Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Facile one-pot synthesis of 3-azabicyclo[3.3.1]nonane scaffold by tandem Mannich reaction

Xiao Yi, Hongxia Tang, Jing Chen, Xiuling Xu, Yongmin Ma*

College of Pharmaceutical Science, Zhejiang Chinese Medical University, Hangzhou, 310053, P R China

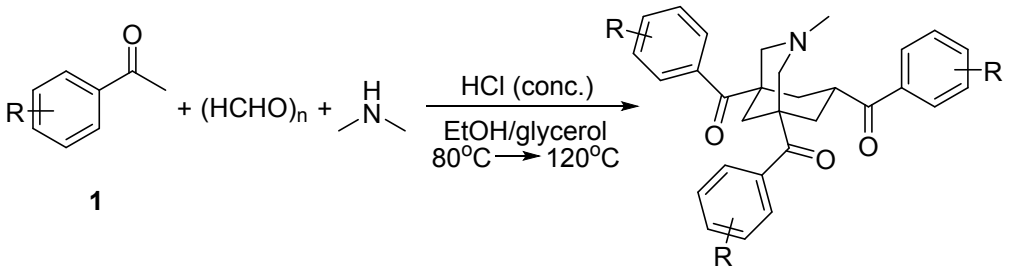
*E-mail: yongmin.ma@zcmu.edu.cn

Contents

General Information

NMR spectra were recorded with tetramethylsilane as the internal standard. ^{1}H NMR spectra were recorded at 600 MHz, 400 MHz or 300 MHz, and ^{13}C NMR spectra were recorded at 151 MHz, 126 MHz or 101 MHz (Bruker Avance). ^{1}H NMR chemical shifts (δ) are reported in ppm relative to tetramethylsilane (TMS) with the solvent signal as the internal standard ($CDCl_3$ at 7.26 ppm). ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ at 77.16 ppm). Data are given as: s (singlet), d (doublet), t (triplet), q (quartet), dd (double of doublet) or m (multiplets), coupling constants (Hz) and integration. Flash column chromatography was carried out using silica gel eluting with ethyl acetate and petroleum ether. High resolution mass spectra were obtained with the Q-TOF-Premier mass spectrometer. Reactions were monitored by TLC and visualized with ultraviolet light. All the solvents were used directly without any purification.

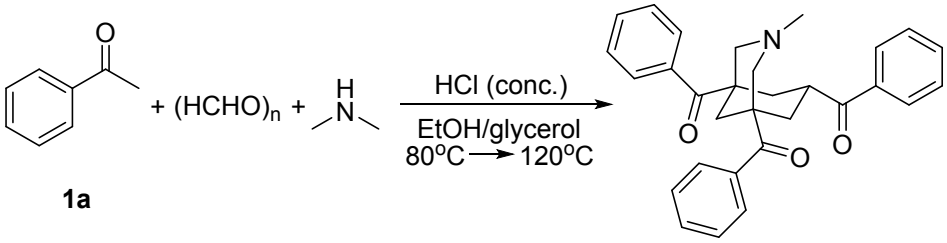
General Procedure for the Synthesis of 3-ABNs



1 **2**

A vial was charged with aromatic ketone **1** (0.3 mmol), paraformaldehyde (30 mg, 1 mmol), Me_2NH (40% *w*/*w* in H_2O, 0.41 mL, 1.5 mmol) and concentrated HCl (0.05 mL, 0.6 mmol) in EtOH/glycerol mixture (1:1 *v*/*v*, 2 mL). The reaction mixture was stirred at 80 °C for 2 h before temperature increasing to 120 °C to remove H_2O-EtOH under open system. The reaction mixture was kept at 120 °C for 4 h. After cooling to room temperature, the reaction mixture was diluted with water (5 mL). The aqueous phase was extracted with dichloromethane and the combined were washed with brine, dried over Na_2SO_4, filtered and concentrated. The mixture was concentrated in vacuo and purified by flash chromatography on silica gel to afford the desired product **2**.

Scale-Up Reaction

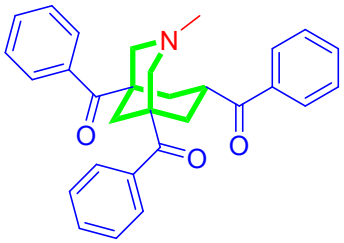


1a **2a**

A round-bottom flask equipped with a magnetic stir bar was charged with an EtOH/glycerol mixture (1:1 *v*/*v*, 80 mL) followed by the addition of acetophenone **1a** (1.44 g, 12 mmol) paraformaldehyde (1.21g, 40 mmol), Me_2NH (40% *w*/*w* in H_2O, 10.34 mL, 60 mmol) and concentrated HCl (2 mL, 24 mmol). The resulting mixture was subsequently was stirred at 80 ^oC for 2 h, and then the temperature was increased 120 ^oC to remove H_2O-EtOH using a Dean-Stark apparatus. The reaction mixture was kept at 120 ^oC for 4 h. After cooling to room temperature, the reaction mixture was diluted with water (200 mL). The aqueous phase was extracted with dichloromethane and the combined were washed with brine, dried over Na_2SO_4, filtered and concentrated. The mixture was concentrated in vacuo and purified by silica gel chromatography with the mixture eluent of ethyl acetate and petroleum ether (1:20 to 1:10 *v*/*v*), to give (3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris(phenylmethanone) **2a** (1.16g, 64%).

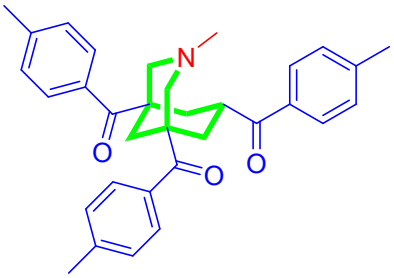
Characterization Data for 3-ABN Compounds

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris(phenylmethanone) (2a):



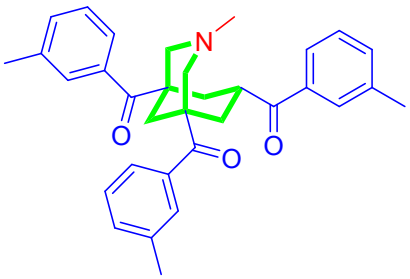
71% yield (32 mg). White solid, m.p. 159-160 °C. R_f = 0.3 (PE/EA=10/1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.64 (dd, *J* = 8.7, 1.0 Hz, 4H), 7.60 – 7.55 (m, 1H), 7.53 – 7.45 (m, 4H), 7.42 – 7.37 (m, 4H), 5.28-5.22 (m, 1H), 3.29 (dd, *J* = 11.9, 1.8 Hz, 2H), 2.40 (dd, *J* = 11.8, 2.0 Hz, 2H), 2.38 (s, 3H), 2.32 (ddd, *J* = 14.1, 5.2, 2.2 Hz, 2H), 2.25 (dt, *J* = 14.0, 1.8 Hz, 1H), 2.10 (dt, *J* = 13.1, 2.3 Hz, 1H), 2.04 – 1.98 (m, 2H). ^{13}C NMR (151 MHz, CDCl3) δ 206.41, 202.87, 138.13, 136.30, 133.32, 131.36, 128.95, 128.59, 128.44, 127.77, 61.73, 48.99, 46.39, 40.21, 37.47, 35.82. HRMS (ESI-TOF): *m/z* calcd for $C_{30}H_{30}NO_3$ $[M+H]^+$: 452.2220, found 452.2233.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris(*p*-tolylmethanone) (2b):



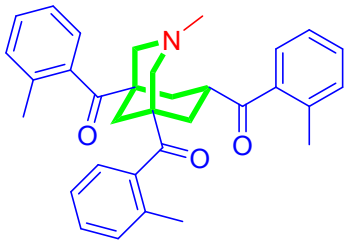
72% yield (35.5 mg). White solid, m.p. 119-121 °C. R_f = 0.32 (PE/EA=10/1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.2 Hz, 2H), 7.63 (d, *J* = 8.2 Hz, 4H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 4H), 5.20 – 5.14 (m, 1H), 3.27 (d, *J* = 10.7 Hz, 2H), 2.42 (d, *J* = 10.0 Hz, 2H), 2.42 (d, *J* = 3.7 Hz, 3H), 2.37 (d, *J* = 3.4 Hz, 9H), 2.31 (ddd, *J* = 13.9, 4.9, 1.8 Hz, 2H), 2.24 (d, *J* = 13.1 Hz, 1H), 2.12 (d, *J* = 13.2 Hz, 1H), 2.00 (t, *J* = 12.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.55, 202.52, 144.08, 142.14, 134.90, 133.74, 129.59, 129.06, 128.70, 128.33, 61.70, 48.85, 46.33, 39.96, 37.58, 36.00, 21.82, 21.62. HRMS (ESI-TOF): *m/z* calcd for $C_{33}H_{36}NO_3$ $[M+H]^+$: 494.2690, found 494.2676.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris(*m*-tolylmethanone) (2c):



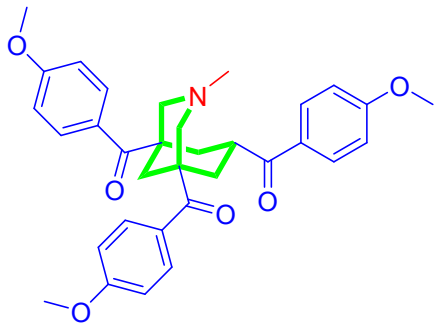
71% yield (35.0 mg). White solid, m.p. 104-106 °C. R_f = 0.32 (PE/EA=10/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (s, 2H), 7.64 – 7.58 (m, 1H), 7.43 (dt, *J* = 4.5, 2.2 Hz, 2H), 7.40 – 7.38 (m, 3H), 7.33 – 7.32 (m, 1H), 7.27 (d, *J* = 4.8 Hz, 3H), 5.26 – 5.19 (m, 1H), 3.27 (d, *J* = 10.7 Hz, 2H), 2.42 (s, 3H), 2.37 (d, *J* = 2.7 Hz, 9H), 2.32 – 2.25 (m, 4H), 2.22 (d, *J* = 13.0 Hz, 1H), 2.08 (d, *J* = 13.0 Hz, 1H), 1.98 (t, *J* = 12.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.88, 203.17, 138.75, 138.30, 136.41, 134.05, 132.83, 132.01, 129.11, 128.73, 128.35, 128.17, 125.78, 125.65, 124.63, 63.94, 61.72, 49.00, 47.16, 46.35, 40.26, 37.54, 35.87, 29.84, 21.60. HRMS (ESI-TOF): *m/z* calcd for $C_{33}H_{36}NO_3$ $[M+H]^+$: 494.2690, found 494.2713.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris(*o*-tolylmethanone) (2d):



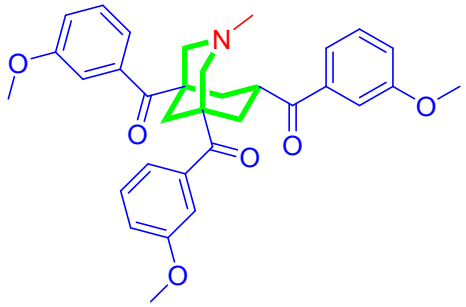
54% yield (26.6 mg). White solid, m.p. 119-121 °C. R_f = 0.33 (PE/EA=10/1). ^{1}H NMR (600 MHz, $CHCl_3$) δ 7.49 (d, *J* = 7.9 Hz, 1H), 7.35 (td, *J* = 7.5, 1.1 Hz, 1H), 7.27 (t, *J* = 7.0 Hz, 3H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 2H), 7.16 (t, *J* = 7.5 Hz, 2H), 7.06 (d, *J* = 7.5 Hz, 2H), 5.06 (tt, *J* = 11.9, 5.2 Hz, 1H), 3.11 (dd, *J* = 11.4, 2.1 Hz, 2H), 2.37 (s, 3H), 2.26 (s, 3H), 2.21 (d, *J* = 10.4 Hz, 2H), 2.17 (s, 6H), 2.15 – 2.11 (m, 2H), 2.00 (d, *J* = 12.6 Hz, 1H), 1.85 (q, *J* = 13.9, 13.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 211.01, 207.25, 139.69, 138.39, 137.62, 134.13, 131.12, 129.21, 127.70, 125.89, 125.09, 124.63, 61.50, 49.39, 46.36, 43.53, 36.97, 34.69, 20.91, 20.06. HRMS (ESI-TOF): *m/z* calcd for $C_{33}H_{36}NO_3$ $[M+H]^+$: 494.2690, found 494.2681.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((4-methoxyphenyl)methanone) (2e):



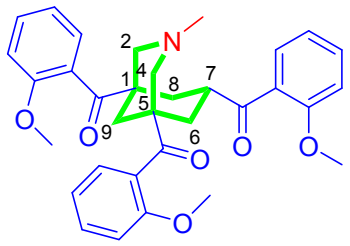
75% yield (40.6 mg). White solid, m.p. 138-140 °C. R_f = 0.25 (PE/EA=5/1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 – 7.95 (m, 2H), 7.89 – 7.85 (m, 4H), 6.99 – 6.95 (m, 2H), 6.91 – 6.87 (m, 4H), 5.07 – 5.01 (m, 1H), 3.89 (s, 3H), 3.85 (s, 6H), 3.21 (d, *J* = 11.4 Hz, 2H), 2.57 (d, *J* = 11.2 Hz, 2H), 2.39 (s, 3H), 2.33 – 2.28 (m, 2H), 2.27 – 2.17 (m, 2H), 2.03 (t, *J* = 12.7 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 203.45, 201.34, 163.66, 162.50, 131.07, 130.87, 129.56, 129.30, 114.08, 113.63, 61.69, 55.65, 55.55, 48.72, 46.21, 39.49, 37.87, 36.35. HRMS (ESI-TOF): *m/z* calcd for $C_{33}H_{36}NO_6$ $[M+H]^+$: 542.2537, found 542.2541.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((3-methoxyphenyl)methanone) (2f):



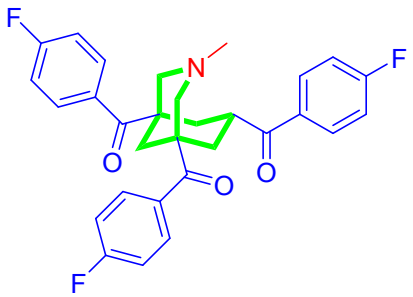
68% yield (36.4 mg). White solid, m.p. 133-135 °C. R_f = 0.25 (PE/EA=5/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.3 Hz, 1H), 7.47 (s, 1H), 7.40 (t, *J* = 6.0 Hz, 1H), 7.34 – 7.31 (m, 1H), 7.30 (s, 1H), 7.25 (dt, *J* = 7.6, 1.2 Hz, 2H), 7.17 – 7.14 (m, 2H), 7.11 (dd, *J* = 8.0, 2.3 Hz, 1H), 7.00 (ddd, *J* = 8.1, 2.5, 0.9 Hz, 2H), 5.21 – 5.14 (m, 1H), 3.84 (s, 3H), 3.80 (s, 6H), 3.26 (d, *J* = 11.5 Hz, 2H), 2.44 (d, *J* = 11.4 Hz, 2H), 2.37 (s, 3H), 2.33 (dd, *J* = 13.8, 5.0 Hz, 2H), 2.22 – 2.15 (m, 2H), 2.03 – 1.95 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.89, 202.45, 160.00, 159.44, 139.10, 137.56, 129.34, 129.30, 120.89, 120.64, 119.80, 119.45, 117.87, 117.06, 113.74, 113.13, 112.95, 63.58, 61.40, 55.35, 48.82, 47.11, 46.13, 40.09, 37.31, 35.77, 30.88. HRMS (ESI-TOF): *m/z* calcd for $C_{33}H_{36}NO_6$ $[M+H]^+$: 542.2537, found 542.2549.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((2-methoxyphenyl)methanone) (2g):



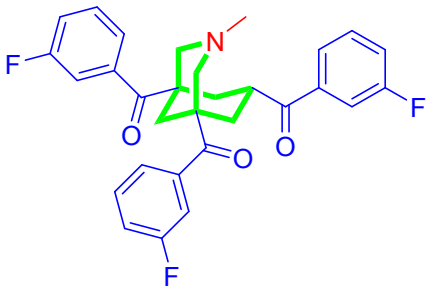
47% yield (25.4 mg). White solid, m.p. 130-132 °C. R*f* = 0.28 (PE/EA=5/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 7.6, 1.4 Hz, 1H, Ar*H*), 7.46 – 7.40 (m, 1H, Ar*H*), 7.35 – 7.28 (m, 2H, Ar*H*), 7.01 – 6.90 (m, 6H, Ar*H*), 6.84 (d, *J* = 8.4 Hz, 2H, Ar*H*), 5.24 – 5.15 (m, 1H, C_7-*H*), 3.87 (s, 3H, C_7-COArCH_3), 3.63 (s, 6H, $C_{1,5}$-COArCH_3), 3.08 (d, *J* = 10.6 Hz, 2H, C_2,C_4-H_2), 2.25 (s, 3H, NCH_3), 2.22 (d, *J* = 9.7 Hz, 2H, C_2,C_4-H_2), 2.16 (dd, *J* = 12.5, 5.1 Hz, 2H, C_6,C_8-H_2), 1.88 – 1.72 (m, 4H, C_6,C_8-H_2, C_9-H_2).^{13}C NMR (101 MHz, $CDCl_3$) δ 210.86, 205.93, 157.98, 155.37, 132.95, 130.37, 130.25, 130.14, 128.79, 126.62, 120.88, 120.51, 111.63, 111.06, 61.11 (C_2, C_4), 55.52 (C_7-COAr*C*H_3), 55.28 (C_1, C_5-COAr*C*H_3), 49.19 (C_1, C_5), 46.31 (NCH_3), 44.76 (C_7), 35.83 (C_9), 34.14 (C_6, C_8). HRMS (ESI-TOF): *m/z* calcd for $C_{33}H_{36}NO_6$ $[M+H]^+$: 542.2537, found 542.2532.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((4-fluorophenyl)methanone) (2h):



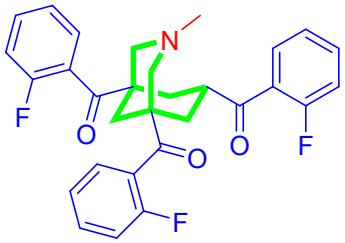
61% yield (30.8 mg). White solid, m.p. 134-135 °C. R$_f$ = 0.35 (PE/EA=10/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 8.0, 5.6 Hz, 2H), 7.79 (dd, *J* = 8.2, 5.5 Hz, 4H), 7.17 (t, *J* = 8.5 Hz, 2H), 7.10 (t, *J* = 8.5 Hz, 4H), 5.13-5.04 (m, 1H), 3.22 (d, *J* = 11.6 Hz, 2H), 2.50 (d, *J* = 11.5 Hz, 2H), 2.39 (s, 3H), 2.33 – 2.25 (m, 2H), 2.16 (q, *J* = 13.2 Hz, 2H), 1.98 (t, *J* = 12.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.88, 201.00, 165.97 (d, $J_{C\text{-}F}$ = 254 Hz), 164.76 (d, $J_{C\text{-}F}$ = 253 Hz), 133.45, 132.52, 131.22 (d, $J_{C\text{-}F}$ = 9 Hz), 130.87 (d, $J_{C\text{-}F}$ = 9 Hz), 116.14 (d, $J_{C\text{-}F}$ = 22 Hz), 115.66 (d, $J_{C\text{-}F}$ = 21 Hz), 61.45, 48.78, 46.24, 39.82, 37.49, 35.92, 29.85. HRMS (ESI-TOF): *m/z* calcd for $C_{30}H_{27}F_3NO_3$ $[M+H]^+$: 506.1938, found 506.1927.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((3-fluorophenyl)methanone) (2i):



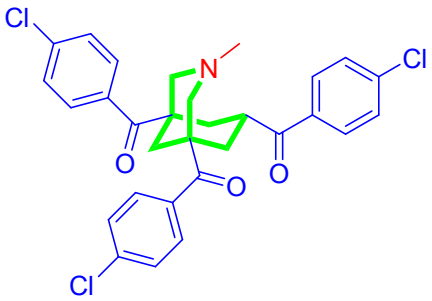
58% yield (29.3 mg). White solid, m.p. 125-127 °C. R_f = 0.34 (PE/EA=10/1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.7 Hz, 1H), 7.62 (d, *J* = 9.2 Hz, 1H), 7.51 – 7.45 (m, 3H), 7.43 – 7.35 (m, 4H), 7.30 (td, *J* = 8.2, 2.4 Hz, 1H), 7.20 (td, *J* = 8.2, 2.2 Hz, 2H), 5.13 – 5.08 (m, 1H), 3.22 (d, *J* = 11.3 Hz, 2H), 2.47 (d, *J* = 11.2 Hz, 2H), 2.40 (s, 3H), 2.28 (dd, *J* = 13.7, 5.0 Hz, 2H), 2.19 – 2.08 (m, 2H), 1.96 (t, *J* = 12.4 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 204.44, 201.25, 163.14 (d, $J_{C\text{-}F}$ = 246 Hz), 162.50 (d, $J_{C\text{-}F}$ = 247 Hz), 139.51 (d, $J_{C\text{-}F}$ = 6 Hz), 138.28 (d, $J_{C\text{-}F}$ = 6 Hz), 130.66 (d, $J_{C\text{-}F}$ = 8 Hz), 130.25 (d, $J_{C\text{-}F}$ = 8 Hz), 124.24, 123.49 (d, $J_{C\text{-}F}$ = 3 Hz), 120.44 (d, $J_{C\text{-}F}$ = 21 Hz), 118.63 (d, $J_{C\text{-}F}$ = 21 Hz), 115.33 (d, $J_{C\text{-}F}$ = 23 Hz), 115.08 (d, $J_{C\text{-}F}$ = 23 Hz), 63.25, 61.26, 48.86, 47.25, 46.18, 40.16, 37.21, 35.58, 32.76. HRMS (ESI-TOF): *m/z* calcd for $C_{30}H_{27}F_3NO_3$ $[M+H]^+$: 506.1938, found 506.1951.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((2-fluorophenyl)methanone) (2j):



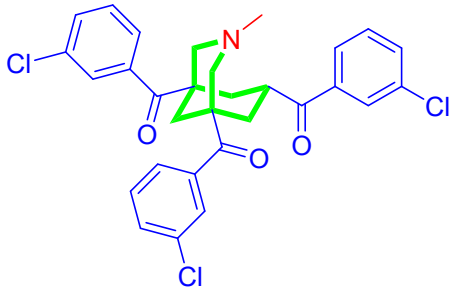
38% yield (19.2 mg). White solid, m.p. 113-115 °C. R_f = 0.34 (PE/EA=10/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.31 (m, 1H), 7.30 – 7.24 (m, 3H), 6.99 (dt, J = 15.4, 7.8 Hz, 5H), 6.93 (t, J = 7.4 Hz, 1H), 6.87 (dd, J = 7.4, 1.4 Hz, 2H), 5.41 – 5.34 (m, 1H), 3.03 (d, J = 10.5 Hz, 2H), 2.19 (s, 3H), 2.10 (dd, J = 11.7, 5.5 Hz, 4H), 1.78 – 1.68 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 214.19, 209.74, 151.83, 150.77, 137.34, 132.99, 131.45, 129.77, 129.52, 126.27, 123.25, 121.06, 119.40, 117.80, 61.81, 49.36, 46.05, 44.88, 44.60, 43.24, 36.12, 35.79, 29.81. HRMS (ESI-TOF): *m/z* calcd for $C_{30}H_{27}F_3NO_3$ $[M+H]^+$: 506.1938, found 506.1962.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((4-chlorophenyl)methanone) (2k):



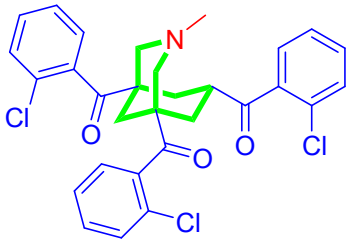
83% yield (45.9 mg). White solid, m.p. 179-180 °C. R_f = 0.35 (PE/EA=10/1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.5 Hz, 2H), 7.65 (d, *J* = 8.5 Hz, 4H), 7.47 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 4H), 5.12 – 5.07 (m, 1H), 3.21 (d, *J* = 11.7 Hz, 2H), 2.45 (d, *J* = 11.3 Hz, 2H), 2.38 (s, 3H), 2.27 (dd, *J* = 13.7, 4.9 Hz, 2H), 2.13 (s, 2H), 1.95 (t, *J* = 12.6 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 204.42, 201.33, 138.09, 135.69, 134.39, 129.97, 129.55, 129.33, 128.82, 61.41, 48.82, 46.27, 39.96, 37.29, 35.71. HRMS (ESI-TOF): *m/z* calcd for $C_{30}H_{27}Cl_3NO_3$ $[M+H]^+$: 554.1051, found 554.1069.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((3-chlorophenyl)methanone) (2l):



