

Supporting Information

Amphiphile catalysed selective synthesis of 4-Amino alkylated- 1H-pyrazol-5-ol via Mannich-aromatization prefer over Knoevenagel-Michael type reaction in water

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1. General information

All reagents and solvents were purchased from commercial sources and used as received. The progress of the reaction was monitored by analytical TLC on silica gel G/GF 254 plates. Reagent grade solvents were used for extraction and flash chromatography. Whereas HPLC grade solvent were used for HPLC. The column chromatography was performed with silica gel 230-400 mesh. NMR (^1H and ^{13}C) spectra were recorded on a 400 MHz using TMS as an internal standard and chemical shifts (δ ppm) (multiplicity, coupling constant (Hz), integration). The abbreviations for multiplicity are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets. Melting points are uncorrected were determined in capillary tubes on a hot stage melting point apparatus containing silicon oil. High-resolution mass spectra (ESI-HRMS) were recorded on Agilent 6520 ESI-QTOP mass spectrometer.. IR spectra were recorded using a FTIR spectrophotometer.

2. General procedure for the preparation of 11.

In a typical experiment, the aromatic aldehyde (1 mmol), secondary amine (1.2 mmol) and SDS (20 mol%) were taken in water (2 mL) in a round-bottom flask and stirred at 80 °C temperature for 4 min. A white turbid mixture was obtained and then 3-methyl-1-phenyl-5-pyrazolinone (1 mmol) was added. The reaction mixture was stirred for 2 h until completion of the reaction (monitored by TLC). After completion of the reaction, the mixture was extracted with ethyl acetate, evaporated under vacuum to give the crude product which was purified by silica gel (230–400 mesh) column chromatography (hexane–ethyl acetate) to afford the corresponding product.

3-Methyl-1-phenyl-4-(phenyl(piperidin-1-yl)methyl)-1H-pyrazol-5-ol (11a).

Physical state: Creamy white solid; **Yield:** 91% (316.1 mg); **Mp:** 219-221 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm):** 1.51 - 1.59 (m, 2 H), 1.59 - 1.68 (m, 4 H), 2.16 (s, 3 H), 2.99 (t, *J* = 5.6 Hz, 4 H), 4.62 (s, 1 H), 7.01 - 7.09 (m, 2 H), 7.17 - 7.22 (m, 1 H), 7.28 - 7.33 (m, 3 H), 7.38 (d, *J* = 7.36 Hz, 1 H), 7.93 - 7.96 (m, 3 H); **¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm):** 13.57, 22.09, 22.72, 35.38, 44.27, 102.44, 119.48, 123.27, 125.29, 127.80, 128.11, 128.68, 141.31, 146.29, 147.31, 157.75. **ESIMS:** *m/z* 348 (M+H)⁺. **IR (KBr):** 3414, 3019, 2400, 1597, 1501, 1384, 1216, 1122, 770, 669 cm⁻¹; **Elemental analysis** calculated for C₂₂H₂₅N₃O: C, 76.05; H, 7.25; N, 12.09%; found: C, 76.07; H, 7.26; N, 12.10%; **HRMS (ES):** calculated for [M+H] 348.2076; found: 348.2068; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); *t*₁ = 11.96 min, *t*₂ = 13.81 min.

4-((4-chlorophenyl)(piperidin-1-yl)methyl)-3-methyl-1-phenyl-1H-pyrazol-5-ol (11b).

Physical state: White solid; **Yield:** 92% (351.3 mg); **Mp:** 221-223 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm):** 1.47 - 1.56 (m, 2 H), 1.56 - 1.65 (m, 4 H), 2.19 (s, 3 H), 2.95 (t, *J* = 5.5 Hz, 4 H), 4.66 (s, 1 H), 7.06 (t, *J* = 7.3 Hz, 1 H), 7.28 (d, *J* = 8.5 Hz, 1 H), 7.34 (t, *J* = 7.9 Hz, 3 H), 7.40 (d, *J* = 8.4 Hz, 1 H), 7.97 (d, *J* = 7.7 Hz, 3 H); **¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm):** 13.52, 22.07, 22.69, 34.75, 44.25, 102.21, 119.56, 123.41, 128.01, 128.73, 129.70, 129.96, 141.25, 146.05, 146.22, 157.75. **ESIMS:** *m/z* 382 (M+H)⁺. **IR (KBr):** 3395, 2927, 2430, 1590, 1485, 1382, 1216, 1116, 1084, 1034, 765, 692 cm⁻¹; **Elemental analysis** calculated for C₂₂H₂₄ClN₃O: C, 69.19; H, 6.33; N, 11.00%; found: C, 69.20; H, 6.32; N, 11.01%; **HRMS (ES):** calculated for [M+H] 382.1686; found: 382.1688; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); *t*₁ = 11.94 min, *t*₂ = 13.78 min.

4-((2-Chlorophenyl)(piperidin-1-yl)methyl)-3-methyl-1-phenyl-1H-pyrazol-5-ol (11c)

Physical state: White solid; **Yield:** 88% (336.0 mg); **Mp:** 203-205 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm):** 1.49 - 1.56 (m, 2 H), 1.58 - 1.65 (m, 4 H), 2.20 (s, 3 H), 2.97 (t, *J* = 5.5 Hz, 4 H), 5.05 (s, 1 H), 7.03 - 7.08 (m, 2 H), 7.30 - 7.35 (m, 4 H), 7.95 (dd, *J* = 8.6, 1.1 Hz, 3 H); **¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm):** 13.79, 22.07, 22.69, 32.74, 44.25, 101.86, 119.60, 123.44, 126.98, 127.25, 128.72, 129.16, 131.50, 141.17, 144.05, 146.08, 158.14. **ESIMS:** *m/z* 382 (M+H)⁺. **IR (KBr):** 3684, 3405, 3021, 2929, 2741, 2401, 1594, 1501,

1428, 1382, 1215, 1119, 758, 670 cm^{-1} ; **Elemental analysis** calculated for $\text{C}_{22}\text{H}_{24}\text{ClN}_3\text{O}$: C, 69.19; H, 6.33; N, 11.00%; found: C, 69.18; H, 6.32; N, 11.02%; **HRMS (ES)**: calculated for $[\text{M}+\text{H}]$ 382.1686; found: 382.1684; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); t_1 = 11.93 min, t_2 = 13.76 min.

4-((2,4-Dichlorophenyl)(piperidin-1-yl)methyl)-3-methyl-1-phenyl-1H-pyrazol-5-ol (11d)

Physical state: White solid; **Yield:** 84% (349.7 mg); **Mp:** 225-227 °C; **^1H NMR (400 MHz, DMSO- d_6) δ (ppm):** 1.48 - 1.57 (m, 2 H), 1.57 - 1.67 (m, 4 H), 2.18 (s, 3 H), 2.98 (t, J = 5.1 Hz, 4 H), 4.98 (s, 1 H), 7.06 (t, J = 7.2 Hz, 1 H), 7.30 - 7.36 (m, 4 H), 7.93 (d, J = 7.9 Hz, 2 H), 8.10 (d, J = 8.5 Hz, 1 H); **^{13}C NMR (100 MHz, DMSO- d_6) δ (ppm):** 13.69, 22.09, 22.72, 32.47, 44.28, 101.42, 119.60, 123.53, 127.05, 128.48, 128.74, 130.80, 132.41, 132.60, 141.07, 142.90, 145.99, 158.09. **ESIMS:** m/z 416 ($\text{M}+\text{H}$)⁺. **IR (KBr):** 3423, 3020, 2518, 1592, 1470, 1382, 1216, 1159, 1115, 1069, 1033, 763, 671 cm^{-1} ; **Elemental analysis** calculated for $\text{C}_{22}\text{H}_{23}\text{Cl}_2\text{N}_3\text{O}$: C, 63.47; H, 5.57; N, 10.09%; found: C, 63.46; H, 5.57; N, 10.10%; **HRMS (ES)**: calculated for $[\text{M}+\text{H}]$ 416.1296; found: 416.1287; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); t_1 = 11.90 min, t_2 = 13.73 min.

4-((4-Fluorophenyl)(piperidin-1-yl)methyl)-3-methyl-1-phenyl-1H-pyrazol-5-ol (11e)

Physical state: pale white solid; **Yield:** 91% (332.5 mg); **Mp:** 218-220 °C; **^1H NMR (400 MHz, DMSO- d_6) δ (ppm):** 1.48 - 1.56 (m, 2 H), 1.57 - 1.67 (m, 4 H), 2.18 (s, 3 H), 2.97 (t, J = 5.4 Hz, 4 H), 4.64 (s, 1 H), 7.00 - 7.08 (m, 3 H), 7.30 - 7.35 (m, 3 H), 7.38 - 7.42 (m, 1 H), 7.96 (d, J = 8.5 Hz, 2 H); **^{13}C NMR (100 MHz, DMSO- d_6) δ (ppm):** 13.52, 22.07, 22.69, 34.61, 44.25, 102.49, 114.52, 114.72, 119.53, 123.37, 128.71, 129.40, 129.47, 141.26, 146.20, 157.72. **ESIMS:** m/z 366 ($\text{M}+\text{H}$)⁺. **IR (KBr):** 3685, 3418, 3021, 2933, 2859, 2740, 2513, 1594, 1501, 1421, 1216, 1118, 769, 671 cm^{-1} ; **Elemental analysis** calculated for $\text{C}_{22}\text{H}_{24}\text{FN}_3\text{O}$: C, 72.31; H, 6.62; N, 11.50%; found: C, 72.33; H, 6.60; N, 11.51%; **HRMS (ES)**: calculated for $[\text{M}+\text{H}]$ 366.1981; found: 366.1971; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); t_1 = 11.92 min, t_2 = 13.82 min.

4-((4-Methoxyphenyl)(piperidin-1-yl)methyl)-3-methyl-1-phenyl-1H-pyrazol-5-ol (11f)

Physical state: White solid; **Yield:** 86% (324.6 mg); **Mp:** 223-225 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm):** 1.49 - 1.55 (m, 2 H), 1.55 - 1.64 (m, 4 H), 2.18 (s, 3 H), 2.95 (t, *J* = 5.1 Hz, 4 H), 3.70 (s, 3 H), 4.61 (s, 1 H), 6.78 (d, *J* = 8.5 Hz, 1 H), 7.05 (t, *J* = 7.2 Hz, 1 H), 7.32 (q, *J* = 7.7 Hz, 5 H), 7.97 (d, *J* = 7.9 Hz, 2 H); **¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm):** 13.55, 22.06, 22.69, 34.46, 44.26, 55.42, 102.81, 113.56, 119.54, 123.33, 128.69, 128.72, 139.30, 141.31, 146.30, 157.34, 157.69. **ESIMS:** *m/z* 378 (M+H)⁺. **IR (KBr):** 3423, 3020, 2518, 1592, 1470, 1382, 1216, 1159, 1115, 763, 671 cm⁻¹; **Elemental analysis** calculated for C₂₃H₂₇N₃O₂: C, 73.18; H, 7.21; N, 11.13%; found: C, 73.20; H, 7.18; N, 11.14%; **HRMS (ES):** calculated for [M+H] 378.2181; found: 378.2175; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); t₁ = 11.12 min, t₂ = 13.96 min.

4-((3,4-Dimethoxyphenyl)(piperidin-1-yl)methyl)-3-methyl-1-phenyl-1H-pyrazol-5-ol (11g)

Physical state: White solid; **Yield:** 88% (358.6 mg); **Mp:** 222-224 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm):** 1.49 - 1.56 (m, 2 H), 1.58 - 1.65 (m, 4 H), 2.20 (s, 3 H), 2.97 (t, *J* = 5.0 Hz, 4 H), 3.63 (s, 3 H), 3.73 (s, 3 H), 4.56 (s, 1 H), 6.87 (s, 1 H), 7.06 (t, *J* = 7.0 Hz, 2 H), 7.34 (t, *J* = 7.5 Hz, 3 H), 7.97 (d, *J* = 7.9 Hz, 2 H); **¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm):** 13.63, 22.08, 22.72, 36.10, 44.29, 56.23, 60.35, 102.54, 105.41, 119.66, 123.38, 128.71, 135.77, 141.26, 143.72, 146.31, 152.70, 157.60. **ESIMS:** *m/z* 408 (M+H)⁺. **IR (KBr):** 3407, 3018, 2927, 1597, 1500, 1456, 1385, 1216, 1118, 759, 668 cm⁻¹; **Elemental analysis** calculated for C₂₄H₂₉N₃O₃: C, 70.74; H, 7.17; N, 10.31%; found: C, 70.72; H, 7.18; N, 10.32%; **HRMS (ES):** calculated for [M+H] 408.2287; found: 408.2279; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); t₁ = 11.16 min, t₂ = 13.31 min.

4-((2,5-Dimethoxyphenyl)(piperidin-1-yl)methyl)-3-methyl-1-phenyl-1H-pyrazol-5-ol (11h)

Physical state: White solid; **Yield:** 86% (350.4 mg); **Mp:** 221-223 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm):** 1.49 - 1.56 (m, 2 H), 1.56 - 1.67 (m, 4 H), 2.14 (s, 3 H), 2.97 (t, *J* = 5.4 Hz, 4 H), 3.65 (s, 3 H), 3.75 (s, 3 H), 5.04 (s, 1 H), 6.62 (dd, *J* = 8.8, 3.2 Hz, 1 H), 6.77 (d, *J* = 8.8 Hz, 1 H), 7.02 - 7.06 (m, 1 H), 7.32 (t, *J* = 7.9 Hz, 2 H), 7.55 (d, *J* = 3.0 Hz, 1 H), 7.95

(d, $J = 7.7$ Hz, 2 H); ^{13}C NMR (100 MHz, DMSO- d_6) δ (ppm): 13.49, 22.10, 22.74, 28.23, 44.29, 55.52, 56.30, 102.40, 109.71, 111.28, 117.03, 119.49, 123.20, 128.68, 136.57, 141.36, 146.46, 150.24, 153.23, 158.19. **ESIMS**: m/z 408 (M+H) $^+$. **IR (KBr)**: 3414, 3019, 2930, 1597, 1503, 1384, 1215, 1119, 669 cm^{-1} ; **Elemental analysis** calculated for $\text{C}_{24}\text{H}_{29}\text{N}_3\text{O}_3$: C, 70.74; H, 7.17; N, 10.31%; found: C, 70.75; H, 7.15; N, 10.33%; **HRMS (ES)**: calculated for [M+H] 408.2287; found: 408.2273; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, $T = 25^\circ\text{C}$, 254 nm); $t_1 = 11.54$ min, $t_2 = 13.26$ min.

3-Methyl-4-(naphthalen-1-yl(piperidin-1-yl)methyl)-1-phenyl-1H-pyrazol-5-ol (11i)

Physical state: Pale brown solid; **Yield**: 81% (321.9 mg); **Mp**: 194-196 $^\circ\text{C}$; ^1H NMR (400 MHz, DMSO- d_6) δ (ppm): 1.48 - 1.55 (m, 2 H), 1.56 - 1.64 (m, 4 H), 2.27 (s, 3 H), 2.96 (t, $J = 4.8$ Hz, 4 H), 5.38 (s, 1 H), 7.02 - 7.06 (m, 2 H), 7.28 - 7.33 (m, 3 H), 7.42 - 7.47 (m, 2 H), 7.68 - 7.78 (m, 2 H), 7.95 (dd, $J = 8.6, 1.0$ Hz, 3 H); ^{13}C NMR (100 MHz, DMSO- d_6) δ (ppm): 13.86, 22.11, 22.74, 31.84, 44.27, 103.23, 119.47, 123.34, 124.59, 125.17, 125.79, 125.84, 125.87, 126.24, 126.72, 127.41, 128.69, 129.21, 129.51, 131.31, 134.06, 135.74, 137.26, 141.22, 145.52, 158.44. **ESIMS**: m/z 398 (M+H) $^+$. **IR (KBr)**: 3418, 3010, 2402, 1596, 1578, 1503, 1422, 1385, 1215, 1125, 928, 769, 693 cm^{-1} ; **Elemental analysis** calculated for $\text{C}_{26}\text{H}_{27}\text{N}_3\text{O}$: C, 78.56; H, 6.85; N, 10.57%; found: C, 78.53; H, 6.87; N, 10.55%; **HRMS (ES)**: calculated for [M+H] 398.2232; found: 398.2226; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, $T = 25^\circ\text{C}$, 254 nm); $t_1 = 12.05$ min, $t_2 = 13.85$ min.

3-Methyl-1-phenyl-4-(piperidin-1-yl(pyridin-4-yl)methyl)-1H-pyrazol-5-ol (11j)

Physical state: pale purple solid; **Yield**: 87% (303.1 mg); **Mp**: 207-209 $^\circ\text{C}$; ^1H NMR (400 MHz, DMSO- d_6) δ (ppm): 1.49 - 1.56 (m, 2 H), 1.57 - 1.65 (m, 4 H), 2.19 (s, 3 H), 2.97 (t, $J = 5.5$ Hz, 4 H), 4.63 (s, 1 H), 7.06 (tt, $J = 7.3, 1.2$ Hz, 1 H), 7.30 - 7.37 (m, 5 H), 7.96 (dd, $J = 8.6, 1.0$ Hz, 2 H), 8.40 (d, $J = 4.7$ Hz, 1 H); ^{13}C NMR (100 MHz, DMSO- d_6) δ (ppm): 13.47, 22.09, 22.72, 34.88, 44.26, 101.28, 119.60, 123.37, 123.51, 128.75, 141.16, 146.28, 149.48, 155.61, 157.82. **ESIMS**: m/z 349 (M+H) $^+$. **IR (KBr)**: 3414, 3020, 2403, 1594, 1496, 1384, 1216, 1116, 1071, 1030, 764, 670 cm^{-1} ; **Elemental analysis** calculated for $\text{C}_{21}\text{H}_{24}\text{N}_4\text{O}$: C, 72.39; H, 6.94; N, 16.08%; found: C, 72.40; H, 6.93; N, 16.09%; **HRMS (ES)**: calculated

349.2028; found: 349.2021; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); t₁ = 9.58 min, t₂ = 10.83 min.

3-Methyl-1-phenyl-4-(phenyl(pyrrolidin-1-yl)methyl)-1H-pyrazol-5-ol (11k)

Physical state: Pale brown solid; **Yield:** 90% (300.9 mg); **Mp:** 215-217 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm):** 1.77 - 1.83 (m, 4 H), 2.18 (s, 3 H), 3.02 - 3.10 (m, 4 H), 4.65 (s, 1 H), 7.03 - 7.09 (m, 2 H), 7.21 (t, *J* = 7.6 Hz, 1 H), 7.30 - 7.35 (m, 3 H), 7.41 (d, *J* = 7.6 Hz, 1 H), 7.95 - 7.98 (m, 3 H); **¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm):** 13.59, 24.07, 35.40, 45.39, 102.47, 119.54, 123.33, 125.32, 127.82, 128.14, 128.71, 141.33, 146.33, 147.30, 157.75. **ESIMS:** m/z 334 (M+H)⁺. **IR (KBr):** 3409, 3019, 2400, 1597, 1501, 1384, 1251, 929, 759, 696 cm⁻¹; **Elemental analysis** calculated for C₂₁H₂₃N₃O: C, 75.65; H, 6.95; N, 12.60%; found: C, 75.66; H, 6.94; N, 12.62%; **HRMS (ES):** calculated for [M+H] 334.1919; found: 334.1911; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); t₁ = 10.32 min, t₂ = 12.20 min.

4-((2-Chlorophenyl)(pyrrolidin-1-yl)methyl)-3-methyl-1-phenyl-1H-pyrazol-5-ol (11l)

Physical state: Brown solid; **Yield:** 92% (338.4 mg); **Mp:** 195-197 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm):** 1.73 - 1.82 (m, 4 H), 2.23 (s, 3 H), 3.04 (t, *J* = 6.7 Hz, 4 H), 5.09 (s, 1 H), 7.05 - 7.16 (m, 3 H), 7.34 (t, *J* = 7.8 Hz, 4 H), 7.98 (d, *J* = 8.1 Hz, 2 H); **¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm):** 13.82, 24.09, 32.79, 45.35, 101.90, 119.66, 123.48, 126.98, 127.26, 128.74, 129.17, 131.53, 131.54, 141.20, 144.07, 146.13, 158.16. **ESIMS:** m/z 368 (M+H)⁺. **IR (KBr):** 3410, 3019, 1598, 1501, 1384, 1215, 1121, 758, 694 cm⁻¹; **Elemental analysis** calculated for C₂₁H₂₂ClN₃O: C, 68.56; H, 6.03; N, 11.42%; found: C, 68.55; H, 6.01; N, 11.44%; **HRMS (ES):** calculated for [M+H] 368.1529; found: 368.1519; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); t₁ = 10.60 min, t₂ = 12.06 min.

4-((4-Methoxyphenyl)(pyrrolidin-1-yl)methyl)-3-methyl-1-phenyl-1H-pyrazol-5-ol (11m)

Physical state: Brown solid; **Yield:** 88% (319.8 mg); **Mp:** 233-235 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm):** 1.78 - 1.85 (m, 4 H), 2.15 (s, 3 H), 3.05 - 3.11 (m, 4 H), 3.68 (s, 3 H), 4.58 (s, 1 H), 6.75 - 6.78 (m, 1 H), 7.01 - 7.06 (m, 1 H), 7.26 - 7.33 (m, 5 H), 7.95 (dd, *J* = 8.6, 1.0 Hz, 2 H); **¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm):** 13.56, 24.08, 34.46, 45.40,

55.41, 102.77, 113.54, 119.47, 123.25, 128.68, 139.34, 141.34, 146.23, 157.31, 157.71. **ESIMS:** m/z 364 (M+H)⁺. **IR (KBr):** 3396, 2922, 2422, 1596, 1500, 1386, 1245, 1031, 769, 691 cm⁻¹; **Elemental analysis** calculated for C₂₂H₂₅N₃O₂: C, 72.70; H, 6.93; N, 11.56%; found: C, 72.72; H, 6.91; N, 11.57%; **HRMS (ES):** calculated for [M+H] 364.2025; found: 364.2010; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); t₁ = 10.49 min, t₂ = 12.32 min.

3-Methyl-1-phenyl-4-(pyridin-4-yl(pyrrolidin-1-yl)methyl)-1H-pyrazol-5-ol (11n)

Physical state: Pale purple solid; **Yield:** 86% (287.6 mg); **Mp:** 208-210 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm):** 1.78 - 1.84 (m, 4 H), 2.18 (s, 3 H), 3.04 - 3.11 (m, 4 H), 4.63 (s, 1 H), 7.04 - 7.08 (m, 1 H), 7.30 - 7.36 (m, 4 H), 7.95 (dd, *J* = 8.6, 1.0 Hz, 3 H), 8.39 (d, *J* = 5.8 Hz, 1 H); **¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm):** 13.49, 24.07, 34.88, 45.40, 101.27, 119.57, 123.35, 123.48, 128.74, 141.18, 146.25, 149.49, 155.59, 157.83. **ESIMS:** m/z 335 (M+H)⁺. **IR (KBr):** 3411, 3019, 1654, 1384, 1215, 1084, 769, 669 cm⁻¹; **Elemental analysis** calculated for C₂₀H₂₂N₄O: C, 71.83; H, 6.63; N, 16.75%; found: C, 71.84; H, 6.64; N, 16.74%; **HRMS (ES):** calculated for [M+H] 335.1872; found: 335.1855; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); t₁ = 9.49 min, t₂ = 10.91 min.

