

Electronic Supplementary Information

Palladium catalyzed synthesis of 2-trifluoromethylquinolines through a domino Sonogashira-alkyne carbocyclization process

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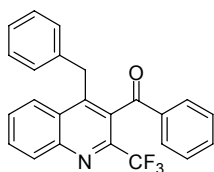
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General:

Melting points were measured on a Melt-Temp apparatus and uncorrected. ¹H NMR spectra were recorded in CDCl₃ on a Bruker AM-300 spectrometer (300 MHz) with TMS as internal standard. ¹⁹F NMR spectra were taken on a Bruker AM-300 (282 MHz) spectrometer using CFC1₃ as external standard. ¹³C NMR spectra were taken on a Bruker AM-400 (100 MHz) spectrometer. IR spectra were obtained with a Nicolet AV-360 spectrophotometer. Solvents and reagents were purchased from commercial sources and used as received. CH₃CN was distilled from calcium hydride. All reactions were carried out under a nitrogen atmosphere in a Schlenk tube, with a stir bar and capped with a Teflon screw-cap. TLC analysis was performed on silica gel plates, column chromatography over silica gel (mesh 300-400) and petroleum ether/ethyl acetate combination was used as the eluent. The β-Trifluoromethyl β-enaminoketones were synthesized according to the literature.¹

General procedure for 2-trifluoromethylquinolines synthesis

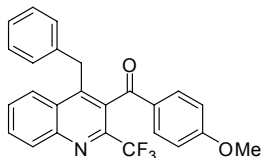
A schlenk tube was charged with 4,4,4-trifluoro-3-(2-iodophenylamino)-1-phenylbut-2-en-1-one (**1a**) (83 mg, 0.2 mmol), and Pd(PPh₃)₂Cl₂ (14 mg, 0.02 mmol), evacuated and backfilled with nitrogen. CH₃CN (2 ml), Phenylacetylene (0.3 mmol), and DBU (2.2 eq) was successively added. Then the reaction mixture was stirred at 60 °C for 2 h. The mixture was partitioned between ethyl acetate and water, the organic layer was washed with brine, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel to provide **3a** as a white solid.

1.1) (4-benzyl-2-(trifluoromethyl)quinolin-3-yl)(phenyl)methanone , 3a.

White solid, mp 131-132 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.28 (d, *J* = 8.3 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.92-7.67 (m, 3H), 7.67-7.46 (m, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.21-6.91 (m, 5H), 4.54-4.17 (m, 2H); ¹⁹F NMR (282 MHz, CDCl₃) δ -62.78 (s); ¹³C NMR (100 MHz, CDCl₃) δ 194.8, 146.8, 145.9, 144.1 (q, *J* = 33.9 Hz), 137.8, 136.9, 134.3, 131.1, 130.9, 130.6, 129.6, 128.8, 128.6, 128.2, 127.8, 126.7, 124.9, 121.4 (q, *J* = 276.8 Hz), 35.6; IR (KBr): 3029, 1672, 1597, 1581, 1496, 1451, 1373, 1184, 1134, 770, 712 cm⁻¹; LRMS (EI) *m/z* (relative intensity) 391 (93) [M⁺], 370 (100), 293 (75), 105 (64), 77 (69). Anal. Calcd. For C₂₄H₁₆F₃NO: C, 73.65; H, 4.12; N, 3.58.

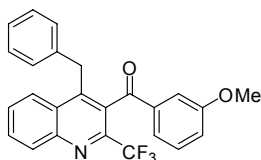
Found: C, 73.34; H, 4.23; N, 3.43.

1.2) (4-benzyl-2-(trifluoromethyl)quinolin-3-yl)(4-methoxyphenyl)methanone, 3b.



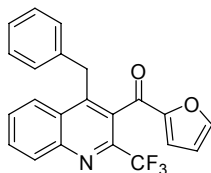
Brown solid, mp 143-145 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.28 (d, J = 8.5 Hz, 1H), 8.01 (d, J = 8.5 Hz, 1H), 7.89 – 7.52 (m, 4H), 7.21 – 6.95 (m, 5H), 6.84 (d, J = 8.6 Hz, 2H), 4.43 – 4.23 (m, 2H), 3.82 (s, 3H); ^{19}F NMR (282MHz, CDCl_3): δ -62.99 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 192.7, 164.0, 146.3, 145.4, 143.7 (q, J = 33.9 Hz), 137.6, 131.6, 130.5, 130.5, 129.8, 129.0, 128.2, 127.8, 127.5, 126.2, 124.5, 121.0 (q, J = 277.2 Hz), 113.6, 55.1, 35.1; IR(KBr): 3063, 2938, 1664, 1604, 1575, 1509, 1497, 1453, 1426, 1371, 1268, 1154, 1023, 763, 719 cm^{-1} ; LRMS (EI) m/z (relative intensity) 421 (79) [M^+], 370 (61), 293 (100), 135 (87), 77 (36). Anal.Calcd. For $\text{C}_{25}\text{H}_{18}\text{F}_3\text{NO}_2$: C, 71.25; H, 4.31; N, 3.32. Found: C, 71.07; H, 4.42; N, 3.19.

1.3) (4-benzyl-2-(trifluoromethyl)quinolin-3-yl)(3-methoxyphenyl)methanone, 3c.



White solid, mp 101-103 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.29 (d, J = 8.5 Hz, 1H), 8.02 (d, J = 8.5 Hz, 1H), 7.82 (t, J = 7.6 Hz, 1H), 7.62 (t, J = 7.7 Hz, 1H), 7.41 (s, 1H), 7.27 – 7.07 (m, 6H), 7.02 (d, J = 7.2 Hz, 2H), 4.44 – 4.21 (m, 2H), 3.79 (s, 3H); ^{19}F NMR (282MHz, CDCl_3): δ -62.88 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 194.5, 159.9, 146.7, 145.8, 144.0 (q, J = 34.3 Hz), 138.2, 137.8, 131.0, 130.9, 130.5, 129.7, 129.5, 128.6, 128.1, 127.7, 126.6, 124.9, 122.8, 121.3 (q, J = 277.0 Hz), 120.9, 112.9, 55.4, 35.6; IR(KBr): 3030, 2973, 1671, 1594, 1582, 1496, 1454, 1370, 1270, 1185, 1130, 1039, 762 cm^{-1} ; LRMS (EI) m/z (relative intensity) 421 (100) [M^+], 370 (79), 293 (46), 135 (46), 77 (35). Anal.Calcd. For $\text{C}_{25}\text{H}_{18}\text{F}_3\text{NO}_2$: C, 71.25; H, 4.31; N, 3.32. Found: C, 70.92; H, 4.30; N, 3.22.

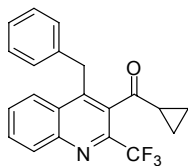
1.4) (4-benzyl-2-(trifluoromethyl)quinolin-3-yl)(furan-2-yl)methanone, 3d.



Brown solid, mp 139-141 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.27 (d, J = 8.5 Hz, 1H), 8.04 (d, J = 8.5 Hz, 1H), 7.81 (t, J = 7.7 Hz, 1H), 7.62 (t, J = 7.7 Hz, 1H), 7.52 (s, 1H), 7.22 – 6.90 (m, 6H), 6.54 – 6.35 (m, 1H), 4.42 (s, 2H); ^{19}F NMR (282MHz, CDCl_3): δ -63.14 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 181.8, 152.8, 148.1, 146.8, 146.5, 143.9 (q, J = 34.1 Hz), 137.8, 131.2, 130.9, 129.5, 129.5, 128.6, 128.2, 127.8, 126.6, 125.0, 121.3 (q, J = 276.8 Hz), 120.6, 112.9, 35.2; IR(KBr): 3131, 3086, 2948, 1642, 1601, 1564, 1497, 1463, 1125, 756 cm^{-1} ; LRMS (EI) m/z (relative intensity) 381 (100) [M^+], 332 (46), 95 (26). Anal.Calcd. For $\text{C}_{22}\text{H}_{14}\text{F}_3\text{NO}_2$: C, 69.29; H, 3.70; N, 3.32.

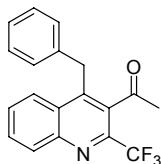
3.67. Found: C, 69.55; H, 4.03; N, 3.55.

1.5) (4-benzyl-2-(trifluoromethyl)quinolin-3-yl)(cyclopropyl)methanone, 3e.



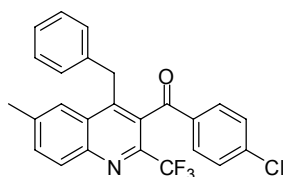
White solid, mp 87-88 °C; ¹HNMR (300 MHz, CDCl₃) δ 8.22 (d, *J* = 8.5 Hz, 1H), 7.98 (d, *J* = 8.5 Hz, 1H), 7.77 (t, *J* = 7.7 Hz, 1H), 7.64 – 7.53 (m, 1H), 7.27 – 7.04 (m, 3H), 4.50 (s, 2H), 2.23 – 2.08 (m, 1H), 1.37 (s, *J* = 33.2 Hz, 1H), 1.05 (s, 1H); ¹⁹FNMR (282MHz, CDCl₃): δ -63.18 (s); ¹³C NMR (100 MHz, CDCl₃) δ 205.4, 146.4, 144.0, 143.1 (q, *J* = 34.2 Hz), 138.1, 134.0, 130.9, 130.8, 129.4, 128.7, 128.1, 127.9, 126.7, 124.9, 121.4 (q, *J* = 276.5 Hz), 35.2, 24.1, 14.4; IR(KBr): 3060, 3034, 1692, 1600, 1570, 1498, 1452, 1357, 1189, 1133, 766, 695 cm⁻¹; LRMS (EI) *m/z* (relative intensity) 355 (24) [M⁺], 327 (40), 306 (100), 77 (4). Anal. Calcd. For C₂₁H₁₆F₃NO: C, 70.98; H, 4.54; N, 3.94. Found: C, 71.04; H, 4.59; N, 3.89.

1.6) 1-(4-benzyl-2-(trifluoromethyl)quinolin-3-yl)ethanone, 3f



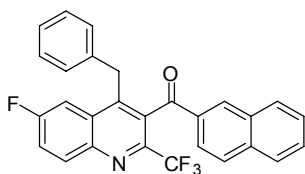
White solid, mp 87-88 °C; ¹HNMR (300 MHz, CDCl₃) δ 8.23 (d, *J* = 8.5 Hz, 1H), 7.98 (d, *J* = 8.5 Hz, 1H), 7.79 (t, *J* = 7.6 Hz, 1H), 7.61 (t, *J* = 7.7 Hz, 1H), 7.34 – 7.13 (m, 3H), 7.13 – 7.00 (m, *J* = 7.2 Hz, 2H), 4.45 (s, 2H), 2.45 (s, 3H); ¹⁹FNMR (282MHz, CDCl₃): δ -63.24 (s); ¹³C NMR (100 MHz, CDCl₃) δ 202.7, 146.4, 143.8, 142.7 (q, *J* = 34.4 Hz), 137.7, 133.3, 131.0, 130.8, 129.6, 128.9, 128.1, 127.9, 126.9, 124.8, 121.4 (q, *J* = 276.1 Hz), 34.7, 32.8 (q, *J* = 2.1 Hz); IR(KBr): 3058, 3026, 1706, 1568, 1496, 1458, 1370, 1192, 1135, 762, 721 cm⁻¹; LRMS (EI) *m/z* (relative intensity) 329 (64) [M⁺], 309 (20), 294 (100), 77 (4). Anal. Calcd. For C₁₉H₁₄F₃NO: C, 69.30; H, 4.28; N, 4.25. Found: C, 69.70; H, 4.39; N, 3.19.

1.7) (4-benzyl-6-methyl-2-(trifluoromethyl)quinolin-3-yl)(4-chlorophenyl)methanone, 3g



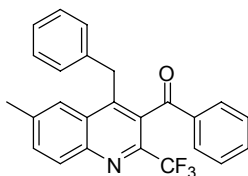
White solid, mp 147-148 °C; ¹HNMR (300 MHz, CDCl₃) δ 8.18 (d, *J* = 8.6 Hz, 1H), 7.81 (s, 1H), 7.72 – 7.54 (m, 3H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.20 – 7.05 (m, 3H), 7.02 – 6.90 (m, 2H), 4.29 (s, 2H), 2.51 (s, 3H); ¹⁹FNMR (282MHz, CDCl₃): δ -62.74 (s); ¹³C NMR (100 MHz, CDCl₃) δ 193.8, 145.5, 144.9, 143.0 (q, *J* = 34.2 Hz), 140.7, 140.2, 137.5, 135.3, 133.6, 130.8, 130.6, 130.0, 129.0, 128.6, 128.2, 127.9, 126.6, 123.6, 121.4 (q, *J* = 276.6 Hz), 35.2, 22.2; IR(KBr): 3029, 2925, 1672, 1586, 1496, 1455, 1375, 1165, 1132, 1093, 900, 772 cm⁻¹; LRMS (EI) *m/z* (relative intensity) 439 (28) [M⁺], 384 (100), 139 (35), 111 (29). HRMS calcd for C₂₅H₁₇ClF₃NO 439.0951, found 439.0954.

1.8) (4-benzyl-6-fluoro-2-(trifluoromethyl)quinolin-3-yl)(naphthalen-2-yl)methanone. 3h.



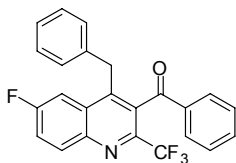
White solid, mp 133-135 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.33 (dd, J = 9.0, 5.5 Hz, 1H), 8.18 – 7.90 (m, 2H), 7.90 – 7.81 (m, 2H), 7.73 (d, J = 8.2 Hz, 1H), 7.70 – 7.41 (m, 4H), 7.21 – 6.94 (m, 5H), 4.28 (s, 2H); ^{19}F NMR (282MHz, CDCl_3): δ -62.90 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 194.0, 161.8(d, J = 253.1 Hz), 145.1(d, J = 6.0 Hz), 143.6, 143.4(q, J = 34.3 Hz), 136.9, 135.7, 133.8, 133.3(d, J = 9.7 Hz), 132.4, 131.8, 131.0, 129.3, 128.9, 128.8(d, J = 10.6 Hz), 128.6, 128.4, 127.7, 127.5, 126.6, 126.5, 123.4, 121.2 (d, J = 26.1 Hz), 121.0(q, J = 277.4 Hz), 108.4(d, J = 23.3 Hz), 35.4; IR(KBr): 3030, 2932, 1663, 1625, 1595, 1573, 1498, 1450, 1197, 1184, 842, 707 cm^{-1} ; LRMS (EI) m/z (relative intensity) 459 (75) [M^+], 438 (43), 361 (54), 311 (38), 155 (29), 127 (100). Anal.Calcld. For $\text{C}_{28}\text{H}_{17}\text{F}_4\text{NO}$: C, 73.20; H, 3.73; N, 3.05. Found: C, 73.12; H, 3.87; N, 2.91.

1.9) (4-benzyl-6-methyl-2-(trifluoromethyl)quinolin-3-yl)(phenyl)methanone, 3i.



White solid, mp 141-142 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.17 (d, J = 8.6 Hz, 1H), 7.85 – 7.60 (m, 4H), 7.53 (t, J = 7.2 Hz, 1H), 7.35 (t, J = 7.6 Hz, 2H), 7.20 – 6.93 (m, 5H), 4.29 (q, J = 15.6 Hz, 2H), 2.49 (s, 3H); ^{19}F NMR (282MHz, CDCl_3): δ -62.72 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 194.9, 145.4, 144.8, 143.1 (q, J = 34.0 Hz), 140.0, 137.7, 136.8, 134.1, 133.4, 130.5, 130.5, 129.5, 128.6, 128.5, 128.1, 127.8, 126.5, 123.6, 121.4 (q, J = 276.6 Hz), 35.4, 22.1; IR(KBr): 3060, 3031, 1676, 1621, 1597, 1580, 1497, 1450, 1373, 1164, 1128, 831, 701 cm^{-1} ; LRMS (EI) m/z (relative intensity) 405 (78) [M^+], 384 (100), 307 (53), 105 (53), 77 (58). Anal.Calcld. For $\text{C}_{25}\text{H}_{18}\text{F}_3\text{NO}$: C, 74.06; H, 4.48; N, 3.45. Found: C, 73.66; H, 4.49; N, 3.32.

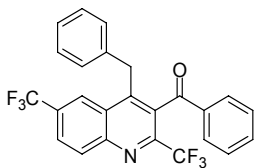
1.10) (4-benzyl-6-fluoro-2-(trifluoromethyl)quinolin-3-yl)(phenyl)methanone, 3j.



White solid, mp 126-127 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.30 (dd, J = 9.1, 5.5 Hz, 1H), 7.74 (d, J = 7.6 Hz, 2H), 7.67 – 7.50 (m, 3H), 7.39 (t, J = 7.7 Hz, 2H), 7.22 – 6.96 (m, 5H), 4.26 (s, 2H); ^{19}F NMR (282MHz, CDCl_3): δ -62.87 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 194.5, 162.2(d, J = 253.2 Hz), 145.3 (d, J = 6.0 Hz), 143.6(q, J = 34.4 Hz), 143.9, 137.2, 136.7, 134.4, 133.7(d, J = 9.6 Hz), 131.2, 129.5, 129.1(d, J = 10.1 Hz), 128.8, 128.8, 128.2, 126.9, 121.6(d, J = 26.1 Hz), 121.3(q, J = 276.3 Hz), 108.7 (d, J = 23.3 Hz), 35.7; IR(KBr): 3089, 1672, 1624, 1597, 1572, 1498, 1445, 1186, 1137, 744, 698, 521 cm^{-1} ; LRMS (EI) m/z (relative intensity) 409 (96) [M^+], 388 (100), 311 (93), 105 (74), 77 (84). Anal.Calcld. For $\text{C}_{24}\text{H}_{15}\text{F}_4\text{NO}$: C, 70.41; H, 3.69; N, 3.42. Found: C, 70.50;

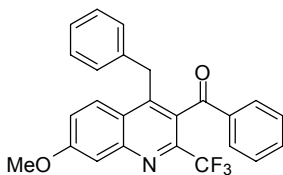
H, 3.80;N, 3.33.