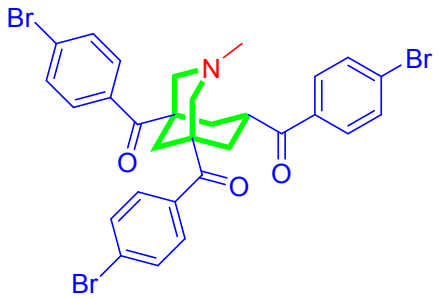
65% yield (35.9 mg). White solid, m.p. 135-137 °C. R_f = 0.33 (PE/EA=10/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (t, *J* = 1.7 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 1.7 Hz, 2H), 7.60 – 7.54 (m, 3H), 7.47 (ddd, *J* = 7.9, 2.1, 1.0 Hz, 3H), 7.37 (t, *J* = 7.9 Hz, 2H), 5.11 – 5.02 (m, 1H), 3.19 (d, *J* = 10.9 Hz, 2H), 2.48 (dd, *J* = 12.0, 1.9 Hz, 2H), 2.41 (s, 3H), 2.26 (ddd, *J* = 14.1, 5.1, 2.1 Hz, 2H), 2.17 (d, *J* = 13.0 Hz, 1H), 2.06 (d, *J* = 13.2 Hz, 1H), 1.93 (t, *J* = 12.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.45, 201.25, 139.12, 137.74, 135.39, 134.81, 133.37, 131.66, 130.31, 129.86, 128.70, 128.06, 126.62, 125.80, 61.19, 48.88, 46.15, 40.07, 37.26, 35.55, 0.14. HRMS (ESI-TOF): *m/z* calcd for $C_{30}H_{27}Cl_3NO_3$ $[M+H]^+$: 554.1051, found 554.1056.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((3-chlorophenyl)methanone) (2m):



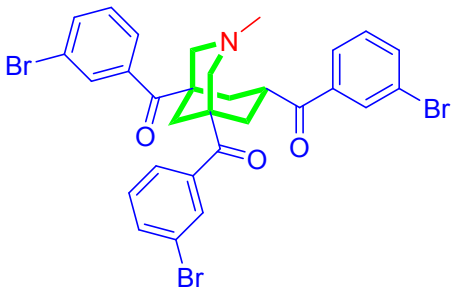
51% yield (28.2 mg). White solid, m.p. 121-122 °C. R_f = 0.35 (PE/EA=10/1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (dt, *J* = 13.3, 6.8 Hz, 4H), 7.34 – 7.30 (m, 4H), 7.29 – 7.25 (m, 2H), 7.07 (dd, *J* = 7.6, 1.4 Hz, 2H), 5.13 – 5.07 (m, 1H), 3.08 (d, *J* = 10.6 Hz, 2H), 2.32 – 2.26 (m, 2H), 2.22 (s, 3H), 2.22 – 2.18 (m, 2H), 1.99 – 1.88 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 207.87, 205.77, 139.38, 139.23, 131.53, 130.76, 130.50, 130.41, 130.14, 129.36, 128.64, 127.06, 126.60, 126.36, 60.91, 49.25, 46.14, 44.75, 36.28, 33.92. HRMS (ESI-TOF): *m/z* calcd for $C_{30}H_{27}Cl_3NO_3$ $[M+H]^+$: 554.1051, found 554.1064.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((4-bromophenyl)methanone (2n):



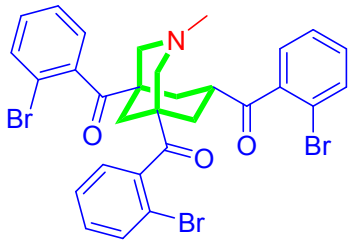
81% yield (55.5 mg). White solid, m.p. 156-158 °C. R_f = 0.33 (PE/EA=10/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.9 Hz, 1H), 7.68 (dd, *J* = 18.3, 8.6 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.59 – 7.55(m, 8H), 5.13 – 5.08 (m, 1H), 3.21 (d, *J* = 11.3 Hz, 2H), 2.43 (d, *J* = 11.5 Hz, 2H), 2.37 (s, 3H), 2.26 (d, *J* = 13.9 Hz, 2H), 2.10 (d, *J* = 13.5 Hz, 2H), 1.95 (t, *J* = 13.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.68, 201.52, 136.31, 134.89, 132.35, 131.93, 131.82, 130.33, 129.83, 129.59, 61.47, 48.87, 47.20, 46.28, 40.03, 37.30, 35.70, 29.84. HRMS (ESI-TOF): *m/z* calcd for $C_{30}H_{27}Br_3NO_3$ $[M+H]^+$: 685.9536, found 685.9548.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((3-bromophenyl)methanone (2o):



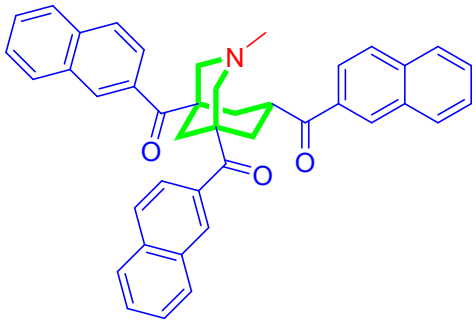
51% yield (34.9 mg). White solid, m.p. 123-124 °C. R_f = 0.32 (PE/EA=10/1). ^{1}H NMR (600 MHz, $CHCl_3$) δ 8.06 (s, 1H), 7.85 (d, *J* = 7.3 Hz, 1H), 7.80 (s, 2H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.65 – 7.59 (m, 4H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 2H), 5.08 – 5.02 (m, 1H), 3.18 (d, *J* = 11.5 Hz, 2H), 2.49 (d, *J* = 11.2 Hz, 2H), 2.41 (s, 3H), 2.25 (d, *J* = 16.5 Hz, 3H), 2.17 (d, *J* = 13.0 Hz, 1H), 2.05 (d, *J* = 12.7 Hz, 1H), 1.94 (q, *J* = 12.8, 11.6 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 204.22, 201.08, 139.28, 136.27, 134.57, 131.66, 131.60, 131.31, 130.97, 130.55, 130.09, 126.88, 126.21, 123.43, 122.89, 61.15, 48.86, 47.28, 46.14, 40.00, 37.27, 35.55, 29.84. HRMS (ESI-TOF): *m/z* calcd for $C_{30}H_{27}Br_3NO_3$ $[M+H]^+$: 685.9536, found 685.9551.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((2-bromophenyl)methanone (2p):



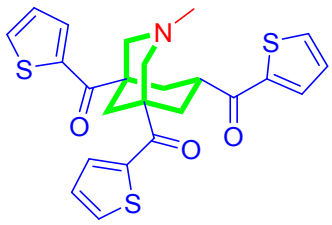
41% yield (28.1 mg). White solid, m.p. 116-117 °C. R_f = 0.34 (PE/EA=10/1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.9 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.39 – 7.26 (m, 6H), 7.26 – 7.24 (m, 1H), 7.08 – 7.05 (m, 2H), 5.11 – 5.05 (m, 1H), 3.09 (d, *J* = 10.7 Hz, 2H), 2.33 (d, *J* = 10.0 Hz, 2H), 2.23 (s, 3H), 2.21 (d, *J* = 5.5 Hz, 2H), 2.03 – 1.92 (m, 4H). ^{13}C NMR (151 MHz, CDCl3) δ 208.27, 202.69, 133.67, 133.34, 131.54, 130.59, 127.61, 127.15, 126.42, 117.76, 61.07, 49.13, 46.16, 44.70, 34.11, 31.57, 30.32, 29.84, 29.84. HRMS (ESI-TOF): *m/z* calcd for $C_{30}H_{27}Br_3NO_3$ $[M+H]^+$: 685.9536, found 685.9521.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris(naphthalen-2-ylmethanone) (2q):



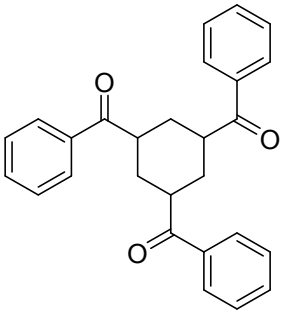
63% yield (37.9 mg). White solid, m.p. 153-155 °C. R*f* = 0.3 (PE/EA = 10/1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.24 (s, 2H), 8.05 – 8.01 (m, 2H), 7.94 (d, *J* = 8.6 Hz, 1H), 7.90 (d, *J* = 7.9 Hz, 3H), 7.85 (dd, *J* = 8.3, 4.7 Hz, 4H), 7.77 (dd, *J* = 8.6, 1.5 Hz, 2H), 7.63 (t, *J* = 6.9 Hz, 1H), 7.60 – 7.58 (m, 1H), 7.57 – 7.51 (m, 4H), 5.45 – 5.39 (m, 1H), 3.41 (d, *J* = 11.4 Hz, 2H), 2.61 (d, *J* = 11.5 Hz, 2H), 2.50 (d, *J* = 14.1 Hz, 2H), 2.48 (s, 3H), 2.41 – 2.37 (m, 1H), 2.36 – 2.30 (m, 1H), 2.17 (t, *J* = 12.6 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 206.09, 202.80, 135.79, 135.16, 134.56, 133.66, 132.77, 132.44, 130.14, 129.82, 129.36, 128.84, 128.65, 128.26, 128.07, 127.95, 127.83, 126.98, 126.91, 124.57, 124.47, 61.78, 49.21, 46.38, 40.26, 37.77, 36.17, 29.84. HRMS (ESI): *m/z* calcd for $C_{42}H_{36}NO_3$ $[M+H]^+$: 602.2690, found 602.2706.

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris(thiophen-2-ylmethanone) (2r):



73% yield (34.2 mg). White solid, m.p. 178-179 °C. R*f* = 0.28 (PE/EA = 10/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 3.6 Hz, 2H), 7.80 (d, *J* = 3.4 Hz, 1H), 7.66 (d, *J* = 4.8 Hz, 1H), 7.60 (d, *J* = 4.9 Hz, 2H), 7.18 (t, *J* = 4.2 Hz, 1H), 7.14 – 7.10 (m, 2H), 5.18 – 5.09 (m, 1H), 3.35 (d, *J* = 11.5 Hz, 2H), 2.51 – 2.42 (m, 4H), 2.39 (s, 3H), 2.28 – 2.17 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.68, 195.49, 143.70, 141.97, 134.19, 133.47, 132.46, 132.20, 128.38, 128.13, 62.15, 48.59, 46.39, 42.18, 37.90, 36.47. HRMS (ESI): *m/z* calcd for $C_{24}H_{24}NO_3S_3$ $[M+H]^+$: 470.0913, found 470.0921.

Cyclohexane-1,3,5-triyltris(phenylmethanone) (3a):

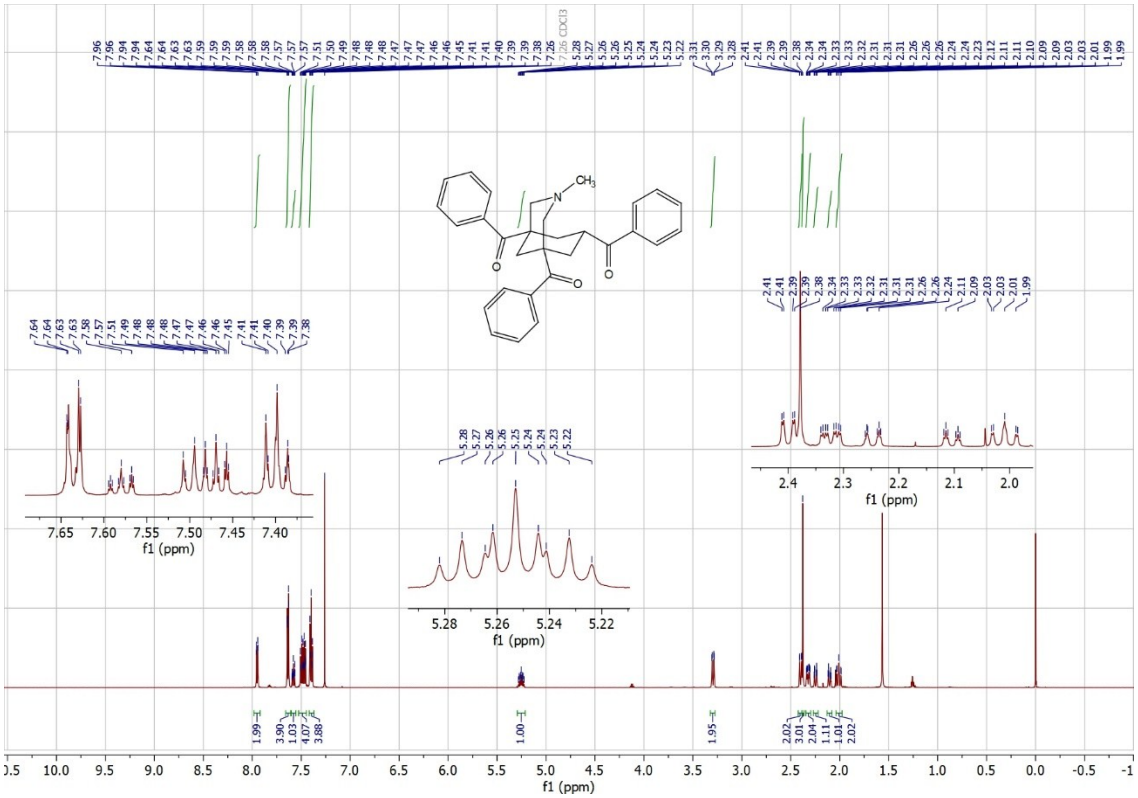


A vial was charged with aromatic ketone **1** (0.3 mmol), paraformaldehyde (30 mg, 1 mmol), Me_2NH (40% *w*/*w* in H_2O, 0.41 mL, 1.5 mmol) and concentrated HCl (0.05 mL, 0.6 mmol) in EtOH/glycerol mixture (1:1 *v*/*v*, 2 mL). The reaction mixture was stirred at 80 °C for 6 h. After cooling to room temperature, the reaction mixture was diluted with water (5 mL). The aqueous phase was extracted with dichloromethane and the combined were washed with brine, dried over Na_2SO_4, filtered and concentrated. The mixture was concentrated in vacuo and purified by flash chromatography on silica gel to afford the desired product **2.** 83% yield (32.9 mg). White solid, m.p. 175-176 °C. R_f = 0.32 (PE/EA = 10/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.91 (m, 6H), 7.56 (t, *J* = 7.4 Hz, 3H), 7.47 (t, *J* = 7.6 Hz, 6H), 3.66 (tt, *J* = 12.4, 2.9 Hz, 3H), 2.23 (d, *J* = 13.1 Hz, 3H), 1.84 (q, *J* = 12.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.35, 135.92, 133.16, 128.78, 128.24, 44.48, 31.47. HRMS (ESI): *m/z* calcd for $C_{27}H_{25}O_3$ $[M+H]^+$: 397.1798, found 397.1773.

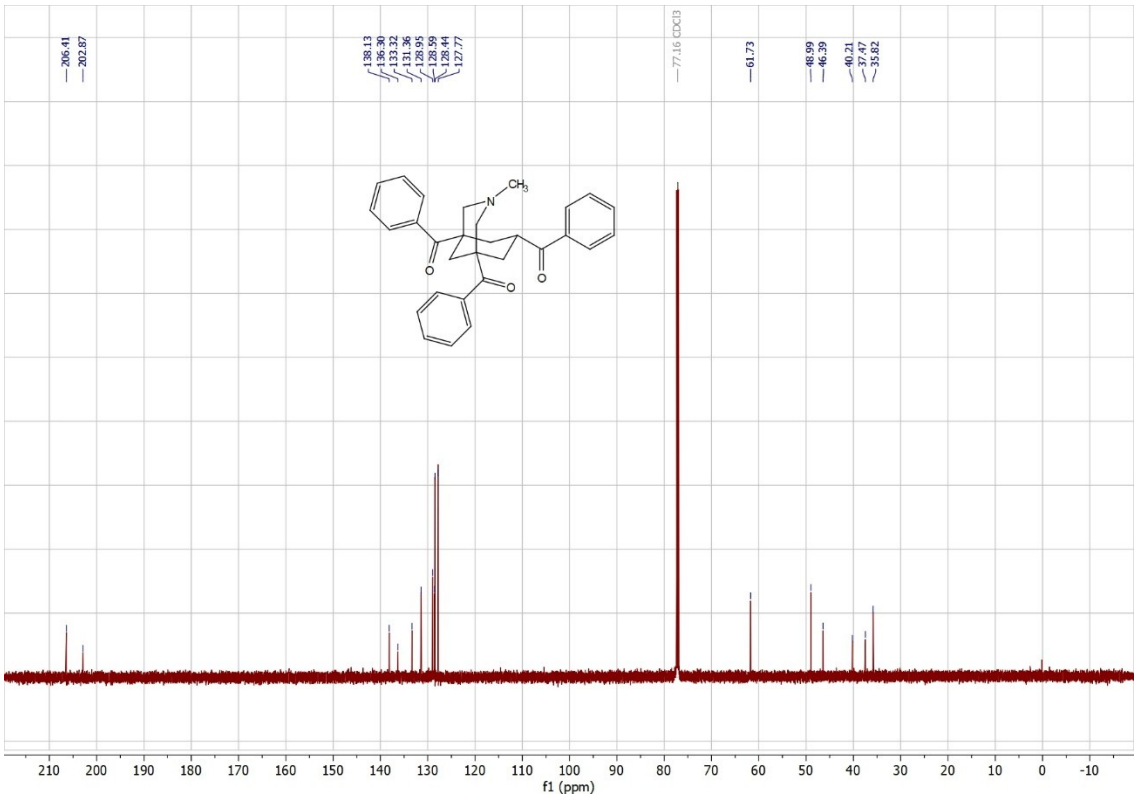
Copies of NMR Spectra

(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris(phenylmethanone) (2a)

^{1}H-NMR

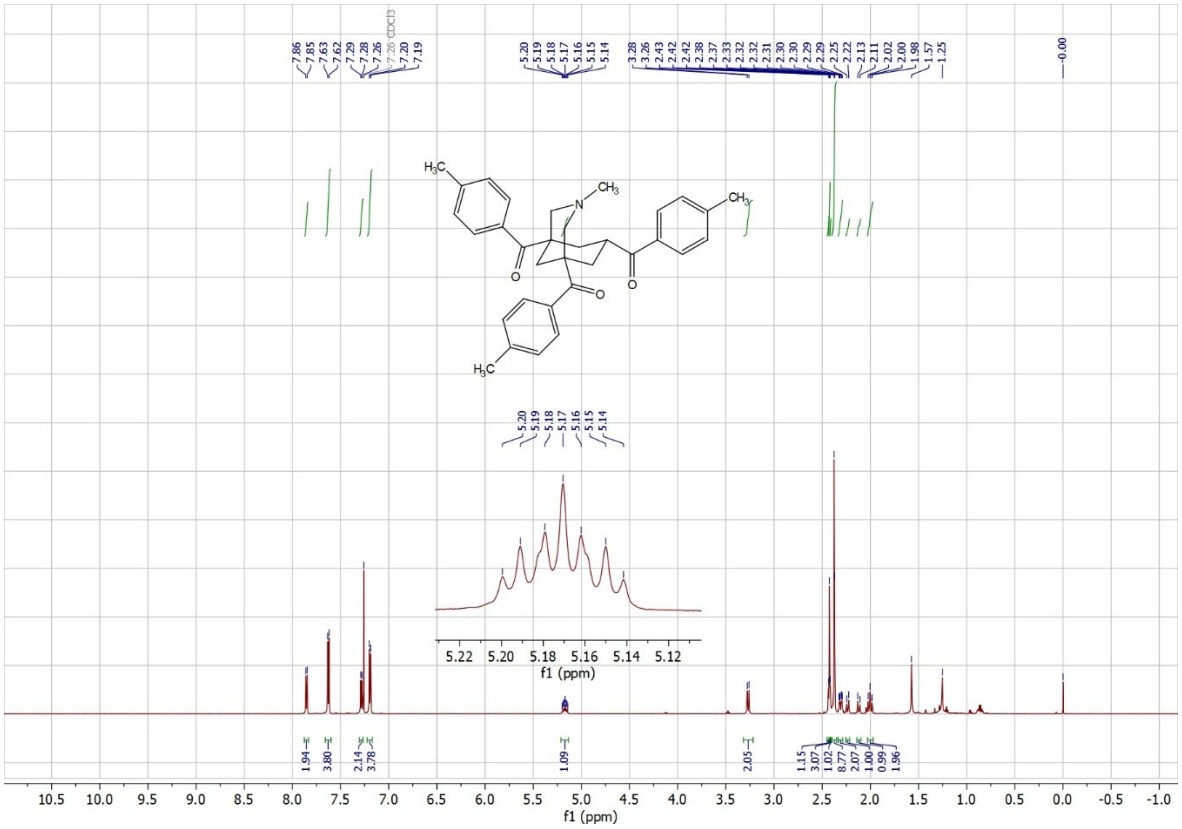


^{13}C-NMR

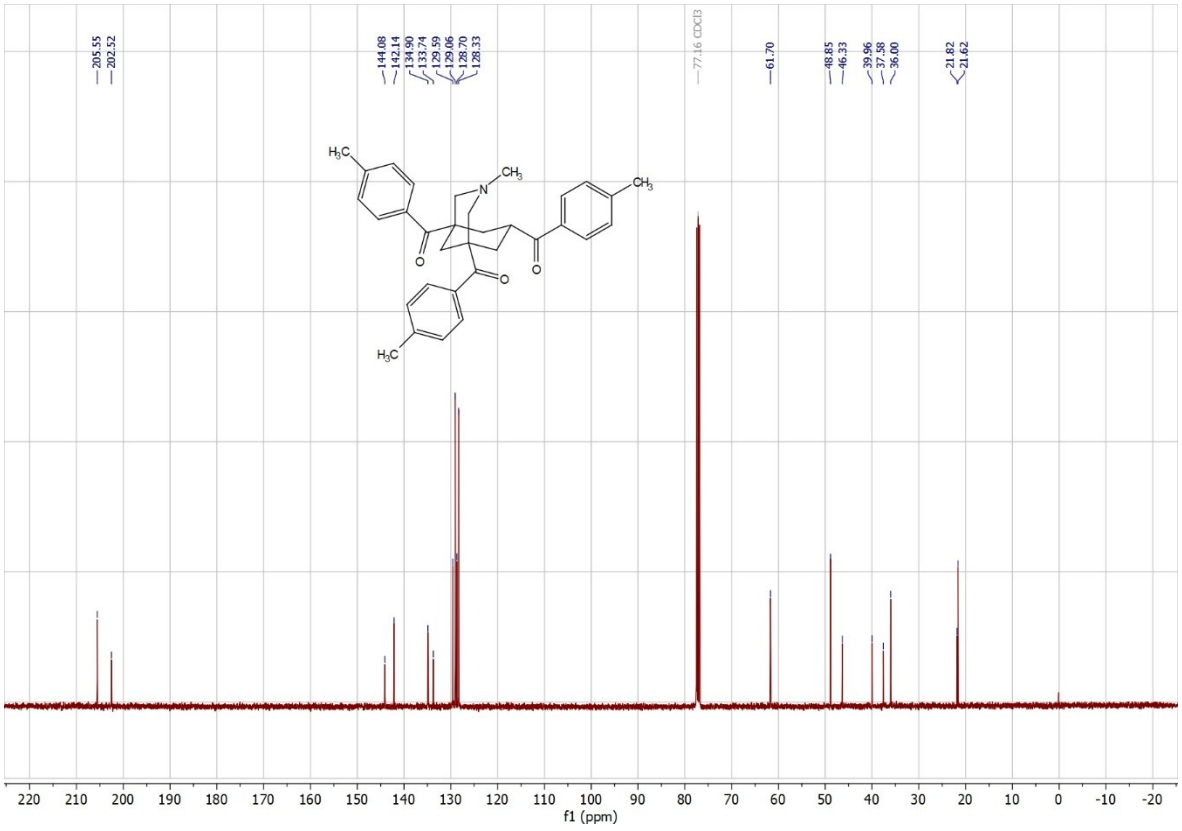


(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris(*p*-tolylmethanone) (2b)

