BEILSTEIN JOURNAL OF ORGANIC CHEMISTRY

Supporting Information

for

Facile preparation and conversion of 4,4,4-trifluorobut-2-yn-1-ones to aromatic and heteroaromatic compounds

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General information, synthetic procedures, and spectral data

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1. General information

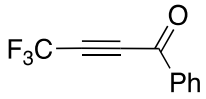
Most of the reactions where an organic solvent was employed were performed under argon, with magnetic stirring using flame-dried glassware. Unless otherwise noted, the materials were obtained from commercial suppliers, including anhydrous THF, Et_2O, and CH_2Cl_2 and were used without further purification. DMSO was freshly dried prior to the reaction over 4 Å molecular sieves, which were activated by irradiating with a microwave for 1 min and heating under vacuum for 1 h. Analytical thin-layer chromatography (TLC) was routinely used for monitoring reactions by generally using a mixture of hexane and ethyl acetate. Spherical neutral silica gel (63–210 μm) was employed for usual column chromatography.

^1H (300.40 MHz), ^{13}C (75.45 Hz), and ^{19}F NMR(282.65 Hz) spectra were recorded in $CDCl_3$ unless otherwise noted, and chemical shifts were reported in parts per million (ppm), downfield from internal tetramethylsilane (Me_4Si: δ 0.00, for ^1H and ^{13}C) or hexafluorobenzene (C_6F_6: δ −163.00 for ^{19}F). Data are tabulated in the following order: number of protons or fluorine atoms, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sex, sextet; sept, septet; m, multiplet; b, broad peak), coupling constants in Hertz. For ^{13}C NMR, because it is difficult to observe perfluoroalkyl carbon atoms even after long-time data acquisition due to multiple coupling, these data are not shown. Infrared (IR) spectra are reported in wave numbers (cm^{-1}). High-resolution mass spectrometry was performed in the positive ionization mode. Melting points were measured by differential scanning calorimetry (DSC; using a Shimadzu DSC-60 device).

2. Synthetic procedure and characterization of new compounds

2.1. General procedure for the oxidation of the propargylic alcohols

2.1.1. 4,4,4-Trifluoro-1-phenylbut-2-yn-1-one (2a) [1]

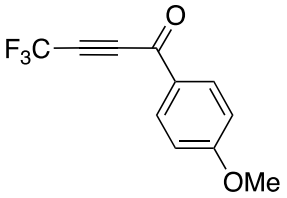


To a 100 mL two-necked round-bottomed flask containing 9.493 g of MnO_2 (10.92 mmol) and CH_2Cl_2 (50 mL) at 0 °C under an argon atmosphere was added 1.31 g of 4,4,4-trifluoro-1-phenylbut-2-yn-1-ol (**1a**, 6.54 mmol) [2], and stirring was continued for 4 h with removing the ice bath. Filtration with Celite®, followed by evaporation of the volatiles afforded a crude mixture in 95% yield determined by ^{19}F NMR spectroscopy, which was found to be unstable towards silica gel and used afterward without further purification. Rf 0.65 (Hexane:AcOEt=4:1). ^1H NMR δ 7.56 (t, *J*=8.0 Hz, 2H), 7.72 (tt, *J*=7.5, 1.5 Hz, 1H), 8.11 (td, *J*=7.2, 1.9 Hz, 2H). ^{13}C NMR δ 75.0 (q, *J*= 54.2 Hz), 79.9 (q, *J*=6.4 Hz), 113.8 (q, *J*=259.6 Hz), 129.0, 129.7, 135.0, 135.5, 174.8. ^{19}F NMR δ –52.84 (s).

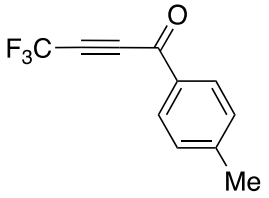
2.1.2. 4,4,4-Trifluoro-1-(4-methoxyphenyl)but-2-yn-1-one (2b) [1]

The reaction of 4,4,4-trifluoro-1-(4-methoxyphenyl)but-2-yn-1-ol (**1b**) [3]and MnO_2 was

continued for 2.5 h to afford the crude product in 93% ^{19}F NMR yield as a red solid. mp 40–41 °C. Rf 0.50 (Hexane: AcOEt=4:1). ^{1}H NMR δ 3.93 (s, 3H), 7.01 (d, *J*=9.0 Hz, 2H), 8.08 (d, *J*=9.0 Hz, 2H). ^{13}C NMR δ 55.7, 74.7 (q, *J*=54.2 Hz), 80.3 (q, *J*=6.4 Hz), 113.9 (q, *J*=259.5 Hz), 114.4, 128.5, 132.3, 165.6, 173.2. ^{19}F NMR δ –52.71 (s).

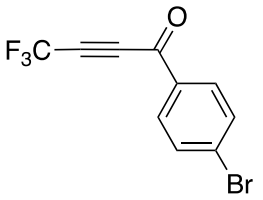


2.1.3. 4,4,4-Trifluoro-1-(4-methylphenyl)but-2-yn-1-one (2c)



The reaction of 4,4,4-trifluoro-1-(4-methylphenyl)but-2-yn-1-ol (**1c**) [4] and MnO_2 was continued for 3 h to afford the crude product in 90% ^{19}F NMR yield as a white oil. Rf 0.57 (Hexane:AcOEt=4:1). ^{1}H NMR δ 2.47 (s, 3H), 7.34 (d, *J*=8.7 Hz, 2H), 7.99 (d, *J*=8.4 Hz, 2H). ^{13}C NMR δ 21.6, 74.6 (q, *J*=53.9 Hz), 80.1 (q, *J*=6.2 Hz), 113.8 (q, *J*=259.2 Hz), 129.7, 129.8, 132.8, 147.1, 174.3. ^{19}F NMR δ –53.78 (s). IR (neat) ν 3301, 3037, 2927, 1661, 1605, 1573, 1450, 1412, 1269, 1153 cm^{-1}. HRMS-FAB (*m*/*z*): [M+H]$^{+}$ calcd. for $C_{11}H_8F_3O$, 213.0527; found, 213.0520.

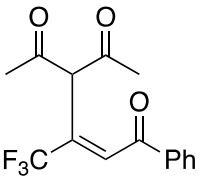
2.1.4. 1-(4-Bromophenyl)-4,4,4-trifluorobut-2-yn-1-one (2d)



The reaction 1-(4-bromophenyl)-4,4,4-trifluorobut-2-yn-1-ol (**1d**) [5] and MnO_2 was continued for 2 h to afford the crude product in 58% ^{19}F NMR yield as a yellow solid. mp 60–61 °C. Rf 0.69 (Hexane: AcOEt=10:1). ^{1}H NMR δ 7.71 (d, *J*=8.7 Hz, 2H), 7.96 (d, *J*=8.7 Hz, 2H). ^{13}C NMR δ 75.7 (q, *J*=55.2 Hz), 79.5 (q, *J*=6.2 Hz), 113.7 (q, *J*=259.8 Hz), 131.0, 131.4, 132.5, 133.9, 174.0. ^{19}F NMR δ –52.86 (s). IR (KBr) ν 3291, 3090, 1662, 1587, 1486, 1401, 1155, 1073, 1011, 838 cm^{-1}. HRMS-FAB (m/z): [M+H]$^{+}$ calcd. for $C_{10}H_5{}^{79}BrF_3O$, 276.9476; found, 276.9478. [M+H]$^{+}$ calcd. for $C_{10}H_5{}^{81}BrF_3O$, 278.9455; found, 278.9465.

2.2. General procedure for the Michael addition reactions

2.2.1. (*E*)-4-Acetyl-1-phenyl-3-(trifluoromethyl)hex-2-ene-1,5-dione (3aa)

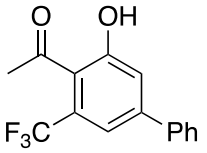


To a 30-mL two-necked round-bottomed flask containing 0.0359 g of NaH (1.50 mmol) and Et_2O (5 mL) at 0 °C under an argon atmosphere was added 0.150 mL of acetylacetone (1.46 mmol), and stirring was continued for 0.5 h where 0.192 g of 4,4,4-trifluoro-1-phenylbut-2-yn-1-one (**2a**, 0.97 mmol) was introduced, and further 0.5 h stirring was carried out. After quenching the reaction with 5 mL of 1 M aq HCl, two extractions with Et_2O afforded an organic phase that was dried with anhydrous Na_2SO_4. Concentration and purification by silica gel column chromatography using hexane/AcOEt 9:1 as an eluent furnished 0.1999 g of 4-acetyl-1-phenyl-3-(trifluoromethyl)hex-2-ene-1,5-dione (0.6702 mmol) in 69% yield as a single isomer as a yellow solid. mp 63–64 °C. Rf 0.30 (Hexane:AcOEt=8:1).

^{1}H NMR δ 2.06 (s, 6H), 7.25–7.91 (m, 6H). ^{13}C NMR δ 23.7 (q, *J*=1.2 Hz), 103.4, 123.0 (q, *J*=274.7 Hz), 128.5, 129.0, 134.0 (q, *J*=4.3 Hz), 134.3, 135.2 (q, *J*=31.6 Hz), 135.8, 189.8, 191.7. ^{19}F NMR δ –69.05 (s). IR (KBr) ν 614, 694, 783, 919, 1001, 1135, 1189, 1284, 1677, 3060 cm^{-1}. Anal. Calcd for $C_{15}H_{13}F_3O_3$, C, 60.40; H, 4.39. Found C, 60.28; H, 4.41.

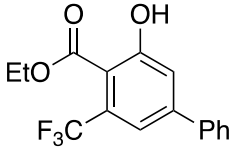
2.3. General procedure for the cyclization to phenol compounds

2.3.1. 1-[2-Hydroxy-4-phenyl-6-(trifluoromethyl)phenyl]ethanone (4aa)



To a 30-mL two-necked round-bottomed flask containing 0.1770 g of *t*-BuOK (1.577 mmol) and Et_2O (5 mL) at 0 °C under an argon atmosphere was added 0.150 mL of acetylacetone (1.46 mmol), and stirring was continued for 0.5 h where 0.206 g of 4,4,4-trifluoro-1-phenylbut-2-yn-1-one (**2a**, 1.04 mmol) was introduced, and further 0.5-h stirring was carried out. To this mixture was added 0.1672 g of *t*-BuOK (1.490 mmol), and stirring was continued for 4 h at room temperature. After quenching the reaction with 5 mL of 1 M aq HCl, two extractions with AcOEt afforded an organic phase that was dried with anhydrous Na_2SO_4. Concentration and purification by silica gel column chromatography using hexane/AcOEt 5:1 as an eluent furnished 0.2155 g of 1-[5-hydroxy-3-(trifluoromethyl)biphenyl-4-yl]ethanone (0.7690 mmol) in 74% yield as a white solid. mp 130–131 °C. Rf 0.16 (Hexane:AcOEt=4:1). ^{1}H NMR δ 2.68 (q, *J*=1.8 Hz, 3H), 7.26–7.63 (m, 7H), 10.13 (s, 1H). ^{13}C NMR δ 31.6 (q, *J*=4.4 Hz), 117.4 (q, *J*=5.6 Hz), 119.5, 121.6 (q, *J*=1.3 Hz), 123.7 (q, *J*=273.5 Hz), 127.0, 128.88, 128.94 (q, *J*=31.6 Hz), 129.0, 138.2, 145.5, 157.5, 205.1. ^{19}F NMR δ –56.78 (s). IR (KBr) ν 761, 877, 943, 1343, 1416, 1614, 1672, 2920, 3036, 3251 cm^{-1}. Anal. Calcd for $C_{15}H_{11}F_3O_2$, C, 64.29; H, 3.96;. Found C, 63.94; H, 4.00.

2.3.2. Ethyl 2-hydroxy-4-phenyl-6-(trifluoromethyl)phenyl-1-carboxylate (4ab)

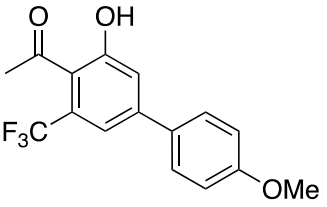


The title compound was obtained in 80% yield as a yellow oil. Rf 0.46 (Hexane: AcOEt=4:1). ^{1}H NMR δ 1.44 (t, *J*=7.1 Hz, 3H), 4.47 (q, *J*=7.2 Hz, 2H), 7.42–7.64 (m, 7H), 11.02 (s, 1H). ^{13}C NMR δ 13.5, 62.6, 109.8 (q, *J*=1.3 Hz), 118.0 (q, *J*=7.0 Hz), 119.7, 123.4 (q, *J*=272.9 Hz), 127.1, 129.0, 129.1, 130.7 (q, *J*=31.6 Hz), 138.3, 146.5, 162.4, 169.1. ^{19}F NMR δ –59.41 (s). IR (neat) ν 2987, 1672, 1620, 1298, 1143, 1060, 1015, 949, 879, 765 cm^{-1}. Anal. Calcd for $C_{16}H_{13}F_3O_3$, C, 61.94; H, 4.22. Found C, 62.11; H, 4.00.

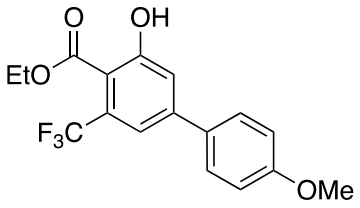
2.3.3. 1-[2-Hydroxy-4-(4-methoxyphenyl)-6-(trifluoromethyl)phenyl]ethanone (4ba)

The title compound was obtained in 67% yield as a white solid. mp 107–108 °C. Rf 0.24 (Hexane:AcOEt=4:1). ^{1}H NMR δ 2.67 (s, 3H), 2.68 (q, *J*=1.9 Hz, 3H), 7.30 (d, *J*=7.8 Hz, 2H), 7.39

(d, *J*=1.5 Hz, 1H), 7.49 (d, *J*=1.8 Hz, 1H), 7.52 (d, *J*=8.1 Hz, 2H), 10.25 (s, 1H). ^{13}C NMR δ 31.5 (q, *J*=4.4 Hz), 55.3, 114.4, 116.8 (q, *J*=5.6 Hz), 118.6, 120.9, 123.7 (q, *J*=271.5 Hz), 128.1, 128.8 (q, *J*=23.9 Hz), 130.4, 145.0, 157.7, 160.3, 205.1. ^{19}F NMR δ –56.69 (s). IR (KBr) ν 3204, 2843, 1686, 1608, 1526, 1340, 1262, 1136, 944, 831 cm^{-1}. Anal. Calcd for $C_{18}H_{13}F_3O_3$, C, 61.94; H, 4.22. Found C, 61.82; H, 4.00.

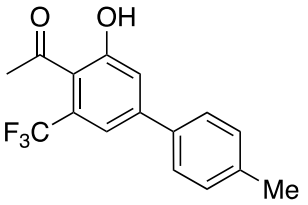


2.3.4. Ethyl 2-hydroxy-4-(4-methoxyphenyl)-6-(trifluoromethyl)phenyl-1-carboxylate (4bb)



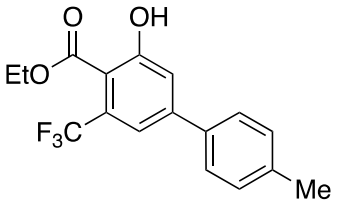
The title compound was obtained in 73% yield as a yellow solid. mp 60–61 °C. Rf 0.29 (Hexane:AcOEt=5:1). ^{1}H NMR δ 1.43 (t, *J*=7.2 Hz, 3H), 3.87 (s, 3H), 4.46 (q, *J*=7.2 Hz, 2H), 7.00 (m, 2H), 7.37 (d, *J*=1.8 Hz, 1H), 7.52 (d, *J*=1.5 Hz, 1H), 7.57 (m, 2H), 11.01 (s, 1H). ^{13}C NMR δ 13.4, 55.2, 62.4, 108.9, 114.4, 117.4 (q, *J*=7.0 Hz), 118.7, 123.4 (q, *J*=273.6 Hz), 128.2, 130.4, 130.5 (q, *J*=31.4 Hz), 145.9, 160.4, 162.4, 169.1. ^{19}F NMR δ –59.33 (s). IR (KBr) ν 2996, 1659, 1606, 1294, 1034, 947, 874, 829, 710, 600 cm^{-1}. Anal. Calcd for $C_{17}H_{15}F_3O_4$, C, 60.00; H, 4.44. Found C, 59.91; H, 4.46.

2.3.5. 1-[2-Hydroxy-4-(4-methylphenyl)-6-(trifluoromethyl)phenyl]ethanone (4ca) [6]



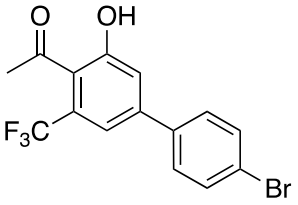
The title compound was obtained in 68% yield as a white solid. Rf 0.26 (Hexane:AcOEt =4:1). ^{1}H NMR δ 2.42 (s, 3H), 2.67 (q, *J*=1.8 Hz, 3H), 7.29 (d, *J*=8.1 Hz, 2H), 7.38 (d, *J*=1.5 Hz, 1H), 7.48–7.52 (m, 3H), 10.13 (s). ^{13}C NMR (acetone-d_6) δ 21.0, 31.8, 116.2, 118.4, 124.7 (q, *J*=273.2 Hz), 127.6, 127.9, 128.4 (q, *J*=30.8 Hz), 130.5, 136.7, 139.2, 144.2, 155.4, 201.8. ^{19}F NMR δ –56.73 (s).

2.3.6. Ethyl [2-hydroxy-4-(4-methylphenyl)-6-(trifluoromethyl)phenyl]-1-carboxylate (4cb)



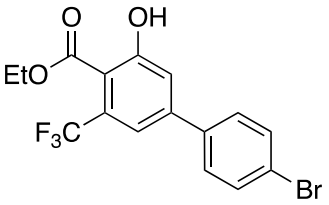
The title compound was obtained in 75% yield as a white solid. mp 64–69 °C. Rf 0.31 (Hexane:AcOEt=5:1). ^{1}H NMR δ 1.43 (t, *J*=7.2 Hz, 3H), 2.42 (s, 3H), 4.47 (q, *J*=7.2 Hz, 2H), 7.29 (d, *J*=8.4 Hz, 2H), 7.41 (d, *J*=1.8 Hz, 1H), 7.51–7.54 (m, 3H), 11.02 (s, 1H). ^{13}C NMR δ 13.4, 21.0, 62.4, 109.3, 117.7 (q, *J*=6.8 Hz), 119.2, 123.4 (q, *J*=271.3 Hz), 126.8, 129.7, 130.5 (q, *J*=31.4 Hz), 135.2, 139.1, 146.3, 162.4, 169.1. ^{19}F NMR δ –59.25 (s). IR (KBr) ν 2988, 1663, 1020, 949, 882, 821, 712, 660, 559, 497 cm^{-1}. Anal. Calcd for $C_{17}H_{15}F_3O_3$, C, 62.96; H, 4.66. Found C, 62.89; H, 4.47.