1.11) (4-benzyl-2,6-bis(trifluoromethyl)quinolin-3-yl)(phenyl)methanone, 3k.



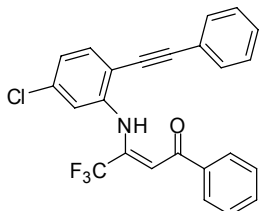
White solid, mp 129-130 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.49 – 8.25 (m, 2H), 7.99 (d, J = 8.9 Hz, 1H), 7.74 (d, J = 7.2 Hz, 2H), 7.59 (t, J = 7.3 Hz, 1H), 7.41 (t, J = 7.7 Hz, 2H), 7.23 – 7.11 (m, 3H), 7.04 (d, J = 6.4 Hz, 2H), 4.57 – 4.14 (m, 2H); ^{19}F NMR (282MHz, CDCl_3): δ -63.13 (s), -63.24 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 193.6, 147.4, 147.1, 145.9 (q, J = 34.3 Hz), 136.8, 136.2, 134.1, 131.9, 131.2, 130.6 (q, J = 33.1 Hz), 129.1, 128.5, 127.8, 126.7, 126.6, 126.3 (d, J = 2.7 Hz), 123.0 (d, J = 273.0 Hz), 122.5 (d, 4.5 Hz), 120.6 (d, J = 277.5 Hz), 35.3; IR(KBr): 3028, 1670, 1596, 1580, 1496, 1451, 1382, 1297, 1189, 1130, 752, 693 cm^{-1} ; LRMS (EI) m/z (relative intensity) 459 (69) [M^+], 438 (57), 361 (78), 105 (100), 77 (78). Anal.Calc'd. For $\text{C}_{25}\text{H}_{15}\text{F}_6\text{NO}$: C, 65.36; H, 3.29; N, 3.05. Found: C, 65.58; H, 3.18; N, 2.90.

1.12) (4-benzyl-7-methoxy-2-(trifluoromethyl)quinolin-3-yl)(phenyl)methanone, 3l.



White solid, mp 157-158 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.90 (d, J = 9.4 Hz, 1H), 7.73 (d, J = 7.5 Hz, 2H), 7.63 – 7.49 (m, 2H), 7.44 – 7.28 (m, 3H), 7.24 – 6.91 (m, 5H), 4.35 – 4.15 (m, 2H), 3.99 (s, 3H); ^{19}F NMR (282MHz, CDCl_3): δ -62.42 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 195.0, 161.7, 149.0, 145.6, 144.4 (q, J = 34.4 Hz), 137.8, 137.1, 134.1, 129.5, 128.7, 128.6, 128.4, 128.2, 126.6, 126.0, 123.0, 122.9, 121.4 (d, J = 276.9 Hz), 108.2, 55.8, 35.5; IR(KBr): 3025, 2934, 1666, 1621, 1596, 1579, 1497, 1453, 1424, 1381, 1221, 1133, 715, 558 cm^{-1} ; LRMS (EI) m/z (relative intensity) 421 (58) [M^+], 400 (61), 323 (24), 185 (91), 105 (46), 77 (42), 75 (100). HRMS calcd for $\text{C}_{25}\text{H}_{18}\text{F}_3\text{NO}_2$ 421.1290, found 421.1293.

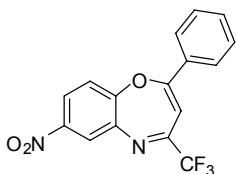
1.13) (Z)-3-(5-chloro-2-(phenylethynyl)phenylamino)-4,4,4-trifluoro-1-phenylbut-2-en-1-one, 3m.



Yellow solid, mp 82-83 °C; ^1H NMR (300 MHz, CDCl_3) δ 12.37 (s, 1H), 7.99 – 7.89 (m, 2H), 7.66 – 7.43 (m, 6H), 7.43 – 7.27 (m, 4H), 7.11 (d, J = 8.5 Hz, 1H), 6.50 (s, 1H); ^{19}F NMR (282MHz, CDCl_3): δ -63.31 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 191.6, 147.1 (q, J = 31.7 Hz), 138.5, 138.2, 136.4, 133.5, 132.8, 131.8, 128.8, 128.7, 128.4, 127.6, 125.8, 123.3, 122.8, 121.5, 120.1 (q, J =

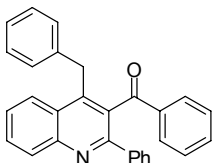
277.6 Hz), 95.4, 93.6(q, $J = 4.7$ Hz, 2C), 85.6; IR(KBr): 3094, 2220, 1632, 1620, 1588, 1497, 1446, 1321, 1291, 1187, 1138, 880, 754, 688, 609 cm^{-1} ; LRMS (EI) m/z (relative intensity) 425 (73) [M^+], 356 (20), 176 (17), 105 (100), 77 (40). HRMS calcd for $\text{C}_{24}\text{H}_{15}\text{ClF}_3\text{NO}$ 425.0794, found 425.0792.

1.14) (2Z,4E)-7-nitro-2-phenyl-4-(trifluoromethyl)benzo[b][1,4]oxazepine, 4n.



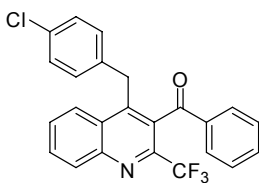
Yellow solid, mp 132-134 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.31 (d, $J = 2.7$ Hz, 1H), 8.20 (dd, $J = 8.9, 2.7$ Hz, 1H), 7.85 (d, $J = 7.5$ Hz, 2H), 7.68 – 7.44 (m, 3H), 7.20 (d, $J = 8.9$ Hz, 1H), 6.44 (s, 1H). ^{19}F NMR (282MHz, CDCl_3): δ -72.45 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 167.2, 157.0 (q, $J = 35.2$ Hz), 155.2, 146.0, 140.5, 132.2, 131.2, 129.2, 126.6, 125.7, 124.9, 122.3, 119.5 (q, $J = 278.8$ Hz), 102.0; IR(KBr): 1615, 1590, 1514, 1493, 1450, 1344, 1190, 1123, 823, 760, 680 cm^{-1} ; LRMS (EI) m/z (relative intensity) 334 (100) [M^+], 265 (31), 219 (24), 105 (62), 77 (21). HRMS calcd for $\text{C}_{16}\text{H}_9\text{F}_3\text{N}_2\text{O}_3$ 334.0565, found 334.0560.

1.15) (4-benzyl-2-phenylquinolin-3-yl)(phenyl)methanone, 3o.²



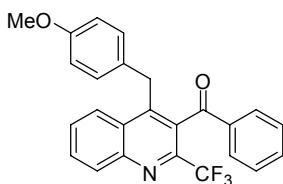
Brown solid, mp 133-135 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.25 (d, $J = 8.2$ Hz, 1H), 8.05 (d, $J = 8.4$ Hz, 1H), 7.76 (t, $J = 7.4$ Hz, 1H), 7.66 – 7.43 (m, 5H), 7.42 – 7.01 (m, 11H), 4.41 (d, $J = 19.2$ Hz, 2H). LRMS (EI) m/z (relative intensity) 399 (100) [M^+], 370 (50), 322 (37), 160 (25), 105 (16), 77 (21).

1.16) (4-(4-chlorobenzyl)-2-(trifluoromethyl)quinolin-3-yl)(phenyl)methanone, 3p.



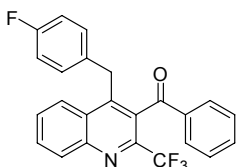
Lightyellow solid, mp 150-152 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.30 (d, $J = 8.4$ Hz, 1H), 7.98 (d, $J = 8.4$ Hz, 1H), 7.84 (t, $J = 7.5$ Hz, 1H), 7.77 – 7.50 (m, 4H), 7.39 (t, $J = 7.5$ Hz, 1H), 7.17 – 7.04 (m, 2H), 7.01 – 6.86 (m, 2H), 4.27 (q, $J = 15.8$ Hz, 2H); ^{19}F NMR (282MHz, CDCl_3): δ -62.83 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 194.7, 146.8, 145.3, 144.1 (q, $J = 34.1$ Hz), 136.8, 136.2, 134.4, 132.5, 131.2, 131.0, 130.6, 129.7, 129.6, 129.5, 128.8, 128.7, 127.6, 124.6, 121.3 (q, $J = 276.8$ Hz), 34.8; IR(KBr): 3058, 1671, 1596, 1581, 1493, 1449, 1411, 1251, 1149, 902, 767, 689 cm^{-1} ; LRMS (EI) m/z (relative intensity) 425 (97) [M^+], 404 (95), 293 (96), 105 (99), 77 (100). HRMS calcd for $\text{C}_{24}\text{H}_{15}\text{ClF}_3\text{NO}$ 425.0794, found 425.0791.

1.17) (4-(4-methoxybenzyl)-2-(trifluoromethyl)quinolin-3-yl)(phenyl)methanone, 3q.



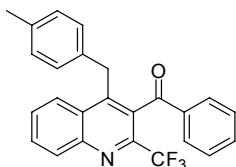
Lightyellow solid, mp 134-135 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.28 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 7.82 (t, J = 7.7 Hz, 1H), 7.74 (d, J = 7.5 Hz, 2H), 7.63 (t, J = 7.7 Hz, 1H), 7.56 (t, J = 7.4 Hz, 1H), 7.39 (t, J = 7.7 Hz, 2H), 6.93 (d, J = 8.5 Hz, 2H), 6.68 (d, J = 8.6 Hz, 2H), 4.25 (q, J = 15.7 Hz, 2H), 3.68 (s, 3H); ^{19}F NMR (282MHz, CDCl_3): δ -62.90 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 194.4, 157.8, 146.4, 146.0, 143.7(q, J = 34.2 Hz), 136.5, 133.8, 130.6, 130.5, 130.0, 129.4, 129.1, 129.1, 128.9, 128.3, 127.4, 124.5, 121.0 (q, J = 276.9 Hz), 113.6, 54.7, 34.3; IR(KBr): 3066, 2933, 2838, 1672, 1610, 1596, 1580, 1512, 1449, 1370, 1257, 1177, 900, 766 cm^{-1} ; LRMS (EI) m/z (relative intensity) 421 (100) [M^+], 400 (56), 293 (87), 105 (57), 77 (71). Anal.Calc'd. For $\text{C}_{25}\text{H}_{18}\text{F}_3\text{NO}_2$: C, 71.25; H, 4.31; N, 3.32. Found: C, 70.87; H, 4.34; N, 3.22.

1.18) (4-(4-fluorobenzyl)-2-(trifluoromethyl)quinolin-3-yl)(phenyl)methanone, 3r.



Brown solid, mp 100-102 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.29 (d, J = 8.5 Hz, 1H), 8.01 (d, J = 8.5 Hz, 1H), 7.89 – 7.78 (m, 1H), 7.73 (d, J = 7.9 Hz, 2H), 7.69 – 7.60 (m, 1H), 7.60 – 7.50 (m, 1H), 7.39 (t, J = 7.6 Hz, 2H), 7.04 – 6.89 (m, 2H), 6.89 – 6.72 (m, 2), 4.28 (q, J = 15.7 Hz, 2H); ^{19}F NMR (282MHz, CDCl_3): δ -62.89 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 194.8, 161.5(d, J = 245.5 Hz), 146.8, 145.6, 144.1(q, J = 34.2 Hz), 136.8, 134.3, 133.4 (d, J = 2.9 Hz), 131.1, 131.0, 130.5, 129.7 (d, J = 8.1 Hz), 129.7, 129.5, 128.8, 127.6, 124.7, 121.3(q, J = 276.8 Hz), 115.4(d, J = 21.5 Hz), 34.7; IR(KBr): 3069, 1668, 1596, 1581, 1512, 1450, 1239, 1182, 902, 771 cm^{-1} ; LRMS (EI) m/z (relative intensity) 409 (76) [M^+], 388 (100), 293 (52), 105 (59), 77 (57). Anal.Calc'd. For $\text{C}_{24}\text{H}_{15}\text{F}_4\text{NO}$: C, 70.41; H, 3.69; N, 3.42. Found: C, 70.52; H, 3.74; N, 3.28.

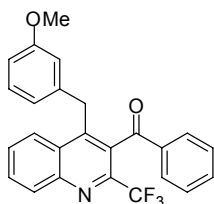
1.19) (4-(4-methylbenzyl)-2-(trifluoromethyl)quinolin-3-yl)(phenyl)methanone, 3s.



Lightyellow solid, mp 167-170 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.28 (d, J = 8.5 Hz, 1H), 8.04 (d, J = 8.5 Hz, 1H), 7.88 – 7.69 (m, 3H), 7.68 – 7.49 (m, 2H), 7.38 (t, J = 7.7 Hz, 2H), 6.93 (q, J = 8.1 Hz, 4H), 4.27 (q, J = 15.7 Hz, 2H), 2.21 (s, 3H); ^{19}F NMR (282MHz, CDCl_3): δ -62.88 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 194.7, 146.7, 146.2, 144.0(q, J = 34.2 Hz), 136.9, 136.2, 134.7, 134.1, 130.9, 130.8, 130.4, 129.5, 129.4, 129.3, 128.7, 128.1, 127.8, 124.9, 121.3(q, J = 277.2 Hz), 35.2, 20.8; IR(KBr): 2924, 1673, 1595, 1568, 1513, 1449, 1135, 902, 769 cm^{-1} ; LRMS (EI) m/z (relative intensity) 405 (100) [M^+], 384 (87), 293 (99), 105 (82), 77 (81). Anal.Calc'd. For

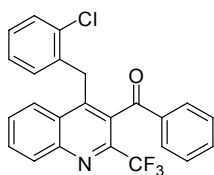
C₂₅H₁₈F₃NO: C, 74.06; H, 4.48; N, 3.45. Found: C, 73.72; H, 4.60; N, 3.35.

1.20) (4-(3-methoxybenzyl)-2-(trifluoromethyl)quinolin-3-yl)(phenyl)methanone, 3t.



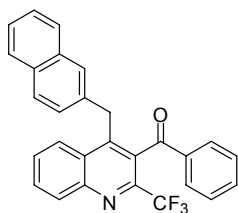
Brown solid, mp 128-129 °C; ¹HNMR (300 MHz, CDCl₃) δ 8.29 (d, *J* = 8.5 Hz, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 7.4 Hz, 2H), 7.64 (t, *J* = 7.7 Hz, 1H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.07 (t, *J* = 7.8 Hz, 1H), 6.72 – 6.53 (m, 3H), 4.47 – 4.11 (m, 2H), 3.66 (s, *J* = 3.2 Hz, 3H); ¹⁹FNMR (282MHz, CDCl₃): δ -62.87 (s); ¹³C NMR (100 MHz, CDCl₃) δ 194.3, 159.3, 146.4, 145.4, 143.7 (q, *J* = 34.2 Hz), 138.9, 136.5, 136.5, 133.8, 130.7, 130.5, 130.1, 129.2, 129.2, 128.3, 127.5, 124.5, 120.9 (q, *J* = 276.7 Hz), 120.2, 113.9, 111.5, 54.6, 35.1; IR(KBr): 3070, 2950, 2835, 1671, 1607, 1582, 1489, 1454, 1371, 1283, 1138, 907, 766 cm⁻¹; LRMS (EI) *m/z* (relative intensity) 421 (72) [M⁺], 400 (39), 293 (100), 105 (56), 77 (62).
Anal.Calcd. For C₂₅H₁₈F₃NO₂: C, 71.25; H, 4.31; N, 3.32. Found: C, 71.25; H, 4.31; N, 3.23.

1.21) (4-(2-chlorobenzyl)-2-(trifluoromethyl)quinolin-3-yl)(phenyl)methanone, 3u.



White solid, mp 136-137 °C; ¹HNMR (300 MHz, CDCl₃) δ 8.32 (d, *J* = 7.9 Hz, 1H), 7.93 – 7.72 (m, 4H), 7.70 – 7.52 (m, 2H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.99 (t, *J* = 7.3 Hz, 1H), 6.71 (d, *J* = 7.6 Hz, 1H), 4.82 – 3.91 (m, 2H); ¹⁹FNMR (282MHz, CDCl₃): δ -62.89 (s); ¹³C NMR (100 MHz, CDCl₃) δ 194.6, 146.7, 145.2, 144.1 (q, *J* = 34.3 Hz), 136.6, 135.4, 134.4, 133.1, 131.2, 131.0, 129.8, 129.8, 129.6, 129.2, 128.8, 128.1, 127.7, 127.1, 124.6, 121.3 (q, *J* = 276.8 Hz), 32.6; IR(KBr): 3060, 1669, 1597, 1579, 1499, 1449, 1253, 1131, 901, 759 cm⁻¹; LRMS (EI) *m/z* (relative intensity) 425 (83) [M⁺], 404 (90), 370 (32), 293 (41), 105 (100), 77 (90). Anal.Calcd. For C₂₄H₁₅ClF₃NO: C, 67.69; H, 3.55; N, 3.29. Found: C, 67.56; H, 3.72; N, 3.14.