^{1}H-NMR

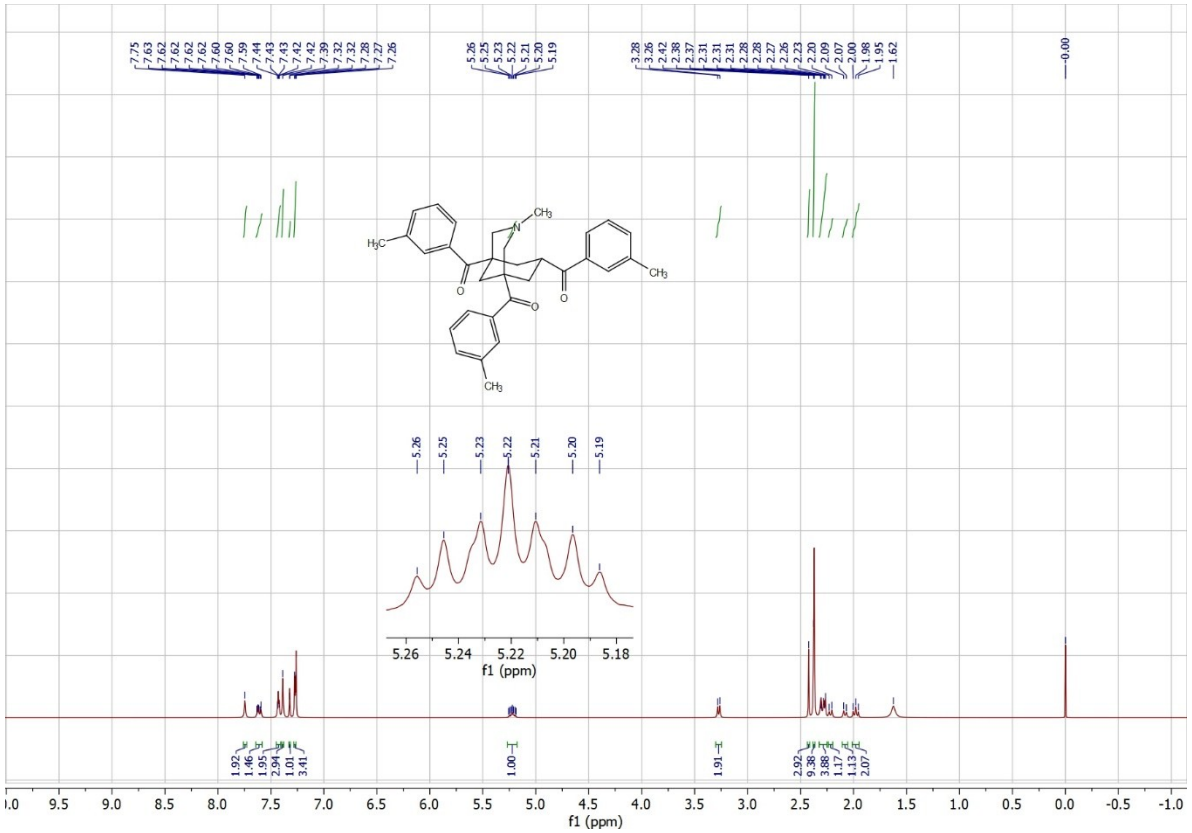


^{13}C-NMR

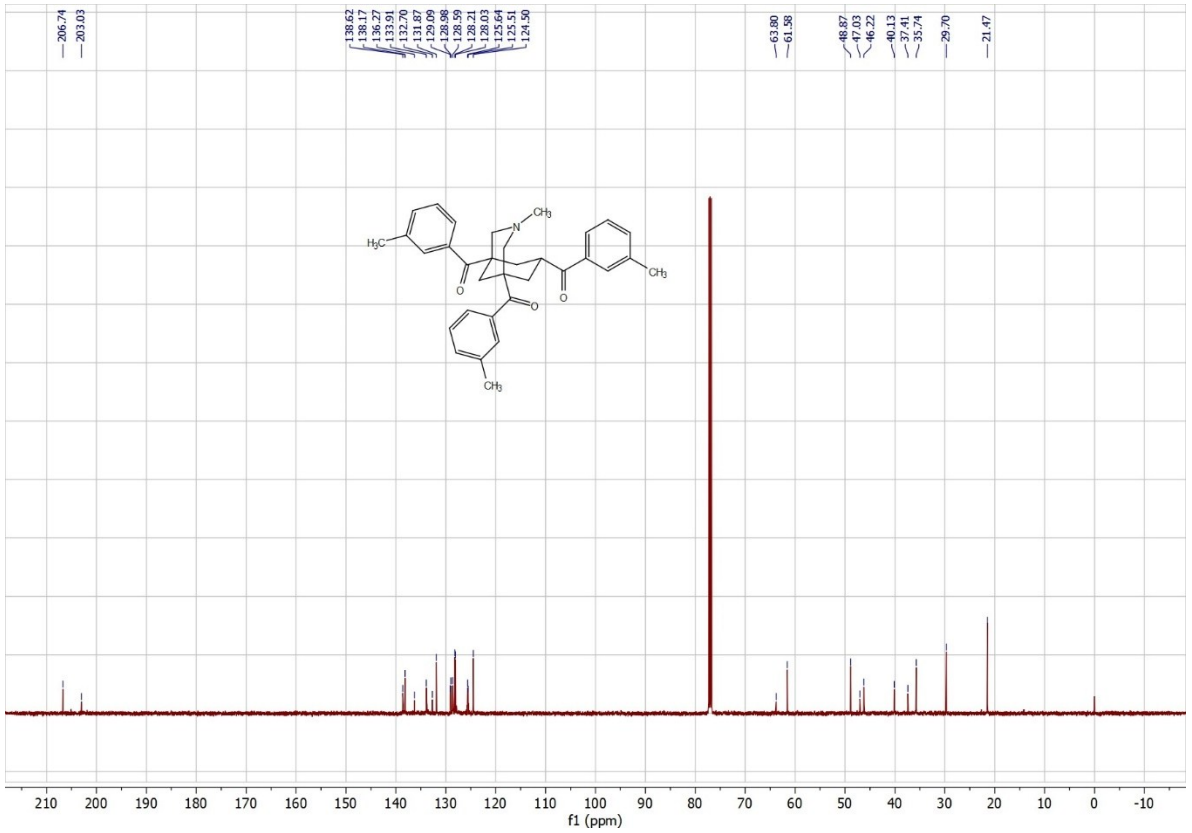


(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris(*m*-tolylmethanone) (2c)

^{1}H-NMR

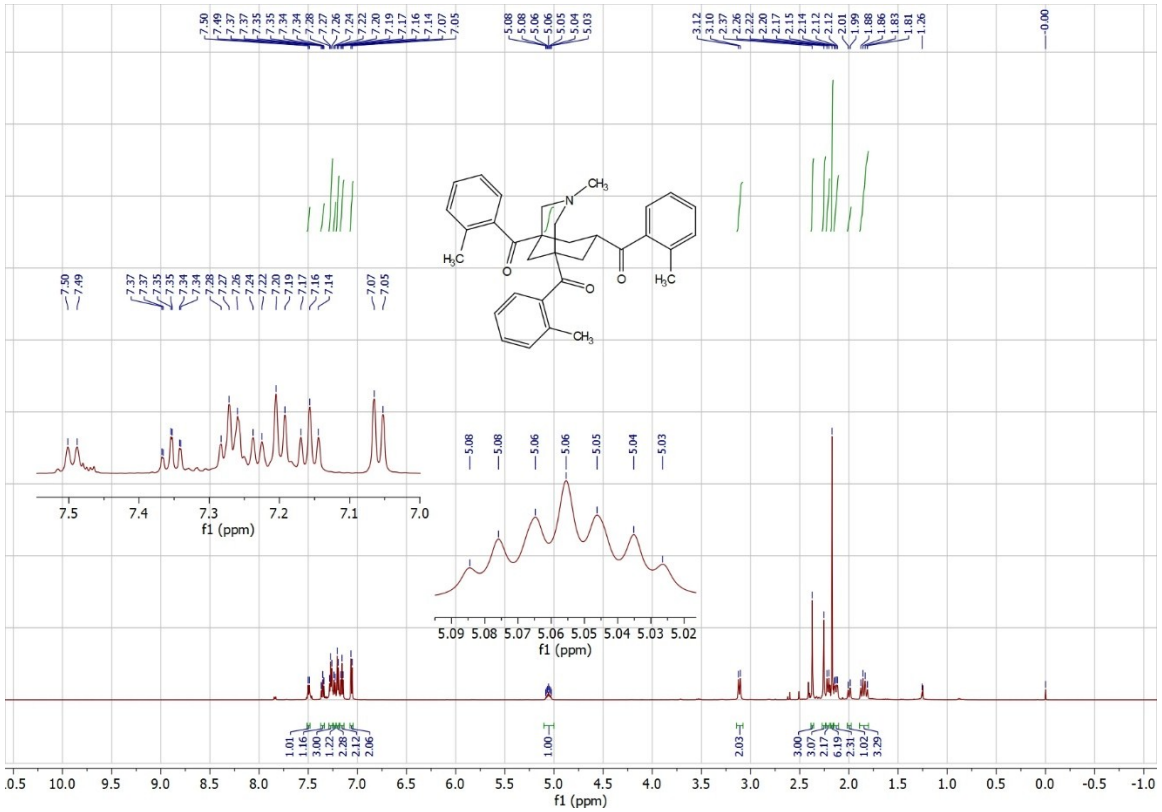


^{13}C-NMR

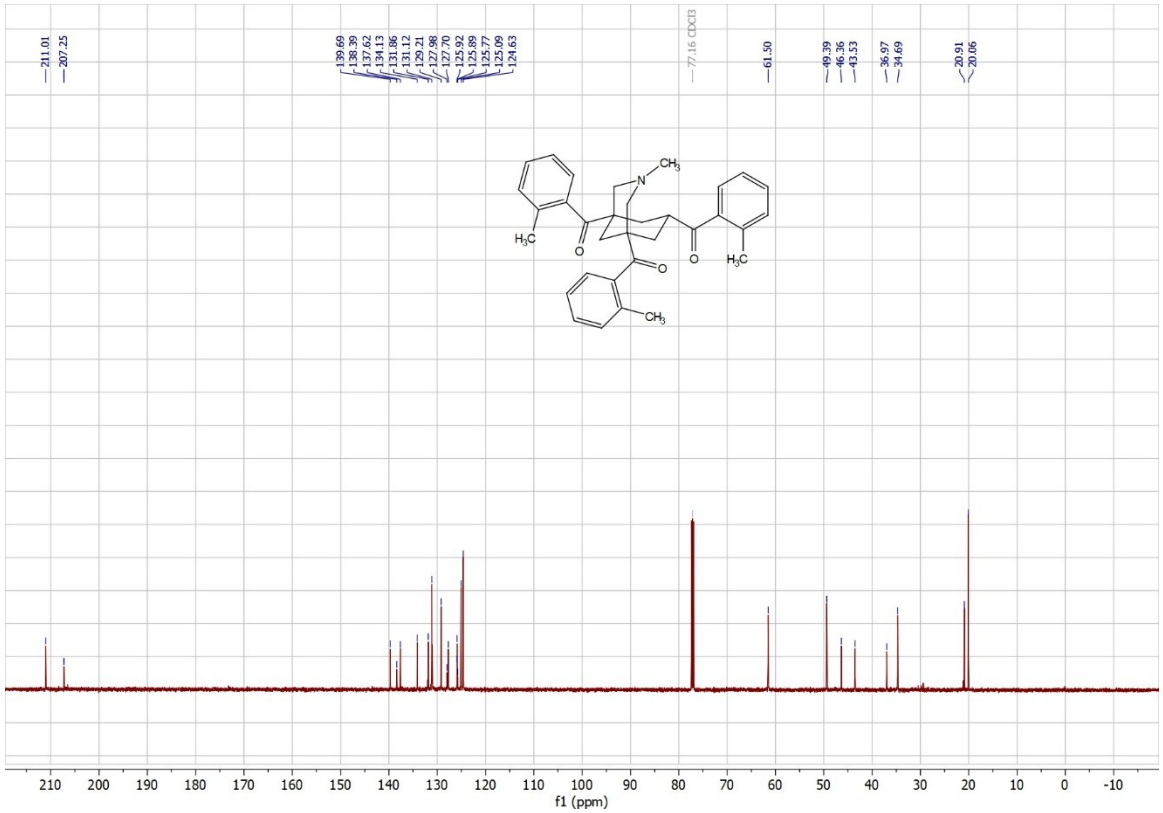


(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris(*o*-tolylmethanone) (2d)

^{1}H-NMR

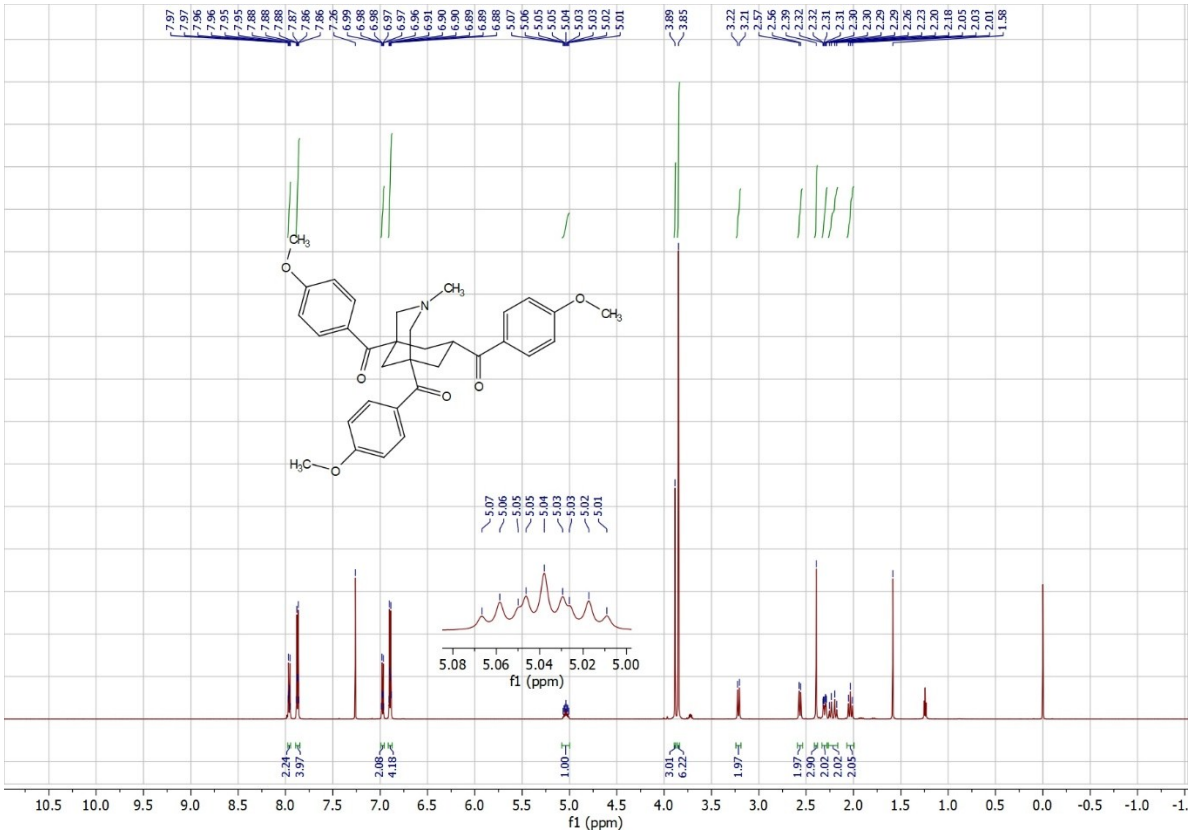


^{13}C-NMR

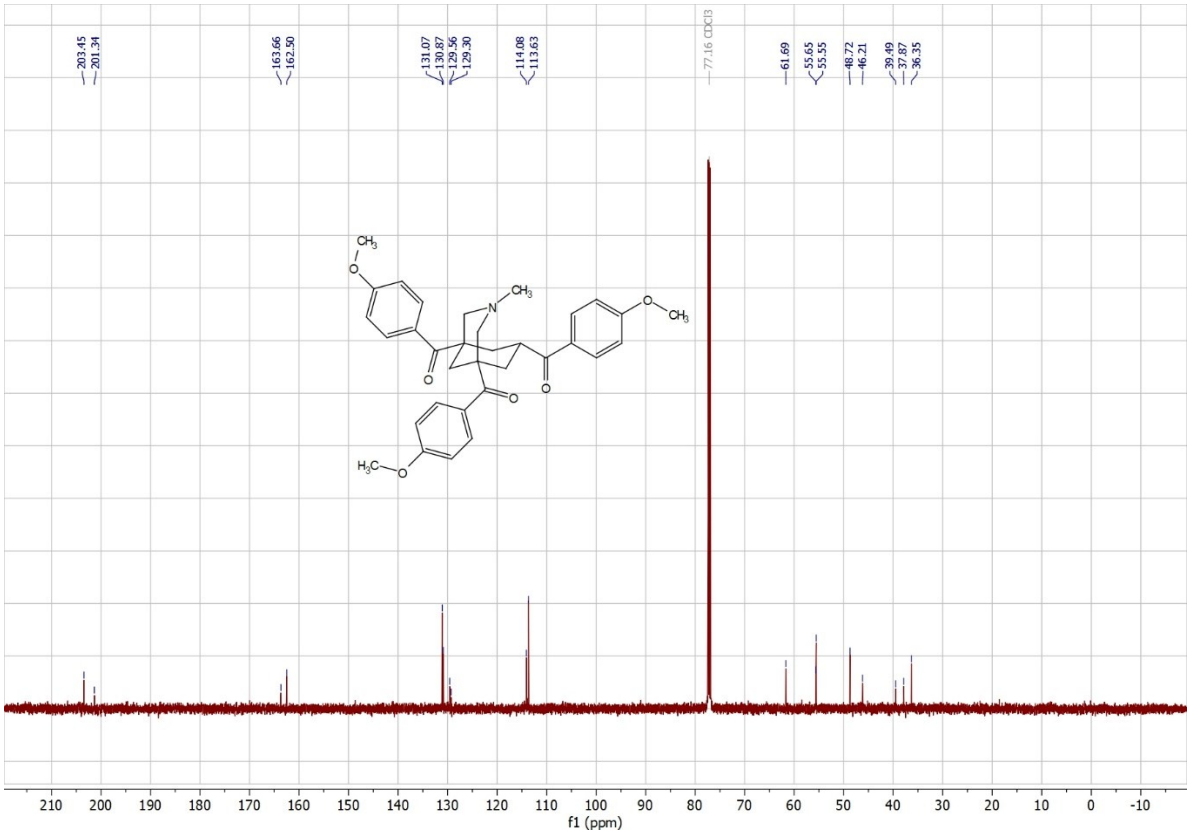


(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((4-methoxyphenyl)methanone) (2e)

^{1}H-NMR

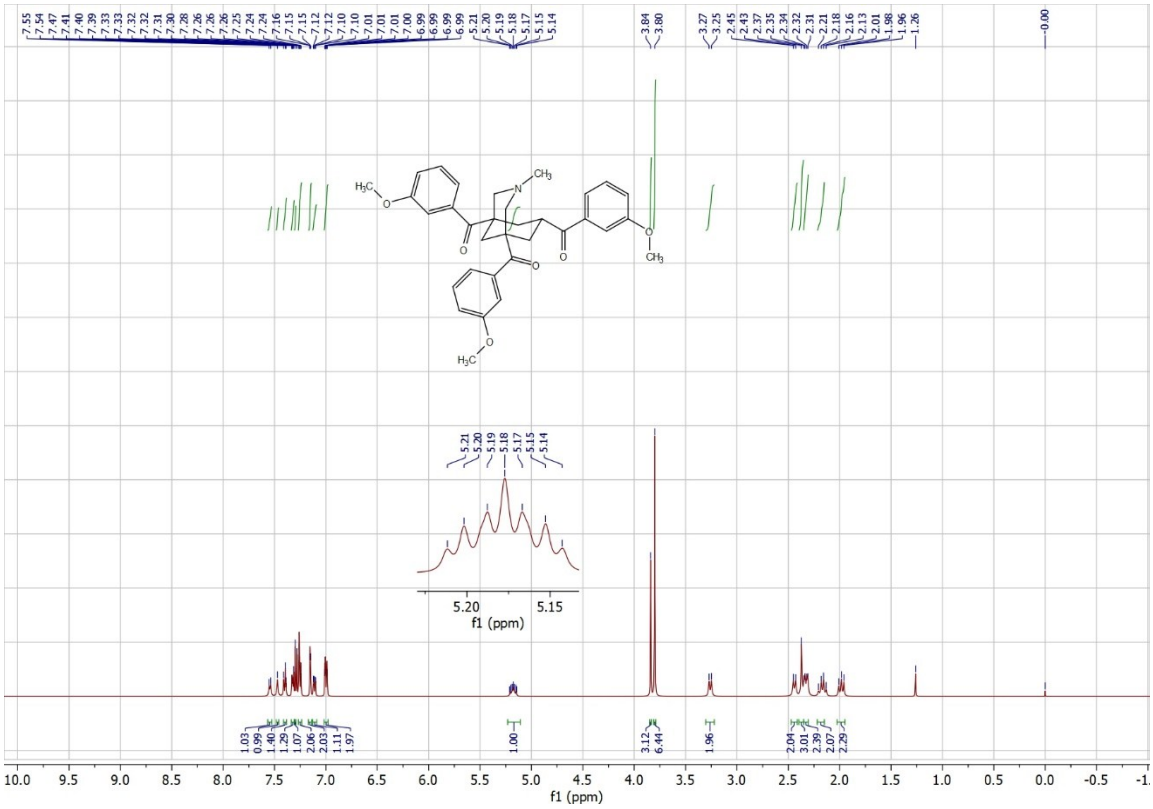


^{13}C-NMR

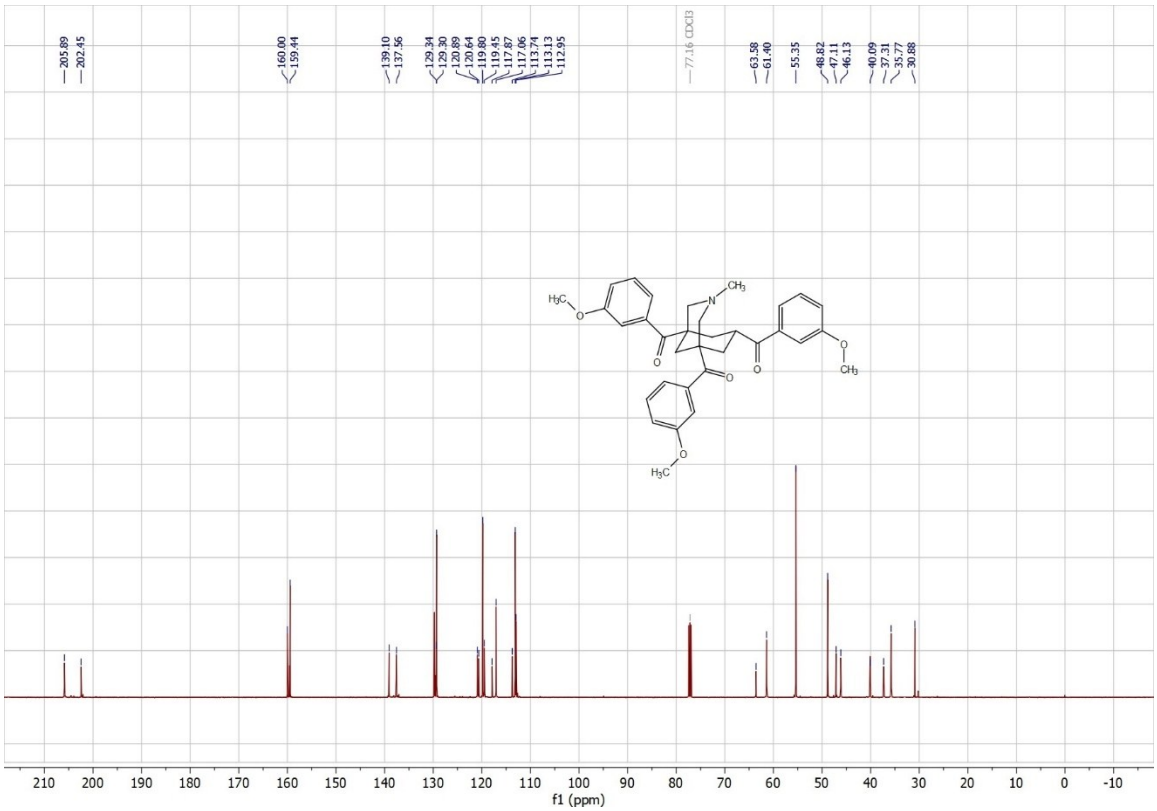


(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((3-methoxyphenyl)methanone) (2f)