4-((4-Fluorophenyl)(morpholino)methyl)-3-methyl-1-phenyl-1H-pyrazol-5-ol (11o)

Physical state: Yellowish brown solid; **Yield:** 87% (319.6 mg); **Mp:** 186-188 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm):** 2.22 (s, 3 H), 3.08 (t, *J* = 4.8 Hz, 4 H), 3.75 (t, *J* = 4.8 Hz, 4 H), 4.73 (s, 1 H), 7.02 - 7.13 (m, 3 H), 7.33 - 7.42 (m, 4 H), 7.93 (d, *J* = 8.0 Hz, 2 H); **¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm):** 13.24, 34.30, 43.41, 63.81, 103.05, 114.65, 114.86, 119.86, 123.94, 128.86, 129.43, 129.50, 140.58, 142.32, 146.33, 157.71, 159.56, 161.95. **ESIMS:** m/z 368 (M+H)⁺. **IR (KBr):** 3422, 3062, 2921, 1490, 1381, 1212, 1162, 750 cm⁻¹; **Elemental analysis** calculated for C₂₁H₂₂FN₃O₂: C, 68.65; H, 6.04; N, 11.44%; found: C, 68.66; H, 6.03; N, 11.42%; **HRMS (ES):** calculated for [M+H] 368.1774; found: 368.1789; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); t₁ = 12.35 min, t₂ = 14.22 min.

4-((Dimethylamino)(4-methoxyphenyl)methyl)-3-methyl-1-phenyl-1H-pyrazol-5-ol (11p)

Physical state: Red solid; **Yield:** 83% (280.0 mg); **Mp:** 123-125 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm):** 2.17 (s, 3 H), 2.30 (s, 6 H), 3.87 (s, 3 H), 5.13 (s, 1 H), 7.10 (d, *J* = 8.9 Hz, 2 H), 7.17 (t, *J* = 7.3 Hz, 1 H), 7.39 – 7.45 (m, 2 H), 7.71 (s, 1 H), 7.92 (dd, *J* = 8.6 Hz, 1.0 Hz, 1 H), 8.68 (d, *J* = 8.9 Hz, 2 H); **¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm):** 13.56, 41.69, 56.15, 101.26, 114.77, 118.77, 124.22, 124.86, 126.64, 129.24, 137.29, 138.85, 148.46, 152.22, 162.30, 164.07. **ESIMS:** *m/z* 338 (M+H)⁺. **IR (KBr):** 3411, 3015, 1589, 1557, 1501, 1432, 1378, 1318, 1264, 1219, 1176, 1147, 763 cm⁻¹; **Elemental analysis** calculated for C₂₀H₂₃N₃O₂: C, 71.19; H, 6.87; N, 12.45%; found: C, 71.21; H, 6.88; N, 12.44%; **HRMS (ES):** calculated for [M+H] 338.1868; found: 338.1889; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); t₁ = 10.28 min, t₂ = 12.11 min.

4-((Dibutylamino)(phenyl)methyl)-3-methyl-1-phenyl-1H-pyrazol-5-ol (11q)

Physical state: Pale white solid; **Yield:** 82% (321.0 mg); **Mp:** 141-143 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm):** 0.89 (t, *J* = 7.3 Hz, 6 H), 1.31 (dq, *J* = 14.9, 7.4 Hz, 4 H), 1.50 - 1.59 (m, 4 H), 2.17 (s, 3 H), 2.84 (t, *J* = 7.9 Hz, 4 H), 4.64 (s, 1 H), 7.02 - 7.09 (m, 2 H), 7.18 - 7.22 (m, 1 H), 7.29 - 7.34 (m, 3 H), 7.39 (d, *J* = 7.4 Hz, 1 H), 7.95 (dd, *J* = 8.6, 1.0 Hz, 3 H); **¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm):** 13.54, 13.93, 19.74, 28.03, 35.36, 46.98, 102.49, 119.52, 123.33, 125.31, 127.80, 128.12, 128.70, 129.33, 141.26, 146.32, 147.23, 157.75. **ESIMS:** *m/z* 392 (M+H)⁺. **IR (KBr):** 3407, 3016, 2924, 1594, 1392, 1213, 1164, 754 cm⁻¹; **Elemental analysis** calculated for C₂₅H₃₃N₃O: C, 76.69; H, 8.50; N, 10.73%; found: C, 76.71; H, 8.48; N, 10.74%; **HRMS (ES):** calculated for [M+H] 392.2702; found: 392.2707; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); t₁ = 12.47 min, t₂ = 14.37 min.

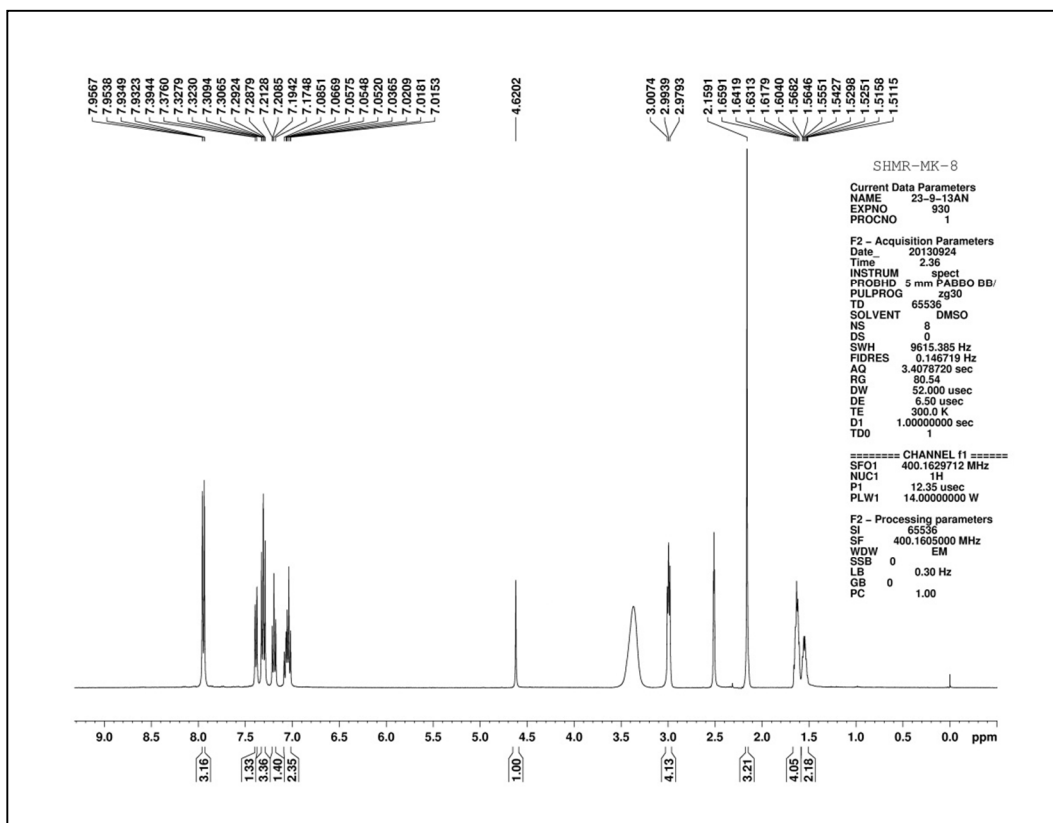
4-((2-Chlorophenyl)(dibutylamino)methyl)-3-methyl-1-phenyl-1H-pyrazol-5-ol (11r)

Physical state: Brown solid; **Yield:** 83% (353.5 mg); **Mp:** 138-140 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm):** 0.89 (t, *J* = 7.3 Hz, 6 H), 1.30 (dq, *J* = 14.9, 7.3 Hz, 4 H), 1.47 - 1.57 (m, 4 H), 2.23 (s, 3 H), 2.82 (t, *J* = 7.8 Hz, 4 H), 5.09 (s, 1 H), 7.06 - 7.16 (m, 2 H), 7.32 - 7.37 (m, 4 H), 7.95 - 7.97 (m, 2 H), 8.16 (dd, *J* = 7.8, 1.2 Hz, 1 H); **¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm):** 13.67, 13.90, 19.70, 28.01, 32.73, 47.05, 102.06, 119.75, 123.66, 127.00, 127.34, 128.77, 129.23, 131.45, 131.60, 140.92, 143.74, 146.16, 158.14. **ESIMS:**

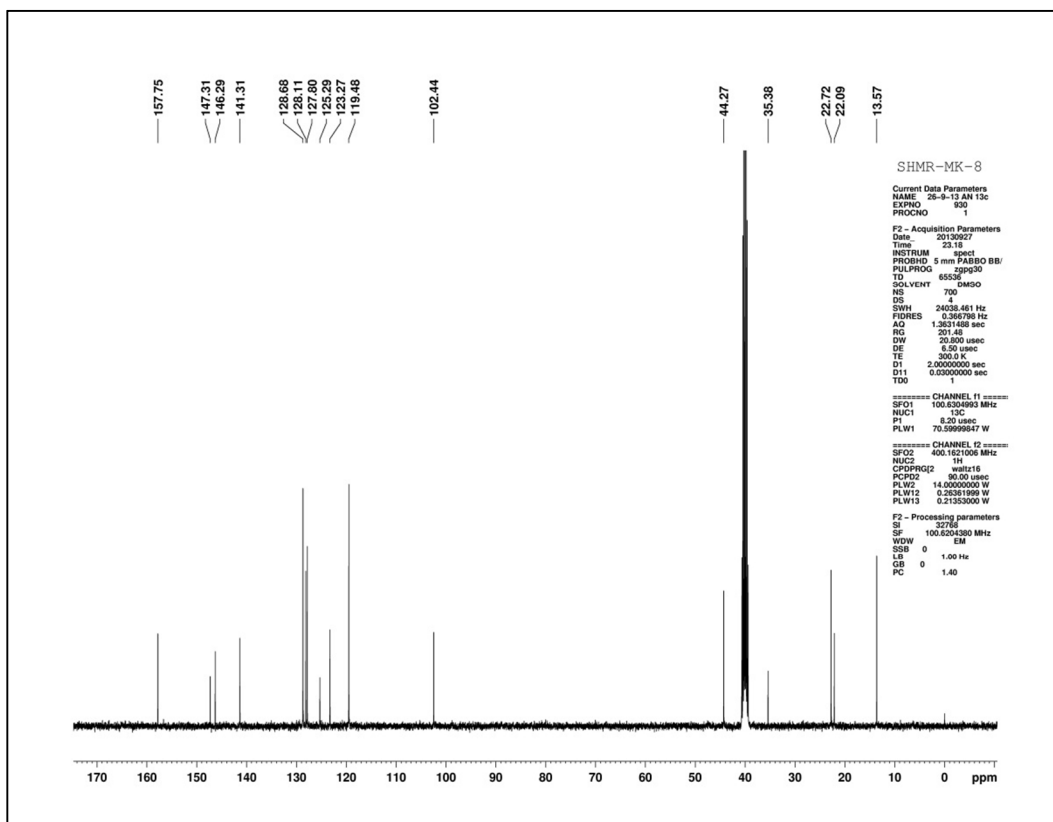
m/z 426 (M+H)⁺. **IR (KBr)**: 3406, 3019, 2963, 1596, 1499, 1384, 1216, 1115, 762, 669 cm⁻¹; **Elemental analysis** calculated for C₂₅H₃₂ClN₃O: C, 70.49; H, 7.57; N, 9.86%; found: C, 70.51; H, 7.54; N, 9.87%; **HRMS (ES)**: calculated for [M+H] 426.2312; found: 426.2333; **HPLC analysis** by using a Chiralpak IA column (hexane/2-propanol = 80/20, flow rate 1.0 ml/min, T = 25°C, 254 nm); t₁ = 12.25 min, t₂ = 14.12 min.

4,4'-(Phenylmethylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (12)

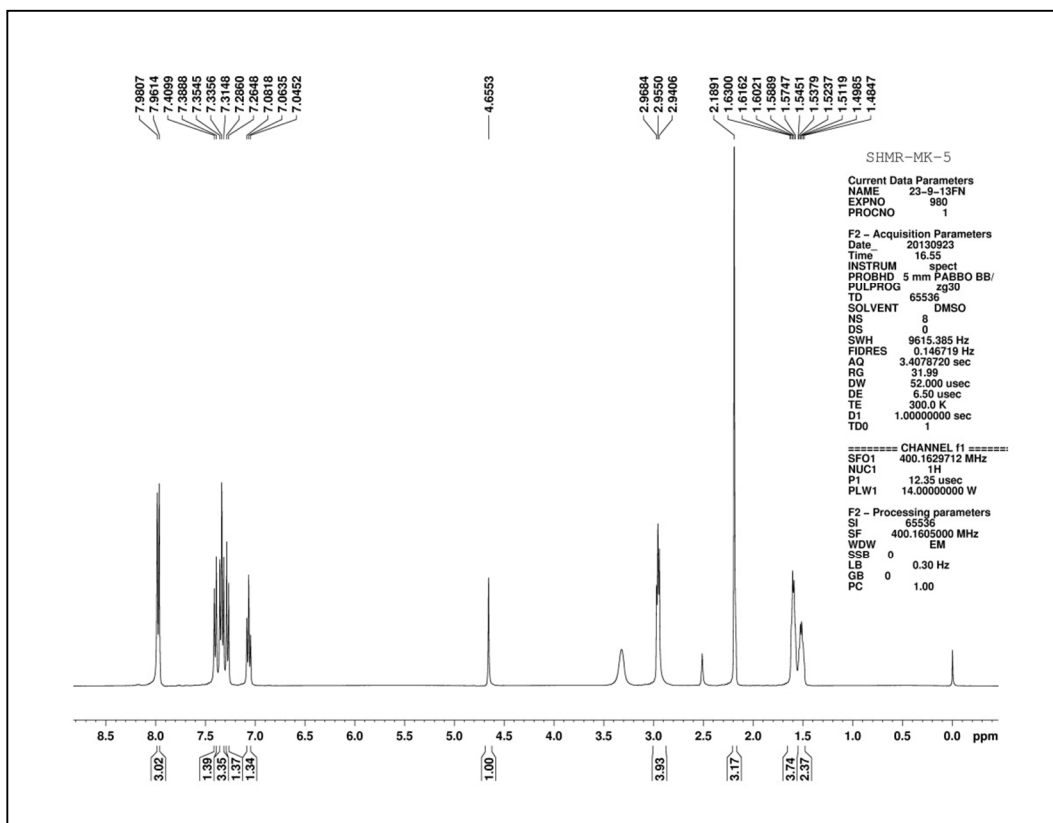
Physical state: White solid; **Mp**: 170-172 °C; **¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm)**: 2.33 (s, 6 H), 4.97 (s, 1 H), 7.18 (dq, *J* = 8.4, 4.1 Hz, 1 H), 7.23 - 7.30 (m, 6 H), 7.45 (t, *J* = 7.8 Hz, 4 H), 7.72 (d, *J* = 7.9 Hz, 4 H), 12.47 (s., 1 H); 14.02 (s., 1 H); **¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm)**: 11.60, 33.14, 120.51, 125.53, 125.86, 127.14, 128.10, 128.88, 137.32, 142.25, 146.27; **ESIMS**: m/z 437 (M+H)⁺. **IR (KBr)**: 3361, 2927, 1625, 1574, 1286, 1189, 1126, 1027, 792 cm⁻¹; **Elemental analysis** calculated for C₂₇H₂₄N₄O₂: C, 74.29; H, 5.54; N, 12.84. Found: C, 74.32; H, 5.56; N, 12.86; **HRMS (ES)**: calculated for [M+H] 437.1967; found: 436.1946.