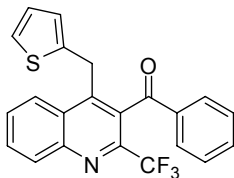
1.22) (4-(naphthalen-2-ylmethyl)-2-(trifluoromethyl)quinolin-3-yl)(phenyl)methanone, 3v.



Brown solid, mp 142-144 °C; ¹HNMR (300 MHz, CDCl₃) δ 8.30 (d, *J* = 8.5 Hz, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.90 – 7.02 (m, 14H), 4.73 – 4.05 (m, 2H); ¹⁹FNMR (282MHz, CDCl₃): δ -62.82 (s); ¹³C NMR (100 MHz, CDCl₃) δ 194.8, 146.8, 145.8, 144.1 (q, *J* = 34.2 Hz), 136.9, 135.3, 134.2,

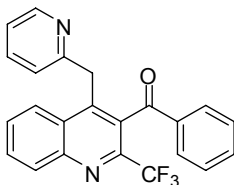
133.3, 132.1, 131.1, 130.9, 130.7, 129.6, 129.5, 128.7, 128.4, 127.9, 127.6, 127.5, 127.0, 126.3, 126.1, 125.7, 124.9, 121.4 (d, $J = 276.1$ Hz), 35.7 cm^{-1} ; IR(KBr): 3060, 2935, 1670, 1595, 1566, 1497, 1449, 1257, 1137, 905, 764; LRMS (EI) m/z (relative intensity) 441 (81) [M^+], 420 (41), 293 (100), 105 (55), 77 (57). Anal.Calcld. For $C_{28}H_{18}F_3NO$: C, 76.18; H, 4.11; N, 3.17. Found: C, 76.57; H, 4.06; N, 3.03.

1.23) phenyl(4-(thiophen-2-ylmethyl)-2-(trifluoromethyl)quinolin-3-yl)methanone, 3w.



White solid, mp 135-136 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.30 (d, $J = 8.5$ Hz, 1H), 8.17 (d, $J = 8.5$ Hz, 1H), 7.86 (t, $J = 7.6$ Hz, 1H), 7.72 (t, $J = 7.8$ Hz, 3H), 7.56 (t, $J = 7.3$ Hz, 1H), 7.38 (t, $J = 7.6$ Hz, 2H), 7.02 (d, $J = 5.0$ Hz, 1H), 6.84 – 6.65 (m, 1H), 6.53 (s, 1H), 4.72 – 4.21 (m, 2H); ^{19}F NMR (282MHz, CDCl_3): δ -62.84 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 194.5, 146.9, 145.2, 144.2 (q, $J = 34.2$ Hz), 139.6, 136.8, 134.3, 131.2, 131.0, 130.1, 129.7, 129.6, 128.8, 127.5, 126.9, 126.3, 124.6, 124.4, 121.3 (q, $J = 277.0$ Hz), 30.0; IR(KBr): 3073, 1674, 1596, 1580, 1496, 1451, 1412, 1264, 1183, 903, 772, 697 cm^{-1} ; LRMS (EI) m/z (relative intensity) 397 (92) [M^+], 376 (41), 293 (100), 105 (32), 77 (48). Anal.Calcld. For $C_{22}H_{14}F_3NOS$: C, 66.49; H, 3.55; N, 3.52. Found: C, 66.41; H, 3.92; N, 3.44.

1.24) phenyl(4-(pyridin-2-ylmethyl)-2-(trifluoromethyl)quinolin-3-yl)methanone, 3x.

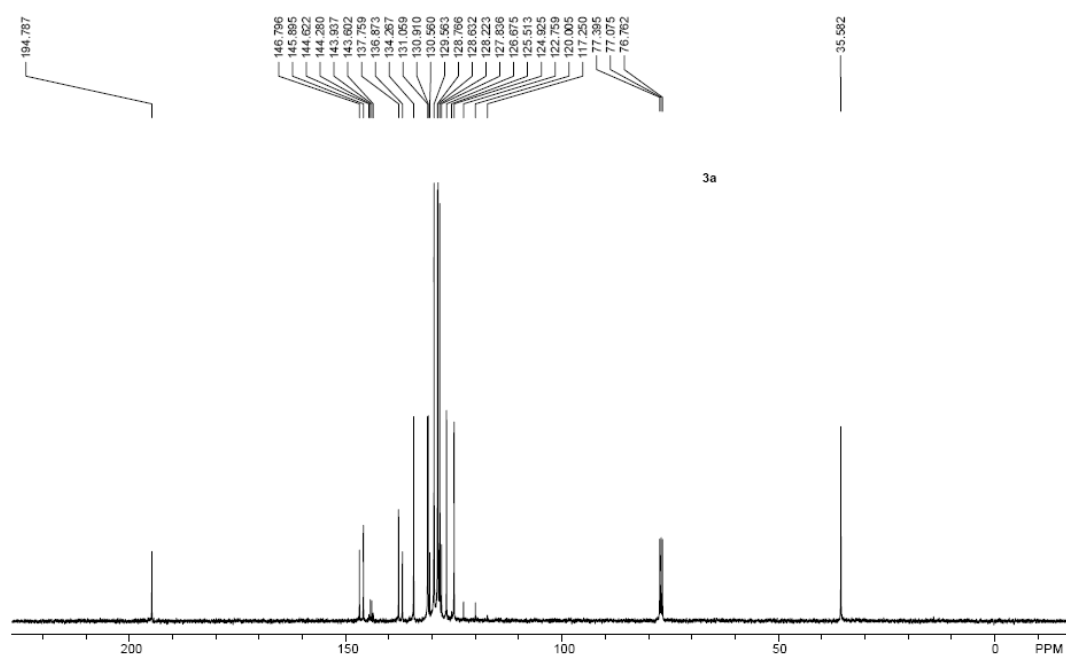
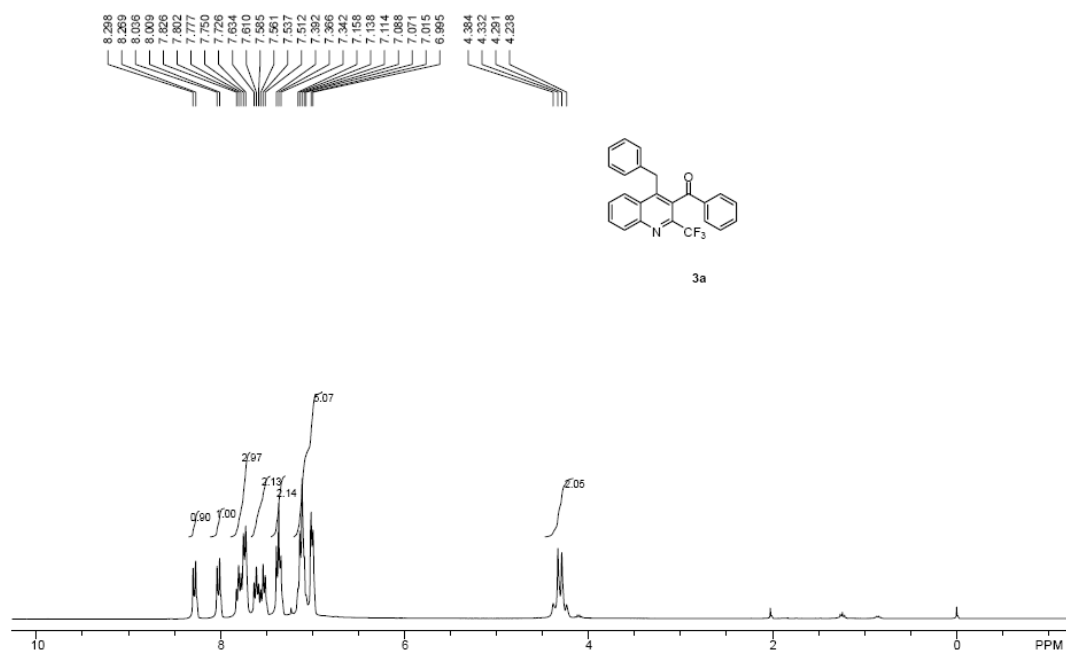


Lightyellow solid, mp 123-125 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.44 (d, $J = 5.1$ Hz, 1H), 8.29 (d, $J = 8.4$ Hz, 1H), 8.19 (d, $J = 8.4$ Hz, 1H), 7.91 – 7.74 (m, 3H), 7.72 – 7.53 (m, 2H), 7.52 – 7.33 (m, 3H), 7.11 – 7.02 (m, 1H), 6.98 (d, $J = 7.9$ Hz, 1H), 4.71 – 4.25 (m, 2H); ^{19}F NMR (282MHz, CDCl_3): δ -62.89 (s); ^{13}C NMR (100 MHz, CDCl_3) δ 195.1, 157.7, 149.1, 146.8, 144.9, 144.1 (q, $J = 34.2$ Hz), 136.9, 136.7, 134.4, 131.1, 130.8, 130.5, 129.7, 129.6, 128.8, 128.0, 125.4, 123.1, 121.8, 121.3 (q, $J = 276.7$ Hz), 38.6; IR(KBr): 3047, 3007, 1664, 1596, 1587, 1498, 1450, 1364, 1258, 1134, 766 cm^{-1} ; LRMS (EI) m/z (relative intensity) 392 (2) [M^+], 287 (100), 105 (6), 77 (9). Anal.Calcld. For $C_{23}H_{15}F_3N_2O$: C, 70.40; H, 3.85; N, 7.14. Found: C, 70.15; H, 4.05; N, 6.92.

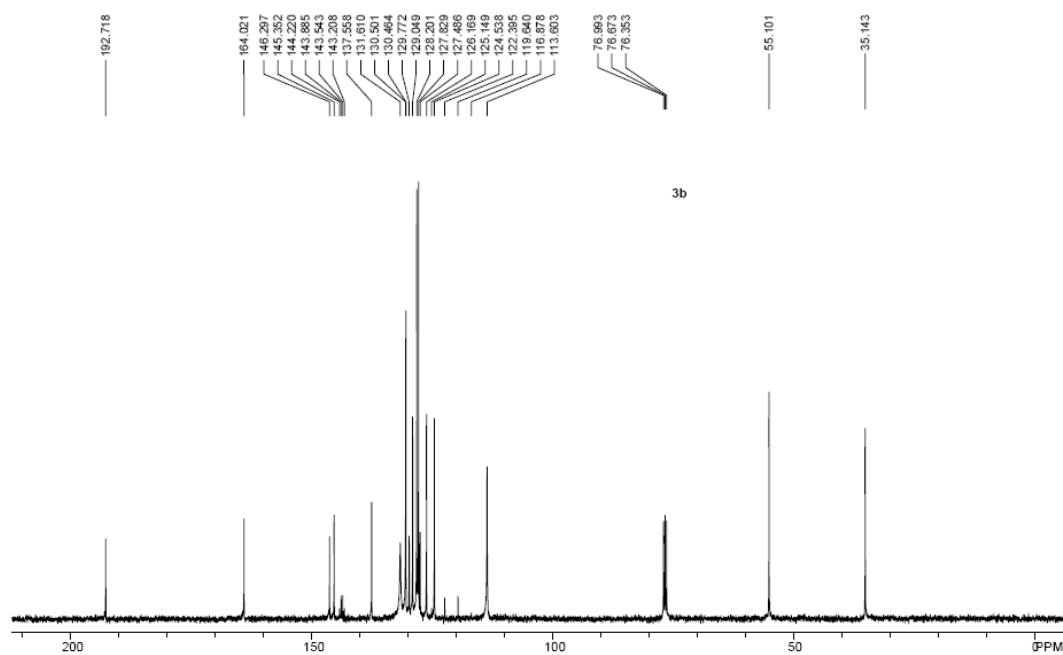
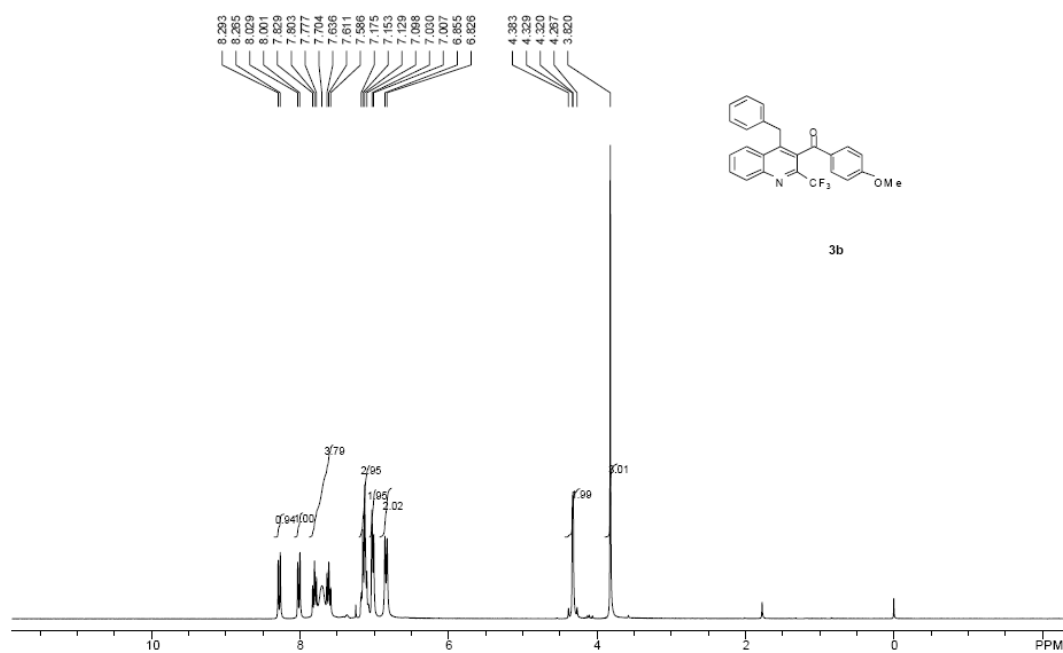
Reference :

- (1) Fustero, S.; Pina, B.; Garcia de la Torre, M., et al. *Org. Lett.* **1999**, *1*, 977-980.
- (2) Roberta Berninia, S. C. G. F. *Synlett* **2009**, 1245-1250.

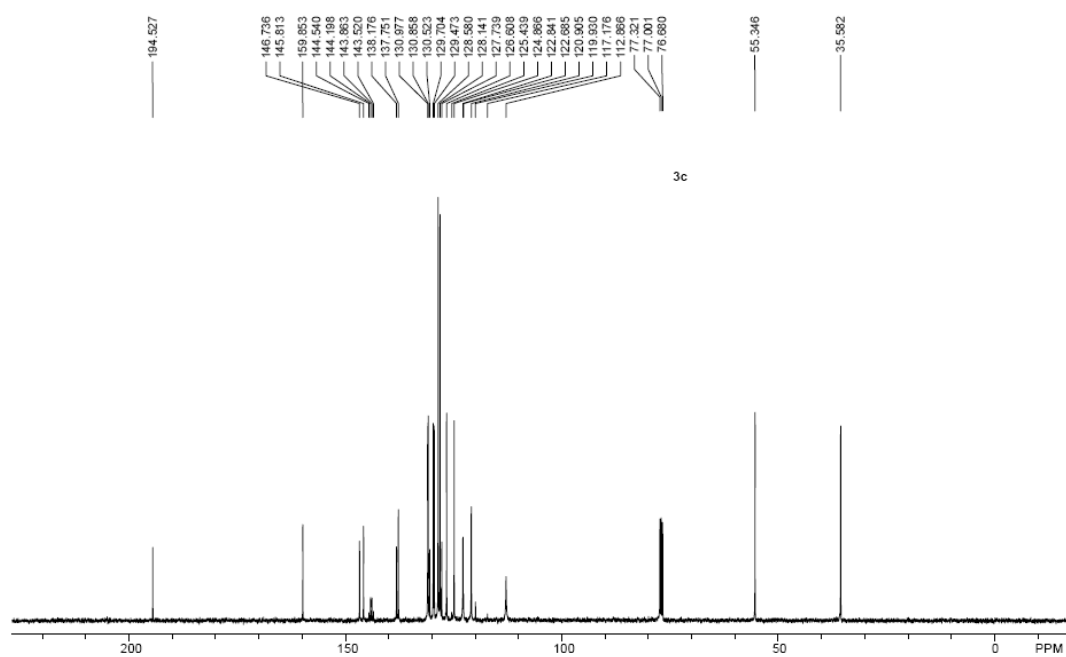
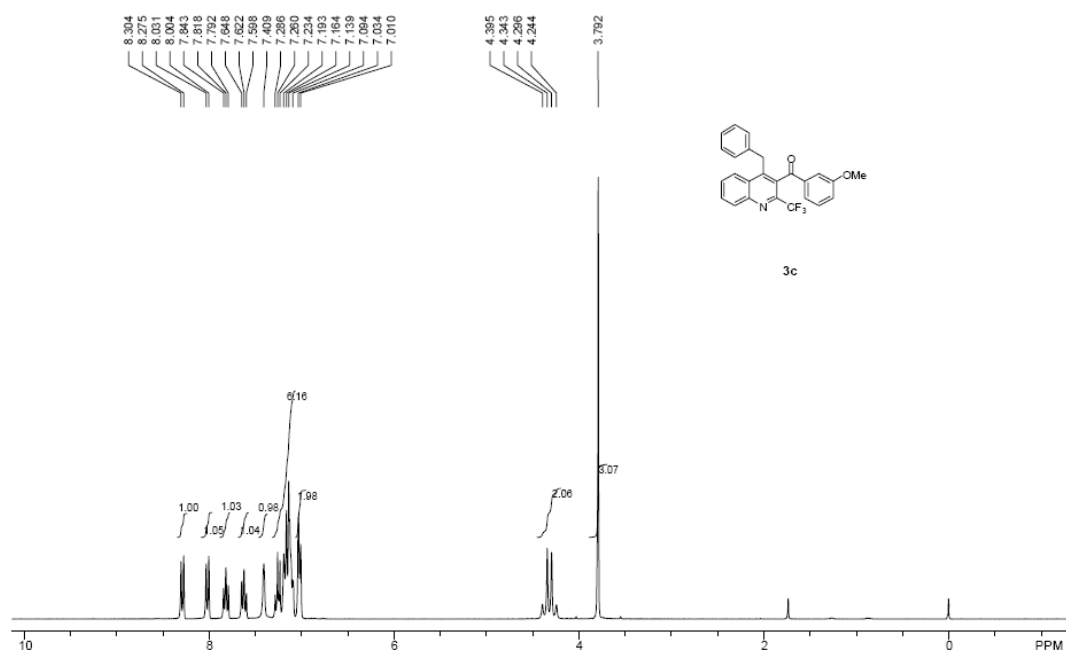
3a



