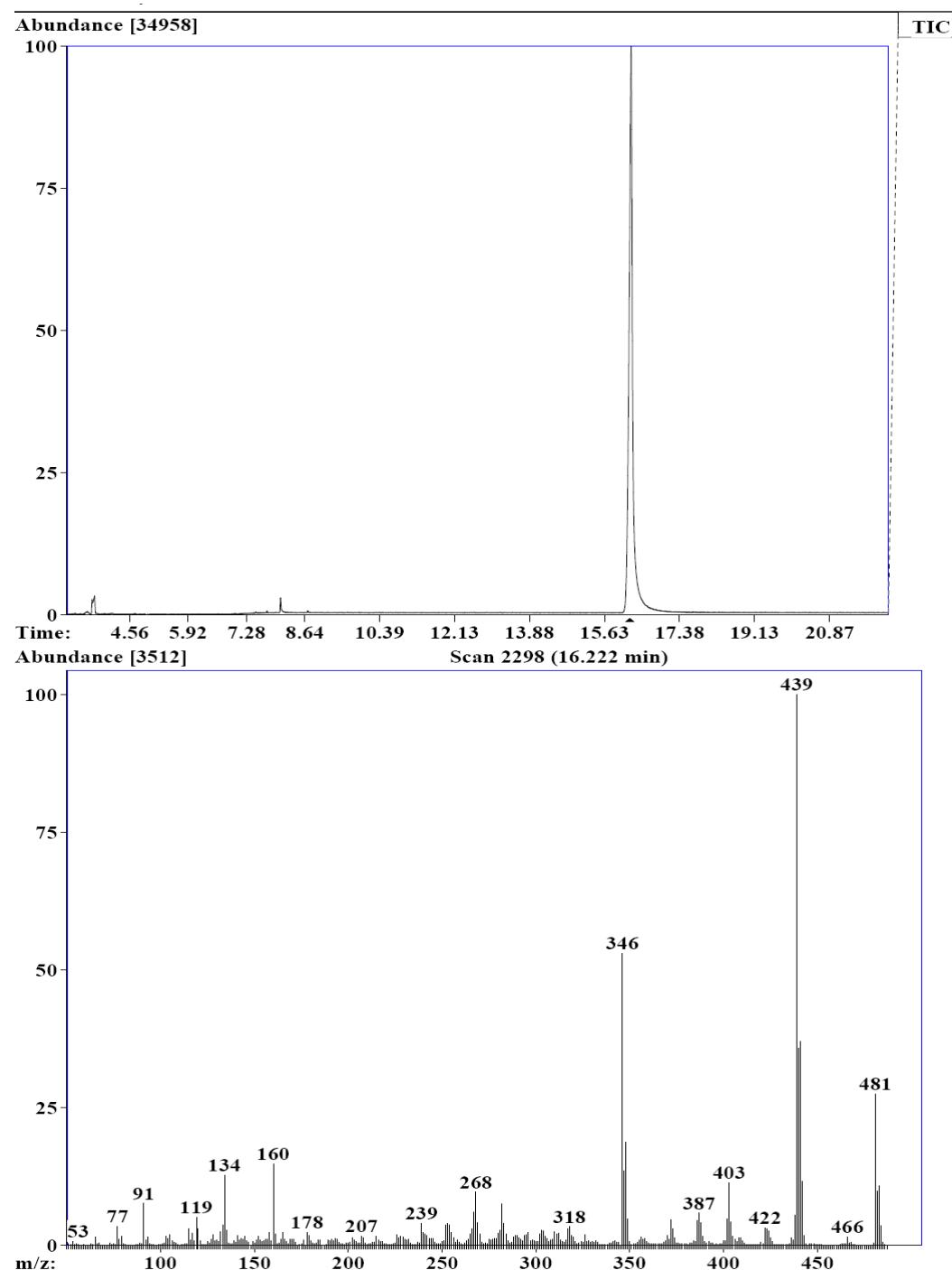
GCMS

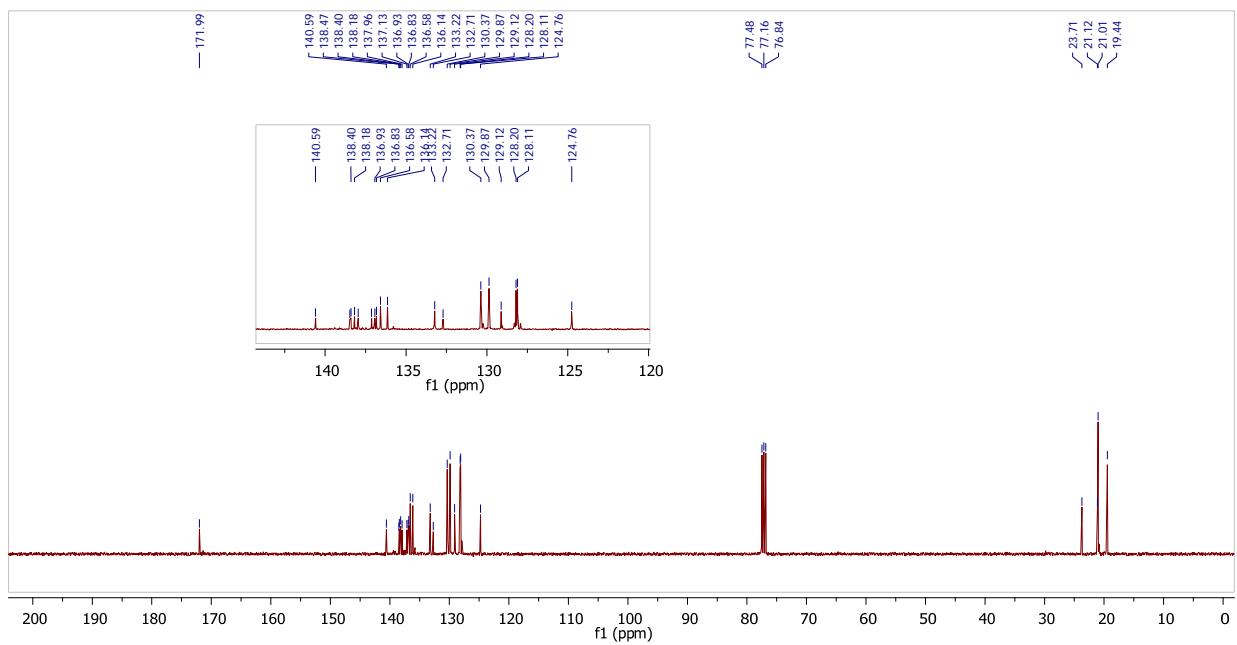
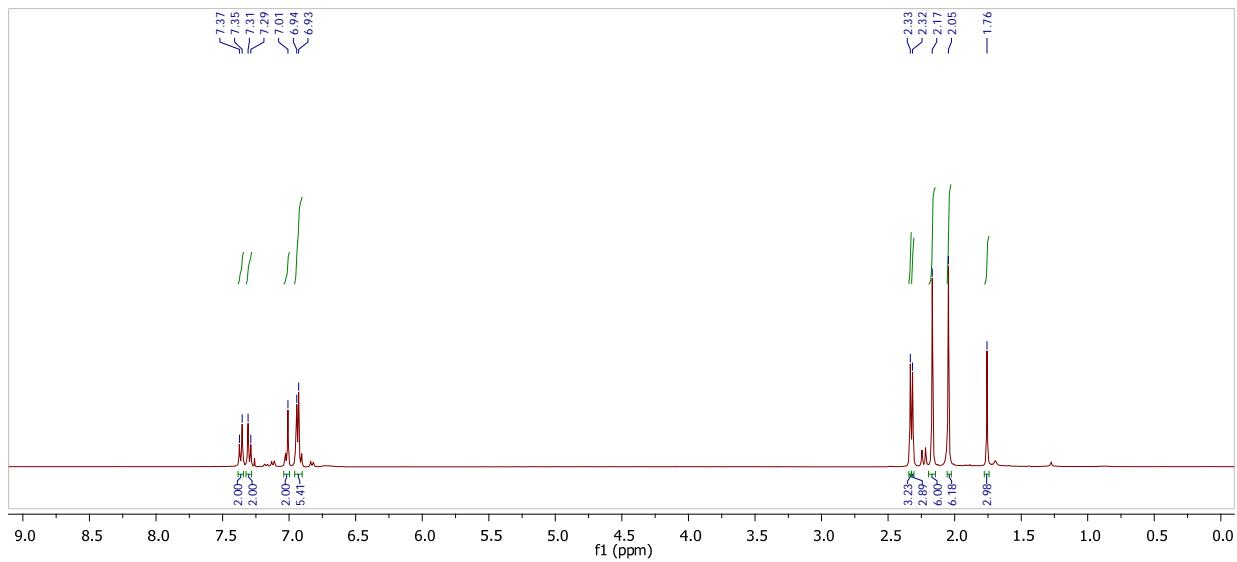
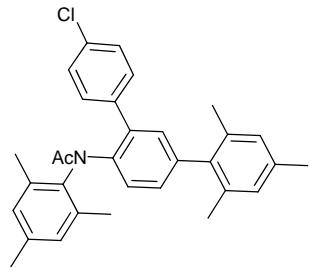


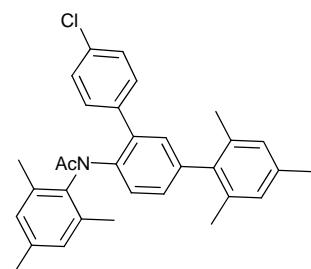




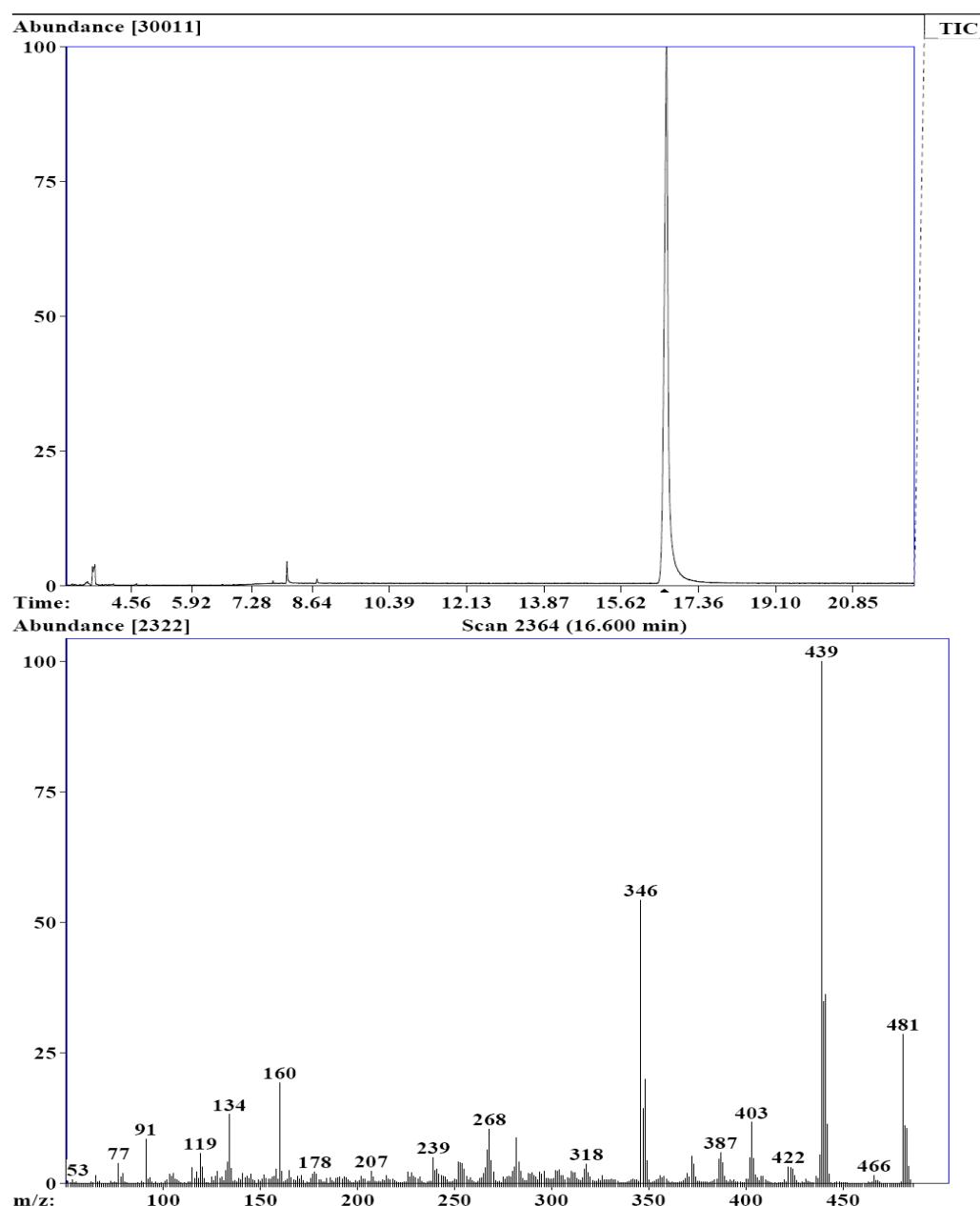
GCMS

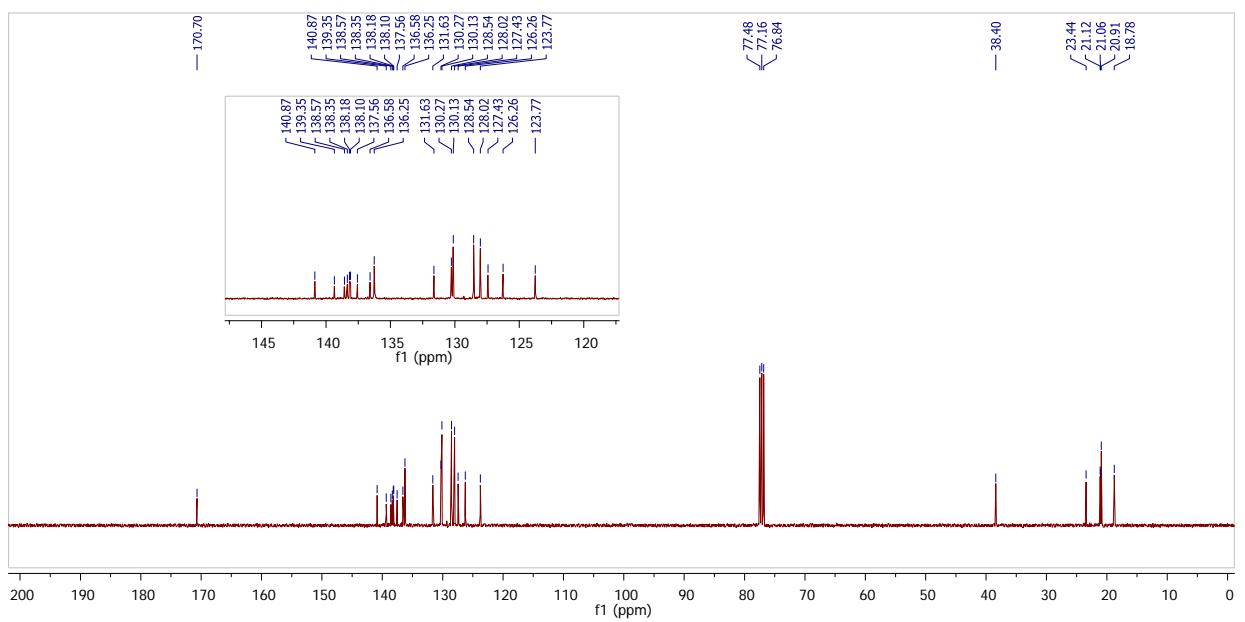
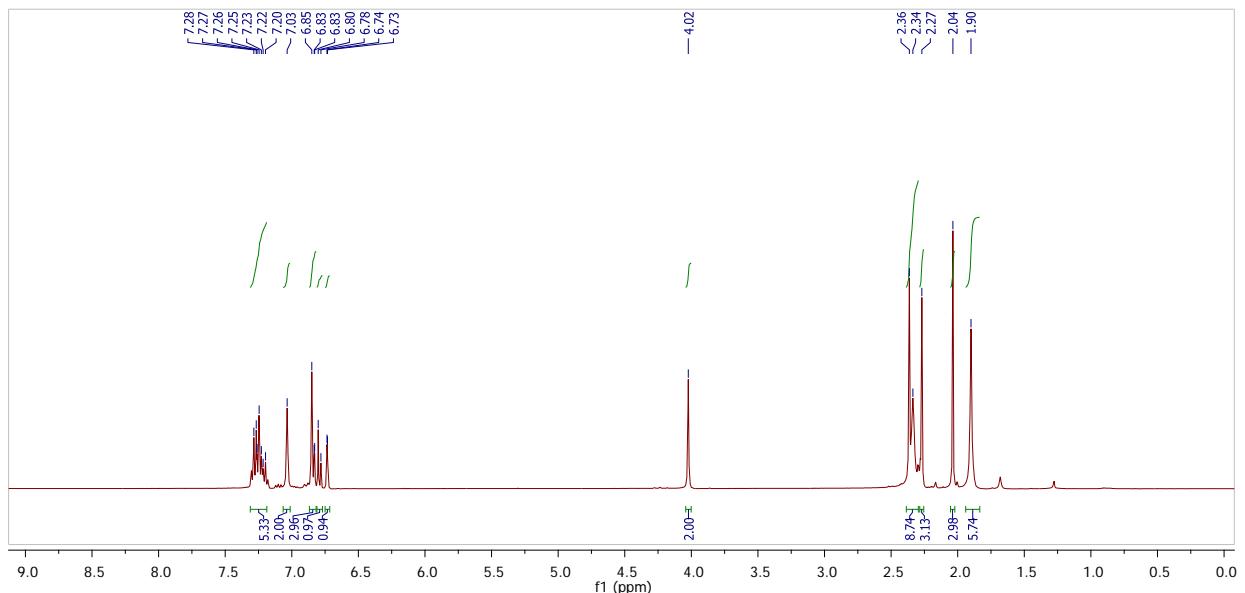
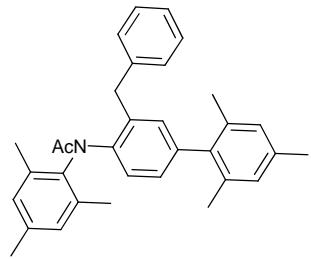