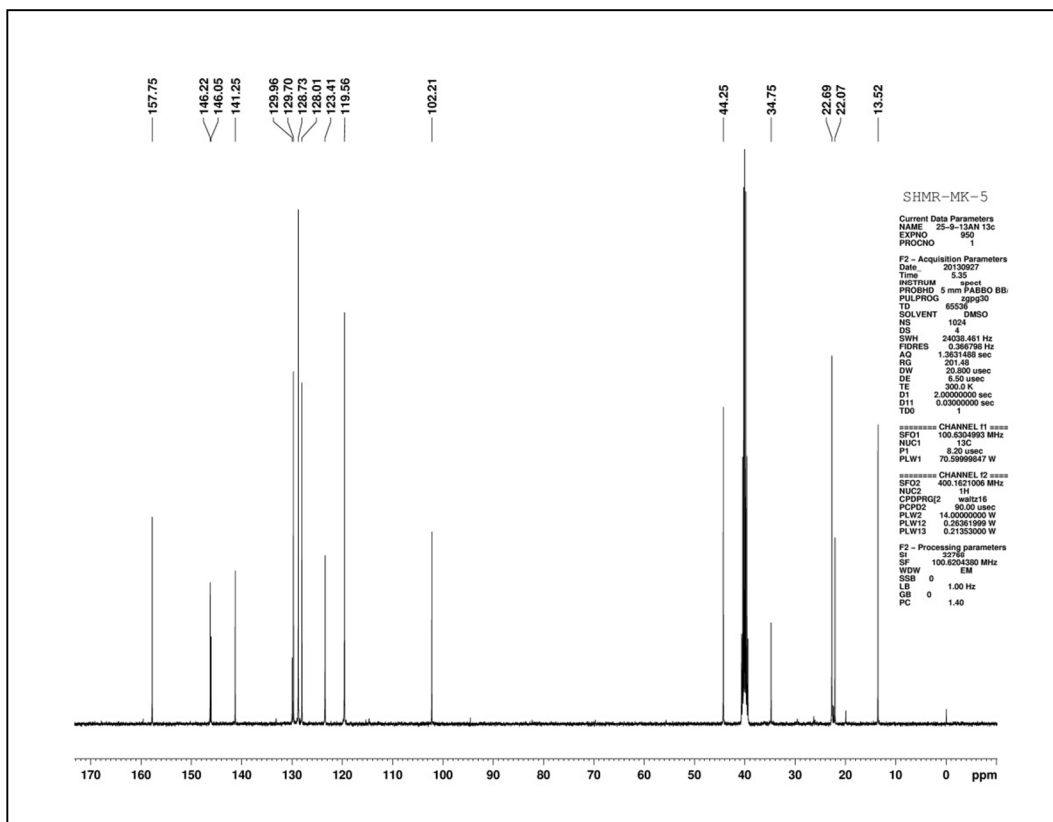
¹H Spectra of 11a



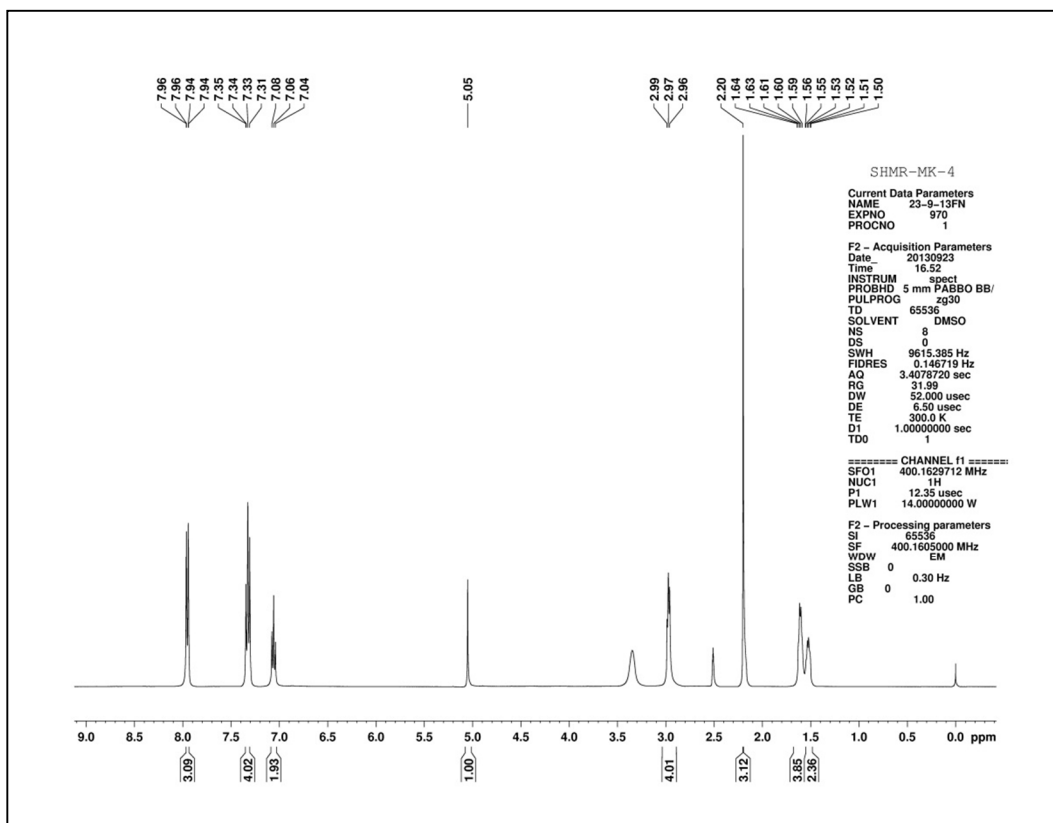
¹³C Spectra of 11a



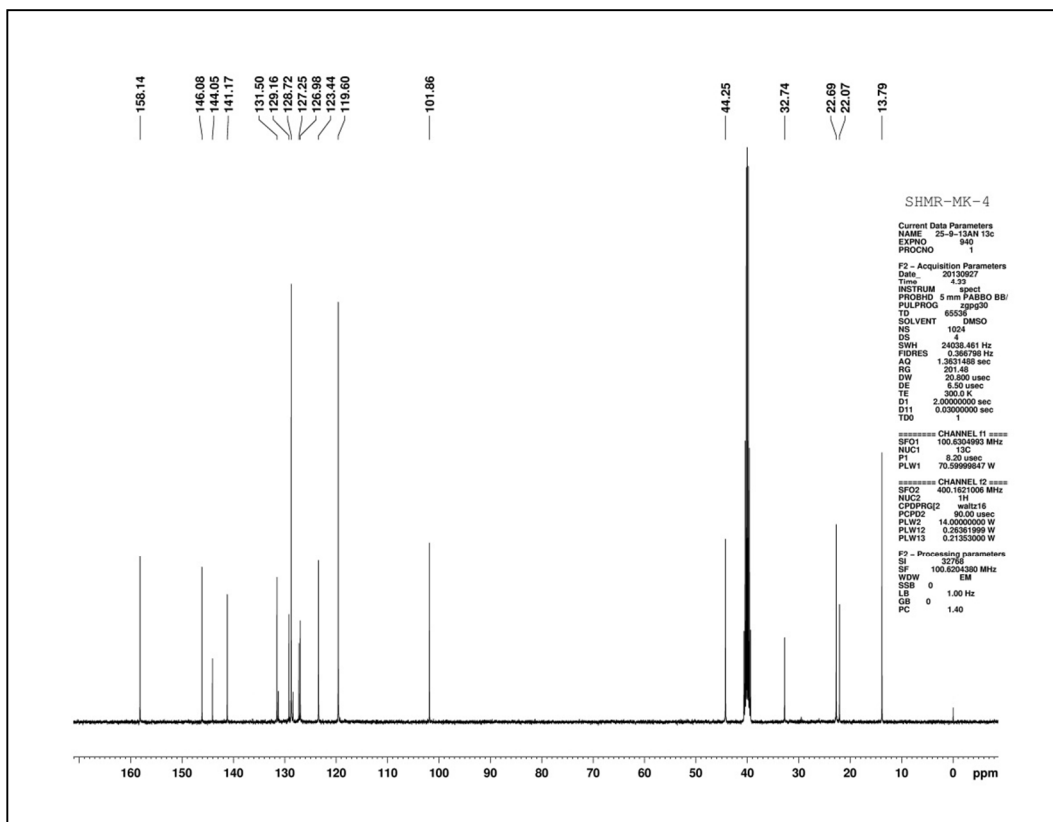
¹H Spectra of 11b



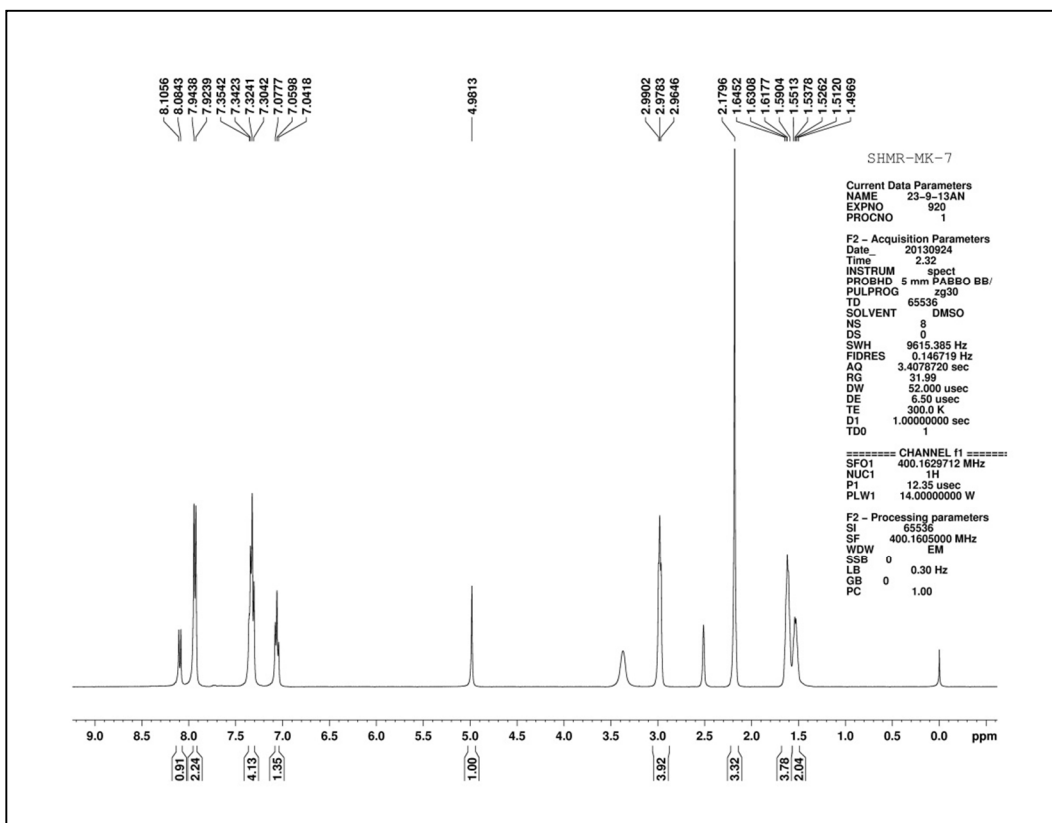
¹³C Spectra of 11b



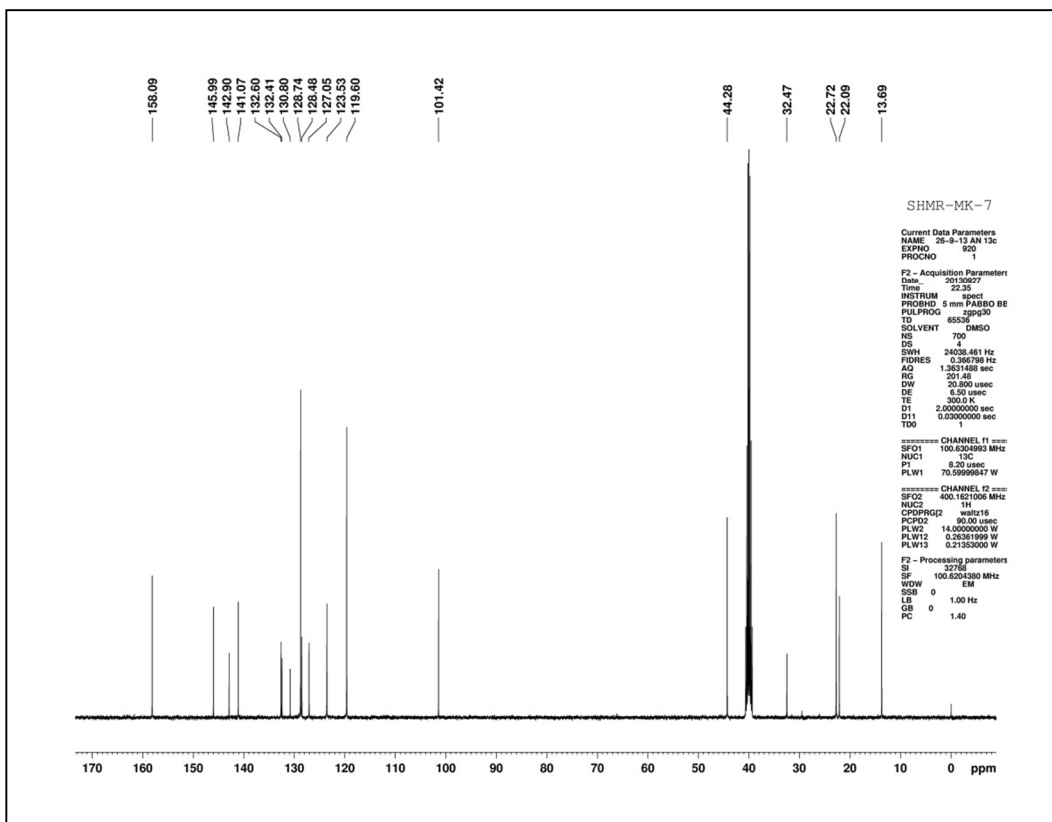
¹H Spectra of 11c



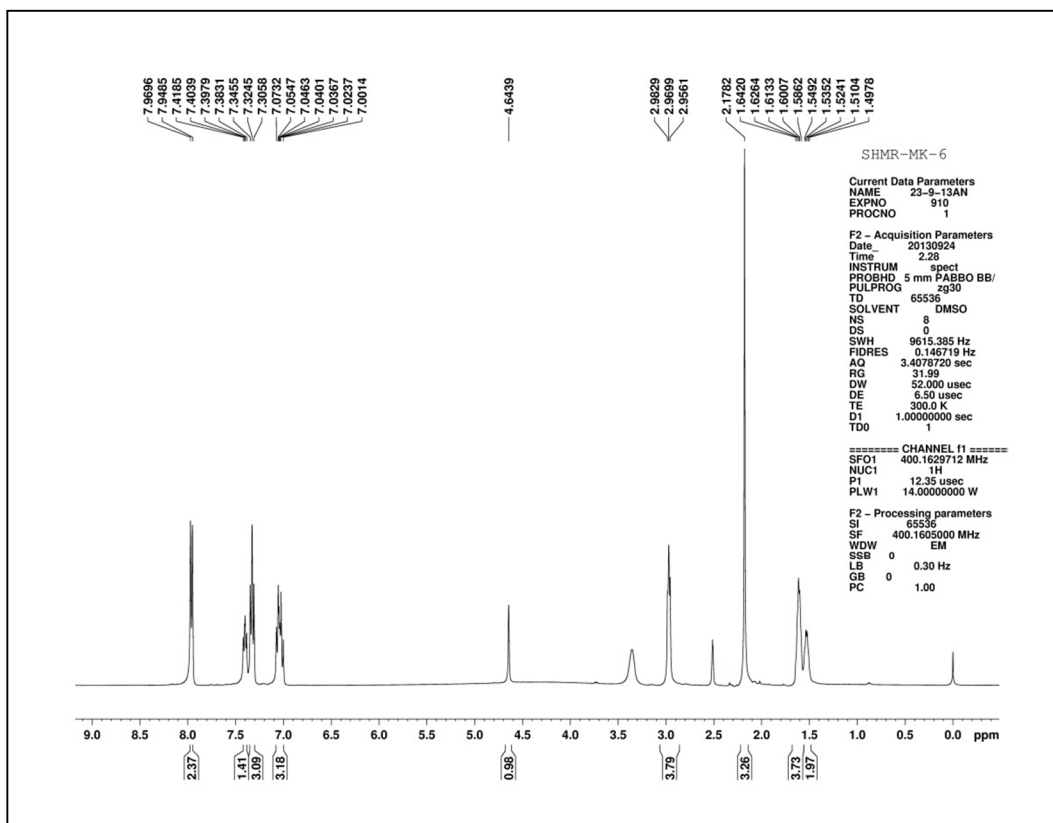
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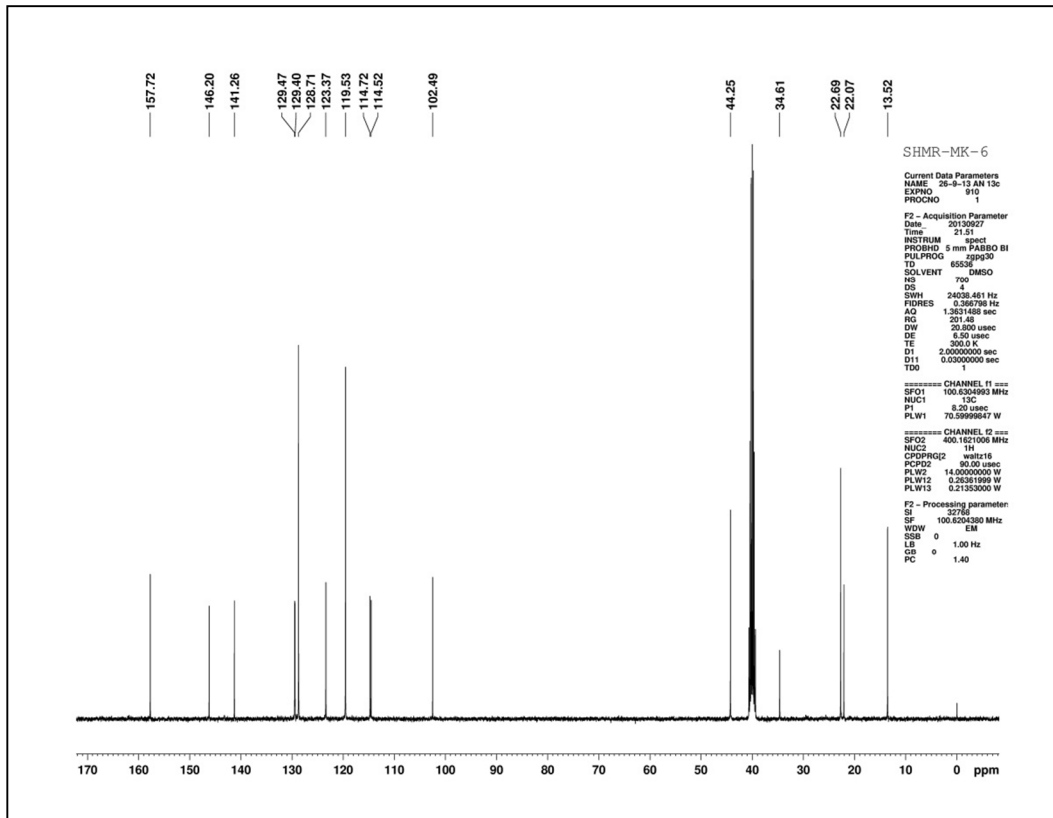
¹H Spectra of 11d



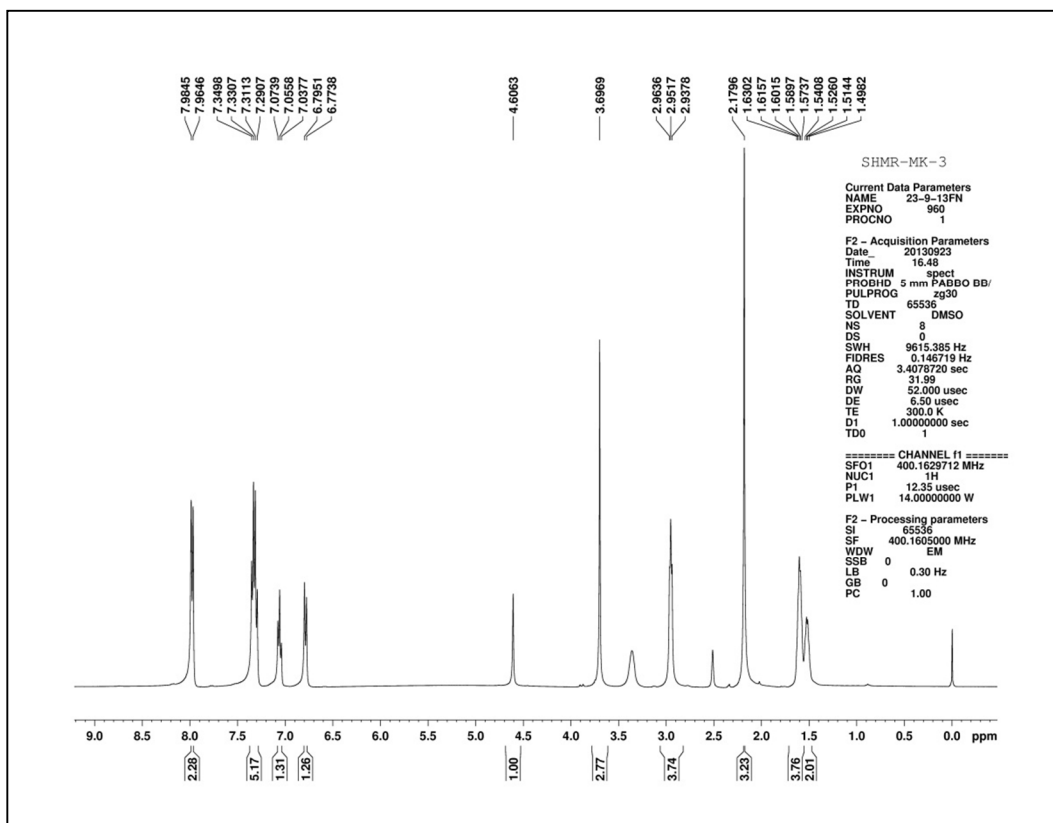
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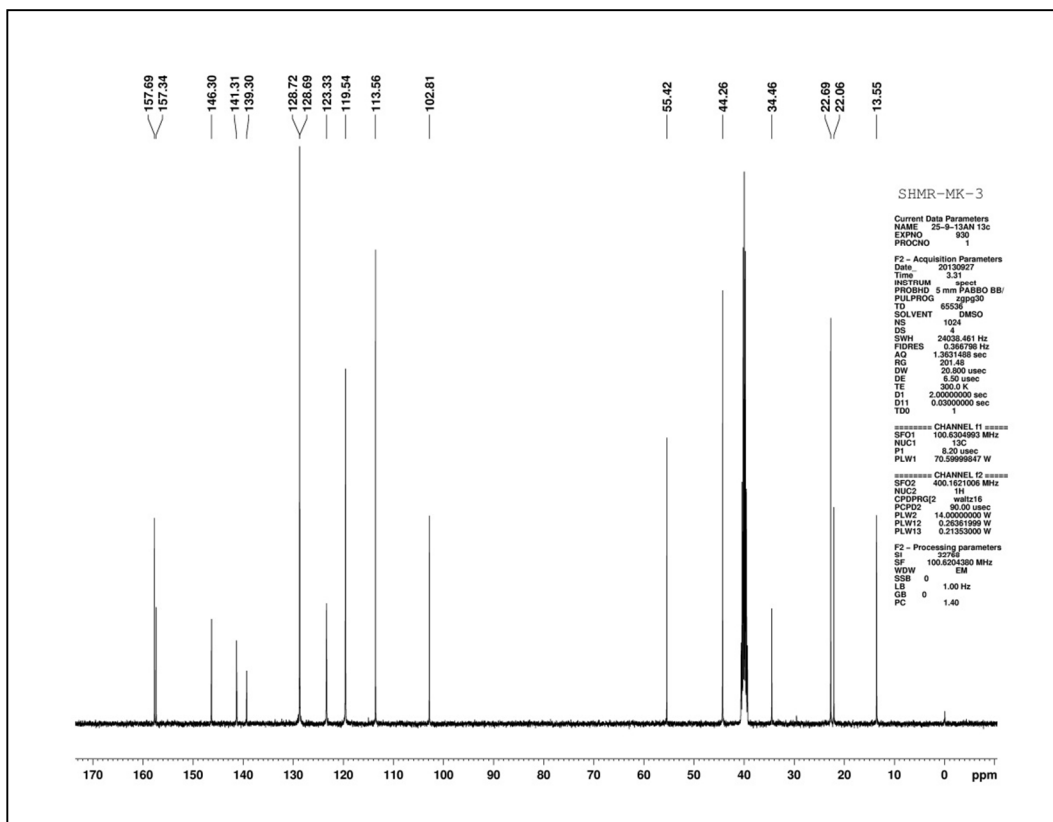
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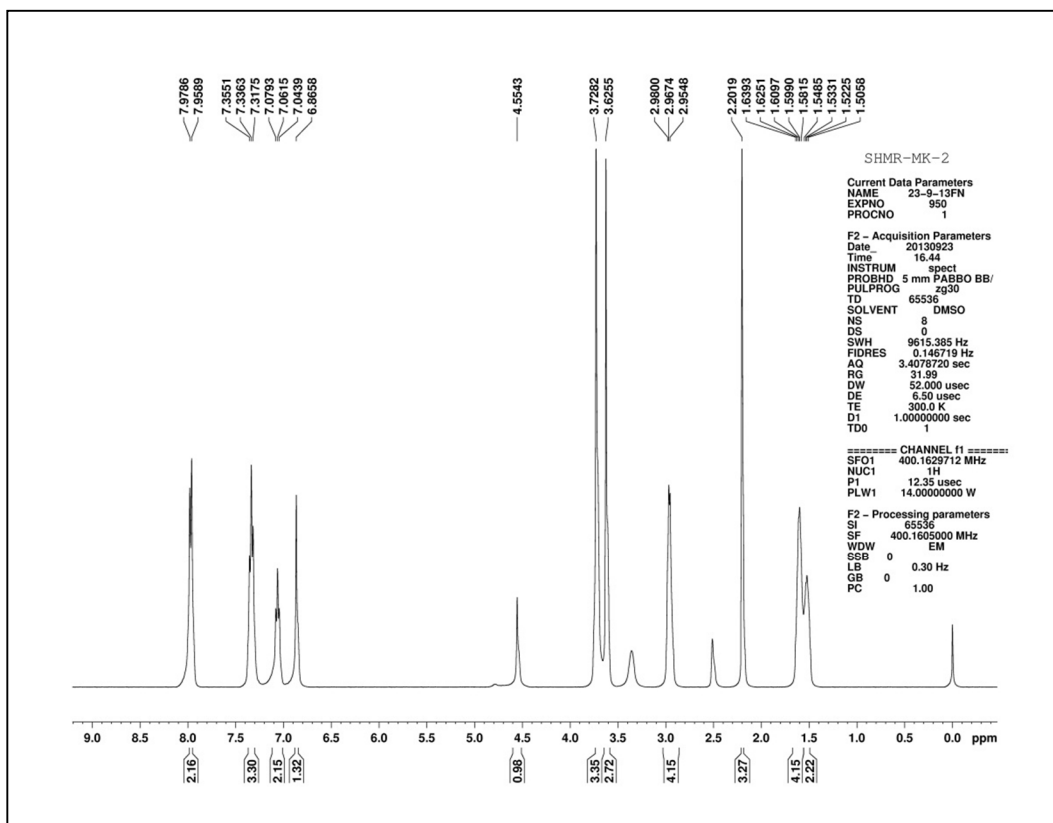
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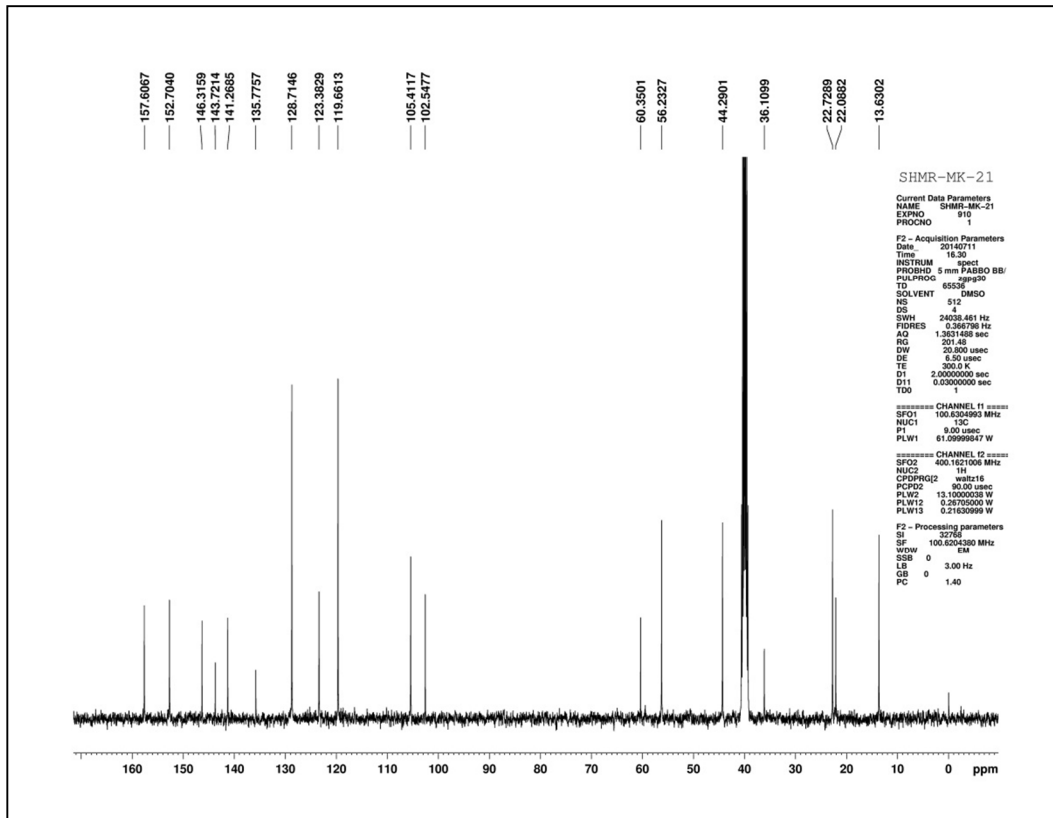
¹H Spectra of 11f