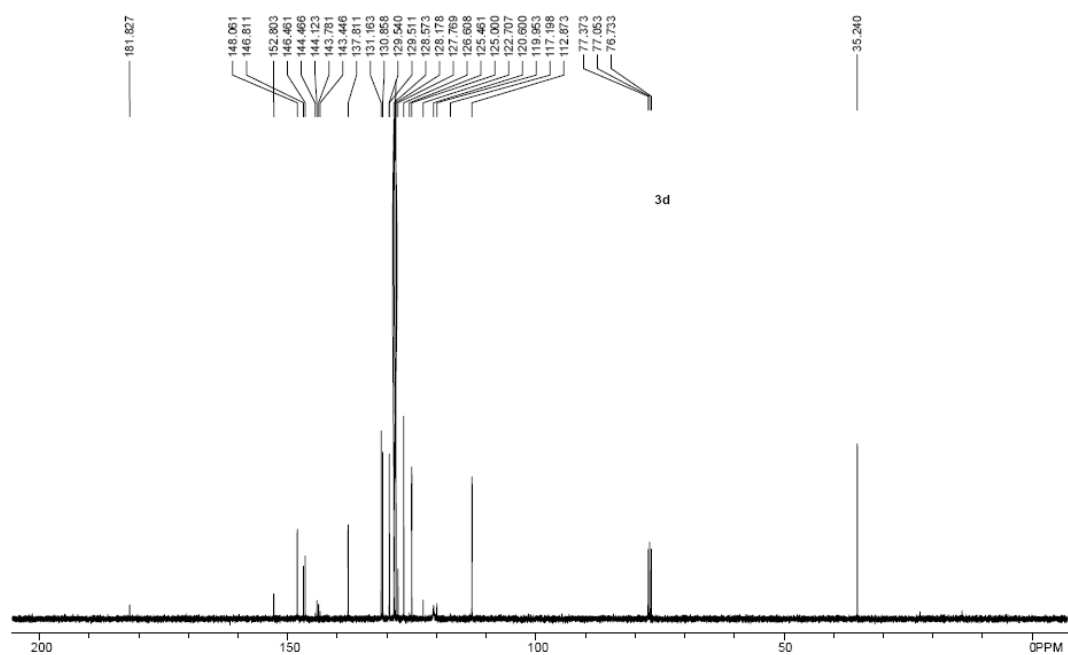
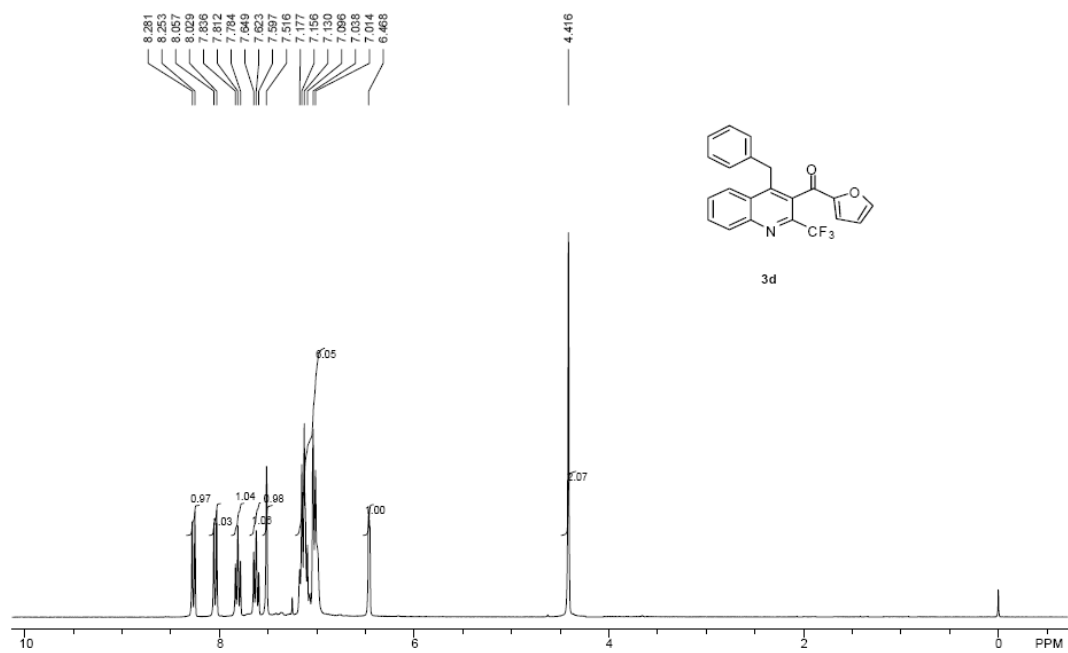
3b



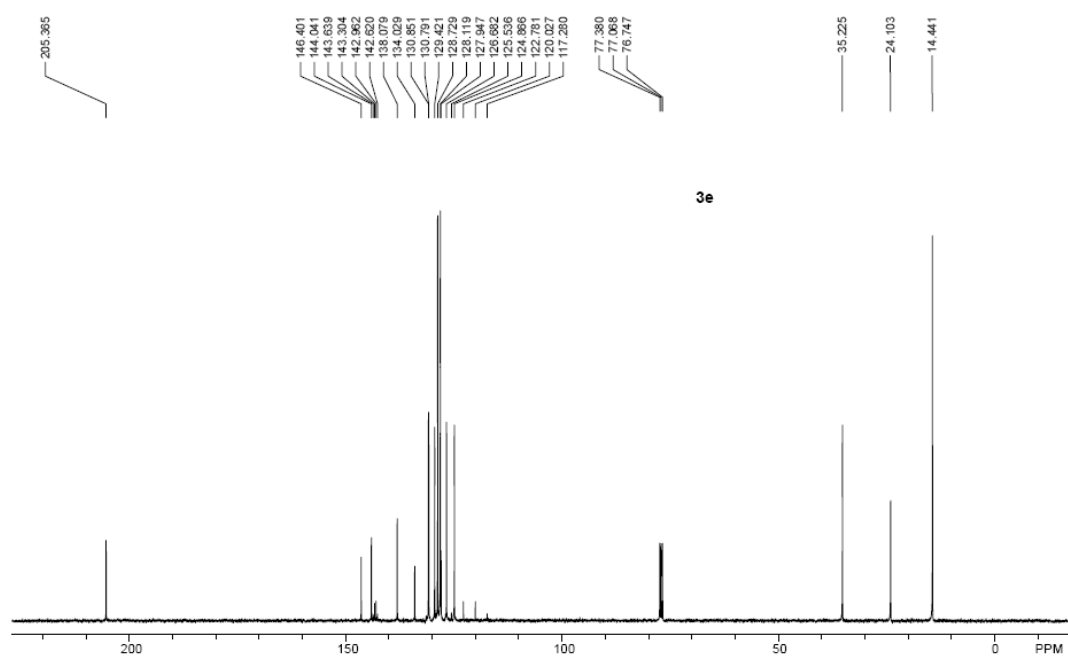
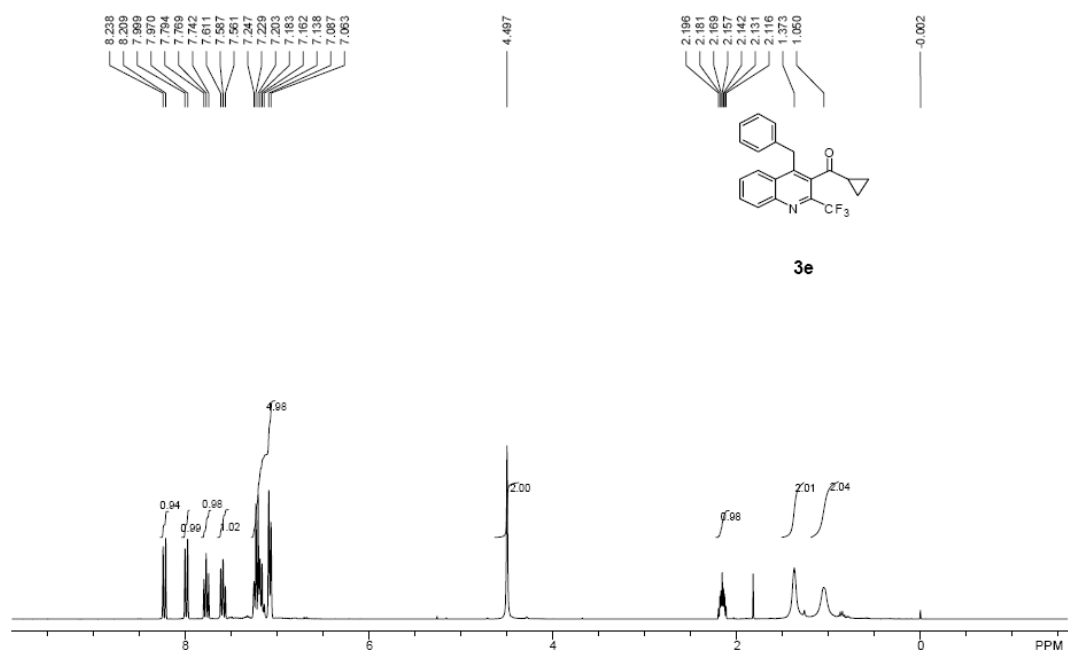
3c



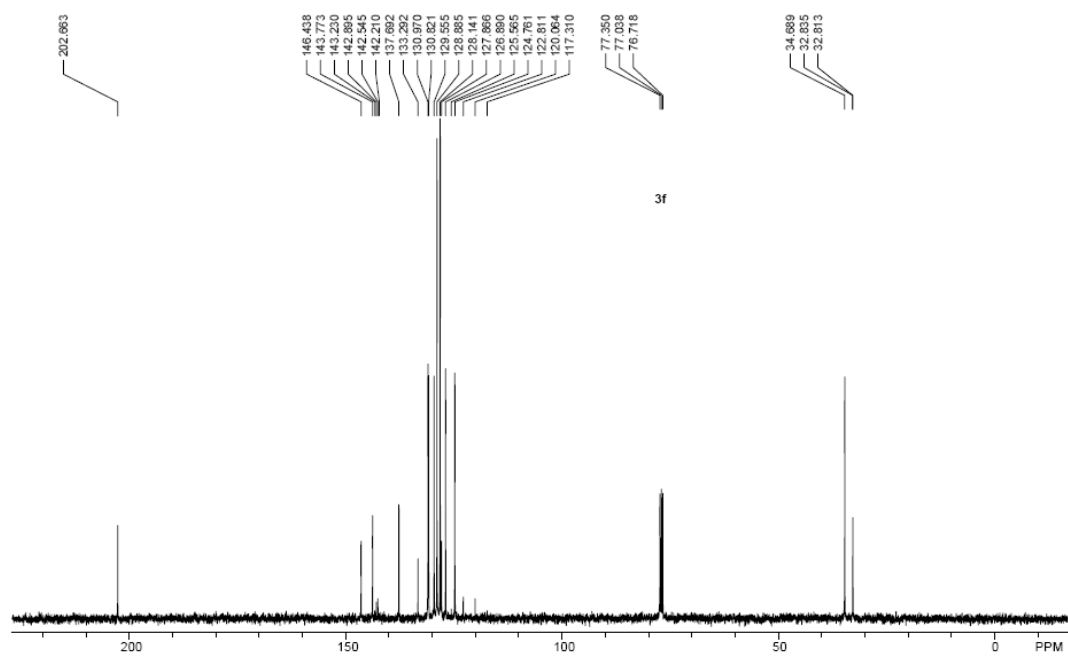
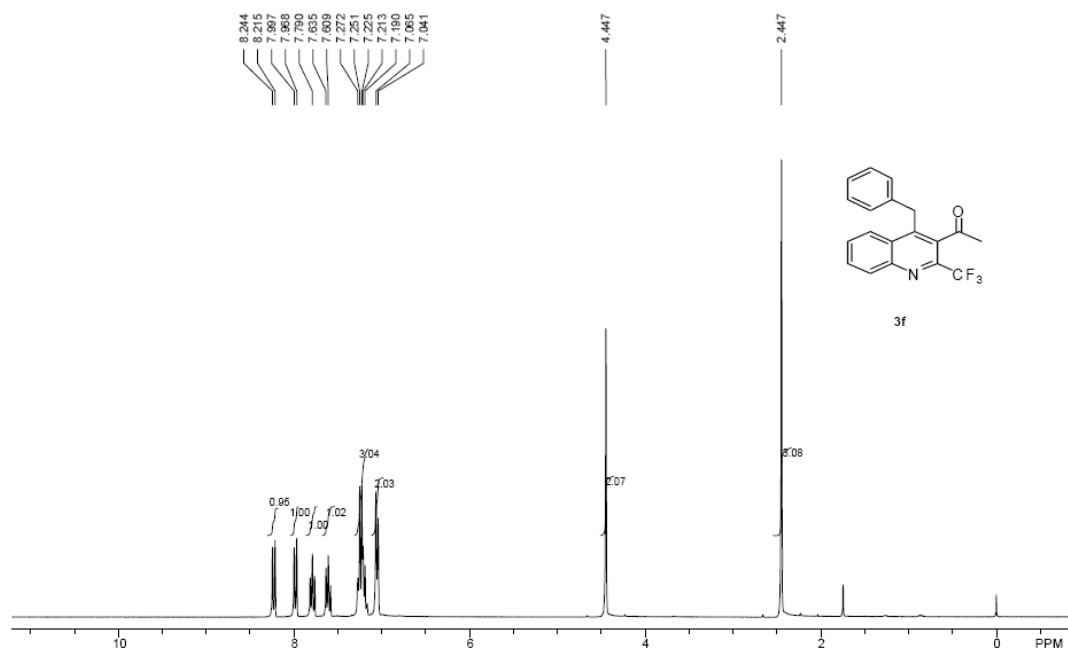
3d



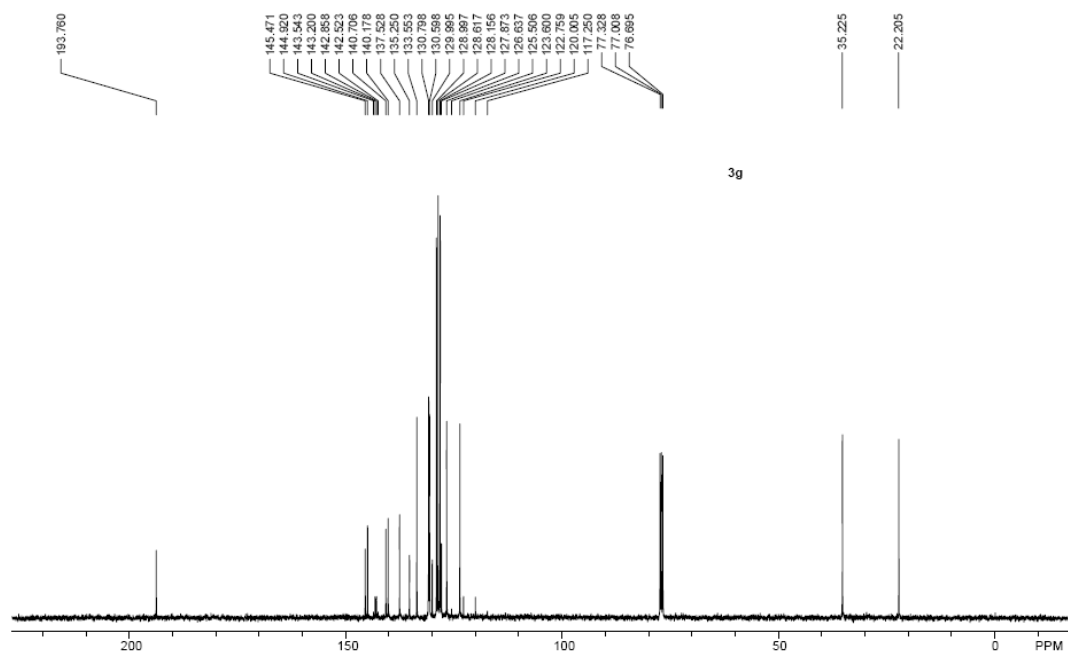
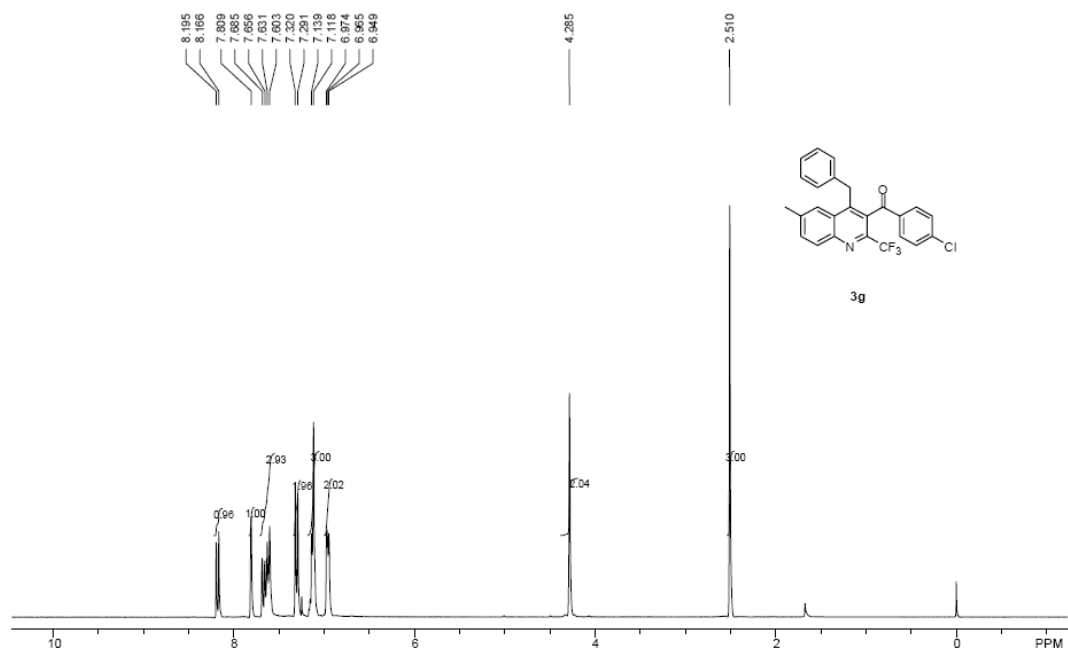
3e