^{1}H-NMR

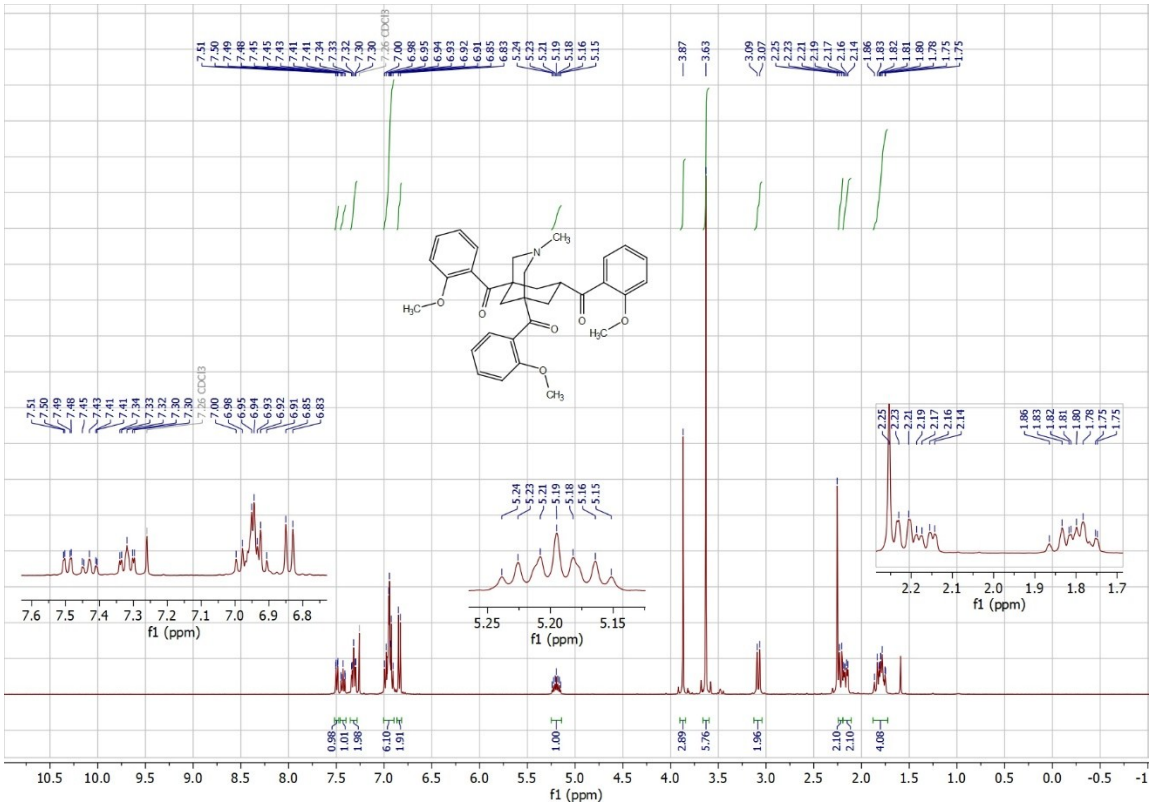


^{13}C-NMR

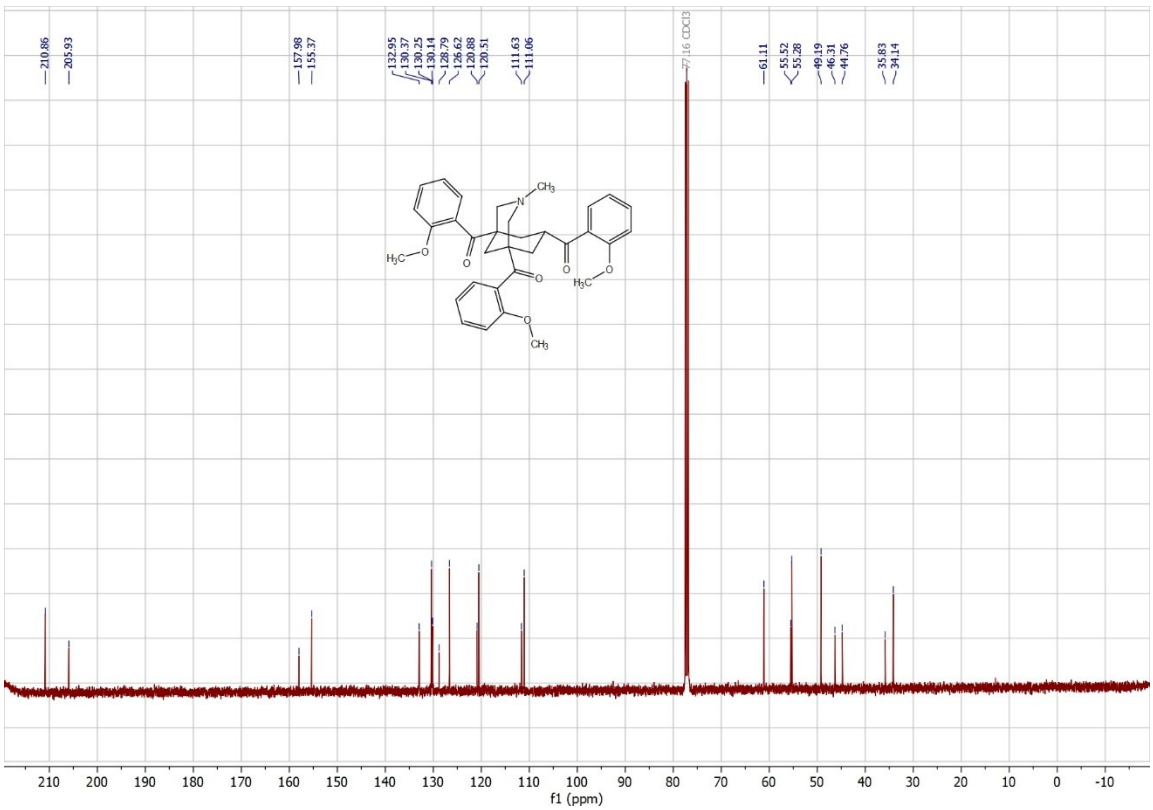


(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((2-methoxyphenyl)methanone) (2g)

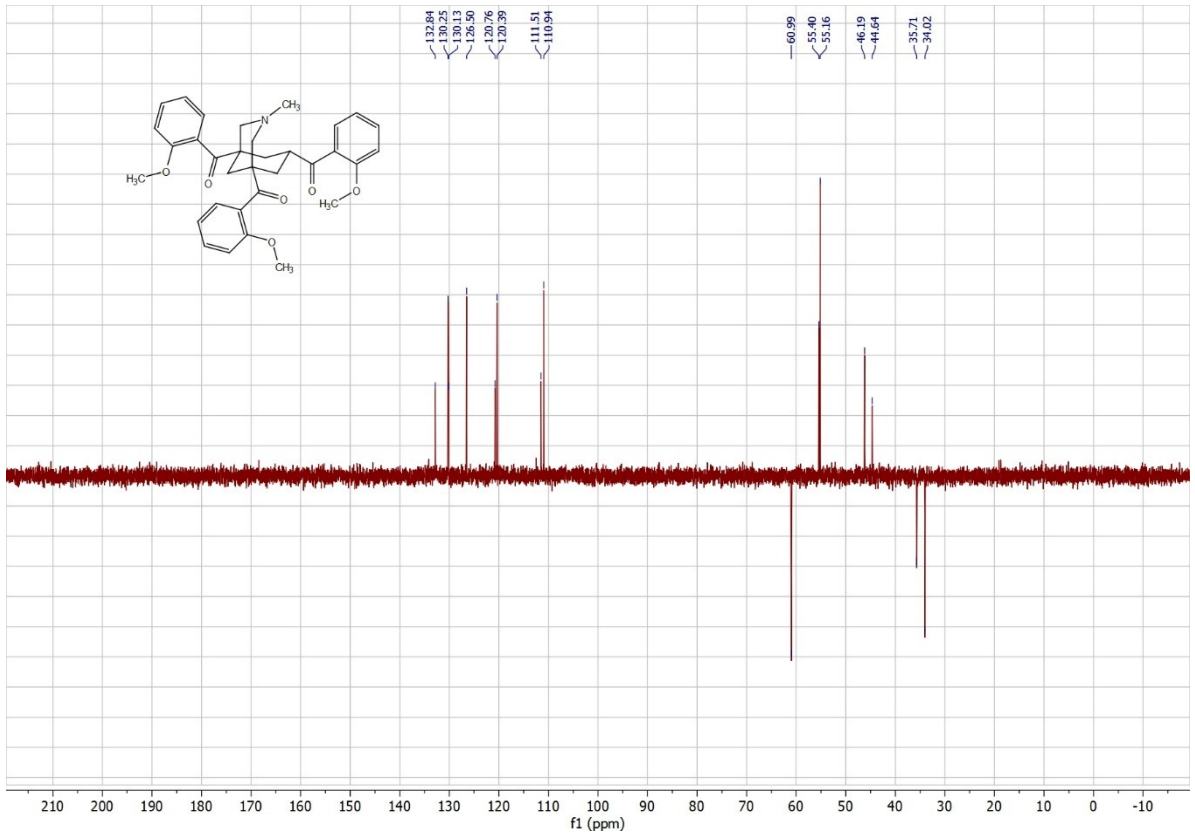
^{1}H-NMR



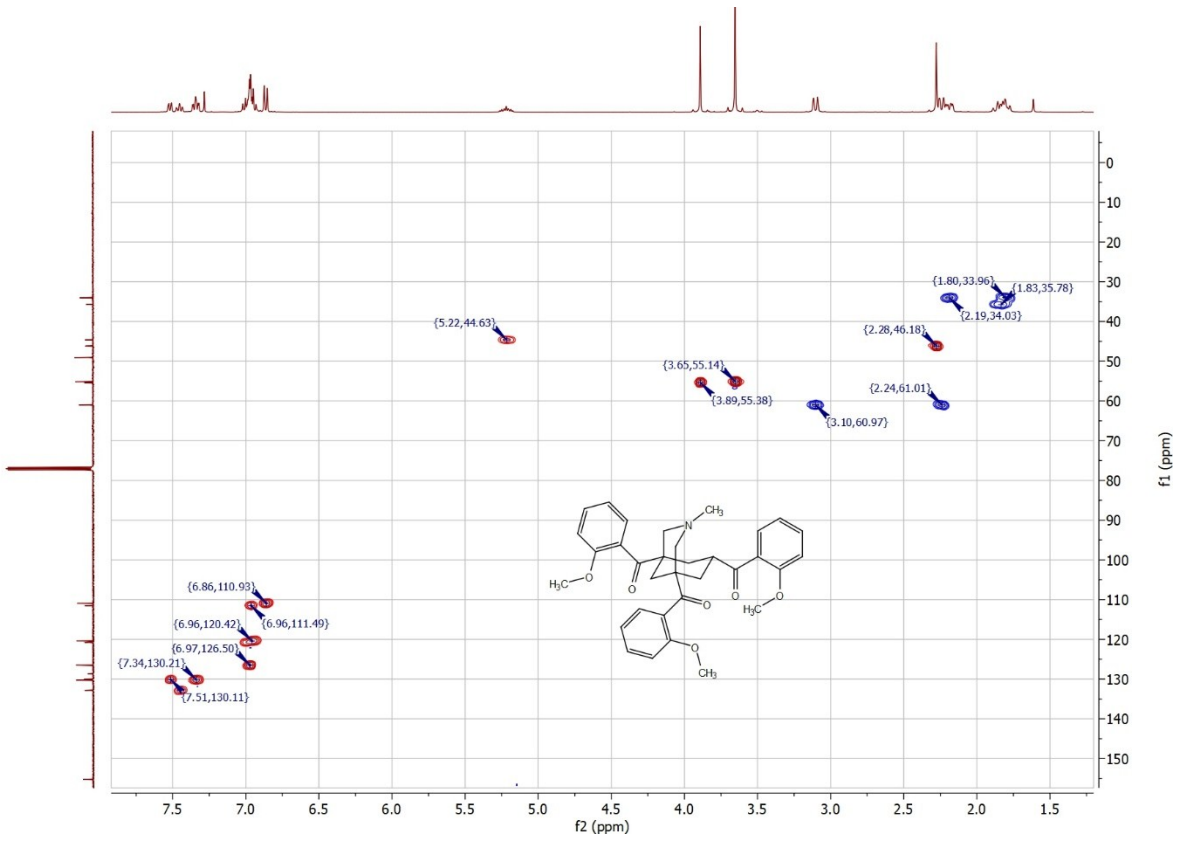
^{13}C-NMR



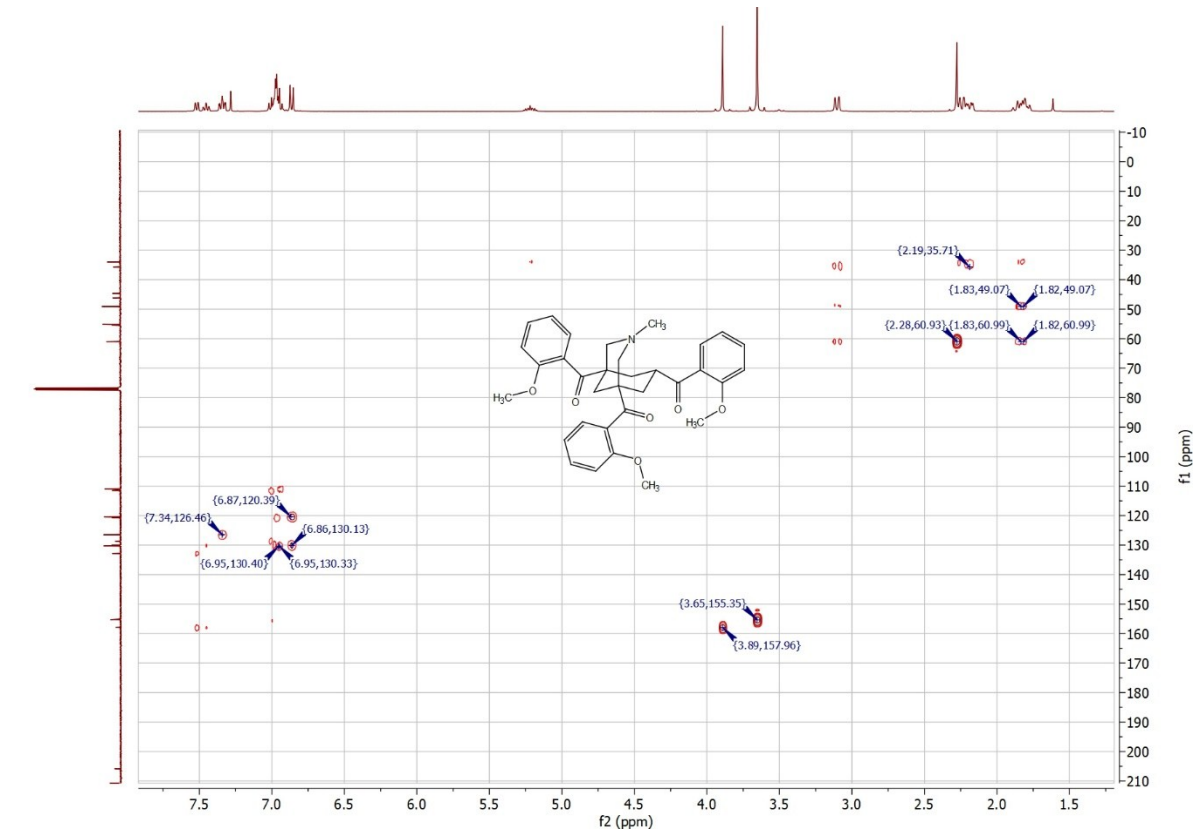
DEPT135



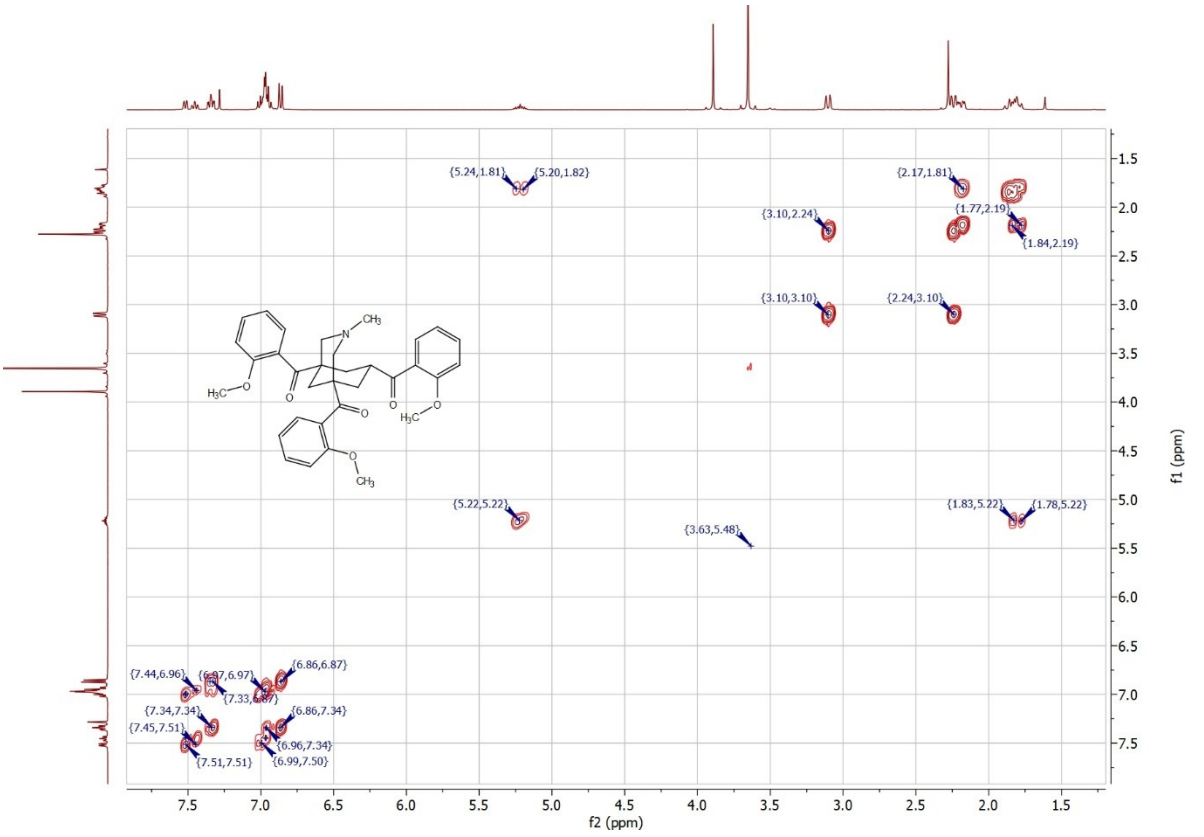
^{1}H-^{13}C HMBC



^{1}H-^{13}C HSQC

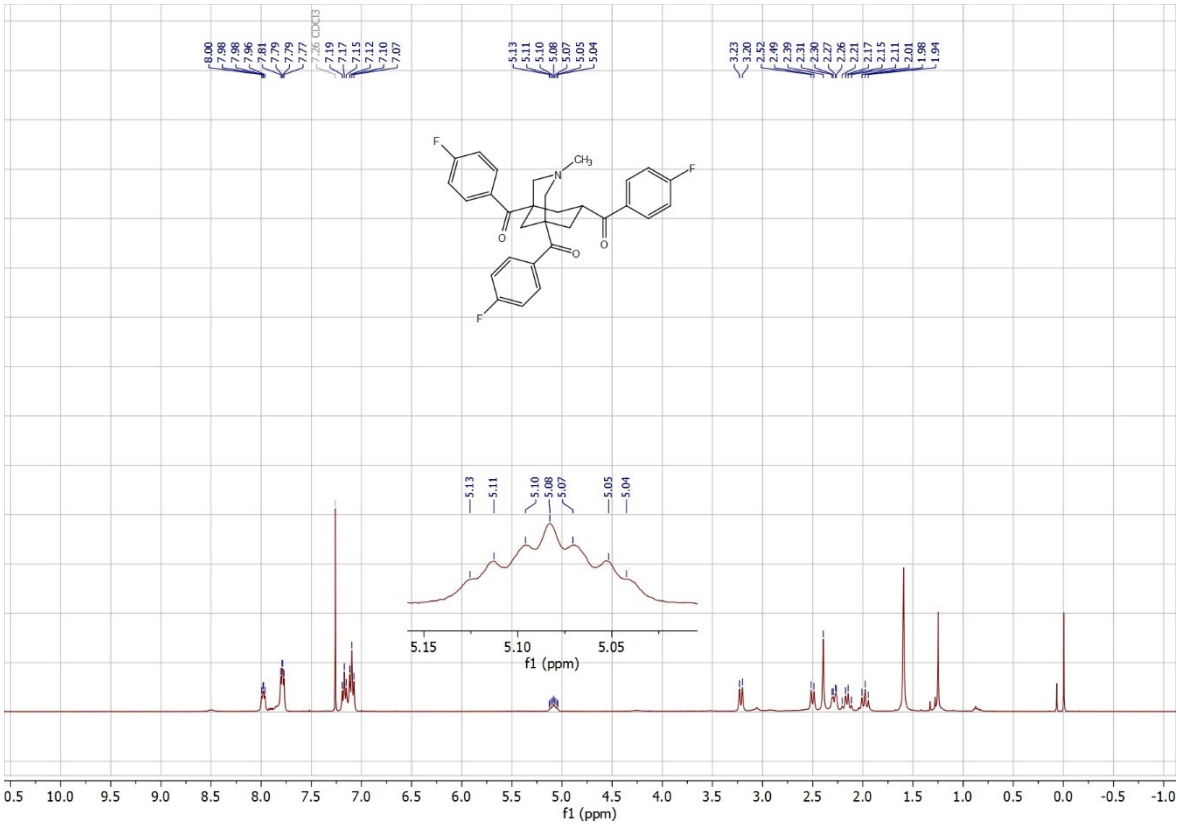


^{1}H-^{1}H COSY

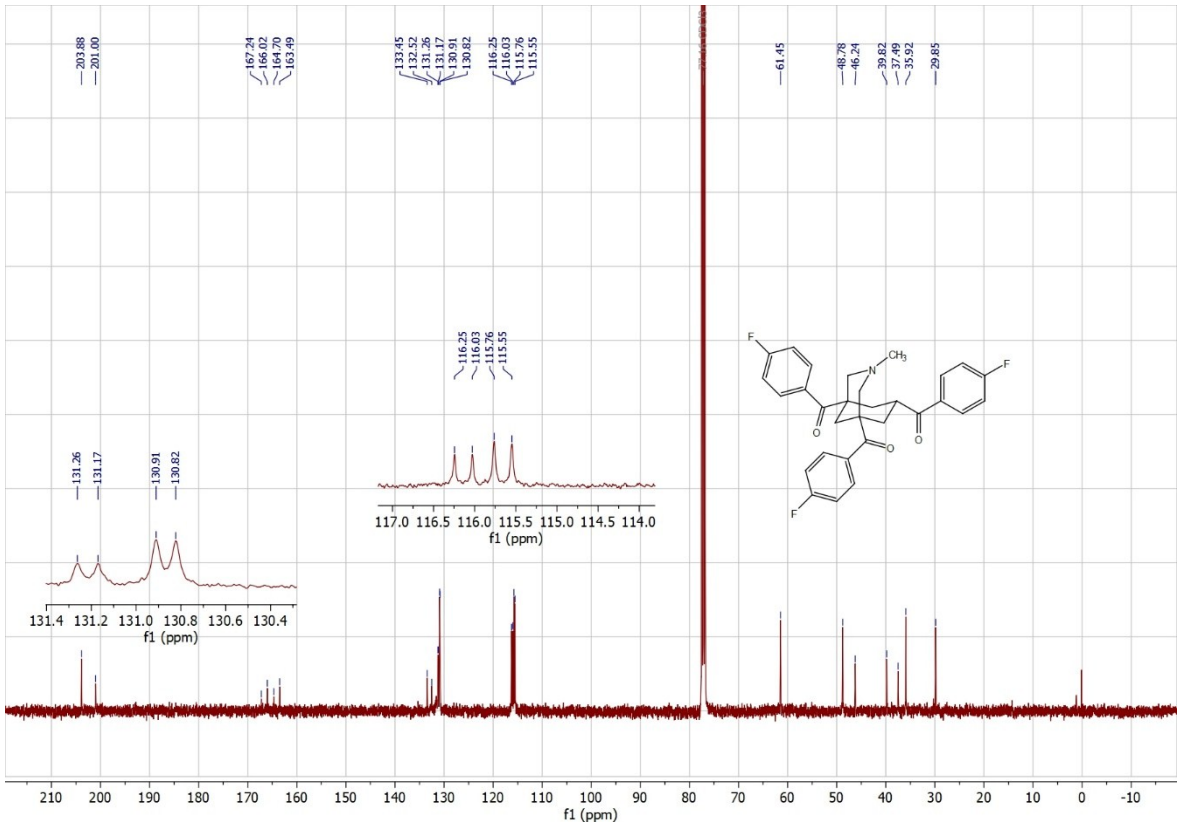


(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((4-fluorophenyl)methanone (2h)