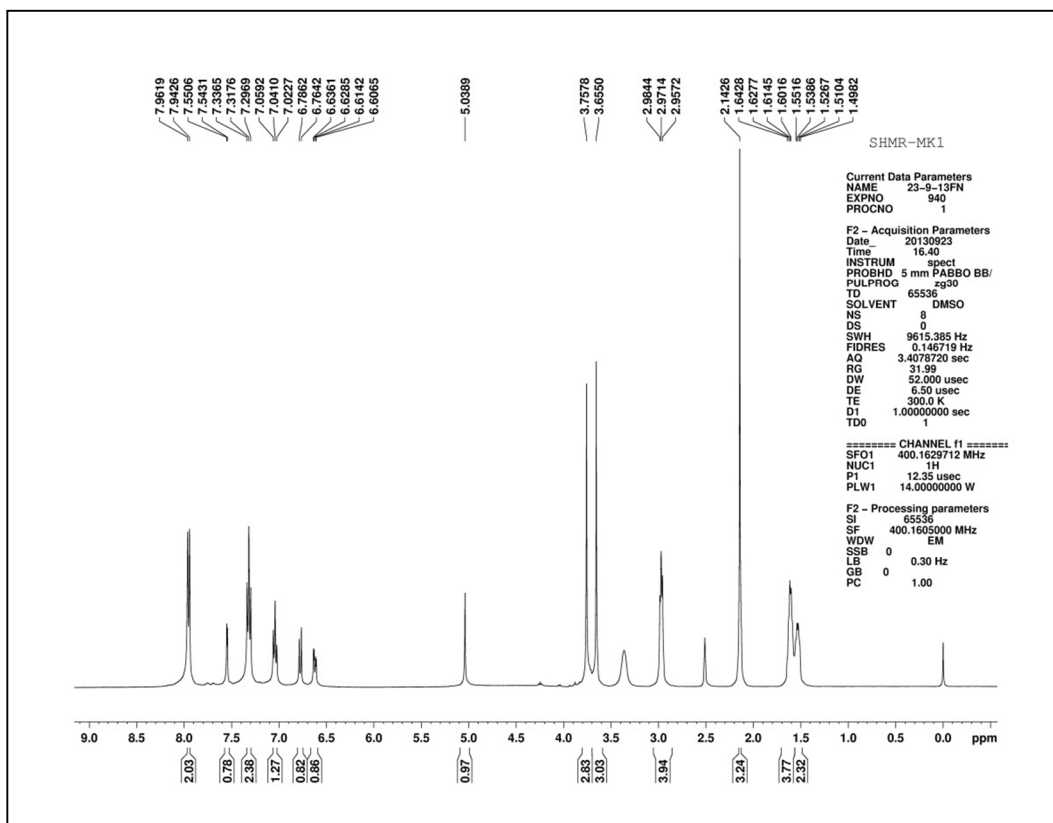
¹³C Spectra of 11f



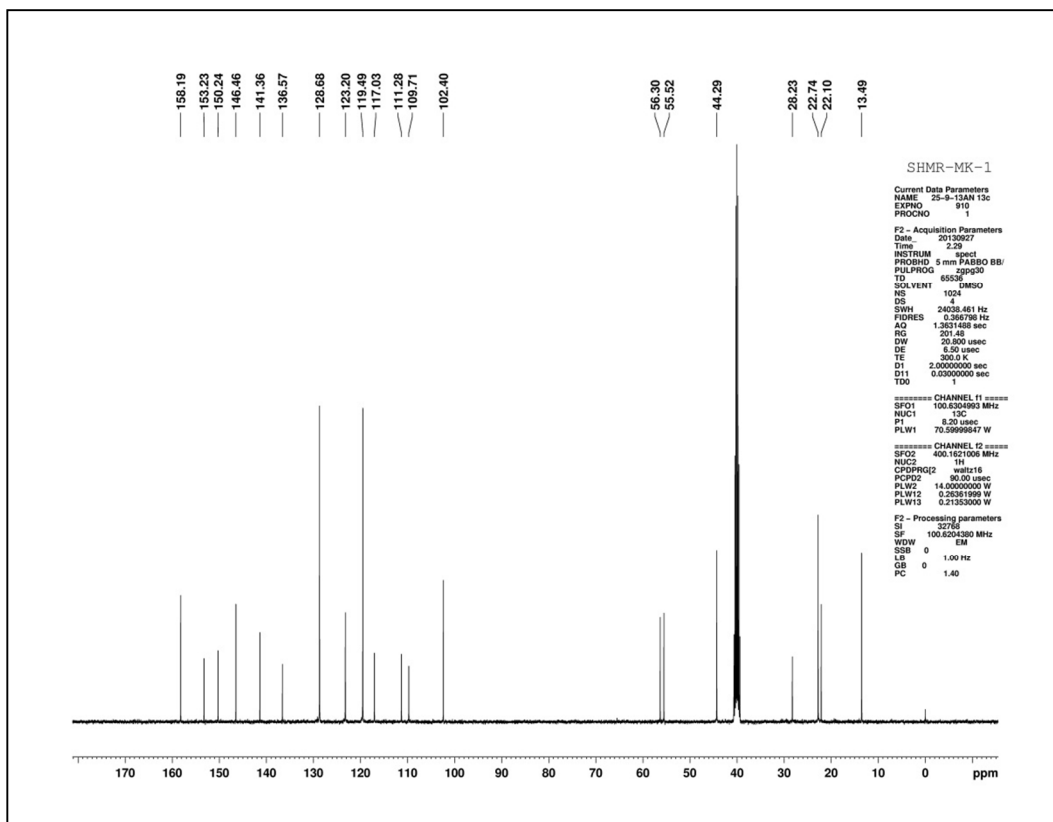
¹H Spectra of 11g



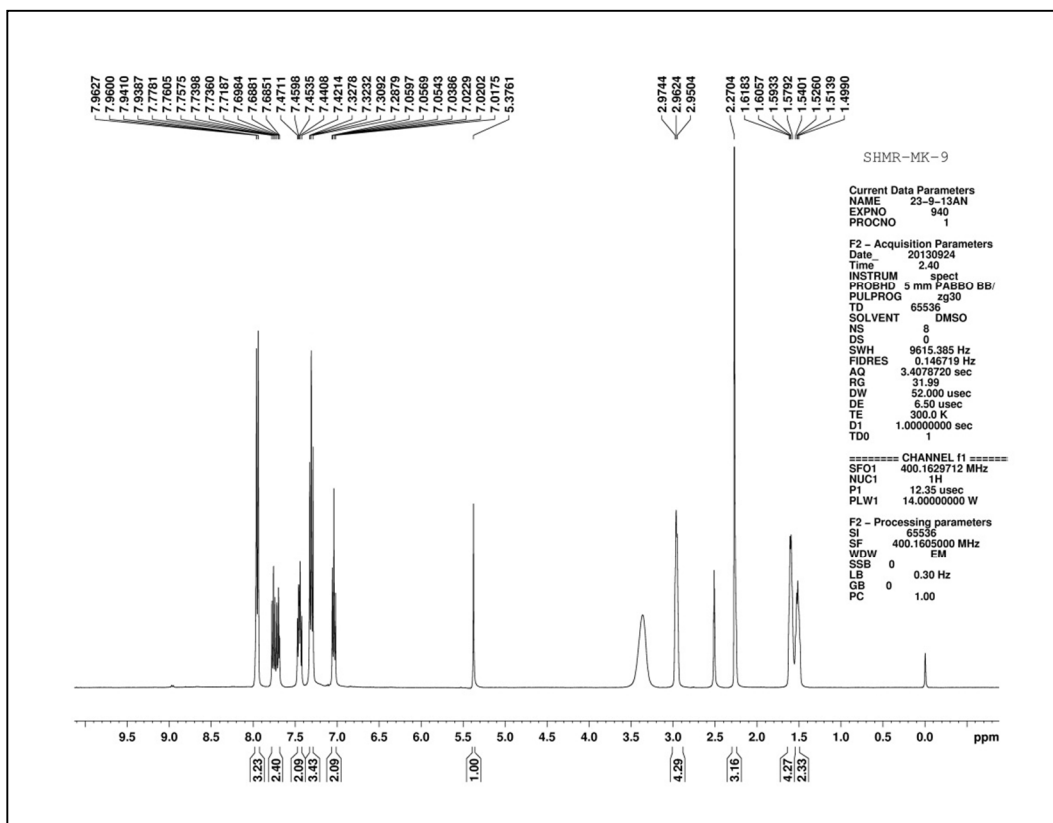
¹³C Spectra of 11g



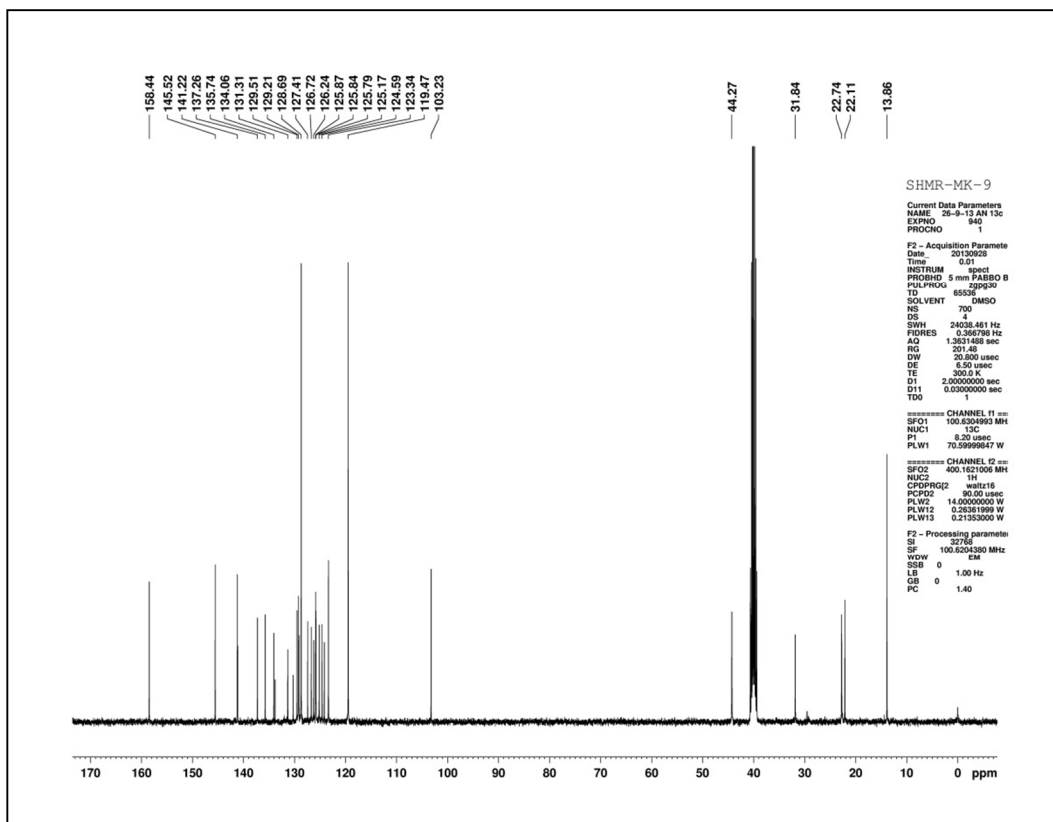
¹H Spectra of 11h



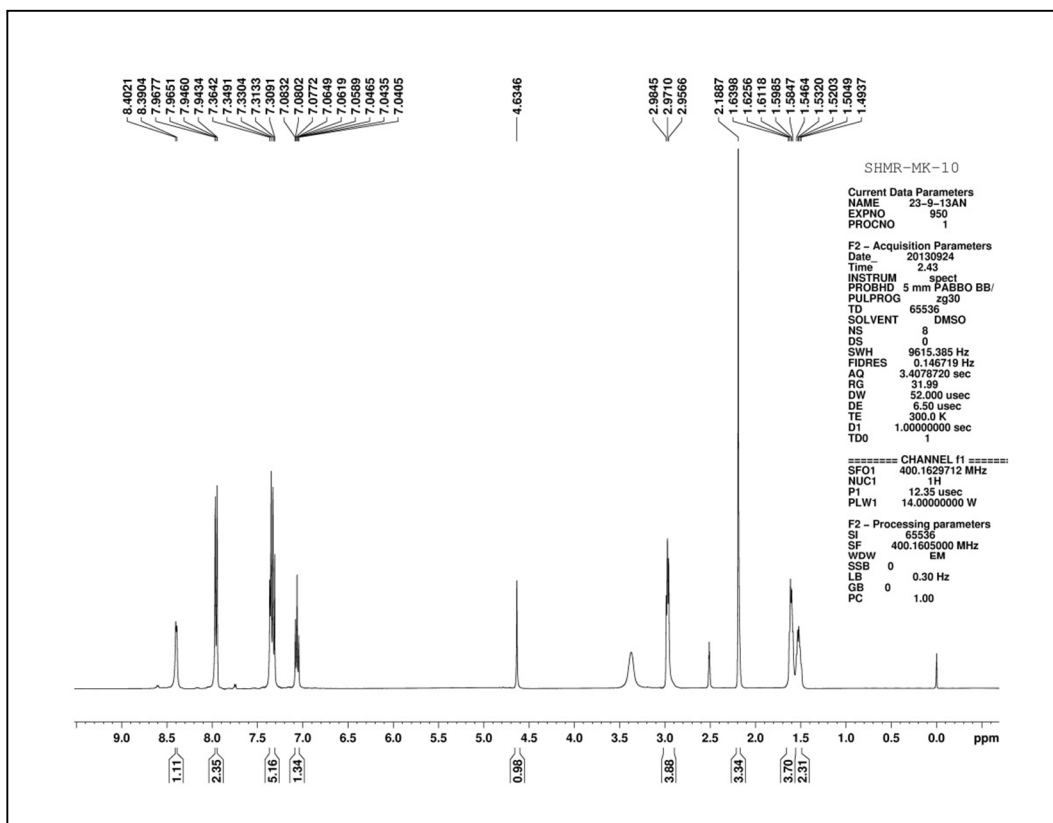
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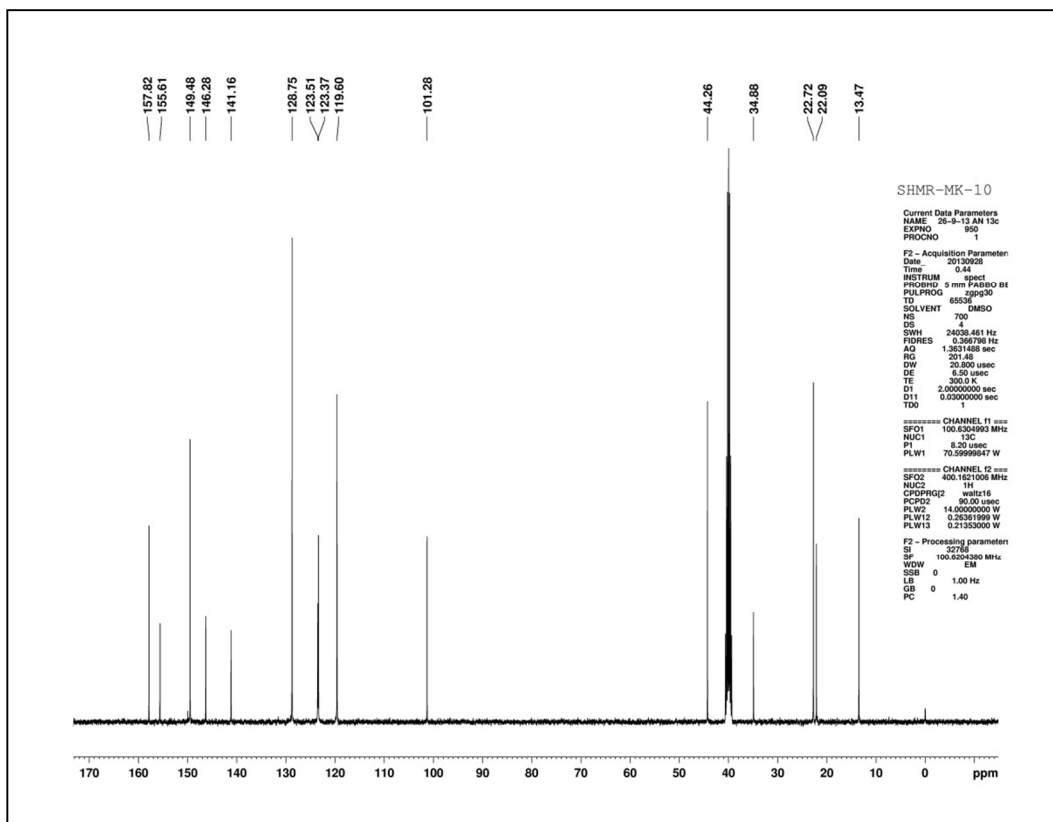
¹H Spectra of 11i