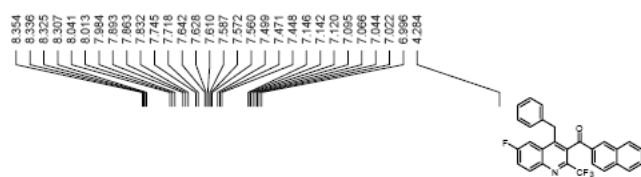
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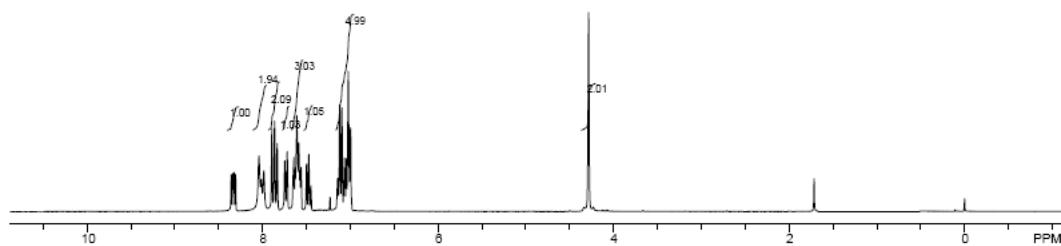
3g



3h

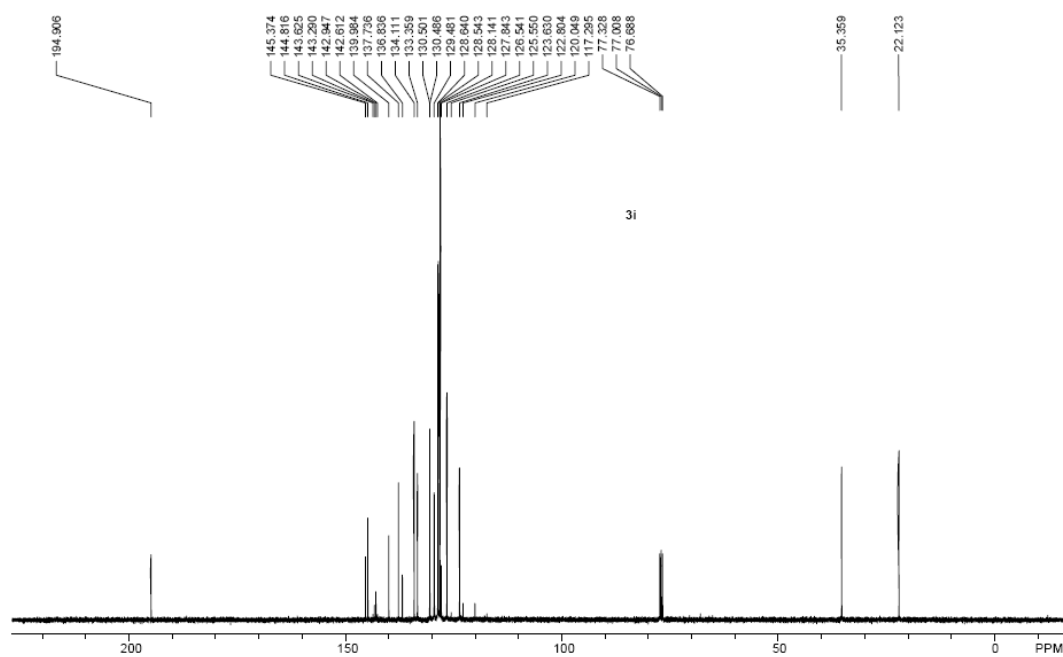
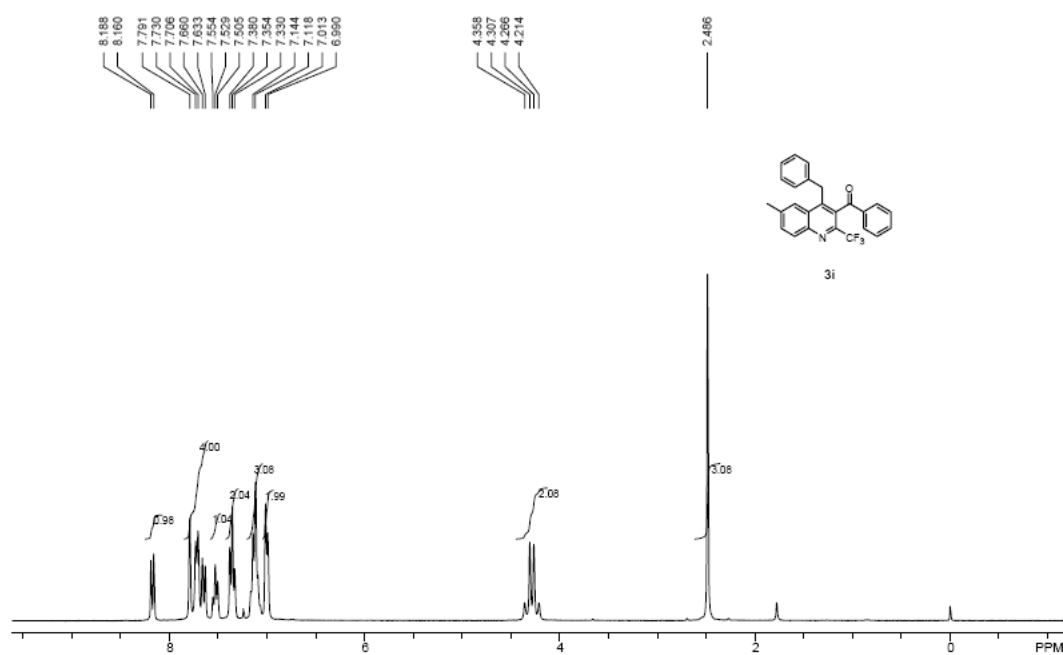


3h

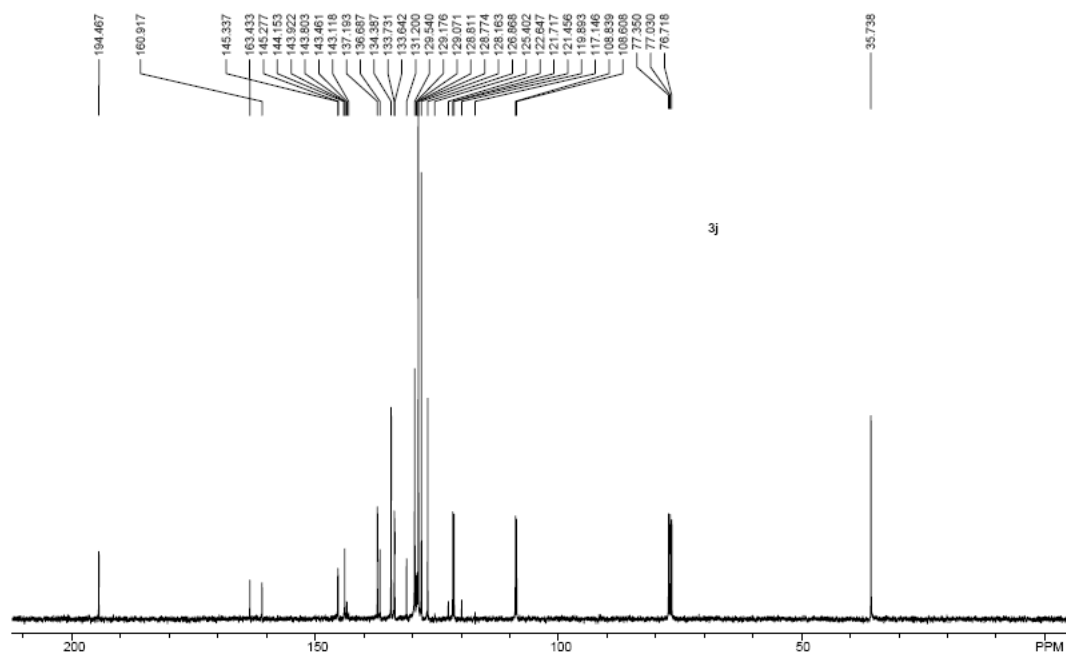
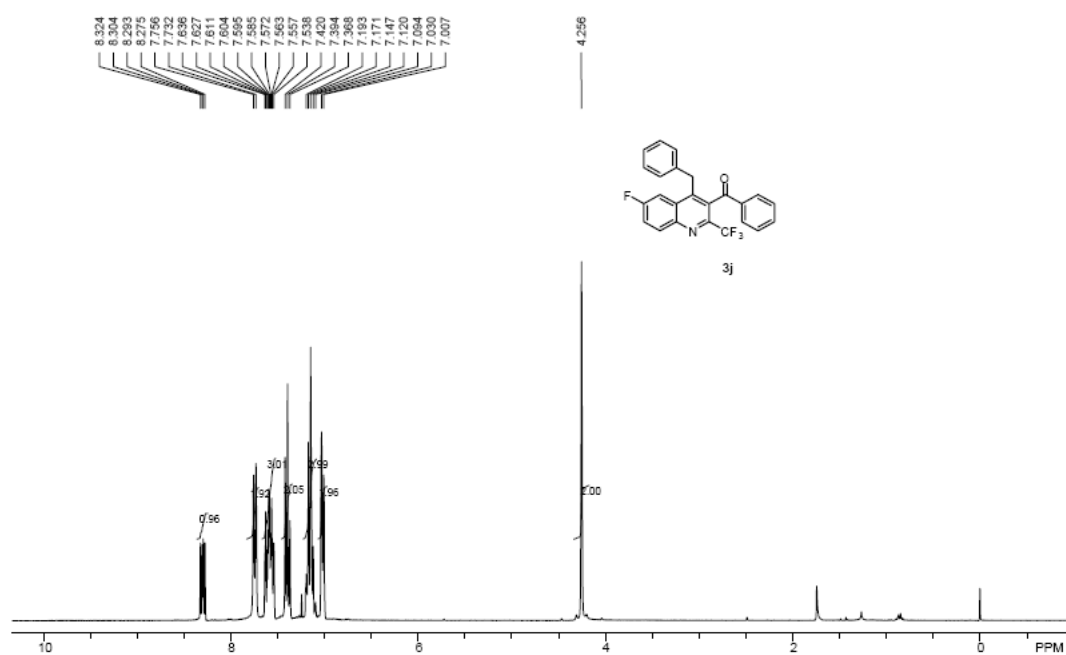


3h

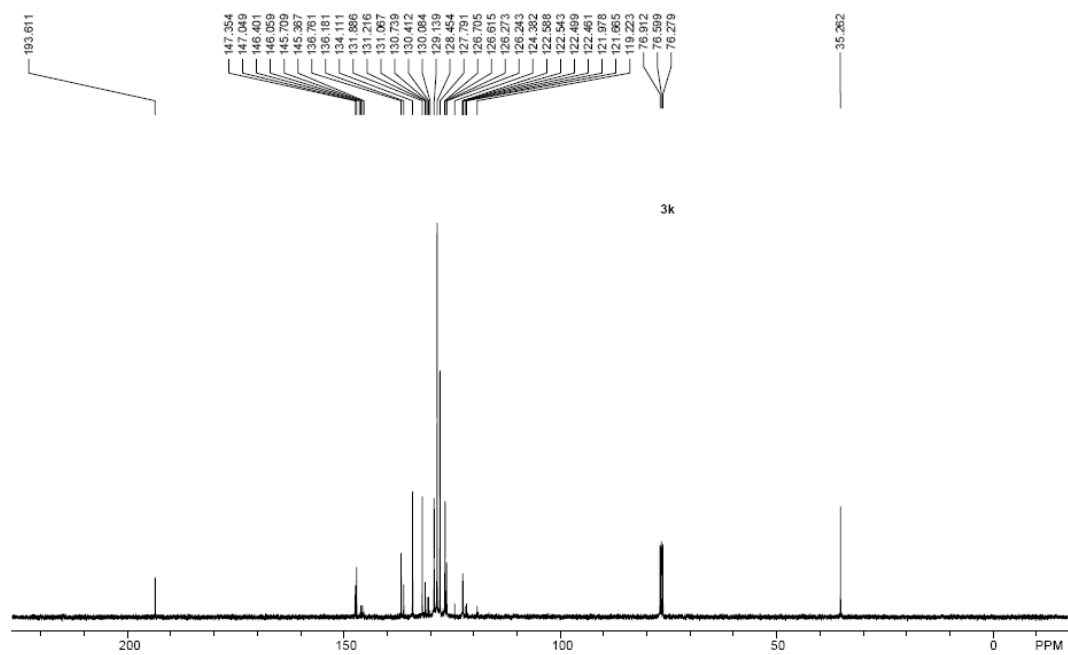
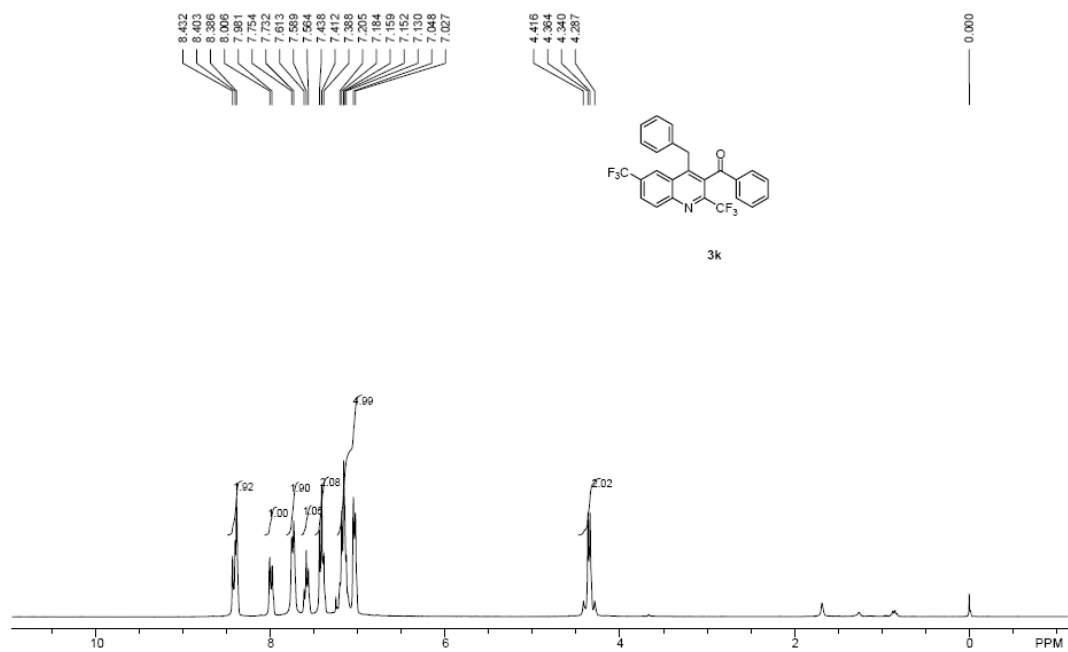
3i