^{1}H-NMR

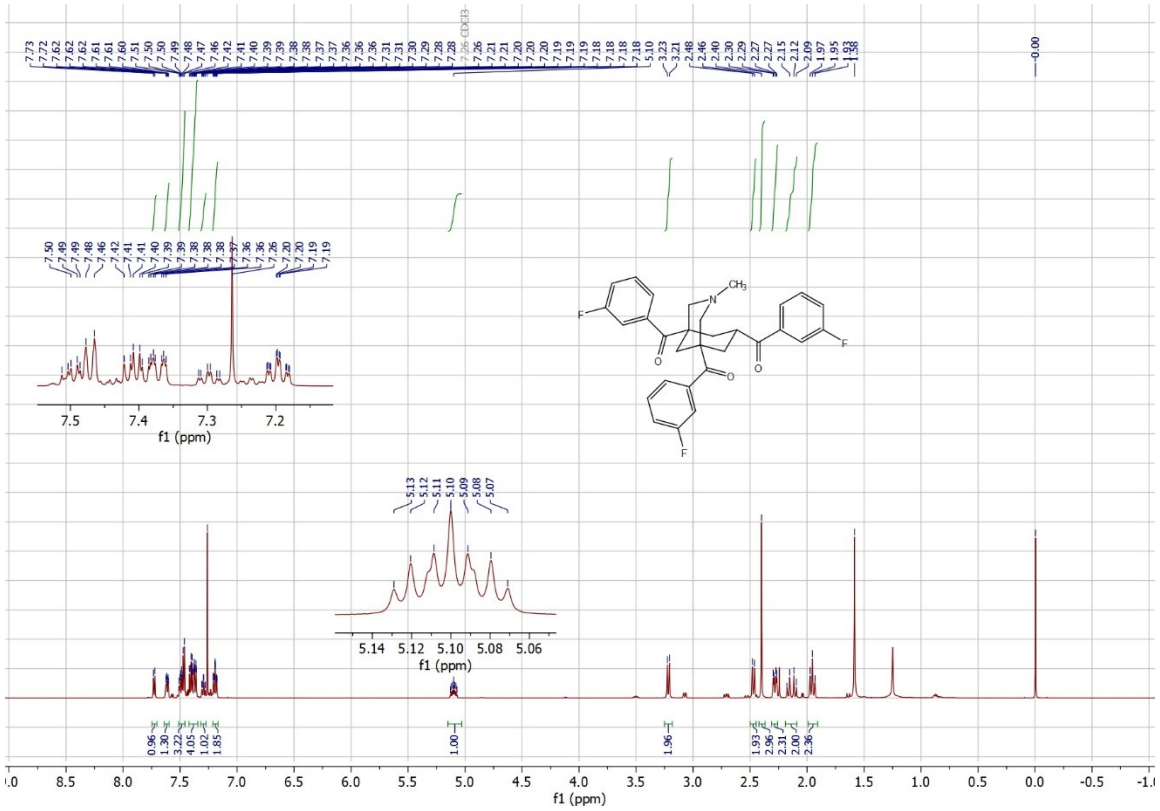


^{13}C-NMR

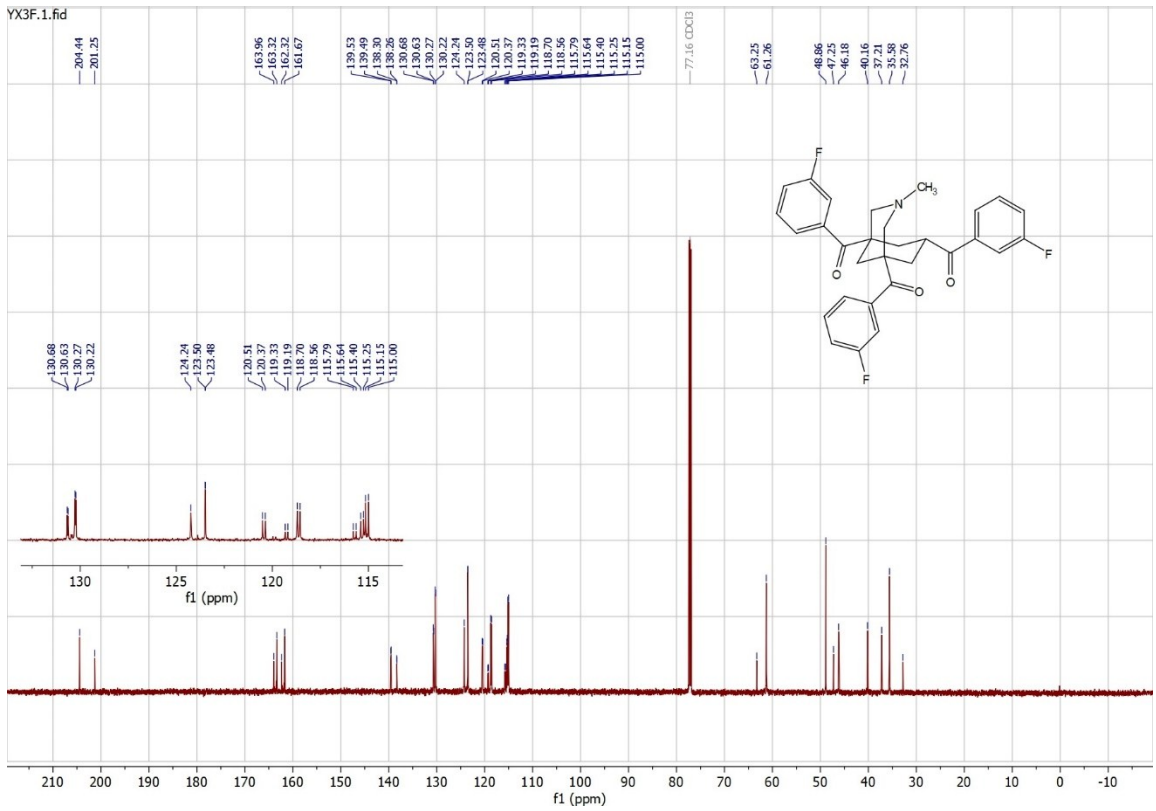


(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((3-fluorophenyl)methanone (2i)

^{1}H-NMR

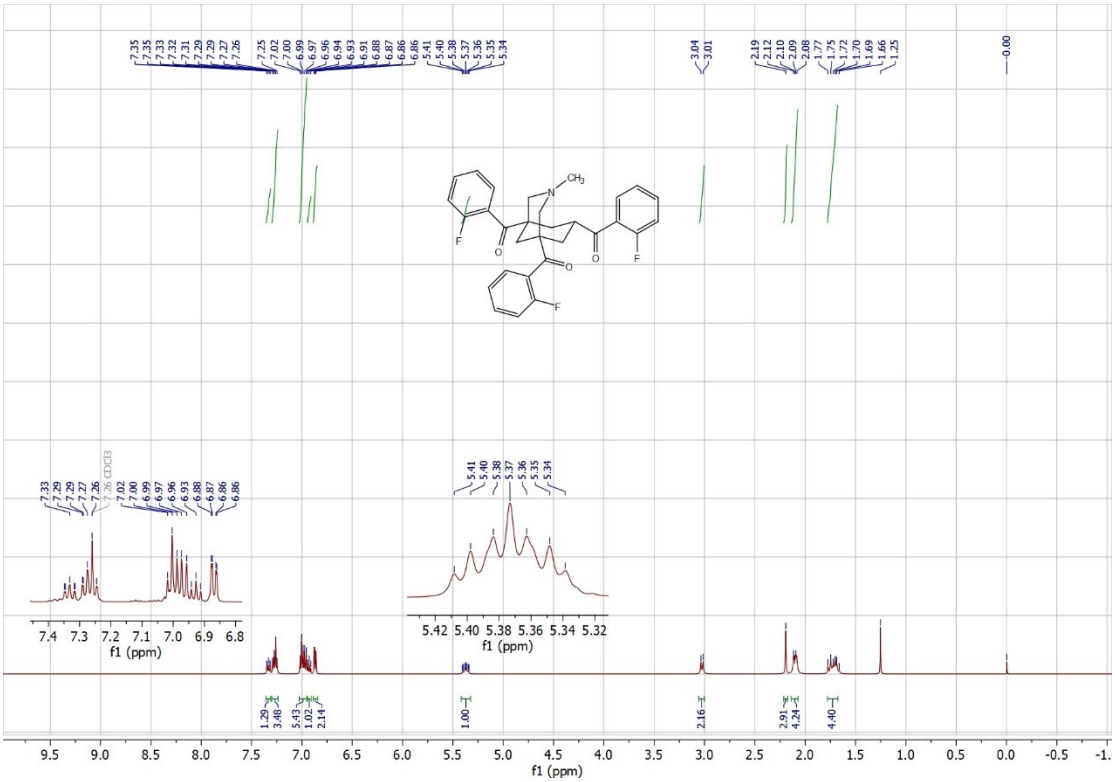


^{13}C-NMR

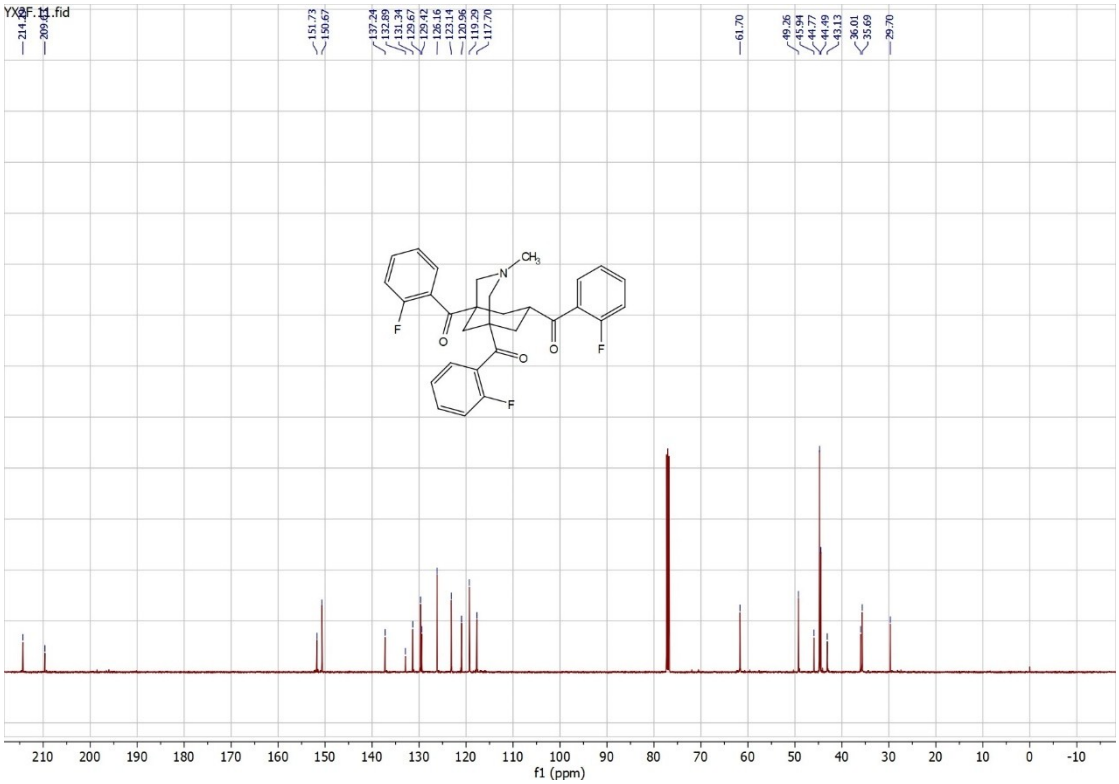


(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((2-fluorophenyl)methanone (2j)

^{1}H-NMR

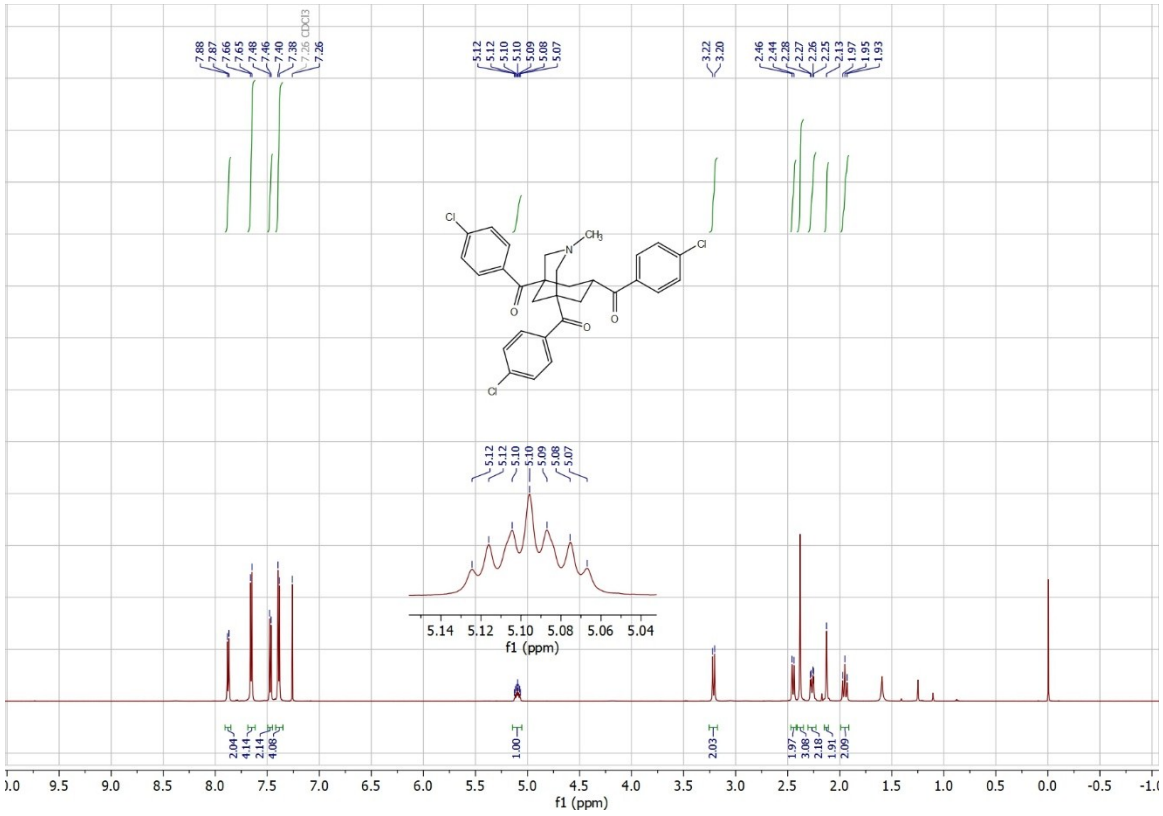


^{13}C-NMR

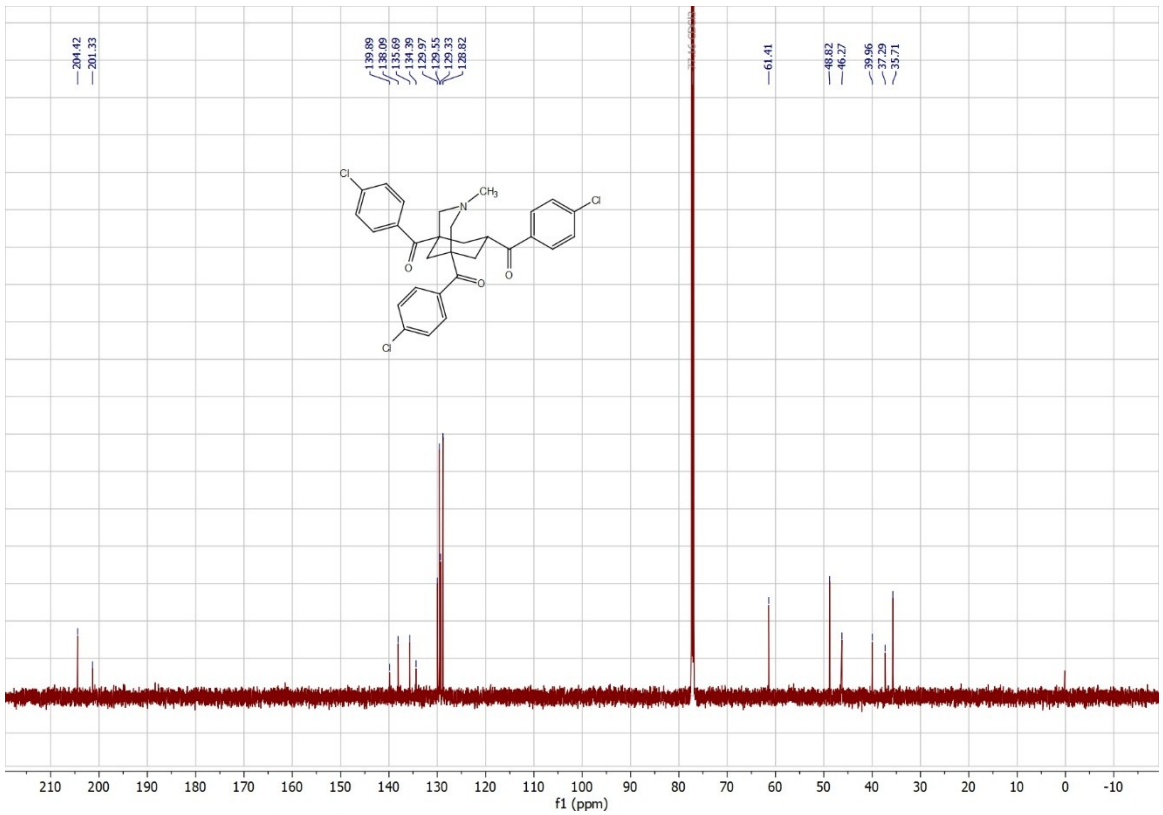


3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((4-chlorophenyl)methanone) (2k)

^{1}H-NMR

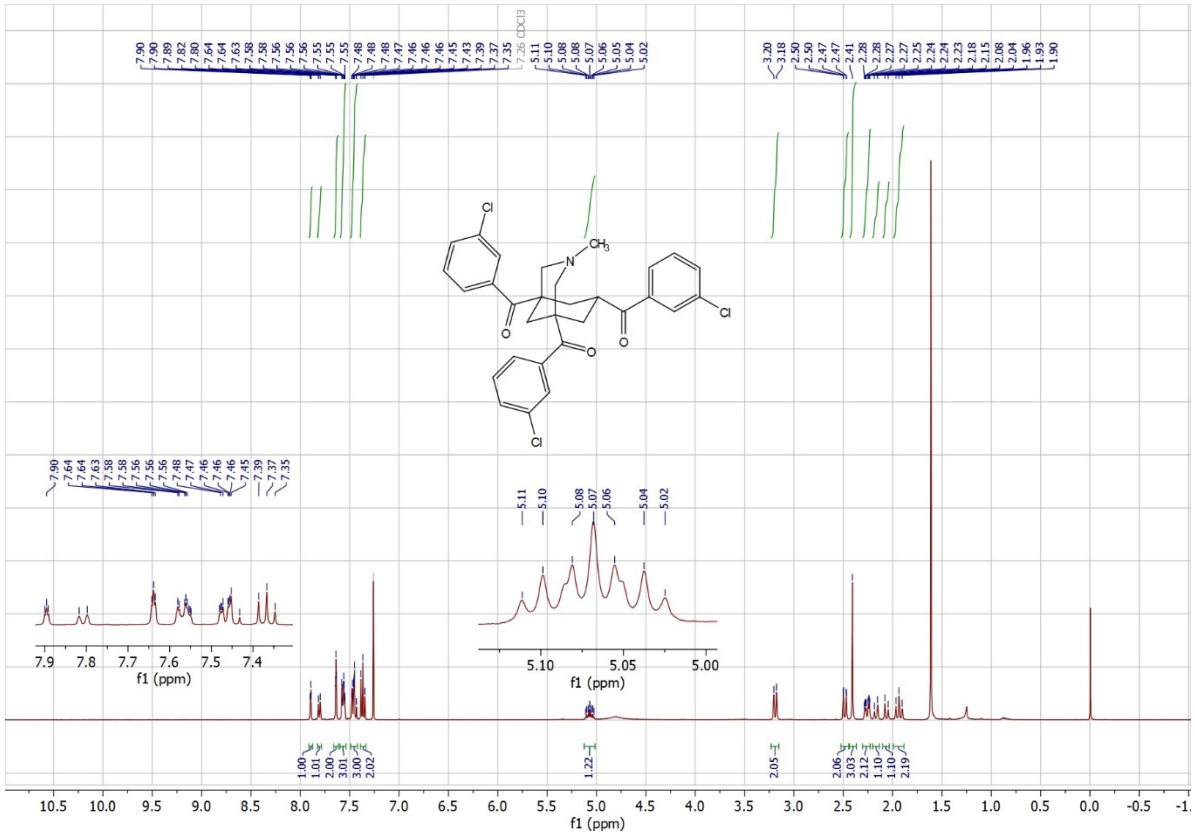


^{13}C-NMR

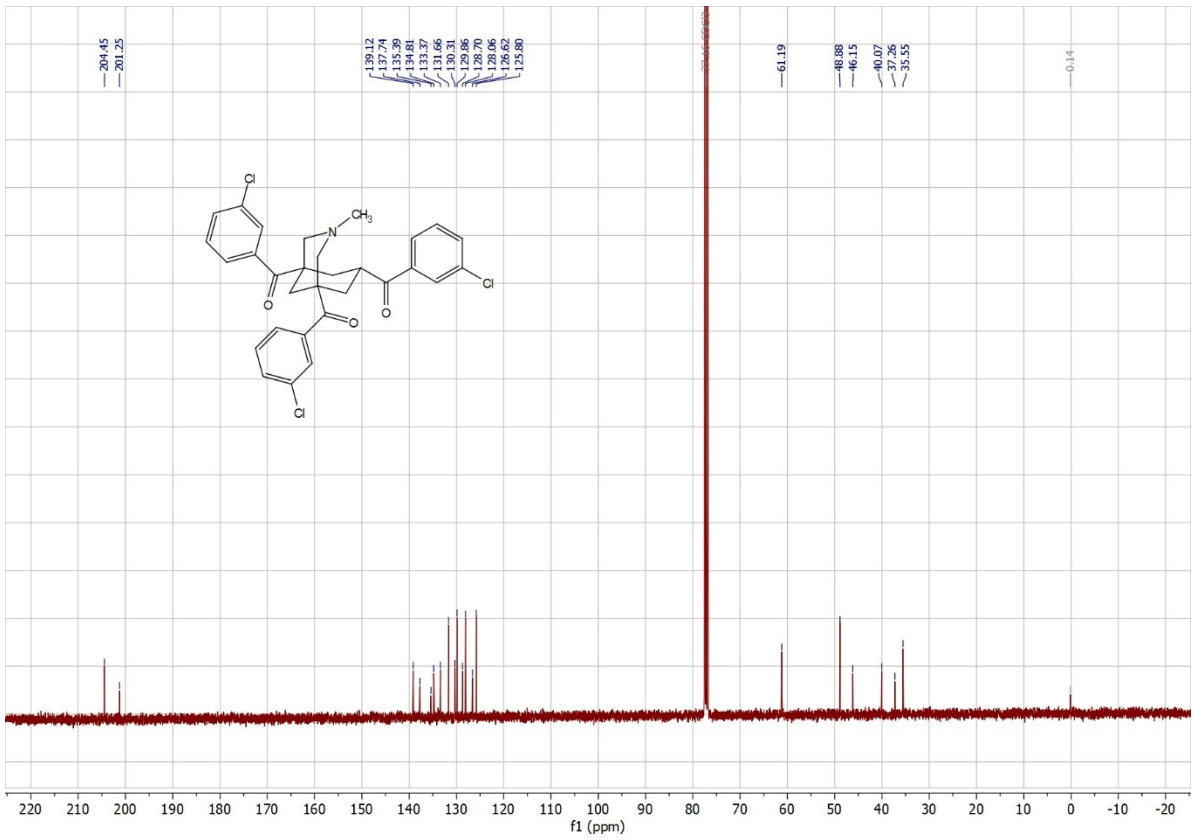


3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((3-chlorophenyl)methanone) (2l)