2.3.7. 1-[2-Hydroxy-4-(4-bromophenyl)-6-(trifluoromethyl)phenyl]ethanone (4da) [6]



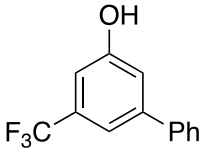
The title compound was obtained in 70% yield as a white solid. mp 136 °C. Rf 0.17 (Hexane:AcOEt=5:1). ^{1}H NMR δ 2.68 (qd, *J*=1.8, 0.9 Hz, 3H), 7.35 (m, 1H), 7.44–7.49 (m, 3H), 7.59–7.64 (m, 2H), 9.94 (s, 1H). ^{13}C NMR δ 31.6 (q, *J*=4.9 Hz), 117.2 (q, *J*=5.6 Hz), 119.6, 121.0, 123.5, 123.6 (q, *J*=271.9 Hz), 128.6, 129.4 (q, *J*=31.4 Hz), 132.3, 137.0, 144.5, 158.3, 204.8. ^{19}F NMR δ –56.82 (s). IR (KBr) ν 3193, 2925, 1690, 1613, 1342, 1136, 1012, 941, 878 826 cm^{-1}. Anal. Calcd for $C_{15}H_{10}F_3O_2$, C, 50.16; H, 2.81. Found C, 50.11; H, 2.48.

2.3.8. Ethyl [4-(4-bromophenyl)-2-hydroxy-6-(trifluoromethyl)]phenyl-1-carboxylate (4db)



The title compound was obtained in 54% yield as a white solid. mp 93–94 °C. Rf 0.40 (Hexane:AcOEt=5:1). ^{1}H NMR δ 1.44 (t, *J*=7.2 Hz, 3H), 4.47 (q, *J*=7.2 Hz, 2H), 7.38 (d, *J*=1.8 Hz, 1H), 7.46–7.50 (m, 3H), 7.60–7.64 (m, 2H), 11.01 (s, 1H). ^{13}C NMR δ 13.4, 62.6, 110.0, 117.5 (q, *J*=6.8 Hz), 119.5, 123.2 (q, *J*=271.3 Hz), 123.5, 128.5, 130.8 (q, *J*=31.7 Hz), 132.2, 137.0, 145.1, 162.3, 168.9. ^{19}F NMR δ –59.40 (s). IR (KBr) ν 3087, 2986, 1671, 1330, 1059, 1011, 949, 828, 720, 567 cm^{-1}. Anal. Calcd for $C_{16}H_{12}F_3O_3$, C, 49.38; H, 3.11. Found C, 49.41; H, 2.76.

2.4. 3-Phenyl-5-(trifluoromethyl)phenol (5a) [7]



To a 30-mL two-necked round-bottomed flask containing 0.0556 g of *t*-BuOK (0.495 mmol) and *t*-BuOH (3 mL) at 0 °C under an argon atmosphere was added a solution of 0.1525 g of 4-acetyl-1-phenyl-3-trifluoromethylhex-2-ene-1,5-dione (0.5113 mmol) in 2 mL of *t*-BuOH, and stirring was continued for 4 h at 60 °C. After quenching the reaction with 3 mL of 1 M aq HCl aq., two extractions with AcOEt afforded an organic phase that was dried with anhydrous Na_2SO_4. Concentration and purification by silica gel column chromatography using hexane/AcOEt 5:1 as an eluent furnished 0.0981 g of 3-phenyl-5-(trifluoromethyl)phenol (0.4118 mmol) in 81% yield as a yellow oil. Rf 0.34 (Hexane:AcOEt=4:1). ^{1}H NMR δ 7.07 (brs, 1H), 7.23 (brs, 1H), 7.37–7.50 (m, 4H), 7.56–7.59 (m, 2H). ^{13}C NMR δ 111.0 (q, *J*=3.7 Hz), 116.5 (q, *J*=3.9 Hz), 117.3, 123.8 (q, *J*=271.7 Hz), 127.1, 128.2, 128.9, 132.4 (q, *J*=31.4 Hz), 139.4, 143.8, 156.0. ^{19}F NMR δ –63.69 (s).

2.5. General procedure for the preparation of the trifluoromethylated pyrimidines

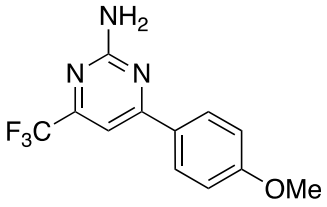
2.5.1. 2-Amino-4-phenyl-6-(trifluoromethyl)pyrimidine (6aa) [8].

To a 30-mL two-necked round-bottomed flask containing 0.1295 g of Na_2CO_3 (1.222 mmol)

and CH_3CN (5 mL), 0.0574 g of guanidine hydrochloride (0.601 mmol) was added. After heating to 80 °C, 0.1029 g of 4,4,4-trifluoro-1-phenylbut-2-yn-1-one (**2a**, 0.501 mmol) was added, and the mixture was stirred for 8 h at that temperature. After quenching the reaction with 3 mL of 1 M aq HCl aq., two extractions with AcOEt afforded an organic phase that was dried with anhydrous Na_2SO_4. Concentration and purification by silica gel column chromatography using hexane/AcOEt 10:1 as an eluent and the following recrystallization furnished 0.0723 g of 2-amino-4-phenyl-6-(trifluoromethyl)pyrimidine (0.3023 mmol) in 60% yield as a white solid. mp 128–129 °C. Rf 0.11 (Hexane:AcOEt=10:1). ^{1}H NMR δ 5.67 (brs, 2H), 7.33 (s, 1H), 7.50-7.52 (m, 3H), 8.03 (dd, *J*=7.8, 1.8 Hz, 2H). ^{13}C NMR (DMSO-d_6) δ 100.9 (q, *J*=2.8 Hz), 121.0 (q, *J*=274.8 Hz), 127.2, 128.8, 131.4, 135.9, 156.1 (q, *J*=33.9 Hz), 164.0, 167.0. ^{19}F NMR δ –71.91 (s).

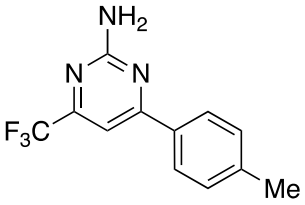
2.5.2. 2-Amino-4-(4-methoxyphenyl)-6-(trifluoromethyl)pyrimidine (6ab) [9]

The title compound was obtained in 55% yield as a white solid. mp 191–192 °C. Rf 0.05 (Hexane:AcOEt=10:1). ^{1}H NMR δ 3.89 (s, 3H), 5.38 (brs, 2H), 7.00 (d, *J*=9.0 Hz, 2H), 7.29 (s, 1H), 8.03 (d, *J*=9.0 Hz, 2H). ^{13}C NMR (DMSO-d_6) δ 55.4, 100.1 (d, *J*=2.5 Hz), 114.2, 121.1 (q, *J*=275.0 Hz), 128.2, 129.0, 155.8 (q, *J*=33.7 Hz), 162.0, 163.8, 166.4. ^{19}F NMR δ –71.98 (s).



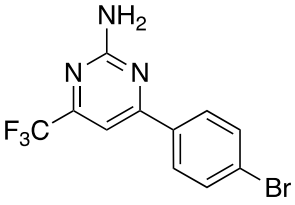
2.5.3. 2-Amino-4-(4-methylphenyl)-6-(trifluoromethyl)pyrimidine (6ac) [10]

The title compound was obtained in 52% yield as a yellow solid. mp 174–175 °C. Rf 0.11 (Hexane:AcOEt=10:1). ^{1}H NMR δ 2.43 (s, 3H), 5.33 (brs, 2H), 7.31 (d, *J*=8.1 Hz, 2H), 7.33 (s, 1H), 7.95 (d, *J*=8.1 Hz, 2H). ^{13}C NMR (DMSO-d_6) δ 21.0, 100.5, 121.1 (q, *J*=275.1 Hz), 127.2, 129.5, 133.2, 141.5, 156.0 (q, *J*=33.9 Hz), 164.0, 166.9. ^{19}F NMR δ –71.98 (s).

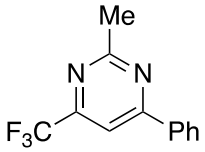


2.5.4. 2-Amino-4-(4-bromophenyl)-6-(trifluoromethyl)pyrimidine (6ad) [10]

The title compound was obtained in 67% yield as a brownish solid. mp 215–216 °C. Rf 0.20 (Hexane:AcOEt=10:1). ^{1}H NMR δ 5.41 (br s, 2H), 7.32 (s, 1H), 7.65 (d, *J*=8.7 Hz, 2H), 7.93 (d, *J*=8.4 Hz, 2H). ^{13}C NMR (DMSO-d_6) δ 100.8 (d, *J*=2.5 Hz), 120.9 (q, *J*=273.8 Hz), 125.3, 129.2, 131.9, 135.1, 156.3 (q, *J*=34.1 Hz), 163.9, 165.8. ^{19}F NMR δ –71.98 (s). IR (KBr) *v* 3486, 3318, 3205, 1643, 1593, 1556, 1481, 1382, 1281, 1259, 1182, 1164, 1140, 1070, 1011, 822 cm^{-1}. HRMS-FAB (m/z) : $[M+H]^+$ calcd. for $C_{11}H_8BrF_3N_3$, 317.9848; found, 317.9820.

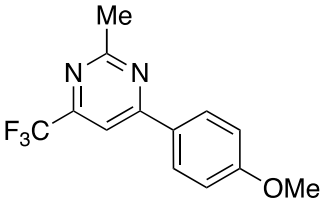


2.5.5. 2-Methyl-4-phenyl-6-(trifluoromethyl)pyrimidine (6ba) [8]



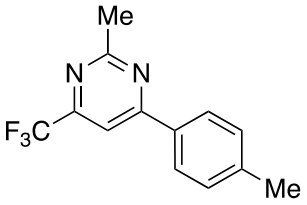
The title compound was obtained in 67% yield as a yellow oil. Rf 0.43 (Hexane:AcOEt= 10:1). ^{1}H NMR δ 2.89 (s, 3H), 7.51-7.56 (m, 3H), 7.83 (s, 1H), 8.12-8.15 (m, 2H). ^{13}C NMR δ 26.1, 109.4 (q, *J*=2.9 Hz), 120.7 (q, *J*=274.8 Hz), 127.4, 129.1, 131.7, 135.7, 156.1 (q, *J*=35.4 Hz), 166.5, 169.5. ^{19}F NMR δ –71.34 (s).

2.5.6. 4-(4-Methoxyphenyl)-2-methyl-6-(trifluoromethyl)pyrimidine (6bb) [11]



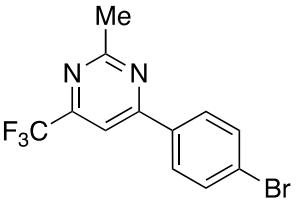
The title compound was obtained in 75% yield as a yellow solid. mp 82–83 °C. Rf 0.28 (Hexane:AcOEt=10:1). ^{1}H NMR δ 2.85 (s, 3H), 3.90 (s, 3H), 7.01-7.06 (m, 2H), 7.76 (s, 1H), 8.10-8.15 (m, 2H). ^{13}C NMR δ 26.1, 55.4, 108.4 (q, *J*=2.9 Hz), 114.4, 120.8 (q, *J*=274.6 Hz), 128.0, 129.0, 155.8 (q, *J*=35.2 Hz), 162.7, 165.8, 169.3. ^{19}F NMR δ –71.41 (s). IR (KBr) *v* 3076, 2979, 2945, 2845, 1549, 1389, 1312, 1298, 1266, 1183, 1144, 1027, 840 cm^{-1}. HRMS-FAB (m/z): $[M+2H]^{+2}$ calcd. for $C_{13}H_{13}F_3N_2O$, 270.0980; found, 270.0994.

2.5.7. 2-Methyl-4-(4-methylphenyl)-6-(trifluoromethyl)pyrimidine (6bc) [12]



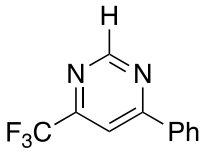
The title compound was obtained in 53% yield as a yellow solid. mp 64–65 °C. Rf 0.42 (Hexane:AcOEt=10:1). ^{1}H NMR δ 2.44 (s, 3H), 2.87 (s, 3H), 7.34 (d, *J*=8.1 Hz, 2H), 7.80 (s, 1H), 8.04 (d, *J*=8.1 Hz, 2H). ^{13}C NMR δ 21.4, 26.1, 109.0 (q, *J*=2.7 Hz), 120.8 (q, *J*=274.6 Hz), 127.3, 129.8, 132.9, 142.4, 156.0 (q, *J*=35.1 Hz), 166.3, 169.4. ^{19}F NMR δ –71.37 (s). IR (KBr) *v* 3036, 2928, 1592, 1550, 1389, 1286, 1264, 1190, 1134, 877, 838 cm^{-1}. HRMS-FAB (m/z) : $[M+H]^{+}$ calcd. for $C_{13}H_{11}F_3N_2$, 252.0874; found, 252.0845.

2.5.8. 4-(4-Bromophenyl)-2-methyl-6-(trifluoromethyl)-pyrimidine (6bd) [11]



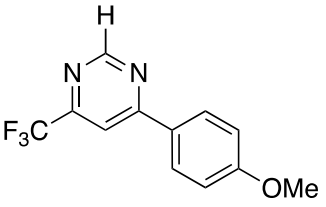
The title compound was obtained in 57% yield as a white solid. mp 79–80 °C. Rf 0.45 (Hexane:AcOEt=10:1). ^{1}H NMR δ 2.89 (s, 3H), 7.68 (d, *J*=8.7 Hz, 2H), 7.81 (s, 1H), 8.03 (d, *J*=8.7 Hz, 2H). ^{13}C NMR δ 26.1, 109.1 (q, *J*=2.9 Hz), 120.6 (q, *J*=275.0 Hz), 126.7, 128.8, 132.3, 134.5, 156.4 (q, *J*=35.6 Hz), 165.2, 169.6. ^{19}F NMR δ –71.36 (s). IR (KBr) *v* 3087, 3009, 2975, 2932, 1592, 1548, 1394, 1274, 1257, 1203, 1158, 1072, 1009, 833 cm^{-1}. HRMS-FAB (m/z) : $[M+H]^{+}$ calcd. for $C_{12}H_9BrF_3N_2$, 316.9896; found, 316.9857.

2.5.9. 4-Phenyl-6-(trifluoromethyl)pyrimidine (6ca) [8]



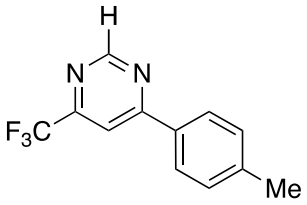
The title compound was obtained in 21% yield as a yellow solid. mp 41–42 °C. Rf 0.42 (Hexane:AcOEt=10:1). ^{1}H NMR δ 7.53-7.60 (m, 3H), 8.05 (s, 1H), 8.16 (dd, *J*=7.7, 2.0 Hz, 2H), 9.41 (s, 1H). ^{13}C NMR δ 112.5 (q, *J*=2.9 Hz), 120.6 (q, *J*=274.8 Hz), 127.4, 129.2, 132.1, 135.3, 156.1 (q, *J*=35.8 Hz), 159.4, 166.5. ^{19}F NMR δ –71.31 (s).

2.5.10. 4-(4-Methoxyphenyl)-6-(trifluoromethyl)pyrimidine (6cb) [11]



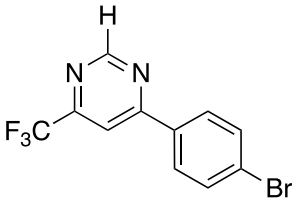
The title compound was obtained in 28% yield as a white solid. mp 52–53 °C. Rf 0.24 (Hexane:AcOEt=10:1). ^{1}H NMR δ 3.91 (s, 3H), 7.04 (d, *J*=8.7 Hz, 2H), 7.95 (s, 1H), 8.14 (d, *J*=9.0 Hz, 2H), 9.31 (s, 1H). ^{13}C NMR δ 55.4, 111.4 (q, *J*=2.7 Hz), 114.6, 120.7 (q, *J*=274.4 Hz), 127.6, 129.1, 155.7 (q, *J*=35.8 Hz), 159.2, 163.0, 165.8. ^{19}F NMR δ –71.39 (s). IR (KBr) *v* 3079, 2972, 2924, 2847, 1596, 1539, 1518, 1394, 1309, 1270, 1175, 1139, 1095, 1063, 1022, 840 cm^{-1}. Anal. Calcd for $C_{12}H_9F_3N_2O$, C, 56.70; H, 3.57; N, 11.02. Found C, 56.67; H, 3.47; N, 10.79.

2.5.11. 4-(4-Methylphenyl)-6-(trifluoromethyl)pyrimidine (6cc)



The title compound was obtained in 22% yield as a white solid. mp 53–54 °C. Rf 0.49 (Hexane:AcOEt=10:1). ^{1}H NMR δ 2.45 (s, 3H), 7.35 (d, *J*=8.1 Hz, 2H), 8.00 (s, 1H), 8.06 (d, *J*= 7.5 Hz, 2H), 9.36 (s, 1H). ^{13}C NMR δ 21.5, 112.1 (d, *J*=2.5 Hz), 120.7 (q, *J*=274.6 Hz), 127.3, 130.0, 132.5, 142.9, 155.9 (q, *J*=35.7 Hz), 159.3, 166.4. ^{19}F NMR δ –71.34 (s). IR (KBr) *v* 3033, 2925, 1597, 1541, 1392, 1322, 1303, 1255, 1144, 1096, 1060, 836, 822 cm^{-1}. Anal. Calcd for $C_{12}H_9F_3N_2$, C, 60.51; H, 3.81; N, 11.76. Found C, 60.51; H, 3.84; N, 11.73.