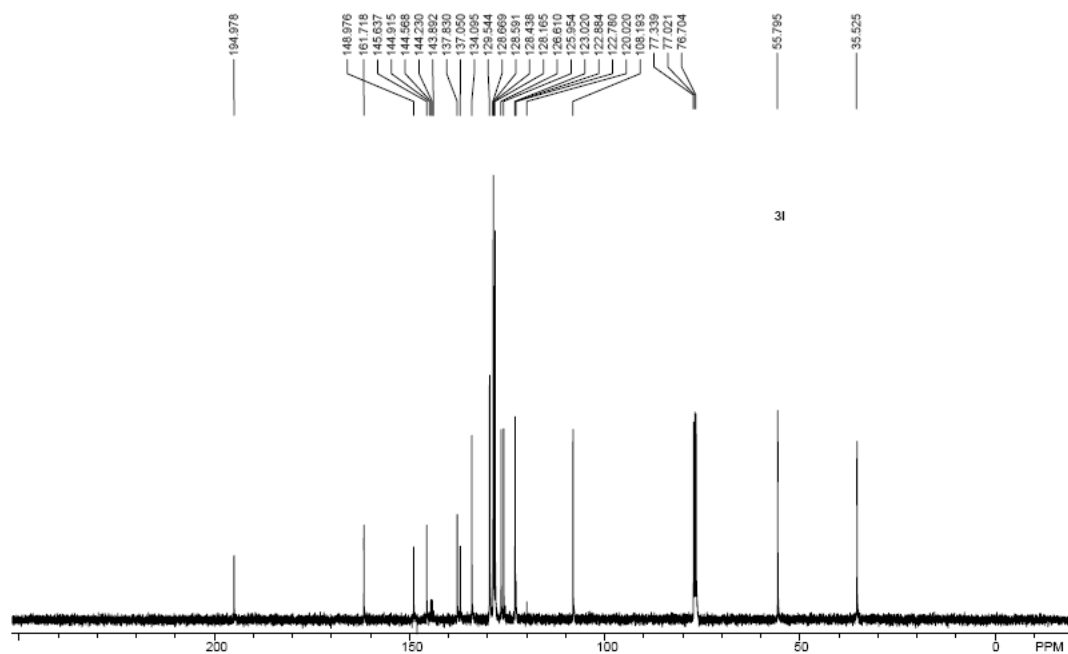
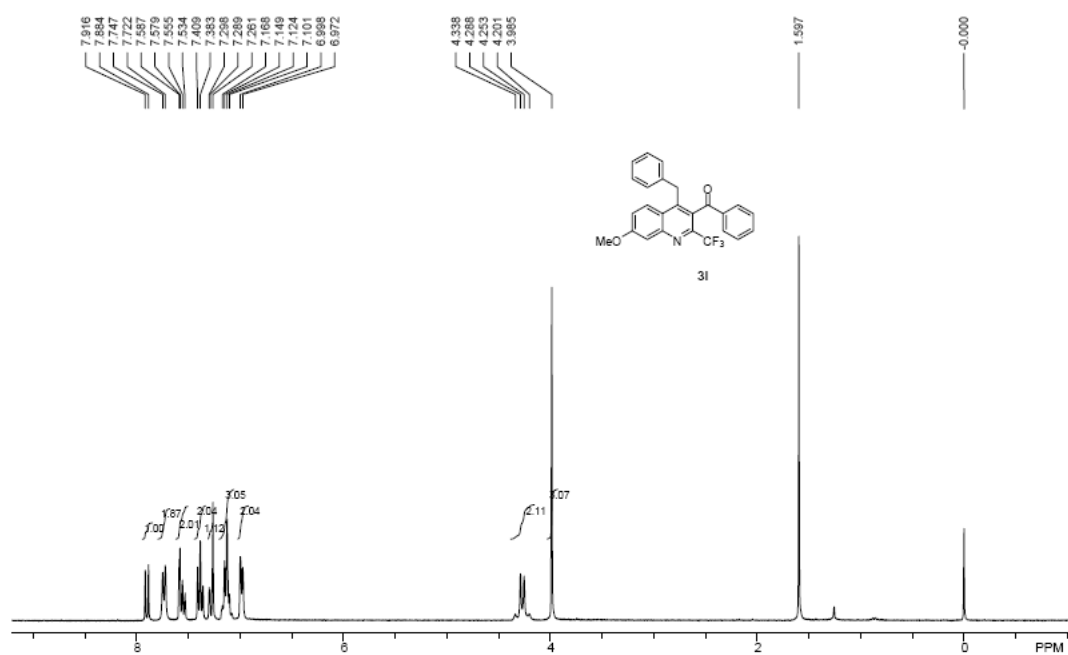


3j

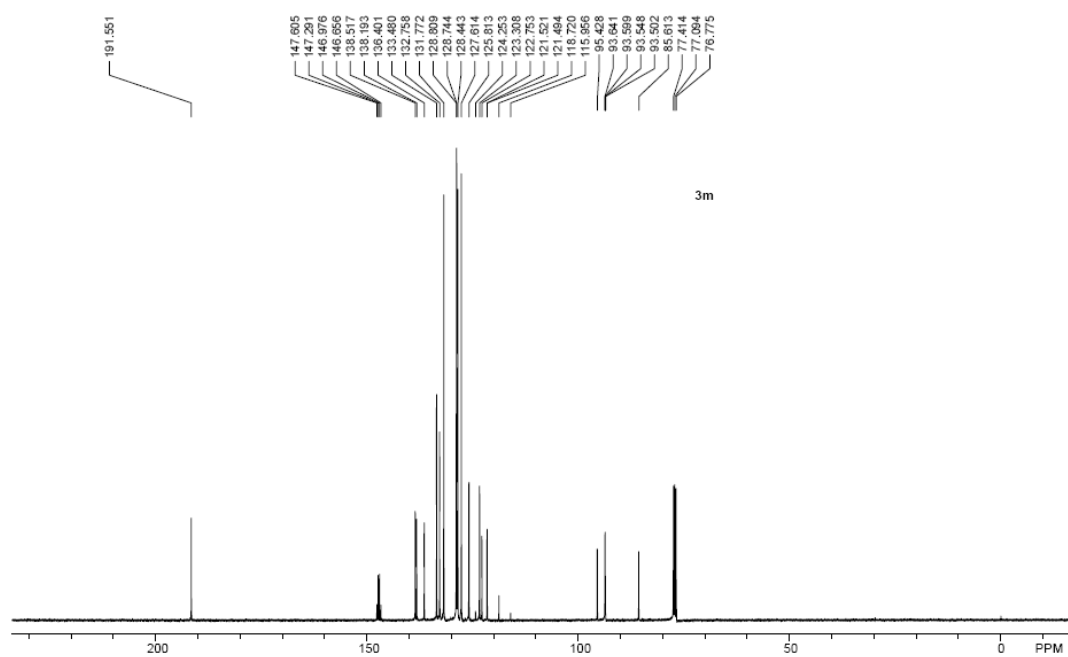
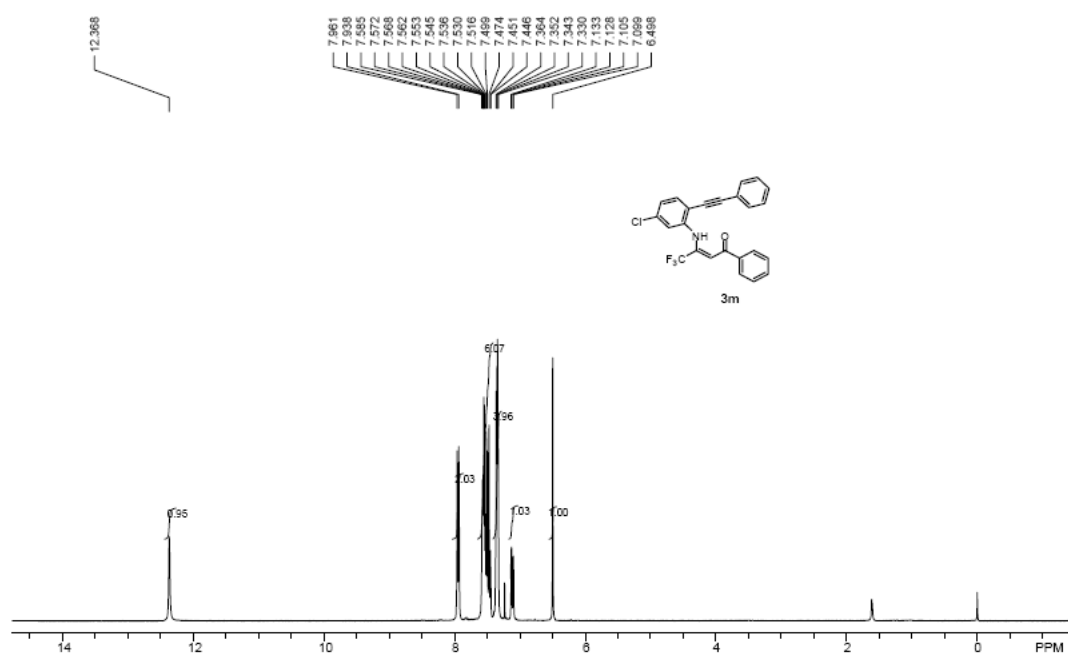


3k

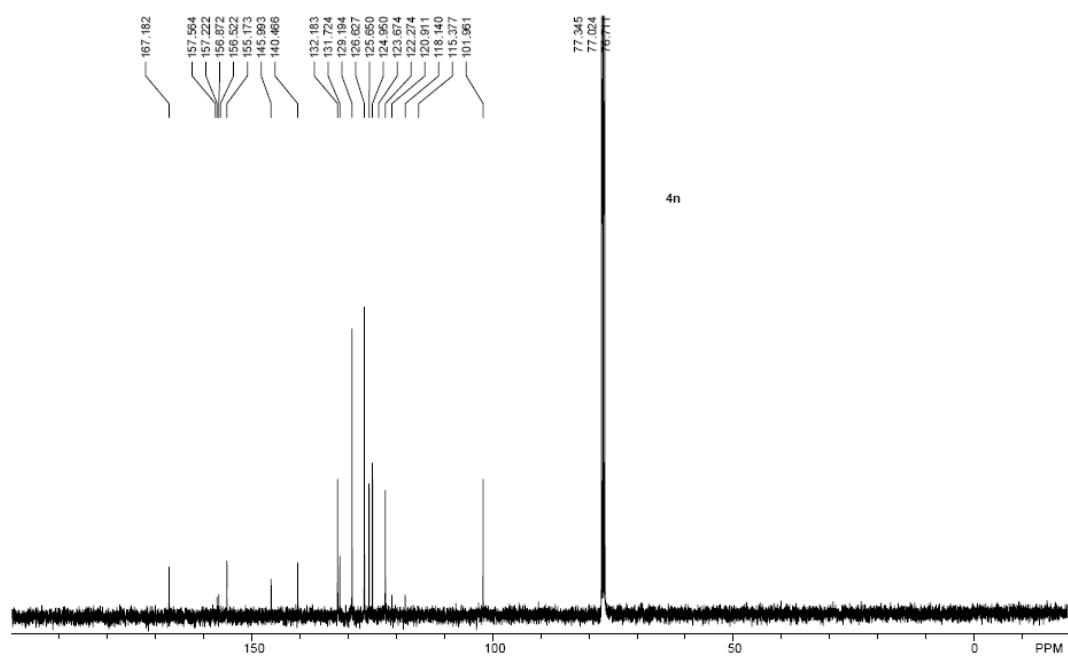
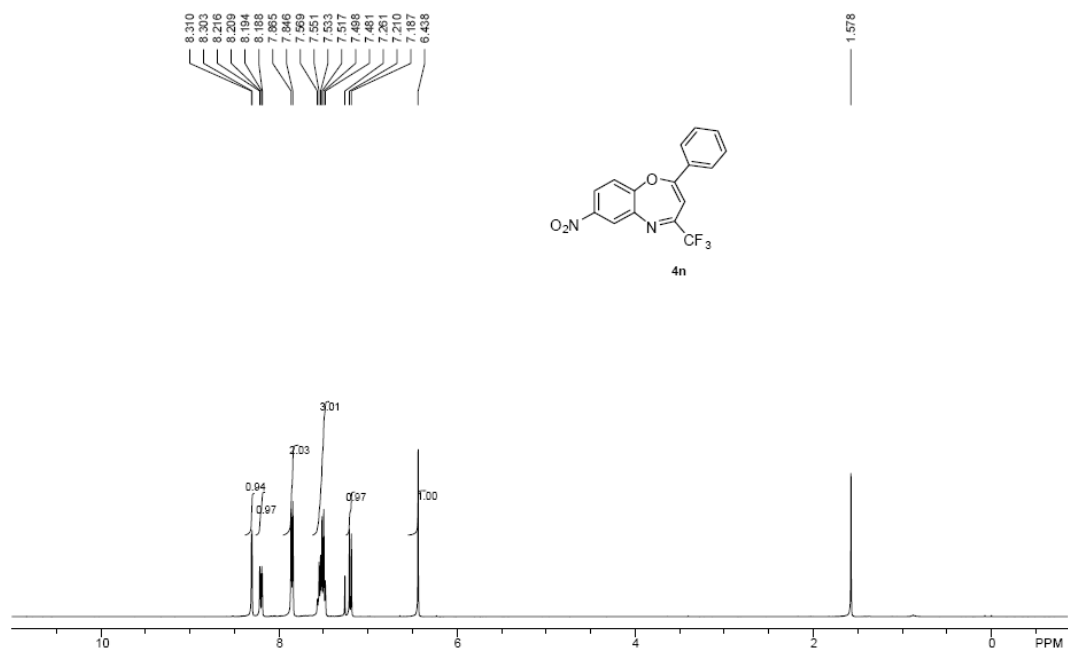




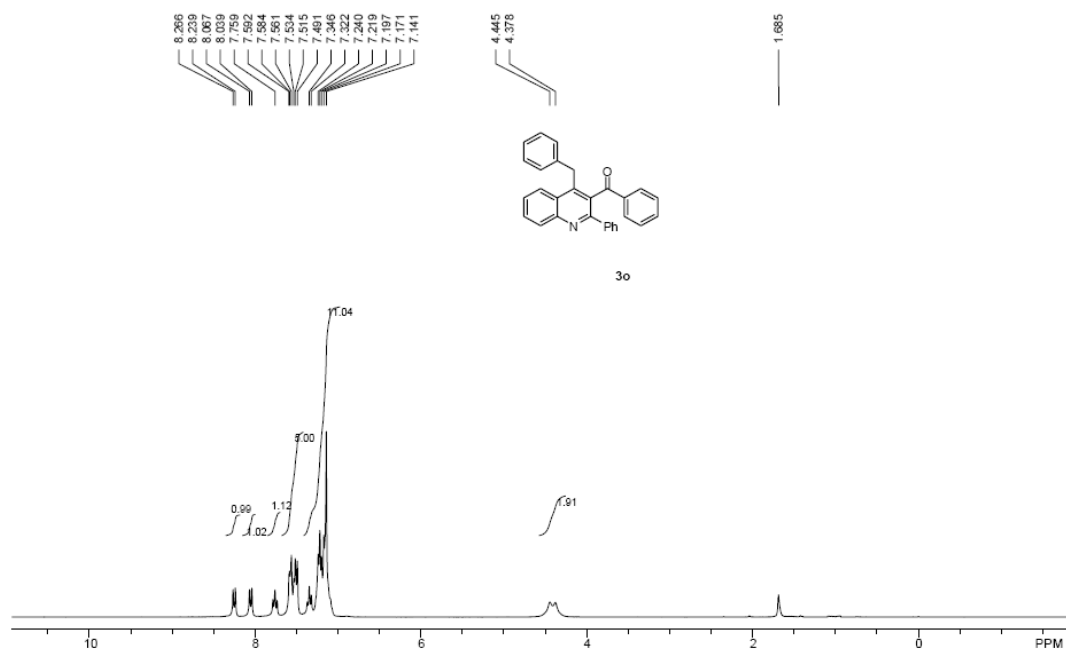
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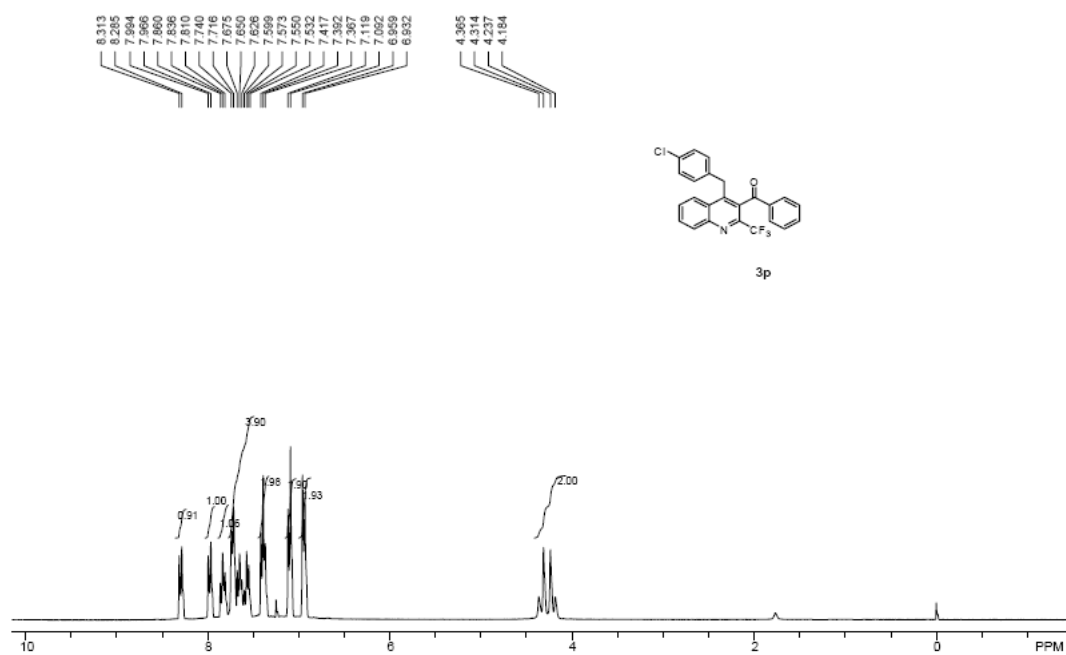
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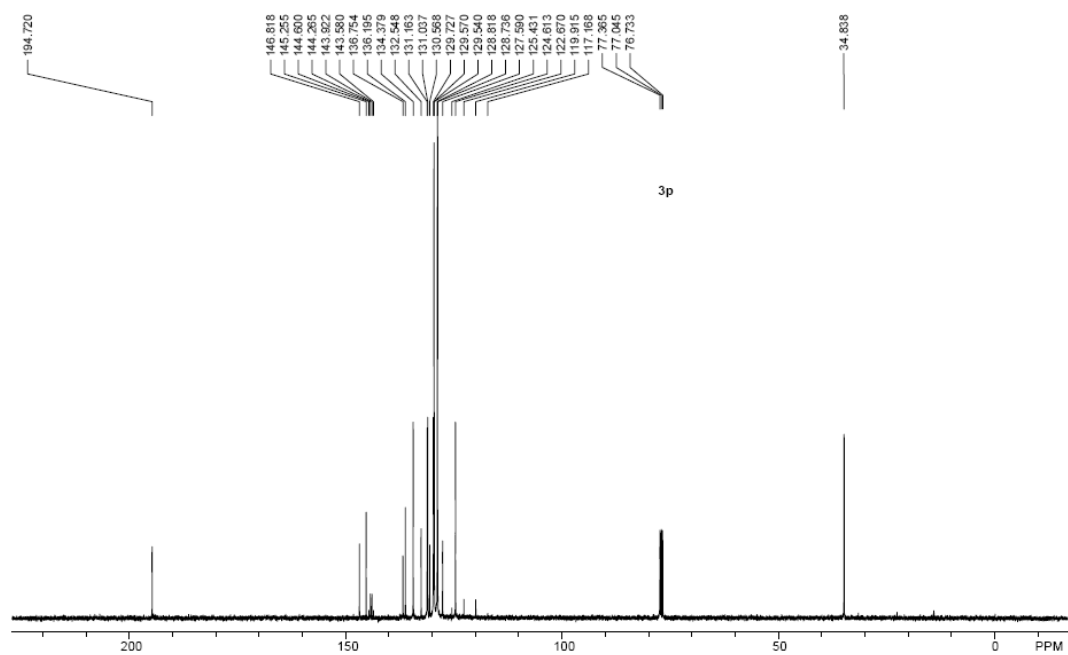