^{1}H-NMR

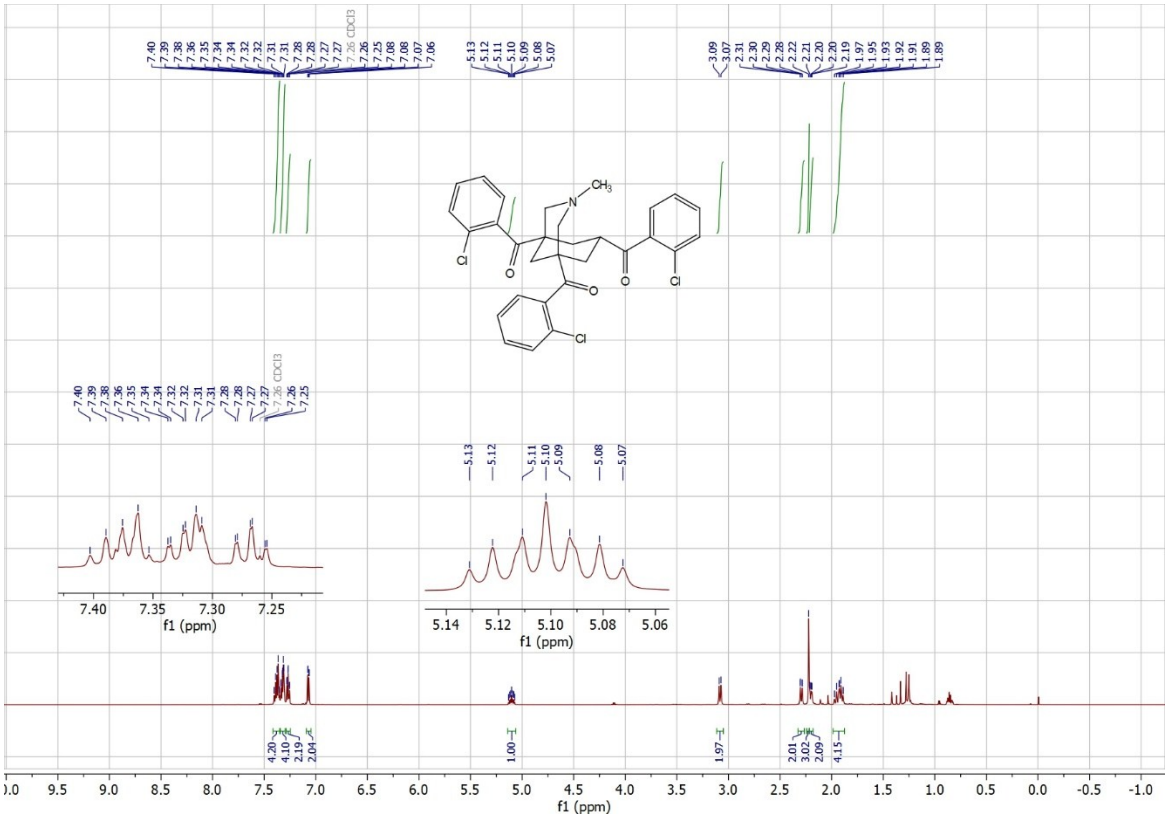


^{13}C-NMR

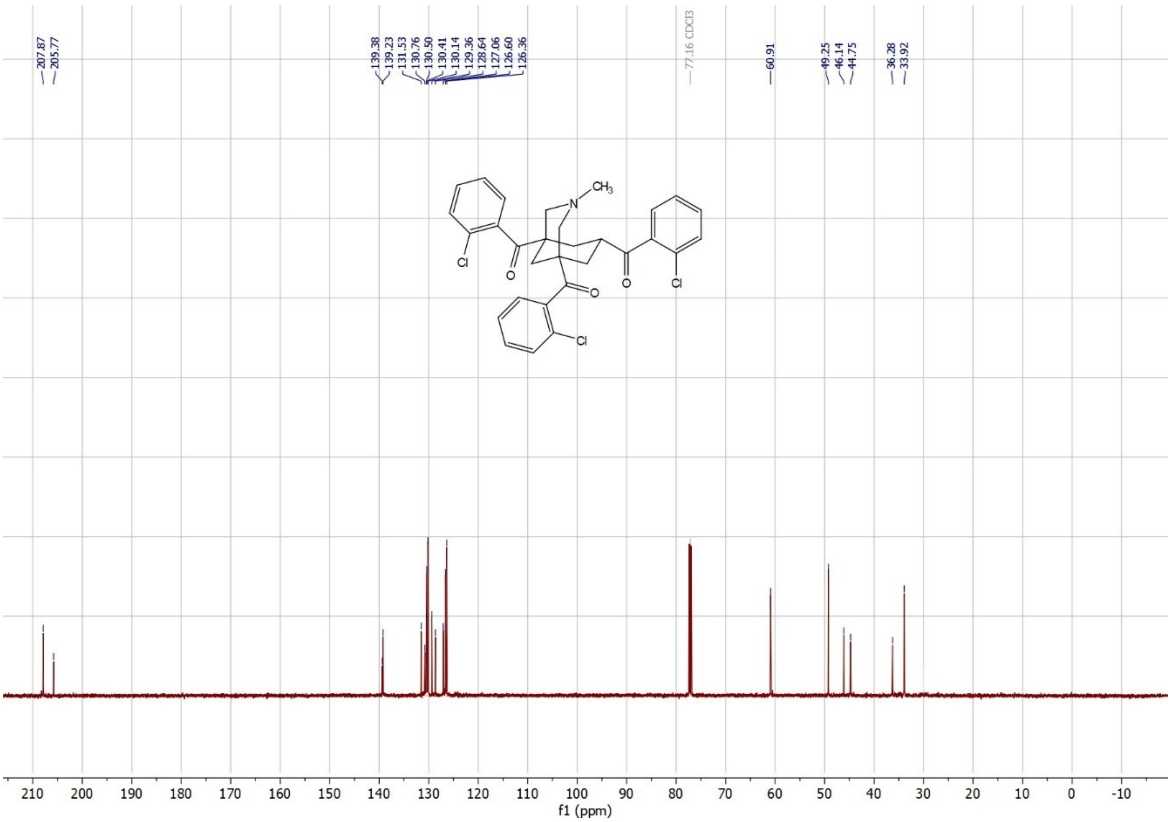


(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((3-chlorophenyl)methanone) (2m)

^{1}H-NMR

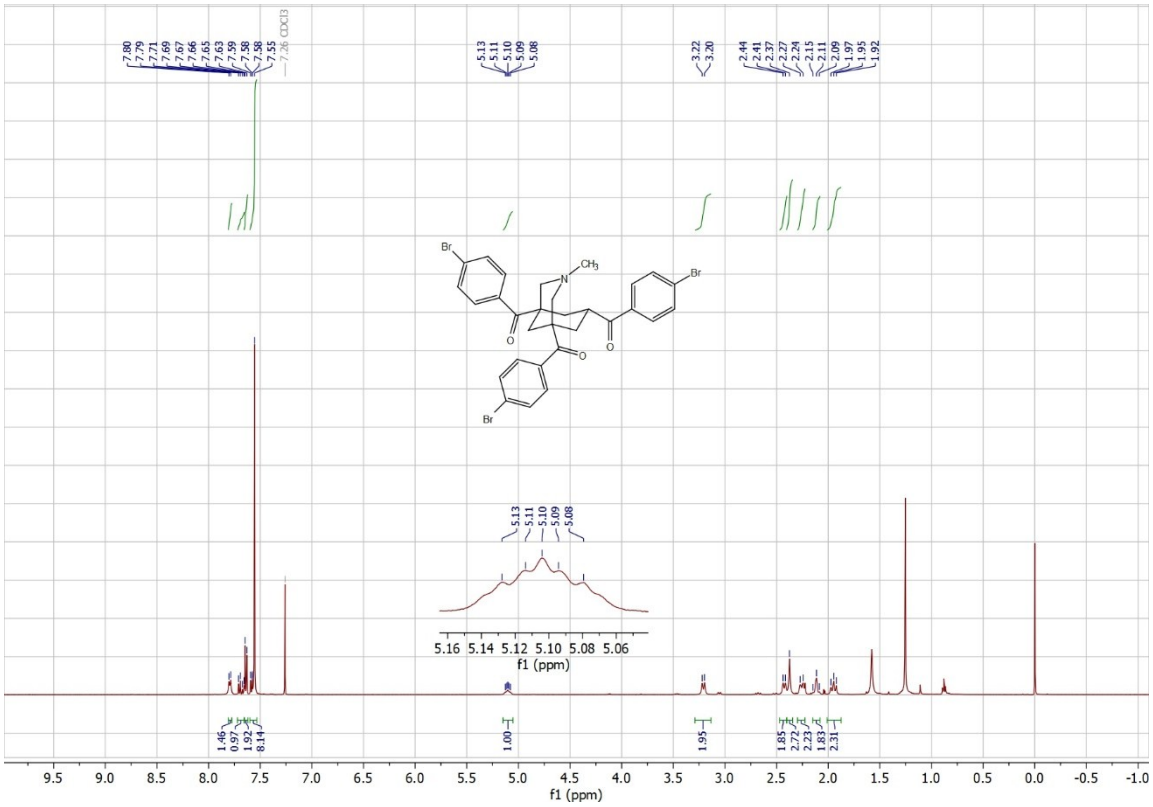


^{13}C-NMR

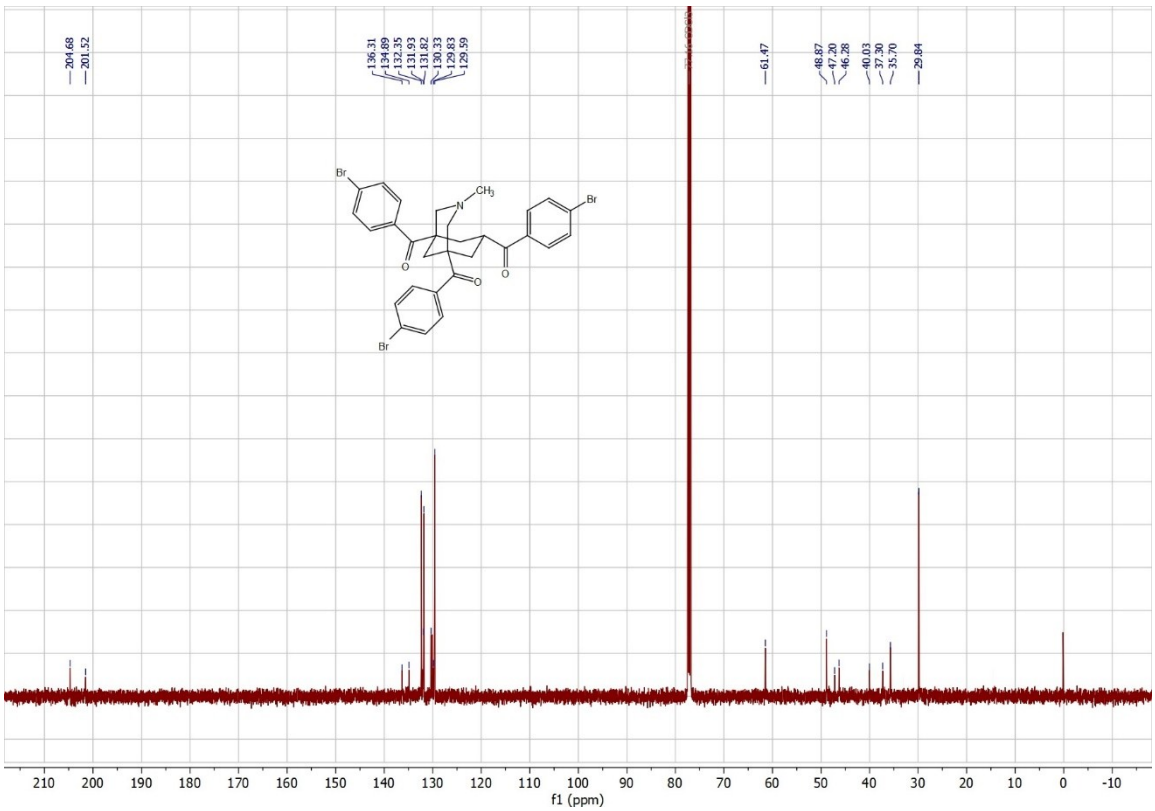


(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((4-bromophenyl)methanone (2n)

^{1}H-NMR

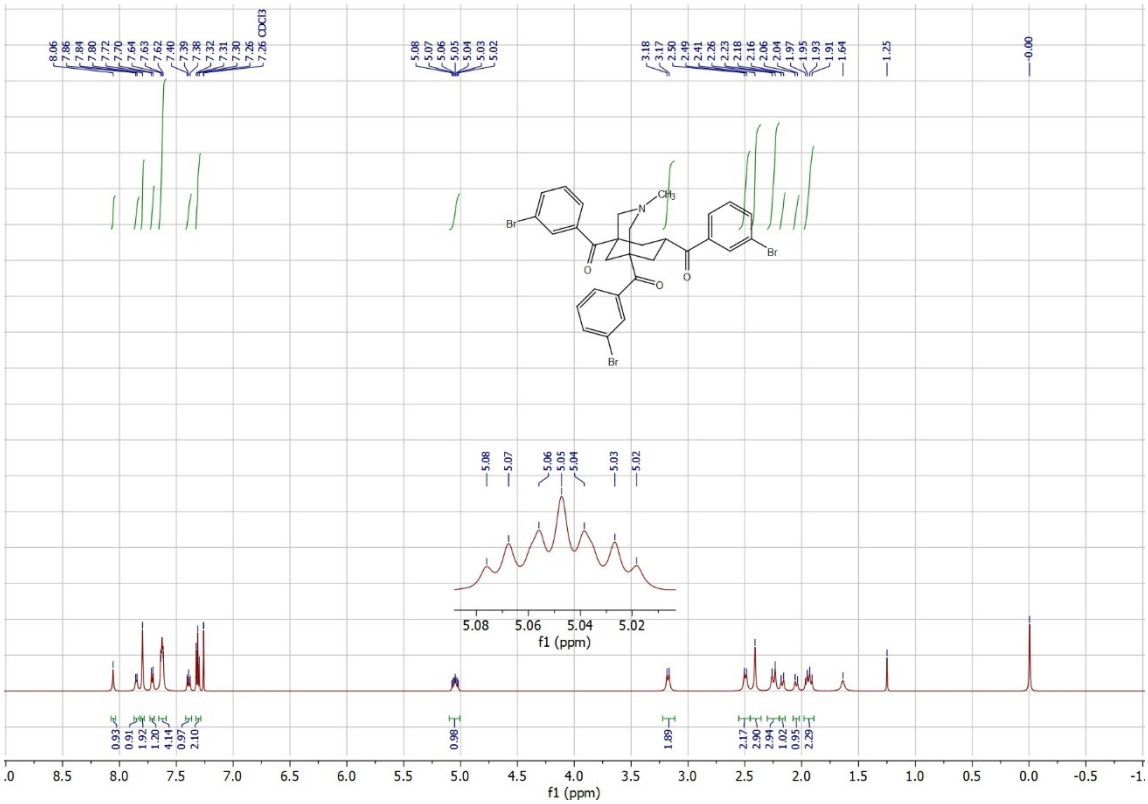


^{13}C-NMR

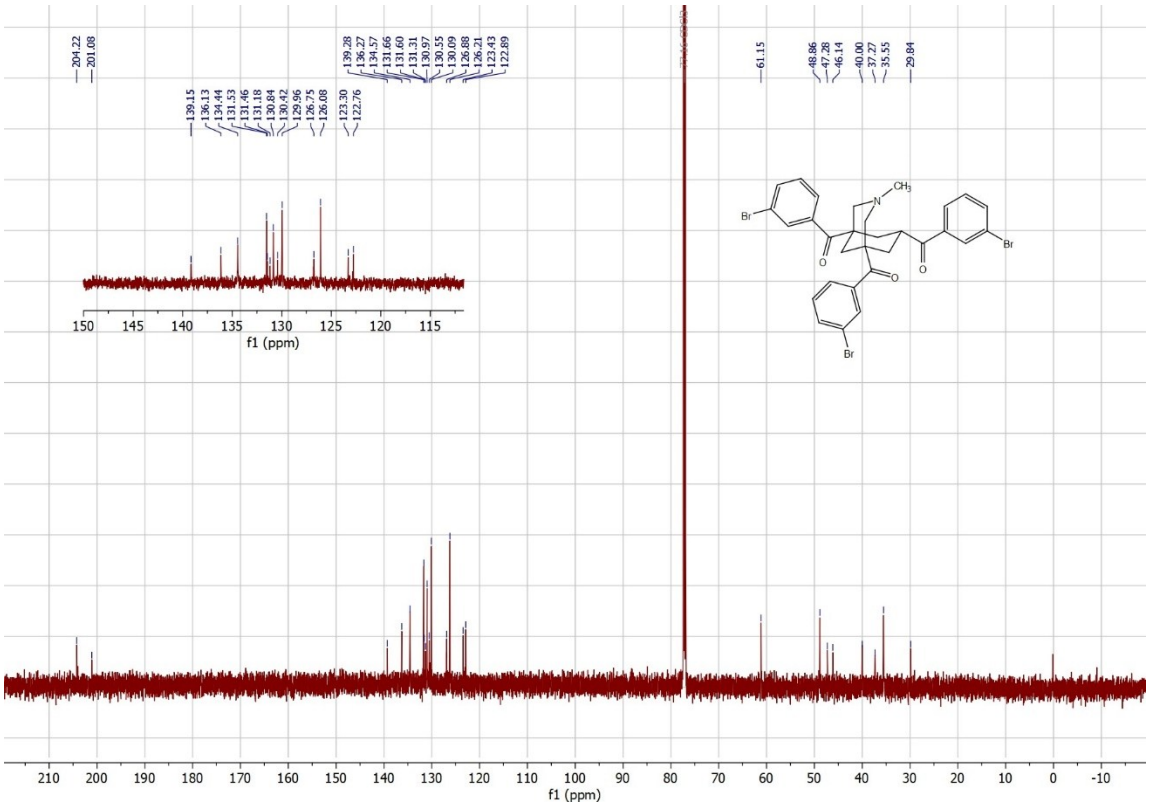


(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((3-bromophenyl)methanone (2o)

^{1}H-NMR

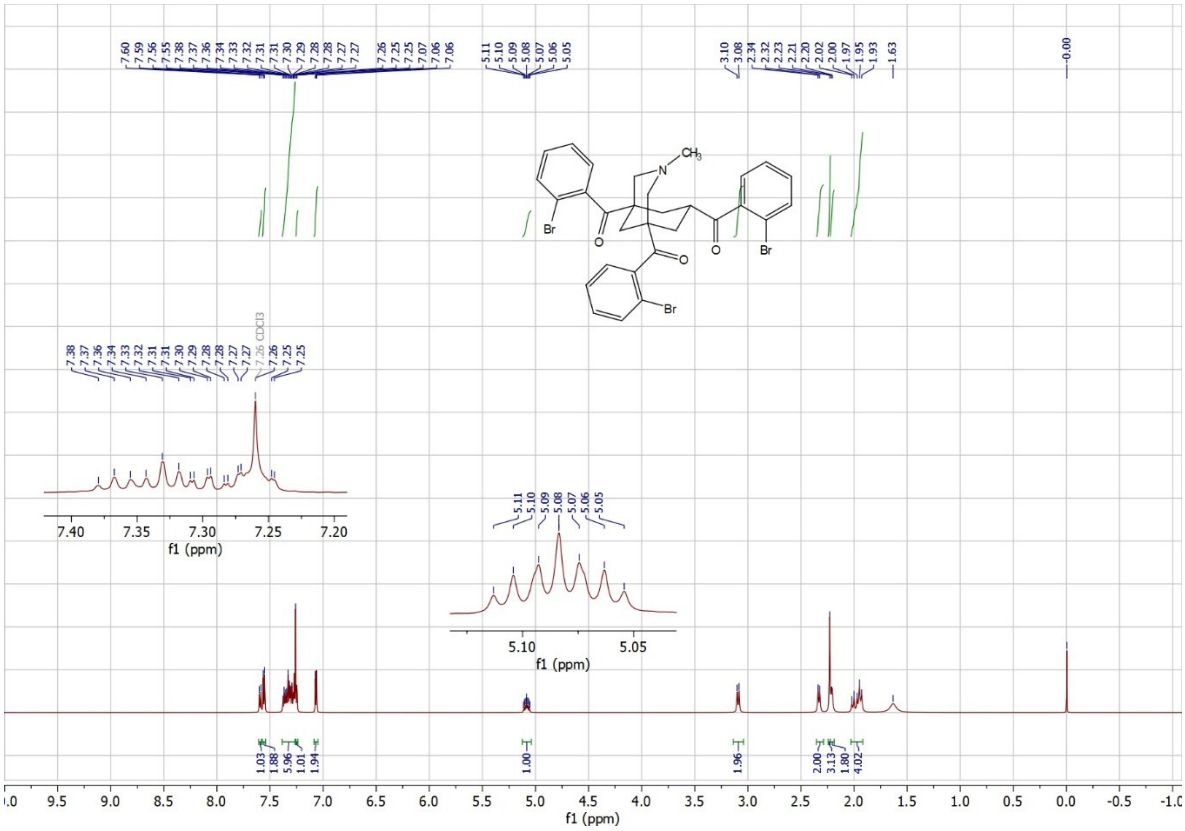


^{13}C-NMR

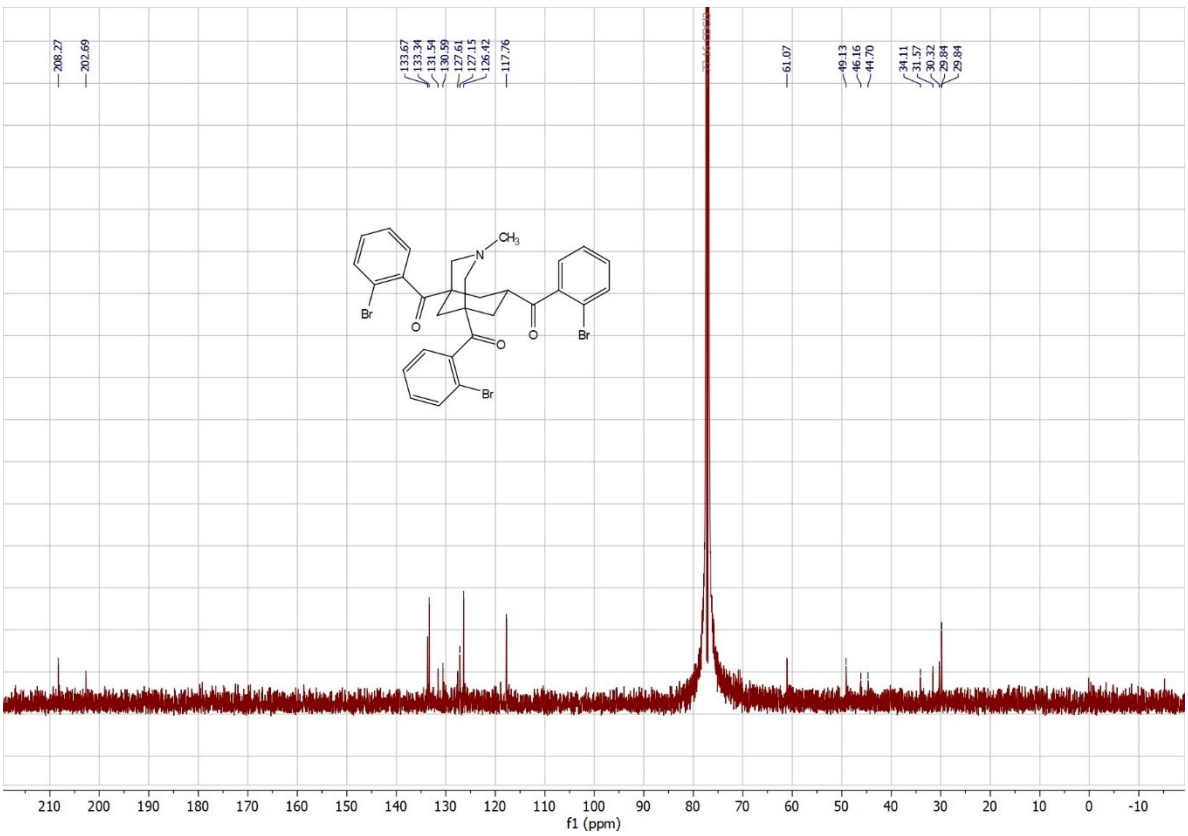


(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris((2-bromophenyl)methanone (2p)

^{1}H-NMR

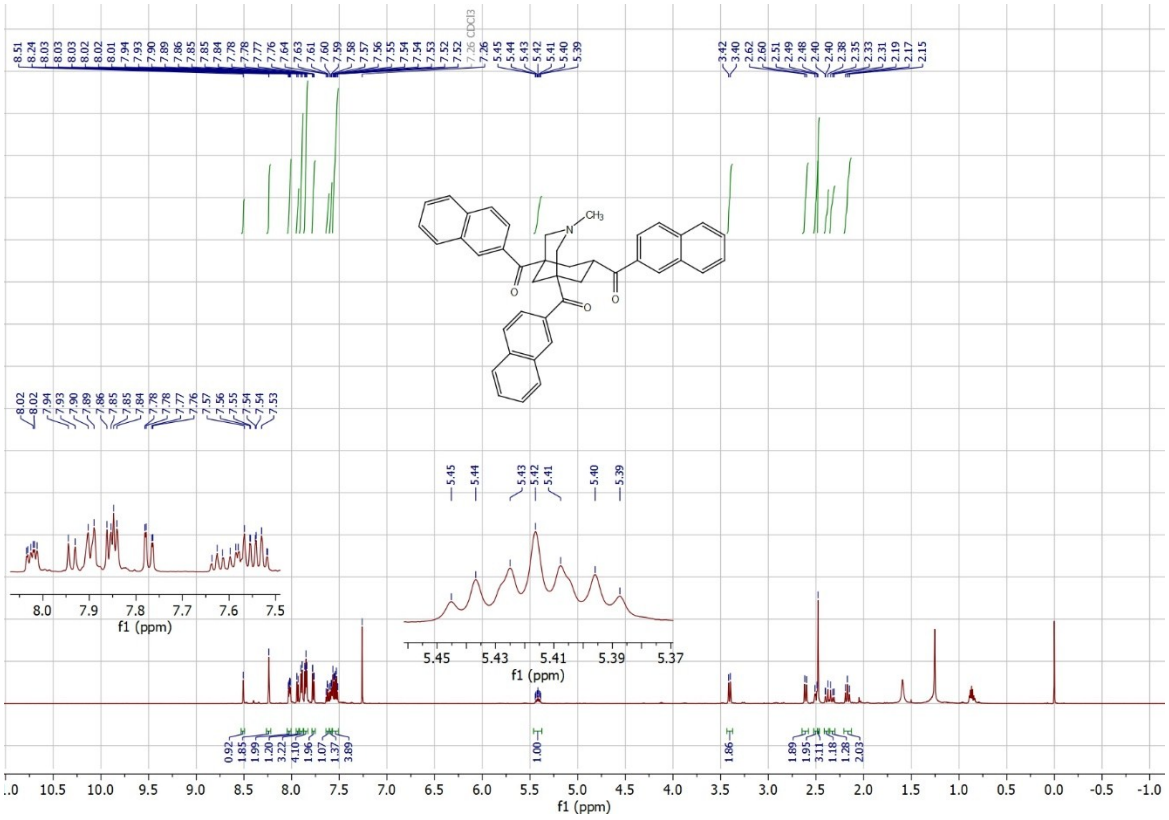


^{13}C-NMR

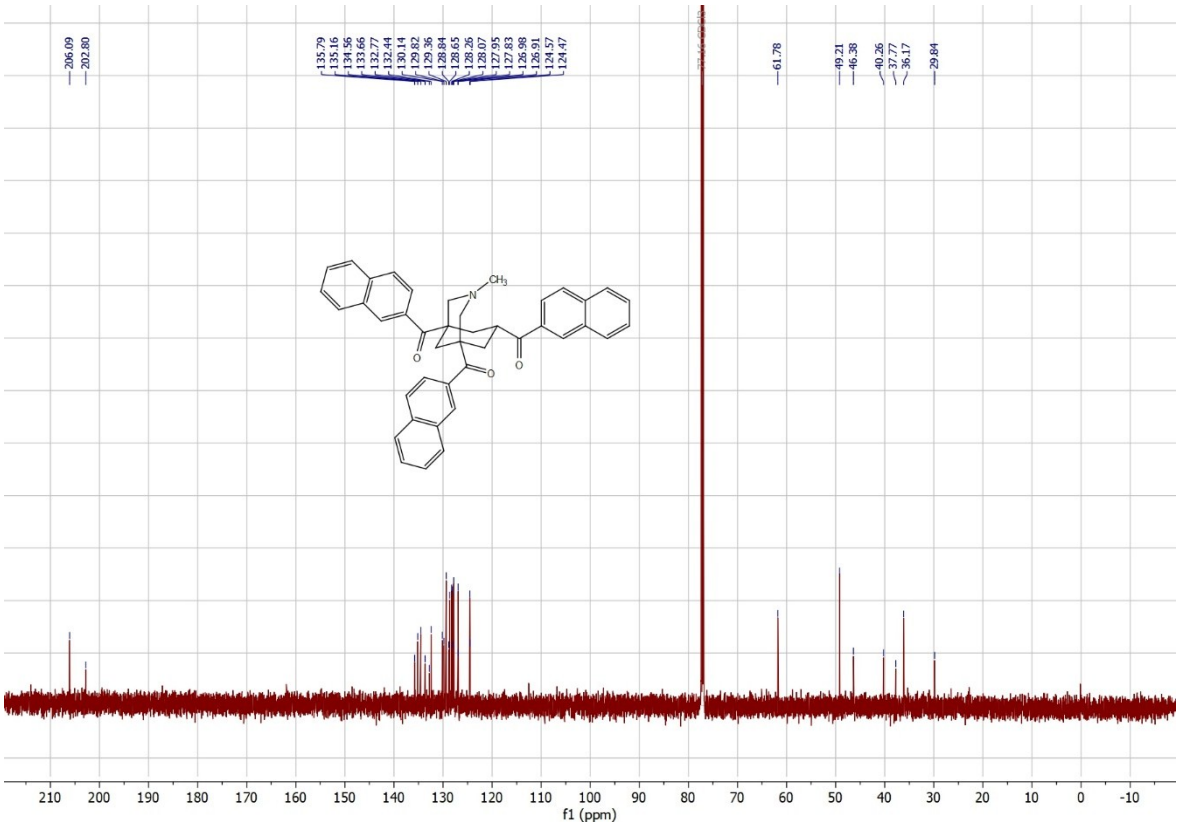


(3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris(naphthalen-2-ylmethanone) (2q)