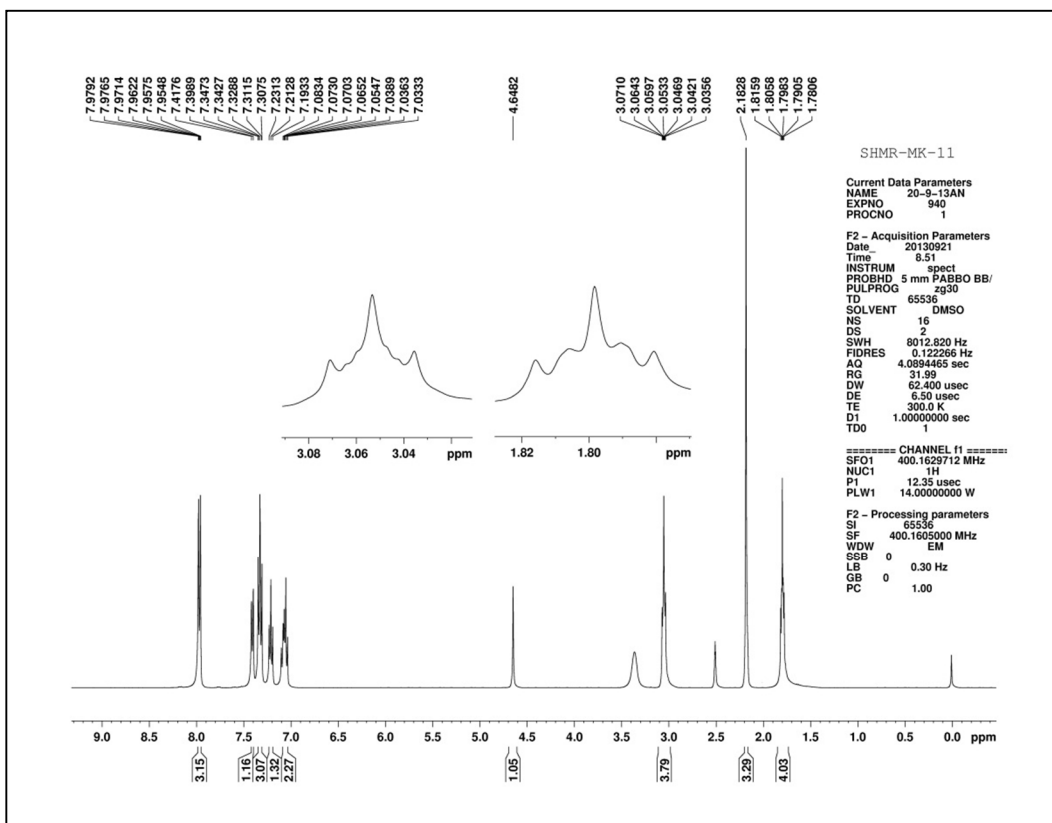
¹³C Spectra of 11i



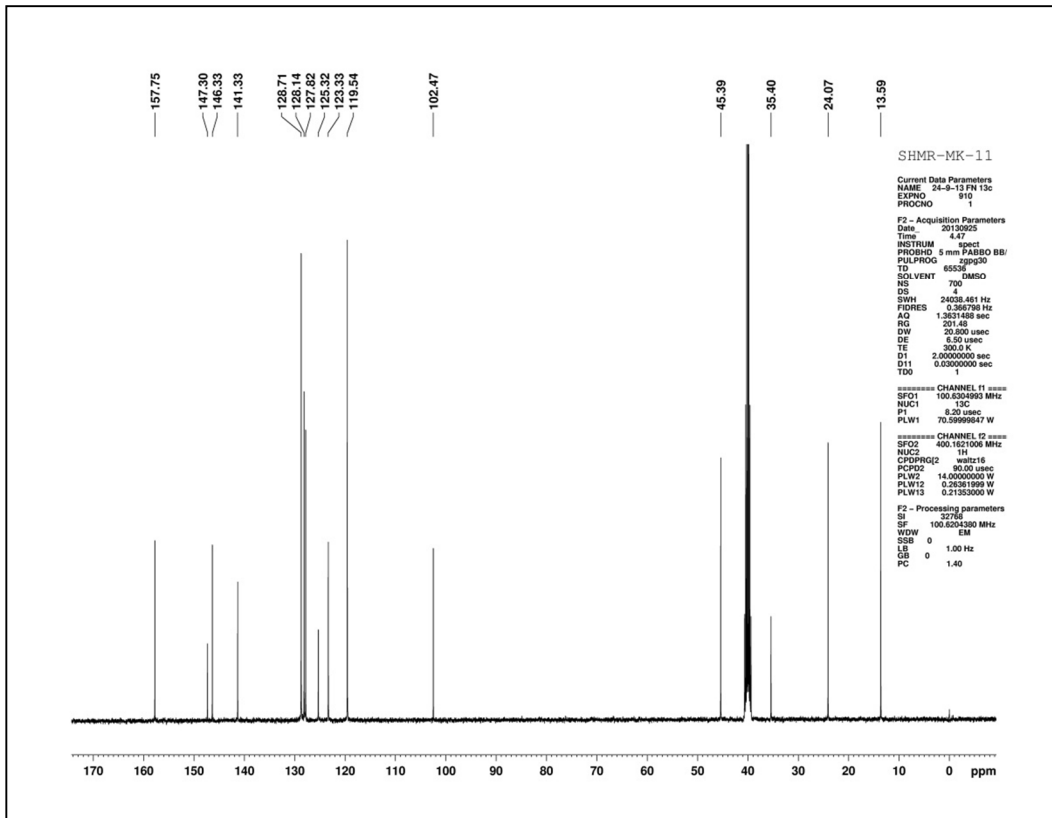
¹H Spectra of 11j



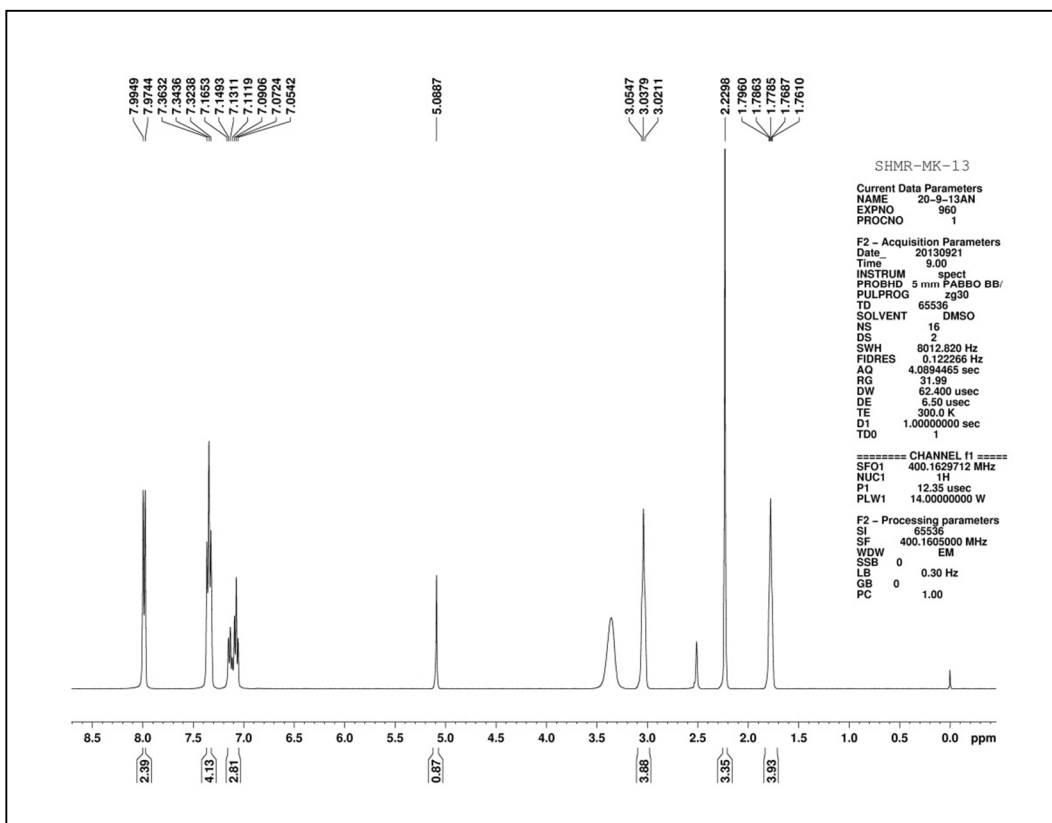
¹³C Spectra of 11j



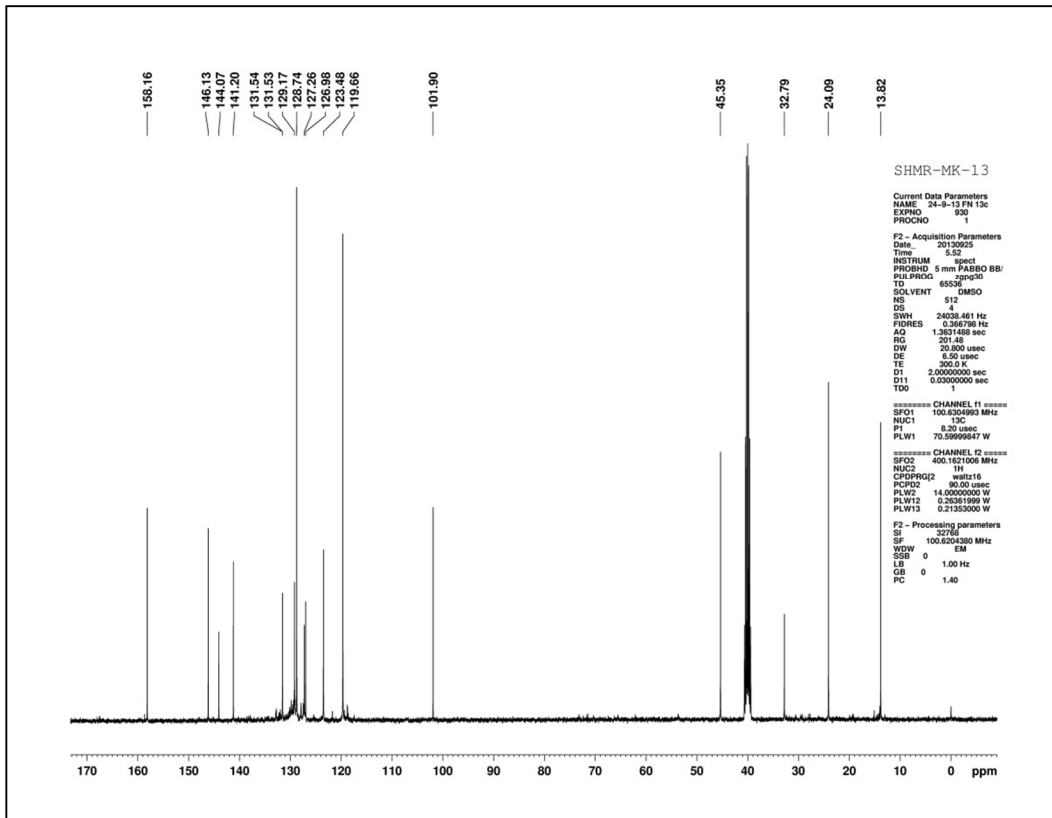
¹H Spectra of 11k



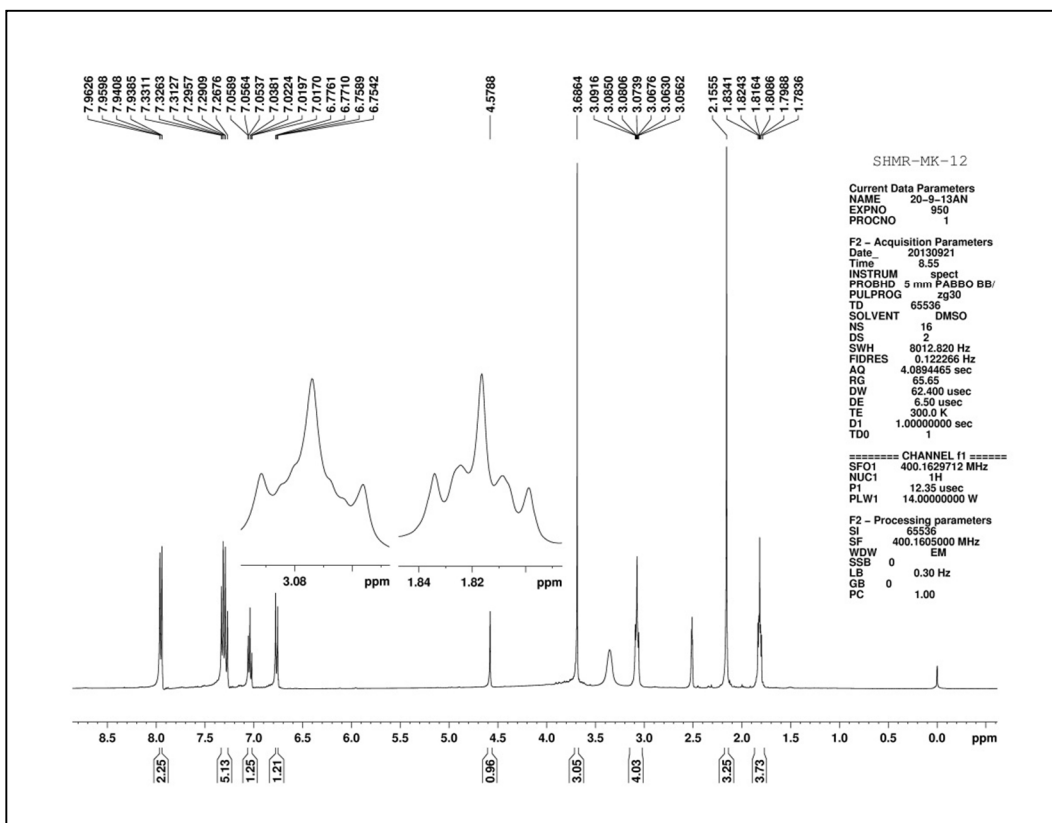
¹³C Spectra of 11k



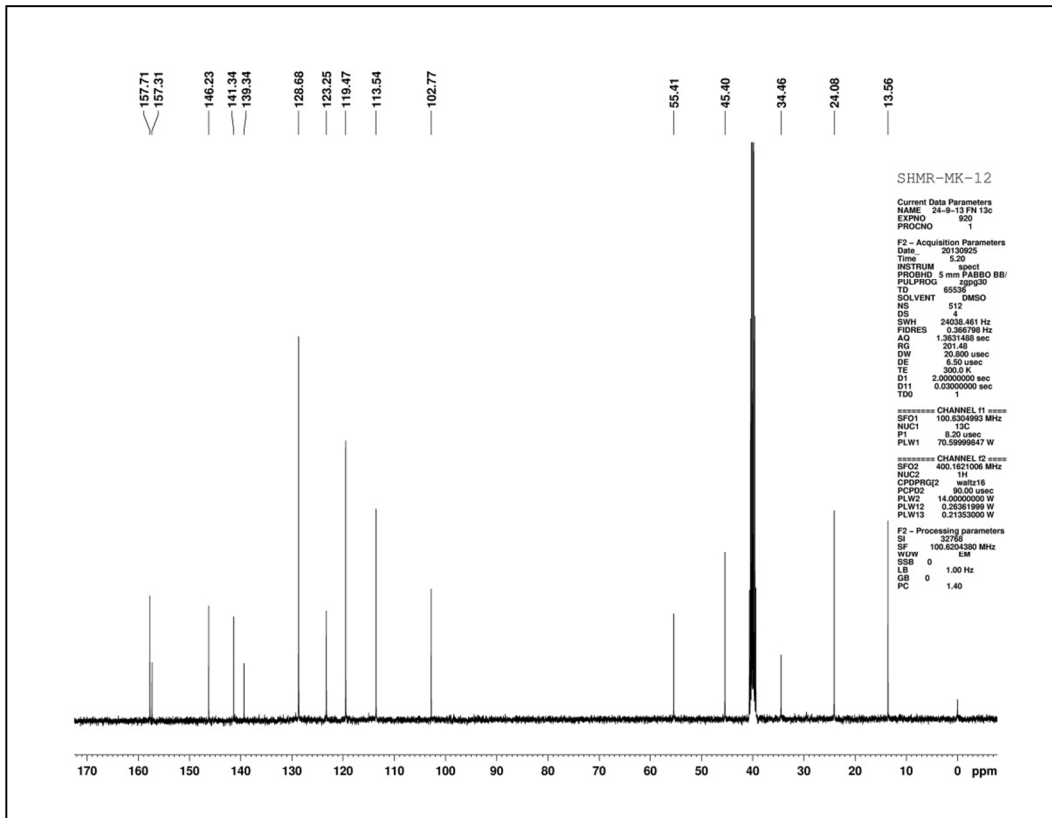
¹H Spectra of 111



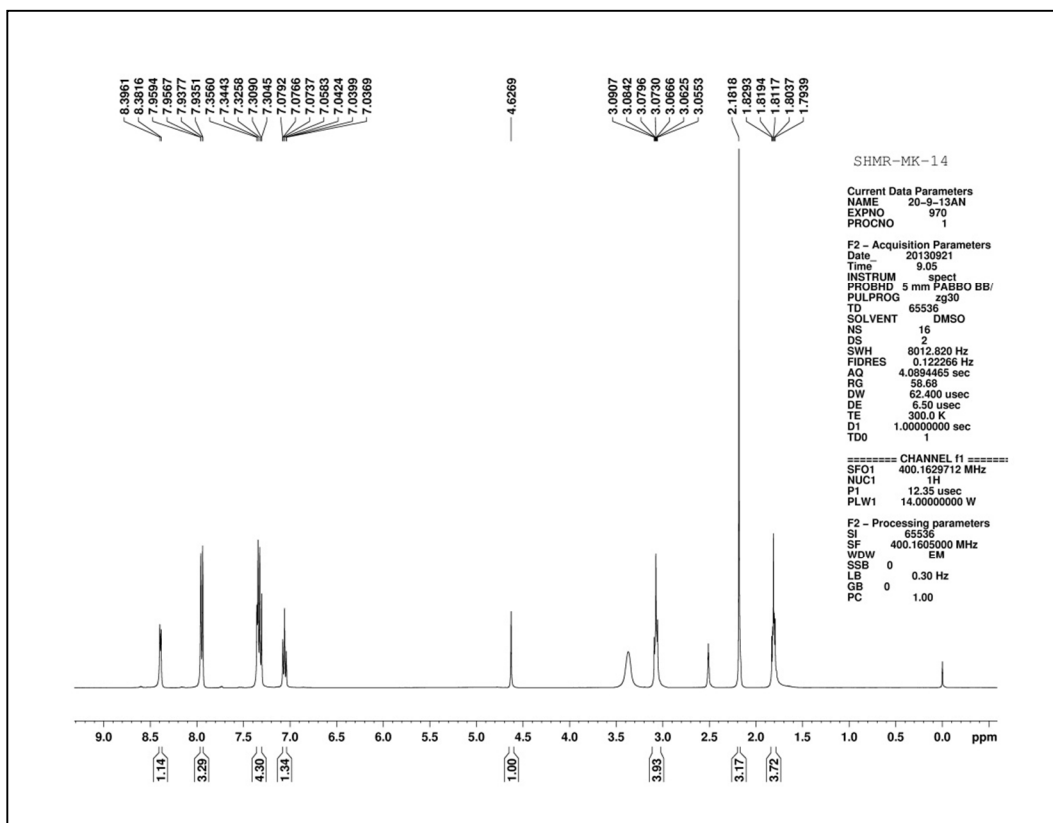
¹³C Spectra of 111



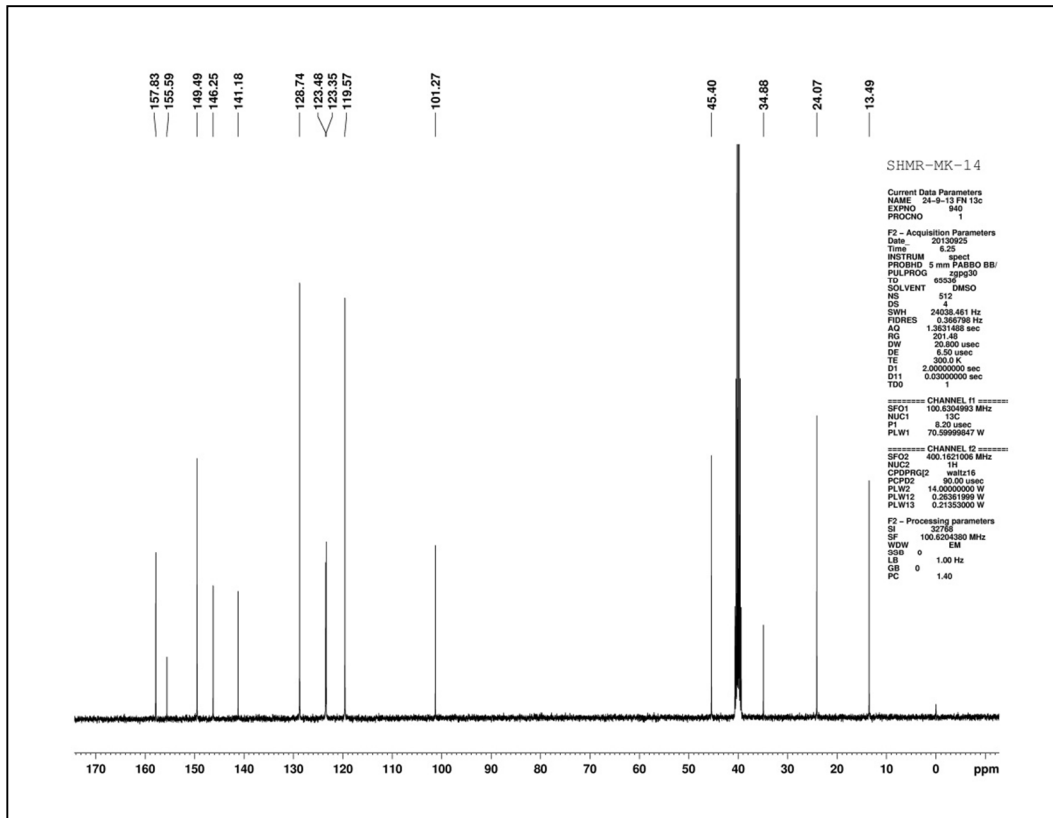
¹H Spectra of 11m



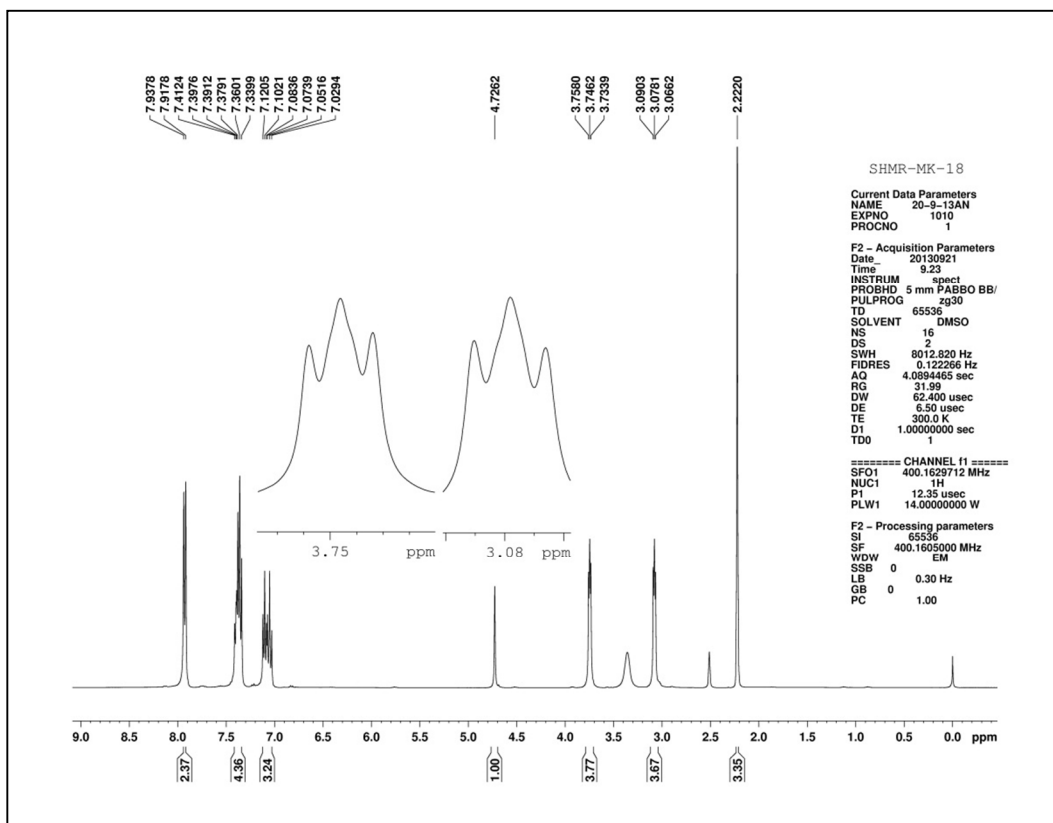
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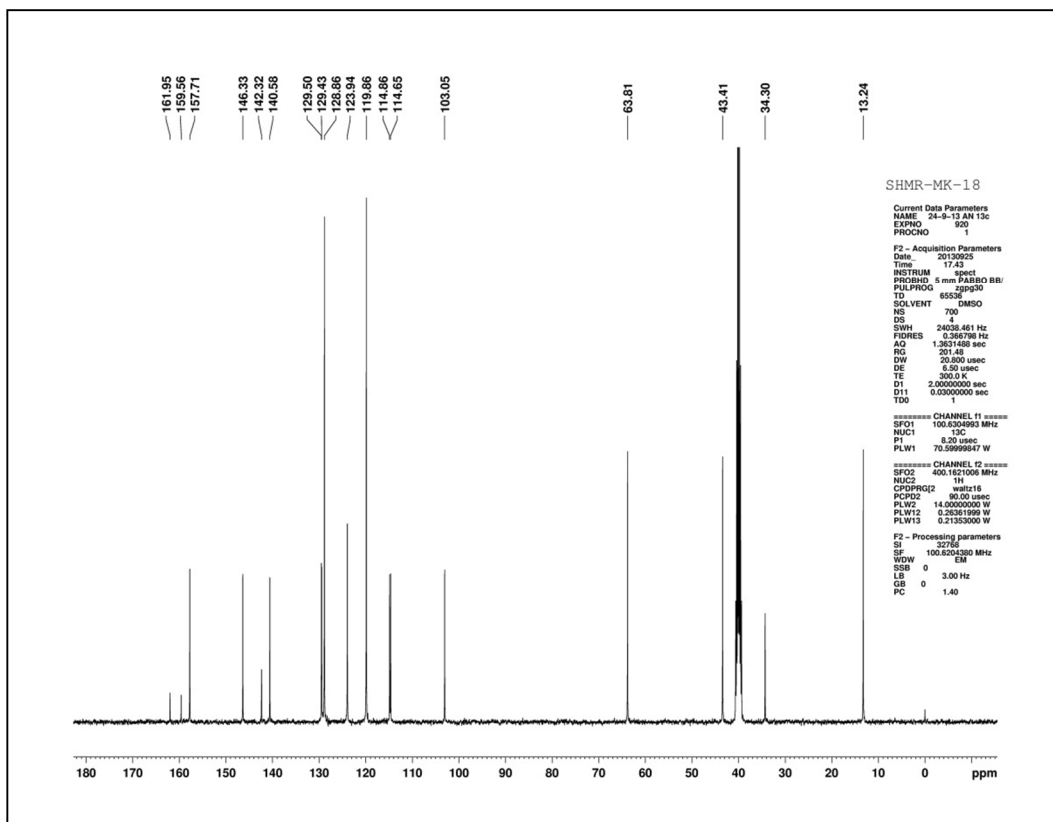
¹H Spectra of 11n



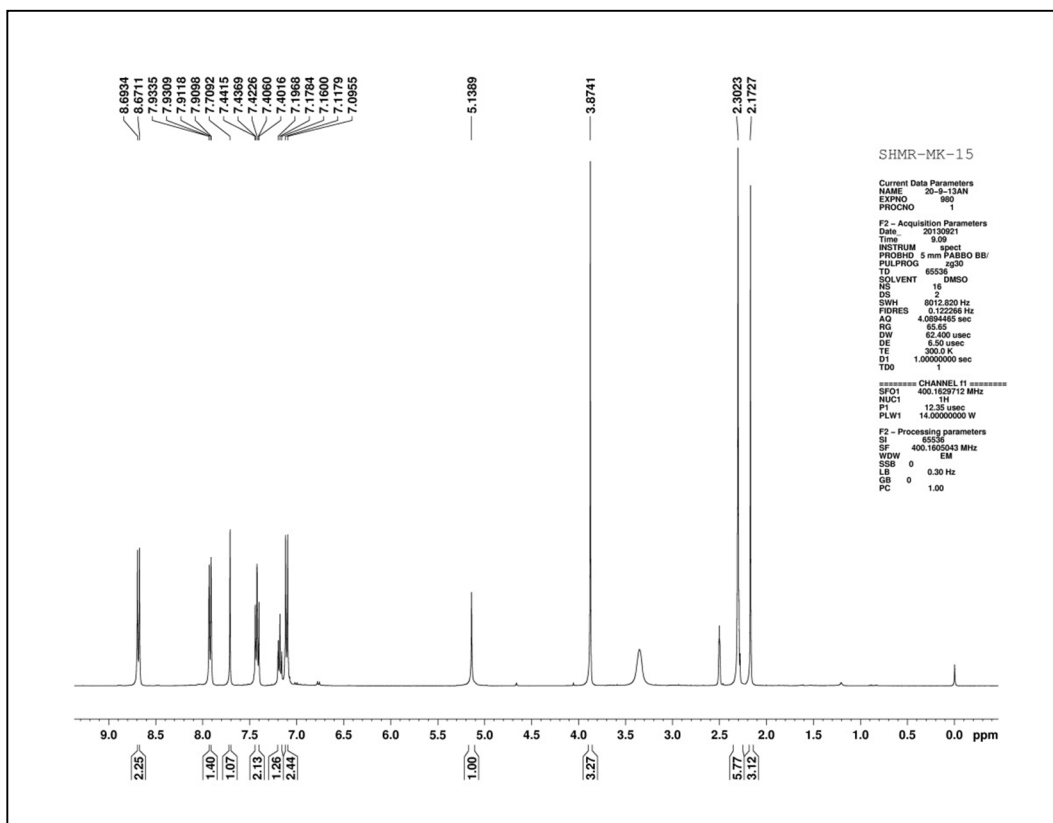
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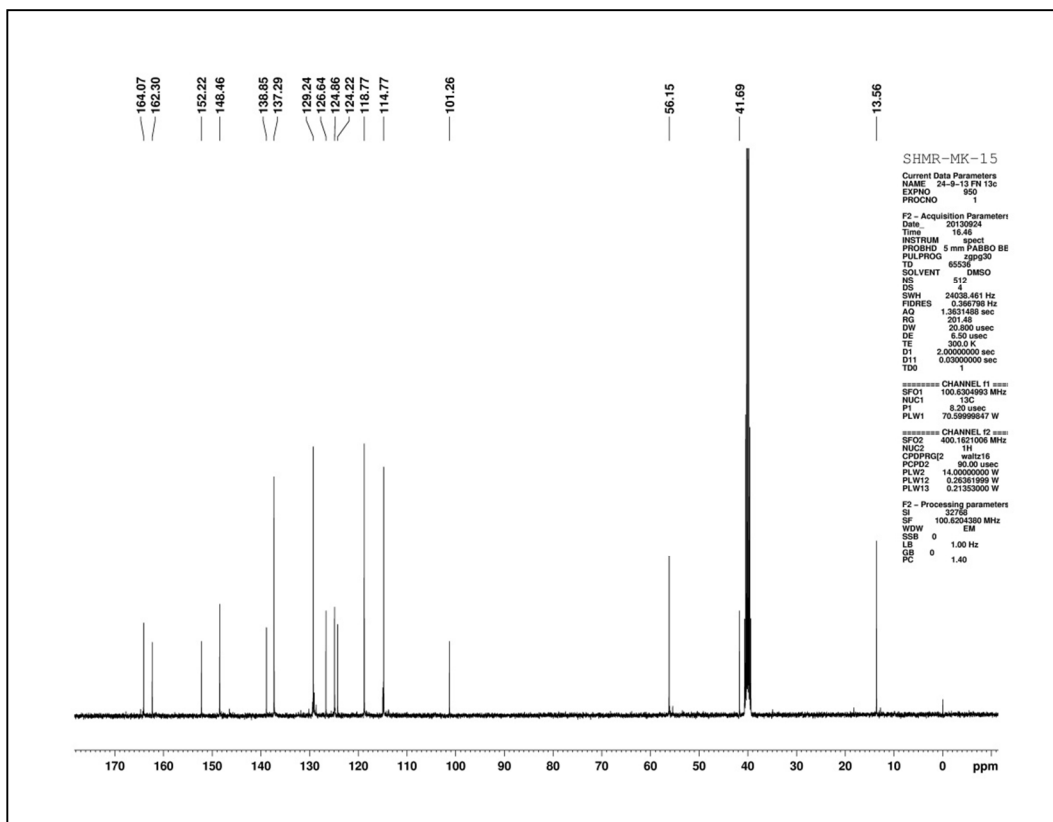
¹H Spectra of 11o