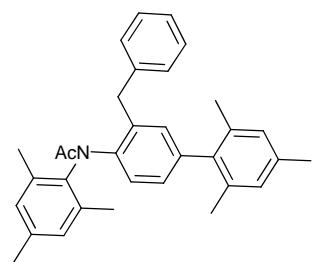




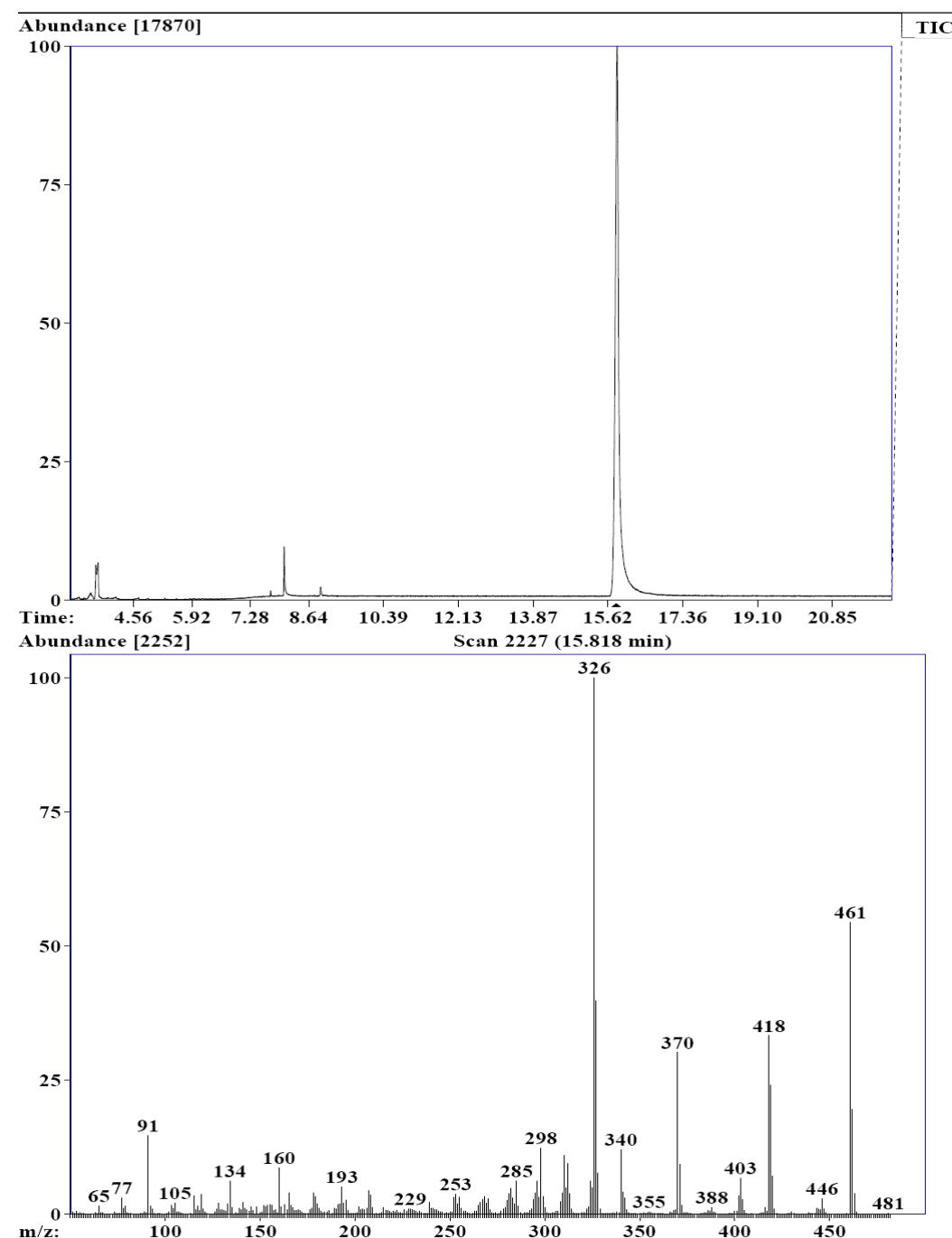
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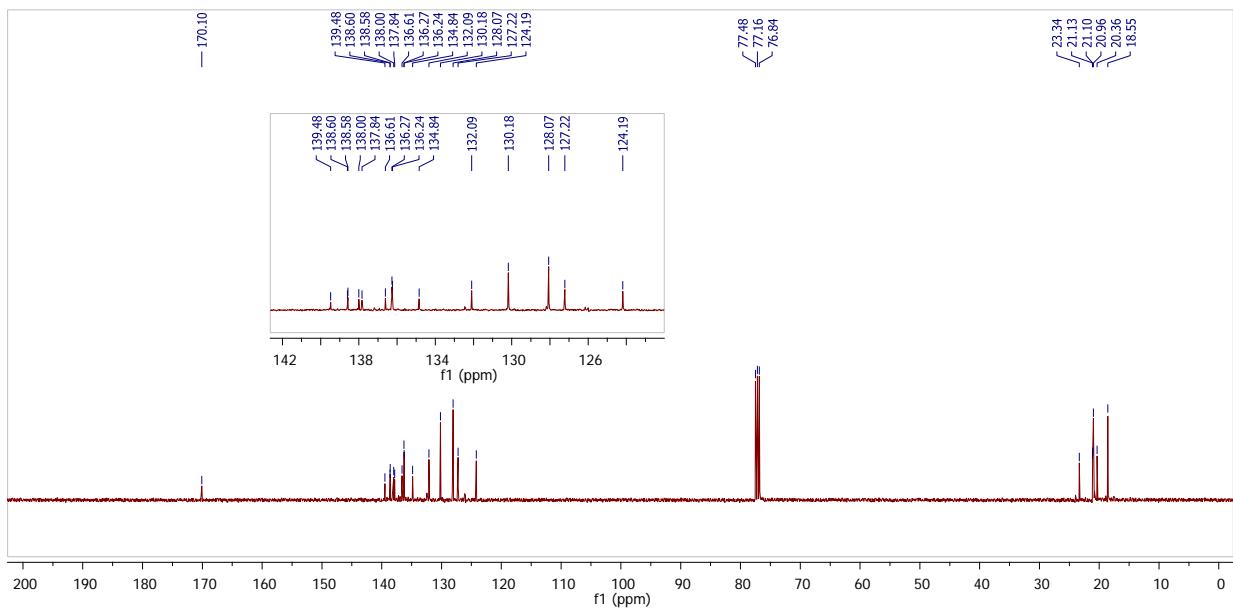
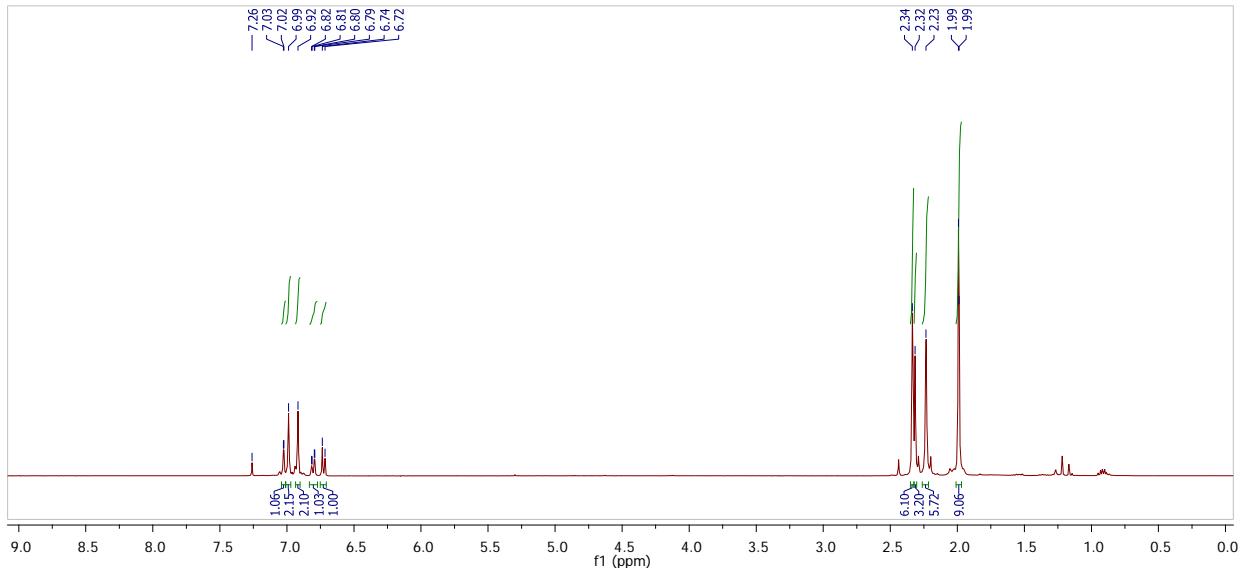
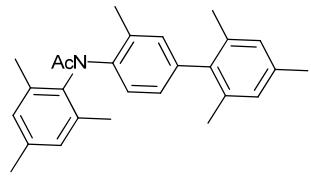


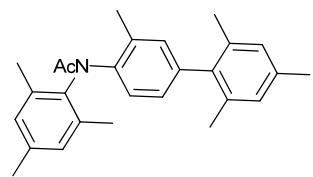




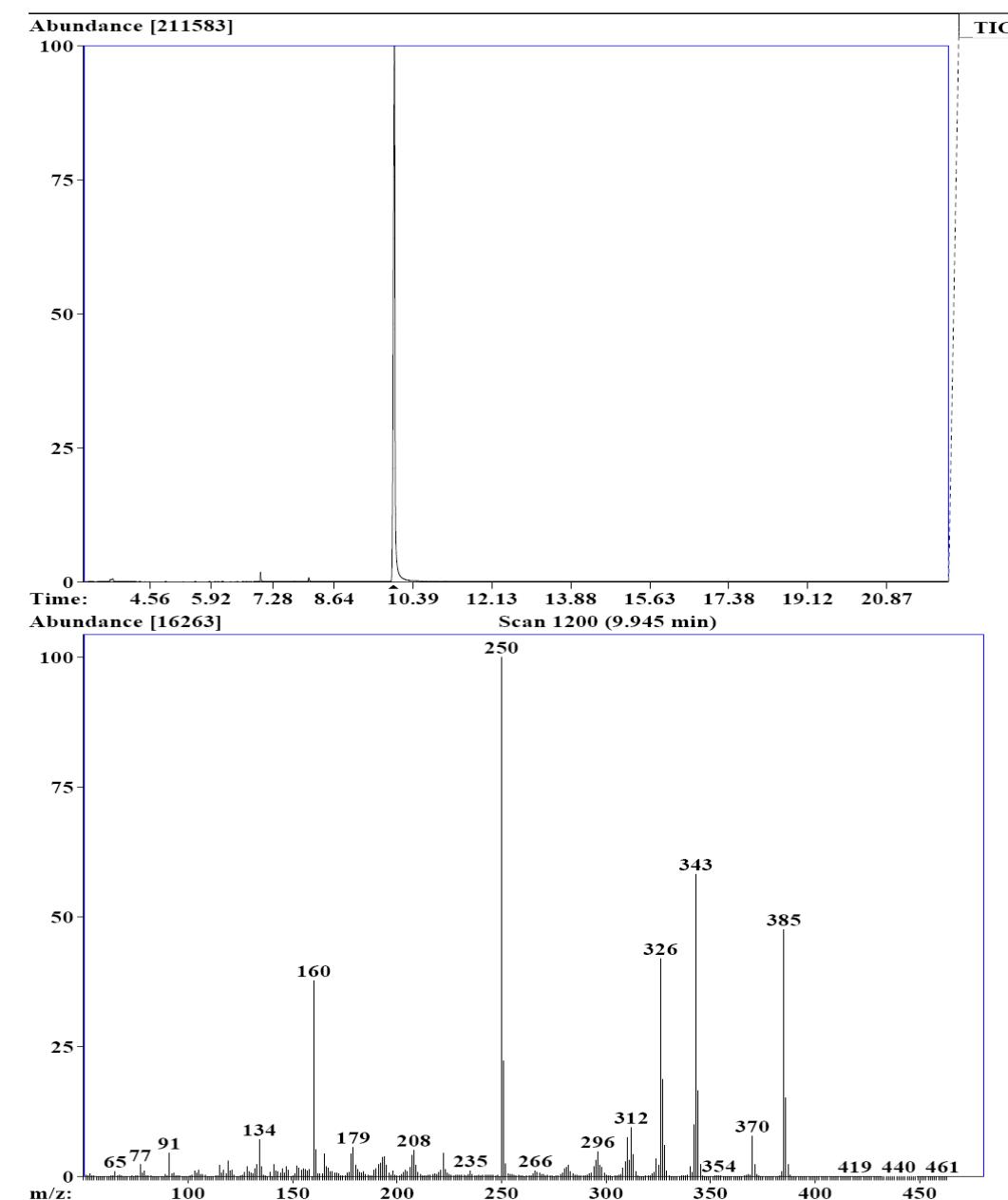
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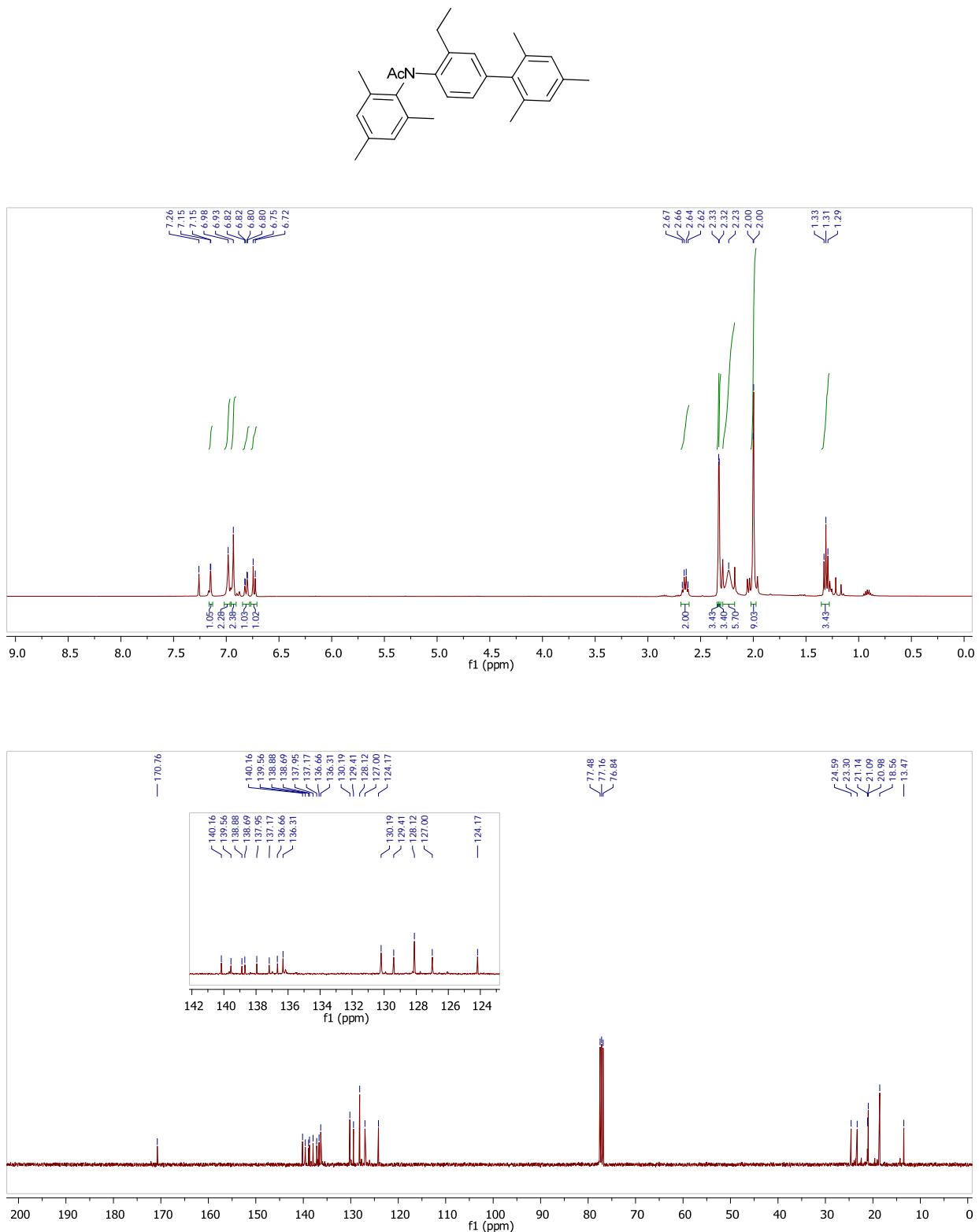


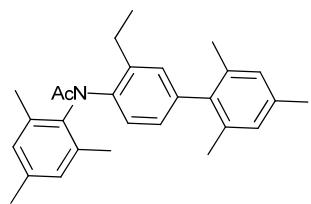




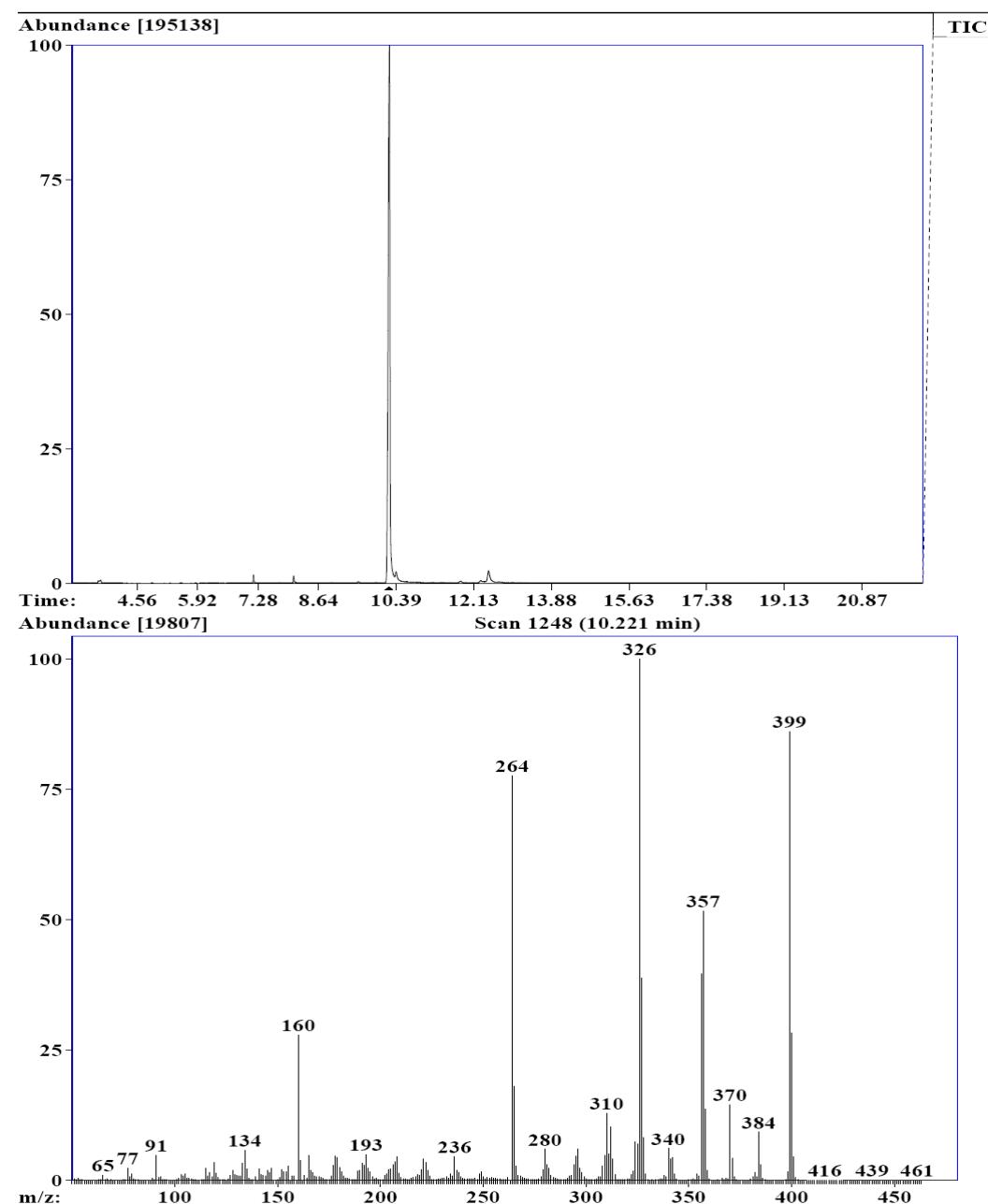
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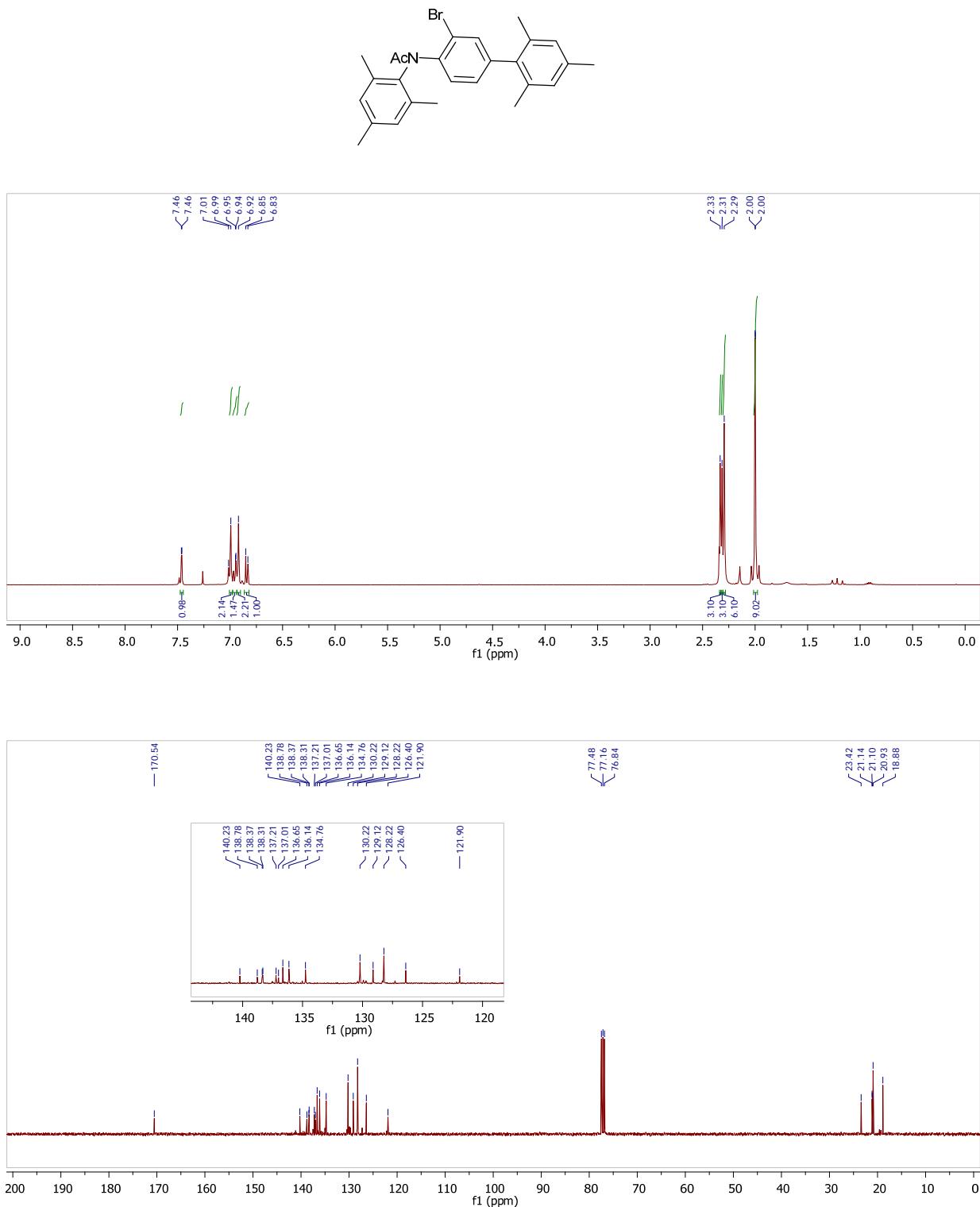