^{1}H-NMR

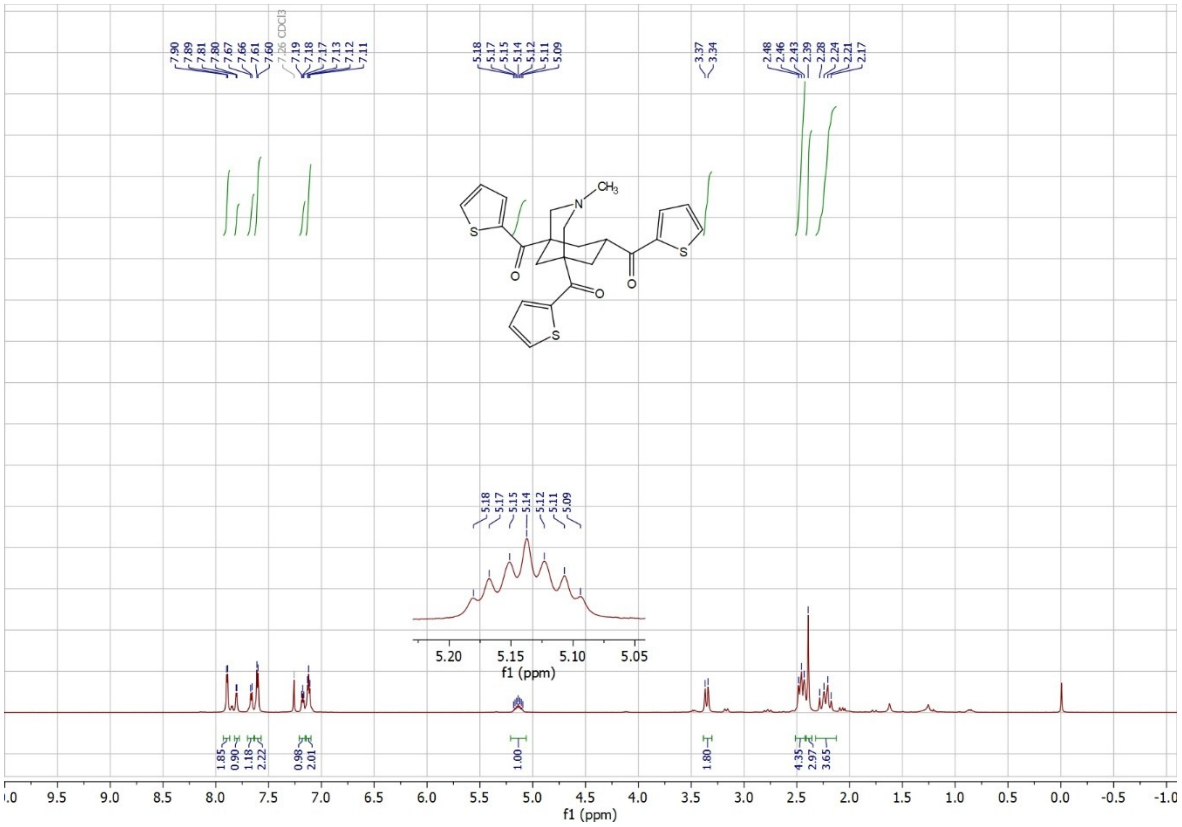


^{13}C-NMR

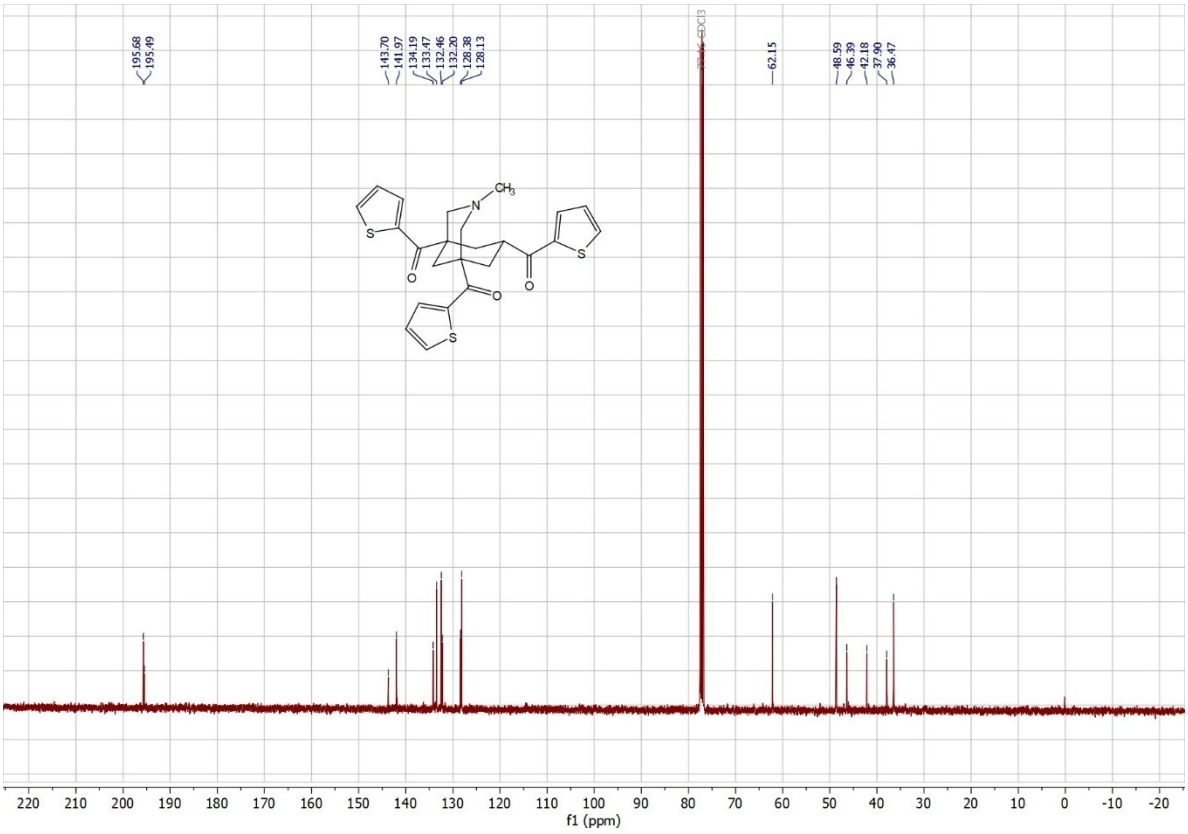


3-methyl-3-azabicyclo[3.3.1]nonane-1,5,7-triyl)tris(thiophen-2-ylmethanone) (2r)

^{1}H-NMR

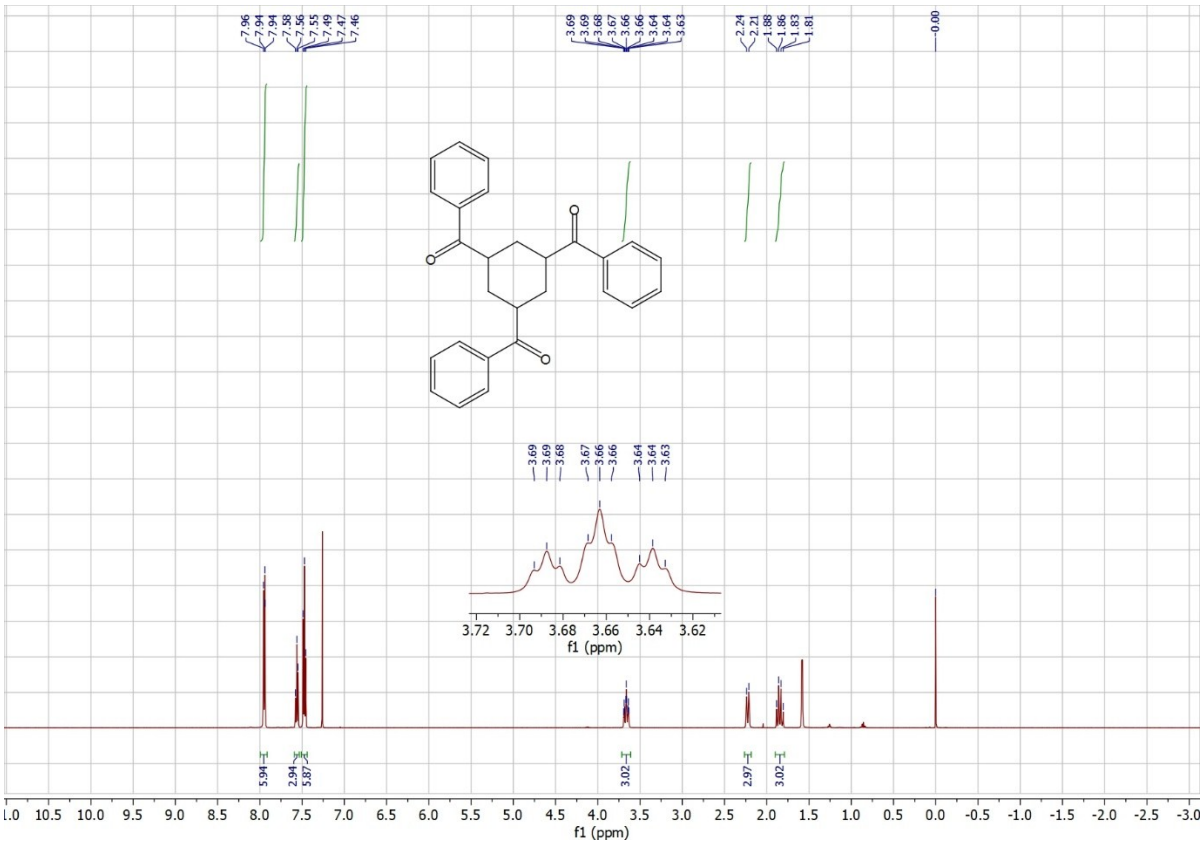


^{13}C-NMR

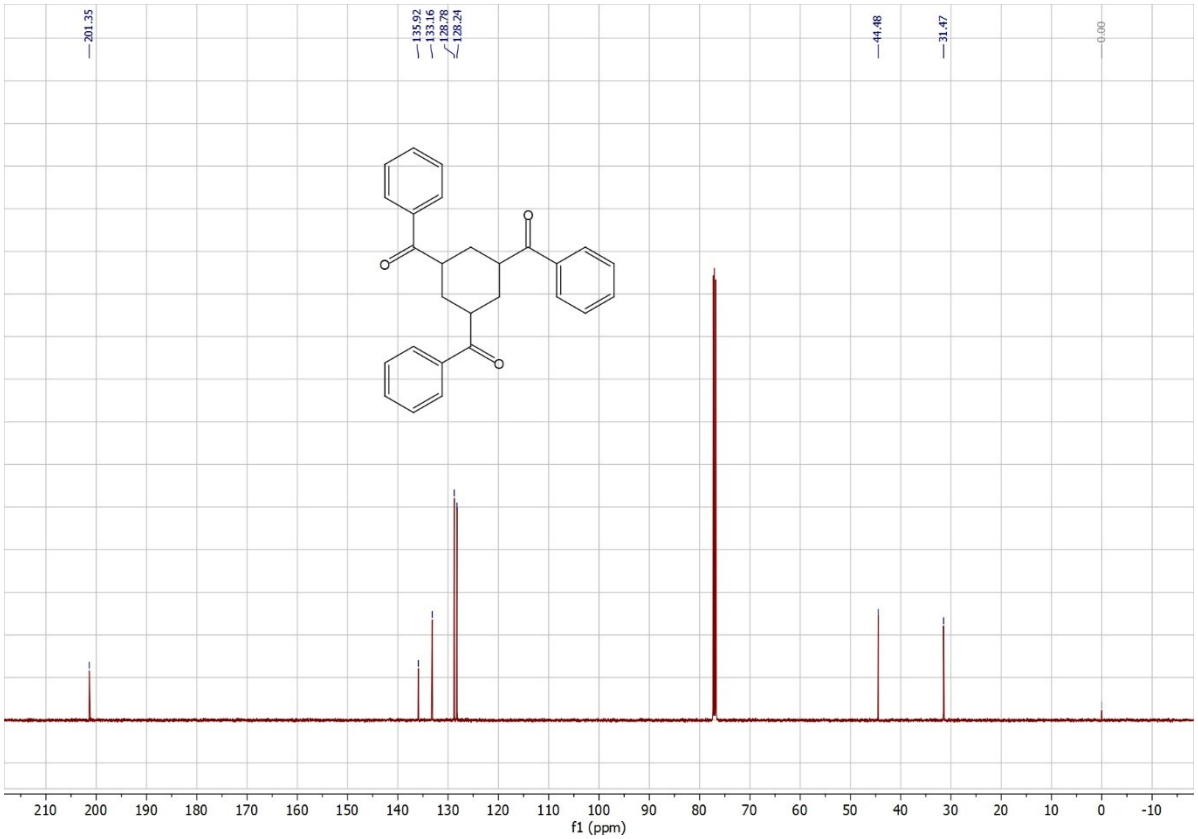


Cyclohexane-1,3,5-triyltris(phenylmethanone) (3a)

^{1}H-NMR

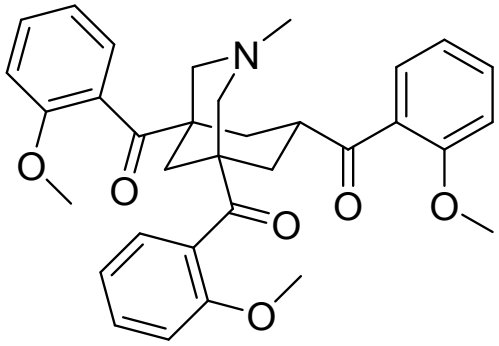


^{13}C-NMR

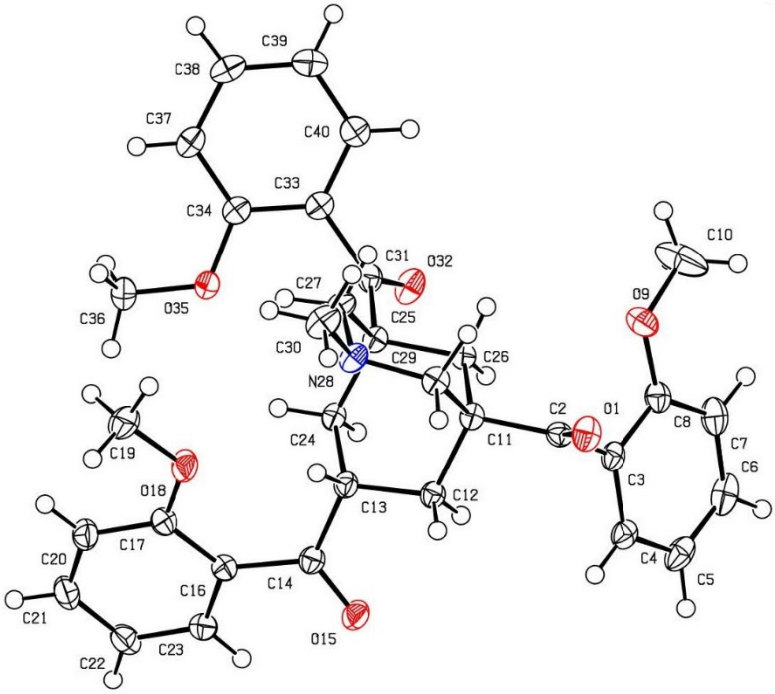


Crystal Data

The crystal of **2g** and **2k** were obtained by leaving alone their solution in ethanol at room temperature in the open air for five days. The structure of compound **2g** and **2k** were assigned by single crystal X-ray analysis. The crystal date of compound **2g** and **2k** have been deposited in CCDC with number **1860930** and **1860931**.



2g



CCDC **1860930**

Table 1 Crystal data and structure refinement for 2g.

Identification code	**2g**
Empirical formula	$C_{33}H_{35}NO_6$
Formula weight	541.65
Temperature/K	100.0
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	17.45405(14)
b/Å	8.11896(7)
c/Å	19.92900(15)
α/°	90
β/°	91.5647(7)
γ/°	90
Volume/Å^3	2823.06(4)
Z	4
ρ_{calc}g/cm^3	1.2743
μ/mm^{-1}	0.707
F(000)	1155.5
Crystal size/mm^3	3 × 1 × 0.4
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	6.64 to 179.44
Index ranges	$-13 \leq h \leq 14$, $-15 \leq k \leq 15$, $-27 \leq l \leq 27$
Reflections collected	14632
Independent reflections	4332 [R_{int} = 0.3380, R_{sigma} = 0.3047]
Data/restraints/parameters	4332/0/501
Goodness-of-fit on F^2	4.213
Final R indexes [I>=2σ (I)]	R_1 = 0.6894, wR_2 = 0.8917
Final R indexes [all data]	R_1 = 0.7193, wR_2 = 0.9141

Largest diff. peak/hole / e Å^{-3} 7.55/-6.70

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 2g. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O1	1750(50)	9610(50)	3230(30)	80(30)
O9	280(110)	6950(110)	3910(50)	40(60)
O15	4530(60)	6860(60)	4660(30)	110(30)
O18	4240(50)	10790(50)	5870(20)	80(30)
O32	1400(80)	6450(90)	6080(40)	130(40)
O35	2480(70)	9130(70)	7120(30)	100(30)
N28	2500(80)	11210(150)	5030(40)	160(40)
C2	1940(100)	8570(150)	3730(70)	160(60)
C3	1640(90)	6590(120)	3510(30)	90(40)
C4	2260(110)	5750(170)	3210(40)	120(70)
C5	2020(120)	4500(300)	2830(70)	180(90)
C6	1390(50)	3210(100)	3060(60)	60(40)
C7	980(140)	4400(200)	3410(100)	90(80)
C8	820(100)	5940(100)	3580(60)	100(50)
C10	-300(40)	6720(70)	4250(40)	60(30)
C11	2330(100)	9030(70)	4270(40)	100(50)
C12	2950(90)	8200(200)	4290(50)	140(60)
C13	3350(90)	8610(80)	5070(50)	80(50)
C14	4170(70)	7580(120)	5090(30)	70(30)
C16	4870(90)	8510(170)	5590(30)	150(60)
C17	4910(140)	9570(100)	5940(50)	220(110)
C19	4250(120)	12380(80)	6250(40)	180(90)
C20	5300(100)	9710(90)	6600(50)	170(60)

C21	6080(120)	8730(190)	6720(30)	150(70)
C22	5860(70)	7240(160)	6330(70)	130(60)
C23	5240(90)	6850(100)	5700(40)	110(40)
C24	3000(100)	7960(100)	5560(50)	140(50)
C25	2170(120)	8890(150)	5600(70)	120(60)
C26	1700(90)	8220(80)	4920(40)	110(40)
C27	1950(70)	10890(80)	5510(60)	110(40)
C29	1890(160)	10880(90)	4460(60)	210(120)
C30	2380(70)	13500(70)	5084(19)	90(50)
C31	1660(80)	8130(100)	6160(50)	120(40)
C33	1450(100)	9010(90)	6750(40)	80(60)
C34	1890(80)	9740(100)	7210(30)	100(50)
C36	3380(110)	9960(110)	7560(40)	130(70)
C37	1650(80)	10530(60)	7730(30)	80(40)
C38	680(100)	10600(100)	7610(50)	90(60)
C39	330(120)	9760(170)	7320(40)	120(60)
C40	450(100)	9340(100)	6750(50)	120(50)

Table 3 Anisotropic Displacement Parameters ($Å^2×10^3$) for 2g. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O1	170(80)	-4(18)	80(30)	-30(30)	-20(50)	40(20)
O9	110(190)	0(40)	30(40)	0(60)	20(70)	10(30)
O15	250(100)	20(30)	60(30)	60(40)	0(40)	-30(20)
O18	220(90)	20(20)	10(20)	60(30)	-10(30)	0(15)
O32	260(120)	20(40)	100(40)	-10(60)	0(60)	-30(30)
O35	250(110)	60(30)	10(20)	-30(50)	50(40)	10(20)
N28	180(120)	210(90)	80(40)	-20(70)	-20(60)	130(50)

C2	290(140)	60(80)	110(110)	10(90)	-150(100)	80(80)
C3	180(130)	90(50)	10(20)	30(80)	10(50)	40(30)
C4	300(200)	80(70)	40(30)	-100(90)	100(60)	10(40)
C5	70(120)	400(200)	100(60)	-20(130)	-10(70)	-170(100)
C6	-20(50)	20(40)	180(110)	-20(30)	40(50)	-40(50)
C7	0(200)	130(80)	120(120)	-60(110)	0(140)	90(90)
C8	180(160)	20(40)	120(60)	-40(60)	-130(90)	50(40)
C10	20(50)	40(30)	120(70)	60(30)	100(50)	90(40)
C11	280(150)	-20(20)	40(40)	10(40)	30(70)	0(20)
C12	100(140)	270(140)	50(50)	-80(110)	-20(70)	120(70)
C13	100(130)	10(30)	130(60)	10(50)	-100(70)	-20(30)
C14	110(100)	90(60)	10(30)	-60(60)	30(40)	0(30)
C16	280(160)	150(110)	20(30)	-150(110)	-60(60)	60(40)
C17	500(300)	-20(30)	160(70)	-30(90)	-120(130)	10(40)
C19	500(300)	0(30)	70(40)	80(70)	130(80)	30(30)
C20	430(170)	10(30)	60(50)	110(60)	140(80)	40(30)
C21	300(200)	190(120)	0(20)	-120(130)	-80(60)	50(40)
C22	100(120)	110(90)	190(110)	70(80)	80(90)	170(90)
C23	240(130)	60(40)	20(30)	-130(60)	10(60)	-10(30)
C24	400(170)	20(30)	20(50)	90(60)	30(70)	10(30)
C25	170(180)	60(70)	130(80)	-20(90)	-30(100)	-50(60)
C26	300(140)	20(30)	20(30)	30(50)	0(50)	40(20)
C27	190(100)	0(30)	130(70)	-40(40)	-50(70)	-30(40)
C29	600(400)	-10(20)	80(80)	70(80)	-60(140)	0(30)
C30	240(150)	40(30)	-16(13)	-30(50)	-10(40)	-48(19)
C31	170(130)	20(40)	170(70)	-80(60)	20(70)	-60(40)
C33	110(170)	20(30)	90(50)	-80(70)	-70(80)	0(30)
C34	250(150)	30(40)	30(30)	50(60)	80(60)	40(30)

C36	300(200)	10(40)	70(40)	70(80)	90(70)	-20(30)
C37	210(130)	0(20)	30(30)	90(40)	40(50)	29(18)
C38	190(170)	20(40)	60(70)	90(70)	70(90)	-20(40)
C39	300(200)	20(60)	20(30)	0(90)	100(60)	20(40)
C40	300(140)	10(40)	70(60)	50(60)	90(80)	30(40)

Table 4 Bond Lengths for 2g.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C2	1.34(8)	C11	C29	1.73(14)
O9	C8	1.4(2)	C12	C13	1.71(14)
O9	C10	1.25(19)	C13	C14	1.66(17)
O15	C14	1.23(11)	C13	C24	1.29(18)
O18	C17	1.5(2)	C14	C16	1.74(15)
O18	C19	1.50(8)	C16	C17	1.11(15)
O32	C31	1.45(10)	C16	C23	1.51(19)
O35	C34	1.15(14)	C17	C20	1.47(18)
O35	C36	1.9(2)	C20	C21	1.6(2)
N28	C27	1.39(16)	C21	C22	1.48(19)
N28	C29	1.6(2)	C22	C23	1.7(2)
N28	C30	1.87(13)	C24	C25	1.6(2)
C2	C3	1.75(17)	C25	C26	1.65(19)
C2	C11	1.32(17)	C25	C27	1.67(15)
C3	C4	1.4(2)	C25	C31	1.57(19)
C3	C8	1.52(19)	C31	C33	1.43(15)
C4	C5	1.3(2)	C33	C34	1.33(14)
C5	C6	1.6(3)	C33	C40	1.77(19)
C6	C7	1.4(3)	C34	C37	1.30(11)

C7	C8	1.3(2)	C37	C38	1.7(2)
C11	C12	1.28(19)	C38	C39	1.1(2)
C11	C26	1.84(15)	C39	C40	1.20(14)

Table 5 Bond Angles for 2g.