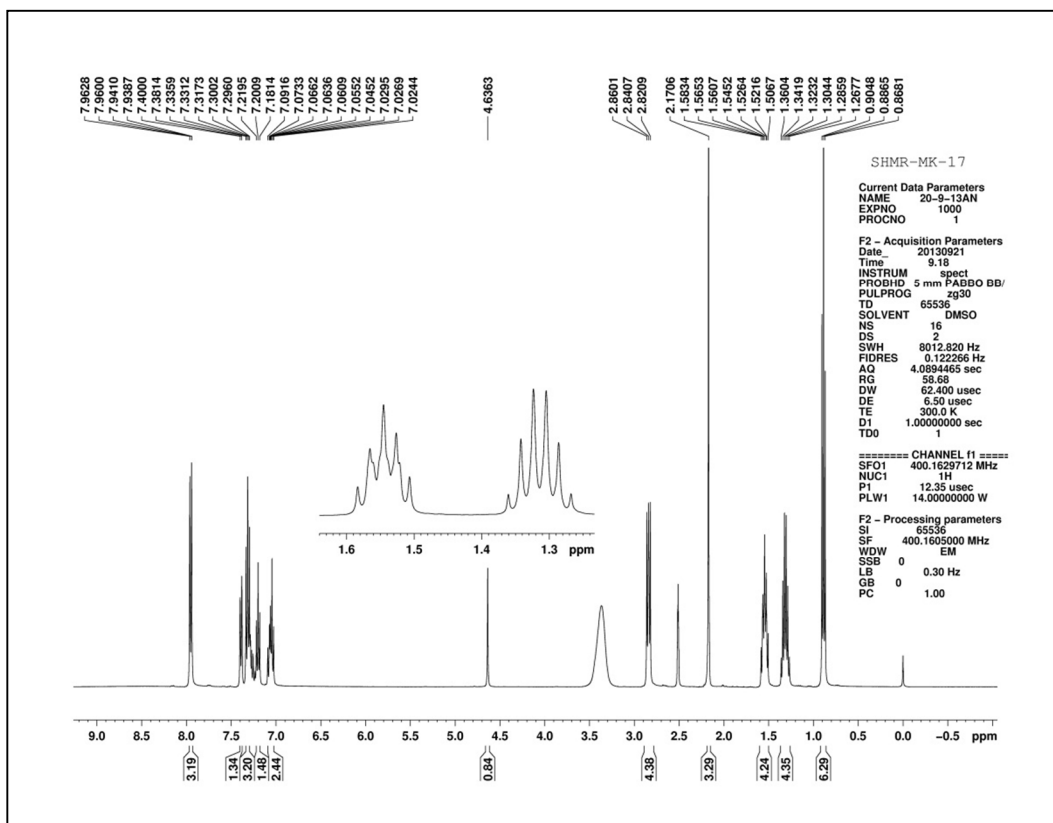
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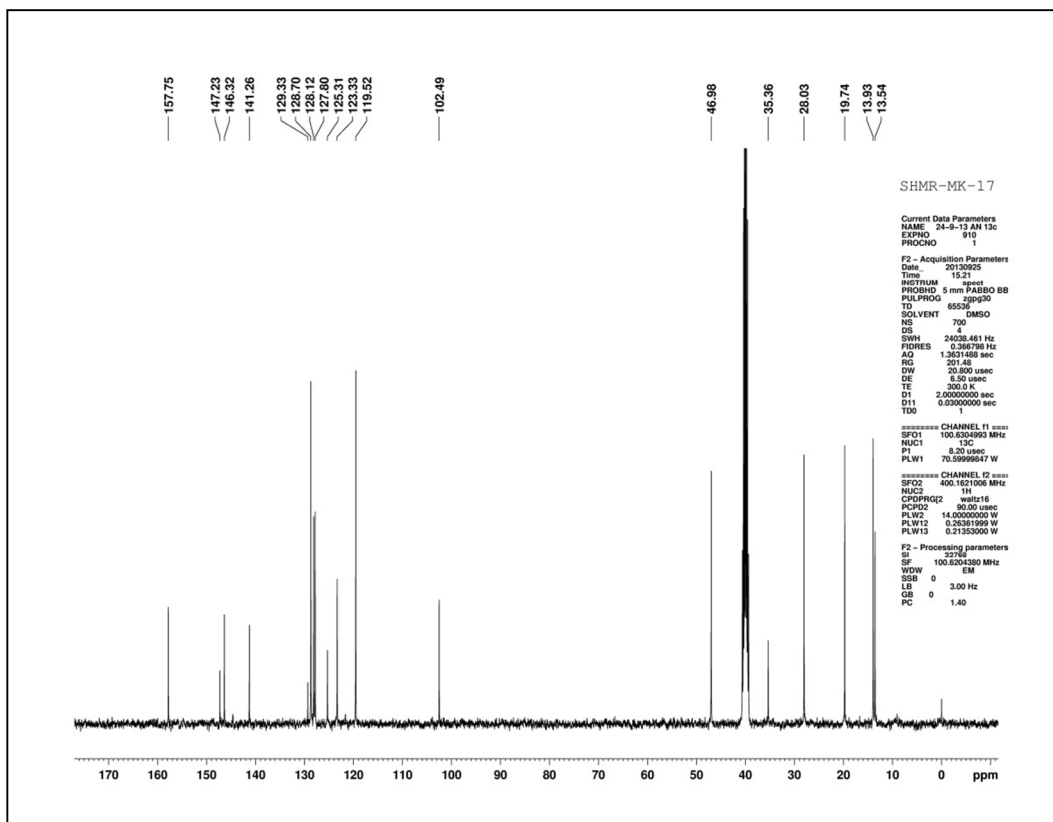
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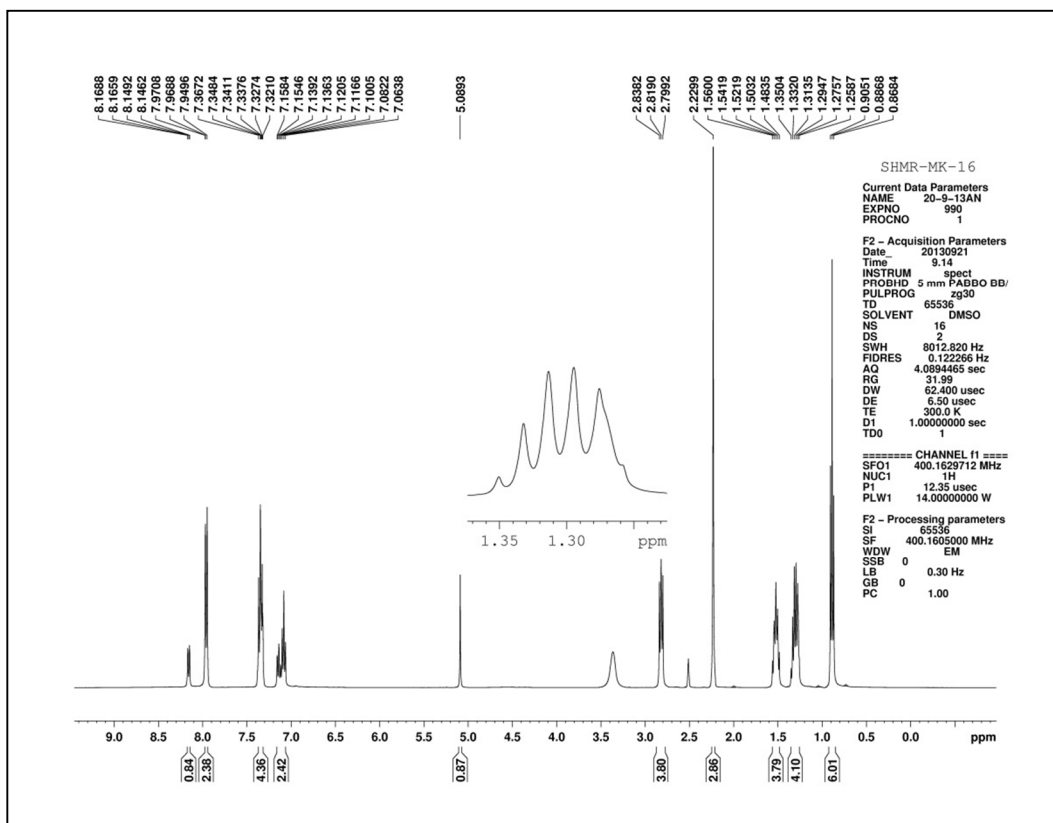
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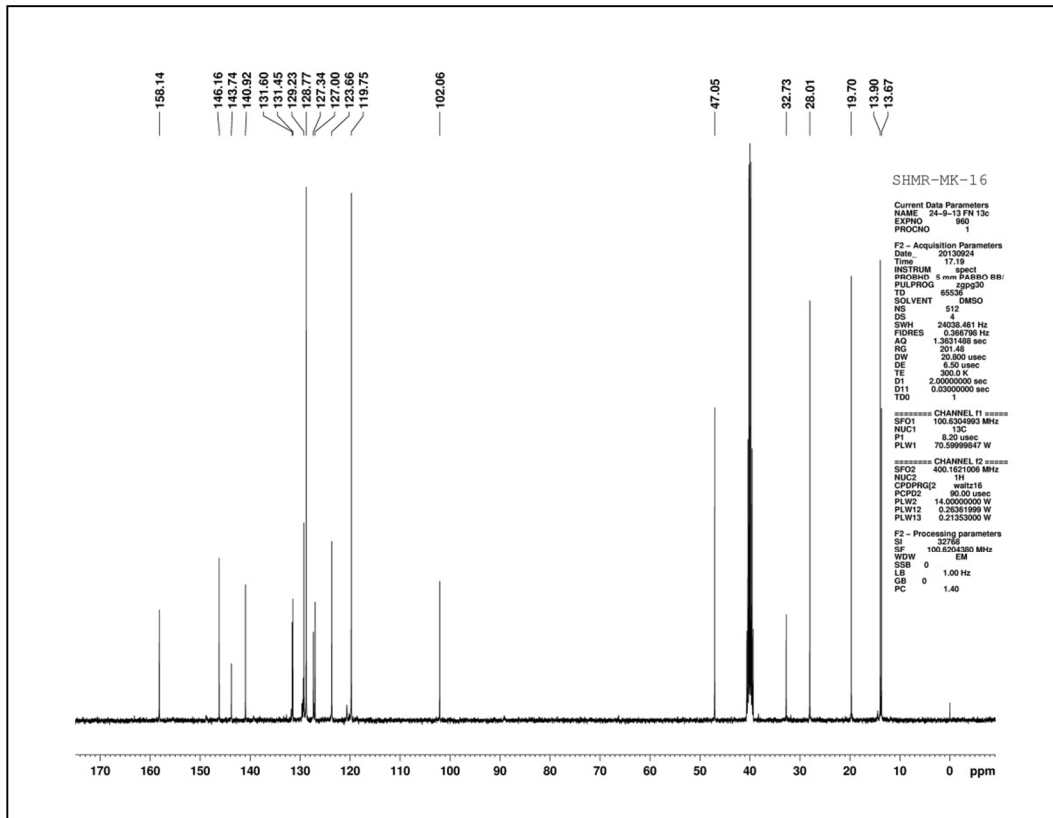
¹H Spectra of 11q



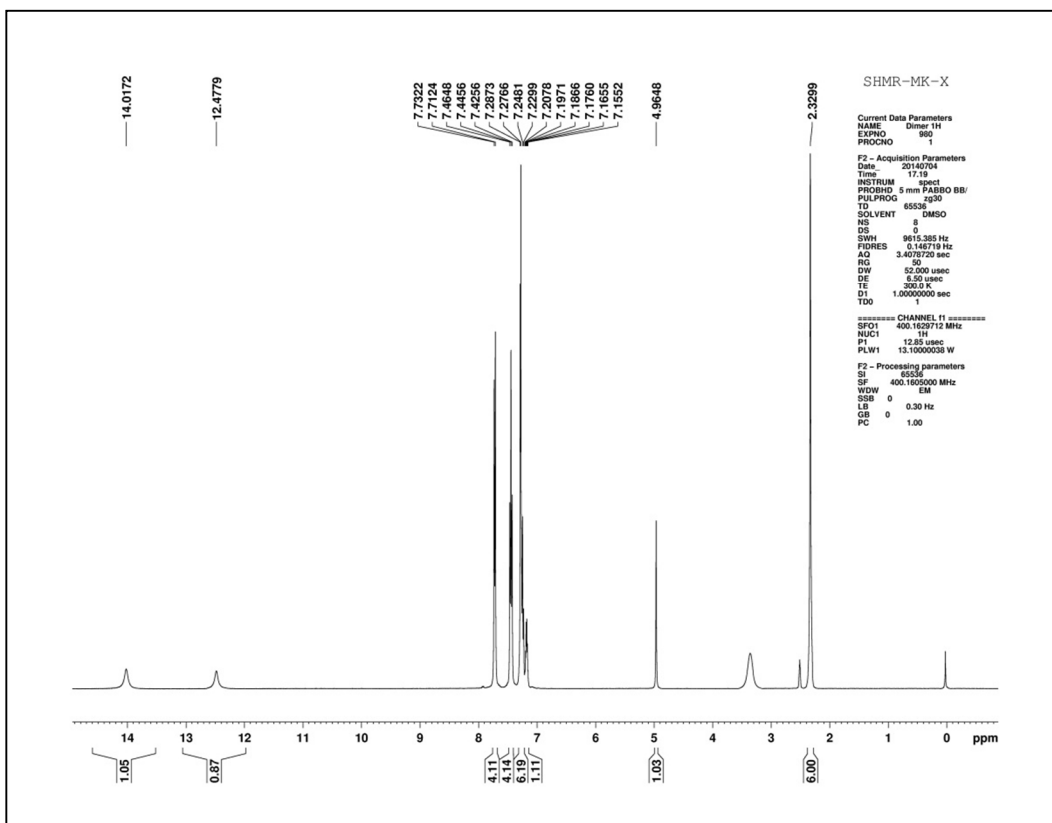
¹³C Spectra of 11q



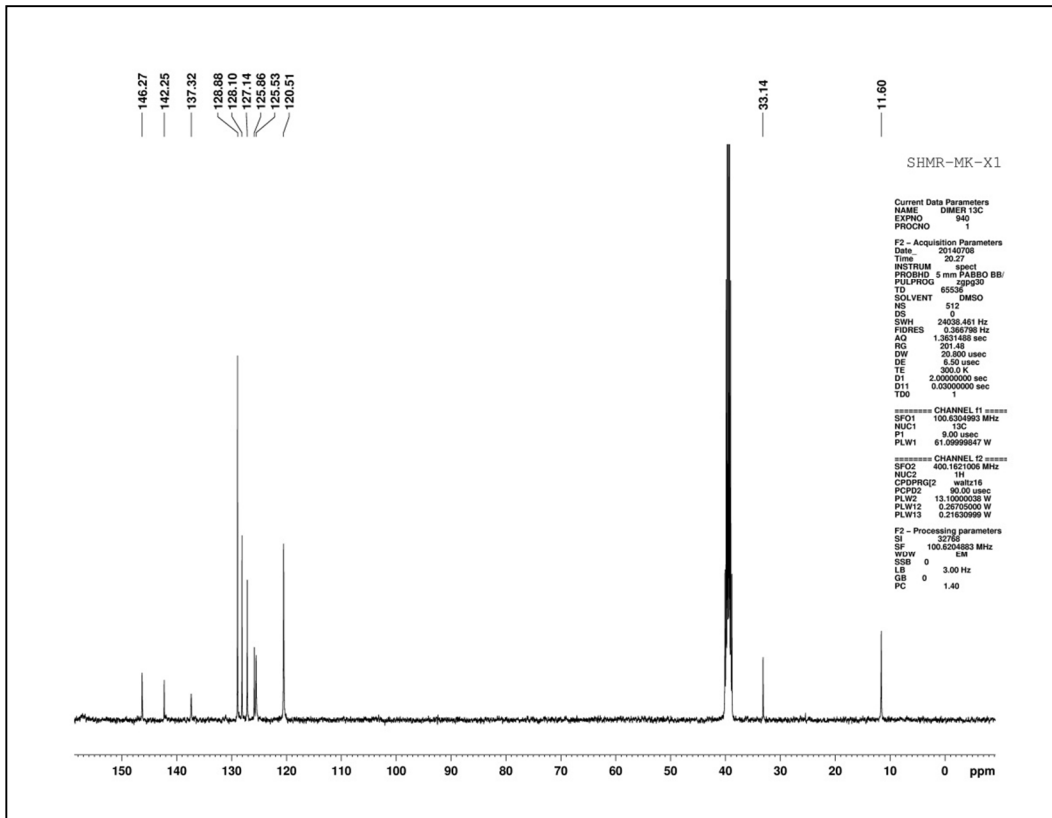
¹H Spectra of 11r



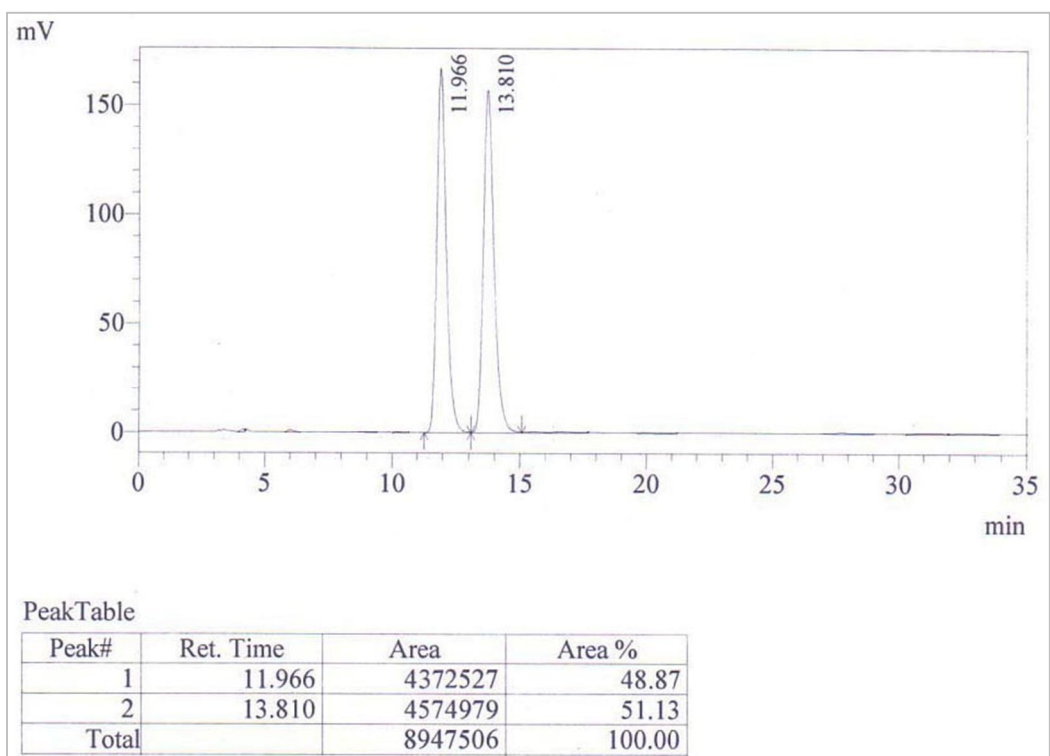
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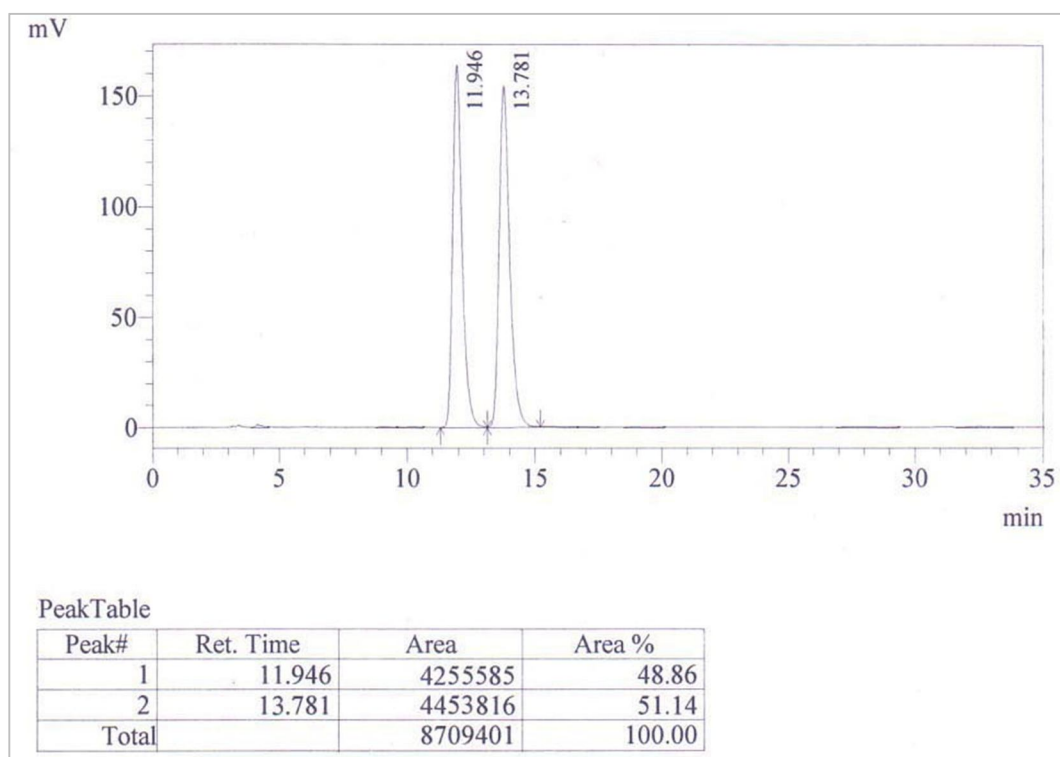
^1H Spectra of 12