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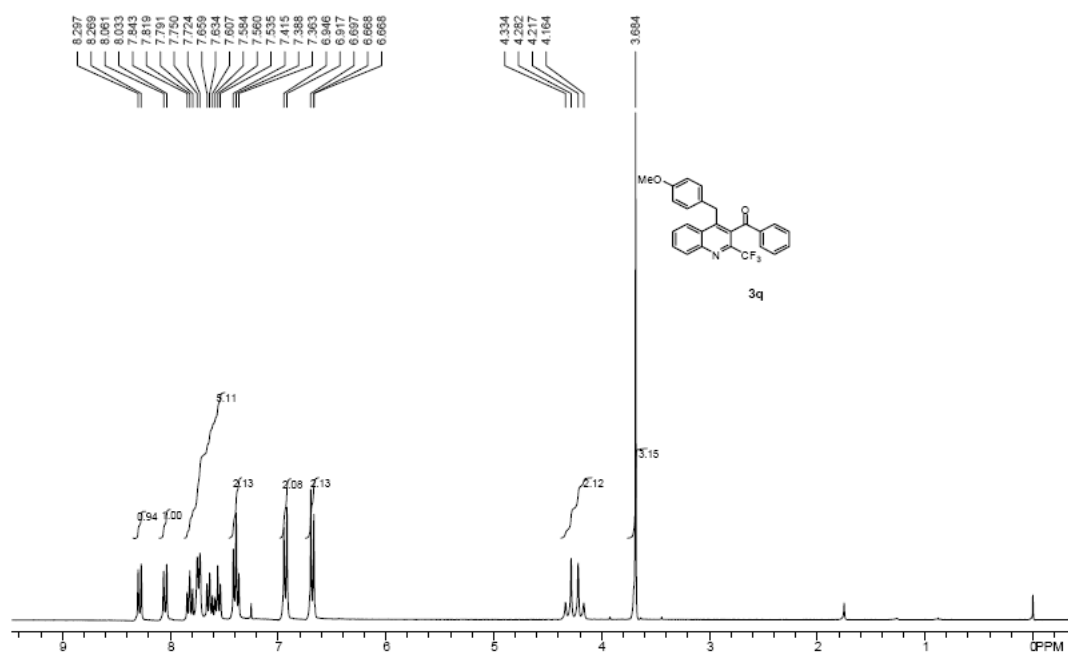


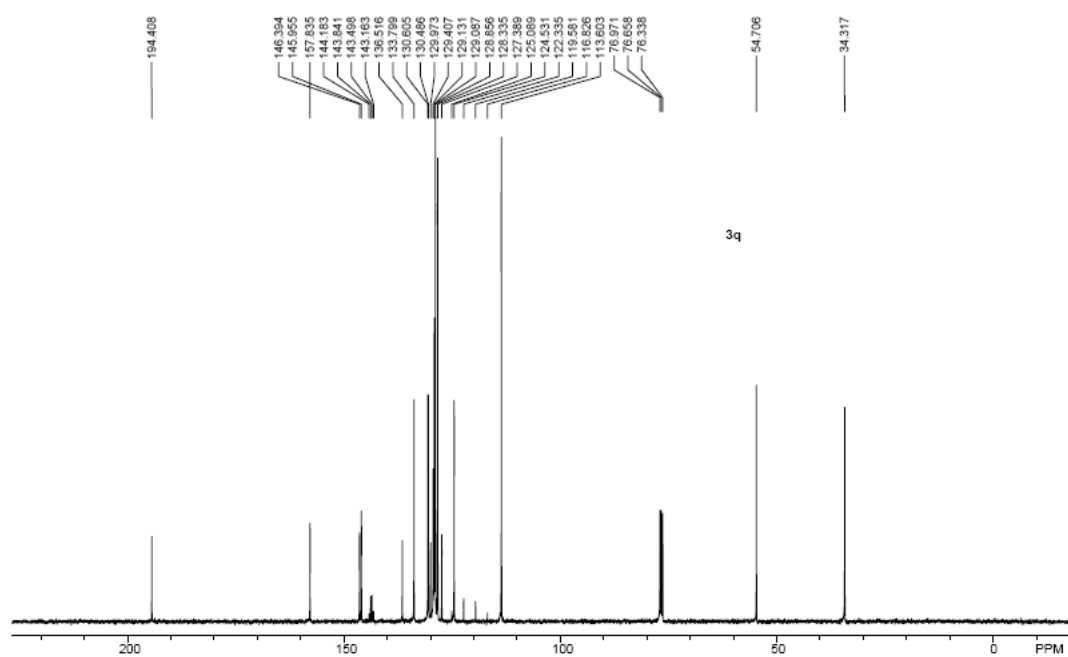
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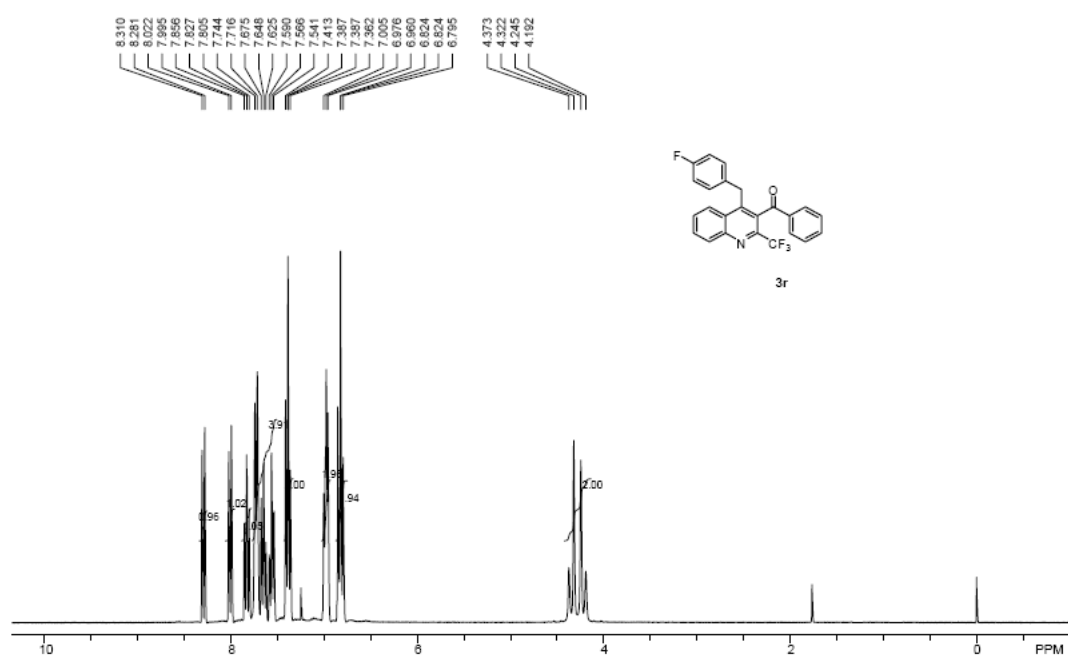


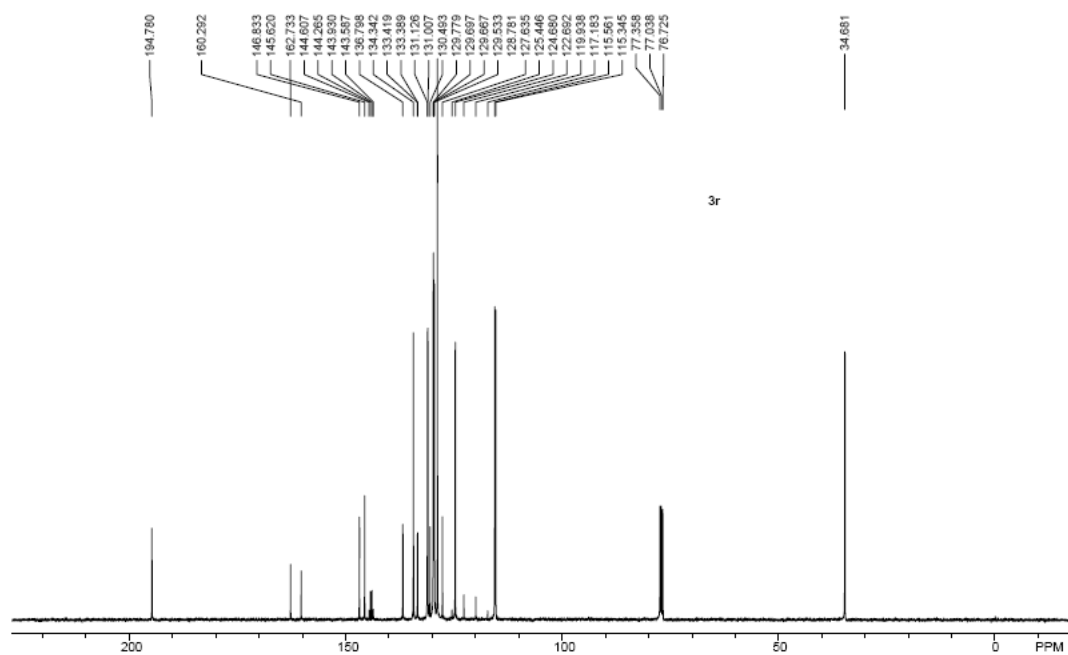
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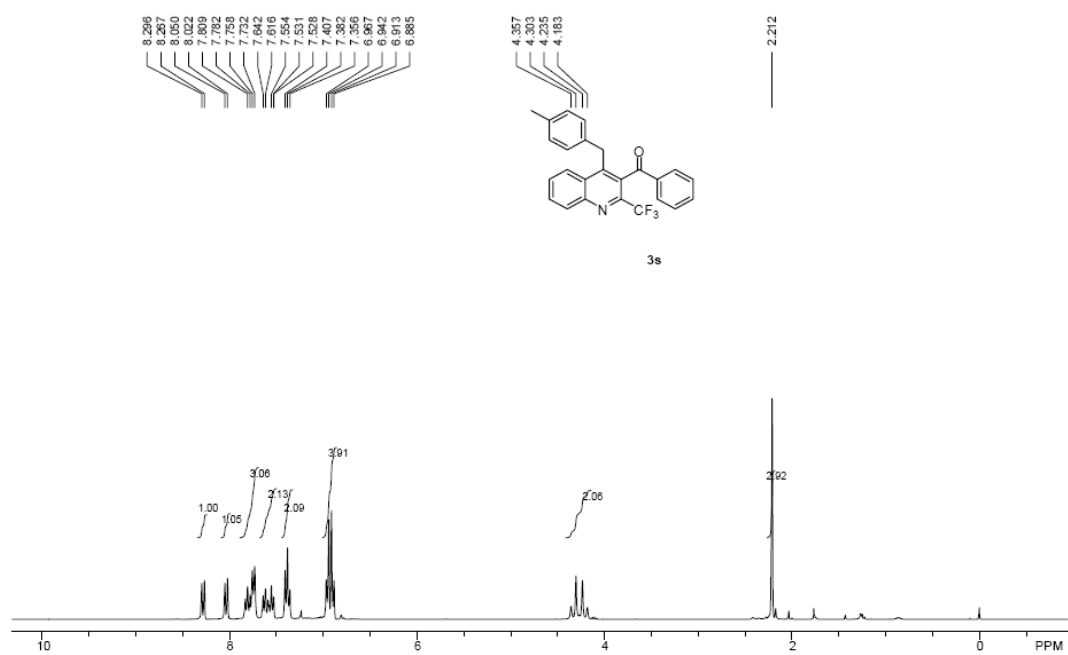


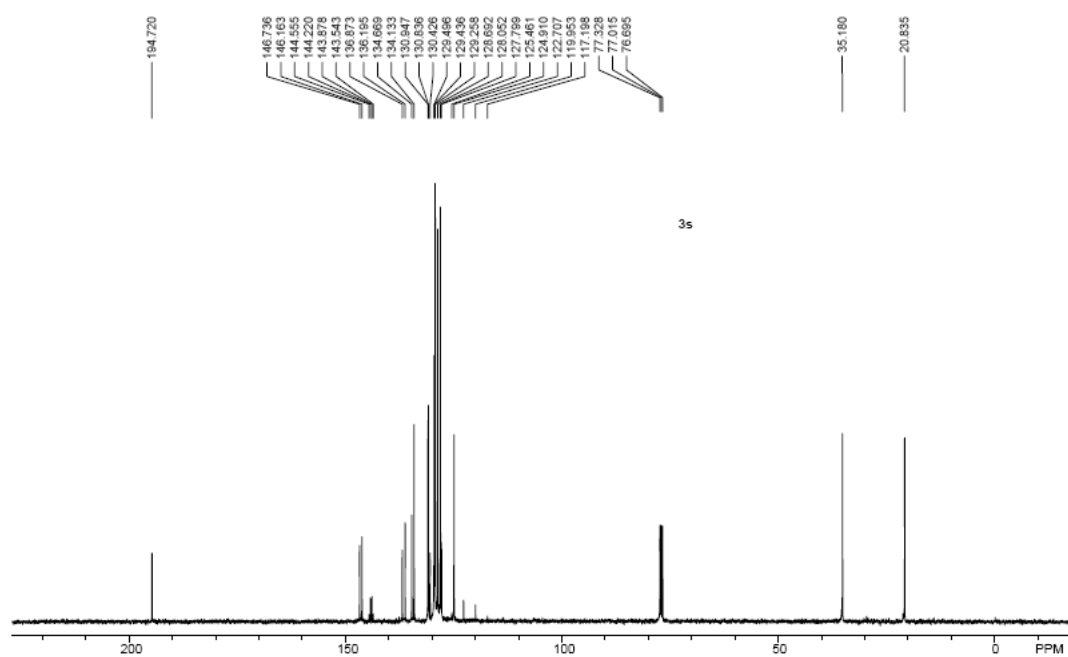
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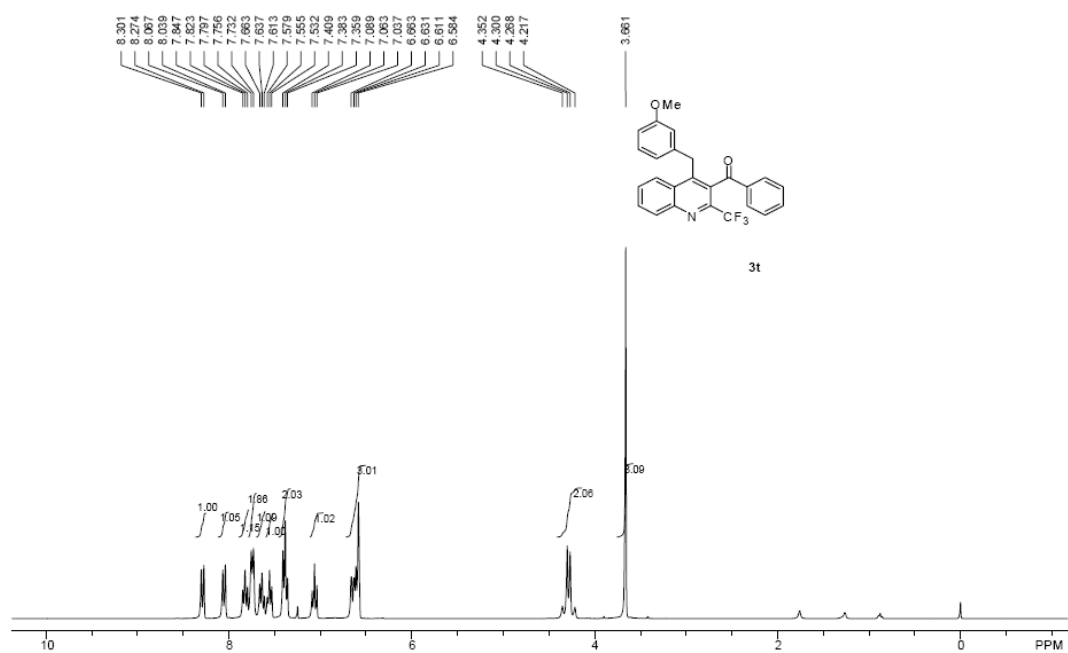