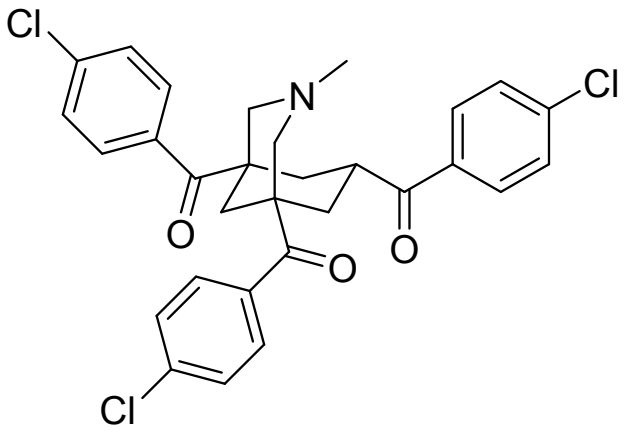
Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C10	O9	C8	136(10)	C23	C16	C14	89(9)
C19	O18	C17	120(10)	C23	C16	C17	126(12)
C36	O35	C34	120(8)	C16	C17	O18	114(17)
C29	N28	C27	91(13)	C20	C17	O18	112(10)
C30	N28	C27	94(8)	C20	C17	C16	129(15)
C30	N28	C29	98(7)	C21	C20	C17	118(10)
C3	C2	O1	110(9)	C22	C21	C20	97(11)
C11	C2	O1	123(11)	C23	C22	C21	134(9)
C11	C2	C3	127(6)	C22	C23	C16	102(7)
C4	C3	C2	108(12)	C25	C24	C13	107(9)
C8	C3	C2	125(10)	C26	C25	C24	103(9)
C8	C3	C4	127(10)	C27	C25	C24	130(12)
C5	C4	C3	112(16)	C27	C25	C26	98(10)
C6	C5	C4	123(13)	C31	C25	C24	112(11)
C7	C6	C5	93(10)	C31	C25	C26	100(11)
C8	C7	C6	154(18)	C31	C25	C27	109(11)
C3	C8	O9	118(10)	C25	C26	C11	100(10)
C7	C8	O9	144(18)	C25	C27	N28	96(10)
C7	C8	C3	96(15)	C11	C29	N28	91(12)
C12	C11	C2	107(11)	C25	C31	O32	118(8)
C26	C11	C2	100(12)	C33	C31	O32	118(9)

C26	C11	C12	109(7)	C33	C31	C25	124(7)
C29	C11	C2	102(12)	C34	C33	C31	129(15)
C29	C11	C12	146(16)	C40	C33	C31	110(8)
C29	C11	C26	83(9)	C40	C33	C34	120(12)
C13	C12	C11	104(14)	C33	C34	O35	102(11)
C14	C13	C12	105(9)	C37	C34	O35	131(12)
C24	C13	C12	115(11)	C37	C34	C33	125(15)
C24	C13	C14	102(8)	C38	C37	C34	104(10)
C13	C14	O15	133(8)	C39	C38	C37	128(12)
C16	C14	O15	104(10)	C40	C39	C38	125(18)
C16	C14	C13	113(8)	C39	C40	C33	104(15)
C17	C16	C14	137(20)				

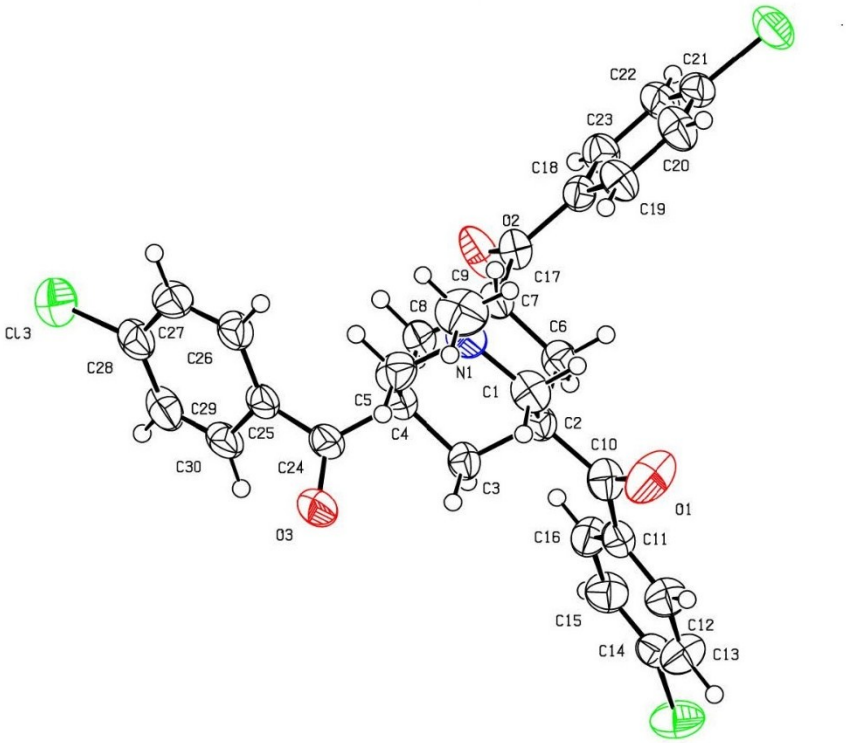
Table 6 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 2g.

Atom	*x*	*y*	*z*	U(eq)
H4	2300(800)	6300(1300)	3000(500)	0(400)
H5	2500(400)	2600(800)	3900(300)	90(160)
H6	500(600)	3300(1100)	3800(400)	300(200)
H7	-700(1100)	5000(2000)	4400(800)	500(600)
H10A	-800(400)	7900(700)	4200(300)	150(150)
H10B	-700(400)	6400(700)	3500(300)	0(150)
H10C	-600(1300)	5400(1900)	3300(900)	500(600)
H12D	2500(400)	6700(700)	3700(300)	0(150)
H12E	3300(600)	7200(1200)	3800(400)	0(300)
H13	3300(400)	10400(700)	4500(300)	0(150)
H19A	4300(400)	15800(700)	5600(300)	50(150)
H19B	1000(7000)	9000(14000)	3000(7000)	1000(11000)

H19C	5800(1300)	12000(3000)	6300(1100)	900(900)
H20	4800(400)	11200(800)	7100(300)	60(150)
H21	7600(1800)	6000(3000)	4100(1800)	1000(1300)
H22	7200(900)	3800(1900)	6900(700)	0(500)
H23	6100(800)	6100(1700)	5800(700)	400(500)
H24A	5000(2000)	5000(4000)	8500(1500)	0(1600)
H24B	3400(400)	7000(700)	4300(300)	170(140)
H26A	1700(400)	8200(800)	5000(300)	20(150)
H26B	2300(400)	6800(700)	4900(300)	0(150)
H27A	1900(600)	10000(1100)	6200(400)	0(200)
H27B	1500(400)	11100(800)	5100(300)	30(160)
H29A	3300(500)	12100(800)	3400(300)	20(140)
H29B	1200(500)	10100(900)	5000(300)	30(160)
H30A	2300(700)	13100(1700)	3400(500)	100(400)
H30B	1700(400)	13600(700)	5500(300)	10(150)
H30C	2700(800)	15500(1700)	6500(600)	0(400)
H36A	3300(600)	9500(1200)	8100(500)	0(300)
H36B	4100(400)	8900(700)	7200(300)	0(150)
H36C	-3000(3000)	6000(7000)	8000(2000)	1000(2000)
H37	700(800)	10400(1700)	8200(700)	0(400)
H38	1000(400)	10000(700)	8500(300)	80(150)
H39	-500(1100)	12000(2000)	7300(900)	200(700)
H40	100(400)	7400(700)	6500(300)	80(140)



2k



CCDC **1860931**

Table 1 Crystal data and structure refinement for 2k.

Identification code	**2k**
Empirical formula	$C_{30}H_{26}Cl_3NO_3$
Formula weight	554.87

Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	11.083(7)
b/Å	21.629(13)
c/Å	12.241(7)
α/°	90
β/°	116.92
γ/°	90
Volume/Å^3	2616(3)
Z	4
ρ_{calc}g/cm^3	1.409
μ/mm^{-1}	0.384
F(000)	1152.0
Crystal size/mm^3	0.3 × 0.1 × 0.1
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.766 to 49.994
Index ranges	$-12 \leq h \leq 13$, $-25 \leq k \leq 25$, $-14 \leq l \leq 14$
Reflections collected	12653
Independent reflections	4056 [R_{int} = 0.1526, R_{sigma} = 0.1431]
Data/restraints/parameters	4056/1/335
Goodness-of-fit on F^2	0.952
Final R indexes [I>=2σ (I)]	R_1 = 0.0998, wR_2 = 0.2507
Final R indexes [all data]	R_1 = 0.1545, wR_2 = 0.2824
Largest diff. peak/hole / e Å^{-3}	0.87/-0.59

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 2k. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ}

tensor.

Atom	*x*	*y*	*z*	U(eq)
C1	5166(7)	3324(3)	6619(6)	48.9(16)
C2	4705(6)	2864(3)	5582(5)	39.9(14)
C3	4165(6)	3229(3)	4375(5)	40.7(14)
C4	5306(6)	3636(3)	4405(6)	42.0(14)
C5	5731(7)	4084(3)	5482(6)	52.1(17)
C6	5856(6)	2431(3)	5692(6)	44.3(15)
C7	7014(6)	2766(3)	5582(5)	38.9(13)
C8	6471(6)	3211(3)	4497(6)	43.2(15)
C9	6556(9)	4188(4)	7647(7)	72(2)
C10	3598(7)	2461(3)	5637(6)	46.6(15)
C11	2598(6)	2083(3)	4589(6)	41.0(14)
C12	1472(7)	1884(3)	4670(6)	51.0(16)
C13	510(7)	1512(3)	3755(7)	58.6(18)
C14	703(6)	1328(3)	2794(6)	46.1(15)
C15	1827(7)	1518(3)	2696(6)	53.9(17)
C16	2770(7)	1886(3)	3580(5)	46.3(15)
C17	7984(6)	2307(3)	5509(6)	43.1(15)
C18	8867(6)	1929(3)	6601(6)	39.6(14)
C19	8951(7)	2021(3)	7755(6)	47.2(16)
C20	9778(7)	1660(3)	8744(6)	53.5(17)
C21	10516(6)	1195(3)	8561(6)	45.5(15)
C22	10458(7)	1092(3)	7441(6)	51.2(17)
C23	9621(6)	1462(3)	6470(6)	46.3(15)
C24	4732(6)	4012(3)	3221(6)	48.2(16)
C25	5587(6)	4209(3)	2629(6)	43.0(15)
C26	6849(7)	4480(3)	3247(6)	46.8(15)

C27	7532(7)	4702(3)	2636(6)	51.0(17)
C28	6953(7)	4641(3)	1368(6)	49.9(16)
C29	5722(8)	4349(3)	749(6)	55.7(18)
C30	5027(7)	4156(3)	1354(6)	50.0(17)
Cl1	-466.6(18)	853.7(10)	1680.7(19)	71.0(6)
Cl2	11515.5(19)	717.2(8)	9770.7(16)	63.4(6)
Cl3	7782(2)	4928.9(9)	595.0(19)	68.2(6)
N1	6186(6)	3765(2)	6639(5)	48.2(13)
O1	3511(6)	2443(3)	6588(5)	78.4(17)
O2	8049(6)	2225(2)	4559(5)	70.4(16)
O3	3551(5)	4154(3)	2708(6)	84.7(19)

Table 3 Anisotropic Displacement Parameters ($Å^2×10^3$) for 2k. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	59(4)	43(3)	42(4)	-4(3)	20(3)	3(3)
C2	44(3)	39(3)	33(3)	1(2)	14(3)	-1(3)
C3	47(4)	33(3)	41(4)	3(3)	19(3)	0(2)
C4	43(3)	36(3)	42(4)	8(3)	15(3)	1(3)
C5	51(4)	38(3)	64(5)	-9(3)	24(4)	-8(3)
C6	51(4)	34(3)	44(4)	-2(3)	19(3)	0(3)
C7	45(3)	34(3)	35(3)	1(2)	16(3)	3(2)
C8	43(3)	43(3)	40(4)	7(3)	15(3)	0(3)
C9	75(5)	64(4)	61(5)	-25(4)	18(4)	-10(4)
C10	60(4)	43(3)	40(4)	-2(3)	25(3)	-1(3)
C11	45(4)	37(3)	42(4)	6(3)	19(3)	5(3)
C12	49(4)	56(4)	49(4)	-7(3)	22(3)	-3(3)

C13	50(4)	67(5)	64(5)	-8(4)	31(4)	-11(3)
C14	38(3)	45(3)	48(4)	7(3)	13(3)	7(3)
C15	55(4)	58(4)	43(4)	-6(3)	17(3)	-4(3)
C16	52(4)	48(3)	39(4)	-3(3)	20(3)	-11(3)
C17	52(4)	38(3)	41(4)	5(3)	23(3)	3(3)
C18	41(3)	39(3)	41(3)	4(3)	21(3)	0(3)
C19	57(4)	41(3)	39(4)	2(3)	18(3)	11(3)
C20	68(5)	40(3)	43(4)	2(3)	16(4)	6(3)
C21	41(3)	43(3)	39(4)	4(3)	6(3)	-6(3)
C22	48(4)	45(4)	57(4)	9(3)	21(4)	14(3)
C23	51(4)	45(3)	48(4)	3(3)	25(3)	5(3)
C24	40(4)	36(3)	57(4)	11(3)	13(3)	6(3)
C25	41(3)	27(3)	48(4)	7(3)	8(3)	2(2)
C26	52(4)	43(3)	35(3)	1(3)	11(3)	-5(3)
C27	48(4)	44(4)	44(4)	-6(3)	6(3)	-9(3)
C28	56(4)	35(3)	51(4)	6(3)	18(4)	8(3)
C29	69(5)	41(4)	39(4)	5(3)	9(4)	0(3)
C30	47(4)	36(3)	42(4)	3(3)	-2(3)	-4(3)
Cl1	48.9(10)	79.6(13)	67.2(13)	-22.6(10)	11(1)	-13.6(9)
Cl2	64.1(12)	58.2(10)	50.6(11)	15.8(8)	10.7(9)	11.8(8)
Cl3	78.0(14)	67.4(12)	63.3(12)	8.0(9)	35.7(11)	1.2(9)
N1	51(3)	34(3)	44(3)	-9(2)	9(3)	-3(2)
O1	90(4)	103(4)	56(3)	-31(3)	44(3)	-46(3)
O2	94(4)	72(3)	55(3)	29(3)	42(3)	43(3)
O3	46(3)	102(4)	101(5)	58(4)	30(3)	22(3)

Table 4 Bond Lengths for 2k.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C1	C2	1.509(8)	C14	Cl1	1.730(7)
C1	N1	1.471(8)	C15	C16	1.368(9)
C2	C3	1.538(8)	C17	C18	1.494(8)
C2	C6	1.538(8)	C17	O2	1.211(7)
C2	C10	1.530(9)	C18	C19	1.387(9)
C3	C4	1.526(8)	C18	C23	1.366(8)
C4	C5	1.528(9)	C19	C20	1.383(9)
C4	C8	1.546(8)	C20	C21	1.376(9)
C4	C24	1.528(8)	C21	C22	1.362(9)
C5	N1	1.445(8)	C21	Cl2	1.733(6)
C6	C7	1.533(8)	C22	C23	1.384(9)
C7	C8	1.526(8)	C24	C25	1.493(9)
C7	C17	1.496(8)	C24	O3	1.207(8)
C9	N1	1.438(8)	C25	C26	1.383(9)
C10	C11	1.503(9)	C25	C30	1.399(9)
C10	O1	1.210(8)	C26	C27	1.370(10)
C11	C12	1.364(9)	C27	C28	1.392(9)
C11	C16	1.400(8)	C28	C29	1.377(10)
C12	C13	1.400(10)	C28	Cl3	1.708(7)
C13	C14	1.346(9)	C29	C30	1.354(10)
C14	C15	1.368(9)			

Table 5 Bond Angles for 2k.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
N1	C1	C2	114.0(5)	C14	C15	C16	120.4(7)
C1	C2	C3	107.7(5)	C15	C16	C11	120.9(6)

C1	C2	C6	112.1(5)	C18	C17	C7	120.5(5)
C1	C2	C10	108.1(5)	O2	C17	C7	120.8(6)
C6	C2	C3	110.0(5)	O2	C17	C18	118.7(6)
C10	C2	C3	111.3(5)	C19	C18	C17	123.2(5)
C10	C2	C6	107.5(5)	C23	C18	C17	119.1(5)
C4	C3	C2	108.4(5)	C23	C18	C19	117.6(6)
C3	C4	C5	108.3(5)	C20	C19	C18	121.5(6)
C3	C4	C8	108.4(5)	C21	C20	C19	118.5(6)
C3	C4	C24	107.4(5)	C20	C21	Cl2	119.6(5)
C5	C4	C8	113.1(5)	C22	C21	C20	121.5(6)
C5	C4	C24	108.3(5)	C22	C21	Cl2	118.9(5)
C24	C4	C8	111.2(5)	C21	C22	C23	118.5(6)
N1	C5	C4	112.2(5)	C18	C23	C22	122.3(6)
C7	C6	C2	113.5(5)	C25	C24	C4	122.0(5)
C8	C7	C6	111.0(5)	O3	C24	C4	121.1(6)
C17	C7	C6	110.2(5)	O3	C24	C25	116.9(6)
C17	C7	C8	112.2(5)	C26	C25	C24	124.2(6)
C7	C8	C4	115.1(5)	C26	C25	C30	118.3(6)
C11	C10	C2	124.7(5)	C30	C25	C24	117.3(6)
O1	C10	C2	118.4(6)	C27	C26	C25	121.5(6)
O1	C10	C11	117.0(6)	C26	C27	C28	119.0(6)
C12	C11	C10	117.1(6)	C27	C28	Cl3	119.4(5)
C12	C11	C16	117.6(6)	C29	C28	C27	119.9(7)
C16	C11	C10	125.2(6)	C29	C28	Cl3	120.7(5)
C11	C12	C13	120.9(6)	C30	C29	C28	120.5(6)
C14	C13	C12	120.3(7)	C29	C30	C25	120.6(6)
C13	C14	C15	119.9(7)	C5	N1	C1	111.6(5)
C13	C14	Cl1	120.3(5)	C9	N1	C1	110.1(6)

C15	C14	Cl1	119.7(5)	C9	N1	C5	112.1(5)

Table 6 Torsion Angles for 2k.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C1	C2	C3	C4	59.6(6)	C10	C11	C12	C13	-177.8(6)
C1	C2	C6	C7	-64.4(7)	C10	C11	C16	C15	177.0(6)
C1	C2	C10	C11	160.9(6)	C11	C12	C13	C14	1.9(11)
C1	C2	C10	O1	-19.1(8)	C12	C11	C16	C15	1.2(9)
C2	C1	N1	C5	54.4(7)	C12	C13	C14	C15	-1.5(11)
C2	C1	N1	C9	179.5(6)	C12	C13	C14	Cl1	178.5(5)
C2	C3	C4	C5	-61.1(6)	C13	C14	C15	C16	1.0(10)
C2	C3	C4	C8	62.0(6)	C14	C15	C16	C11	-0.9(10)
C2	C3	C4	C24	-177.8(5)	C16	C11	C12	C13	-1.7(10)
C2	C6	C7	C8	-46.7(7)	C17	C7	C8	C4	171.2(5)
C2	C6	C7	C17	-171.5(5)	C17	C18	C19	C20	179.8(6)
C2	C10	C11	C12	-163.1(6)	C17	C18	C23	C22	-179.8(6)
C2	C10	C11	C16	21.1(9)	C18	C19	C20	C21	-0.7(10)
C3	C2	C6	C7	55.6(7)	C19	C18	C23	C22	-0.7(10)
C3	C2	C10	C11	42.8(8)	C19	C20	C21	C22	0.7(10)
C3	C2	C10	O1	-137.3(7)	C19	C20	C21	Cl2	-177.8(5)
C3	C4	C5	N1	59.1(7)	C20	C21	C22	C23	-0.7(10)
C3	C4	C8	C7	-56.0(7)	C21	C22	C23	C18	0.7(10)
C3	C4	C24	C25	-149.2(6)	C23	C18	C19	C20	0.7(10)
C3	C4	C24	O3	29.4(9)	C24	C4	C5	N1	175.3(5)
C4	C5	N1	C1	-54.6(7)	C24	C4	C8	C7	-173.9(5)
C4	C5	N1	C9	-178.6(6)	C24	C25	C26	C27	-174.0(6)

C4	C24	C25	C26	-47.4(9)	C24	C25	C30	C29	177.2(6)
C4	C24	C25	C30	137.4(6)	C25	C26	C27	C28	-1.5(10)
C5	C4	C8	C7	64.1(7)	C26	C25	C30	C29	1.7(9)
C5	C4	C24	C25	94.0(7)	C26	C27	C28	C29	-1.2(10)
C5	C4	C24	O3	-87.5(8)	C26	C27	C28	Cl3	178.8(5)
C6	C2	C3	C4	-63.0(6)	C27	C28	C29	C30	4.1(10)
C6	C2	C10	C11	-77.8(7)	C28	C29	C30	C25	-4.4(10)
C6	C2	C10	O1	102.2(7)	C30	C25	C26	C27	1.2(9)
C6	C7	C8	C4	47.5(7)	Cl1	C14	C15	C16	-179.0(5)
C6	C7	C17	C18	-70.0(7)	Cl2	C21	C22	C23	177.8(5)
C6	C7	C17	O2	108.4(7)	Cl3	C28	C29	C30	-175.9(5)
C7	C17	C18	C19	-7.0(9)	N1	C1	C2	C3	-56.6(7)
C7	C17	C18	C23	172.1(6)	N1	C1	C2	C6	64.7(7)
C8	C4	C5	N1	-61.1(7)	N1	C1	C2	C10	-177.0(5)
C8	C4	C24	C25	-30.8(8)	O1	C10	C11	C12	17.0(9)
C8	C4	C24	O3	147.8(7)	O1	C10	C11	C16	-158.9(7)
C8	C7	C17	C18	165.8(5)	O2	C17	C18	C19	174.6(7)
C8	C7	C17	O2	-15.8(9)	O2	C17	C18	C23	-6.3(9)
C10	C2	C3	C4	178.0(5)	O3	C24	C25	C26	134.0(7)
C10	C2	C6	C7	176.9(5)	O3	C24	C25	C30	-41.2(9)

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 2k.

Atom	*x*	*y*	*z*	U(eq)
H1A	4385	3554	6557	59
H1B	5538	3101	7390	59
H3A	3860	2947	3686	49
H3B	3405	3484	4284	49

H5A	6454	4346	5509	63
H5B	4970	4347	5356	63
H6A	6215	2221	6476	53
H6B	5488	2119	5056	53
H7	7503	3011	6329	47
H8A	6157	2972	3748	52
H8B	7212	3470	4550	52
H9A	7275	4451	7693	107
H9B	6853	3959	8396	107
H9C	5787	4436	7525	107
H12	1343	1998	5342	61
H13	-264	1390	3811	70
H15	1951	1397	2025	65
H16	3536	2008	3508	56
H19	8441	2334	7867	57
H20	9833	1729	9515	64
H22	10969	780	7331	61
H23	9570	1390	5701	56
H26	7241	4512	4096	56
H27	8371	4892	3062	61
H29	5365	4285	-91	67
H30	4169	3985	918	60