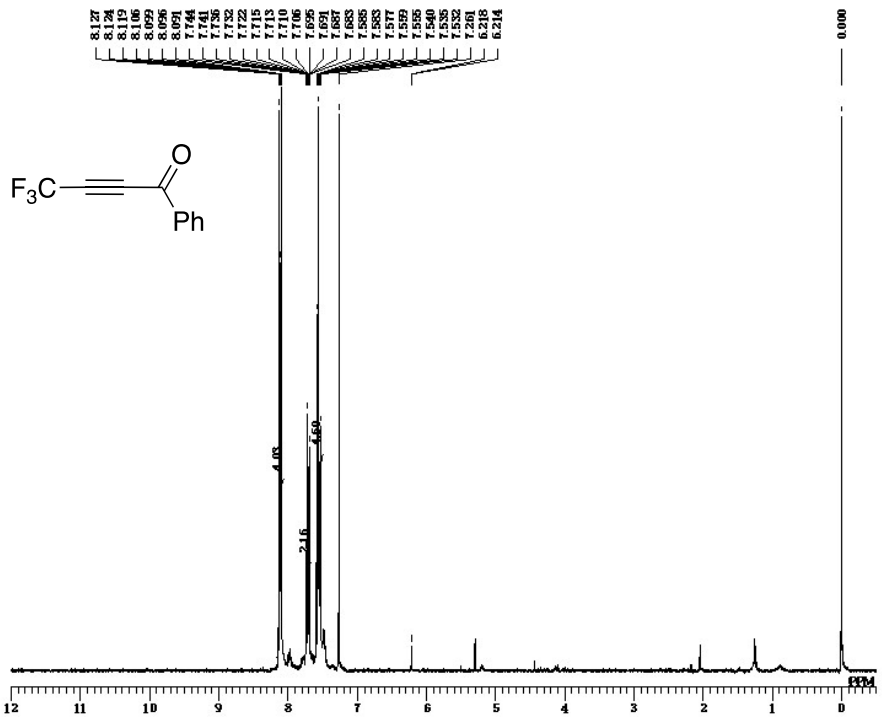
2.5.12. 4-(4-Bromophenyl)-6-(trifluoromethyl)pyrimidine (6cd)

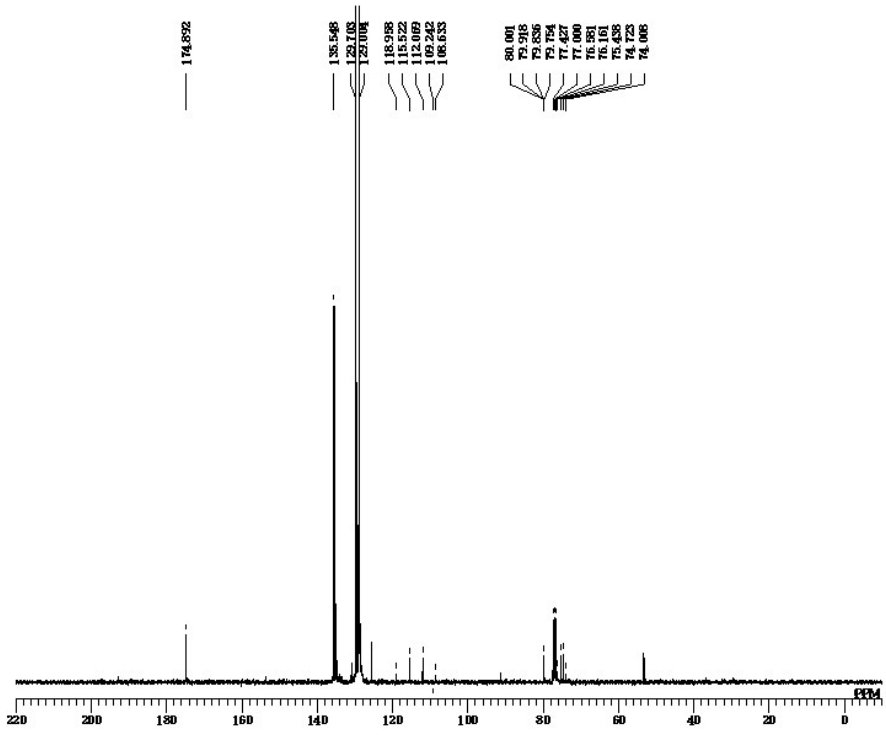


The title compound was obtained in 26% yield as a yellow solid. mp 39–40 °C. Rf 0.37 (Hexane:AcOEt=10:1). ^{1}H NMR δ 7.70 (d, *J*=8.4 Hz, 2H), 8.02 (d, *J*=6.0 Hz, 2H), 8.06 (s, 1H), 9.40 (s, 1H). ^{13}C NMR δ 112.3 (q, *J*=2.5 Hz), 120.5 (q, *J*=274.6 Hz), 127.1, 128.8, 132.5, 134.1, 156.4 (q, *J*=35.4 Hz), 159.5, 165.3. ^{19}F NMR δ –71.32 (s). IR (KBr) *v* 3070, 1595, 1537, 1403, 1324, 1307, 1290, 1264, 1202, 1133, 1095, 835 cm^{-1}. Anal. Calcd for $C_{11}H_6BrF_3N_2$, C, 43.59; H, 2.00; N, 9.24. Found C, 43.55; H, 1.68; N, 9.10.

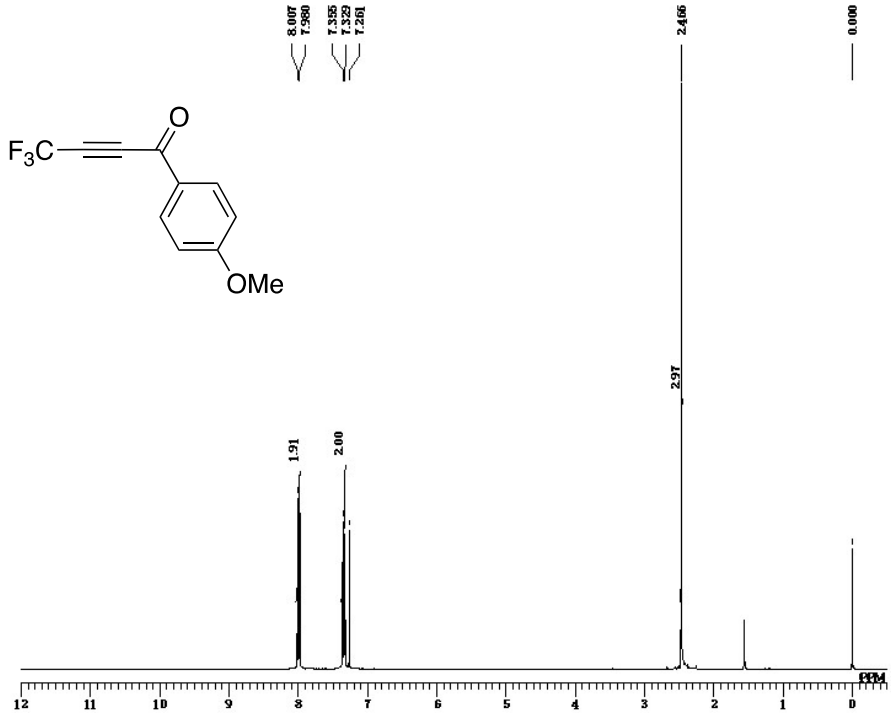
3. Spectral data

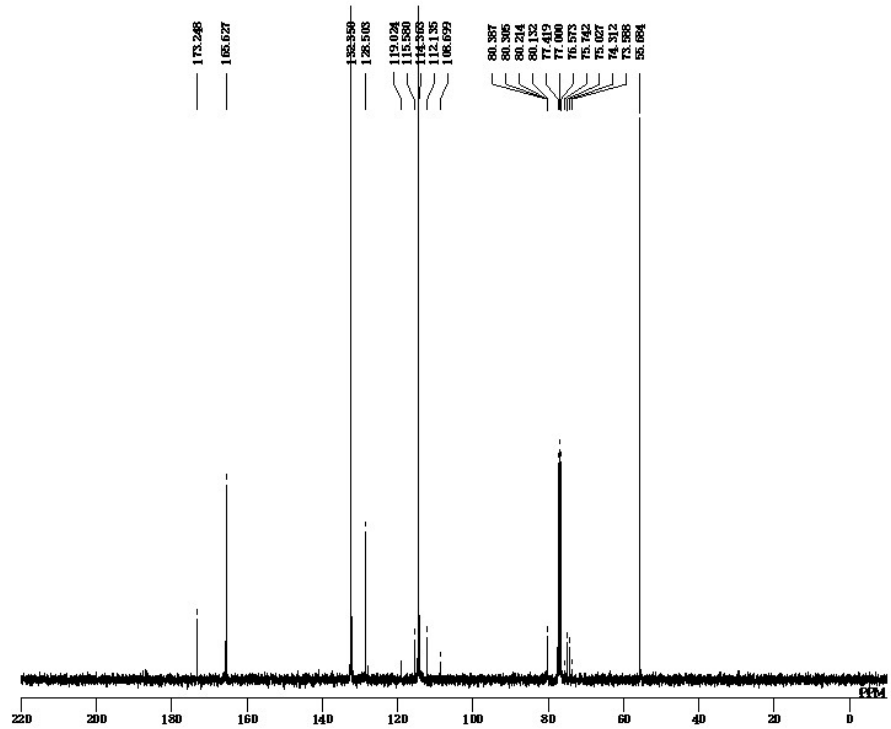
4,4,4-Trifluoro-1-phenylbut-2-yn-1-one (2a)



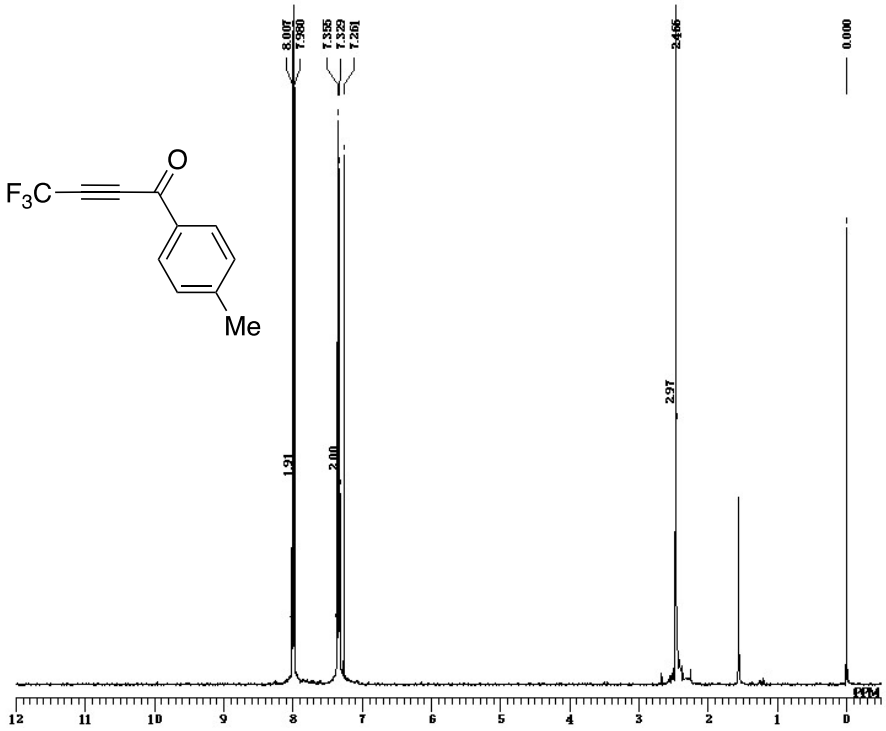


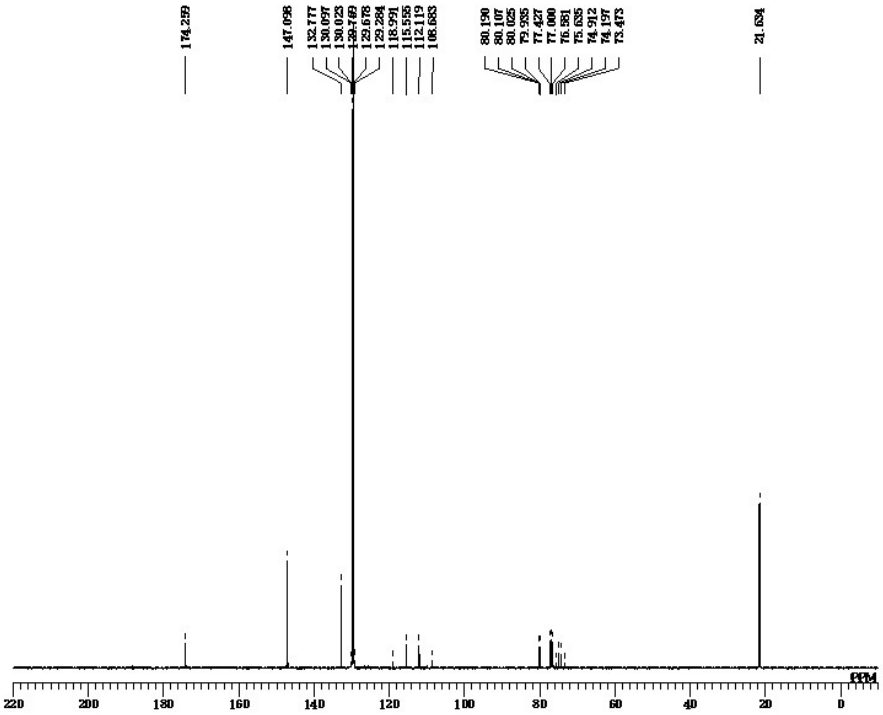
4,4,4-Trifluoro-1-(4-methoxyphenyl)but-2-yn-1-one (2b)



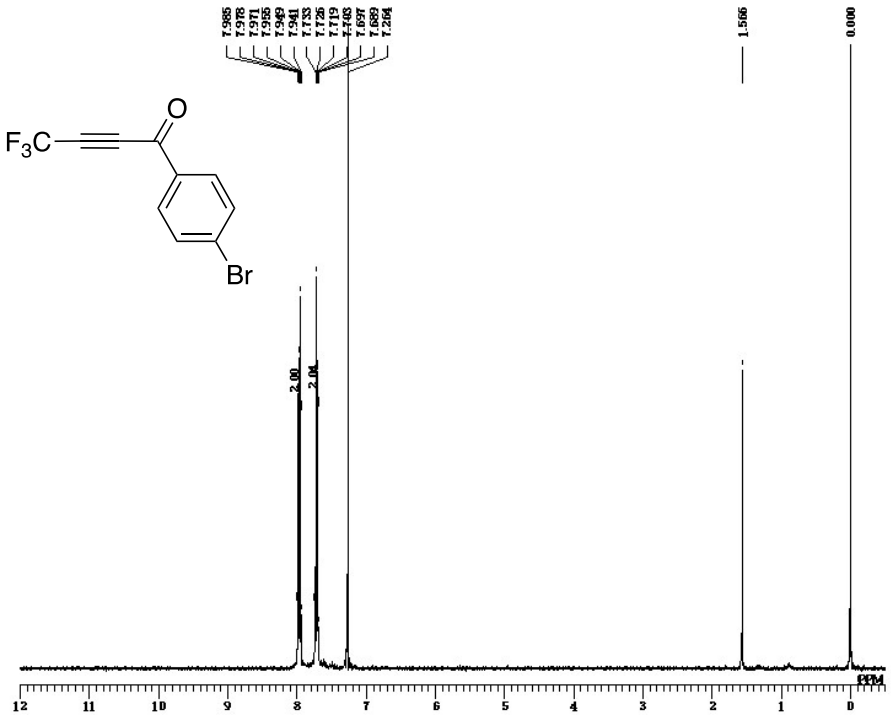


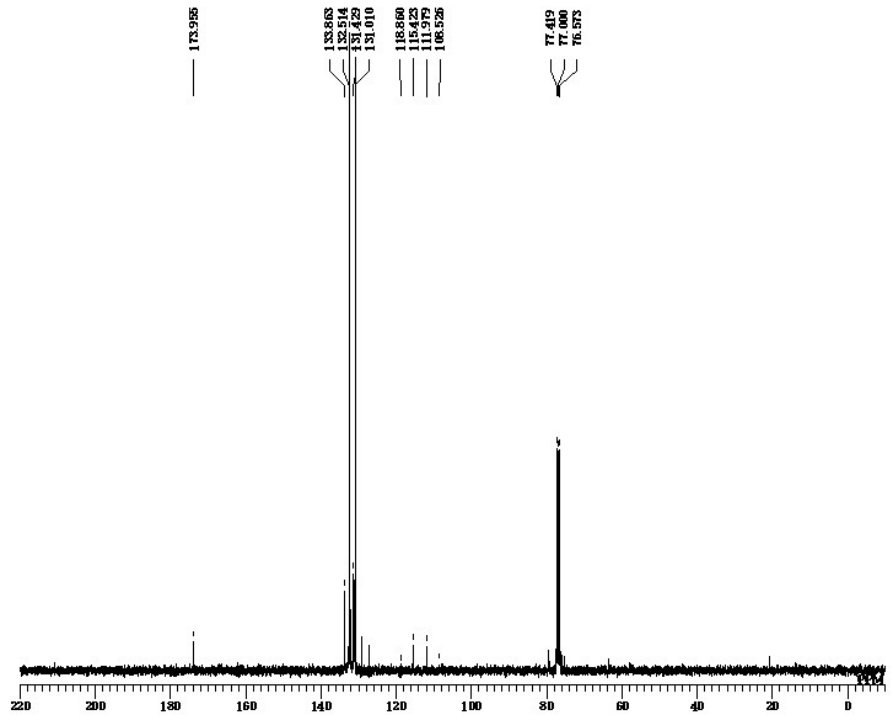
4,4,4-Trifluoro-1-(4-methylphenyl)but-2-yn-1-one (2c)



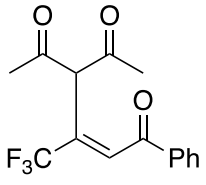


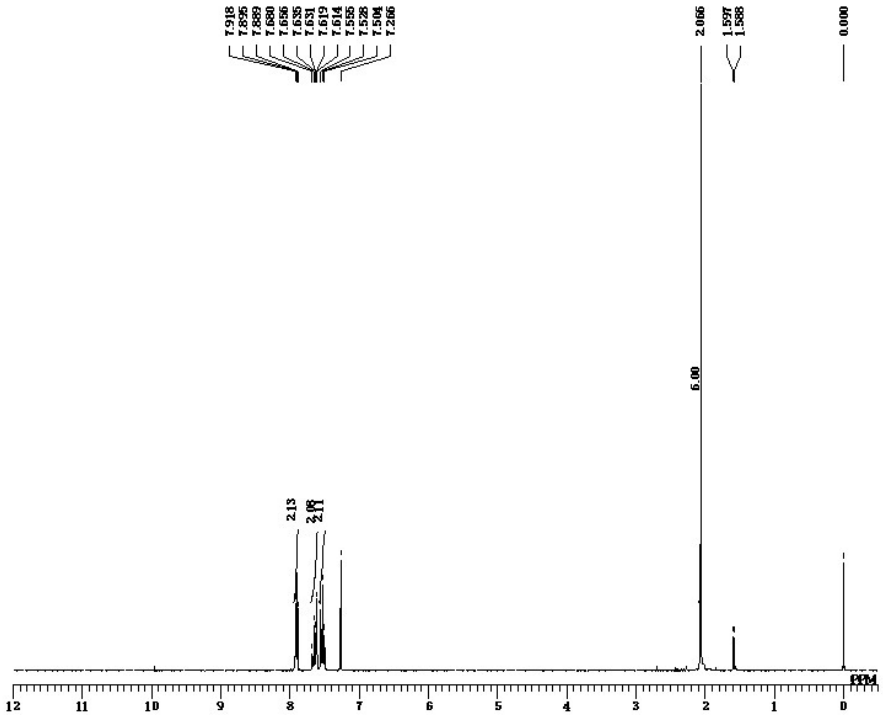
1-(4-Bromophenyl)-4,4,4-trifluorobut-2-yn-1-one (2d)

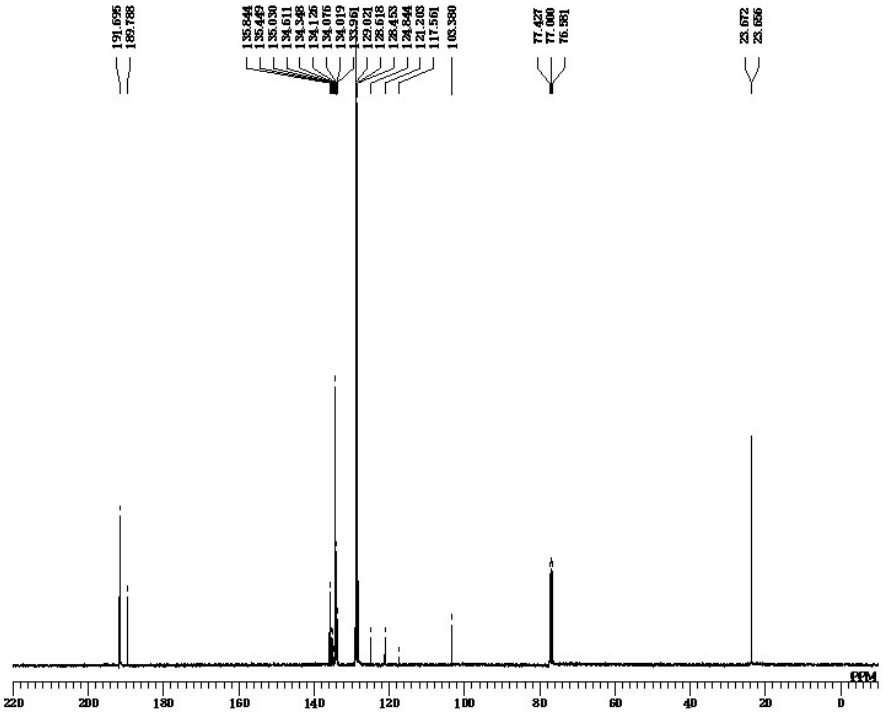




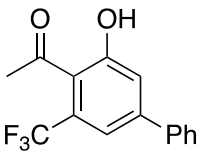
(*E*)-4-Acetyl-1-phenyl-3-(trifluoromethyl)hex-2-ene-1,5-dione (3aa)