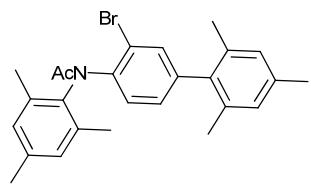




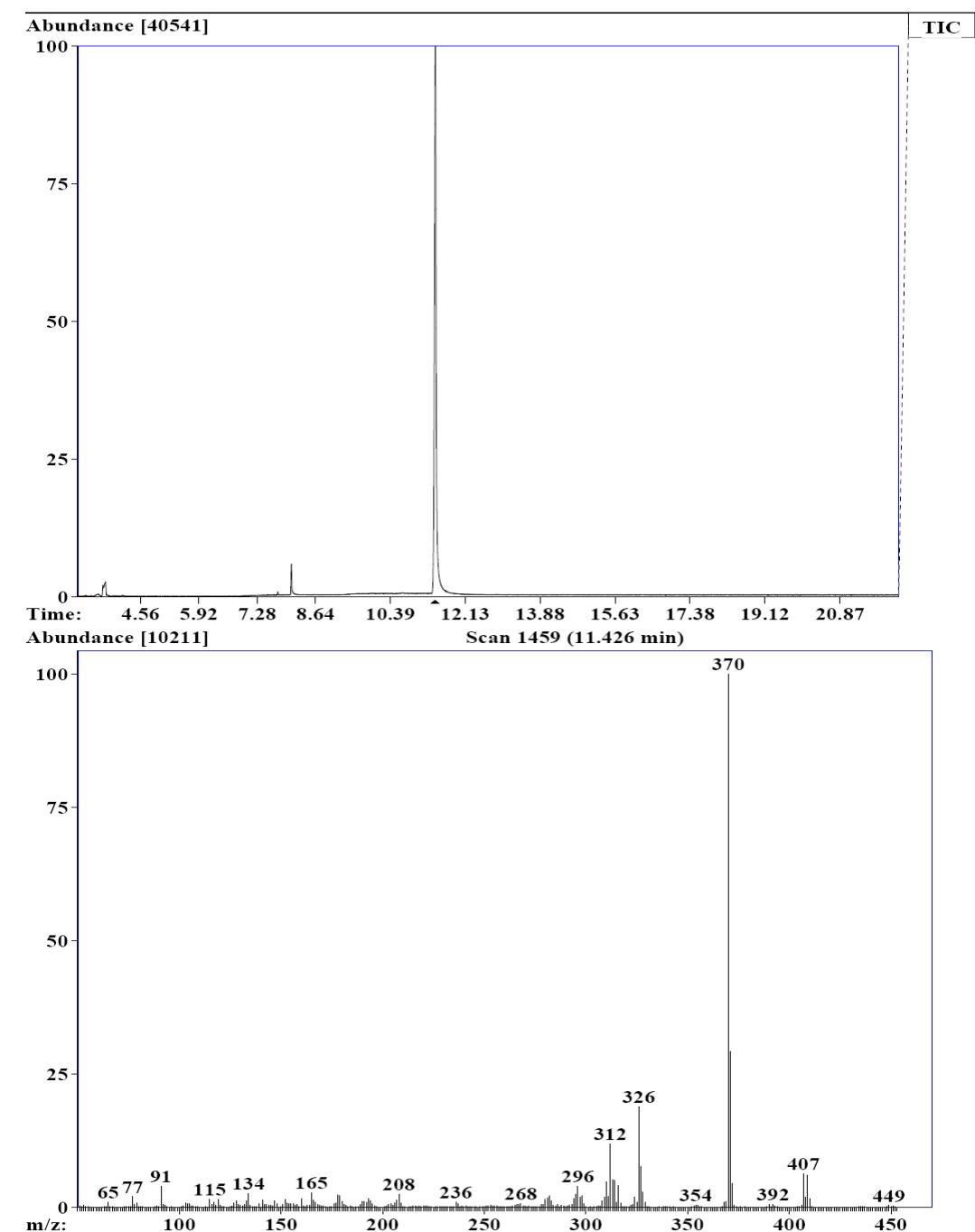
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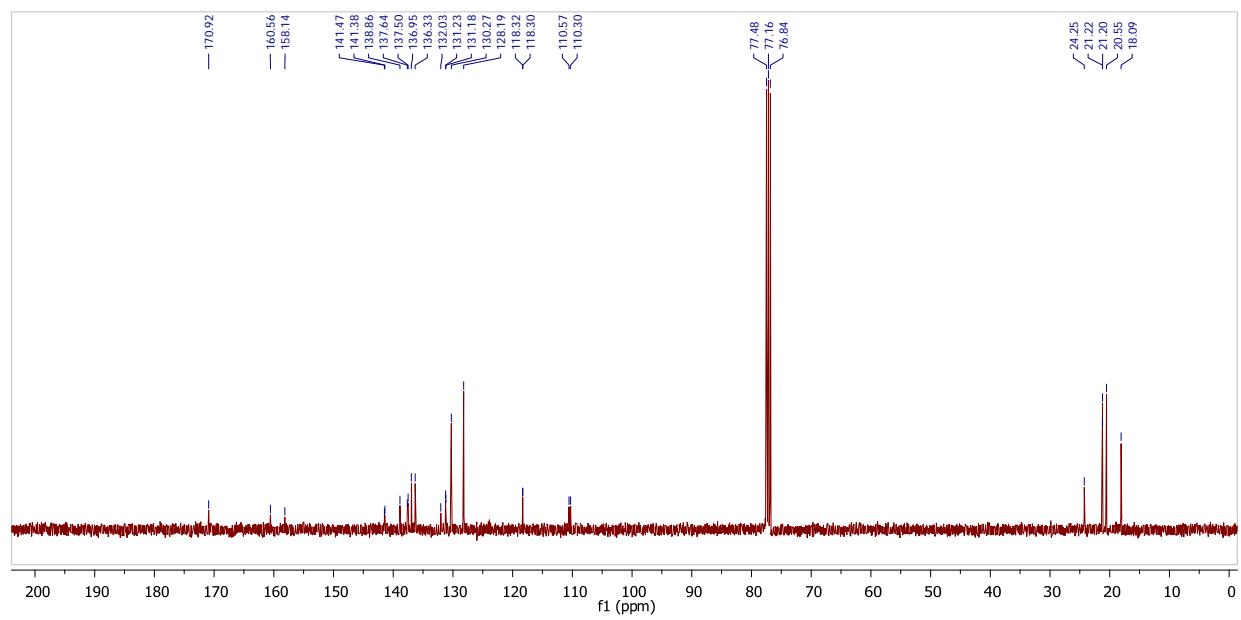
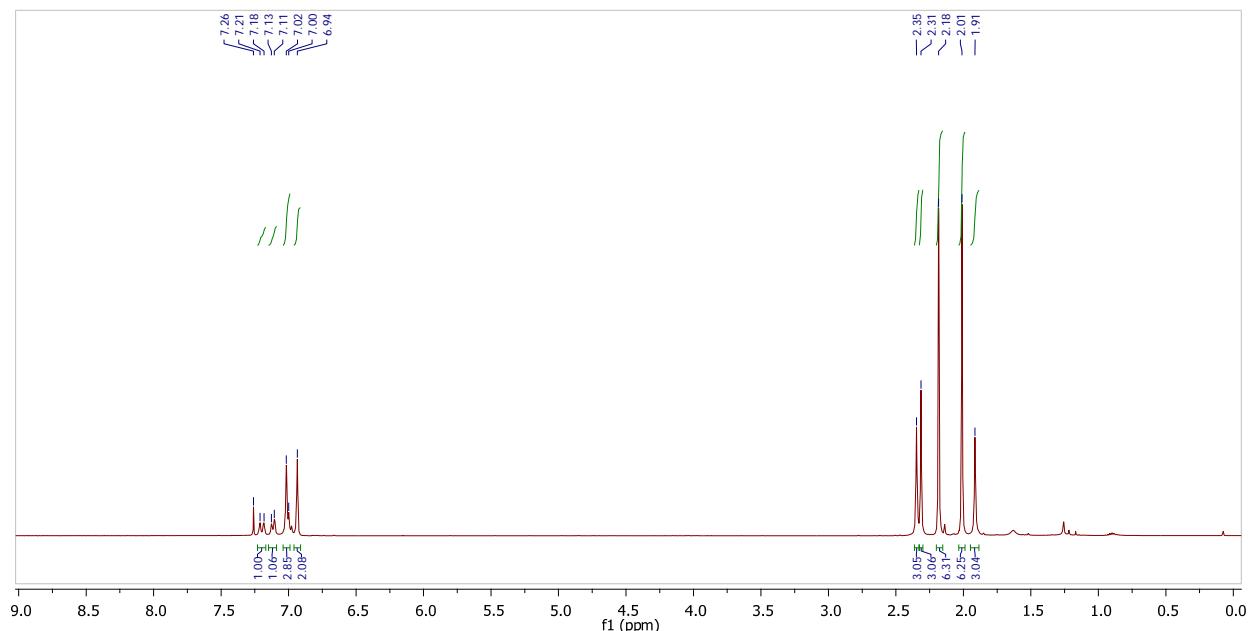
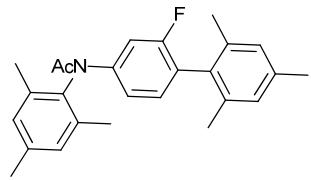


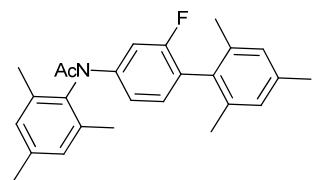




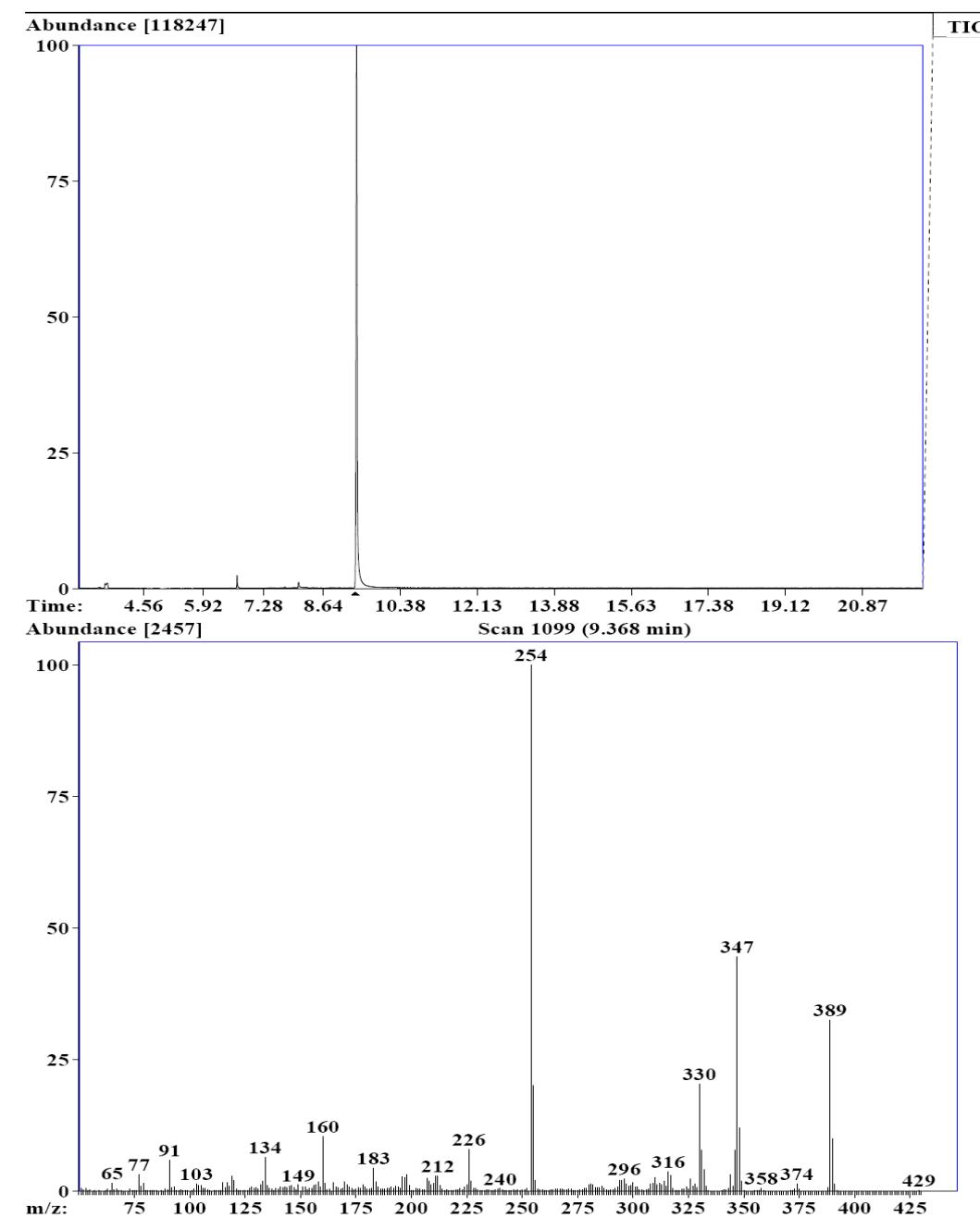
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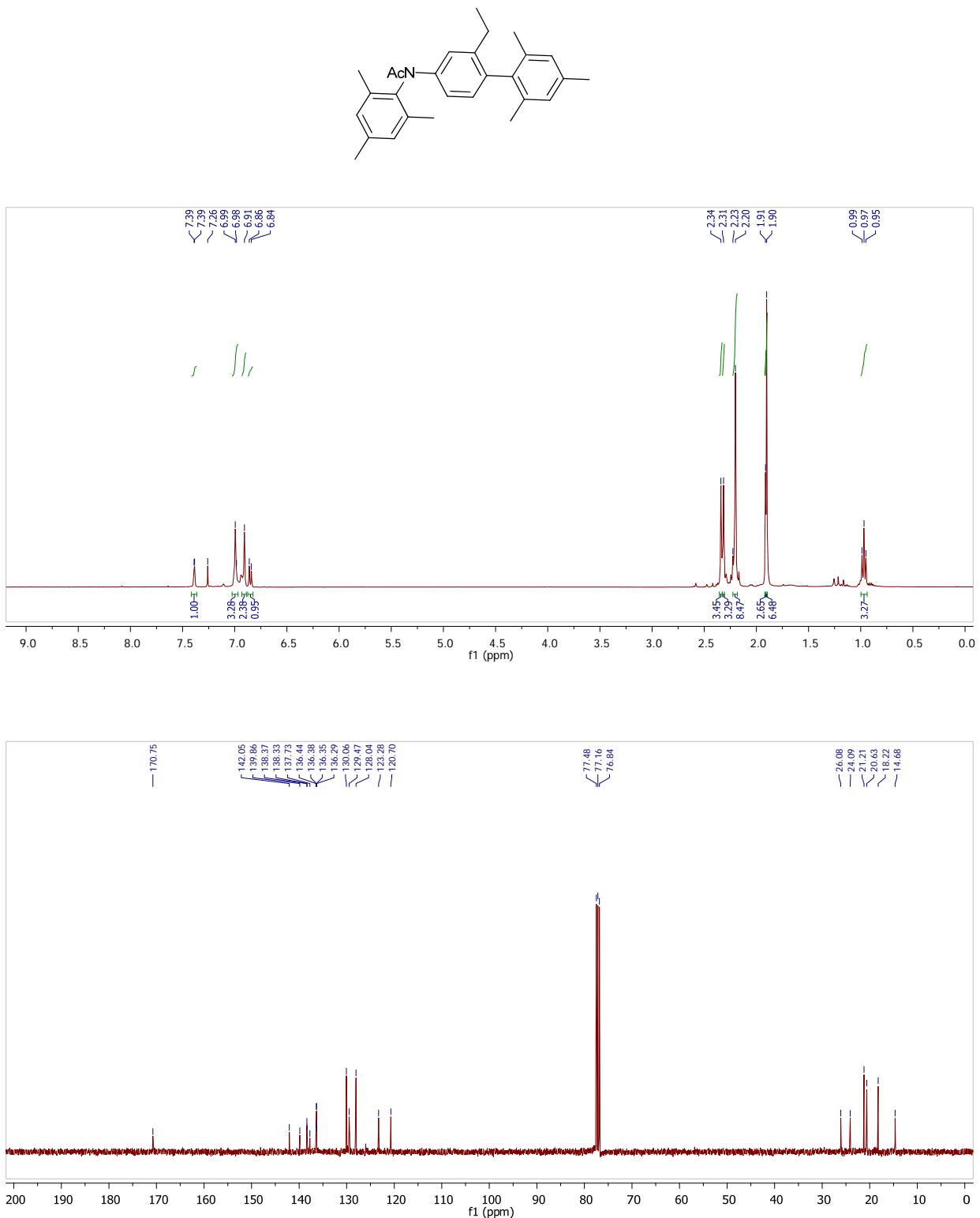


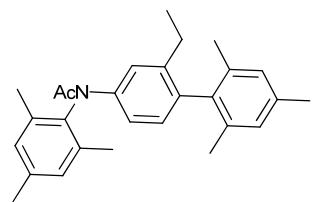




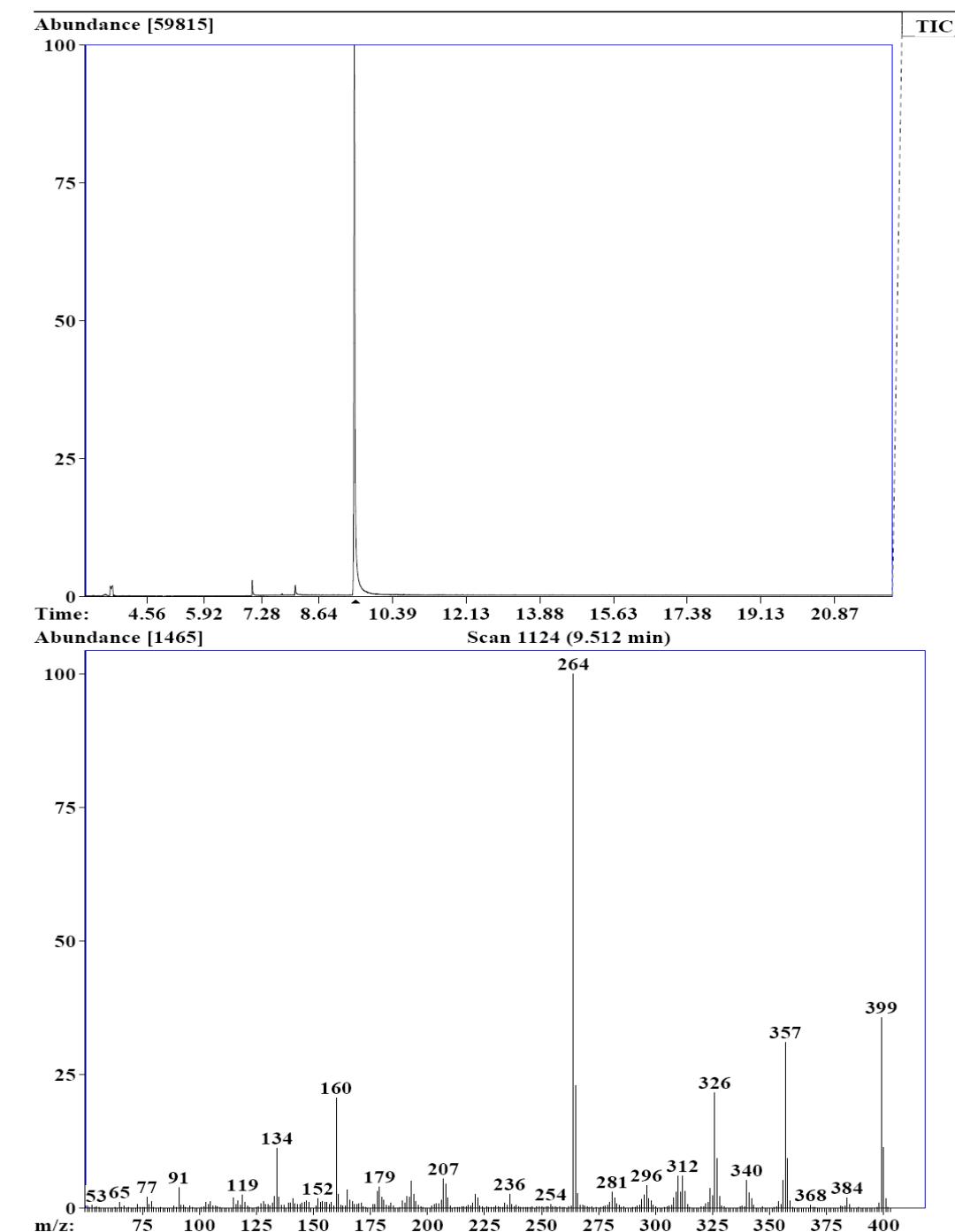
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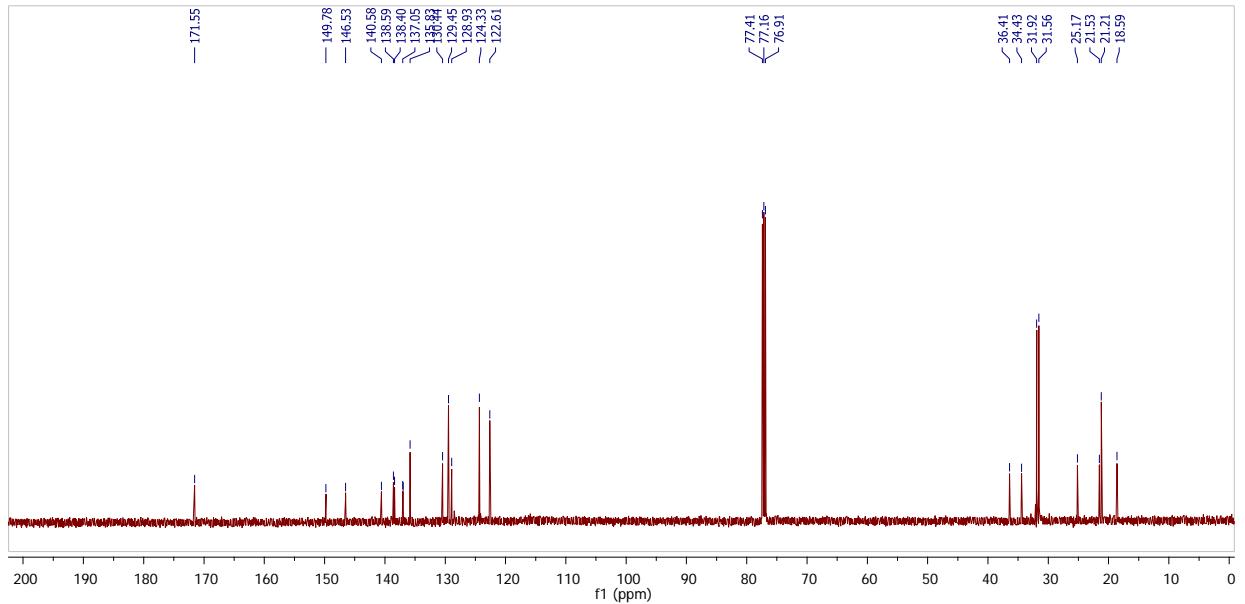
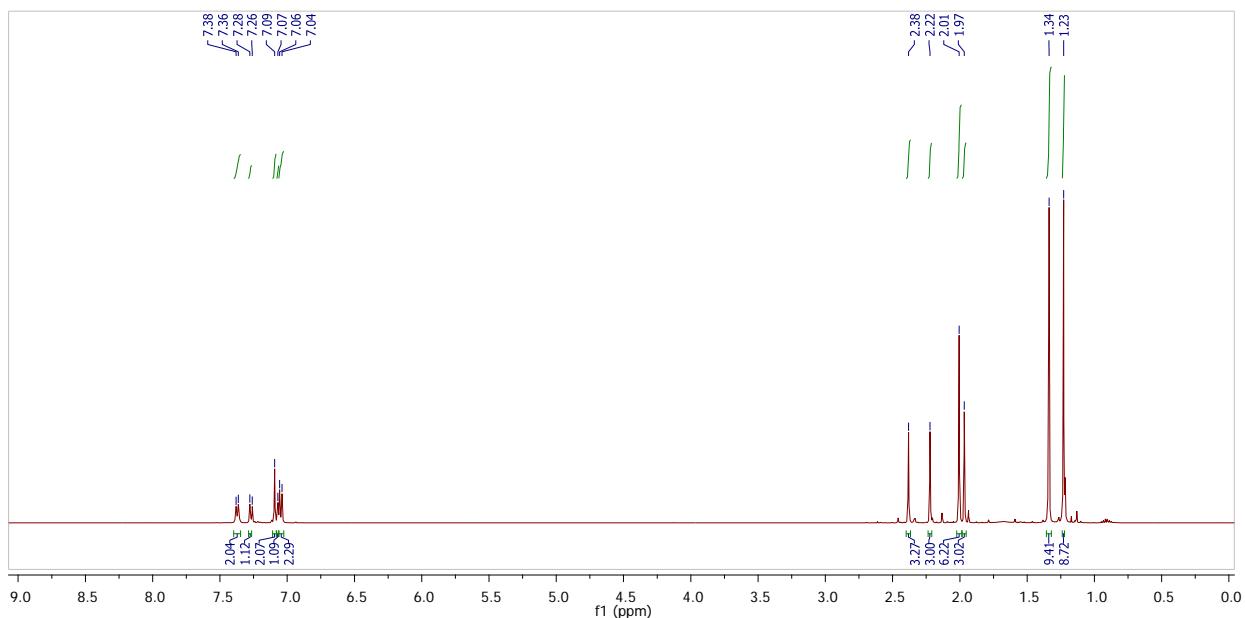
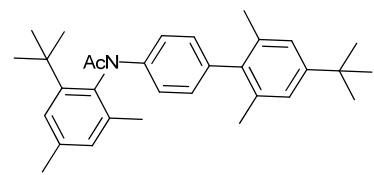