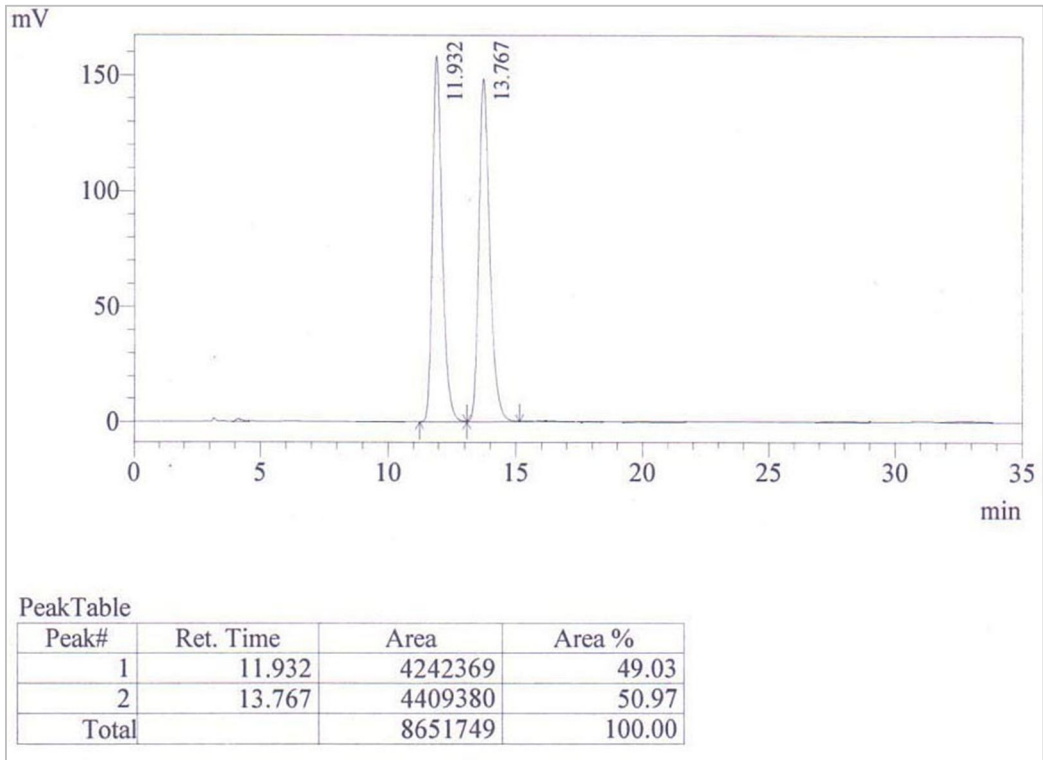
^{13}C Spectra of 12



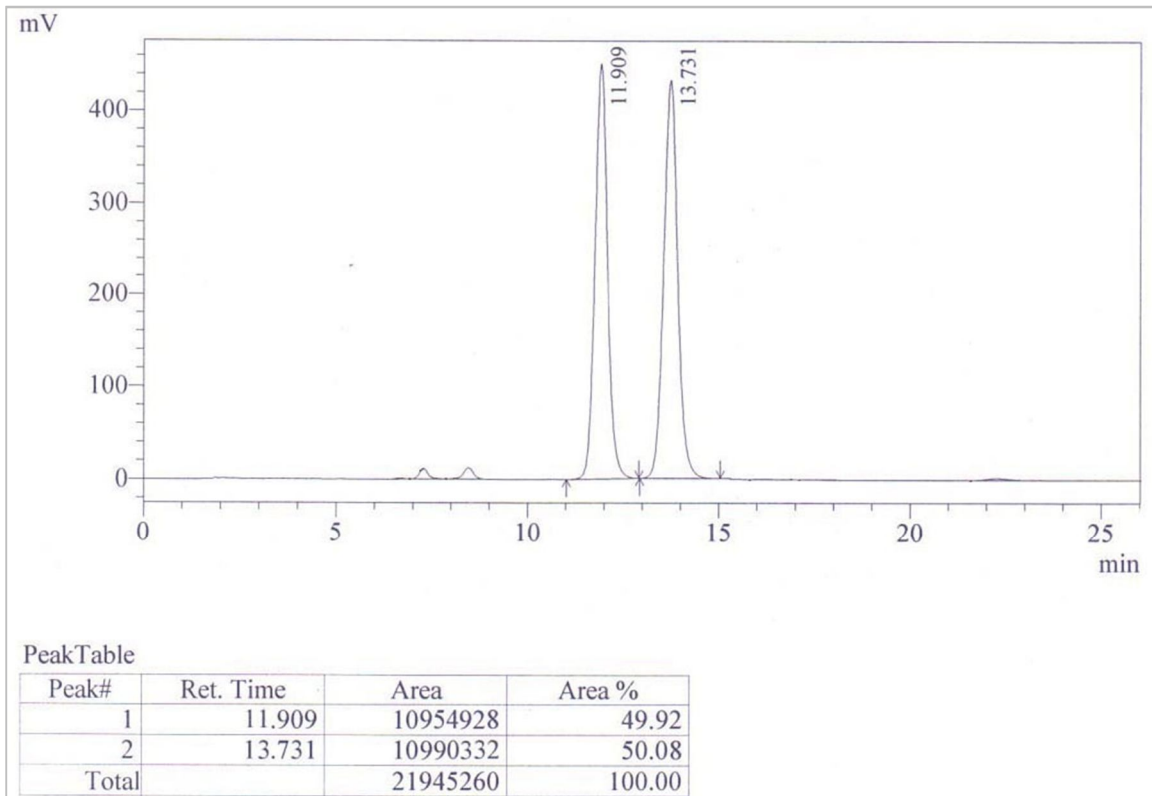
HPLC Parameter of 11a



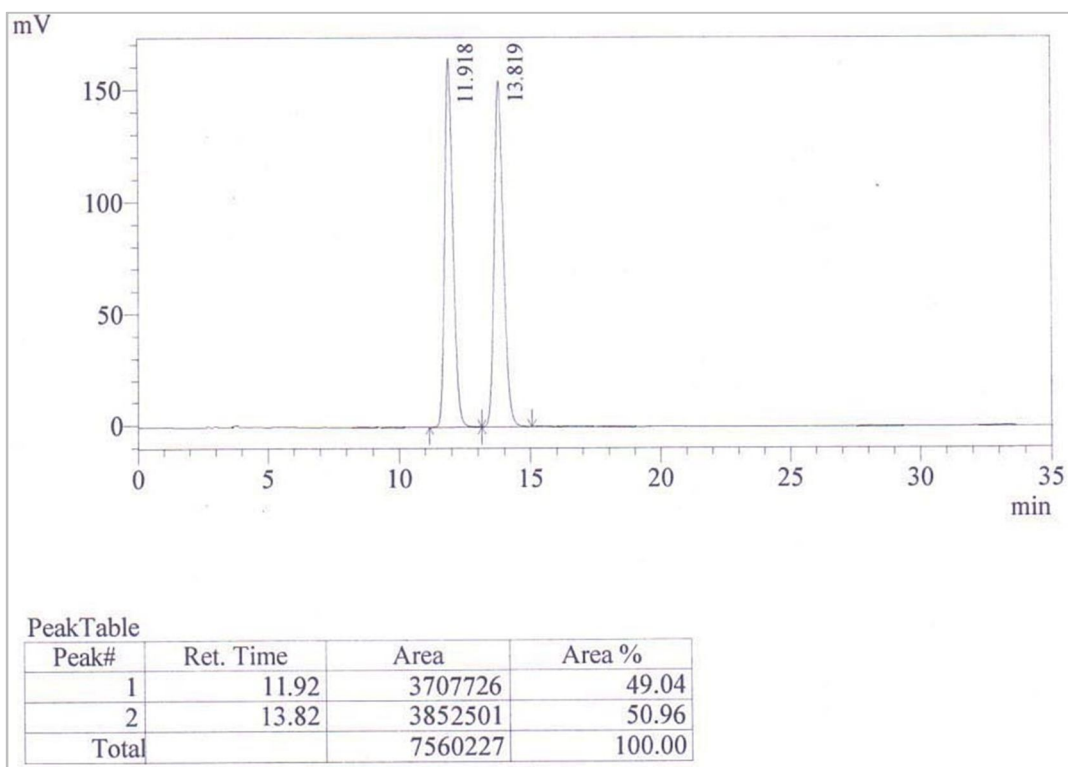
HPLC Parameter of 11b



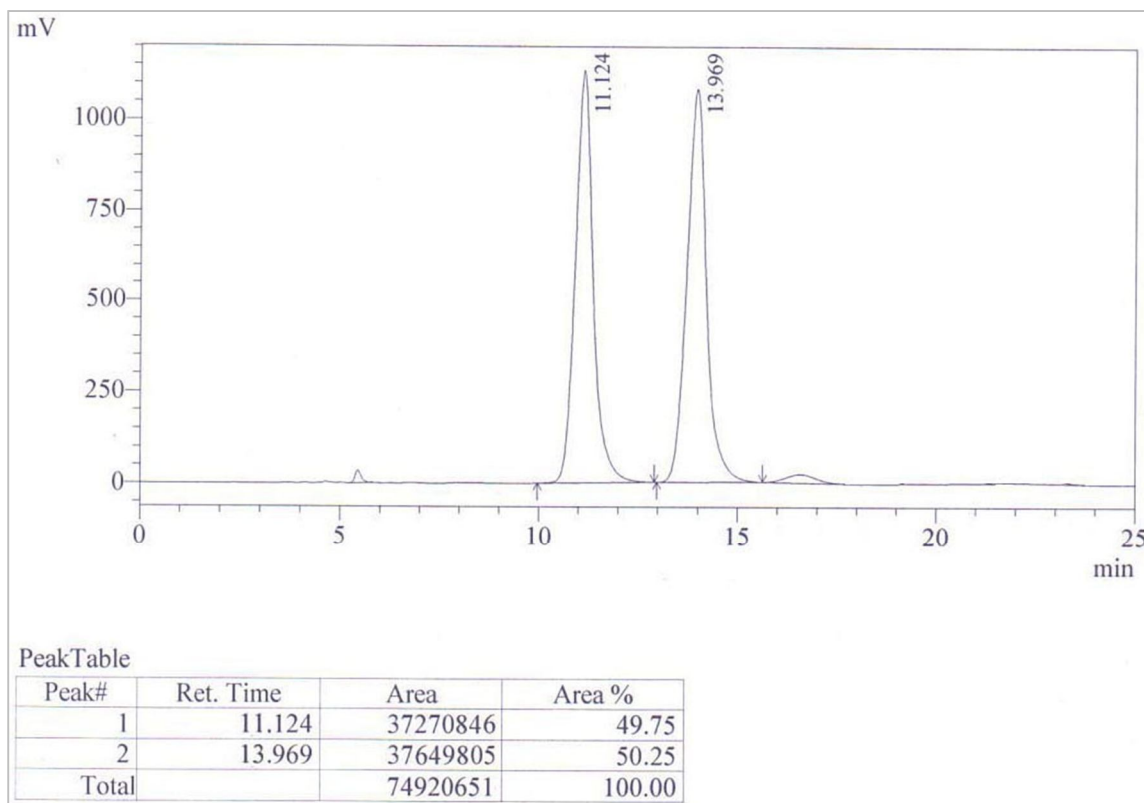
HPLC Parameter of 11c



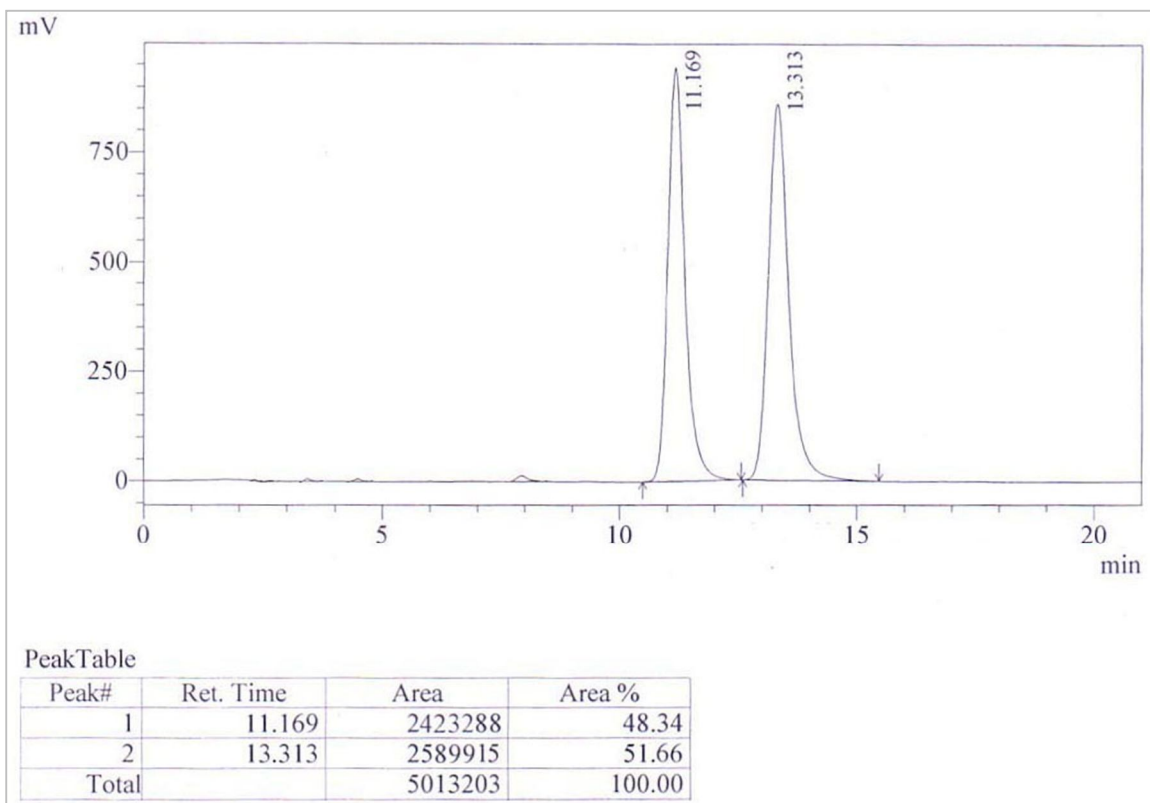
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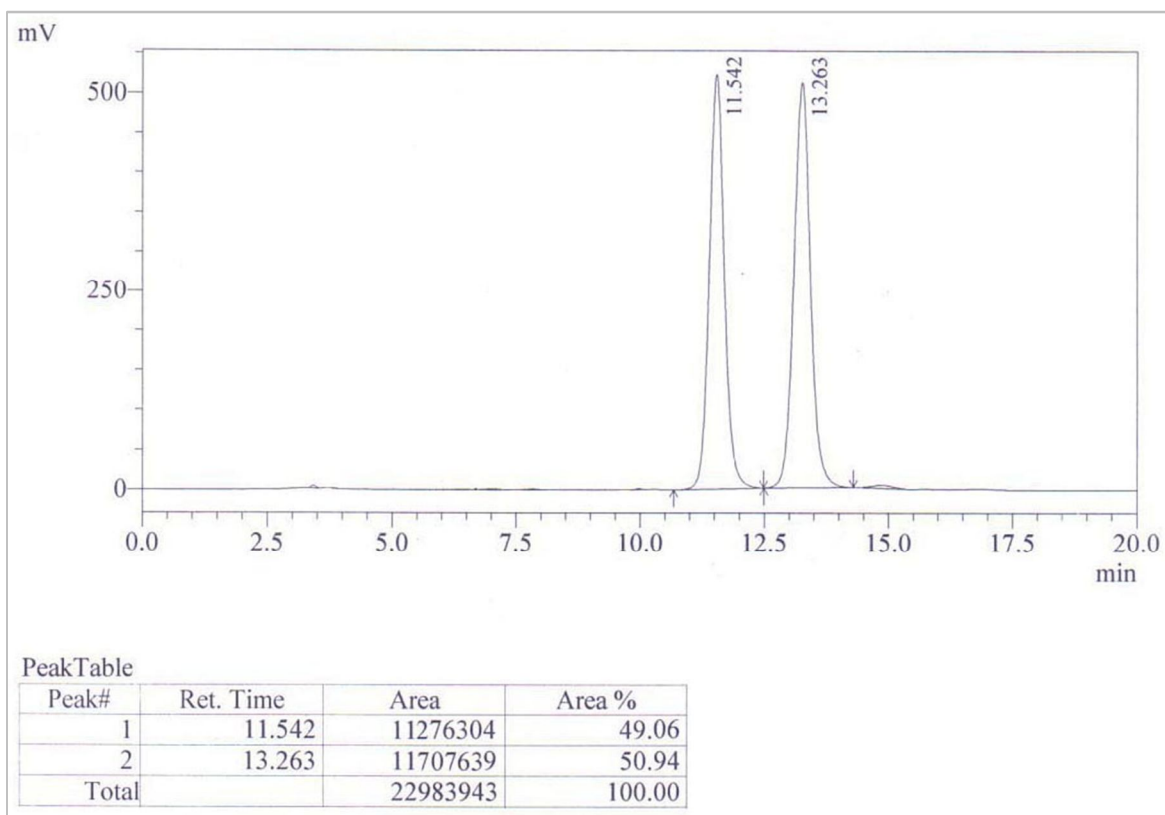
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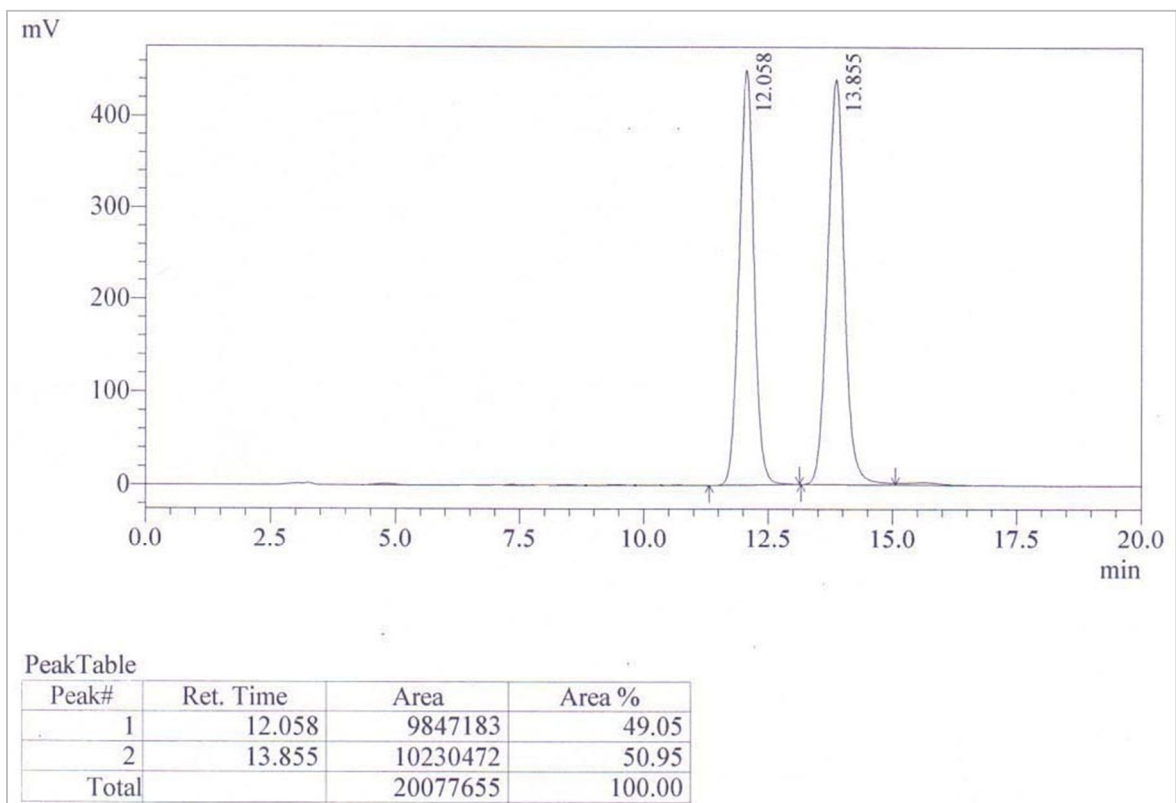
HPLC Parameter of 11f