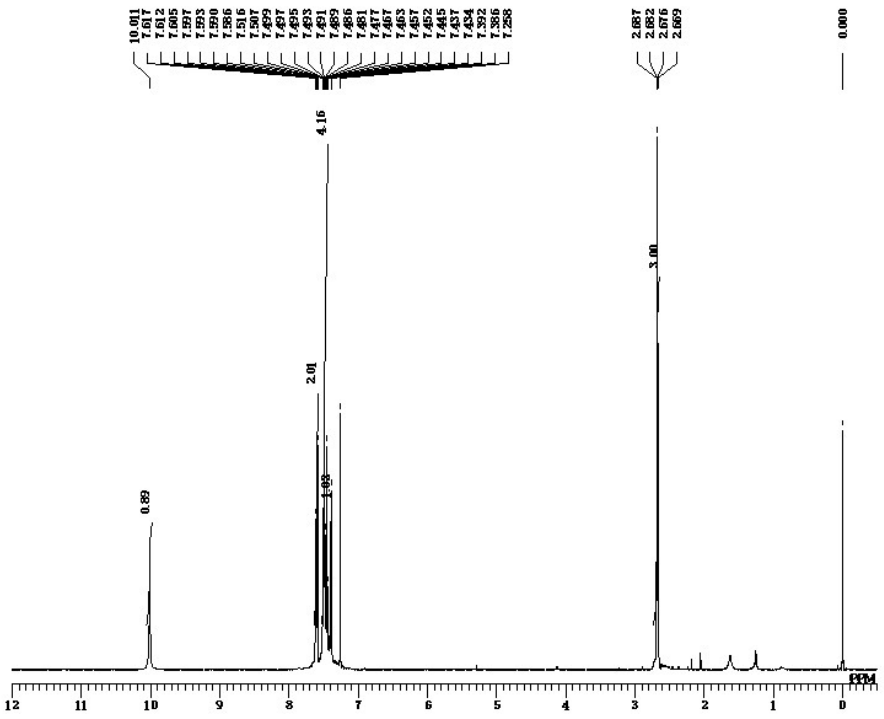


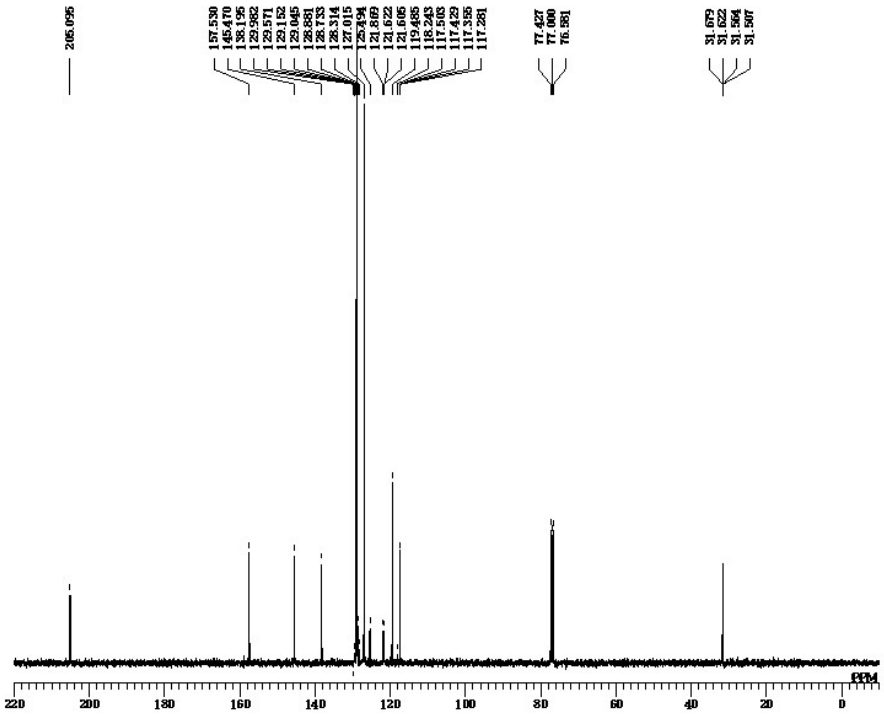




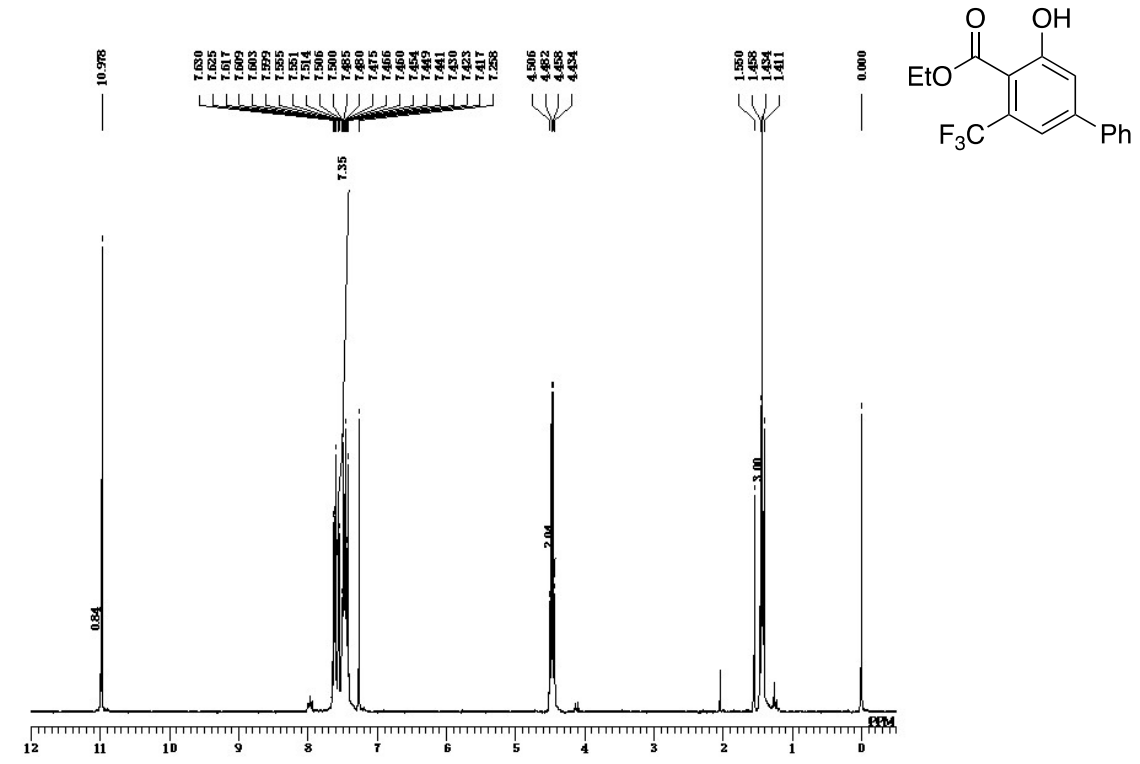
1-[2-Hydroxy-4-phenyl-6-(trifluoromethyl)phenyl]ethanone (4aa)

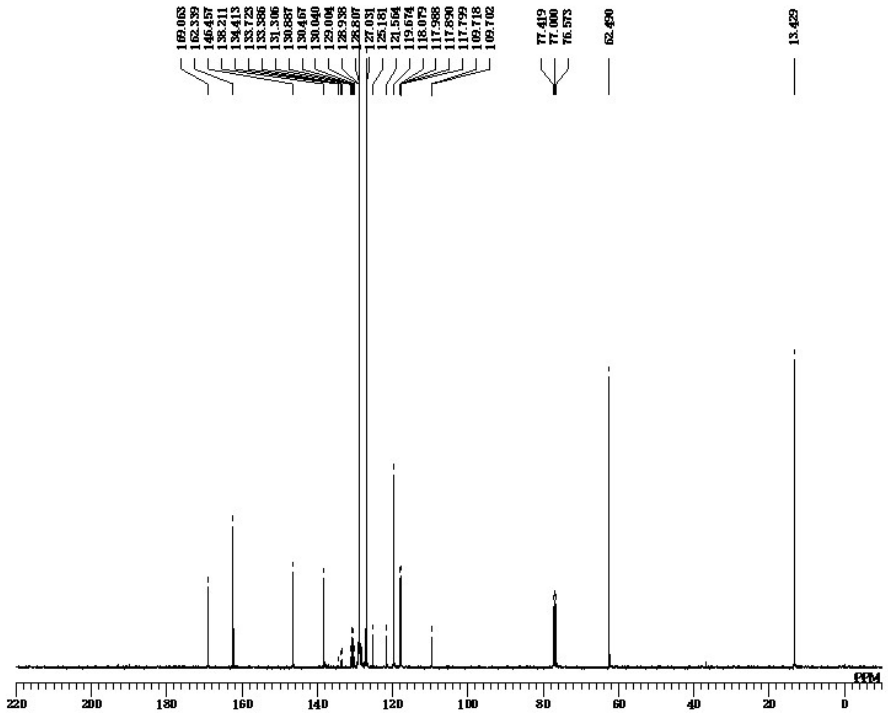




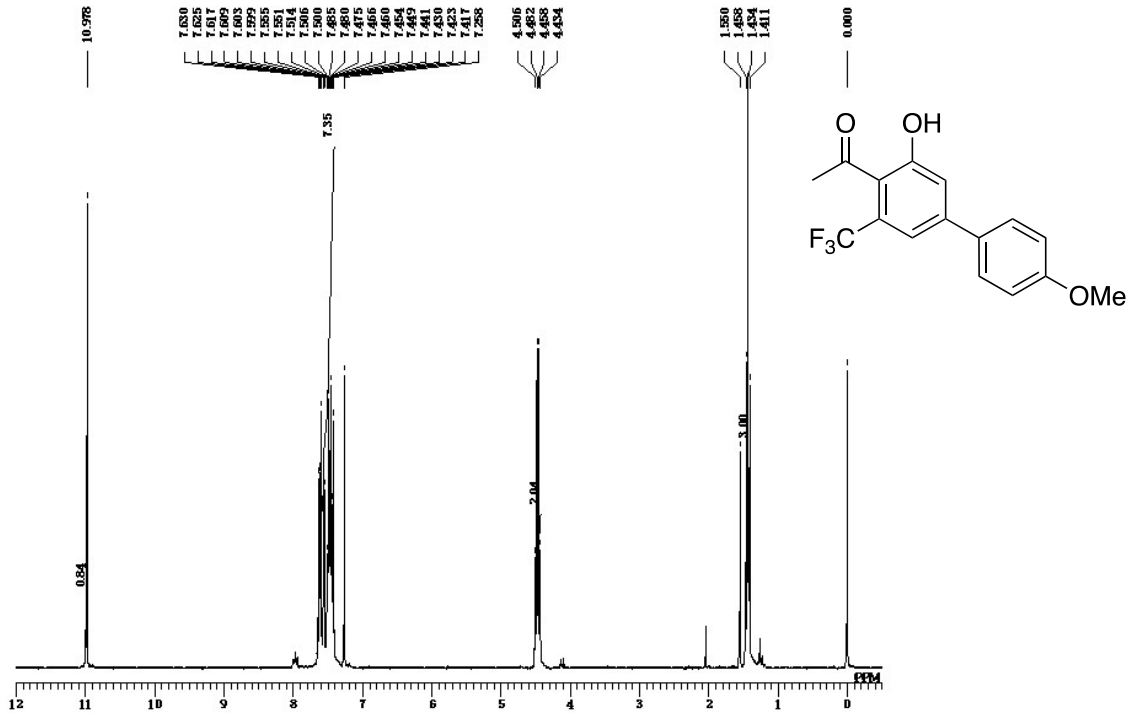


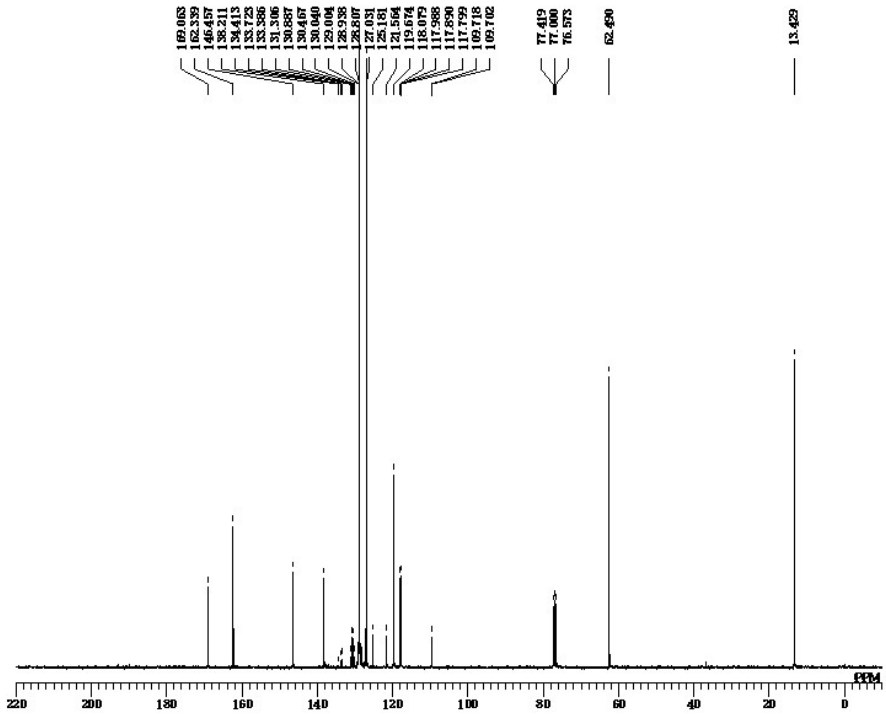
Ethyl 2-hydroxy-4-phenyl-6-(trifluoromethyl)phenyl-1-carboxylate (4ab)



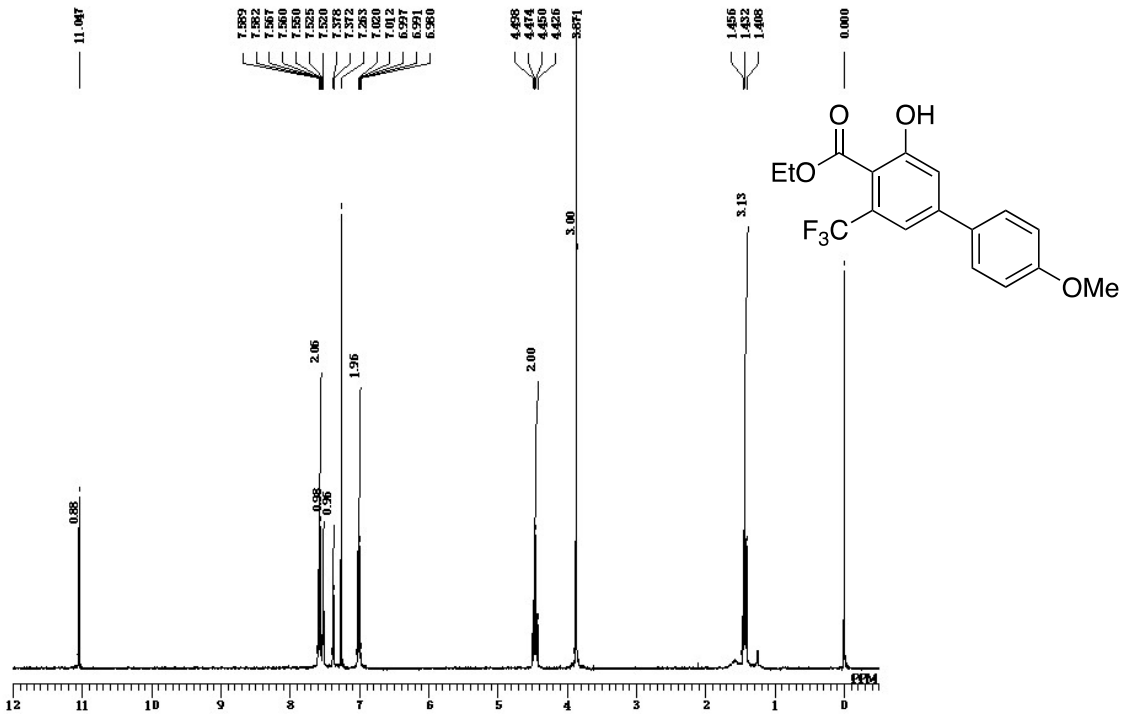


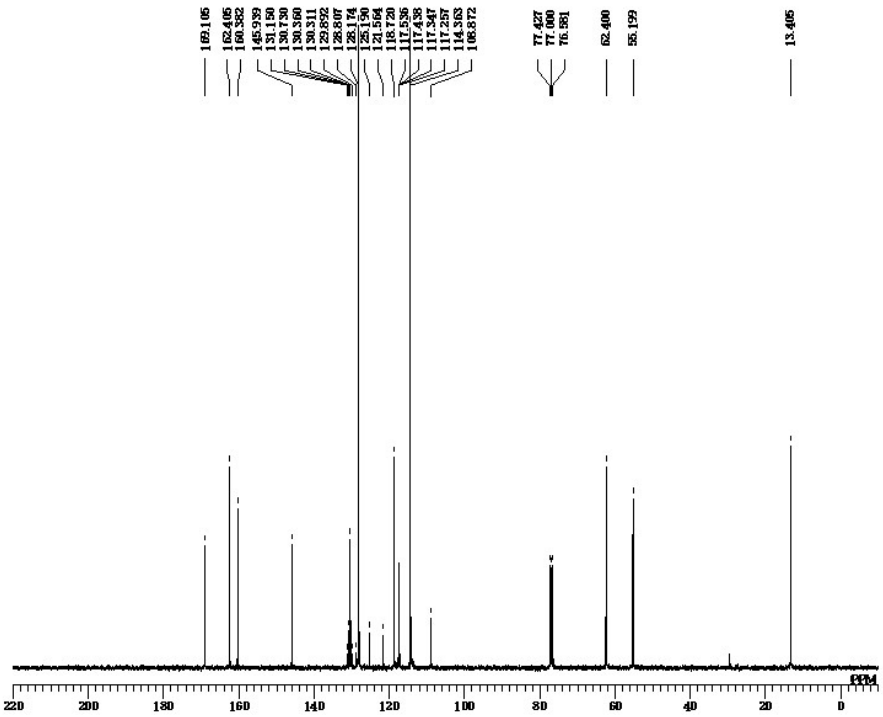
1-[2-Hydroxy-4-(4-methoxyphenyl)-6-(trifluoromethyl)phenyl]ethanone (4ba)