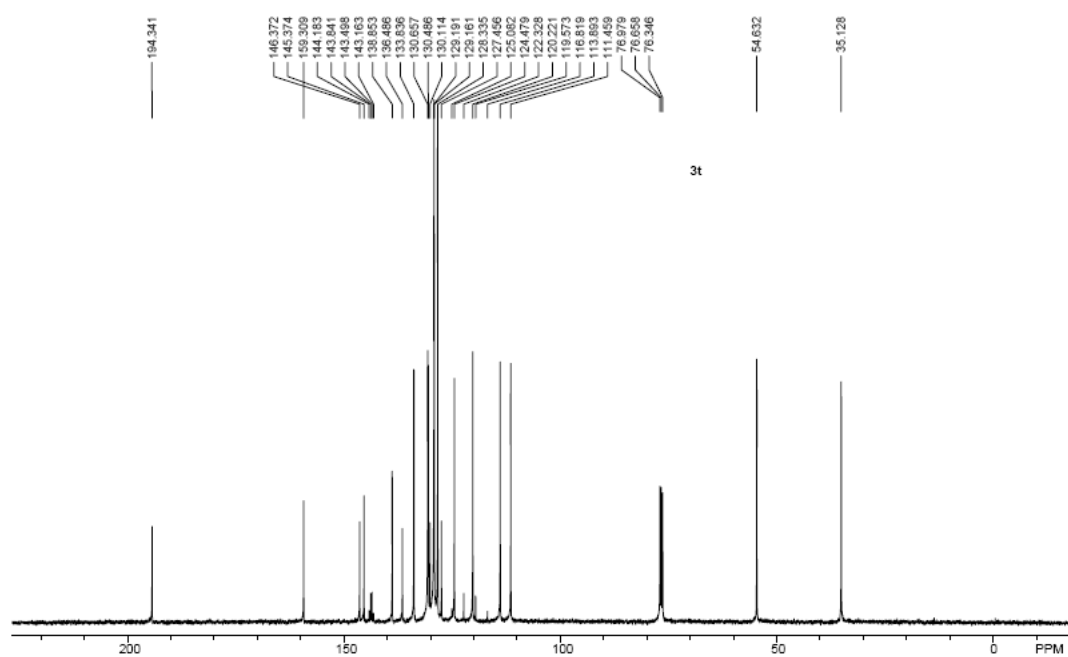
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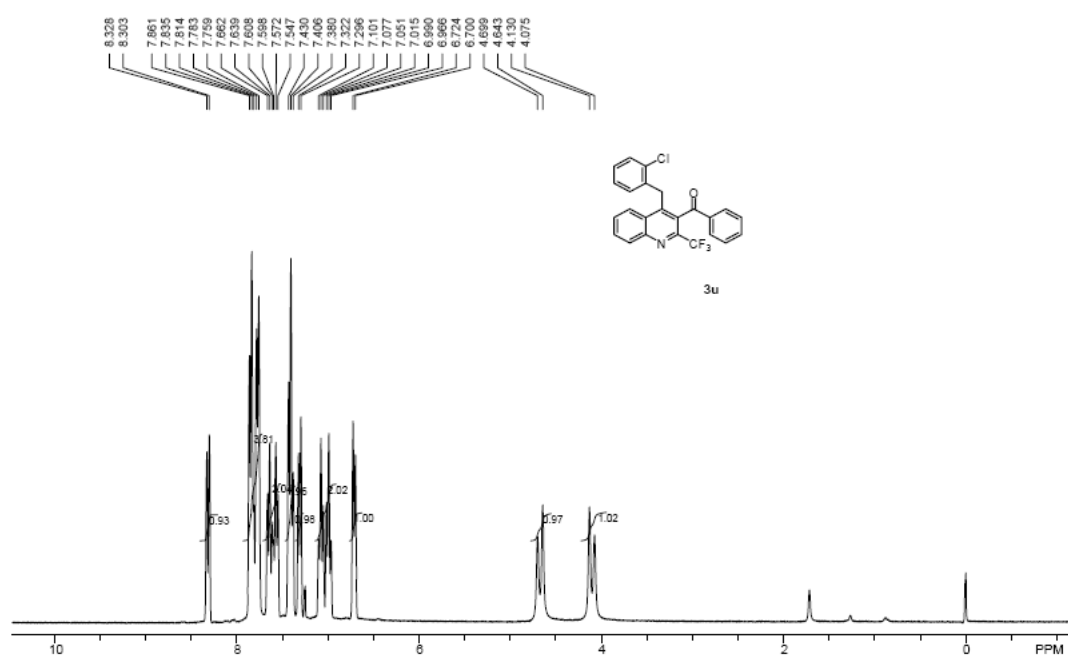


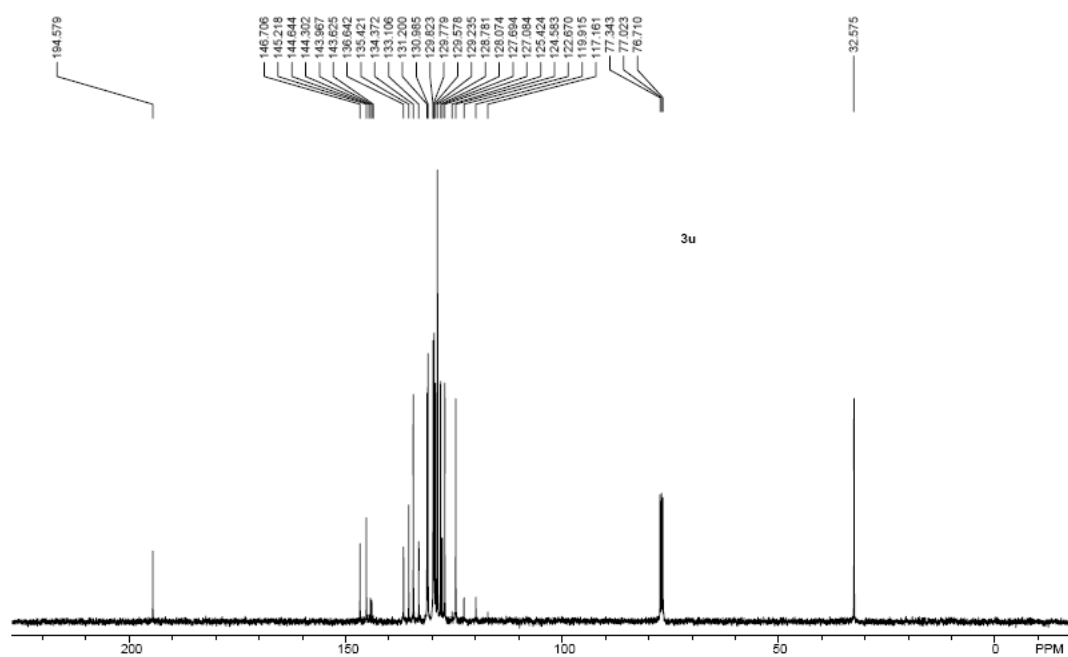
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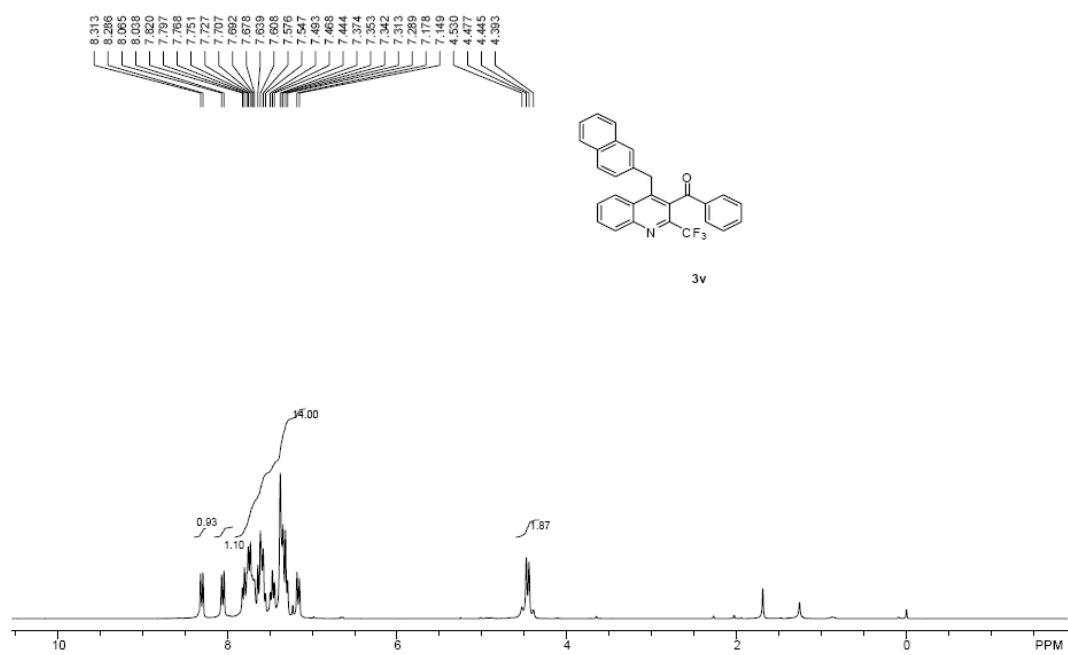


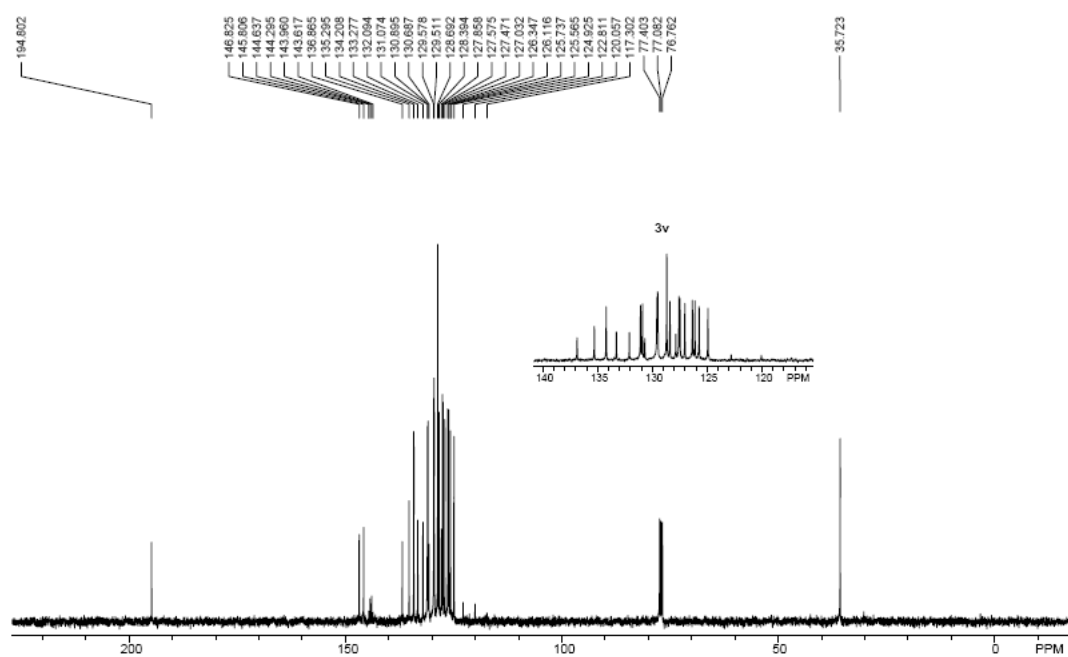
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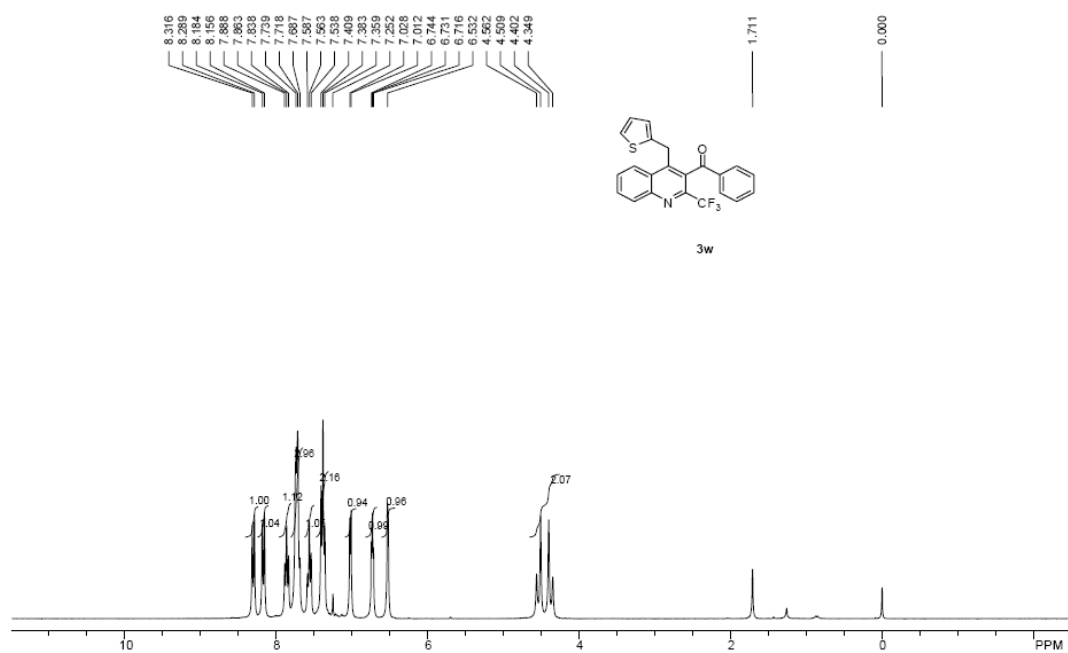


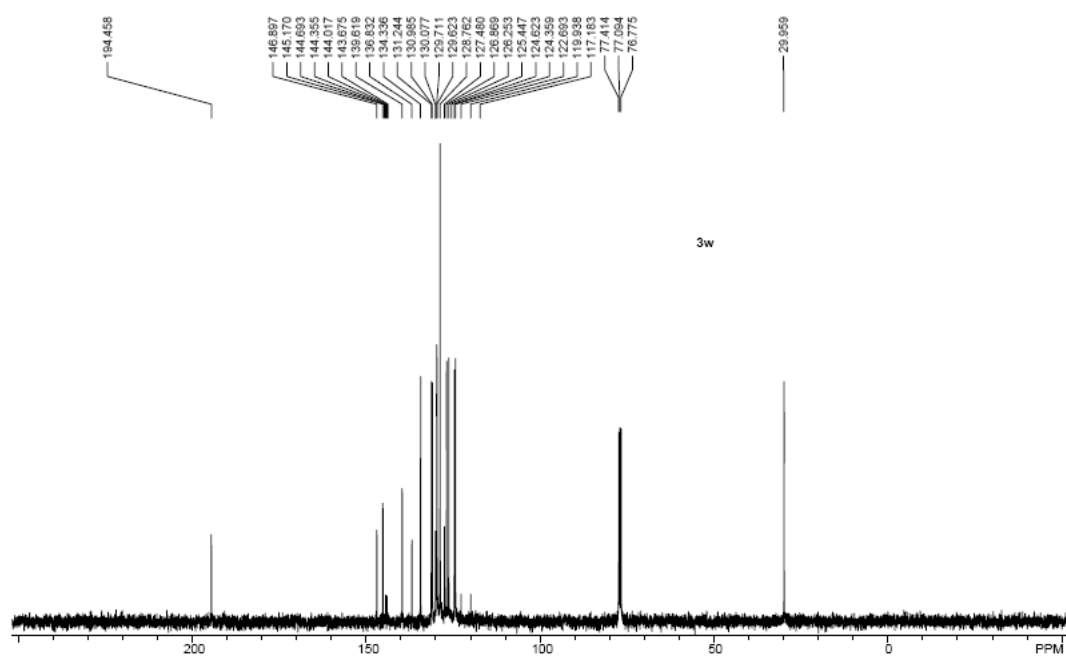
3v





3w





3x