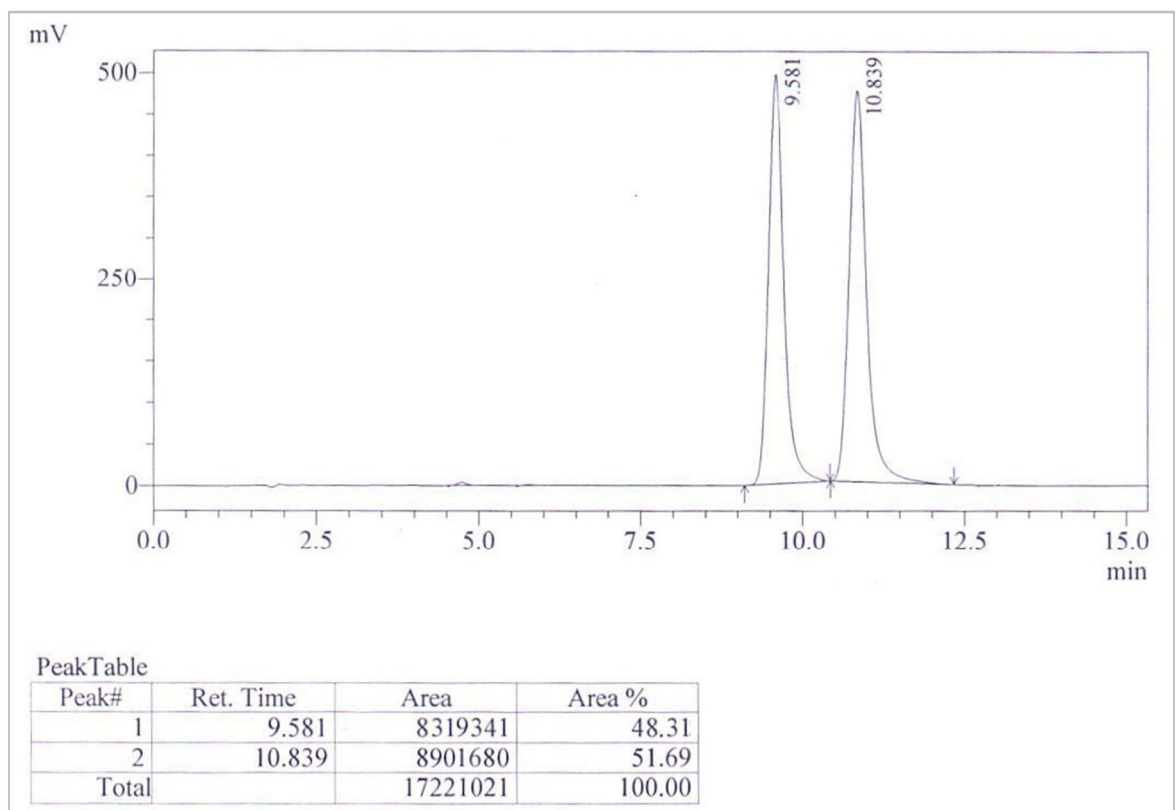
HPLC Parameter of 11g



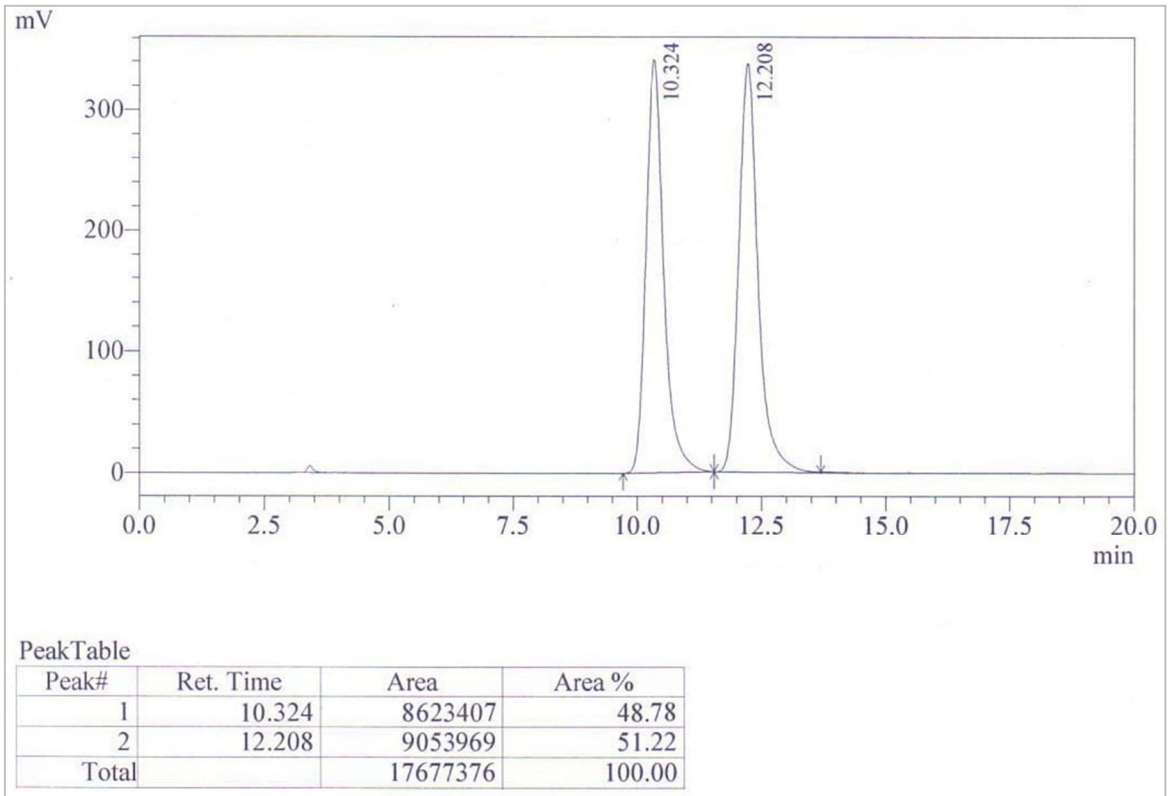
HPLC Parameter of 11h



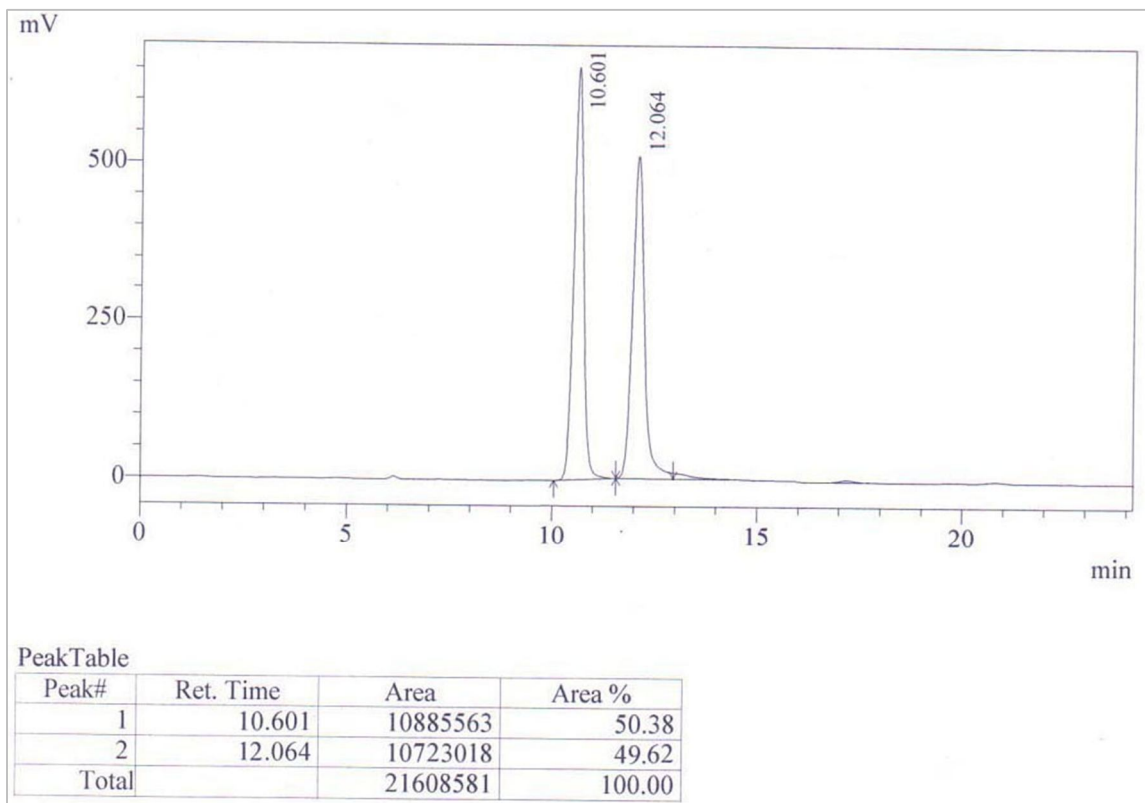
HPLC Parameter of 11i



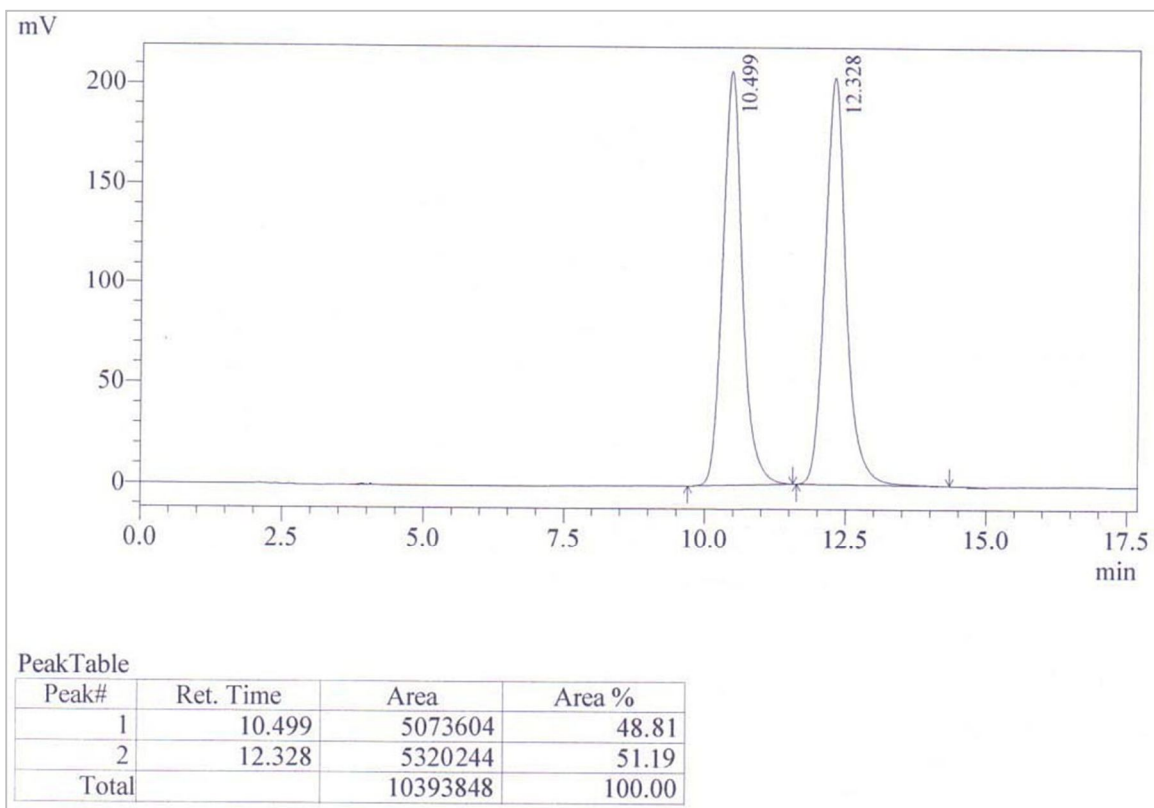
HPLC Parameter of 11j



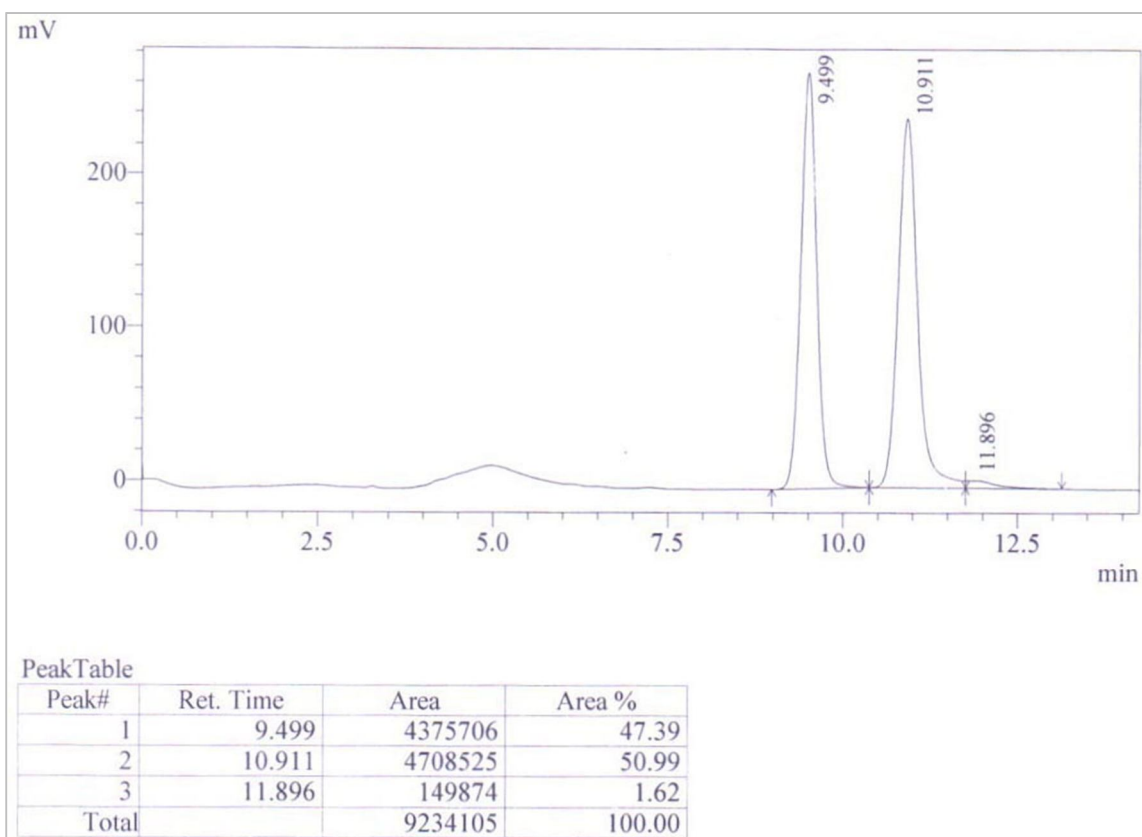
HPLC Parameter of 11k



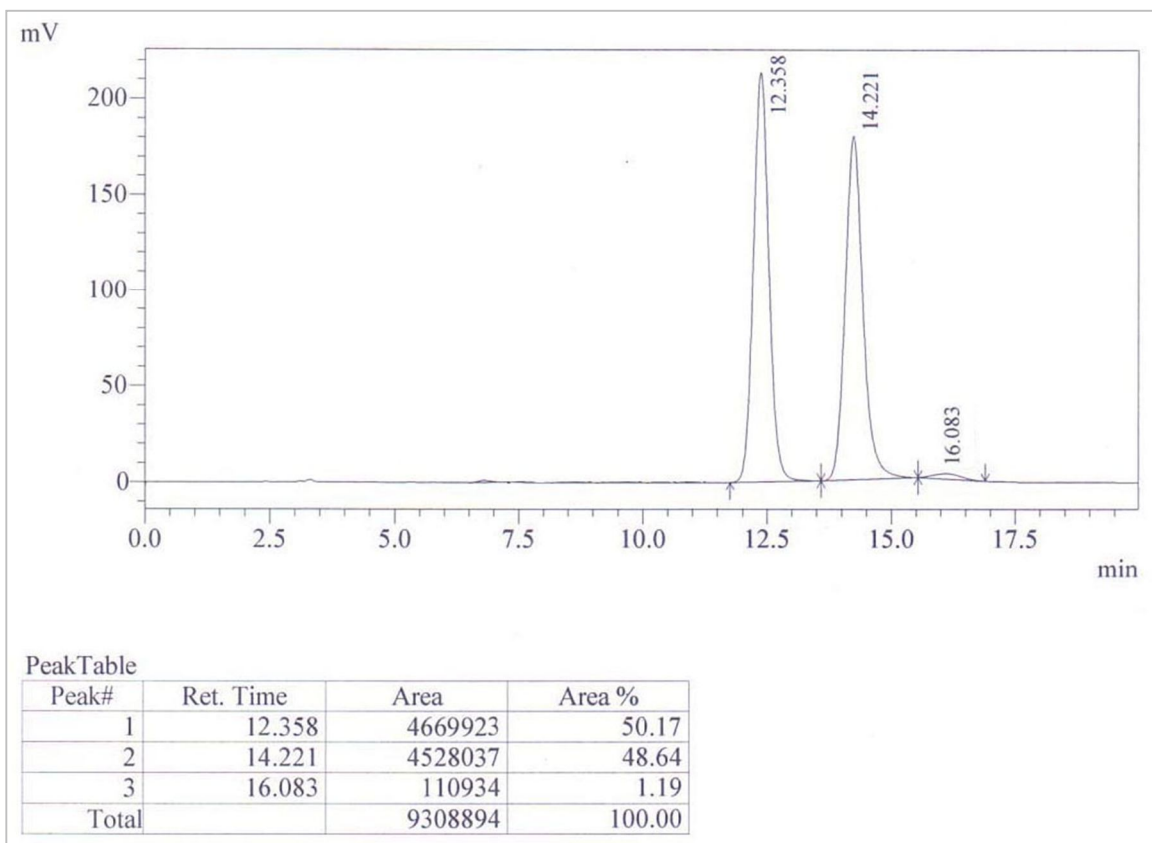
HPLC Parameter of 11l



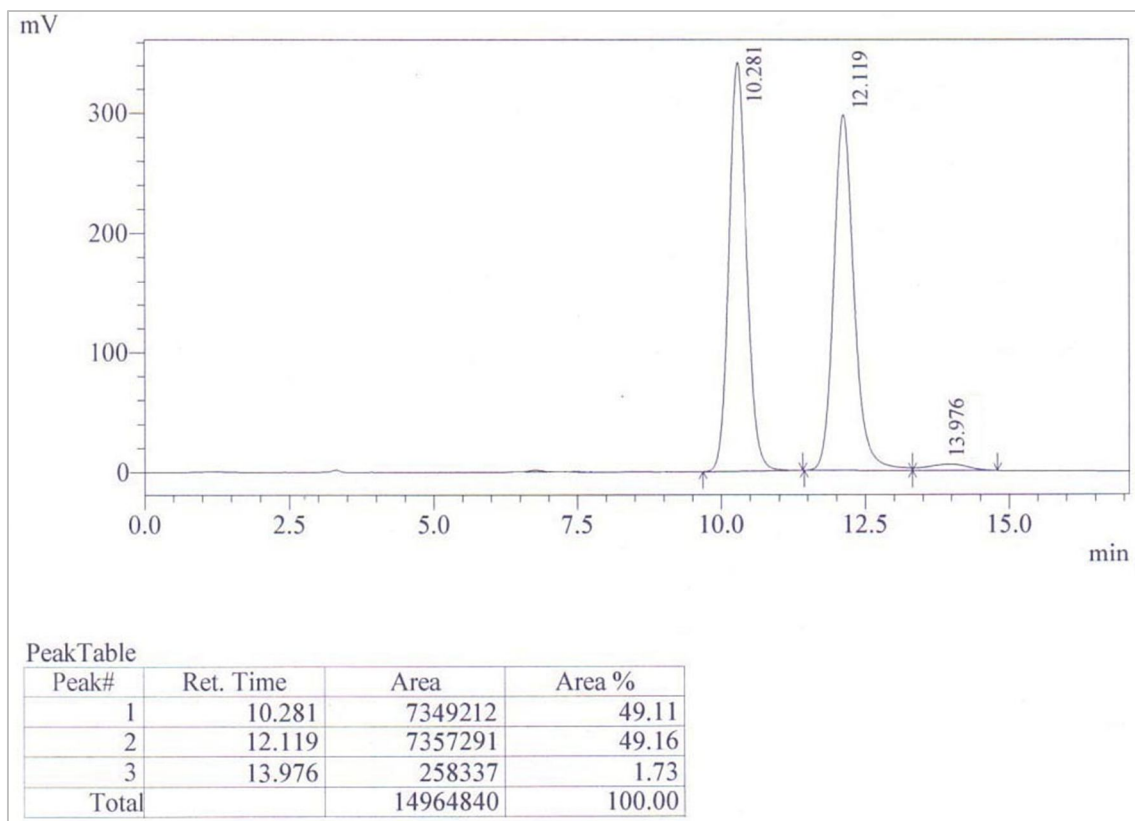
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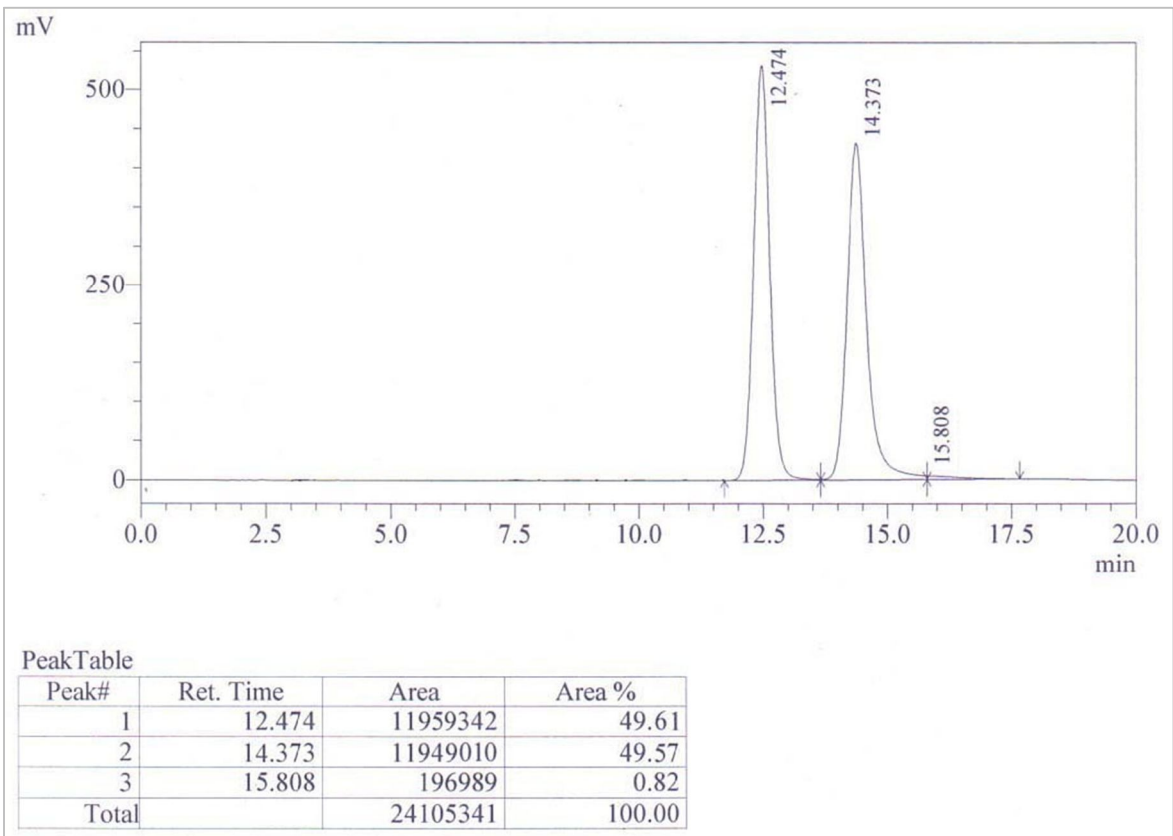
HPLC Parameter of 11n



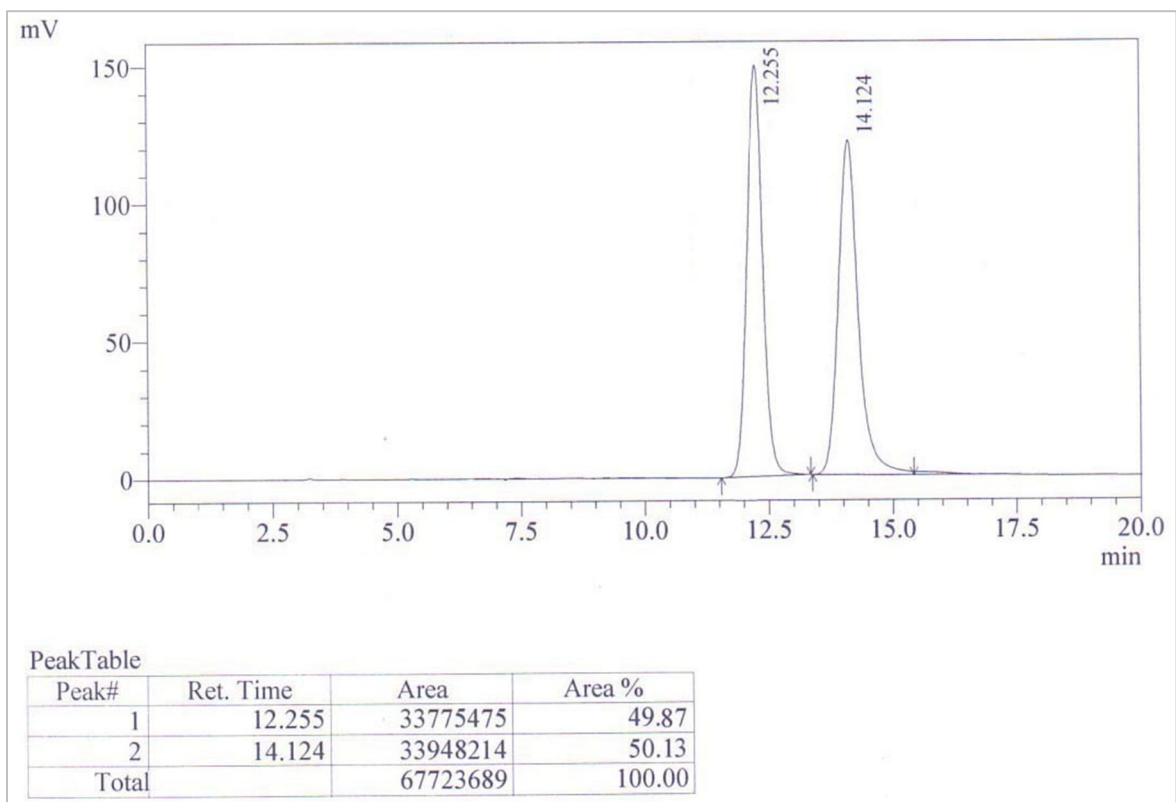
HPLC Parameter of 11o



HPLC Parameter of 11p



HPLC Parameter of 11q



HPLC Parameter of 11r