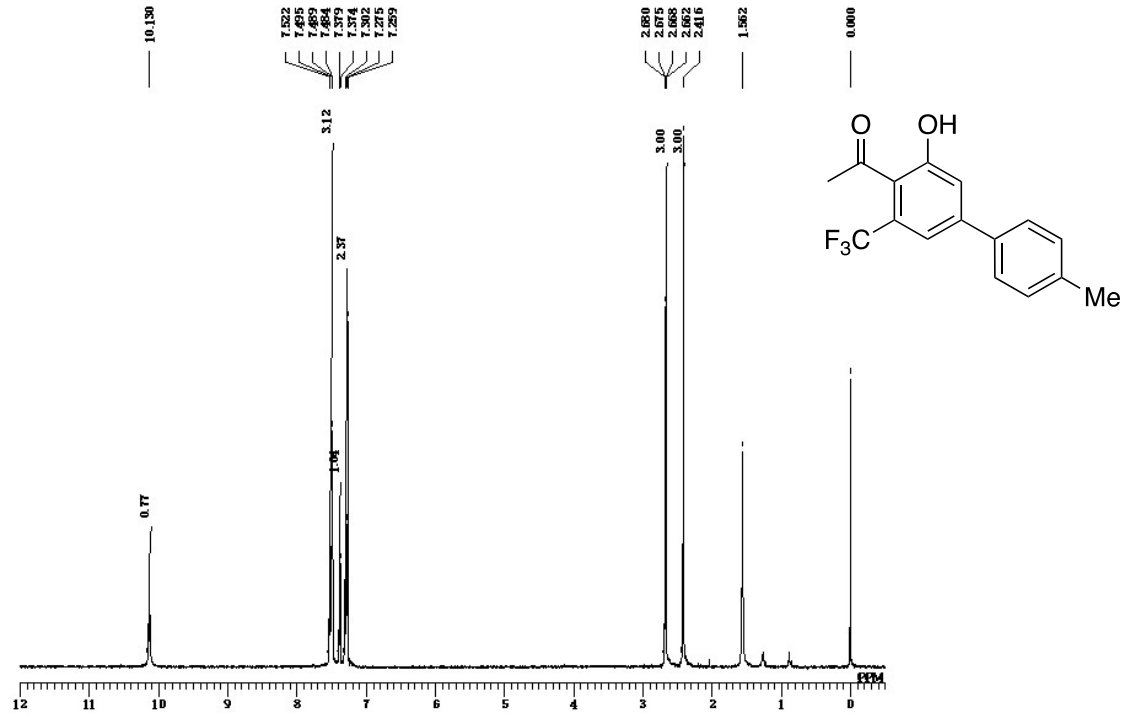


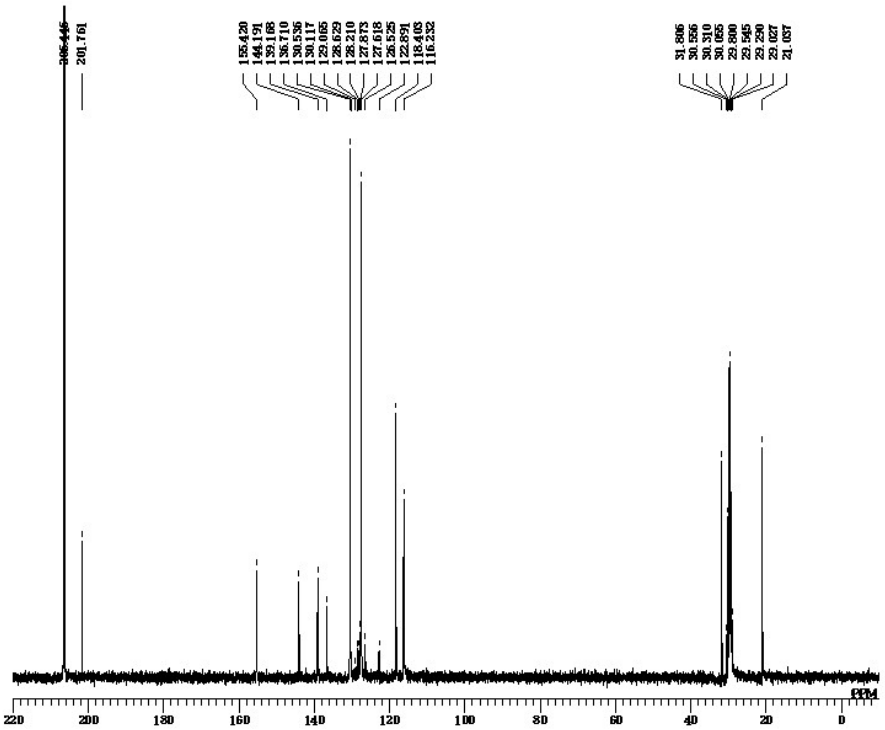
Ethyl 2-hydroxy-4-(4-methoxyphenyl)-6-(trifluoromethyl)phenyl-1-carboxylate (4bb)



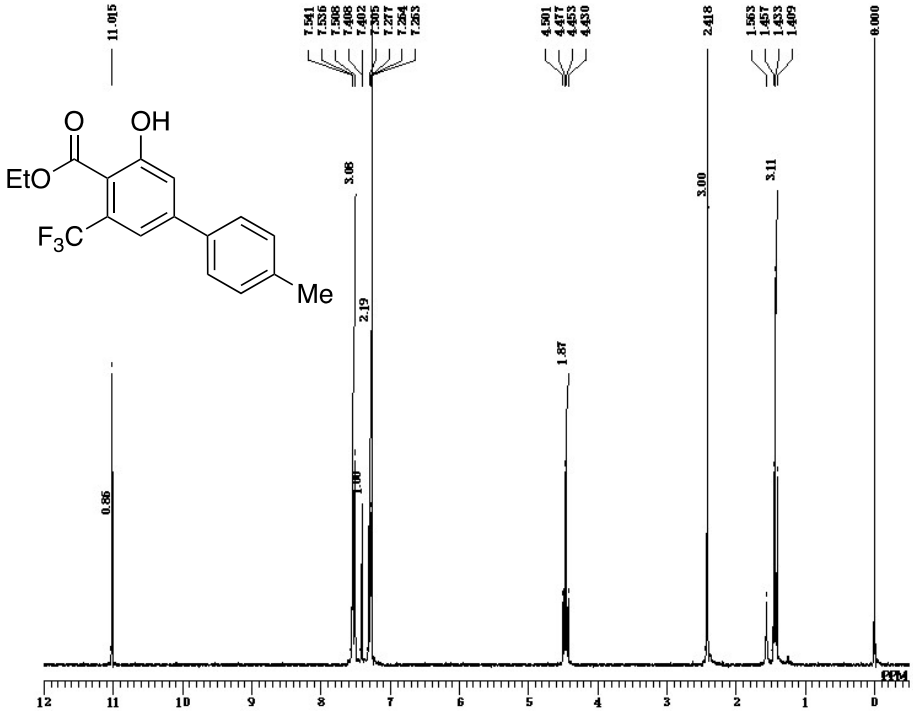


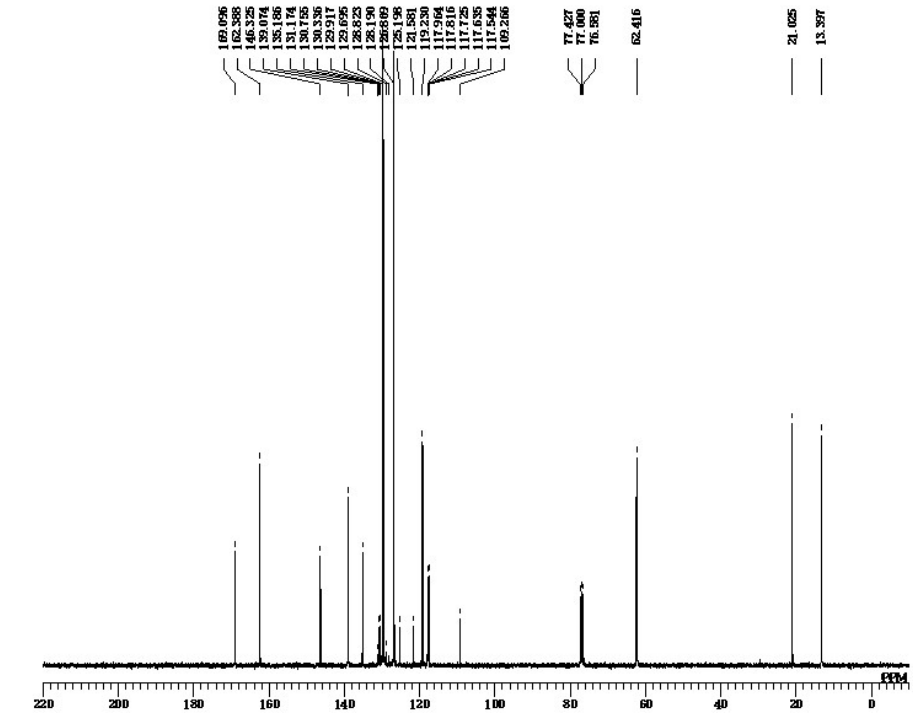
1-[2-Hydroxy-4-(4-methylphenyl)-6-(trifluoromethyl)phenyl]ethanone (4ca)



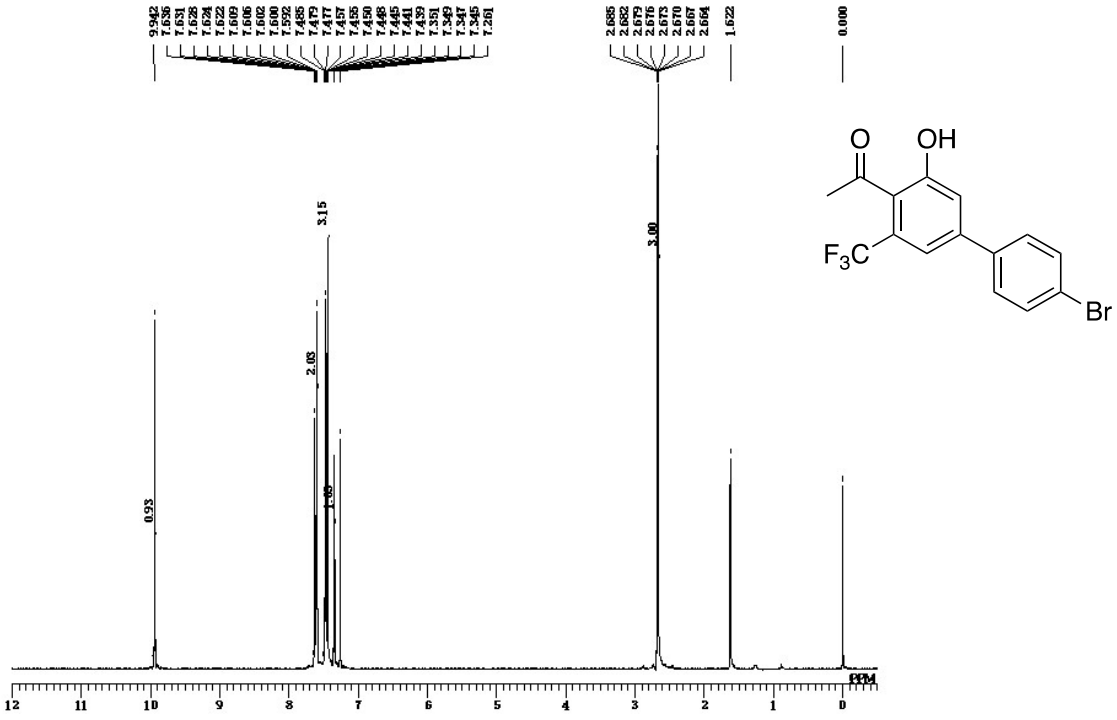


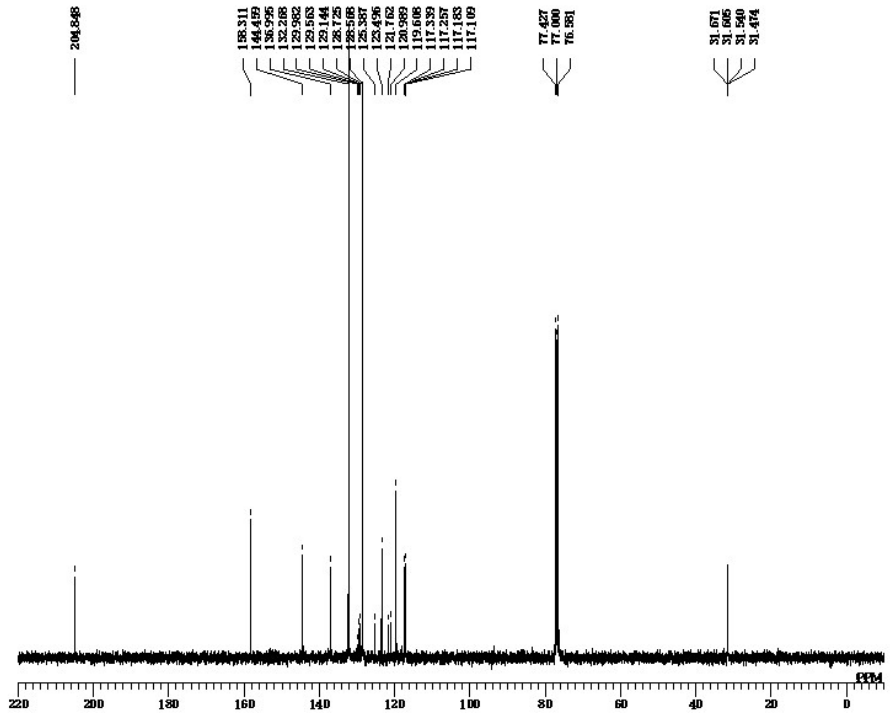
Ethyl [2-hydroxy-4-(4-methylphenyl)-6-(trifluoromethyl)phenyl]-1-carboxylate (4cb)



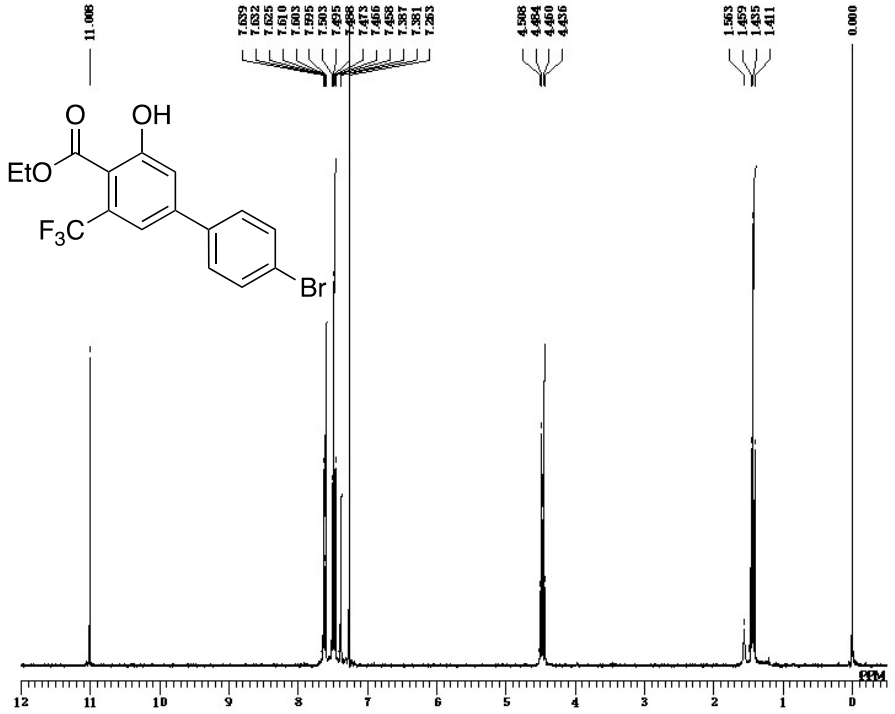


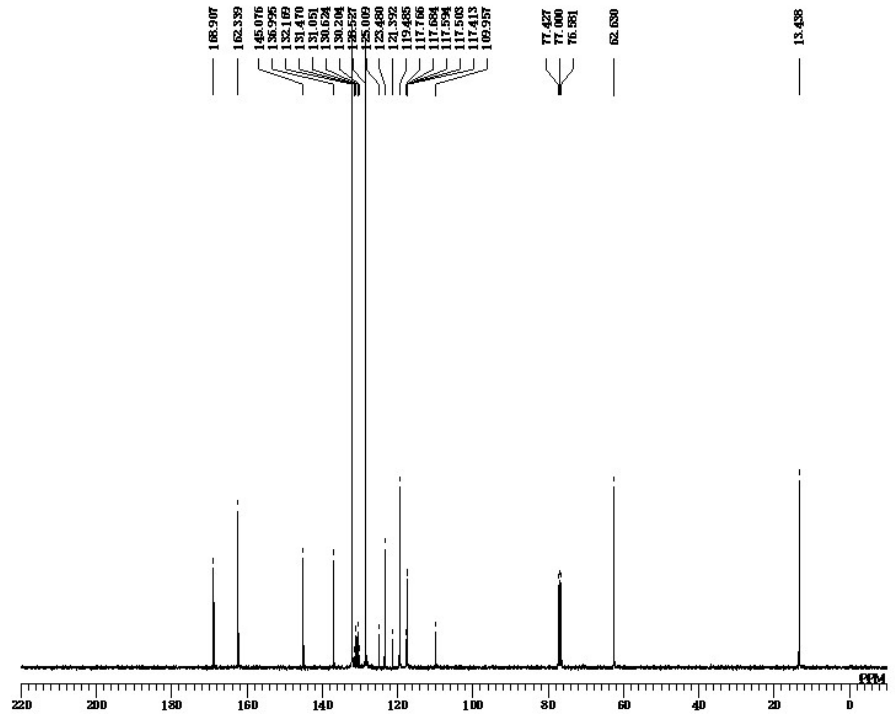
2.4.7. 1-[2-Hydroxy-4-(4-bromophenyl)-6-(trifluoromethyl)phenyl]ethanone (4da)



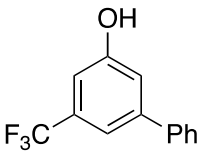


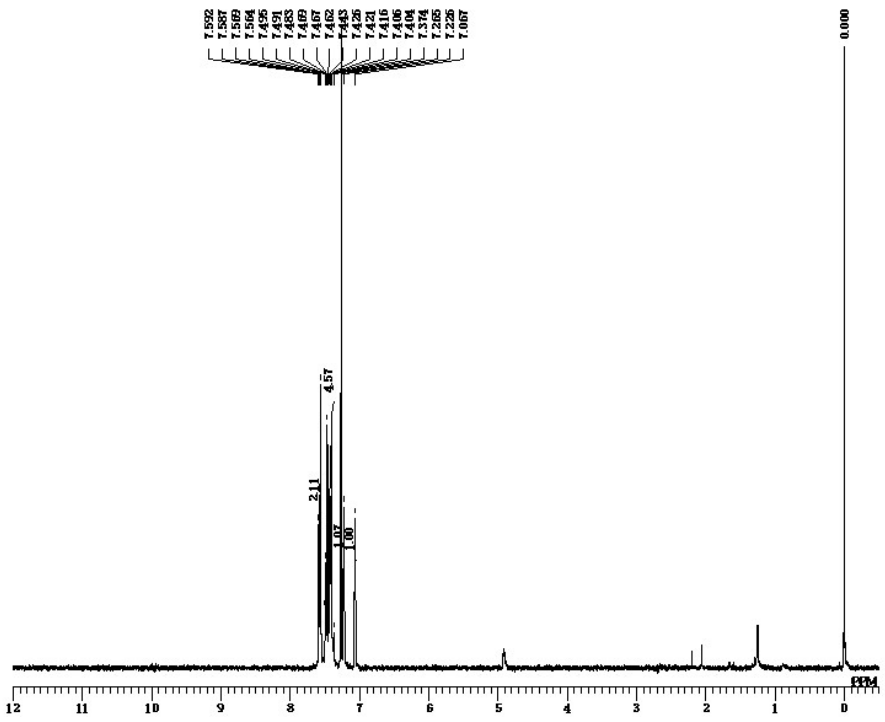
Ethyl [4-(4-bromophenyl)-2-hydroxy-6-(trifluoro-methyl)]phenyl-1-carboxylate (4db)