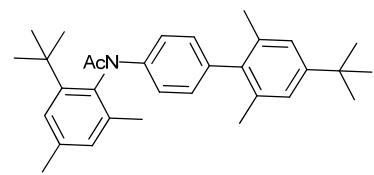




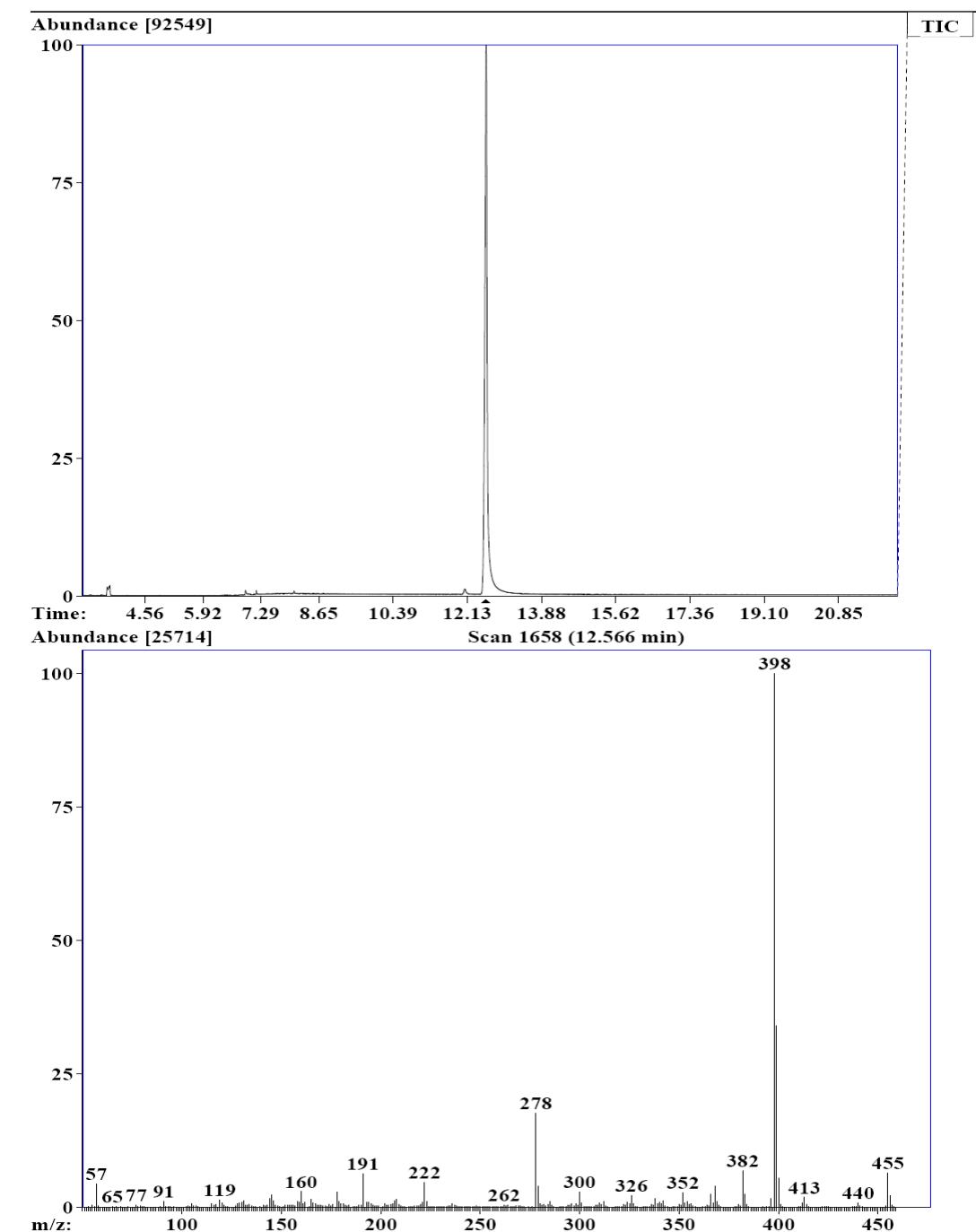
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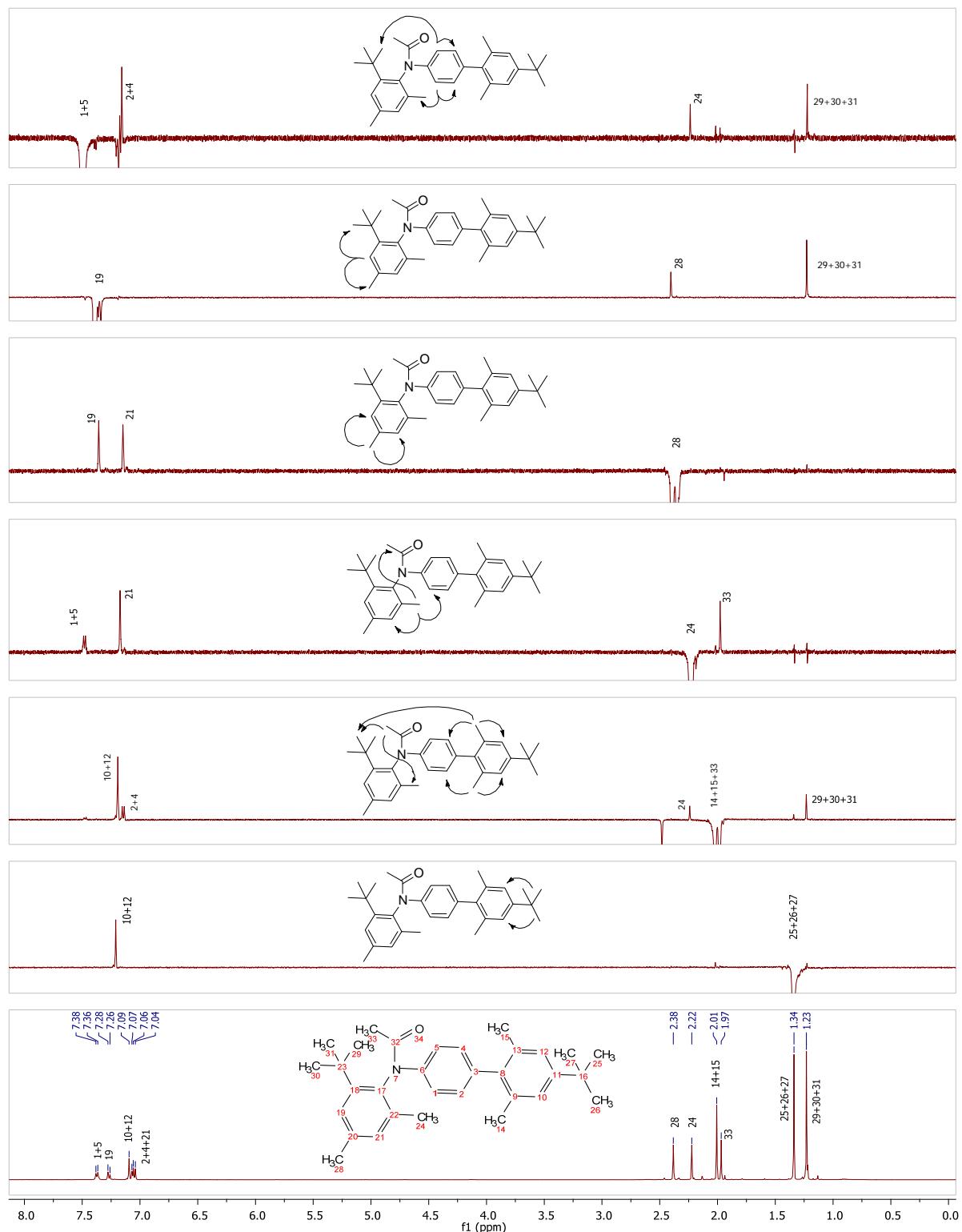


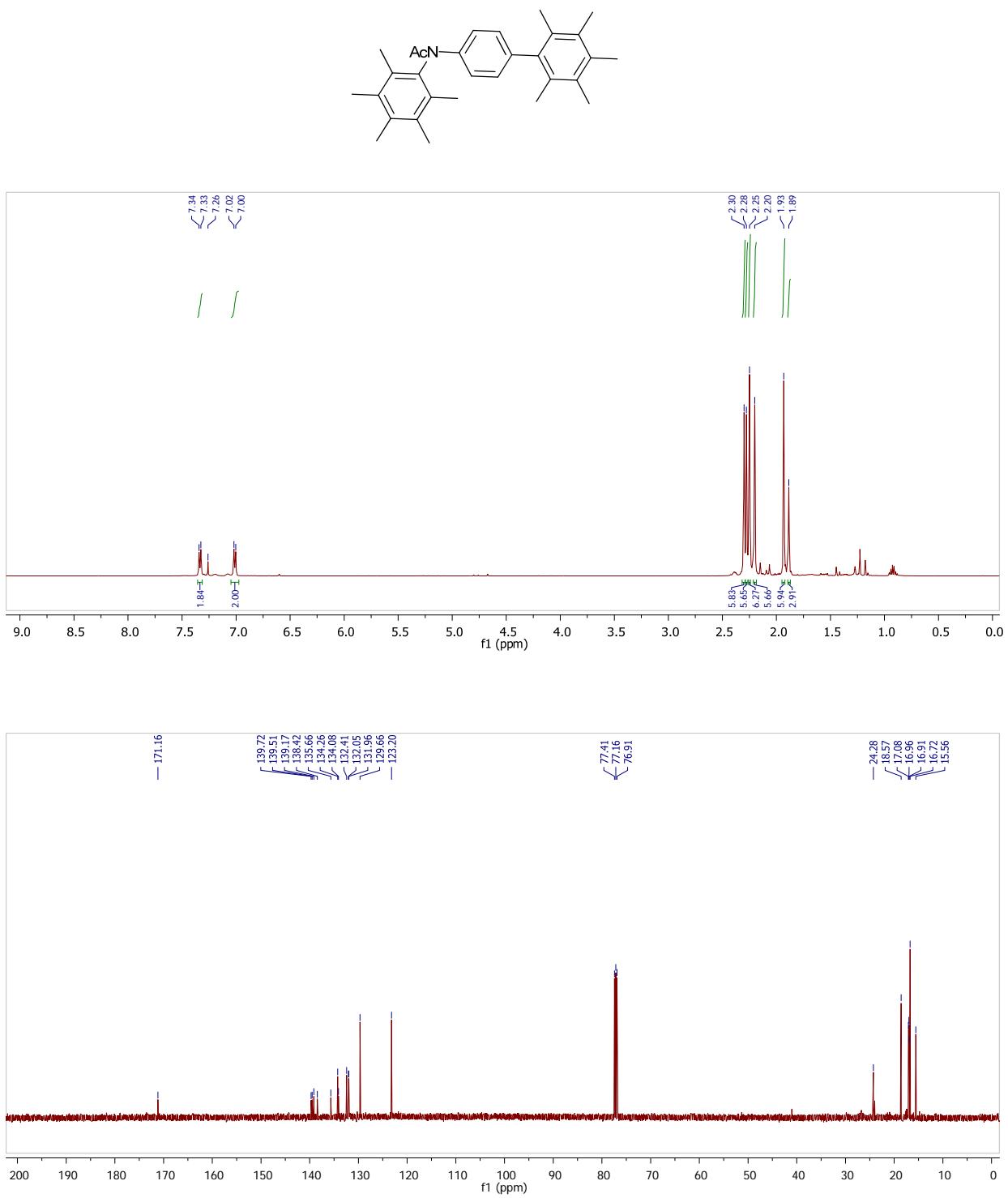


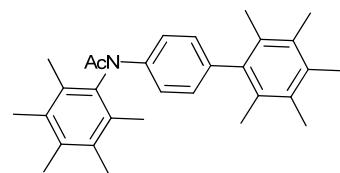
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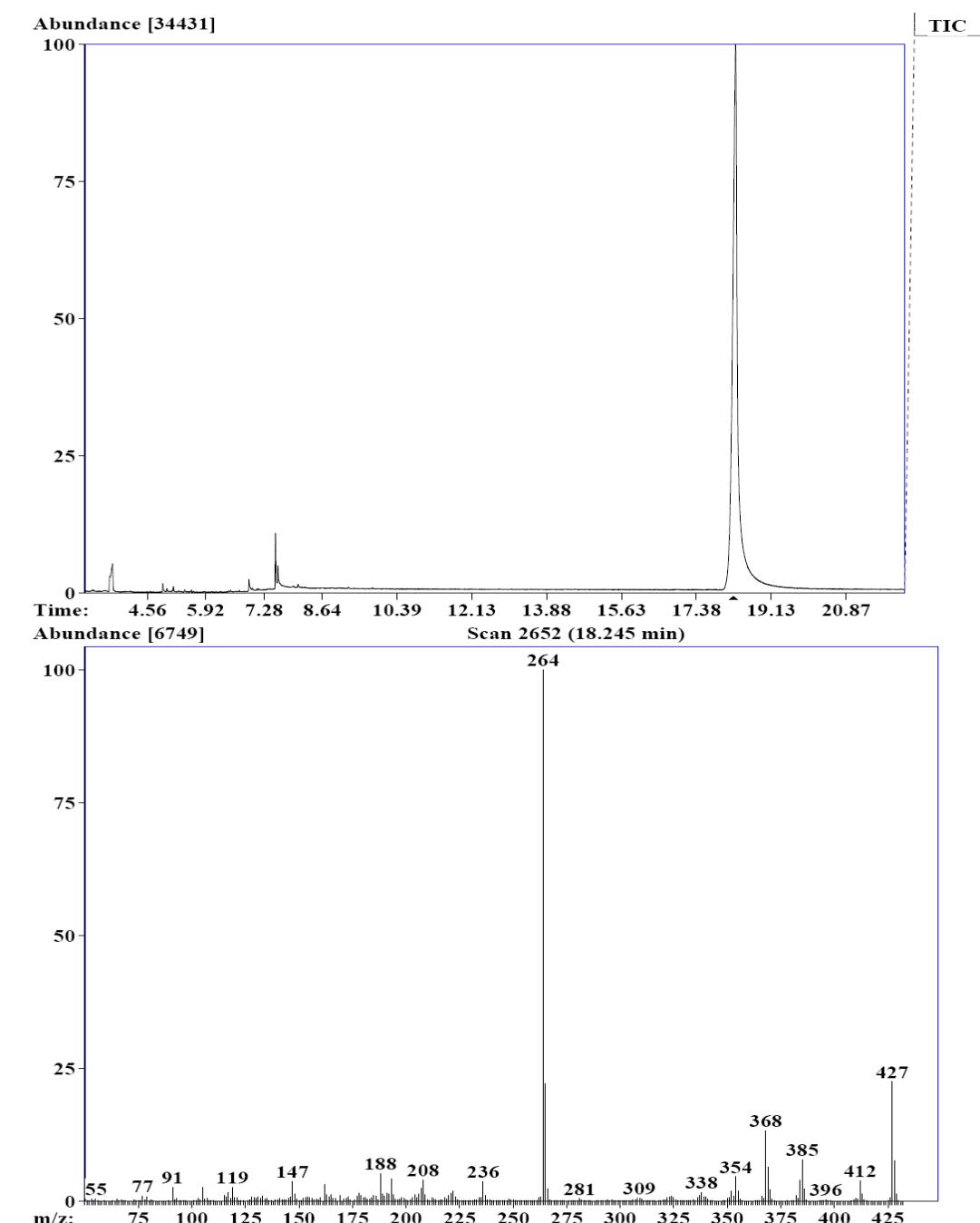
1D-NOE Experiments of compound 3eh:

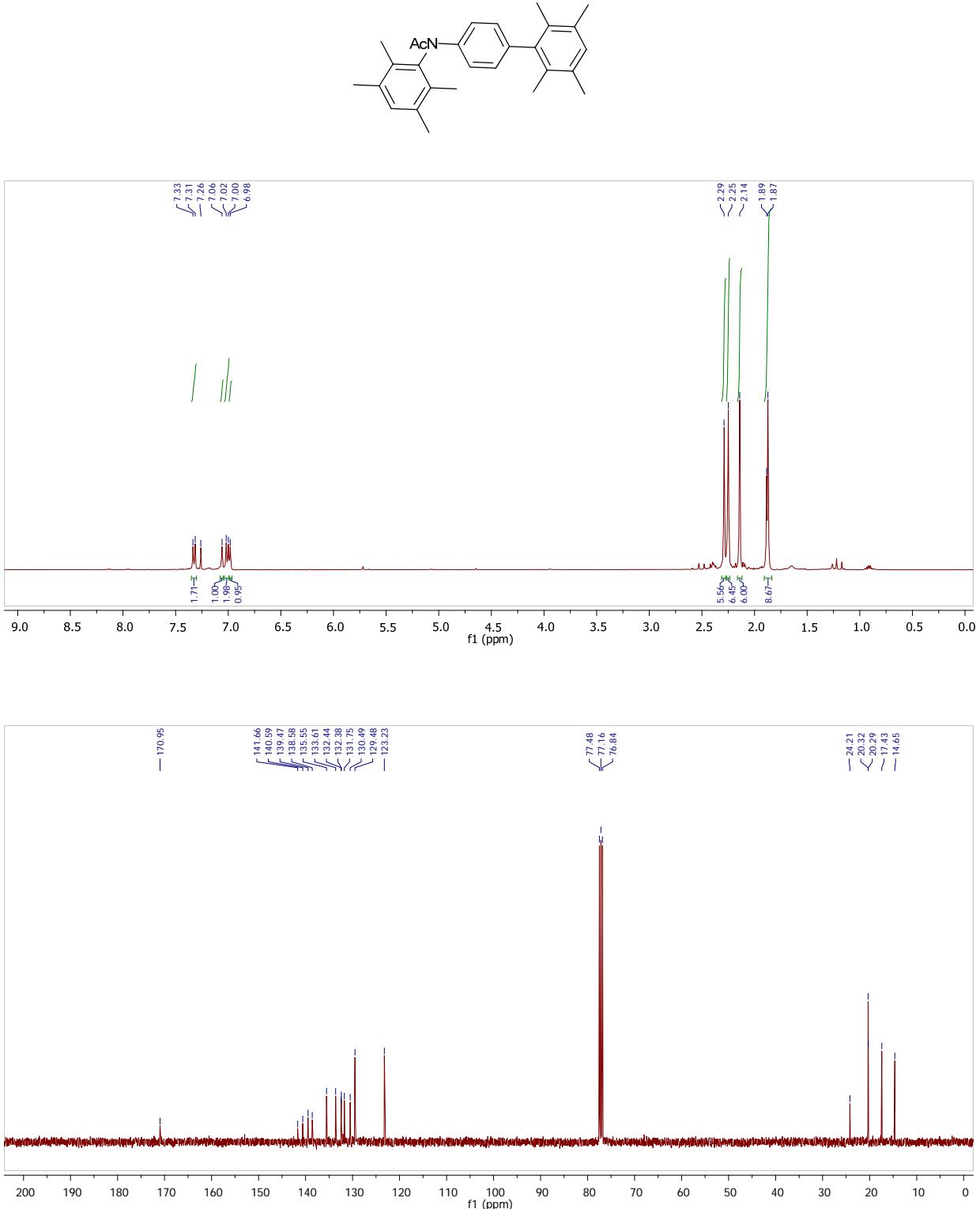


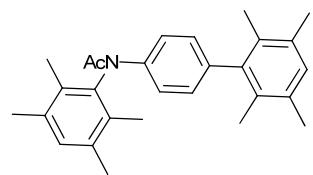




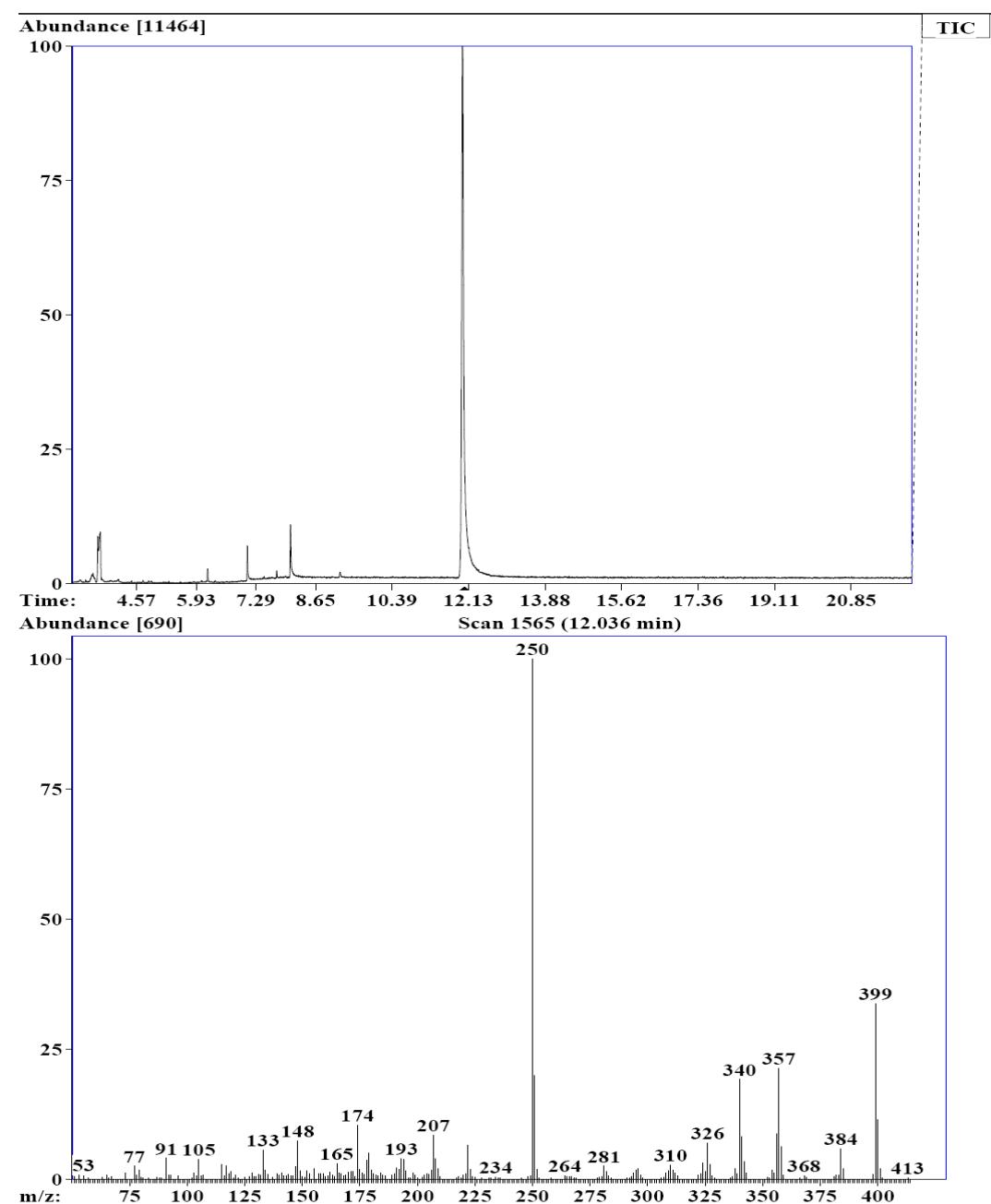
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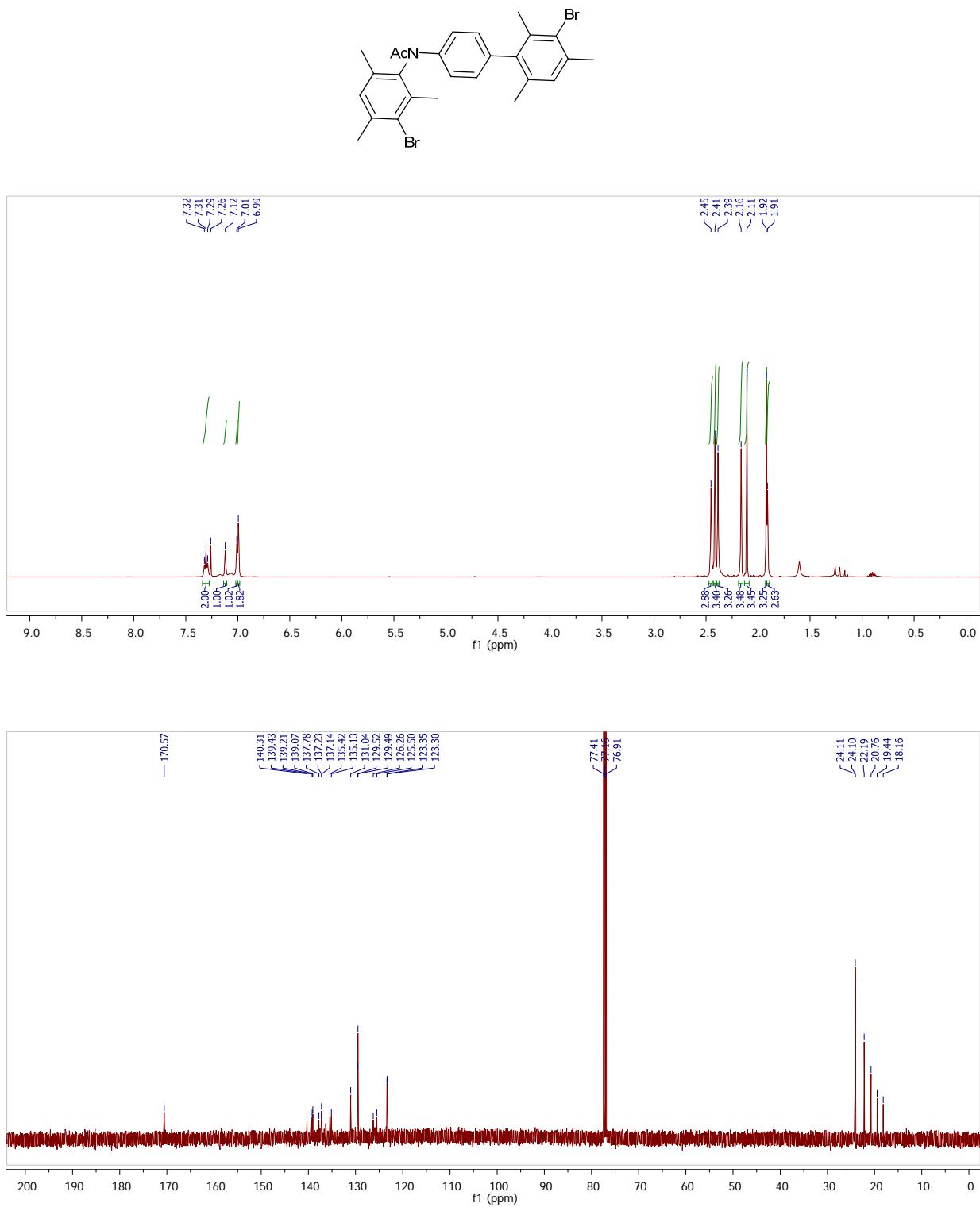


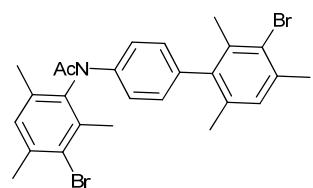




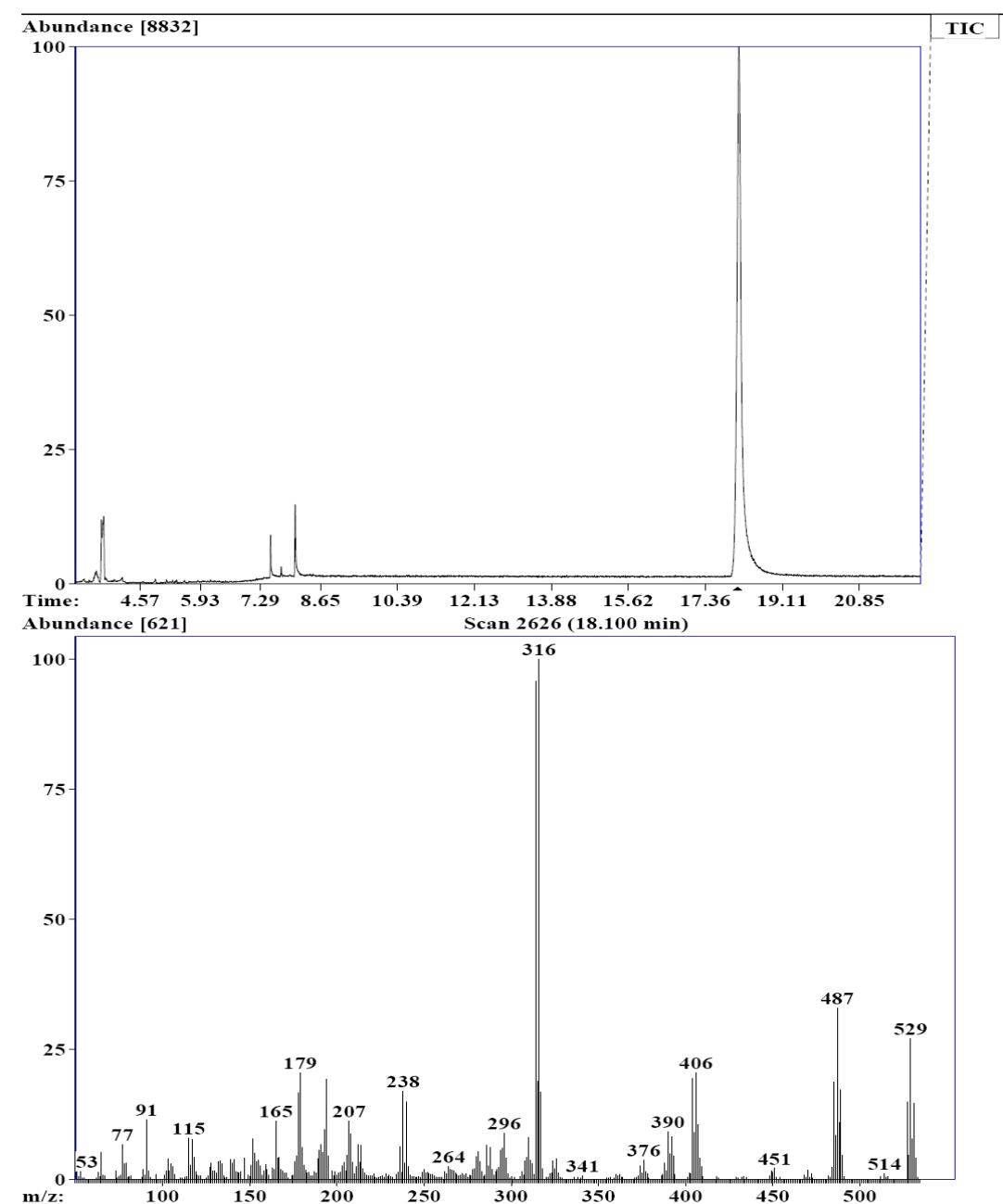
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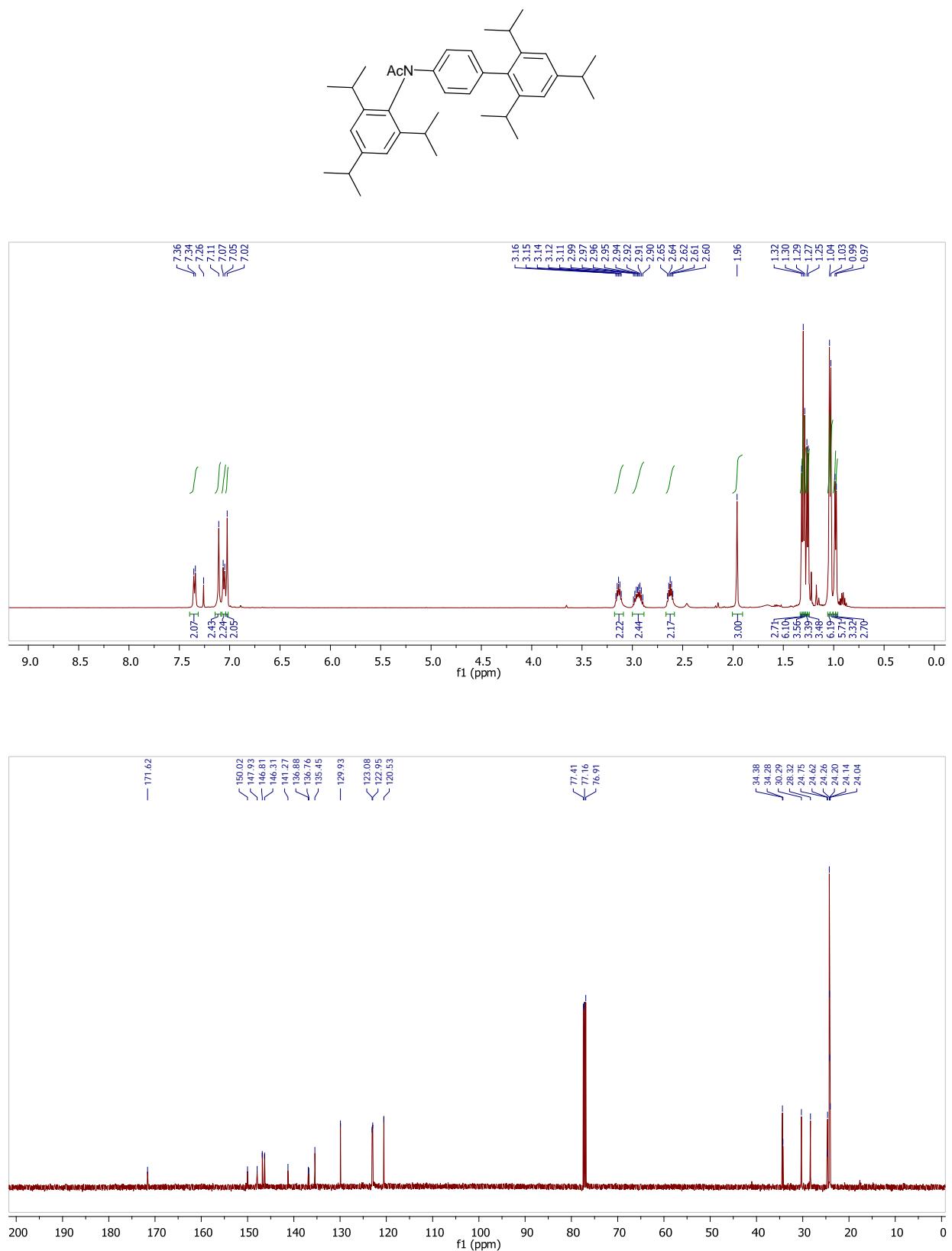


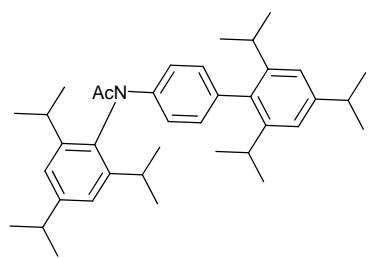




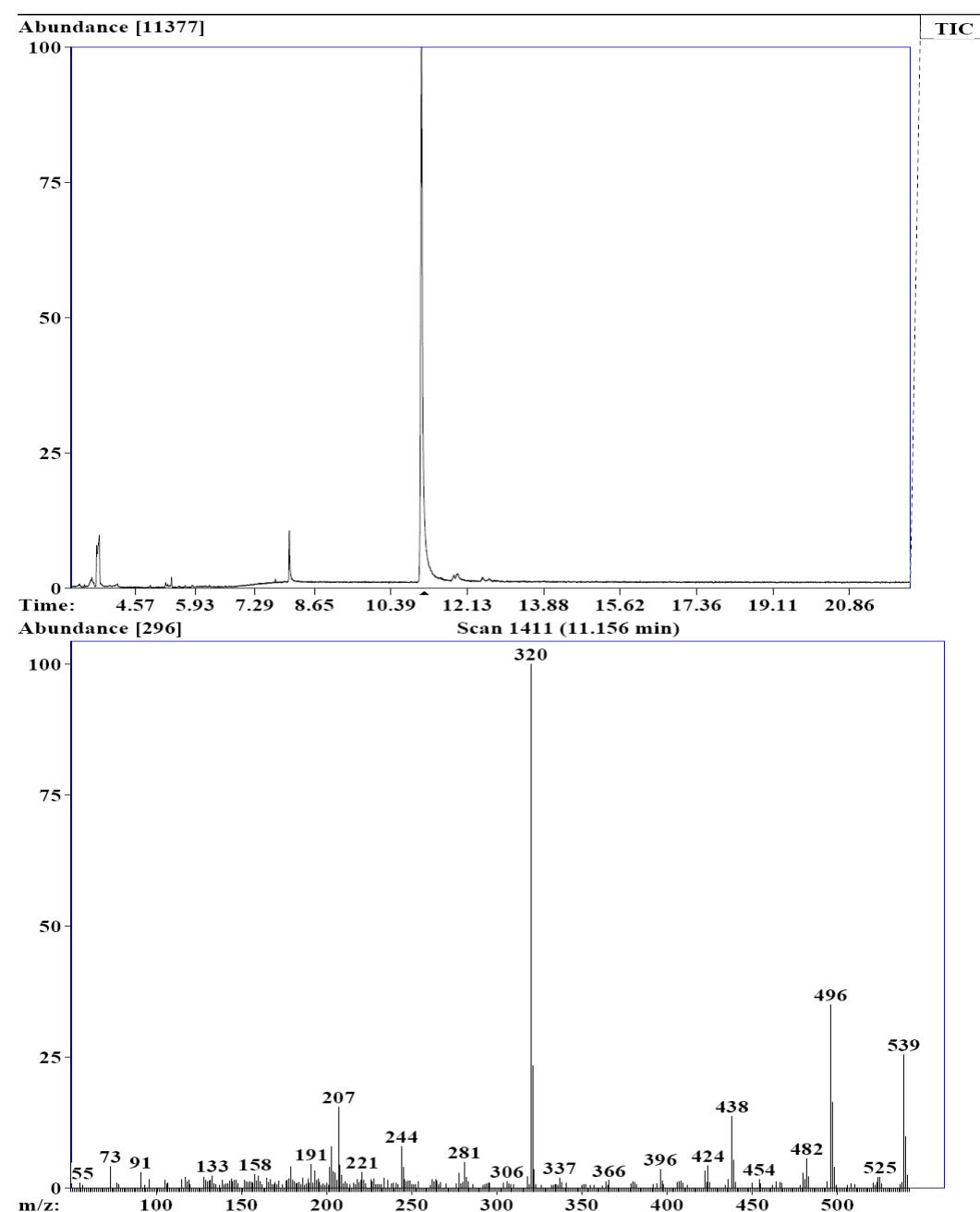
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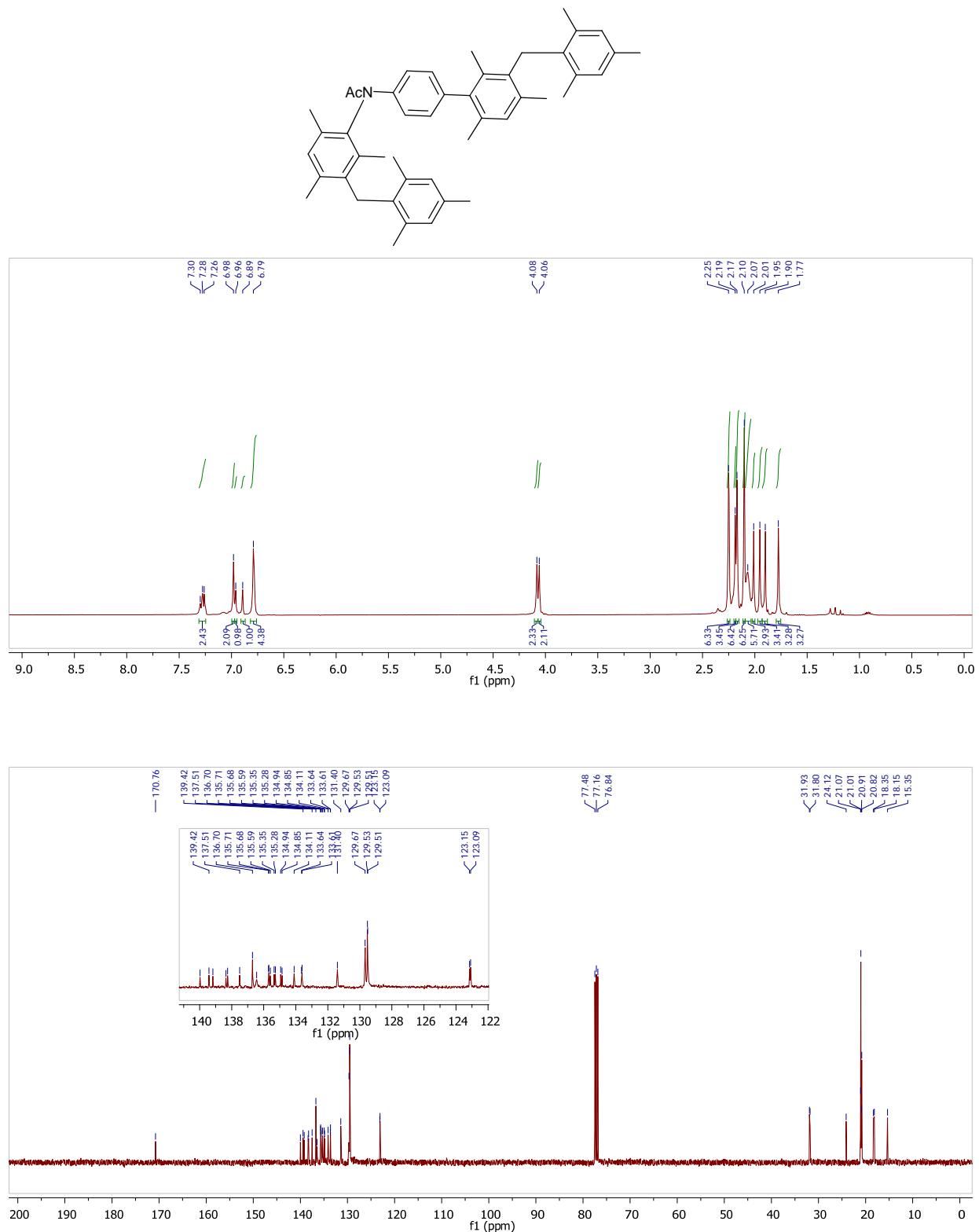