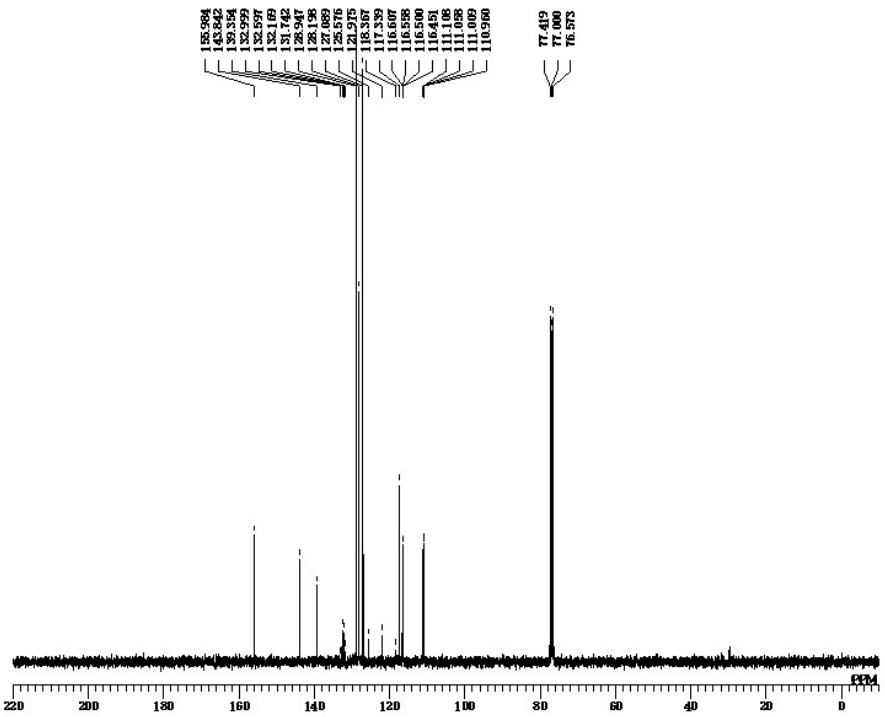




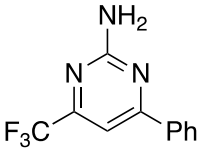
3-Phenyl-5-(trifluoromethyl)phenol (5a)

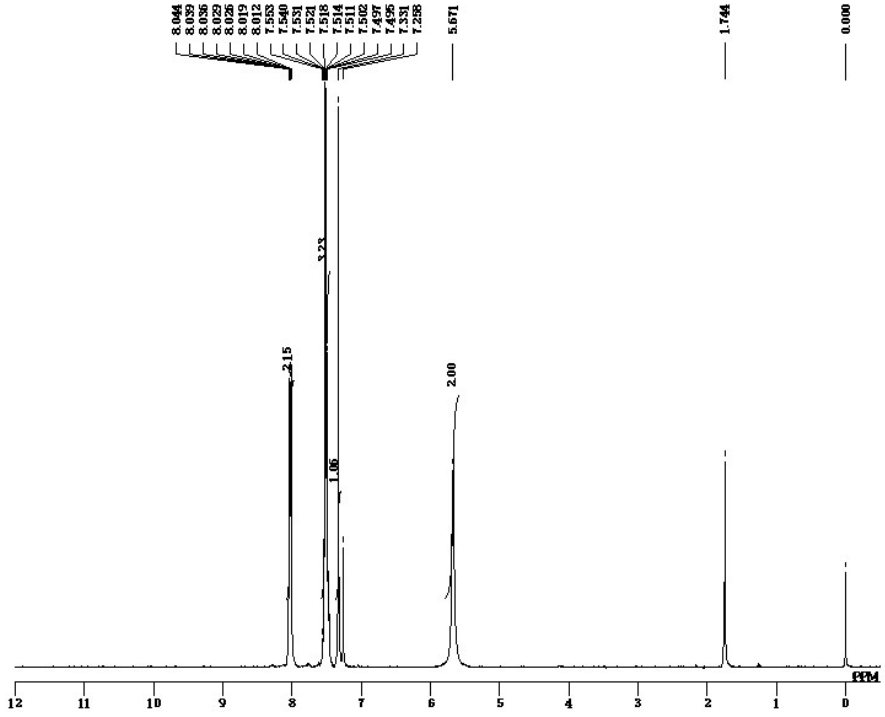


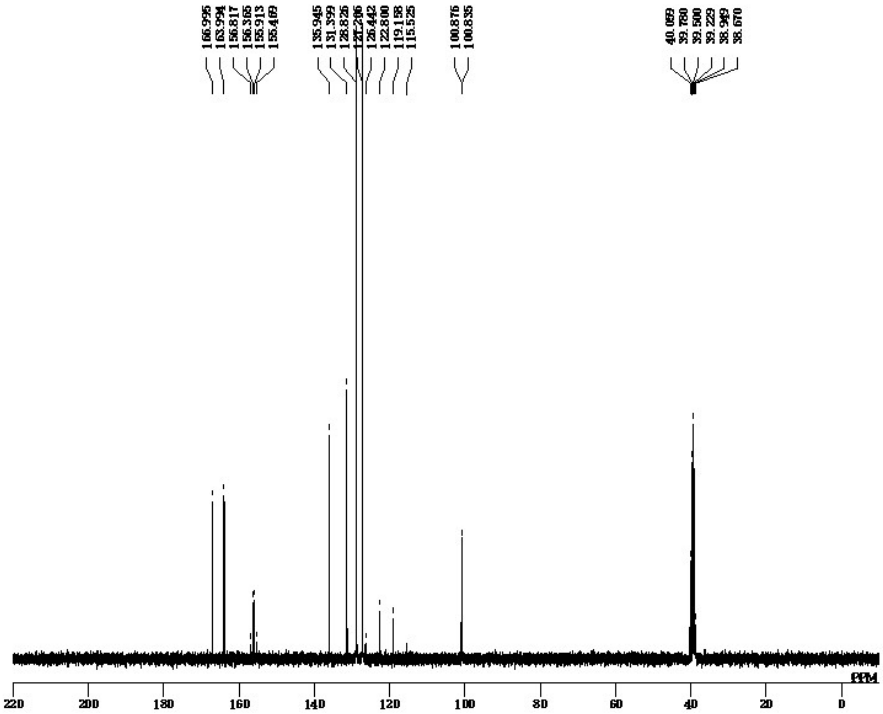




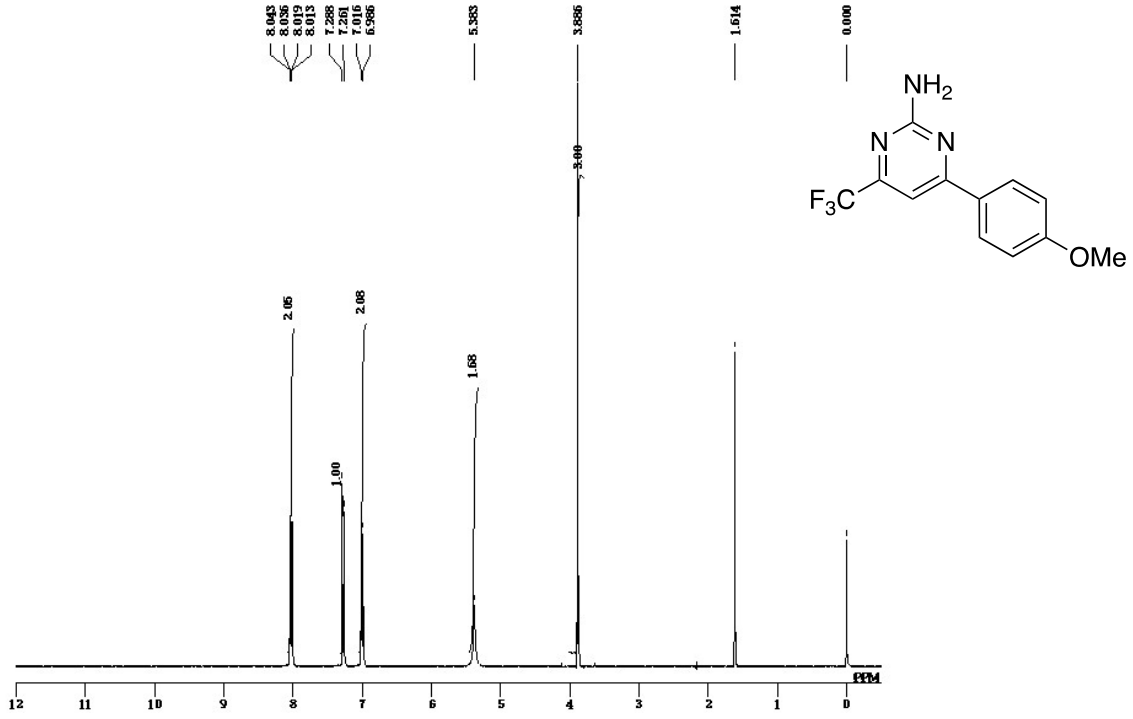
2-Amino-4-phenyl-6-(trifluoromethyl)pyrimidine (6aa)

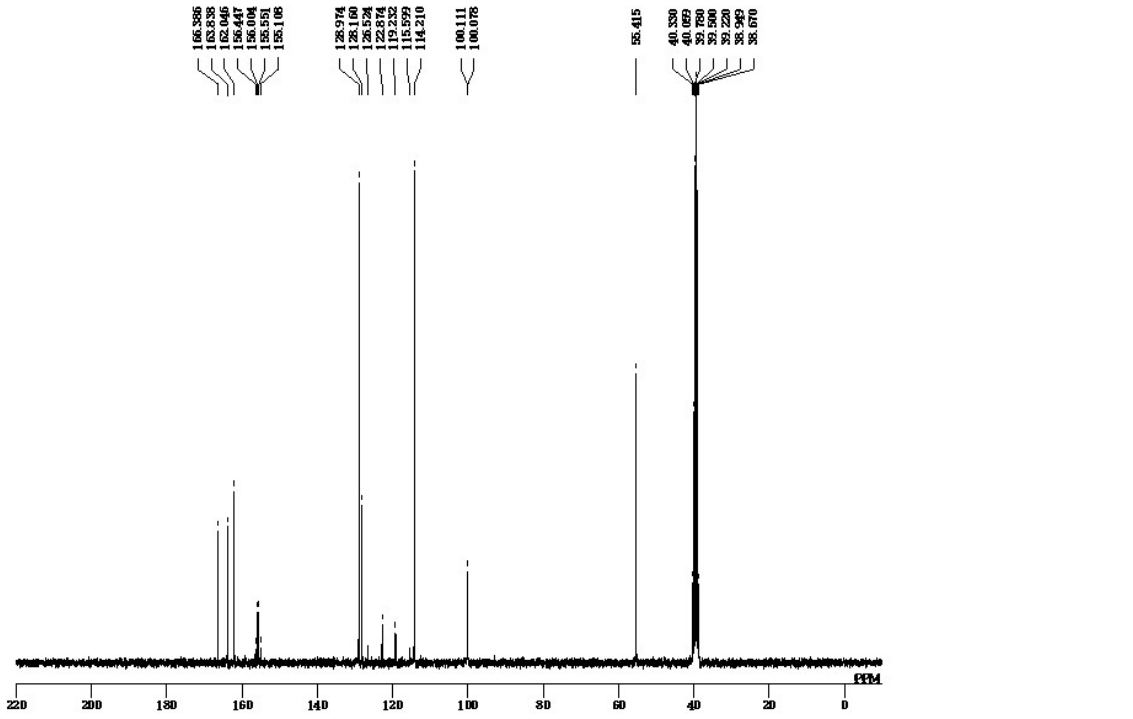




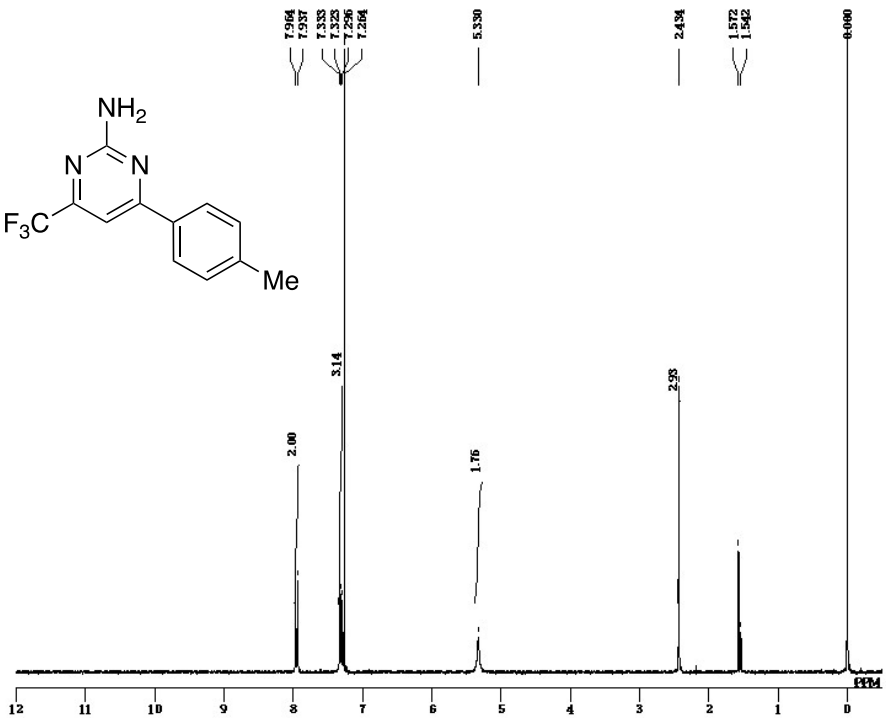


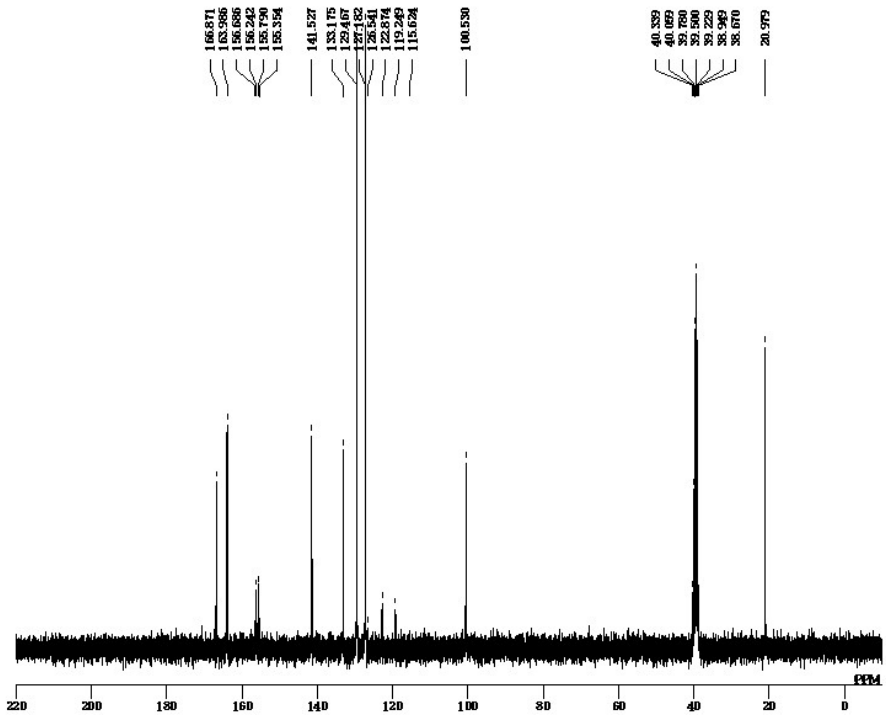
2-Amino-4-(4-methoxyphenyl)-6-(trifluoromethyl)pyrimidine (6ab)



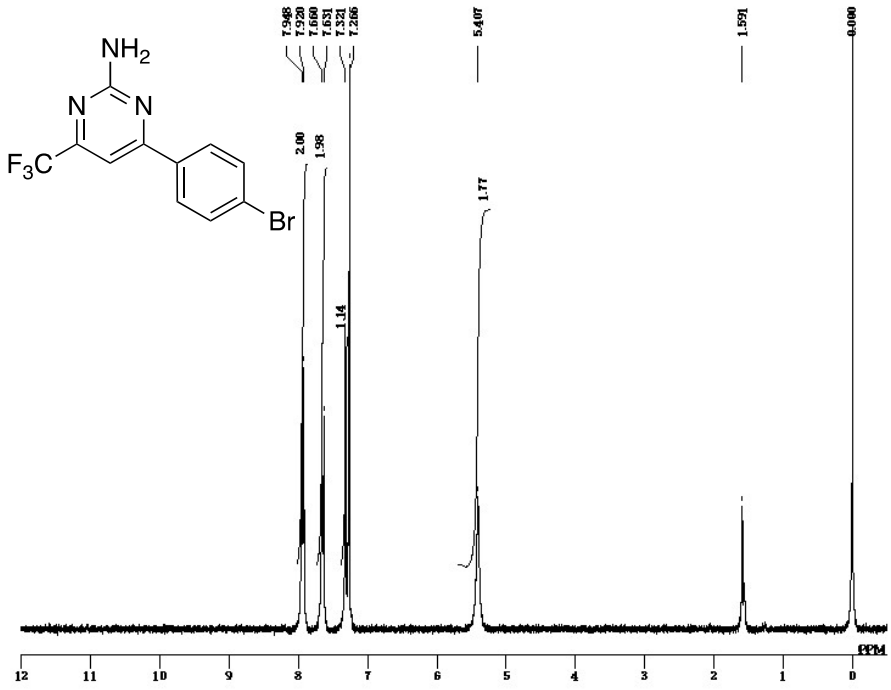


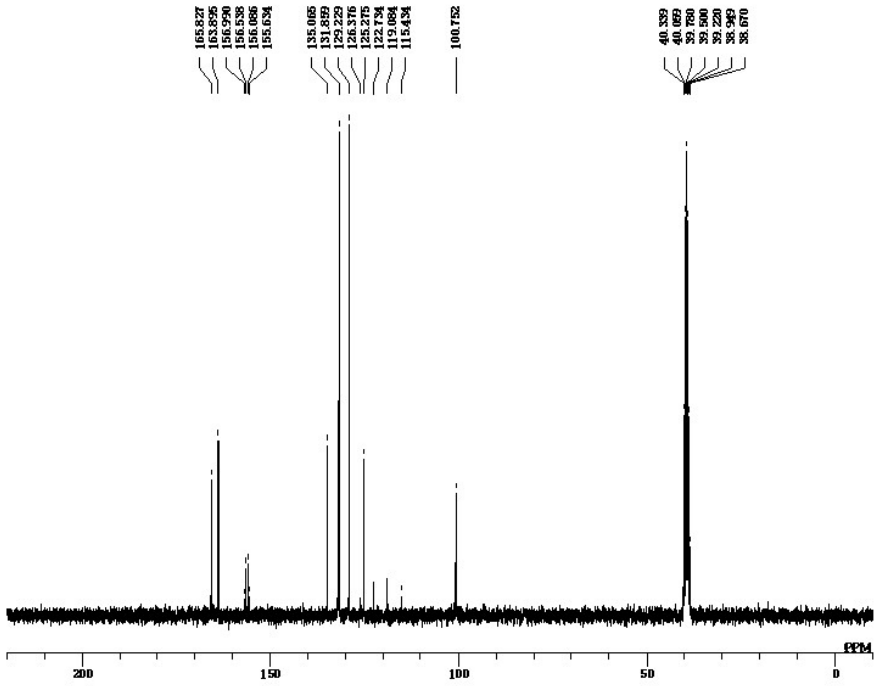
2-Amino-4-(4-methylphenyl)-6-(trifluoromethyl)pyrimidine (6ac)



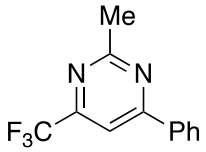


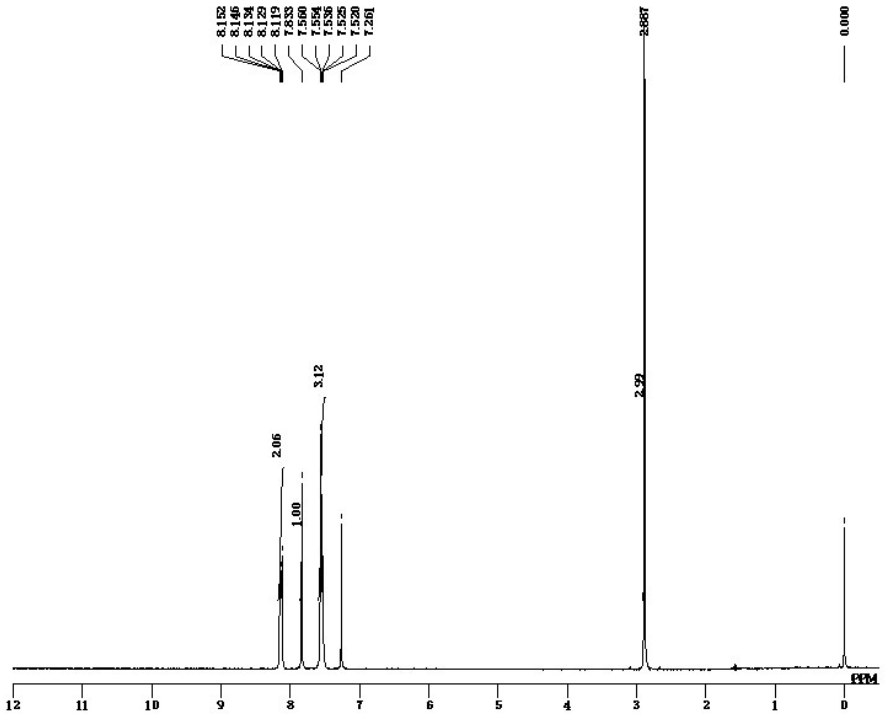
2-Amino-4-(4-bromophenyl)-6-(trifluoromethyl)pyrimidine (6ad)

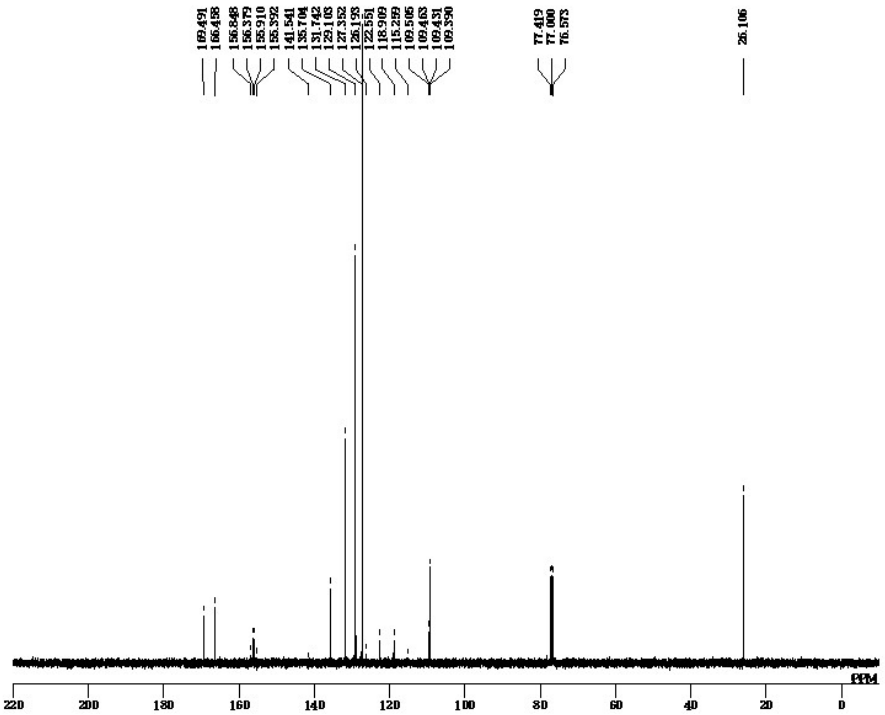




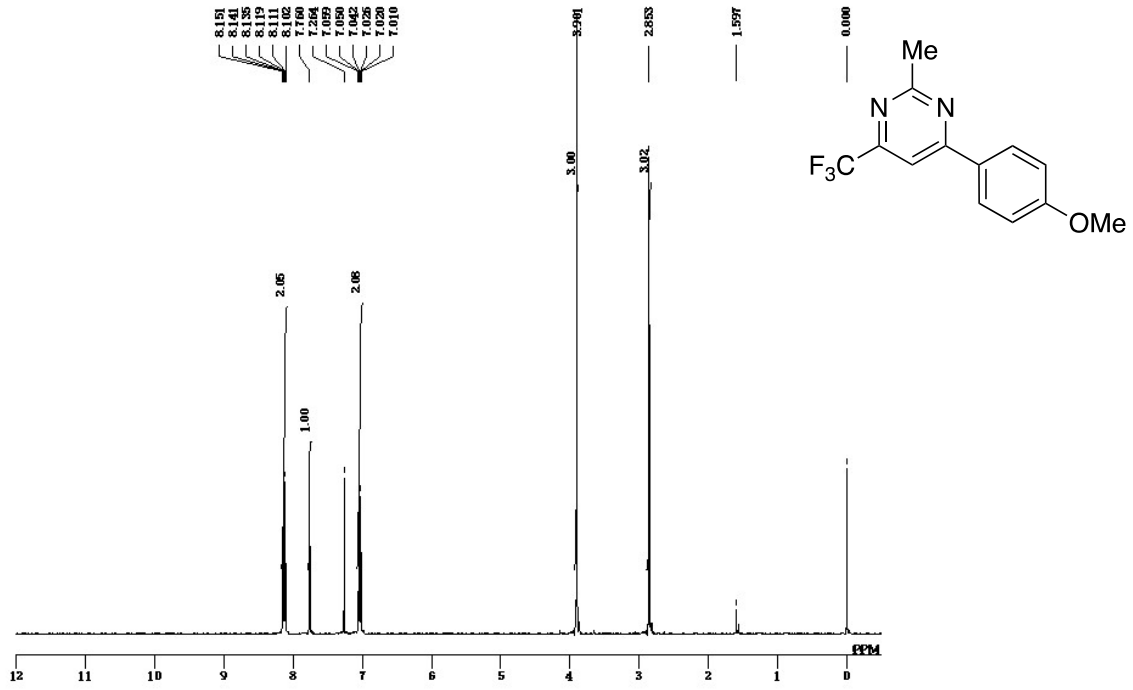
2-Methyl-4-phenyl-6-(trifluoromethyl)pyrimidine (6ba)

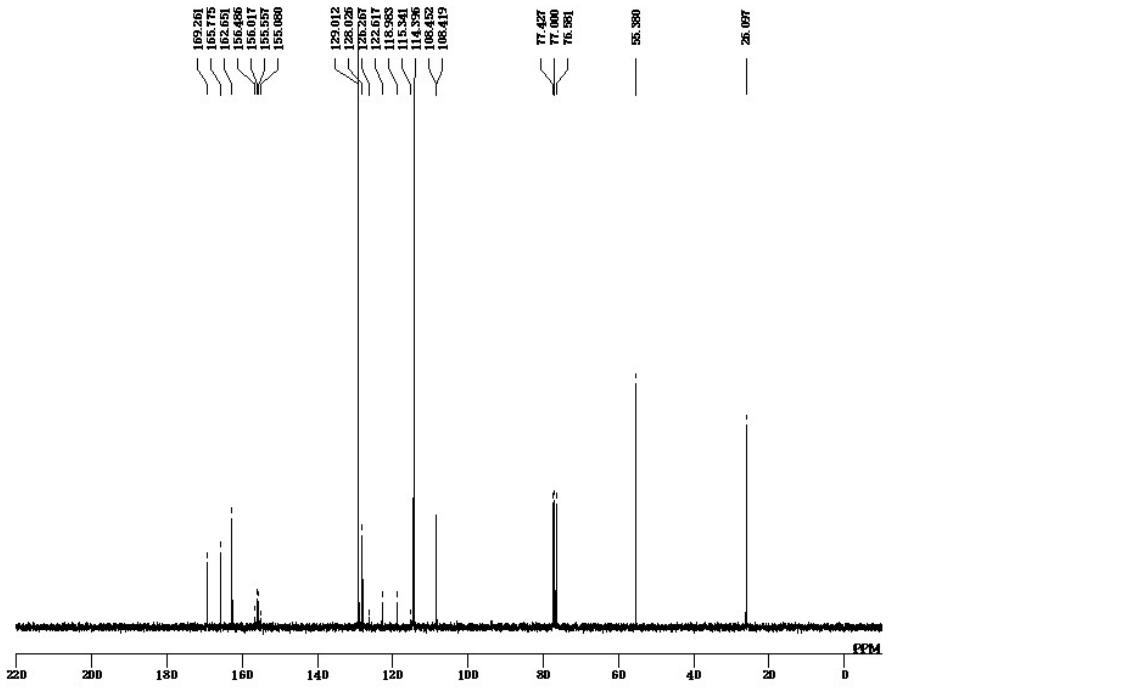




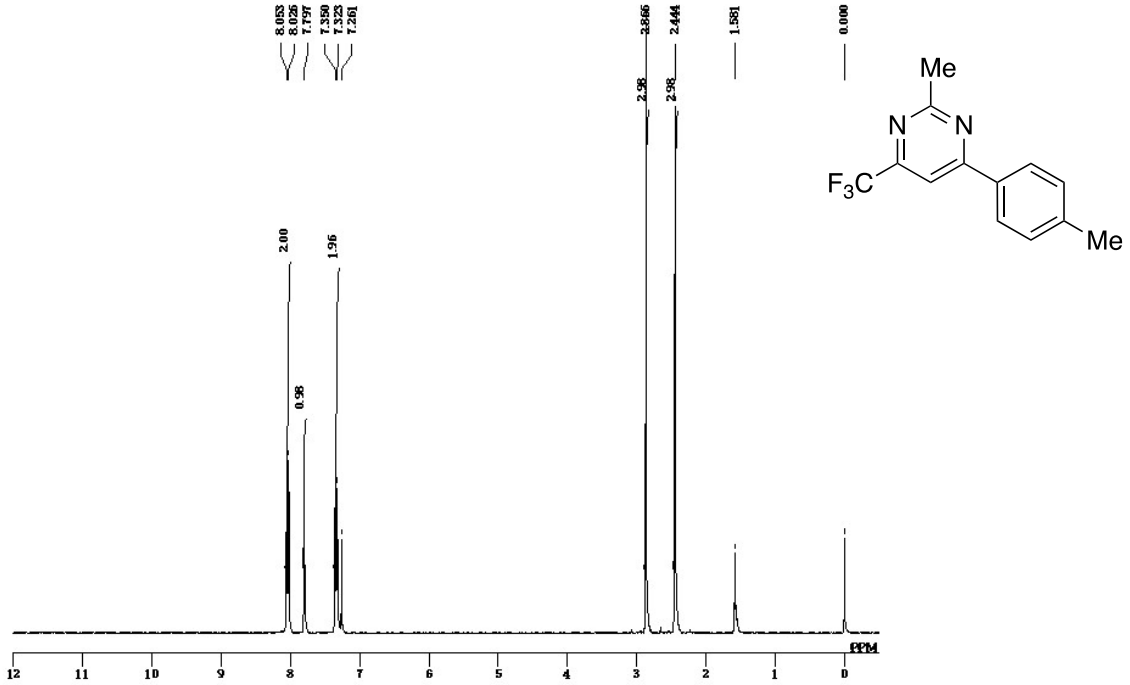


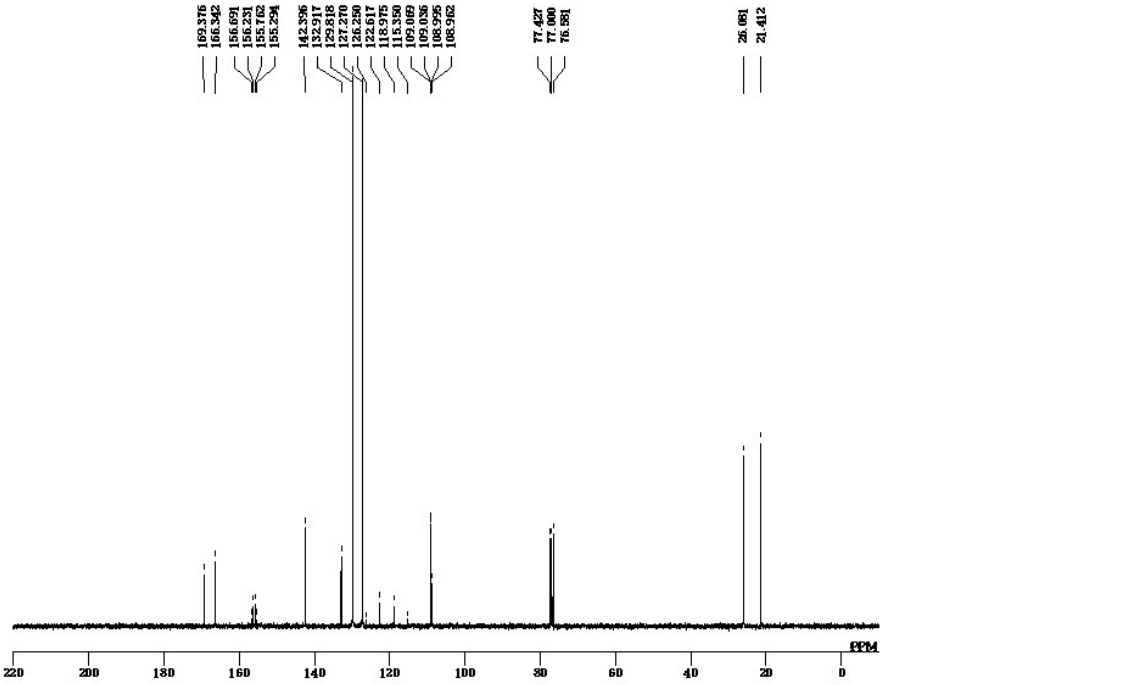
4-(4-Methoxyphenyl)-2-methyl-6-(trifluoromethyl)pyrimidine (6bb)



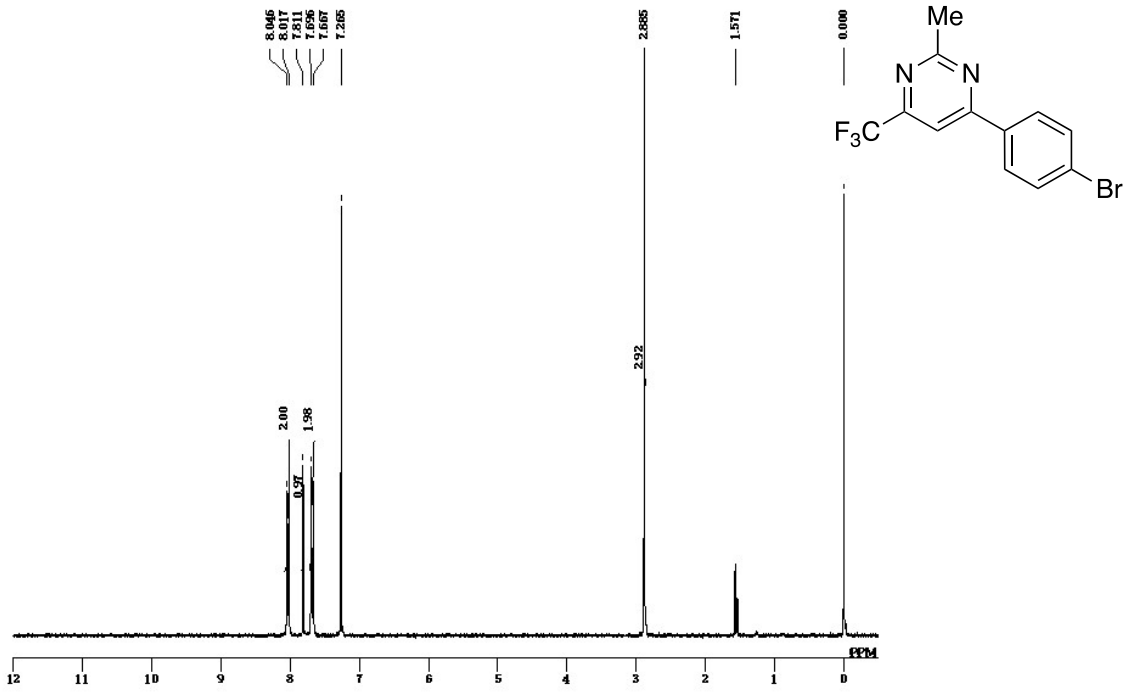


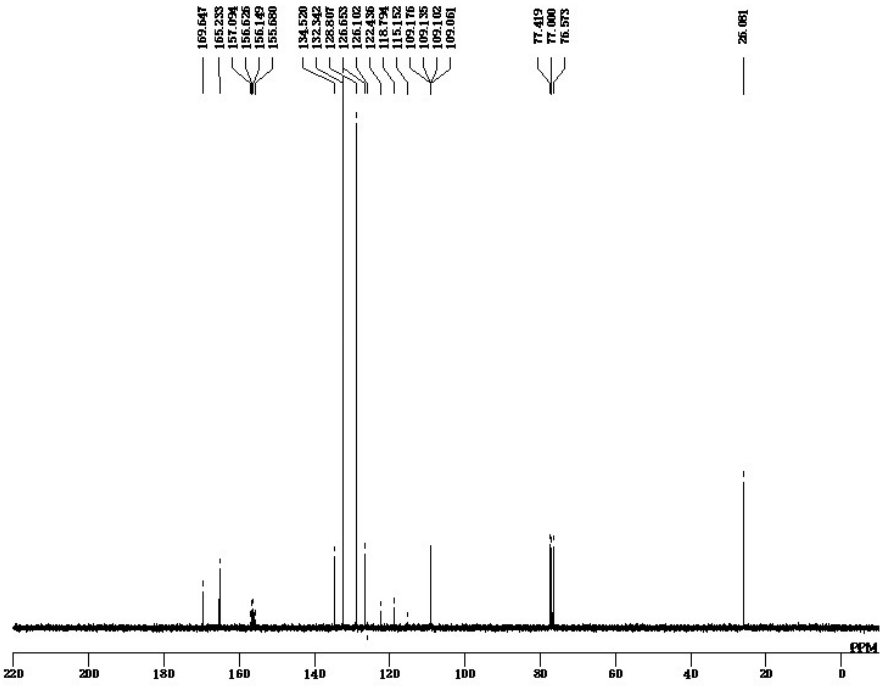
2-Methyl-4-(4-methylphenyl)-6-(trifluoromethyl)pyrimidine (6bc)