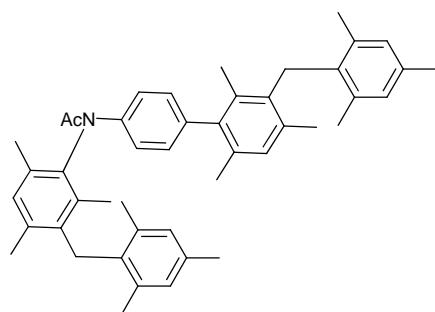




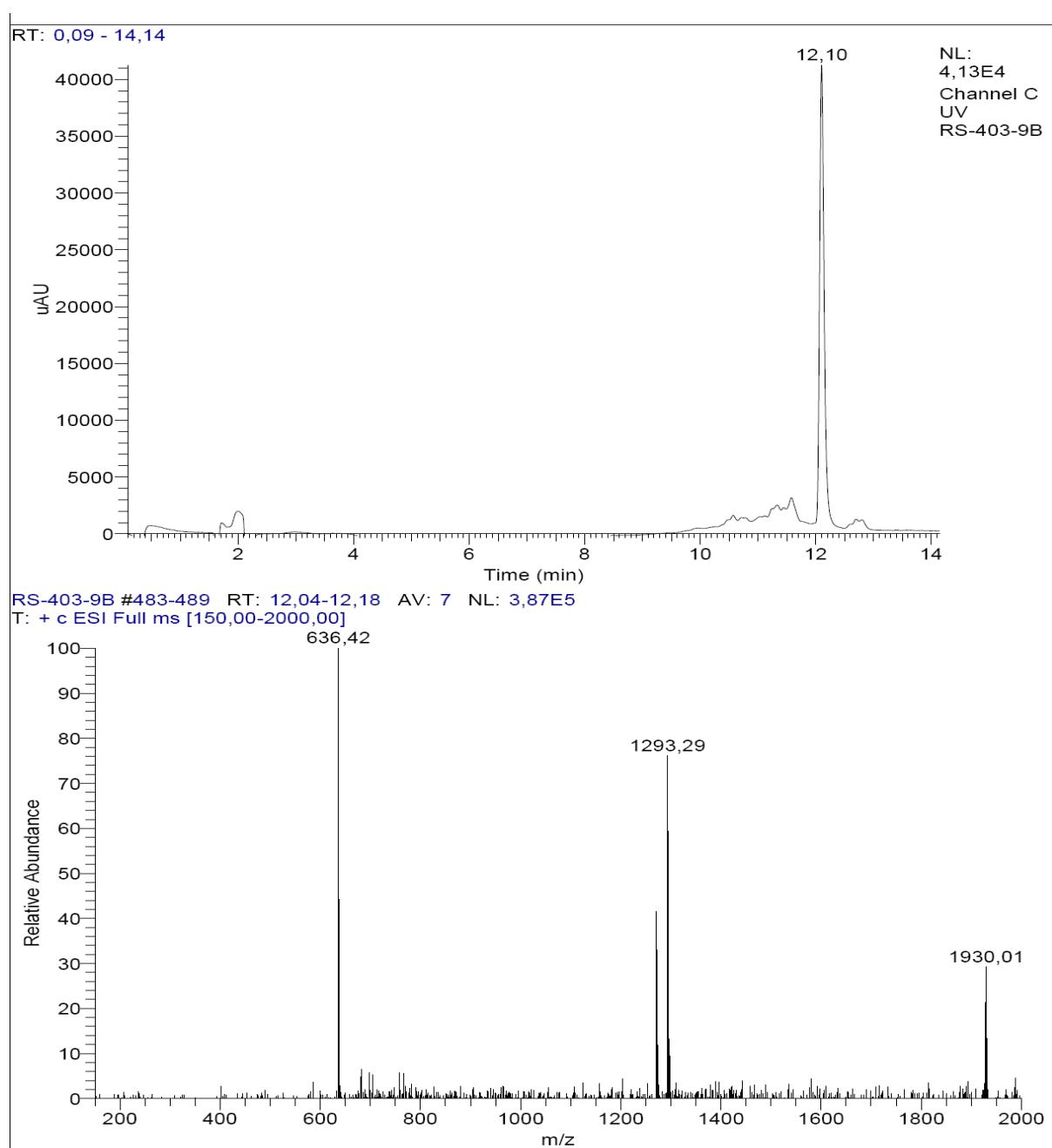
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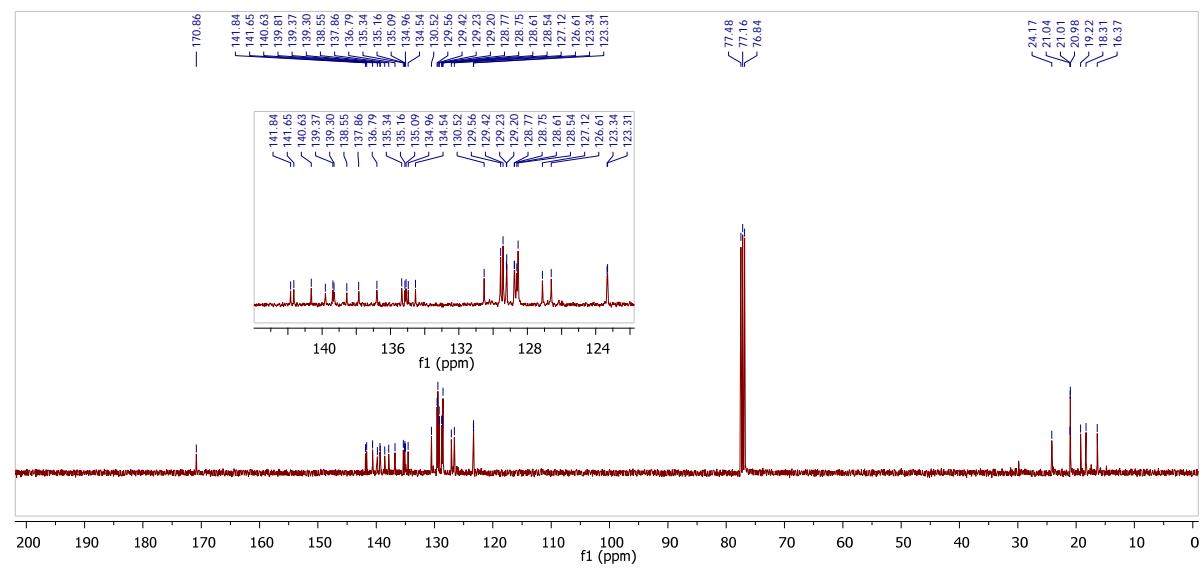
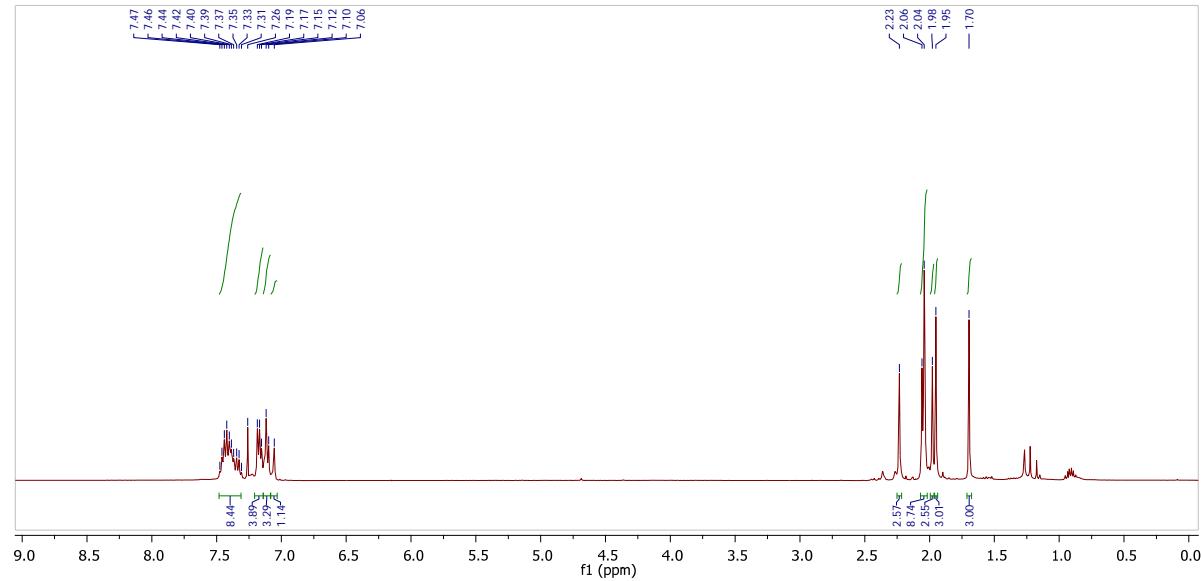
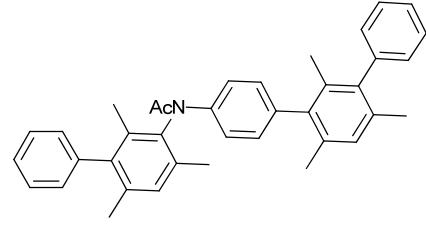


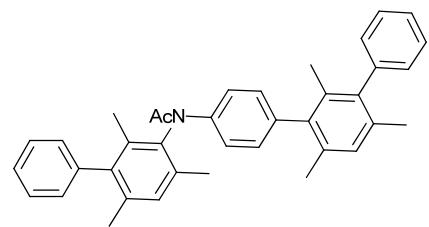




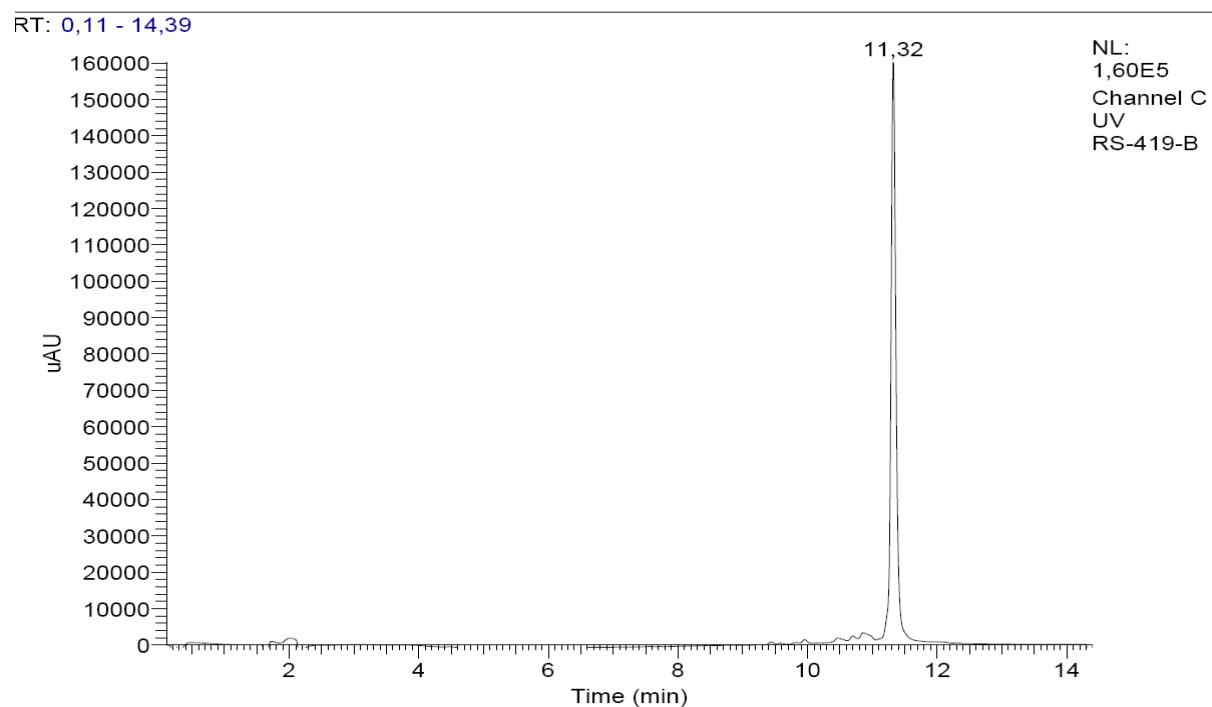
HPLC-MS



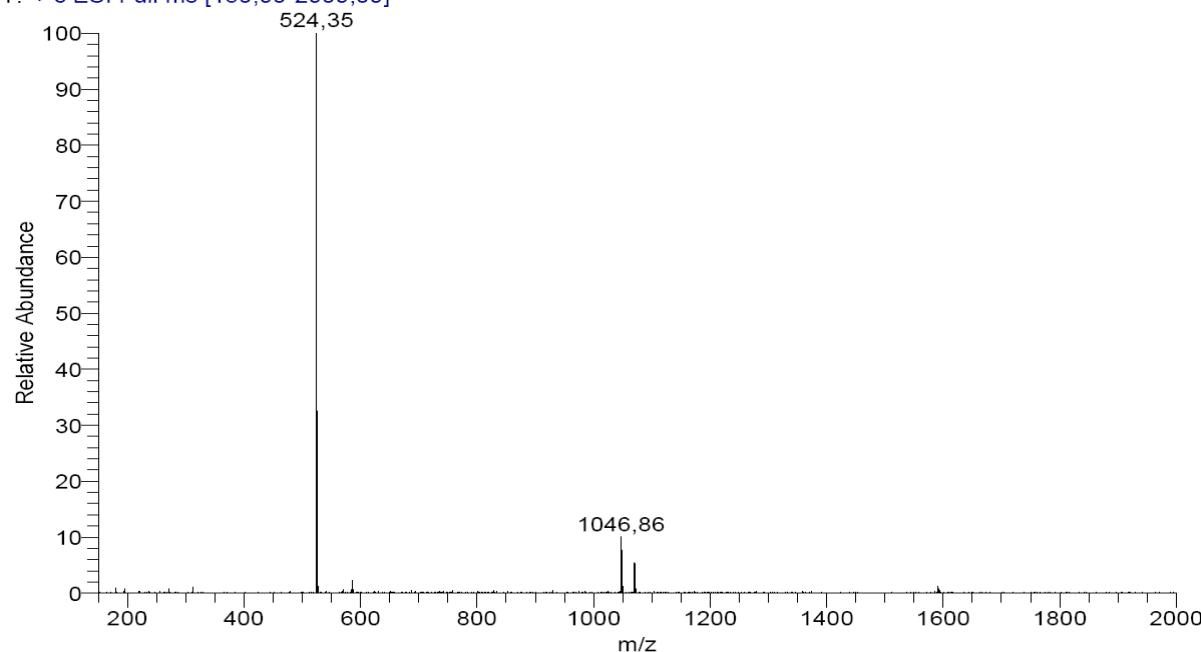


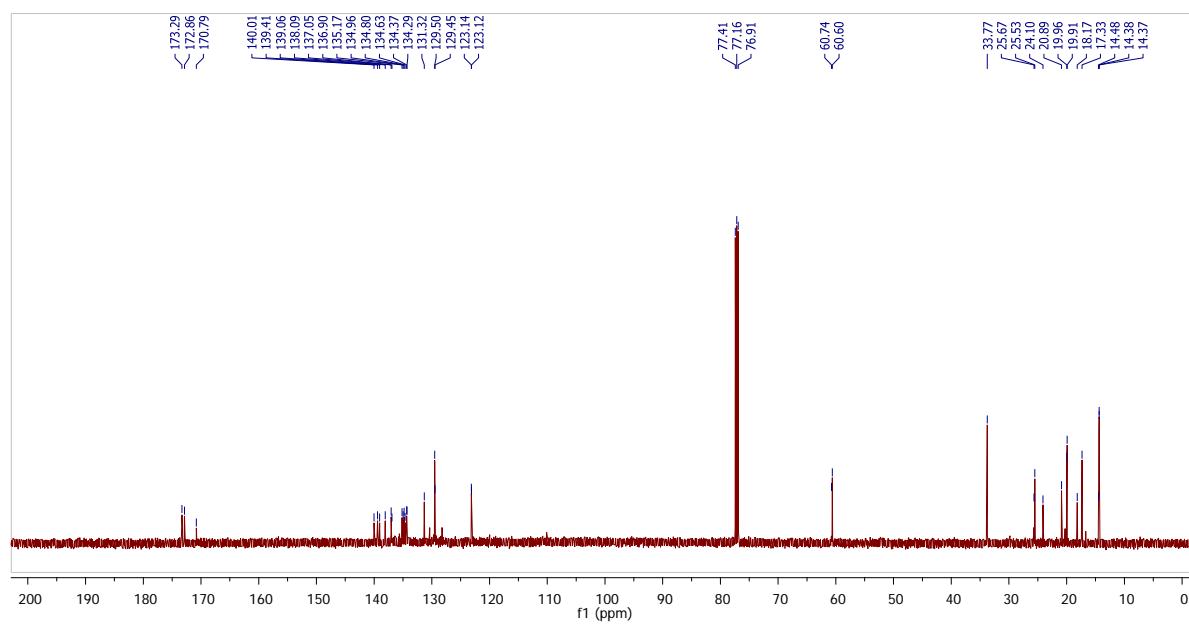
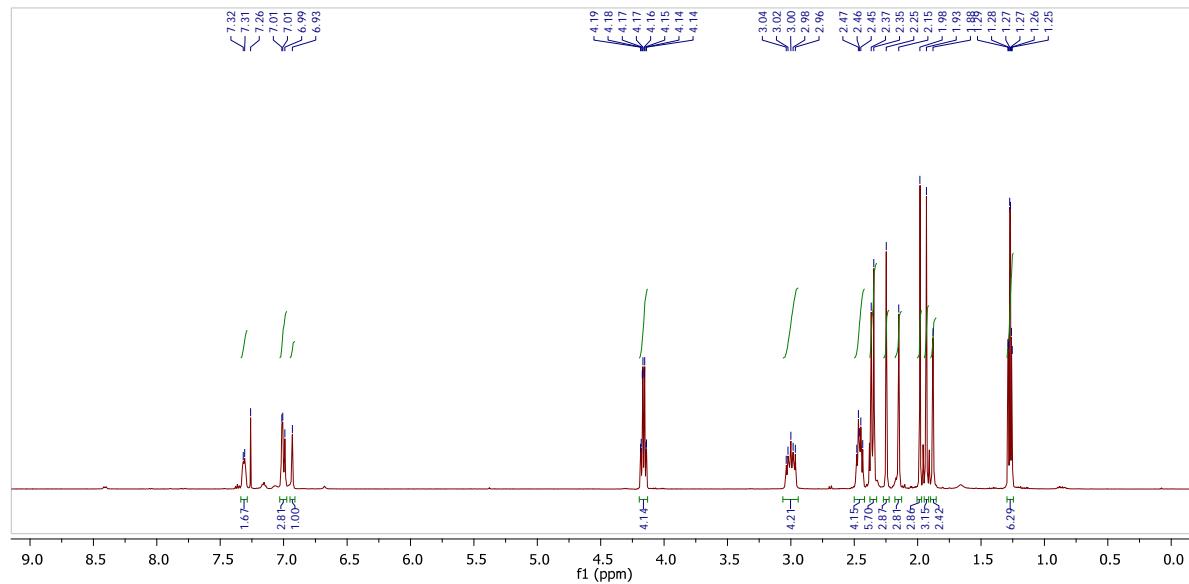
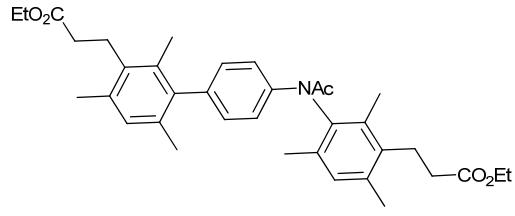


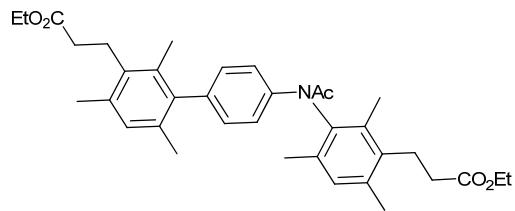
HPLC-MS



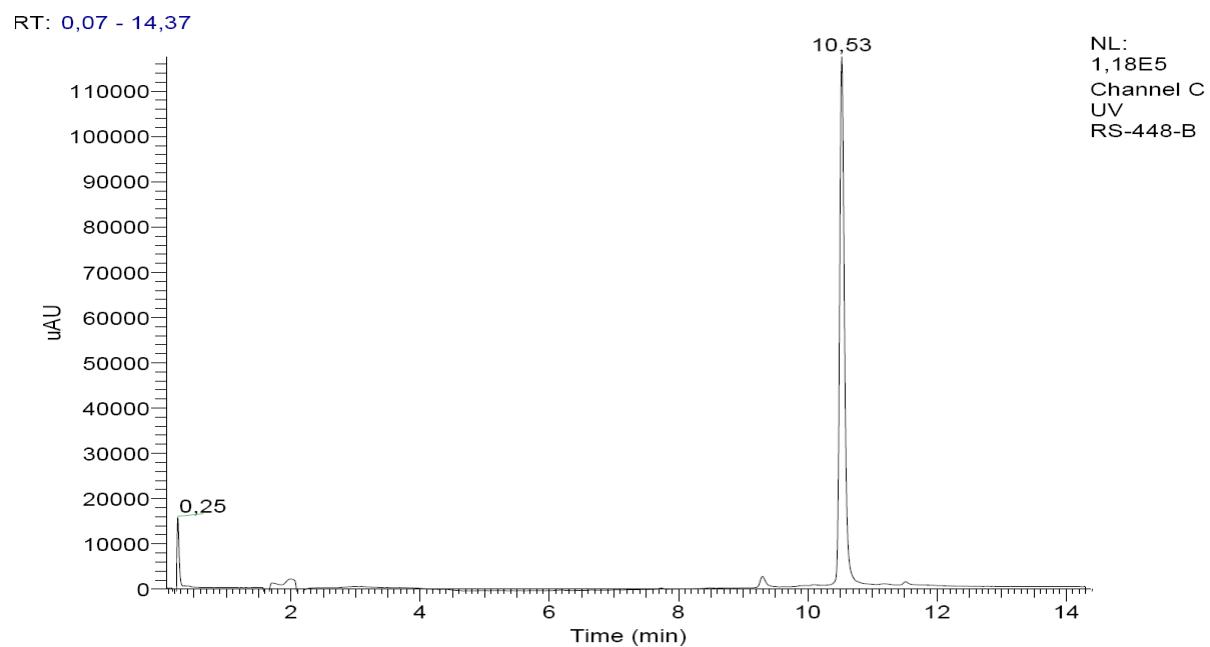
RS-419-B #453-458 RT: 11,27-11,39 AV: 6 NL: 7,58E6
T: + c ESI Full ms [150,00-2000,00]