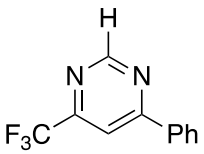


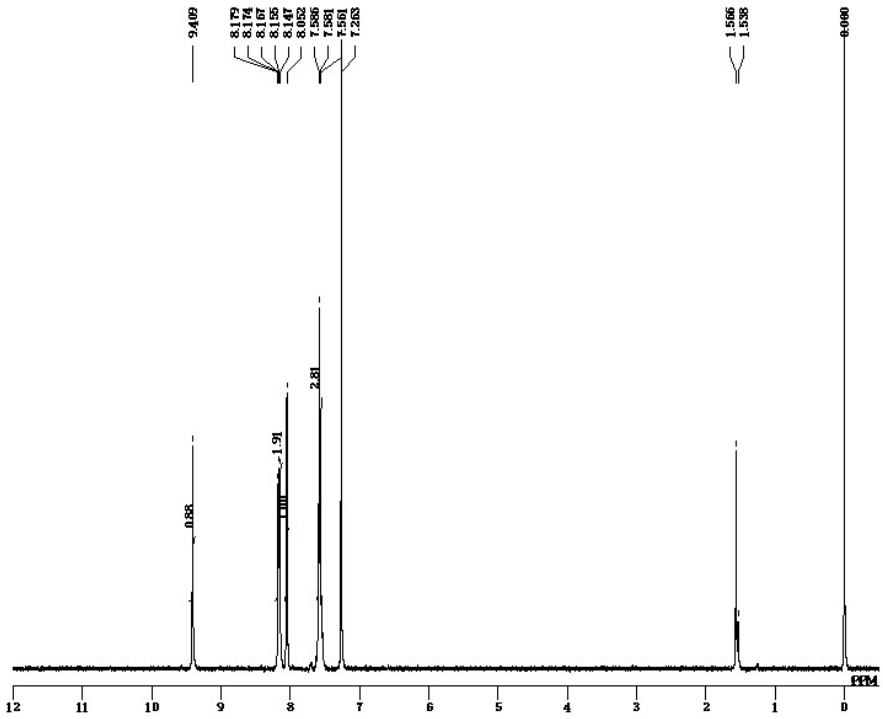
4-(4-Bromophenyl)-2-methyl-6-(trifluoromethyl)-pyrimidine (6bd)

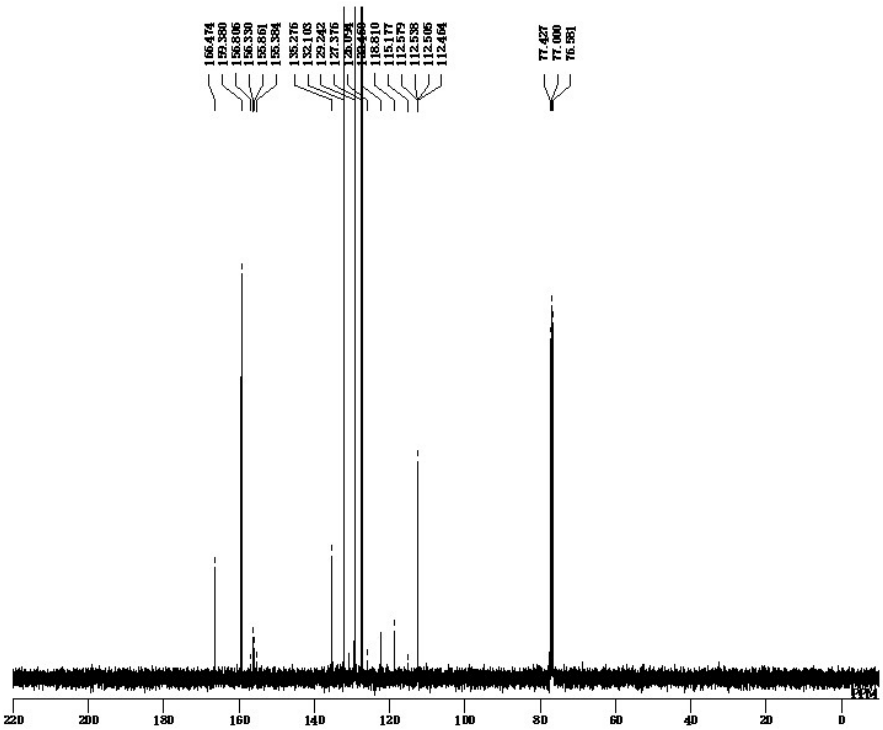




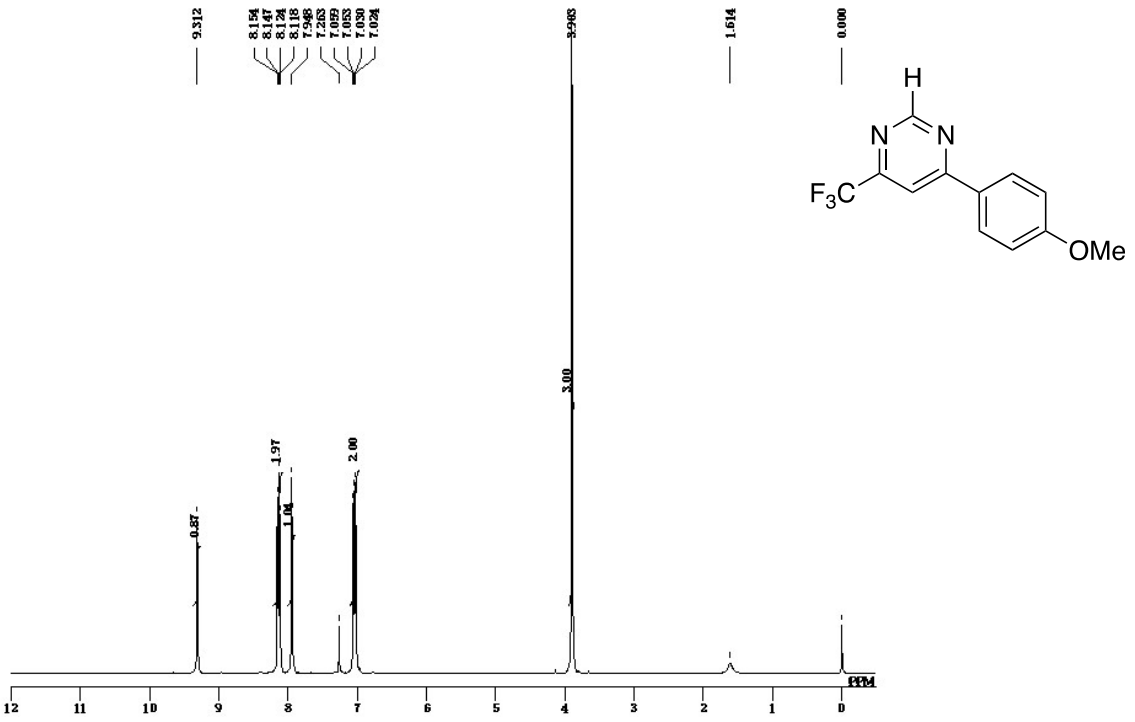
4-Phenyl-6-(trifluoromethyl)pyrimidine (6ca)

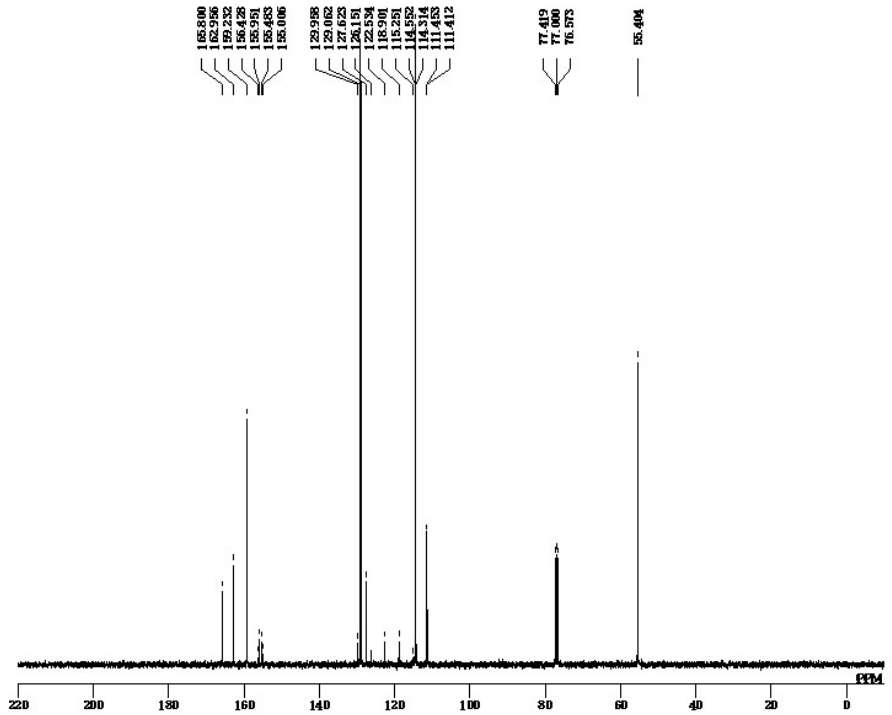




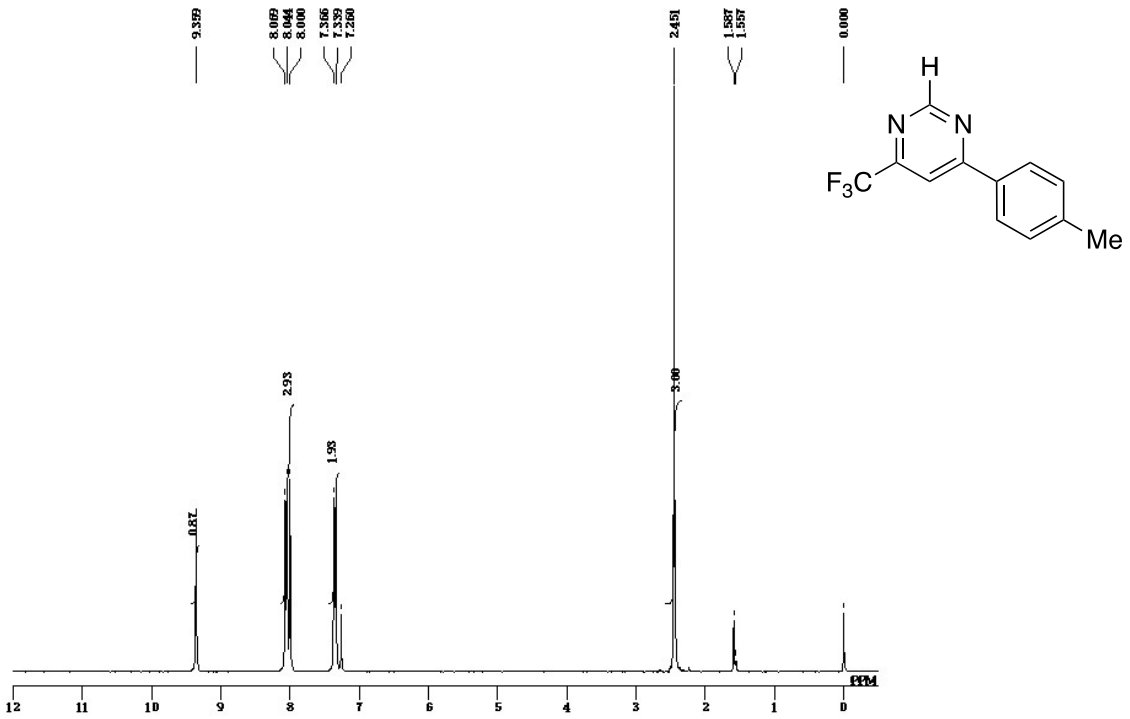


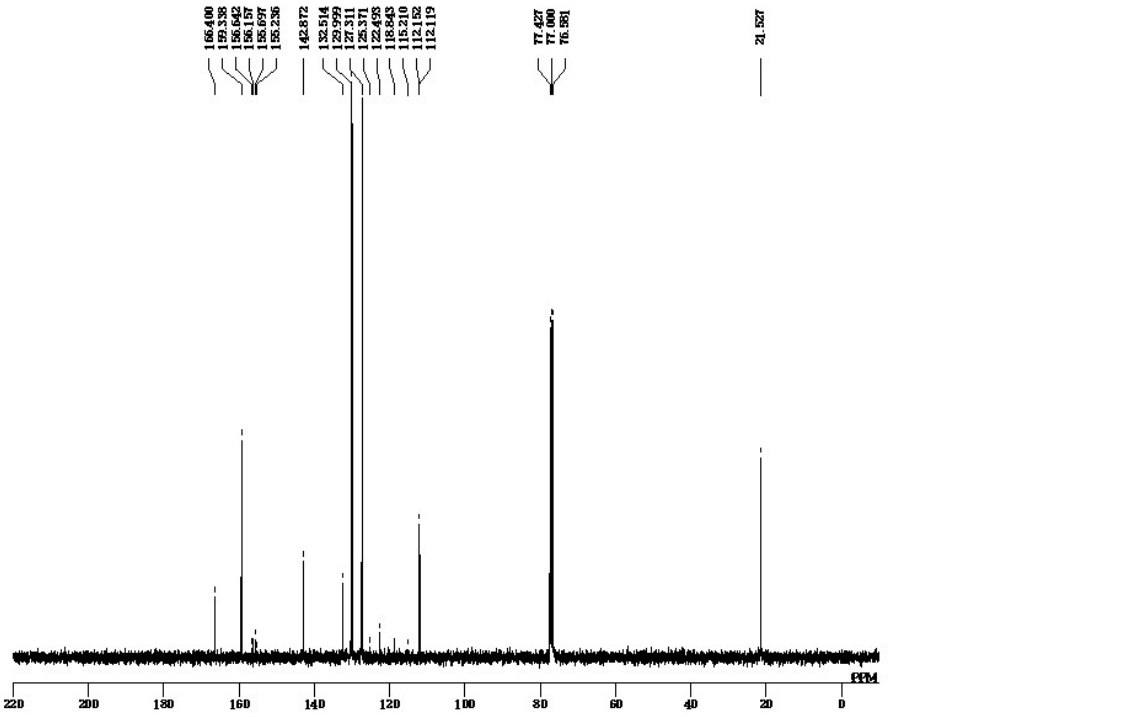
4-(4-Methoxyphenyl)-6-(trifluoromethyl)pyrimidine (6cb)



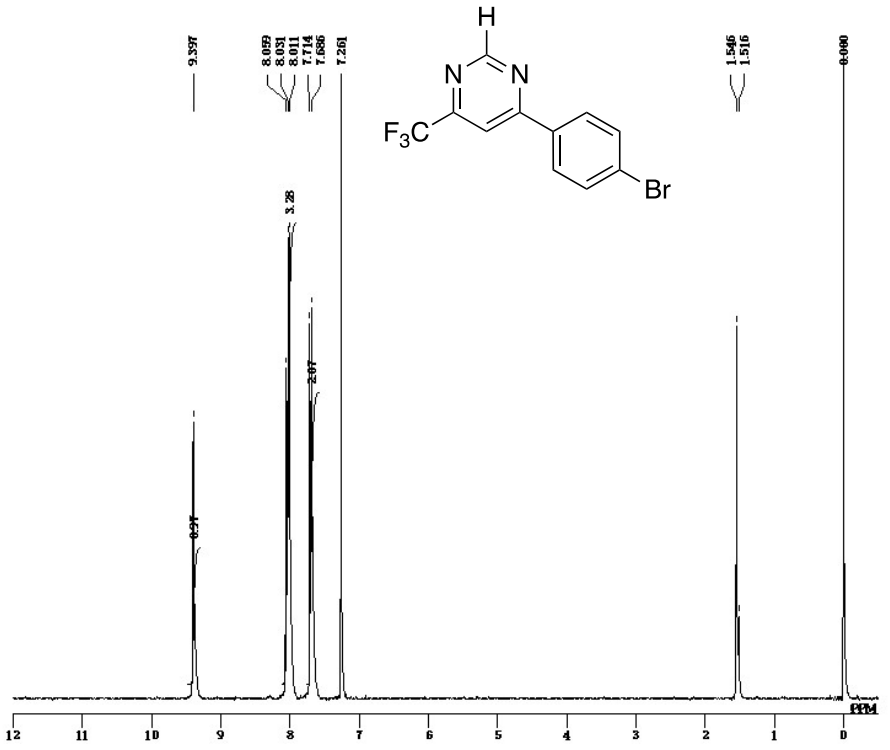


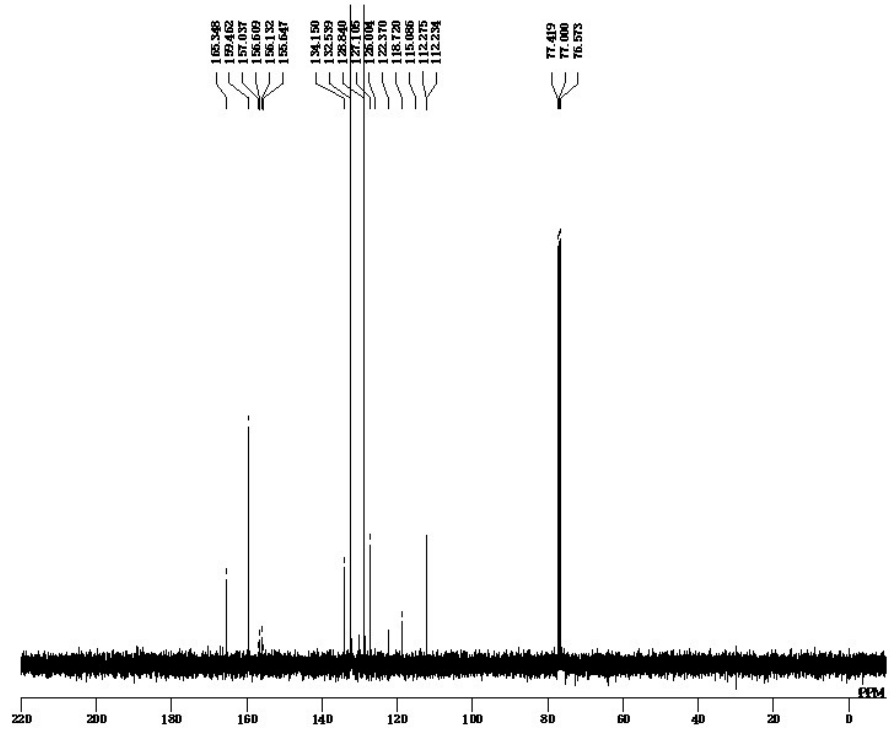
4-(4-Methylphenyl)-6-(trifluoromethyl)pyrimidine (6cc)





4-(4-Bromophenyl)-6-(trifluoromethyl)pyrimidine (6cd)





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