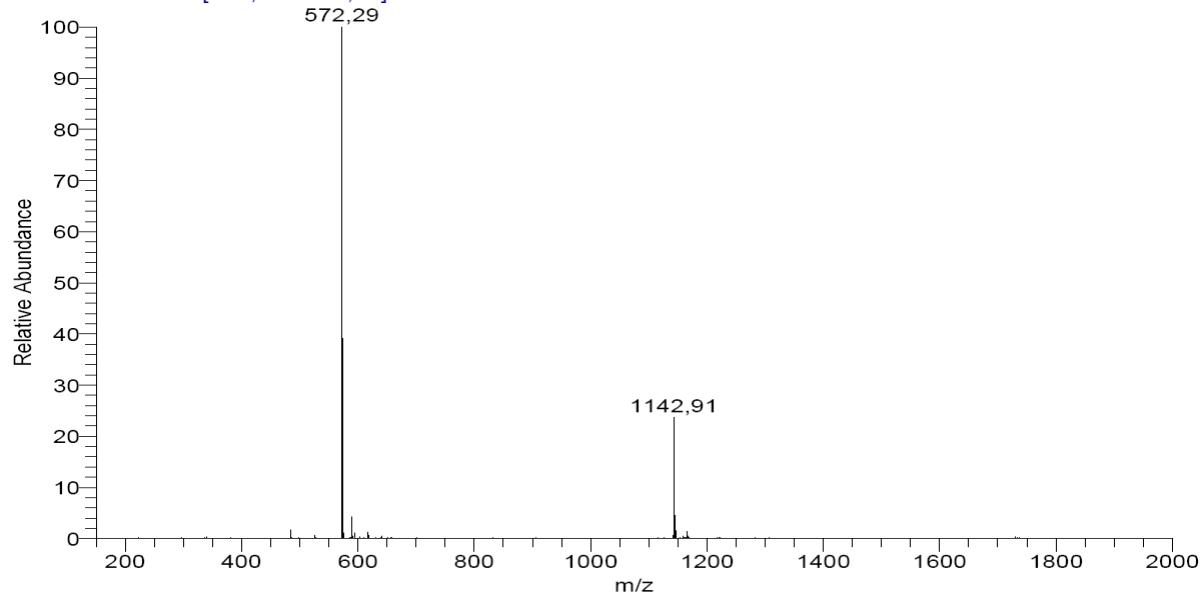


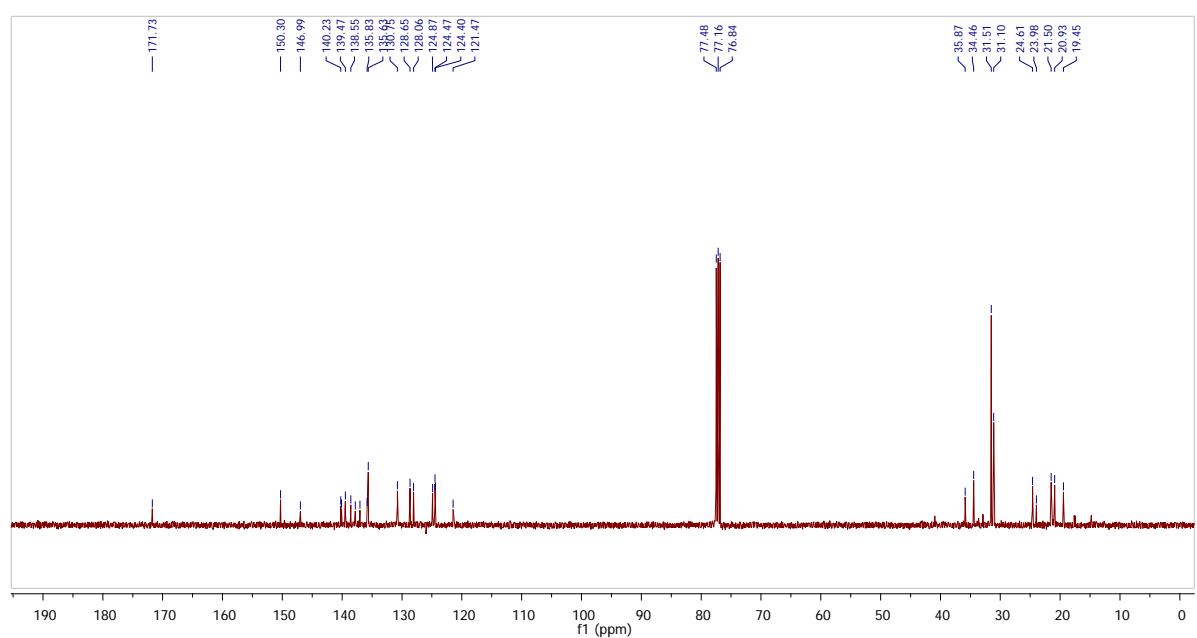
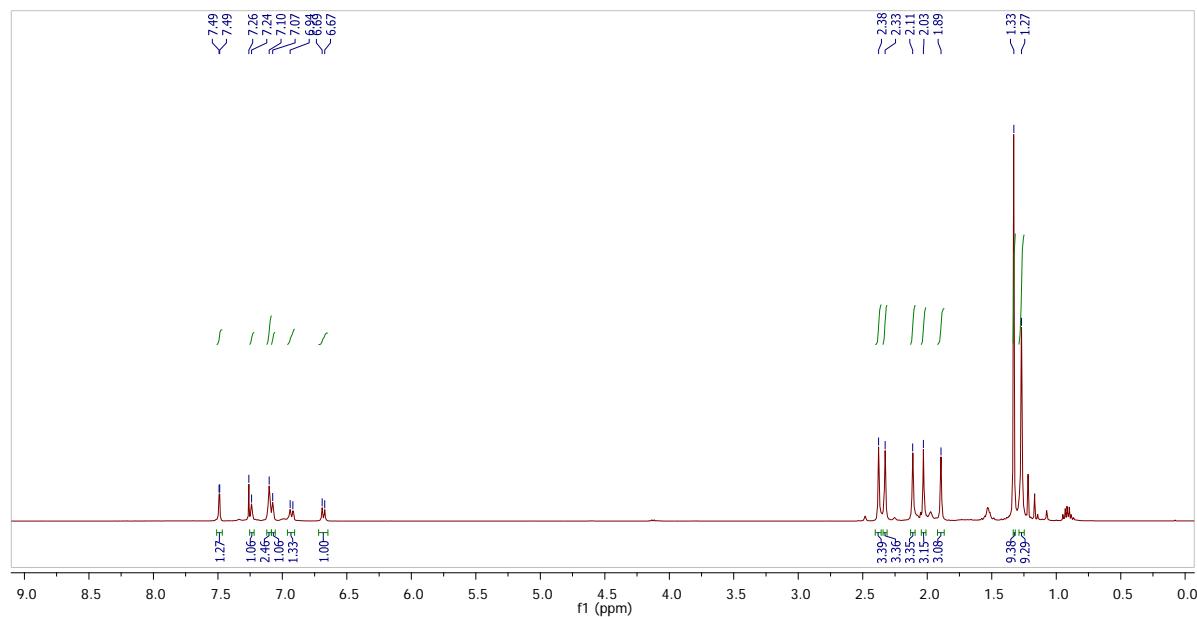
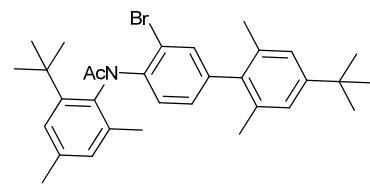


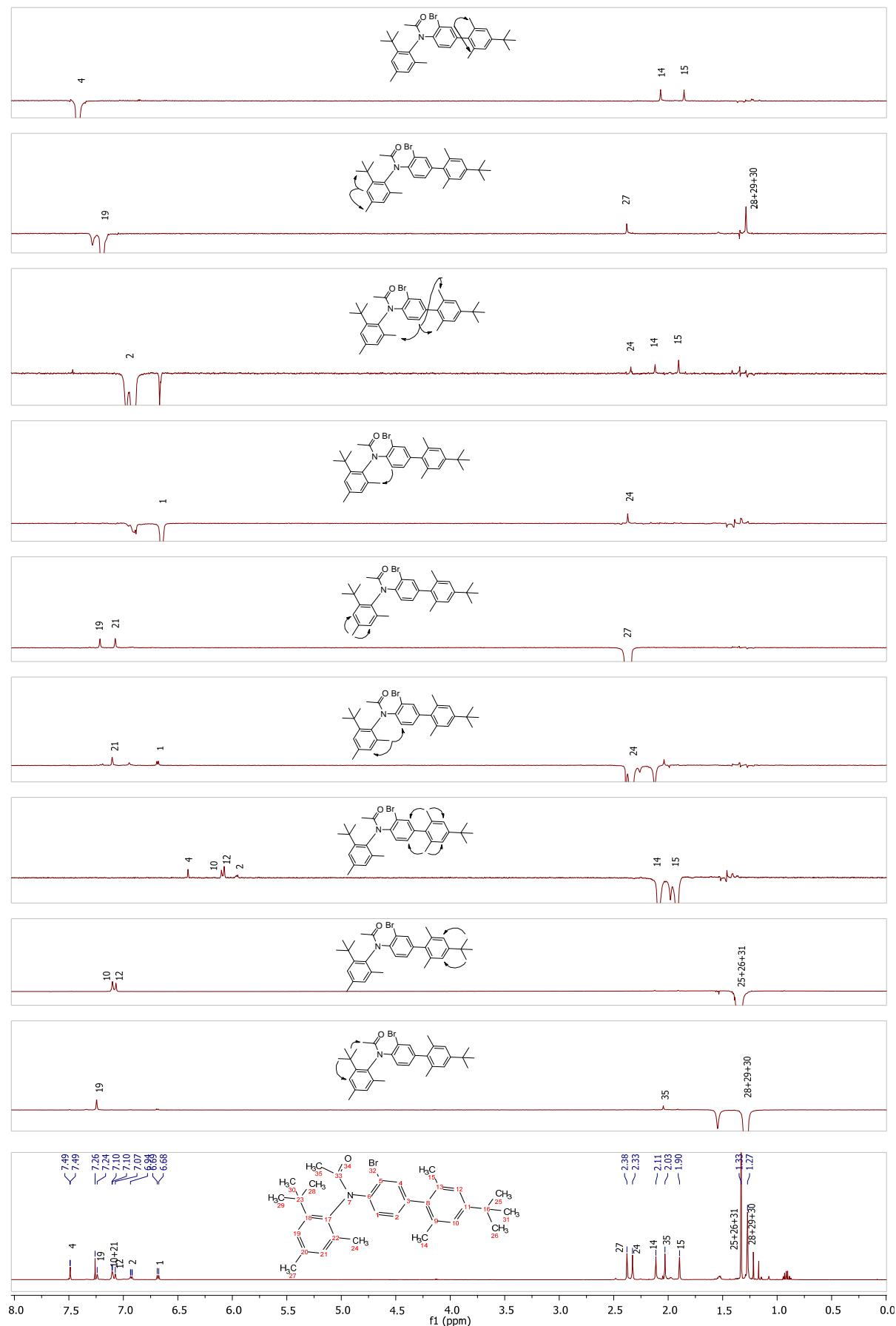
HPLC-MS

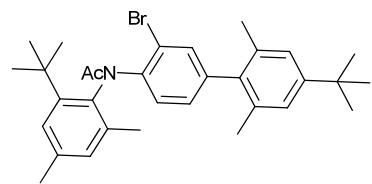


RS-448-B #419-427 RT: 10,43-10,61 AV: 9 NL: 7,22E7
T: + c ESI Full ms [150,00-2000,00]

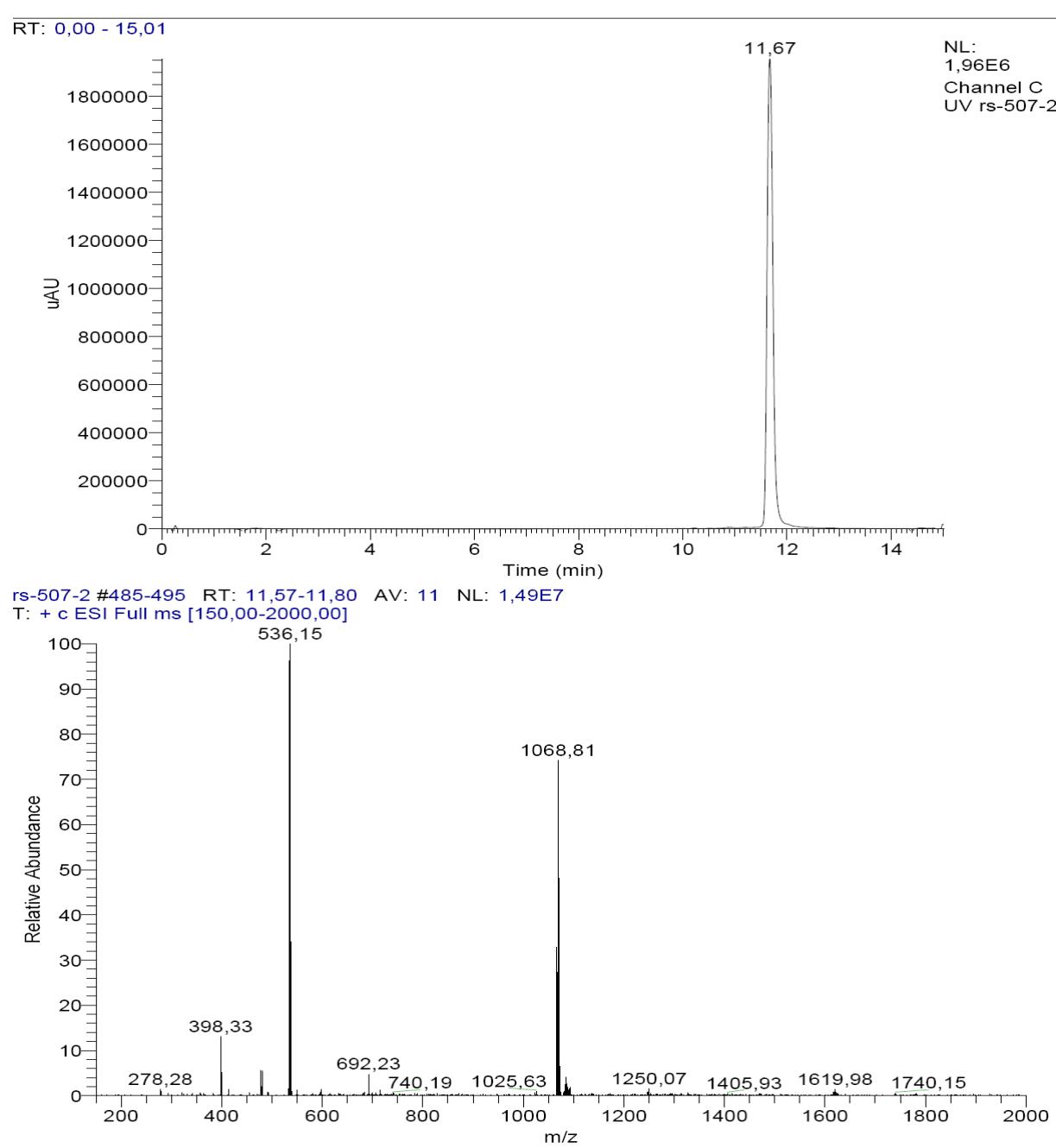


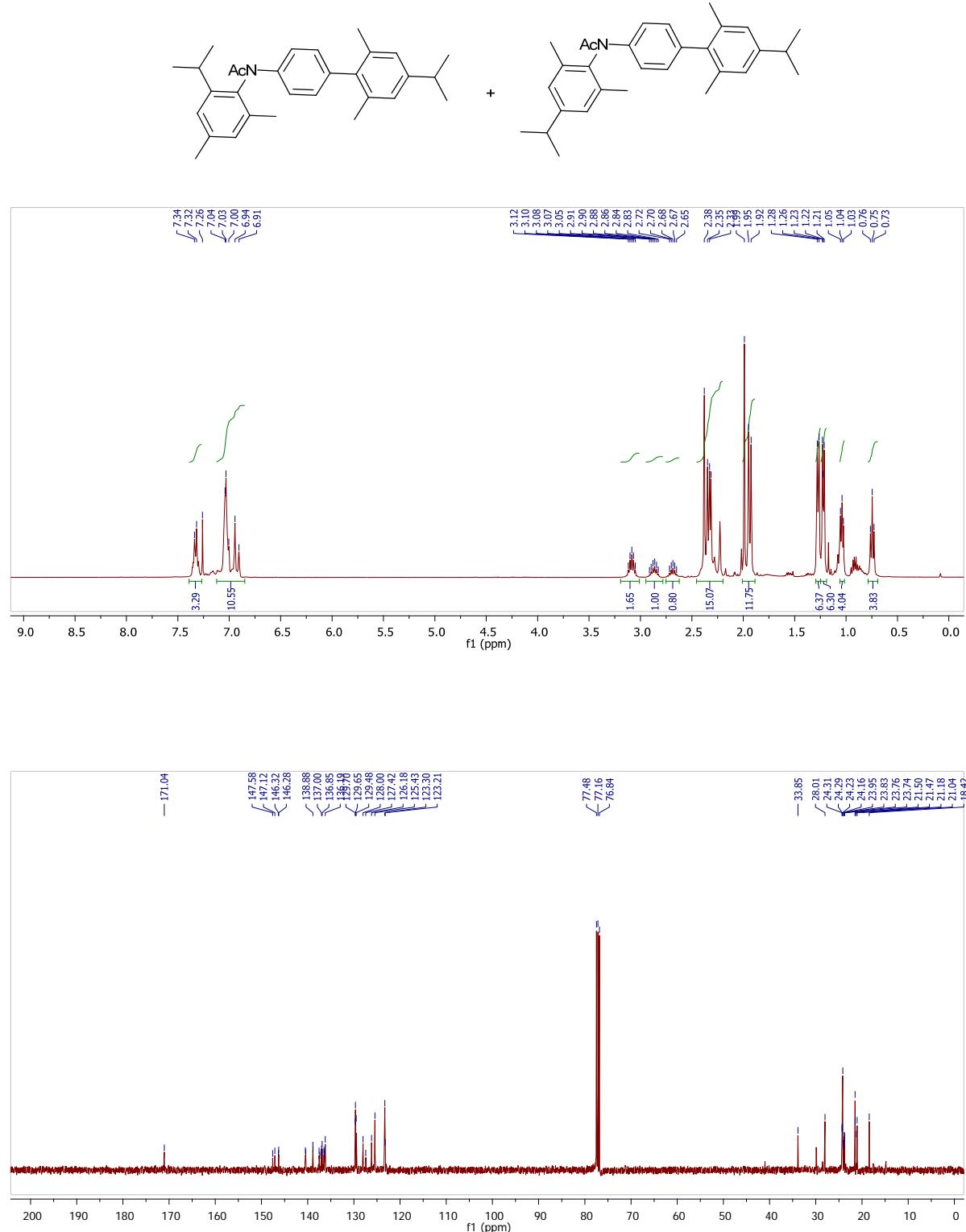


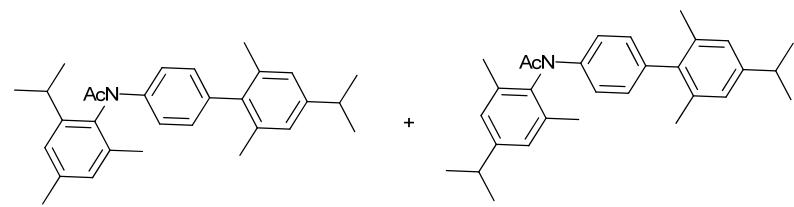




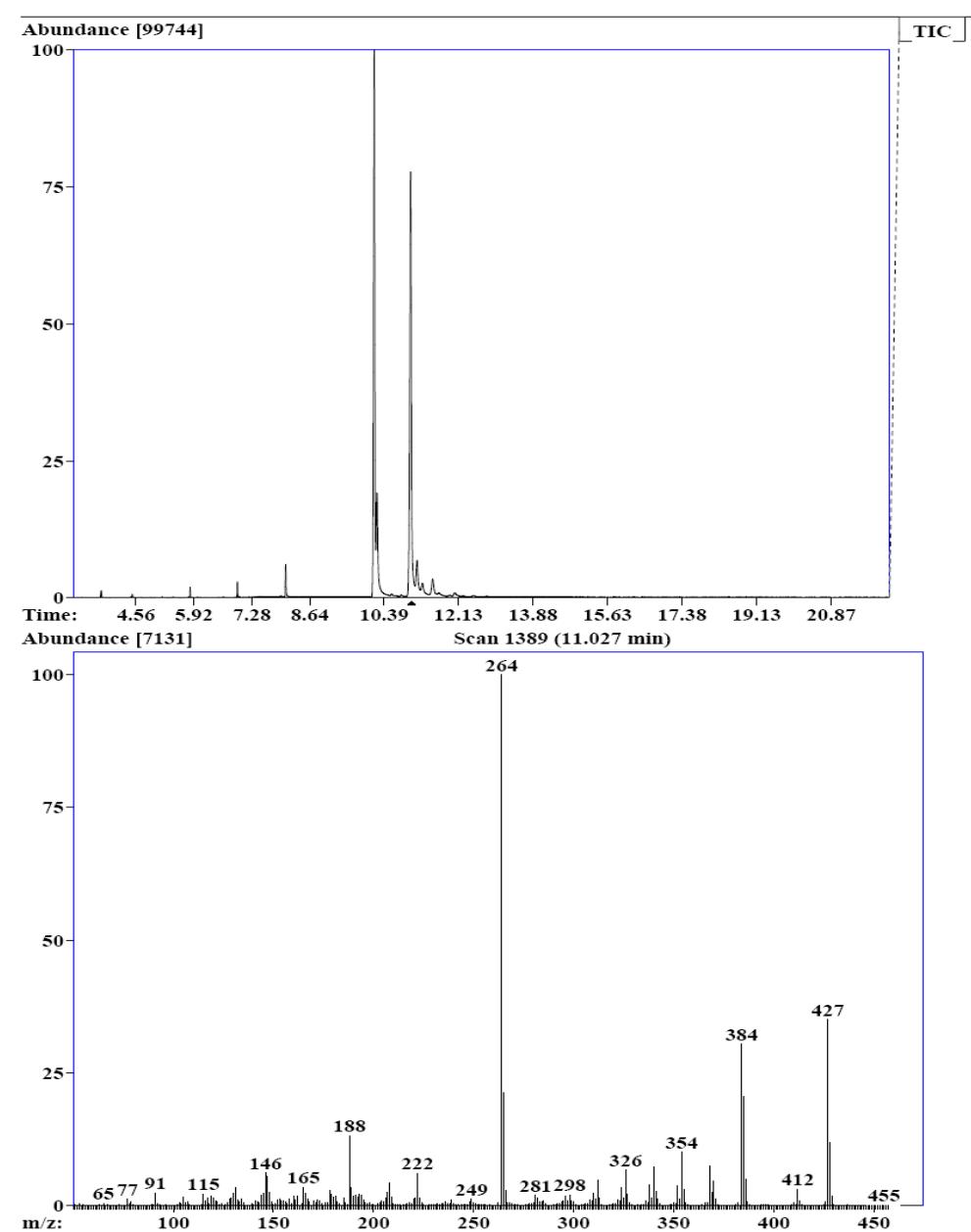
HPLC-MS

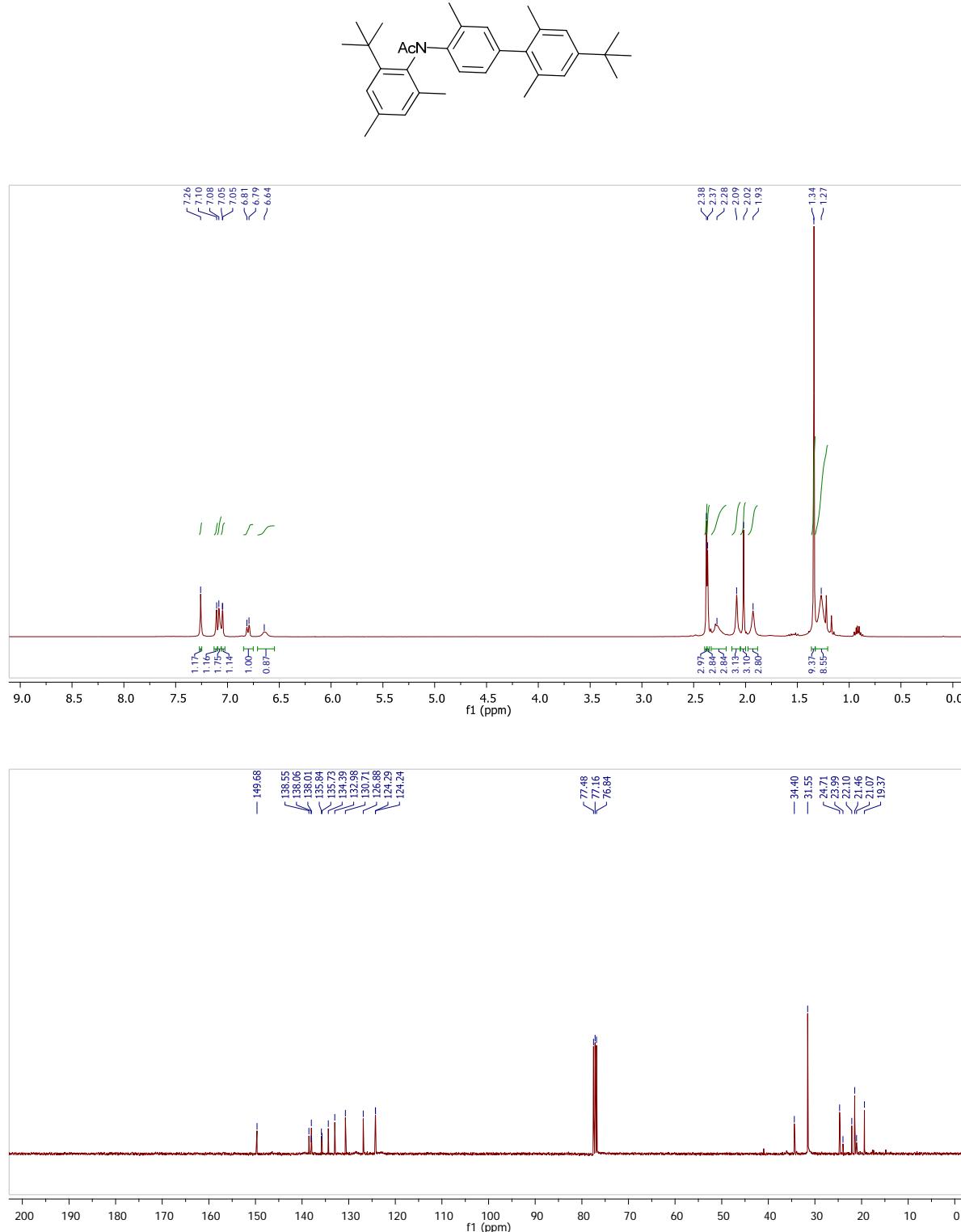


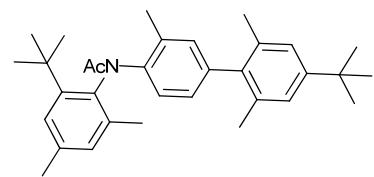




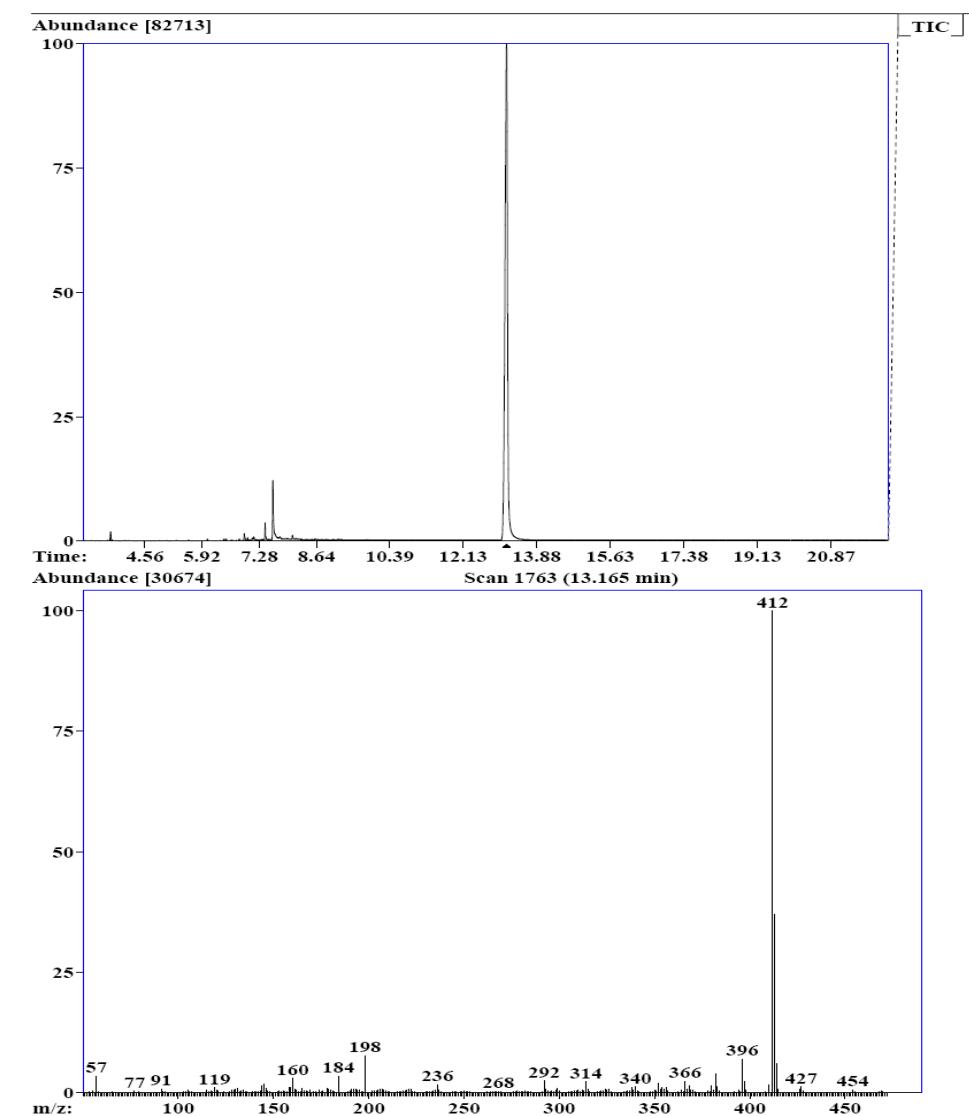
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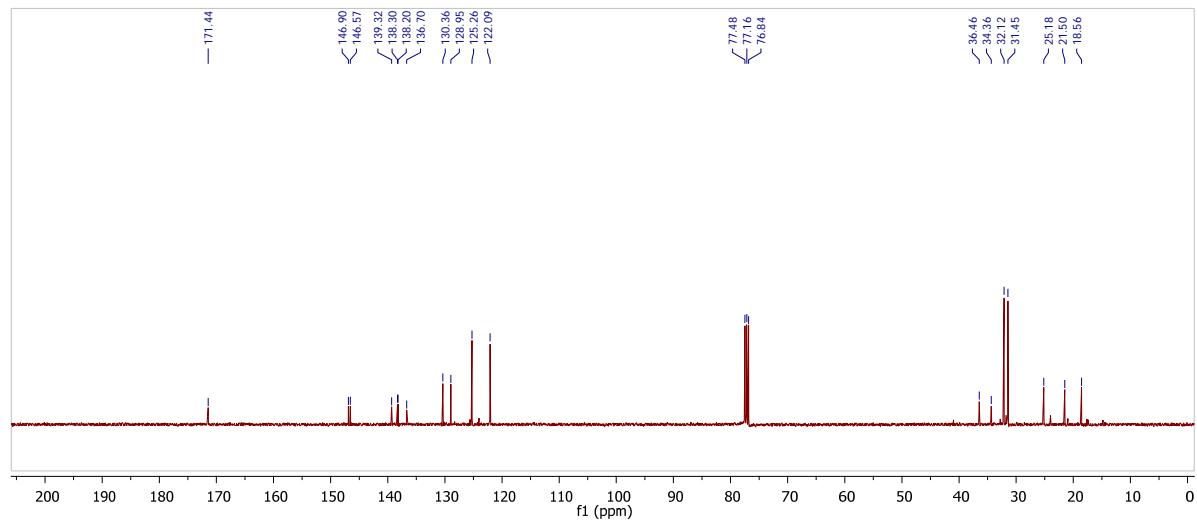
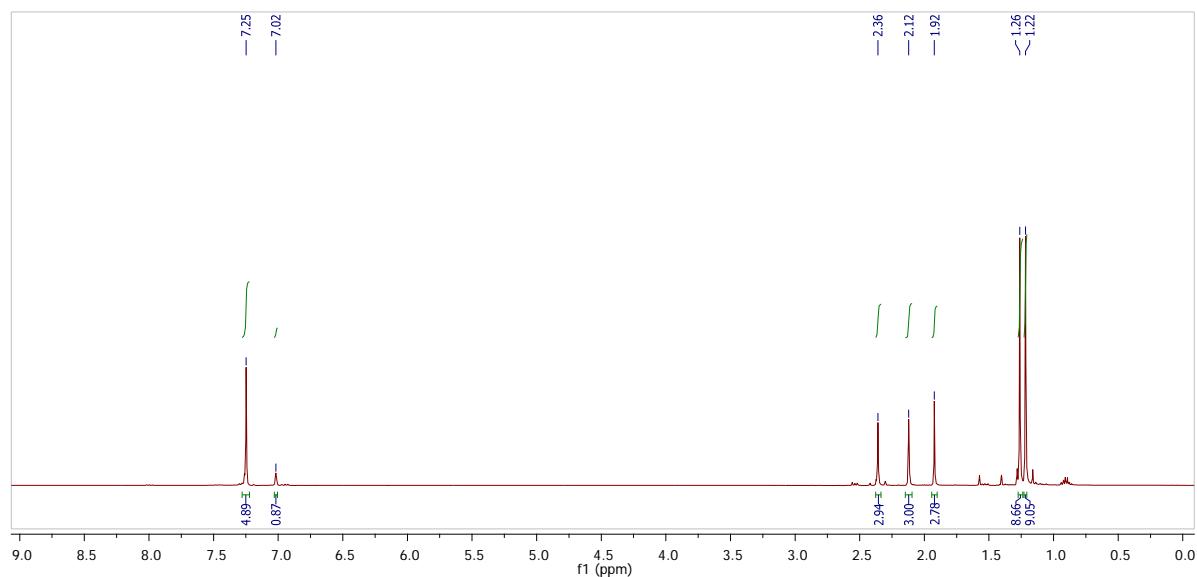
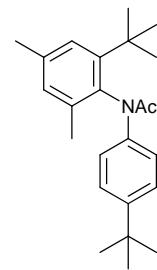


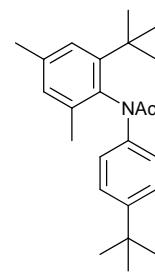




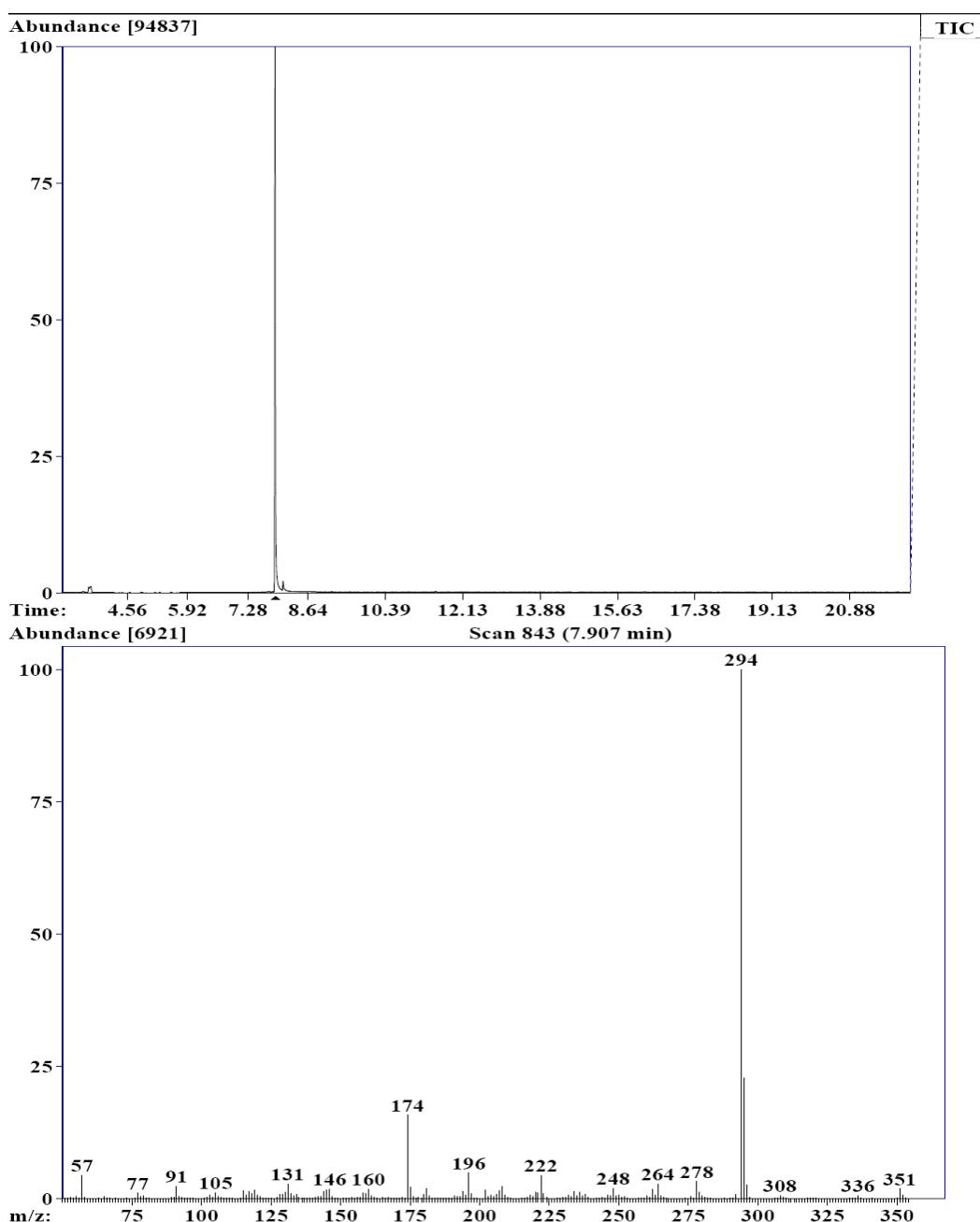
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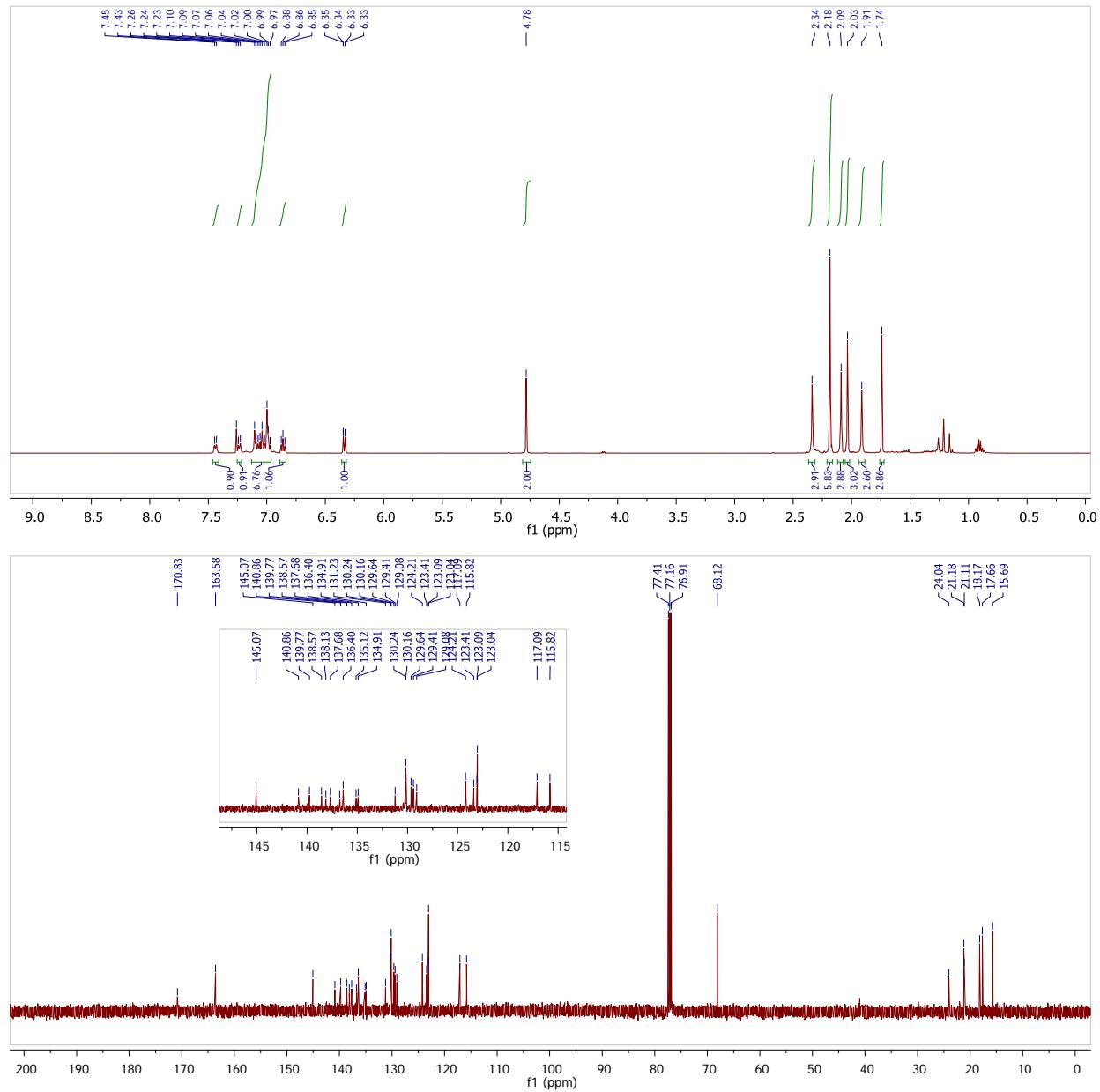
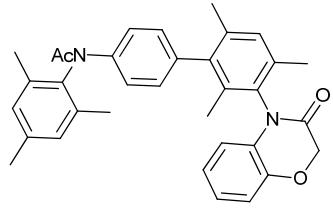






GCMS





1D-NOE Experiments of compound 4:

