Electronic Supplementary Information

Chromene-triazole-pyrimidine based chemosensor therapeutics for the in vivo and in vitro detection of Fe^{3+} ions

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Table of Contents

Experimental Section

General

IR spectra were recorded on a JASCO-FT/IR-4100 Fourier transform infrared spectrometer and measured as KBr pellets. ^{1}H and ^{13}C NMR spectra were determined in DMSO with a Bruker amx 500 MHz spectrometer. The chemical shifts (δ) are given relative to tetramethylsilane (TMS) and the coupling constants (J) are reported in hertz (Hz). Electron spray ionization mass spectra were recorded with a Thermo scientific exactive mass spectrometer and on a JEOL JMS600H. . Absorption spectra of the compounds were recorded on a JASCO V-550 UV/Vis spectrophotometer and fluorescence measurements were carried out with a Jasco spectrofluorometer.

General procedure for the synthesis of chlorinated 3, 4-dihydropyrimidinone (a1-a3): A mixture of benzaldehyde (1 mmol), ethyl-4-chloroacetoacetate (1mmol), and urea (1.5 mmol) was heated at 80 °C in an oil bath. After 1 hour the reaction mixture was cooled to room temperature and poured into crushed ice. The precipitate of pyrimidinone derivatives obtained was washed with cold water. Filtered, and dried under vacuum to give the crude product in pure form. Recrystallization from hot ethanol provided the analytically pure product.

a1:ethyl6-(chloromethyl)-4-(4-chlorophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5 carboxylate: White Solid, Mp 234-237^{0}C, Yield: 85%; ^{1}H-NMR (DMSO-(d_6) 500MHz) δ_H (ppm): 7.84-7.09 (m,5H), 6.98 (s, 1H), 6.85-6.84 (d, 1H,J=7.5), 4.97 (s, 1H), 4.90 (s,1H), 4.40-4.34 (q, 2H), 1.29 (s, 1H), 1.07-1.02 (t, 3H), FT-IR(KBr)(ν_{max},cm^{-1}): 3386, 3087, 1768, 1701,1616, 1530, 1479, 1443, 1351, 1201, 1098, 906, 811, 732, 689,604; MS: m/z Calcd for $C_{14}H_{14}Cl_2N_2O_3$, [M] $^{+}$: 328.04, Found: [M] $^{+}$: 328.0

a2:ethyl6-(chloromethyl)-4-(3-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate: Brown solid, Mp 236-238^{0}C,Yield: 83%; ^{1}H-NMR (DMSO-(d_6) 500MHz) δ_H (ppm): 8.19-8.178(d,1H,J=9),7.90-7.77(d,2H),7.47-7.45(d,1H,J=8.5),7.37-7.35(d,2H,J=8.5),5.92(s,1H),5.18-5.16 (d,1H,J=7.5)3.48 (s,1H), 3.417-3.35 (q,2H),1.66-1.62 (t,3H);FTIR(KBr) (ν_{max},cm^{-1}): 3437, 3291, 1665, 1597, 1520, 1475, 1433, 1351, 1293, 1235, 1201,1137,1105,1024,1000 ,964 ,924 ; MS:m/z Calcd for $C_{14}H_{14}ClN_3O_5$, [M] $^{+}$: 339.0, Found: [M] $^{+}$: 339.0

a3:ethyl6-(chloromethyl)-4-(4-hydroxyphenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5 carboxylate:White Solid, Mp 235-237^{0}C, Yield: 85%; ^{1}H-NMR (DMSO-(d_6) 500MHz) δ_H (ppm):7.54 -7.15 (m,5H),5.37 (s,1H),5.19-5.17(d,1H,J=9.5),5.07(s,1H),4.97-4.92(d,1H),1.96(s,1H),1.81-1.755(t,3H); FT-IR(KBr)(ν_{max},cm^{-1}): 3568, 3381, 3234, 3105, 2917, 1683, 1645, 1612, 1595, 1513, 1464, 1431, 1389, 1366, 1325,1304,1281,1229,1169; MS: m/z Calcd for $C_{14}H_{15}ClN_2O_4$, [M+H^{+}]: 311.1, Found: [M+H^{+}]: 311.1

General procedure for the synthesis of azide derivatives of dihydropyrimidinones (P1-P3): Chloroderivative of dihydropyrimidinone (1 mmol), and sodium azide (1 mmol) were stirred at 0^{0}c in acetone. After completion of the reaction (6 h,TLC) the mixture was poured into ice cold water. The solid product obtained was filtered, washed with petroleum ether and ehtylacetate(4:1), and dried under vacuum to afford the dihydropyrimidinone azide.

P1:ethyl6-(azidomethyl)-4-(4-chlorophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5carboxylate: White Solid, Mp 164-166^{0}C, Yield: 80%; ^{1}H-NMR (DMSO-(d_6) 500MHz) δ_H (ppm):1.00-0.97 (t,3H),1.62 (s,1H),2.17 (s,2H),3.98-3.94 (q,2H),4.97-4.95 (d, 1H,J=11.5), 5.19 (s, 1H), 6.12 (s, 1H), 7.26 (s, 1H),7.36-

7.31 (m, 5H); FT- IR (KBr) (ν_{max}, cm^{-1}): 3421,3298,3212, 2923, 2749, 2122, 1723, 1677, 1602, 1577, 1508,1427,1302,1250,1137,1021,861,828,761,653,611,511; MS: m/z Calcd for $C_{14}H_{14}ClN_5O_3$, $[M]^+$: 335.08, Found: $[M]^+$: 335.0

P2:ethyl6-(azidomethyl)-4-(3-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5carboxylate: Yellow solid, Mp 163-165^{0}C, Yield: 82%; ^{1}H-NMR (DMSO-(d_6) 500MHz) δ_H (ppm):0.97-1.00 (t, 3H); 2.17 (s, 2H); 3.93-4.03 (m, 2H); 4.97 (s, 1H); 5.19 (s, 1H); 6.12 (s, 1H); 7.26-7.36 (m, 4H); FT-IR(KBr)ν_{max} 3383, 3090, 2982, 2931, 2113, 1698, 1652, 1530, 1476, 1446, 1350, 1303, 1096, 1018, 904, 861, 809, 761,736,691,553,479: HRMS (EI)m/z calcd for $C_{14}H_{14}N_6O_5$ $[M+Na]^+$: 369.09234, found $[M+Na]^+$: 369.09718.

P3:ethyl6-(azidomethyl)-4-(4-hydroxyphenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5carboxylate: Yellow solid, Mp 166-167^{0}C, Yield: 85%; ^{1}H-NMR (DMSO-(d_6) 500MHz) δ_H (ppm): 1.13-1.15 (t,3H);2.24-2.25 (d,H);4.01 (s,1H),4.05 (s,1H);5.22 (s,1H);5.54 (s,1H);6.82 (s,1H); 6.84 (s,1H);7.00-7.35 (m,4H);FT-IR(KBr)(ν_{max},cm^{-1}):3442,2922,2852,2057, 1638, 1529, 1418, 1350, 1212, 1157,1113,1020,873,664,553; HRMS (EI) m/z calcd for $C_{14}H_{15}N_5O_4$ $[M+Na]^+$:340.10217 , found: $[M+Na]^+$: 340.10574.

General experimental procedure for the synthesis alkynes (C1-C3): A mixture of propargylated aromatic aldehyde (160 mg, 1mmol),2-naphthol (144mg, 1 mmol), malononitrile (66mg, 1mmol), and sodium carbonate(0.106 mg, 0.01mmol) were mixed by using a mortar and pestle. The resulting solid was heated in an oven at 80^{O}C for 10 min. After cooling, the mixture was washed with hot water and the solid separated was filtered and dried. Recrystallized from hot ethanol to obtain pure product

C1:.3-amino-1-(2-(prop-2-yn-1-yloxy)phenyl)-1H-benzo[f]chromene-2-carbonitrile:Yellow solid, M.p. 110-112 ^{o}C,Yield:93%; 1H NMR (500 MHz, DMSO): δH (ppm): 3.31 (s,1H), 3.68 (s,2H),4.97 (S,1H),7.09 (d,2H, J=9Hz),7.11(S,2H),7.67-7.77(m,3H),8.00-7.90(d,1H, J=8.5Hz), 8.42(d,1H), ^{13}C NMR (DMSO-(d6), 125 MHz) *δc* (ppm):22.4, 56.4, 59.2, 78.2, 79.2, 112.9, 117.1, 117.9, 121.7, 122.8, 126.9, 128.5, 128.5, 129.8, 130.5, 130.5, 132.7, 133.8, 133.9, 156.5, 171.9, 200.8. FT- IR (KBr) (ν_{max}, cm^{-1}): 3420, 3274, 3030, 2224, 2130, 1586, 1559, 1509;EI-MS:m/z calculated for $C_{23}H_{16}N_2O_2$:352.3847 and found EI-MS: 353.37 (M+).

C2:*3-Amino-1-(4-(prop-2-yn-1-yloxy)phenyl)-1H-benzo[f]chromene-2-carbonitrile*:Yellow solid, M.p.110-113^{o}C, Yield:96%, ^{1}H-NMR (DMSO-(d_6) 500MHz) δ_H (ppm): 3.31 (s,1H), 3.68 (s,2H), 4.978 (S,1H), 7.09(d,2H,J=9Hz),7.11(S,2H),7.67-7.77(m,3H),8.00-7.90(d,1H, J=8.5Hz), 8.42(d,1H). FT- IR (KBr) (ν_{max}, cm^{-1}): 3420, 3274, 3030, 2224, 2130, 1586, 1559, 1509; EI-MS: m/z calculated for $C_{23}H_{16}N_2O_2$:352.3847 and found EI-MS: 353.37 (M+).

C3*:3-Amino-1-(3-methoxy-4-(prop-2-yn-1-yloxy)phenyl)-1H-benzo[f]chromene-2carbonitrile:* Yellow solid, M.p.111-114^{o}C, Yield: 98%; ^{1}H-NMR (DMSO-(d_6) 500MHz) δ_H (ppm):3.33 (s, 1H), 3.67(s, 1H), 3.82(s, 3H) 4.98 (s, 1H), 7.08(d, 2H, J=8.5Hz), 7.13 (s, 2H), 7.20 (d, 2H J=7.5Hz),7.37(d, 1H, J=8Hz),7.67-7.77(m, 3H), 8.00 (d, 1H, J=8Hz), 8.022(d, 1H,J=8Hz). ^{13}C NMR (DMSO-(d6), 125 MHz) *δc* (ppm):27.9, 54.3, 56.2, 59.3, 78.2, 79.2, 112.9, 117.1, 117.9, 121.8, 122.8, 122.8, 128.7, 128.8, 128.9, 129.8, 129.8, 130.9, 130.9, 132.7, 134.8, 139.8, 157.4, 172.9. FT- IR (KBr) (ν_{max}, cm^{-1}): 3363, 3279, 2223, 2129, 1629, 1598, 1417; EI- MS: m/z calculated for $C_{24}H_{18}N_2O_3$:382.4106 and found EI-MS: 382.32 (M+).

General procedure for the synthesis of 1, 4-disubstituted chromene pyrimidinone diad via Cu (I) catalyzed Huisgen cycloaddition(CP1-CP6): An equimolar mixture of azide and alkyne was mixed with 0. 2 equiv of CuSO4 and 0.4 equiv of sodium ascorbate in a mixed solvent system containing tert-butanol, water, and

DMSO (4:2:1) at room temperature. After 12 h, the reaction mixture was diluted with cold water, filtered, and washed with water to afford the click product in solid form.

CP1:ethyl6-((4-((4-(3-amino-2-cyano-1H-benzo[f]chromen-1-yl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-4-(4-hydroxyphenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate: Brown solid, Mp 145-147^{0}C,Yield 85%;1H NMR (500 MHz, DMSO): δH (ppm): 8.57 (s, 2H), 7.85-7.22 (m,14H),7.58 (s,1H),6.21(s,2H),5.96(s,1H),5.52(s,1H),5.23-5.11(d,1H),5.02(s,2H),4.30(s,2H),4.15-4.09 (q,2H),1.35-1.31(t,3H);13CNMR(DMSO-(d6),500MHz): 35.80, 39.50, 39.67, 39.83, 40.00, 40.17, 40.26, 40.33, 40.42,40.50,40.59,55.79,71.25,79.45,80.32,81.00,104.50,114.73,115.79,116.21,116.42,123.78,124.43,128.15,131.83,132.15,133.64,152.76,158.16,165.13,171.23;FT-IR(KBr)(ν_{max},cm^{-1}:3383, 2928, 2227, 1697, 1552, 1504, 1512, 1487, 1457, 1369,1307, 1227, 1175, 1097, 1030, 756; HRMS m/z calcd for $C_{37}H_{31}N_7O_6$ $[M]^+$:669.23358,found: $[M]^+$: 669.23352 .

CP2:ethyl6-((4-((4-(3-amino-2-cyano-1H-benzo[f]chromen-1-yl)-2-methoxyphenoxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-4-(4-hydroxyphenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate: Brown solid, Yield 87%, M.p 148-151^{0}C; 1H NMR (500 MHz, DMSO): δH(ppm): 8.23(s,2H), 7.91-6.94 (m,13H),7.59(s,1H),5.69(s,1H),5.50(s,1H),5.35(s,1H),4.98 (s,1H),4.77-4.71 (q,2H), 3.76 (s,3H),1.34-1.32 (t,3H);13CNMR(DMSO-(d6),500MHz): 34.05, 39.51, 39.67, 39.84, 40.01, 40.17, 40.27, 40.34, 40.43, 40.51,56.53,57.13,68.05,78.25,79.31,103.70,113.64,116.93,121.73,122.94,125.01,128.87,130.27,131.62,133.13,152.60,154.53,156.08,165.01,173.03; FT-IR(KBr)(ν_{max},cm^{-1}):3403, 2920, 2223, 1696, 1585, 1510, 1451, 1425, 1375, 1341,1274, 1145,1097,1015,804,624; HRMS m/z calcd for $C_{38}H_{33}N_7O_7$ $[M]^+$: 669.24415 , found: $[M]^+$: 669.24405.

CP3:ethyl 6-((4-((4-(3-amino-2-cyano-1H-benzo[f]chromen-1-yl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-4-(3-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate: Yellow solid, M.p 144-147^{0}C, Yield 86%.1H NMR (500 MHz, DMSO) δH (ppm): 8.53(s, 2H),7.83-7.19 (m,13H),7.53 (s,1H),6.19 (s,1H),5.90 (s,1H),5.16-5.11 (d,1H),4.98 (s,2H),4.25 (s,2H),4.13-4.07 (q,2H),1.33-1.29 (s,3H) ;13CNMR(DMSO-(d6),500MHz): 27.78, 36.29, 39.50, 39.66, 39.83, 40.00, 40.17, 40.26, 40.33, 40.42, 40.50,59.13,63.16,69.19,71.13,76.94,78.94,101.64,104.13,108.53,110.04,113.35,116.75,122.09,122.80,123.51,126.30,136.64,137.04,149.63,151.51,155.20,157.07,158.62,159.63,174.59;FT-IR(KBr)(ν_{max},cm^{-1}):3083, 3031, 2923, 2224, 1745, 1683, 1601, 1587, 1559,1509,1454,1429,1375, 1318, 1262, 1238, 1186, 1158, 1126, 1071,1009; HRMS m/z calcd for $C_{37}H_{30}N_8O_7$[M+Na]$^+$:725.22375,found: [M+Na]$^+$: 725.23396

CP4:ethyl6-((4-((2-(3-amino-2-cyano-1H-benzo[f]chromen-1-yl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-4-(3-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate: Brown solid, M.p 155-157^{0}C, Yield 83%.1H NMR (500 MHz, DMSO) δH (ppm): 8.08 (s,2H), 7.69 (s, 1H), 7.59-7.05 (m,14H),6.28 (s,1H),6.01 (s,1H),5.18-5.14 (d,1H), 5.08-4.95 (d, 2H), 4.83-4.75 (d,1H), 1.39-1.35 (t,3H); 13C NMR (DMSO-(d6), 500 MHz): 23.07, 39.51, 39.68, 39.84, 40.01, 40.18, 40.34, 40.51, 44.76, 48.85, 64.81,66.12,67.62,69.18,84.88,103.36,106.94,111.73,113.14,128.45,128.62,129.04,129.19,131.80,133.74, 136.98,142.55,156.80,158.93,160.18,168.89,182.39;FT-IR(KBr)(ν_{max},cm^{-1}): 3376, 2923, 2853, 2227, 1747,1675,1583,1562,1486,1456,1393,1365, 1224, 1108, 1016, 849, 810, 754, 727, 614,570;HRMS m/z calcd for $C_{37}H_{30}N_8O_7$[M]$^+$: 698.22375 , found: [M]$^+$: 698.02643

CP5:ethyl 6-((4-((2-(3-amino-2-cyano-1H-benzo[f]chromen-1-yl)phenoxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-4-(4-chlorophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate: pale yellow solid, M.p

143-145^{0}C,Yield 84%.1H NMR (500 MHz, DMSO) δH (ppm): 7.99 (s, 2H), 7.97-7.26 (m,13H),7.41 (s,1H),5.83-5.82 (d,1H),5.68-5.63 (d,1H),4.13-4.07 (q,2H), 1.41-1.37 (t,3H); 13C NMR (DMSO-(d6), 500 MHz): 23.10, 39.52, 39.69, 39.86, 40.02, 40.19, 40.28, 40.36, 40.52, 48.78, 48.87, 56.60, 78.61, 79.92,111.44,114.62,116.59,118.77,124.76,125.48,131.24,135.02,137.04,145.86,147.78,149.56,155.02,158.96,168.69,195.29; FT-IR(KBr)(ν_{max},cm^{-1}): 3353, 2924, 2205, 1654, 1530, 1457, 1350, 1225, 1158, 1100, 1028,755;HRMS m/z calcd for $C_{37}H_{30}ClN_7O_5$[M+Na]$^+$: 710.19969 , found: [M+Na]$^+$: 710.19903

CP6:ethyl6-((4-((4-(3-amino-2-cyano-1H-benzo[f]chromen-1-yl)-2-methoxyphenoxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-4-(4-chlorophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate:Brown solid, M.p 141-144^{0}C, Yield 83%;1H NMR (500 MHz, DMSO)δH(ppm):8.19 (s,2H),7.79-7.36 (m,13H),7.49 (s,1H),5.93 (s,1H),5.68 (s,1H),4.81-4.79 (d,2H),4.27-4.25 (d,2H), 3.11-3.07 (t,3H), 1.41-1.38 (t,3H); 13C NMR (DMSO-(d6), 500 MHz): 36.50, 39.50, 39.67, 39.84, 40.00, 40.17, .26, 40.34, 40.43, 40.50, 40.59,71.29,71.47,82.19,83.07,111.69,118.04,121.60,123.27,124.21,125.17,137.06,140.59,145.42,147.02, 155.84,157.76,159.58,165.02,168.92,178.89;FT-IR(KBr)(ν_{max},cm^{-1}):3403, 2920.18, 2223, 1696, 1585, 1510, 1451, 1425, 1375, 1341, 1274, 1145,1097,1015,804,624;HRMS m/z calcd for $C_{38}H_{32}ClN_7O_6$ [M]$^+$: 717.21026 , found: [M]$^+$: 717.21045

Preparation of stock solutions for the measurement

The stock solution of probe CP1 (100 mL of 1.0×10^{-4} M) was prepared in DMSO. Stock solutions of different ions in 0.1mM concentration were prepared in distilled water from their respective salts. From the above stock solutions, 1 equivalent (0.8 ml) of each of the ions were added to 2.5ml of probe solution taken in the cuvette. After mixing, absorbance and fluorescence were measured using a UV-Visible spectrophotometer and fluorescent spectrometer at room temperature respectively.

Analysis of Fe3+ in normal drinking water and distilled water

Stock solutions of Fe^{3+} were prepared in distilled water and normal drinking water at .01mM, .02mM and .03mM concentrations. Calculated amounts of stock solutions of Fe^{3+} and sample solutions (0.01mM) were added to a vial containing different concentrations of normal water and distilled water.

Calculation of the Fluorescence Quantum Yield, Limit of detection (LOD) and Association constant

The fluorescence quantum yield was determined using quinine sulfate (0.54) as standard and was calculated using equation $\Phi_f = \Phi_f^R F_S A_R \eta_S^2 / F_R A_S \eta_R^2$

Where F_S and F_R are the integrated fluorescence intensities of the sample and reference, A_S and A_R are the absorbance of the sample and reference at the excitation wavelength, and η_S and η_R are the refractive indexes of the solvents used for the sample and reference.

The limit of detection (LOD) was calculated from the fluorescence spectra. It was calculated using the plots of concentration versus fluorescence intensity using the equation LOD=3σ/K, where σ stands for the standard deviation and K stands for the slope of the graph.

Association constant, Ka was calculated using the equation 1/(F-F0)=1/[Kass(Fmax-F0)] x 1/[ion]+1/(Fmax-F0), where F= fluorescence intensity after the addition of metal ions,F0= fluorescence

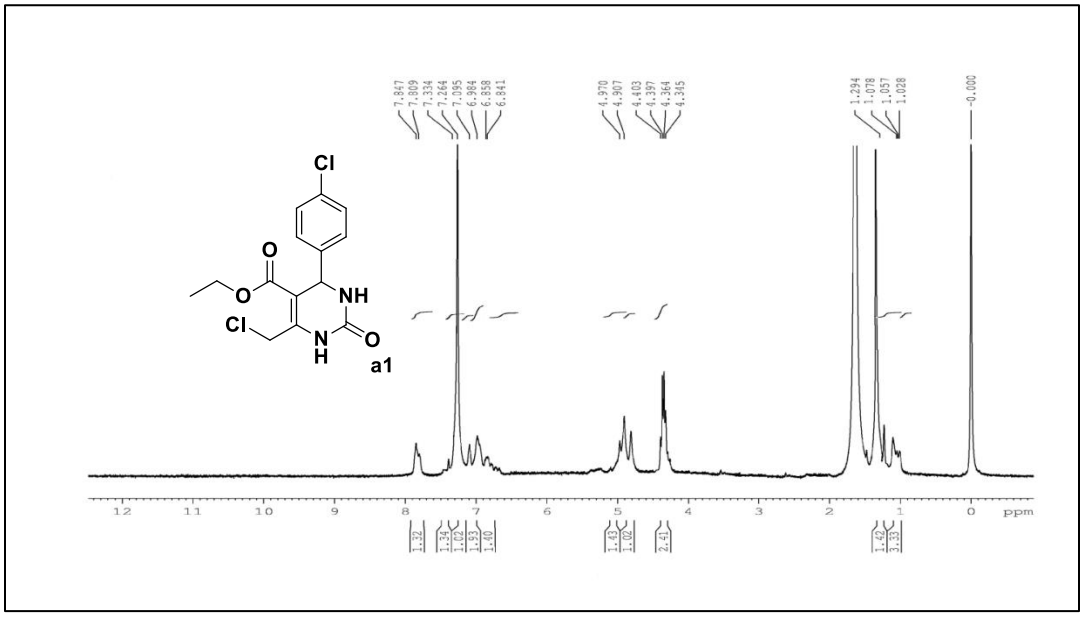
intensity before the addition of metal ions, and Fmax=maximum fluorescence intensity observed after the addition of metal ions.

Molecular docking to find the binding affinities with CDK2

Docking studies were carried out using Auto Dock Vina 1.1.2. The pdb structure of the protein was recovered from the Brookhaven protein database (http://www.rcsb.org). Water molecules were removed in the first step and then have removed the original inhibitors from the protein structure. The synthesized molecules were optimized through the B3LYP/6-31G basis set using the Gaussian 09 program and were changed to pdbqt coordinates by Autodock Tools, version 1.5.4. After deleting the water molecules, polar hydrogens were added. The docking sites were assigned by making 1Å spacing between grid points by the Auto grid. The center of the grid box was placed at the center of donepezil with coordinates x = 23.903, y = 29.002, z = 25.954, and with exhaustiveness 8. The dimensions of the active site box were set at 24 × 22 × 18 Å. Then these parameters were noted into a conf file split out file using vinasplit and the docking interaction was scanned using Autodock tools.

In vitro cytotoxicity against human cervical cancer cell line HeLa

Hela cells were procured from National Centre for Cell Science (Pune, India). The cells were maintained in Dulbecco's Modified Eagles medium supplemented with 10% FBS, 2 mM l-glutamine, and Earle's BSS adjusted to contain 1.5 g/L Na bicarbonate, 0.1 mM nonessential amino acids, and 1.0 mM of Na pyruvate in a humidified atmosphere containing 5% CO_2 at 37 $^{\circ}$C. The media were changed every two days, and the cells were passaged by trypsinization before the confluence. Cell viability was determined by MTT assay. Cytotoxicity of different sized compounds in the log phase was seeded in 96-well plates at a concentration of $1.0x10^4$ cells/well and incubated overnight at 37 ^{0}C in a 5% CO_2 humidified environment. The cells were then treated with different concentrations of the samples such as 10, 20, 30, 40, 50, 60, 70, 80, 90, and 100 µg/mL (dissolved with RPMI medium 1640), respectively. Controls were also cultivated under the same conditions without the addition of samples. The treated cells were incubated for 24 h for cytotoxicity analysis. The cells were then subjected to MTT assay. The stock concentration (5 mg/mL) of MTT-(3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, a yellow tetrazole)was prepared and 100 µL of MTT was added in each sample treated wells and incubated for 4 h. Purple color formazone crystals were observed and these crystals were dissolved with 100 µL of dimethyl sulphoxide (DMSO) and read at 620 nm in a multi well ELISA plate reader (Thermo, Multiskan). The dose-dependent cytotoxicity was observed when the samples treated Hela cells. Fifty percentage of cell death, which determines the inhibitory concentration (IC50) value of samples against Hela cells in 48 h. To study the morphological changes, Hela cells were grown (1×10^5 cells/coverslip) and incubated with samples at their IC50 concentrations, and then they were fixed in a mixture of methanol and acetic acid (3:1, v/v). The coverslips were gently mounted on glass slides for the morphometric analysis. Morphological changes of these cells were analyzed under a Nikon (Japan) bright-field inverted light microscope at 40 magnifications.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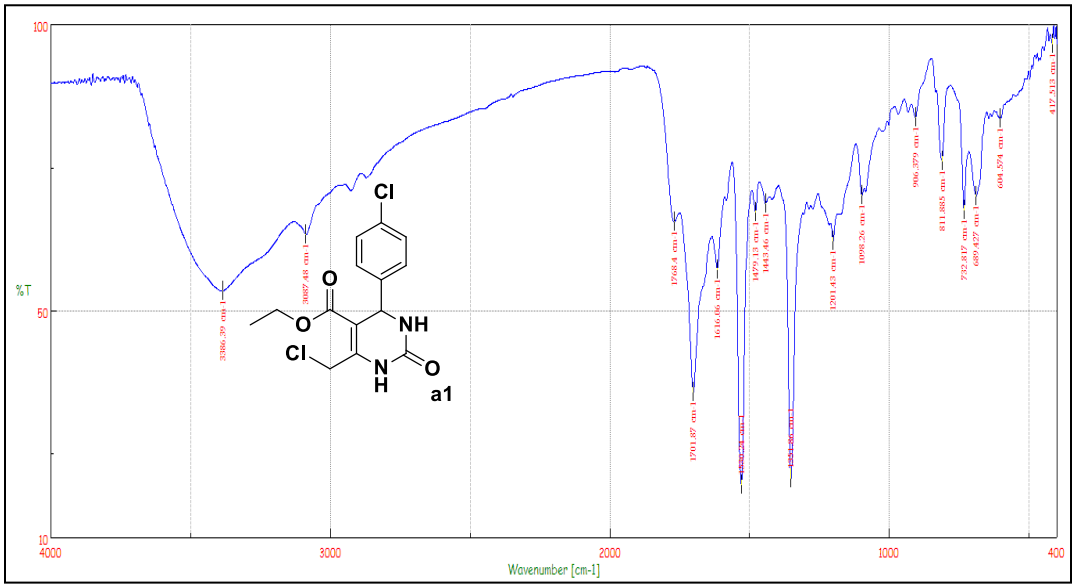
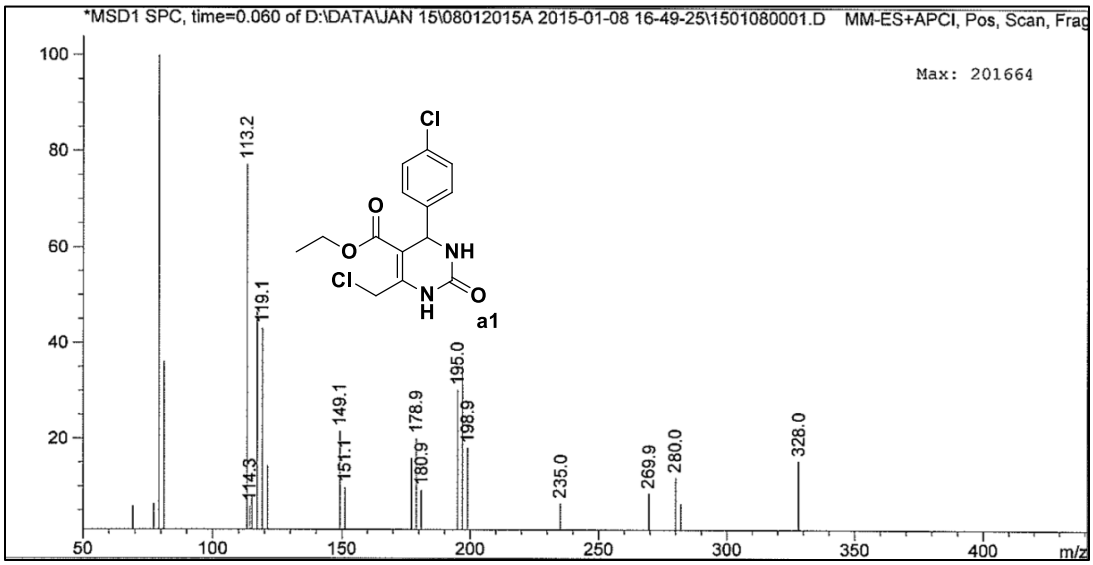
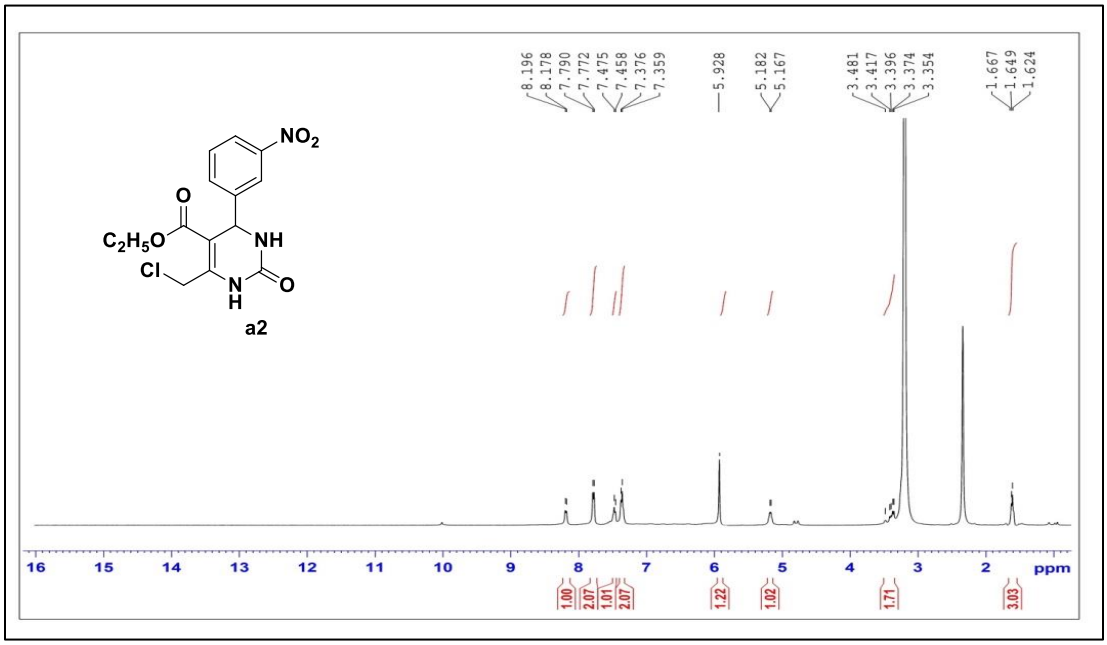
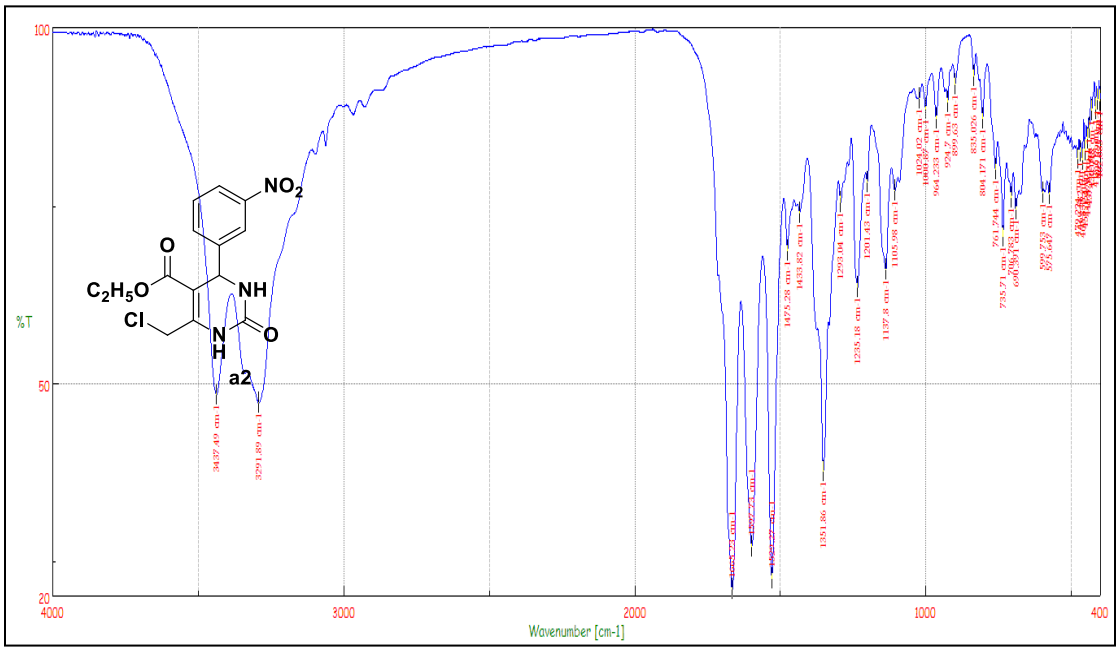
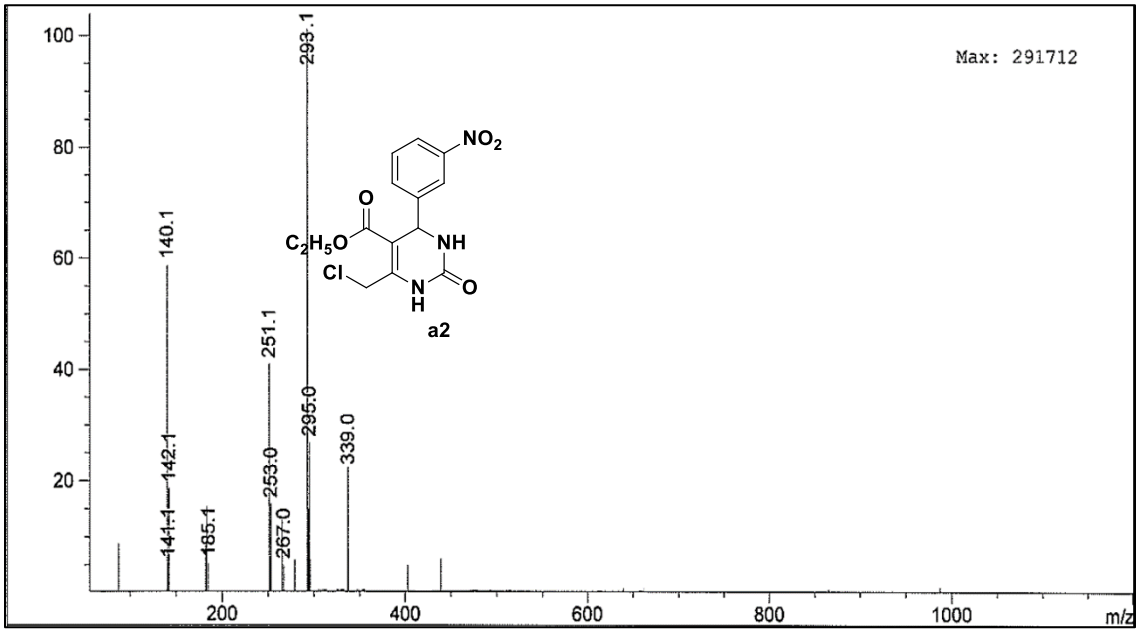
1.42
3.33

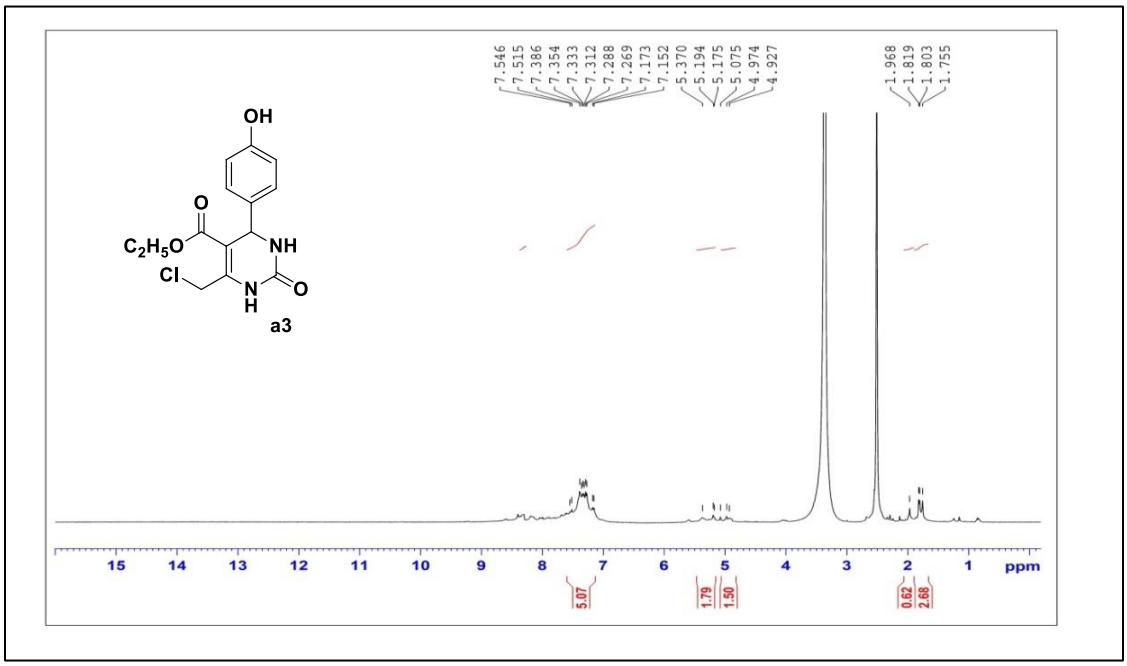

100
%T
50
10
4000
3000
2000
1000
400
Wavenumber [cm-1]
3386.39 cm-1
3087.48 cm-1
1768.4 cm-1
1701.87 cm-1
1616.06 cm-1
1479.13 cm-1
1443.46 cm-1
1291.43 cm-1
1098.26 cm-1
986.379 cm-1
831.885 cm-1
732.817 cm-1
689.427 cm-1
604.574 cm-1
417.513 cm-1
Cl
O
O
NH
Cl
N
H
O
a1

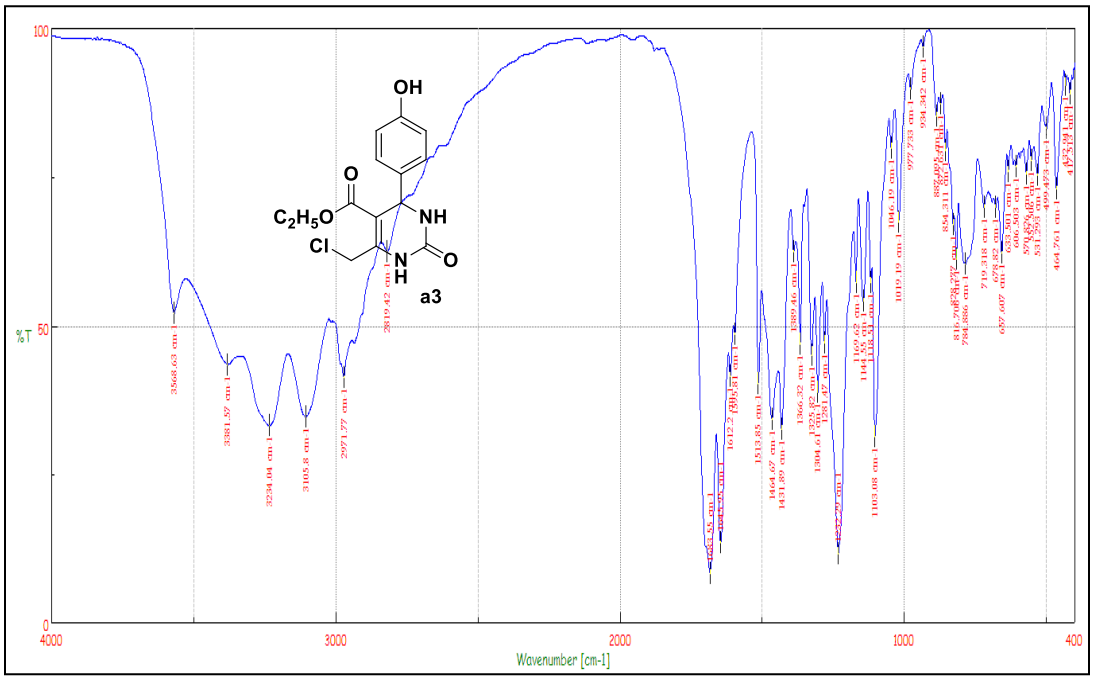

*MSD1 SPC, time=0.060 of D:\DATA\JAN 15\08012015A 2015-01-08 16-49-25\1501080001.D MM-ES+APCI, Pos, Scan, Frag
Max: 201664
113.2
119.1
114.3
149.1
151.1
178.9
180.9
195.0
198.9
235.0
269.9
280.0
328.0
m/z
a1

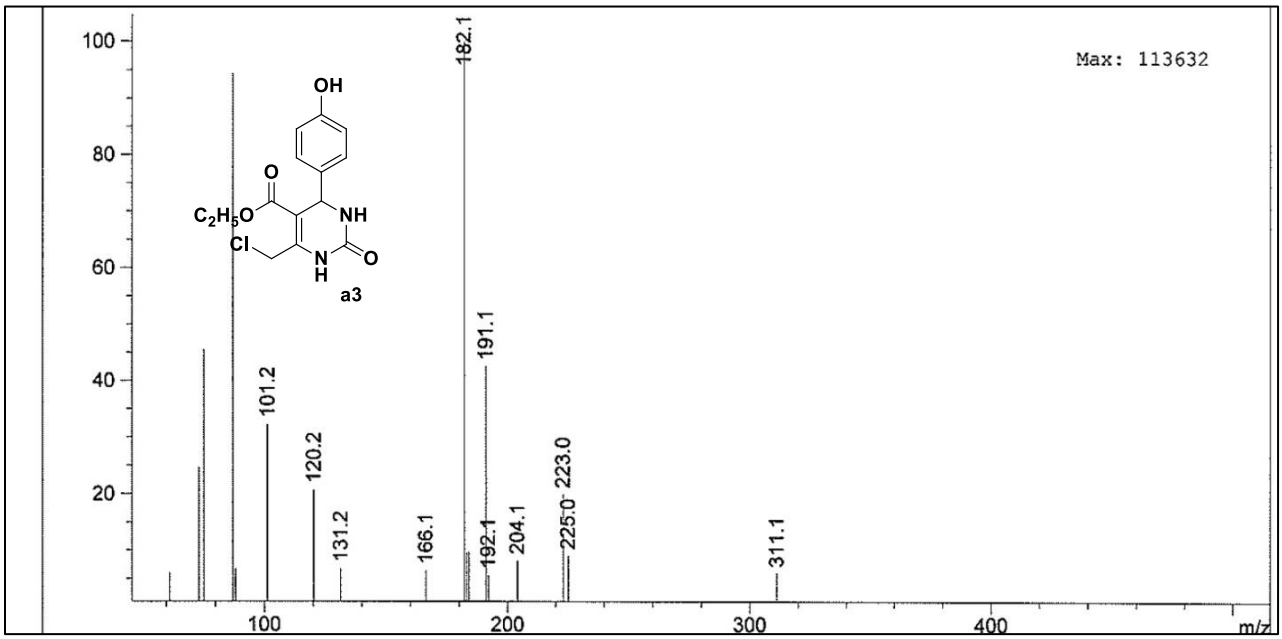

8.196
8.178
7.790
7.772
7.475
7.458
7.376
7.359
5.928
5.182
5.167
3.481
3.417
3.396
3.374
3.354
1.667
1.649
1.624
ppm
a2

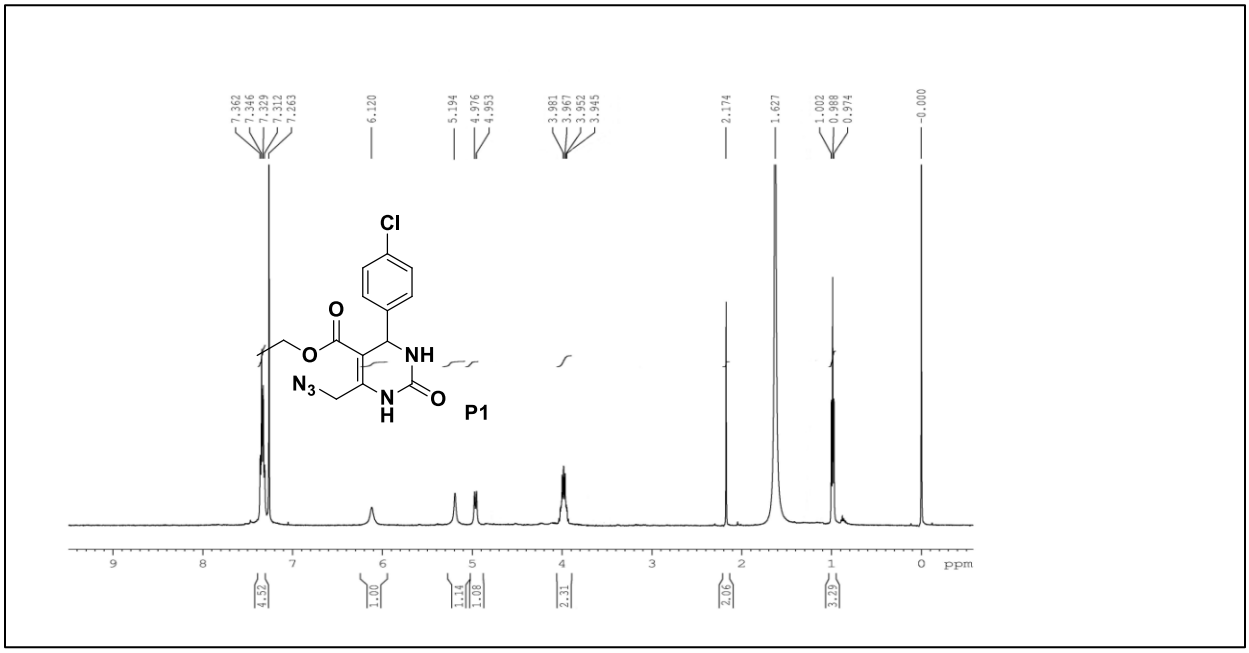

100
50
20
%T
4000
3000
2000
1000
400
Wavenumber [cm-1]
NO2
O
C2H5O
NH
Cl
N
H
O
a2
3437.49 cm-1
3291.89 cm-1
1475.28 cm-1
1433.82 cm-1
1351.86 cm-1
1293.04 cm-1
1201.43 cm-1
1235.18 cm-1
1137.8 cm-1
1105.98 cm-1
964.233 cm-1
924.7 cm-1
894.171 cm-1
761.744 cm-1
735.71 cm-1
690.396 cm-1
575.649 cm-1

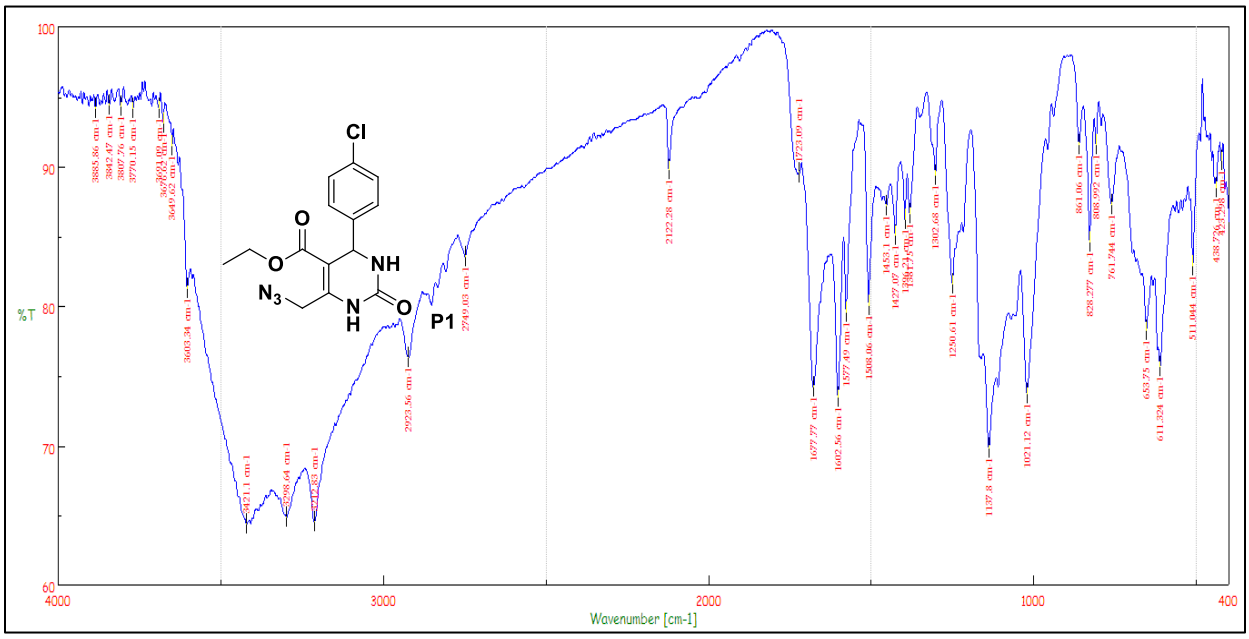

Max: 291712
100
80
60
40
20
200
400
600
800
1000
m/z
293.1
140.1
251.1
295.0
339.0
142.1
253.0
141.1
185.1
267.0
NO2
O
C2H5O
NH
Cl
N
H
O
a2

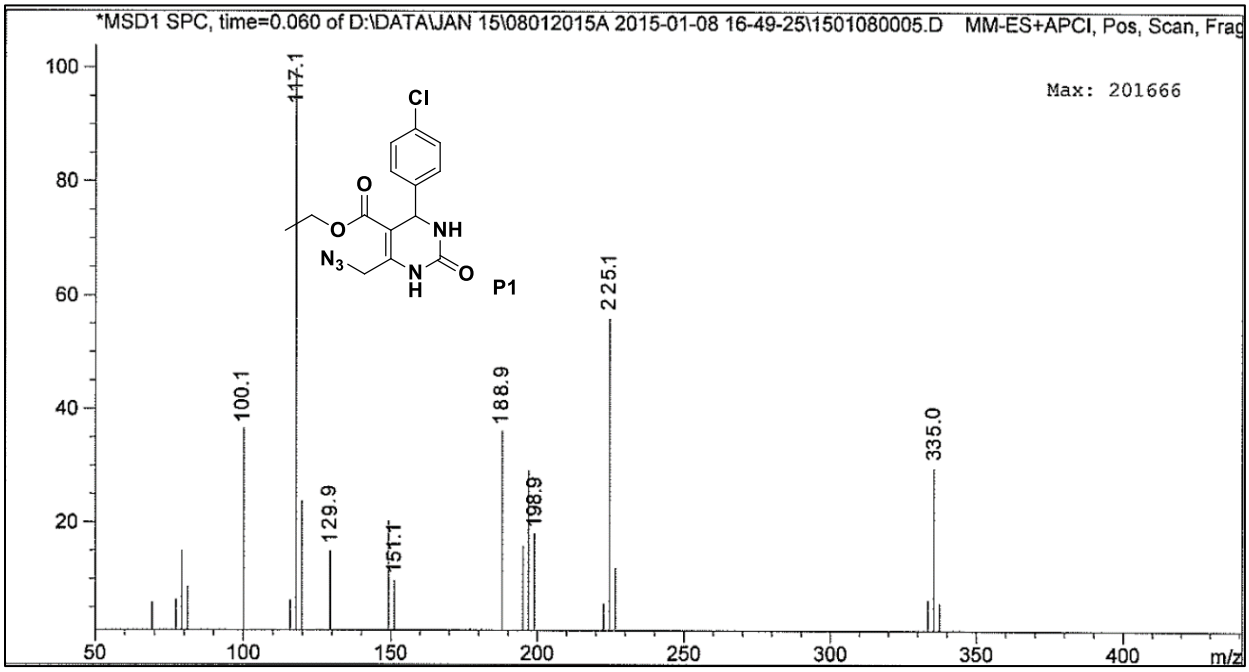

7.546
7.515
7.386
7.354
7.333
7.312
7.288
7.269
7.173
7.152
5.370
5.194
5.175
5.075
4.974
4.927
1.968
1.819
1.803
1.755
OH
O
C_2H_5O
NH
Cl
N
H
O
a3
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
5.07
1.79
1.50
0.62
2.68

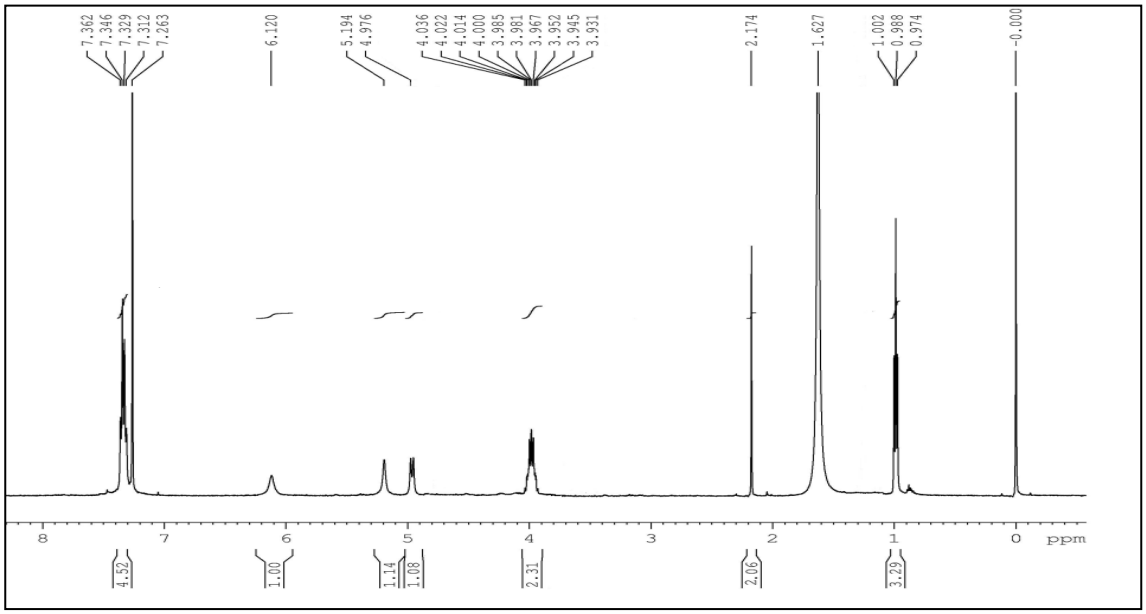

100
%T
50
0
4000
3000
2000
1000
400
Wavenumber [cm-1]
OH
O
C_2H_5O
NH
Cl
N
H
O
a3
3568.63 cm-1
3381.57 cm-1
3234.04 cm-1
3105.8 cm-1
2971.77 cm-1
2819.42 cm-1
1612.2 cm-1
1533.85 cm-1
1464.67 cm-1
1431.89 cm-1
1389.46 cm-1
1366.32 cm-1
1325.82 cm-1
1304.61 cm-1
1169.62 cm-1
1144.55 cm-1
1103.08 cm-1
1046.19 cm-1
1019.19 cm-1
977.753 cm-1
934.342 cm-1
719.318 cm-1
678.82 cm-1
657.607 cm-1
633.501 cm-1
606.503 cm-1
499.473 cm-1
464.761 cm-1

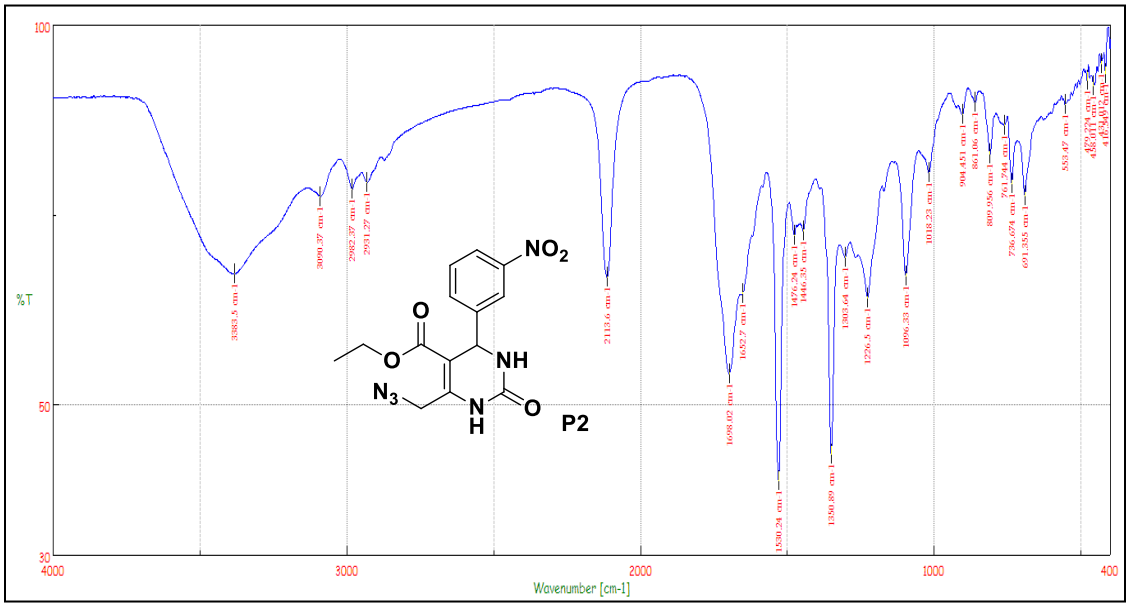

Max: 113632
182.1
191.1
101.2
120.2
131.2
166.1
192.1
204.1
225.0
223.0
311.1
OH
O
C_2H_5O
NH
Cl
N
H
O
a3
100
80
60
40
20
100
200
300
400
m/z

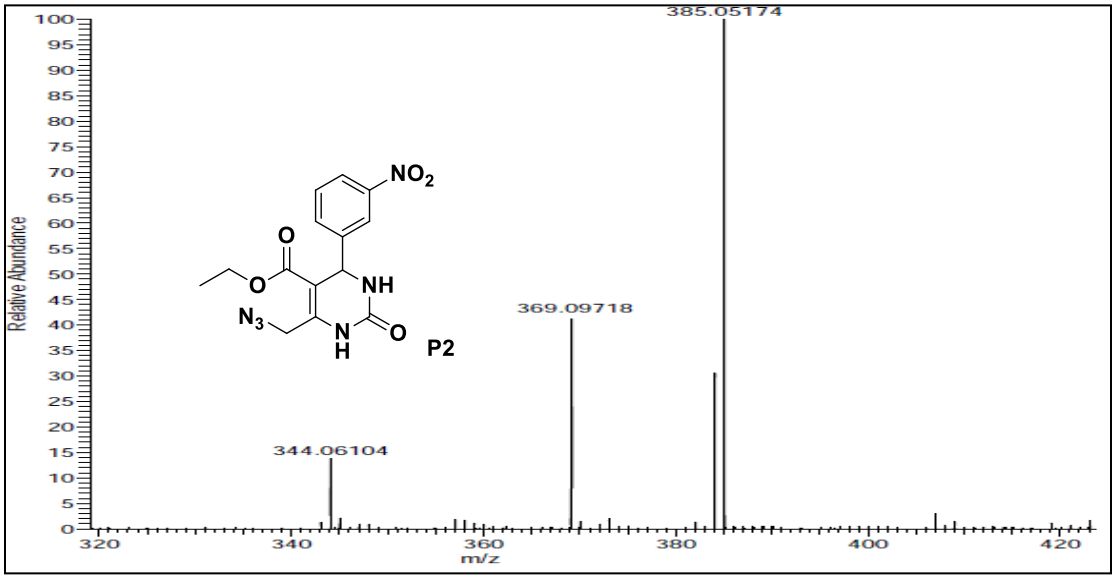

7.362
7.346
7.329
7.312
7.263
6.120
5.194
4.976
4.953
3.981
3.967
3.952
3.945
2.174
1.627
1.002
0.988
0.974
-0.000
Cl
O
O
NH
N_3
N
H
O
P1
9
8
7
6
5
4
3
2
1
0
ppm
4.52
1.00
1.14
1.08
2.31
2.06
3.29

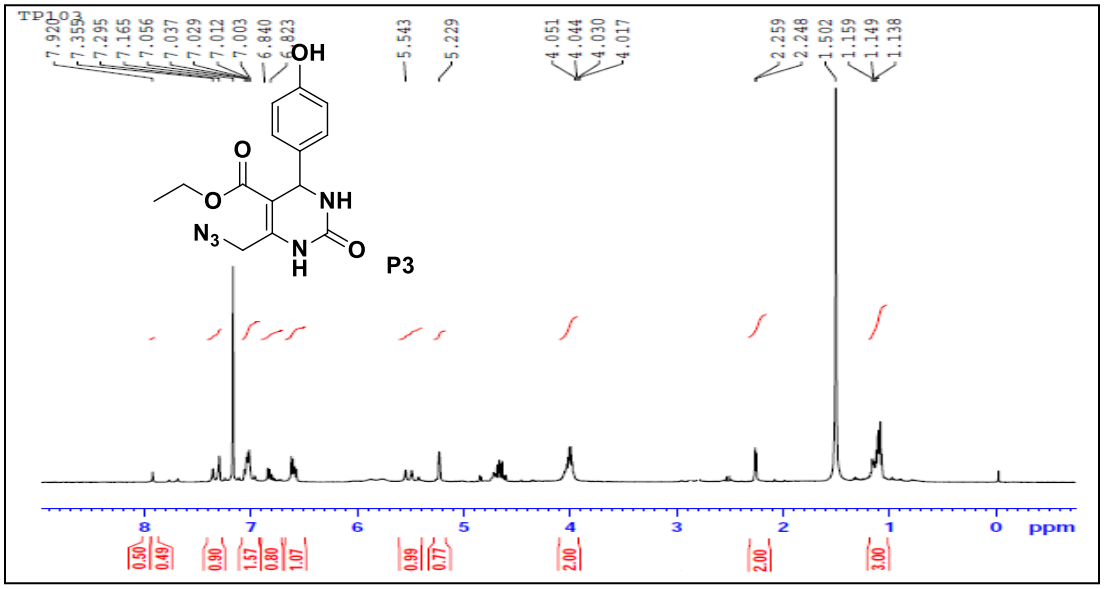

100
90
80
70
60
%T
4000
3000
2000
1000
400
Wavenumber [cm-1]
Cl
O
O
NH
N3
N
H
O
P1

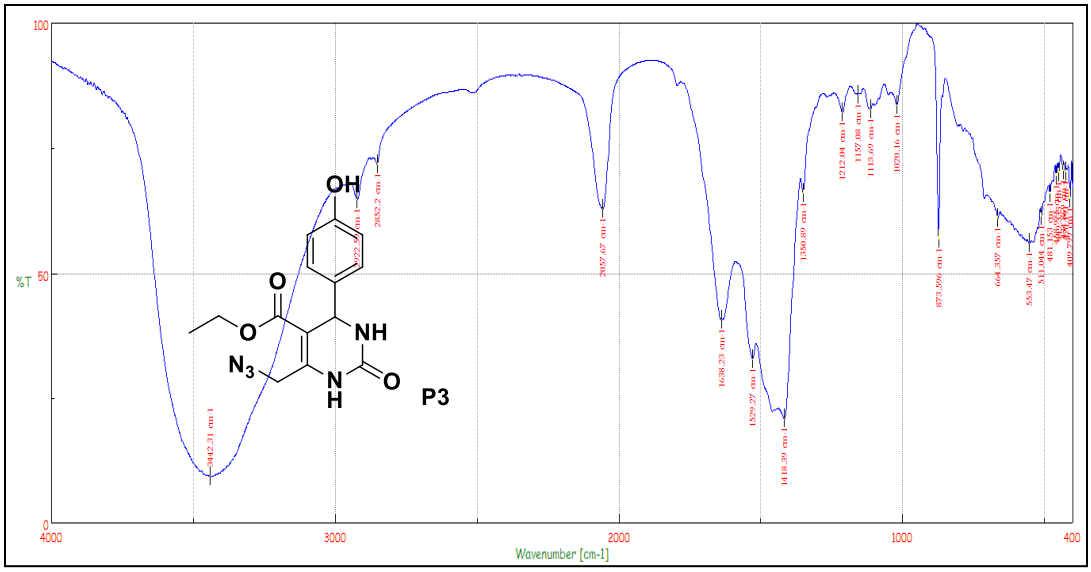

*MSD1 SPC, time=0.060 of D:\DATA\JAN 15\08012015A 2015-01-08 16-49-25\1501080005.D MM-ES+APCI, Pos, Scan, Frag
Max: 201666
100
80
60
40
20
147.1
100.1
129.9
151.1
188.9
198.9
225.1
335.0
50
100
150
200
250
300
350
400
m/z
Cl
O
O
NH
N3
N
H
O
P1

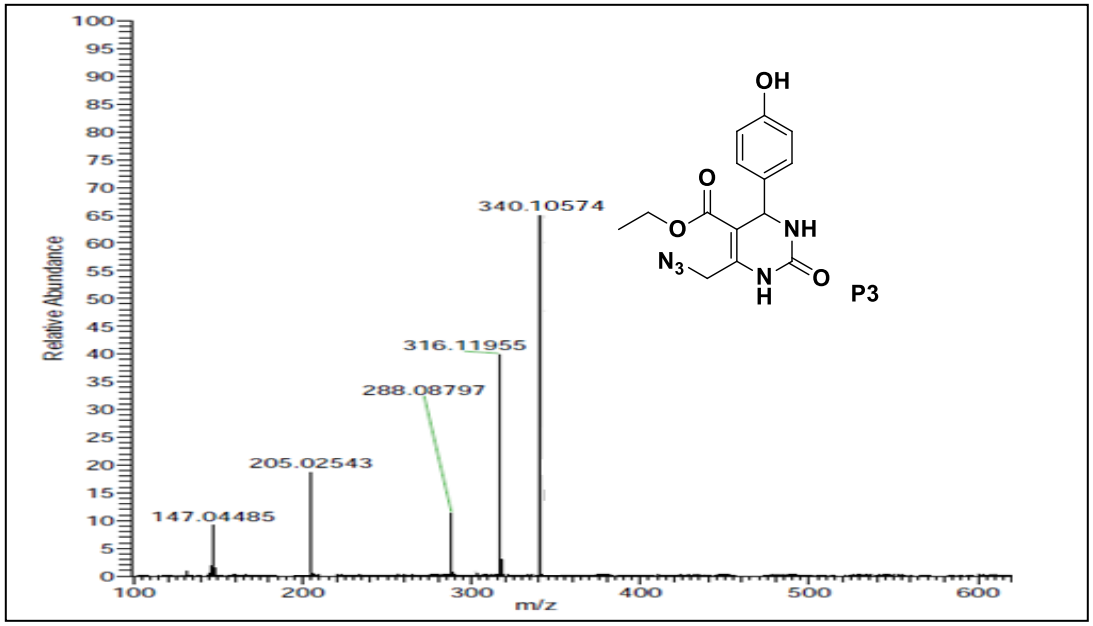

7.362
7.346
7.329
7.312
7.263
6.120
5.194
4.976
4.036
4.022
4.014
4.000
3.985
3.981
3.967
3.952
3.945
3.931
2.174
1.627
1.002
0.988
0.974
-0.000
8
7
6
5
4
3
2
1
0
ppm
4.52
1.00
1.14
1.08
2.31
2.06
3.29

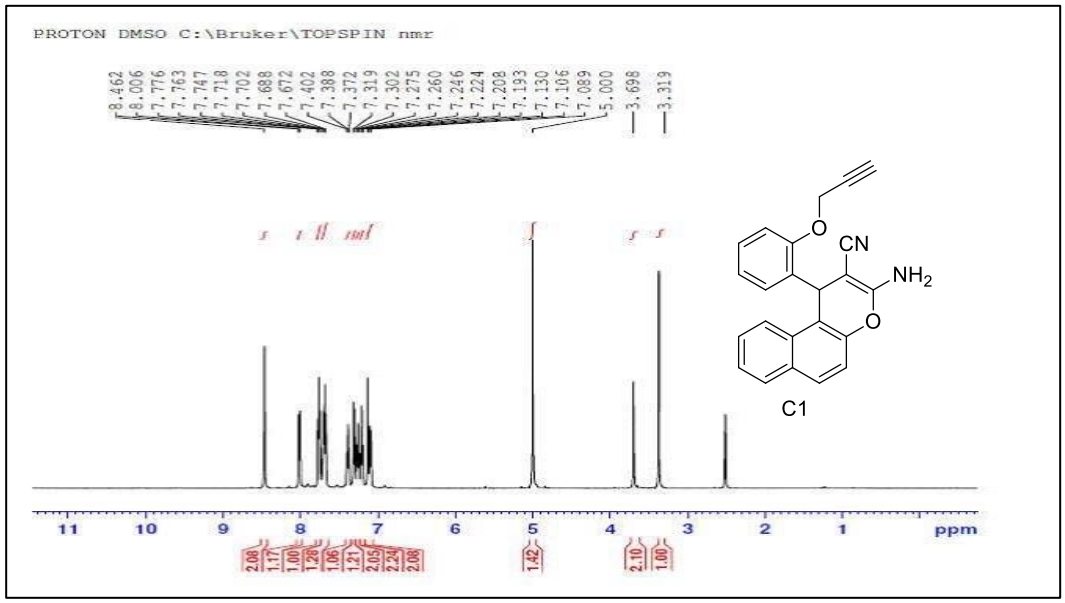

100
%T
50
30
4000
3000
2000
1000
400
Wavenumber [cm-1]
3383.5 cm-1
3090.37 cm-1
2982.39 cm-1
2931.27 cm-1
2113.6 cm-1
1698.92 cm-1
1652.7 cm-1
1530.24 cm-1
1476.24 cm-1
1446.53 cm-1
1350.89 cm-1
1303.64 cm-1
1256.5 cm-1
1096.33 cm-1
1038.23 cm-1
994.451 cm-1
861.06 cm-1
809.956 cm-1
761.748 cm-1
736.674 cm-1
691.355 cm-1
553.47 cm-1
NO2
O
O
NH
N3
N
H
O
P2

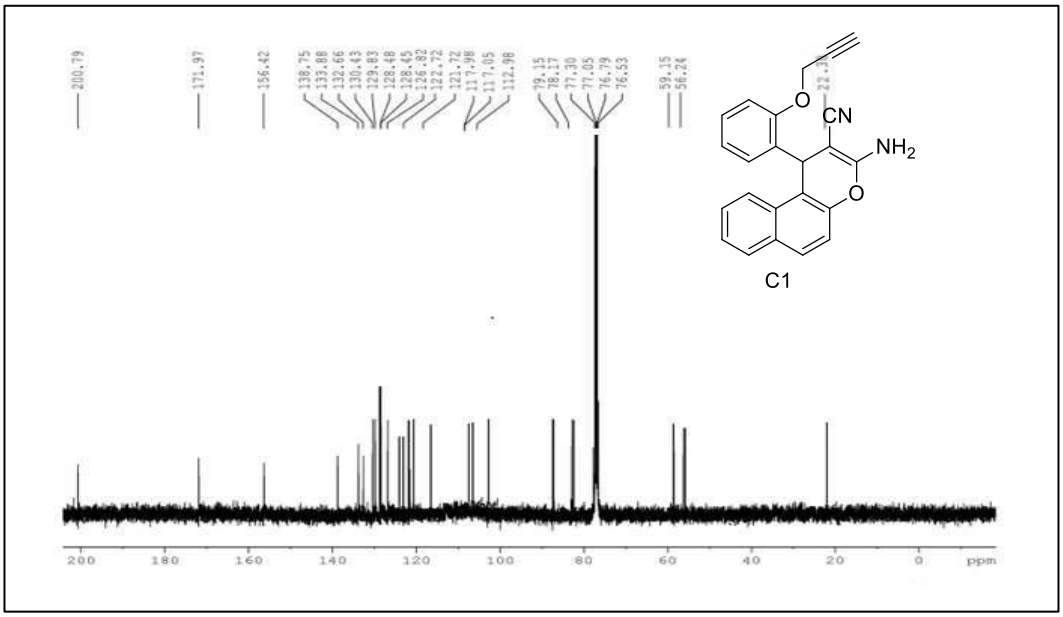

385.05174
369.09718
344.06104
Relative Abundance
m/z
P2

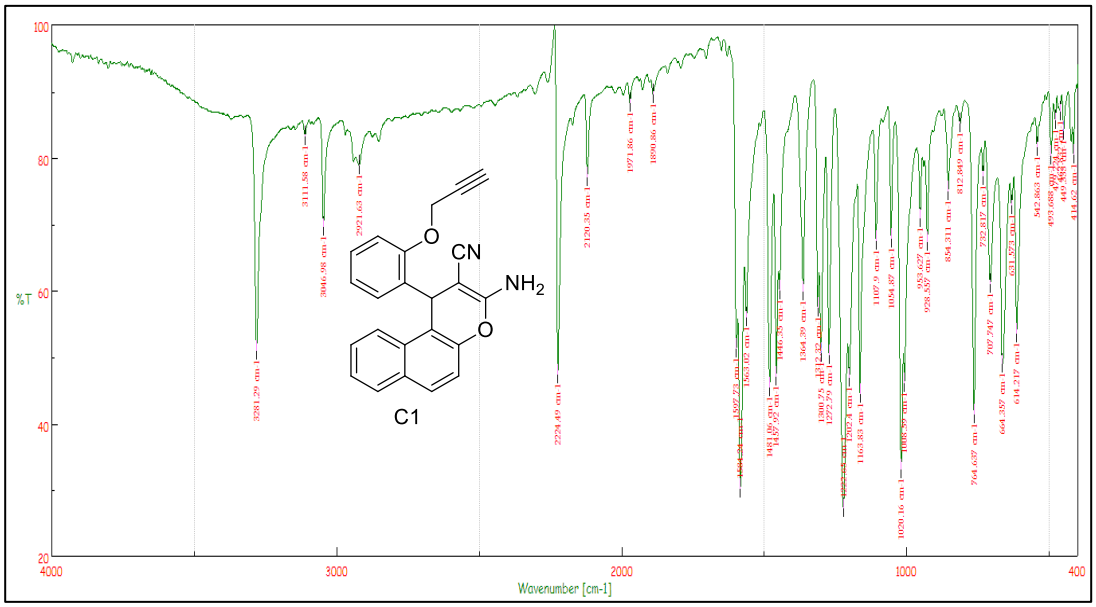

TP103
OH
P3
ppm

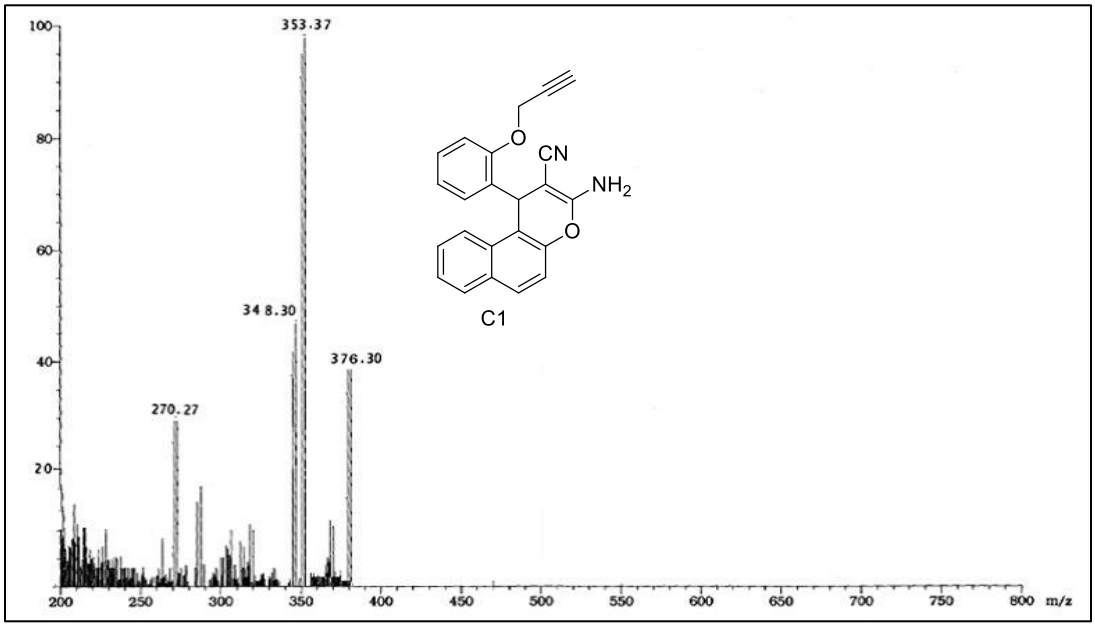

%T
100
50
0
4000
3000
2000
1000
400
Wavenumber [cm-1]
OH
O
O
NH
N3
N
H
O
P3

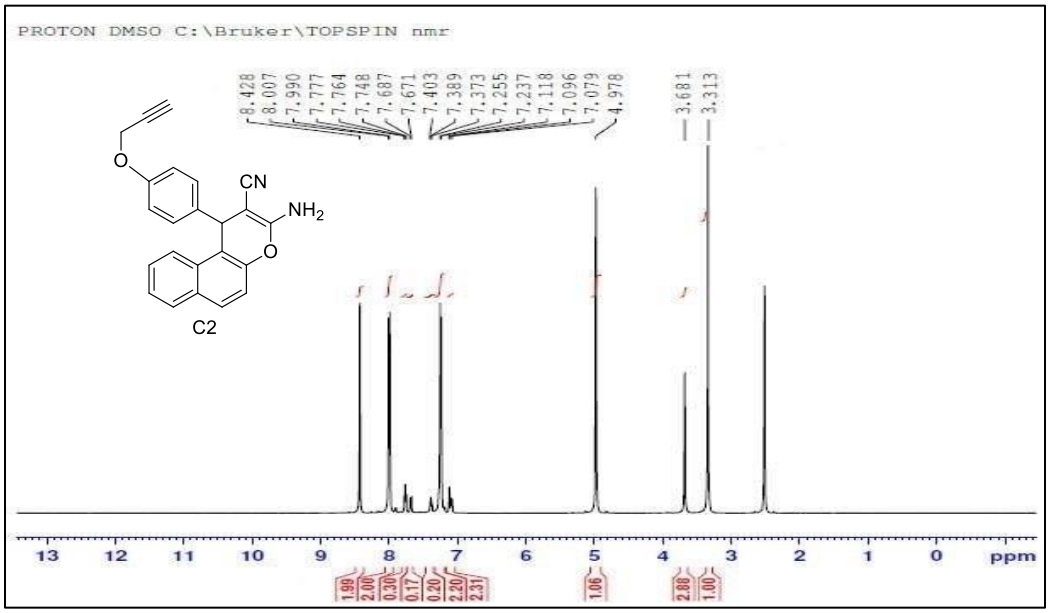

Relative Abundance
m/z
340.10574
316.11955
288.08797
205.02543
147.04485
OH
O
O
NH
N3
N
H
O
P3

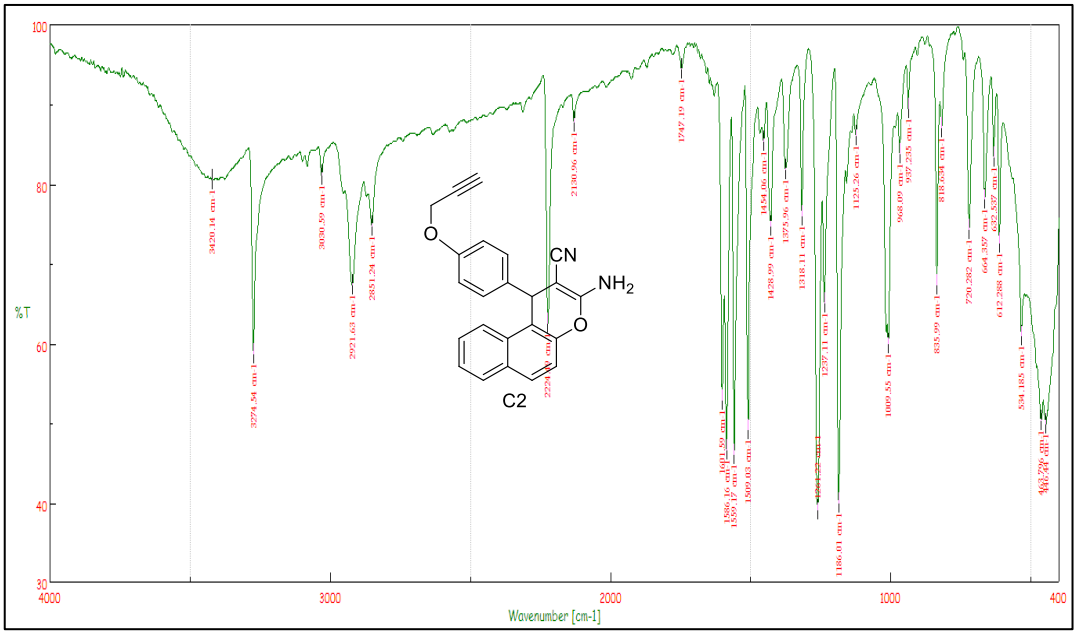

PROTON DMSO C:\Bruker\TOPSPIN nmr
8.462
8.006
7.776
7.763
7.747
7.718
7.702
7.688
7.672
7.402
7.388
7.372
7.319
7.302
7.275
7.260
7.246
7.224
7.208
7.193
7.130
7.106
7.089
5.000
3.698
3.319
CN
NH2
O
O
C1
11
10
9
8
7
6
5
4
3
2
1
ppm
2.06
1.17
1.00
1.28
1.06
1.21
2.05
2.24
2.08
1.42
2.10
1.00

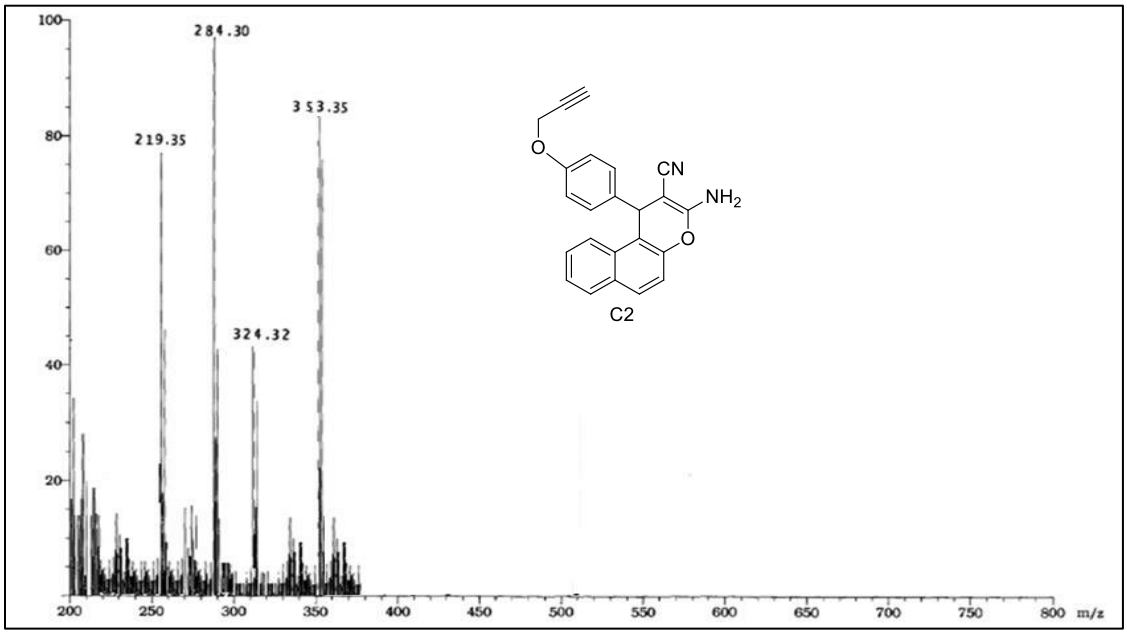

200.79
171.97
156.42
138.75
133.88
132.66
130.43
129.83
128.48
128.45
126.82
122.72
121.72
117.98
117.05
112.98
79.15
78.17
77.30
77.05
76.79
76.53
59.15
56.24
22.43
CN
NH2
O
O
C1
200
180
160
140
120
100
80
60
40
20
0
ppm

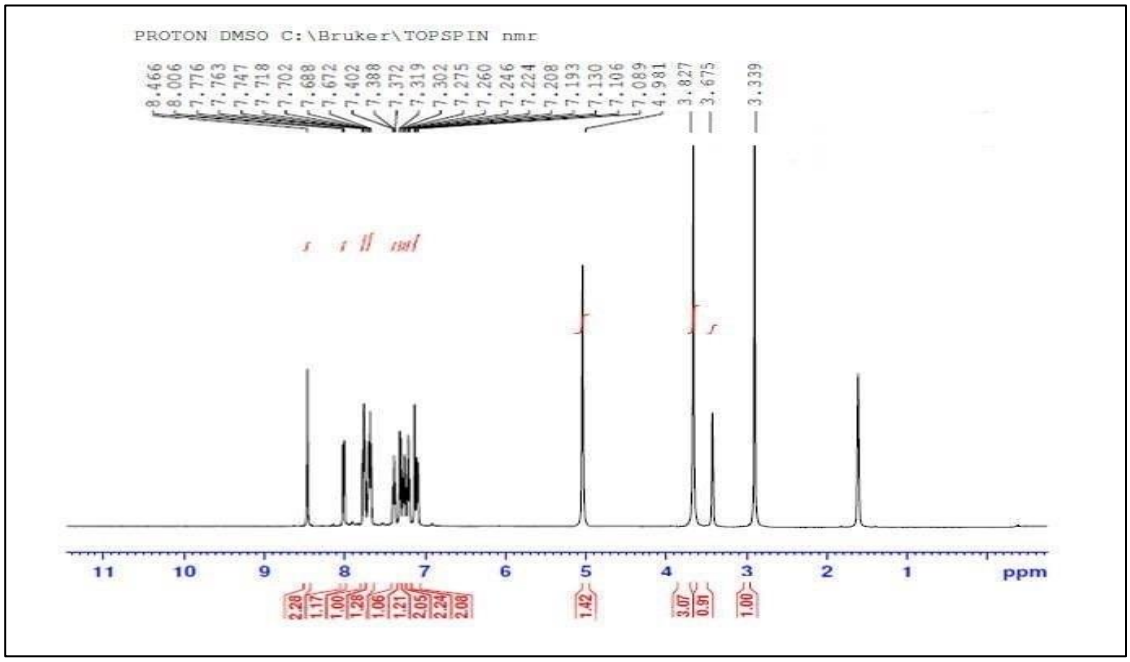

%T
Wavenumber [cm-1]
C1

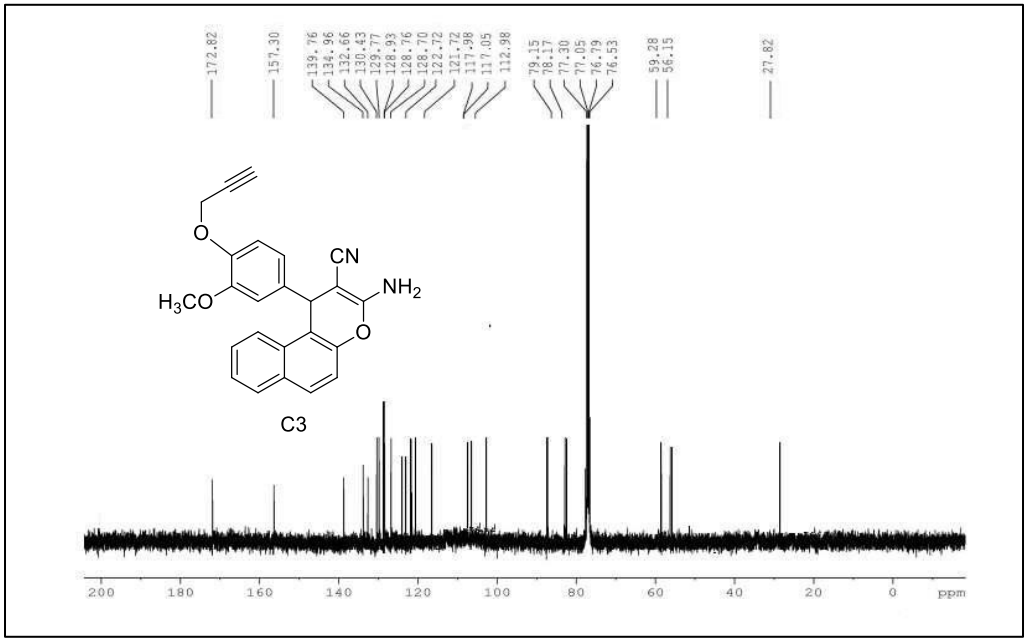

353.37
348.30
376.30
270.27
m/z
C1

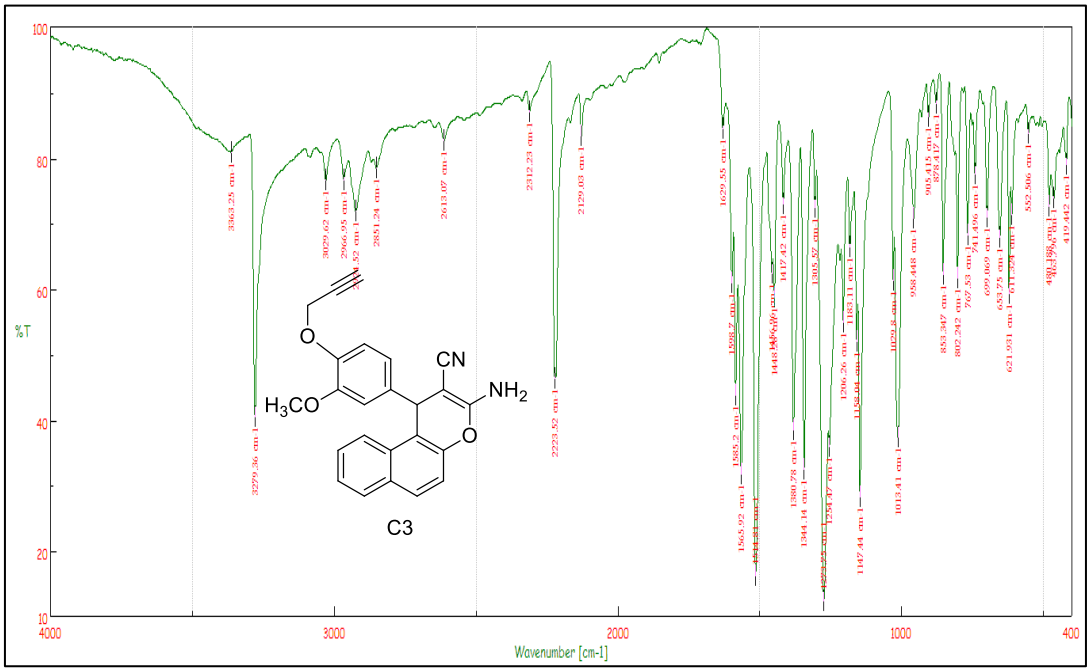

PROTON DMSO C:\Bruker\TOPSPIN nmr
8.428
8.007
7.990
7.777
7.764
7.748
7.687
7.671
7.403
7.389
7.373
7.255
7.237
7.118
7.096
7.079
4.978
3.681
3.313
CN
NH2
O
O
C2
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.90
2.00
0.30
0.17
0.20
2.20
2.31
1.06
2.80
1.00

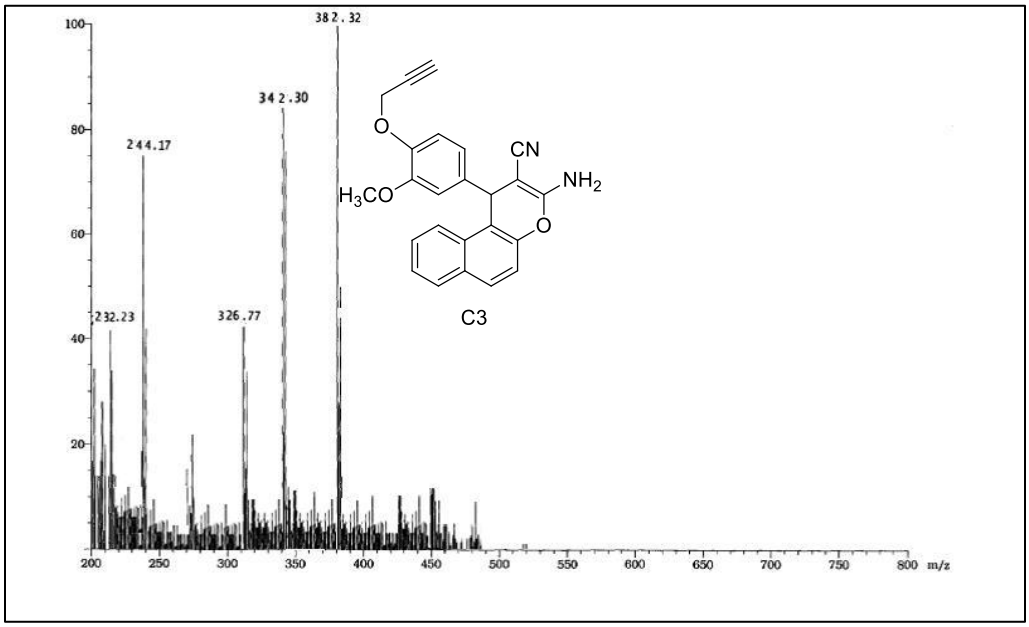

100
80
60
40
30
%T
4000
3000
2000
1000
400
Wavenumber [cm-1]
3420.14 cm-1
3274.54 cm-1
3030.59 cm-1
2921.63 cm-1
2851.24 cm-1
2130.96 cm-1
2224.97 cm-1
1747.19 cm-1
1601.59 cm-1
1586.19 cm-1
1569.83 cm-1
1458.06 cm-1
1428.99 cm-1
1379.96 cm-1
1318.11 cm-1
1239.11 cm-1
1186.01 cm-1
1125.26 cm-1
1089.55 cm-1
968.09 cm-1
937.235 cm-1
835.99 cm-1
818.264 cm-1
729.282 cm-1
664.357 cm-1
632.537 cm-1
612.288 cm-1
534.185 cm-1
463.726 cm-1
446.44 cm-1
CN
NH2
O
O
C2

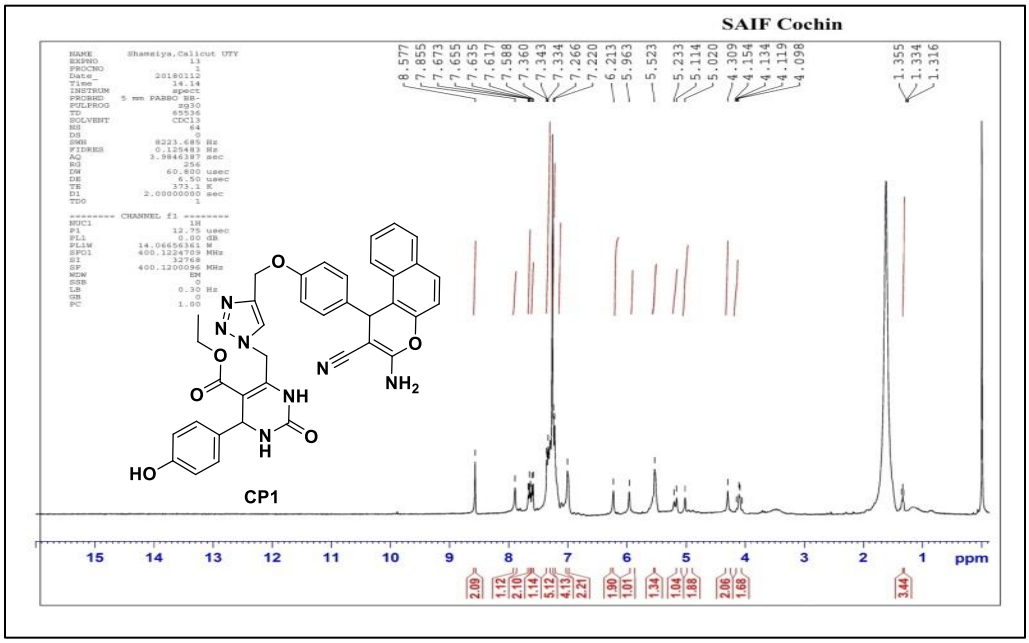

284.30
353.35
219.35
324.32
CN
NH2
O
O
C2
m/z

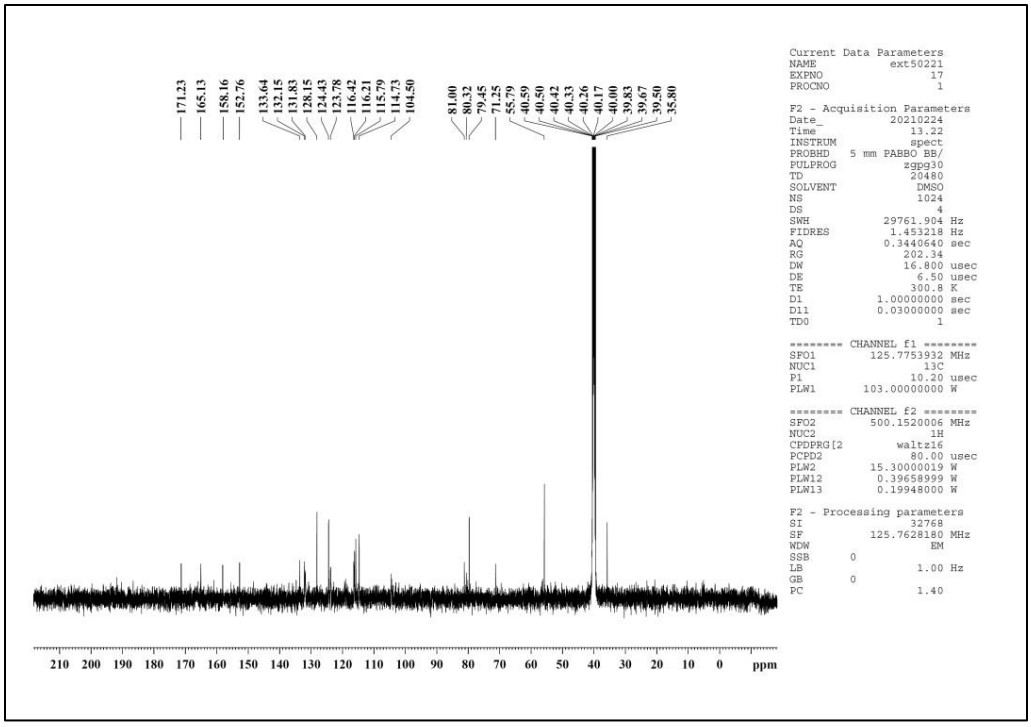

PROTON DMSO C:\Bruker\TOPSPIN nmr
8.466
8.006
7.776
7.763
7.747
7.718
7.702
7.688
7.672
7.402
7.388
7.372
7.319
7.302
7.275
7.260
7.246
7.224
7.208
7.193
7.130
7.106
7.089
4.981
3.827
3.675
3.339
ppm

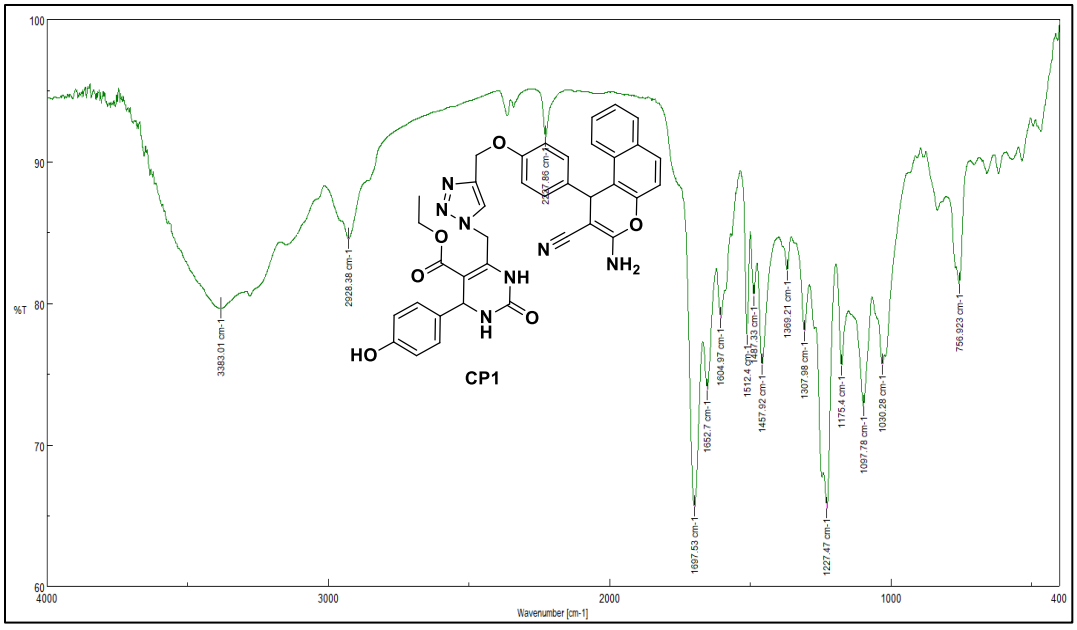

172.82
157.30
139.76
134.96
132.66
130.43
129.77
128.93
128.76
128.70
122.72
121.72
117.98
117.05
112.98
79.15
78.17
77.30
77.05
76.79
76.53
59.28
56.13
27.82
O
CN
NH2
H3CO
O
C3
200
180
160
140
120
100
80
60
40
20
0
ppm

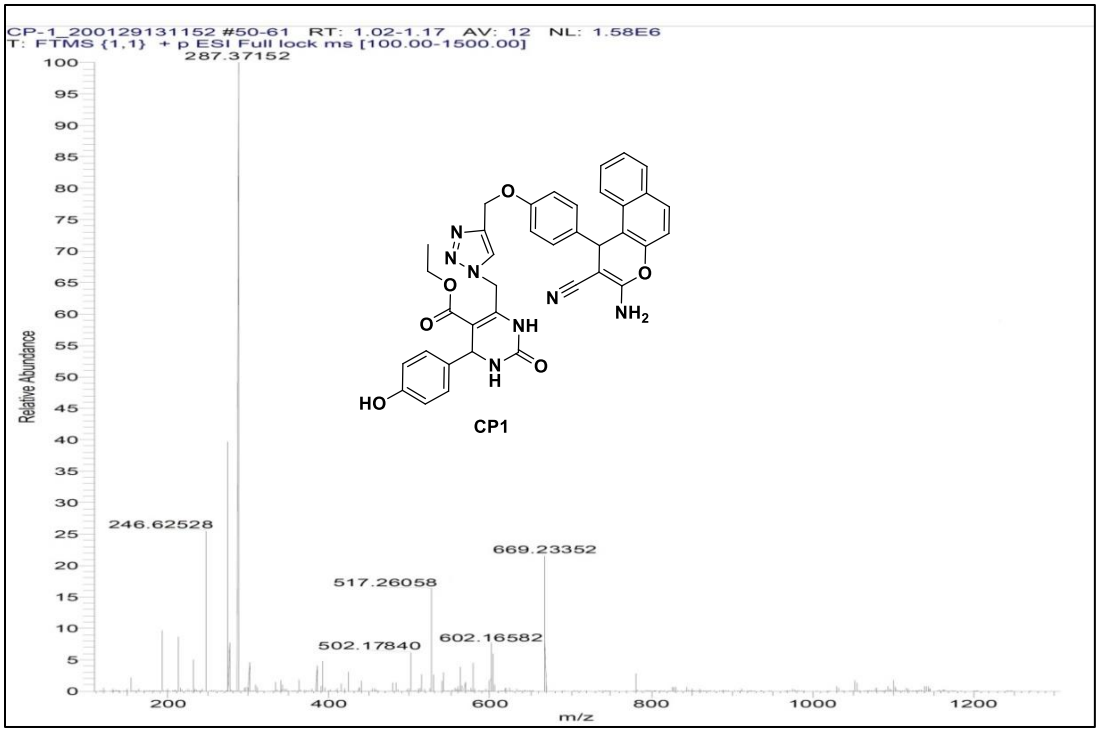

100
80
60
40
20
10
%T
4000
3000
2000
1000
400
Wavenumber [cm-1]
3363.25 cm-1
3279.36 cm-1
3029.62 cm-1
2966.95 cm-1
2851.24 cm-1
2613.07 cm-1
2312.23 cm-1
2223.52 cm-1
2129.03 cm-1
1629.55 cm-1
1598.7 cm-1
1565.92 cm-1
1417.47 cm-1
1385.57 cm-1
1380.78 cm-1
1344.14 cm-1
1254.37 cm-1
1206.26 cm-1
1183.11 cm-1
1158.08 cm-1
1147.44 cm-1
1029.8 cm-1
1013.41 cm-1
988.448 cm-1
905.415 cm-1
874.417 cm-1
853.597 cm-1
802.242 cm-1
767.53 cm-1
741.436 cm-1
699.069 cm-1
653.75 cm-1
621.991 cm-1
611.324 cm-1
552.506 cm-1
480.188 cm-1
419.442 cm-1
O
CN
NH2
H3CO
O
C3

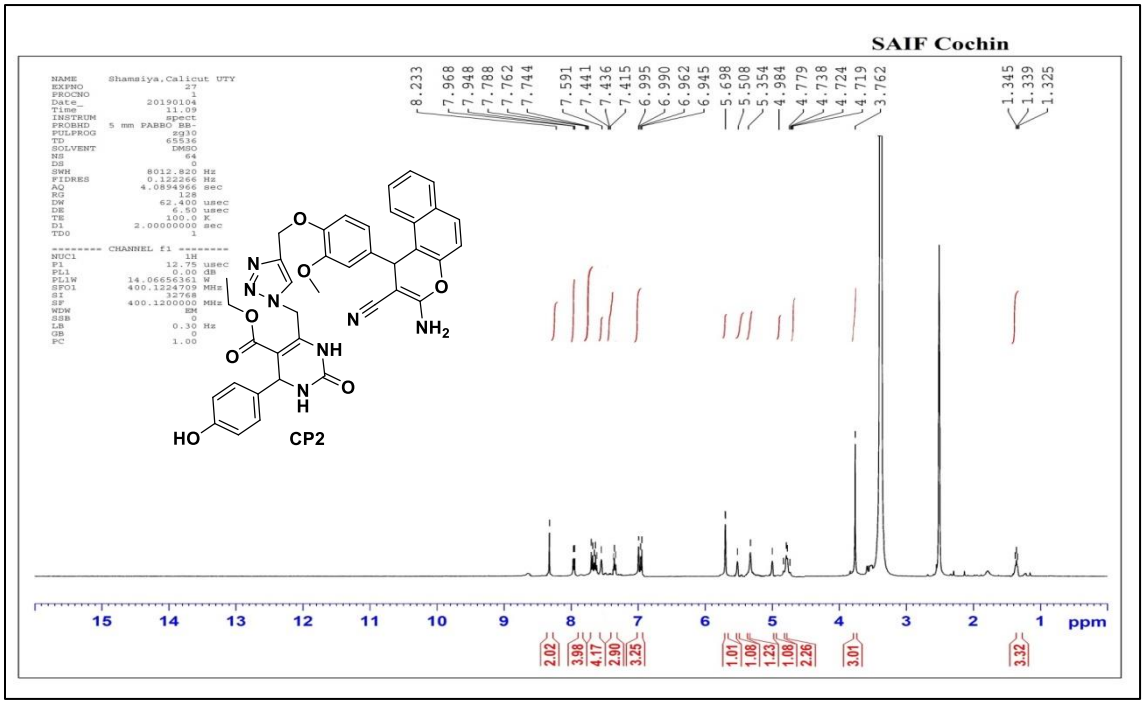

382.32
342.30
244.17
232.23
326.77
100
80
60
40
20
200
250
300
350
400
450
500
550
600
650
700
750
800 m/z
O
CN
NH2
H3CO
O
C3

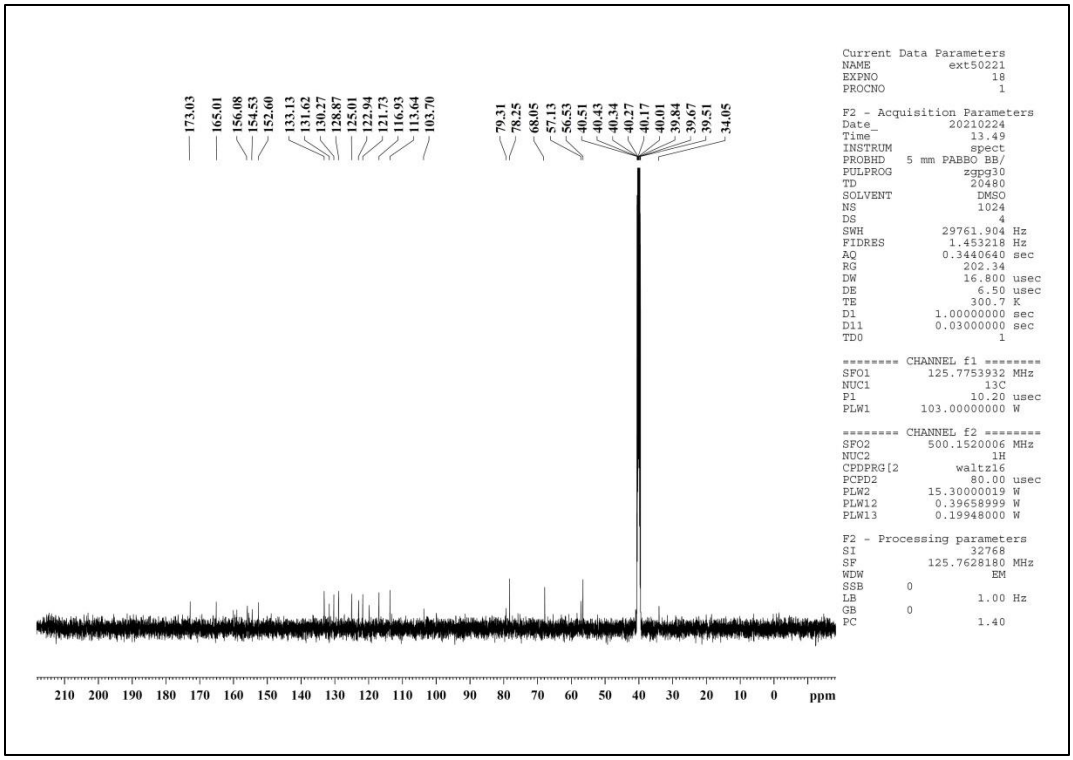

SAIF Cochin
8.577
7.855
7.673
7.655
7.635
7.617
7.588
7.360
7.343
7.334
7.266
7.220
6.213
5.963
5.523
5.233
5.114
5.020
4.309
4.154
4.134
4.119
4.098
1.355
1.334
1.316
O
N
N
N
O
O
NH
N
H
O
HO
N
O
NH2
CP1
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
2.09
1.12
2.10
1.14
5.12
4.13
2.21
1.90
1.01
1.34
1.04
1.88
2.06
1.68
3.44

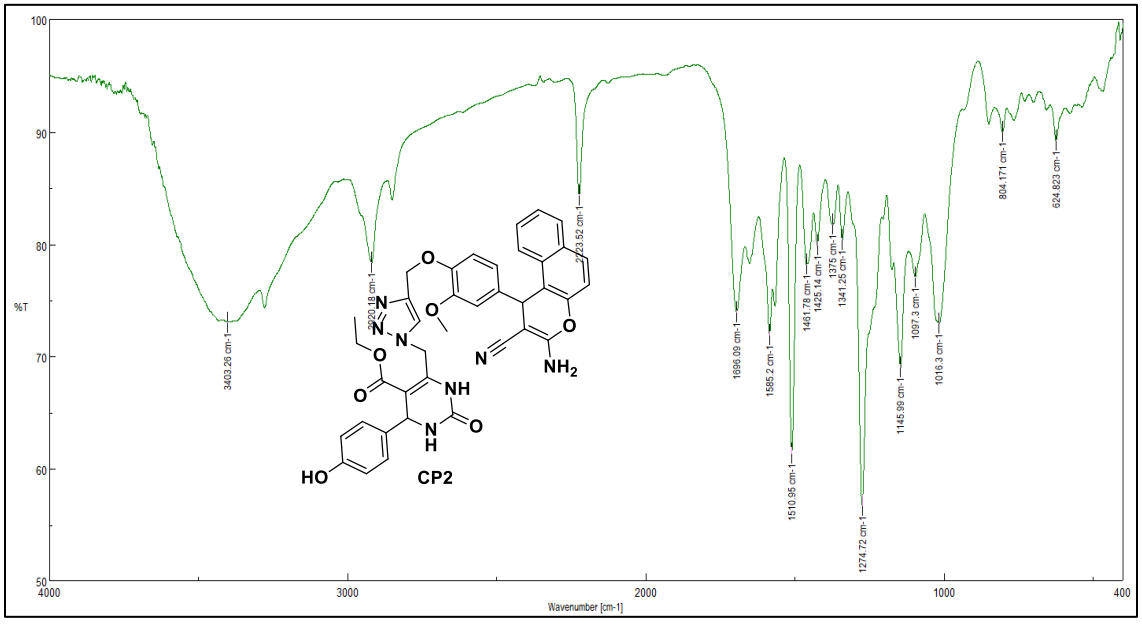

171.23
165.13
158.16
152.76
133.64
132.15
131.83
128.15
124.43
123.78
116.42
116.21
115.79
114.73
104.50
81.00
80.32
79.45
71.25
55.79
40.59
40.50
40.42
40.33
40.26
40.17
40.00
39.83
39.67
39.50
35.80
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Current Data Parameters
NAME ext50221
EXPNO 17
PROCNO 1
F2 - Acquisition Parameters
Date_ 20210224
Time 13.22
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 20480
SOLVENT DMSO
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 1.453218 Hz
AQ 0.3440640 sec
RG 202.34
DW 16.800 usec
DE 6.50 usec
TE 300.8 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7753932 MHz
NUC1 13C
P1 10.20 usec
PLW1 103.00000000 W
======== CHANNEL f2 ========
SFO2 500.1520006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 15.30000019 W
PLW12 0.39658999 W
PLW13 0.19948000 W
F2 - Processing parameters
SI 32768
SF 125.7628180 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

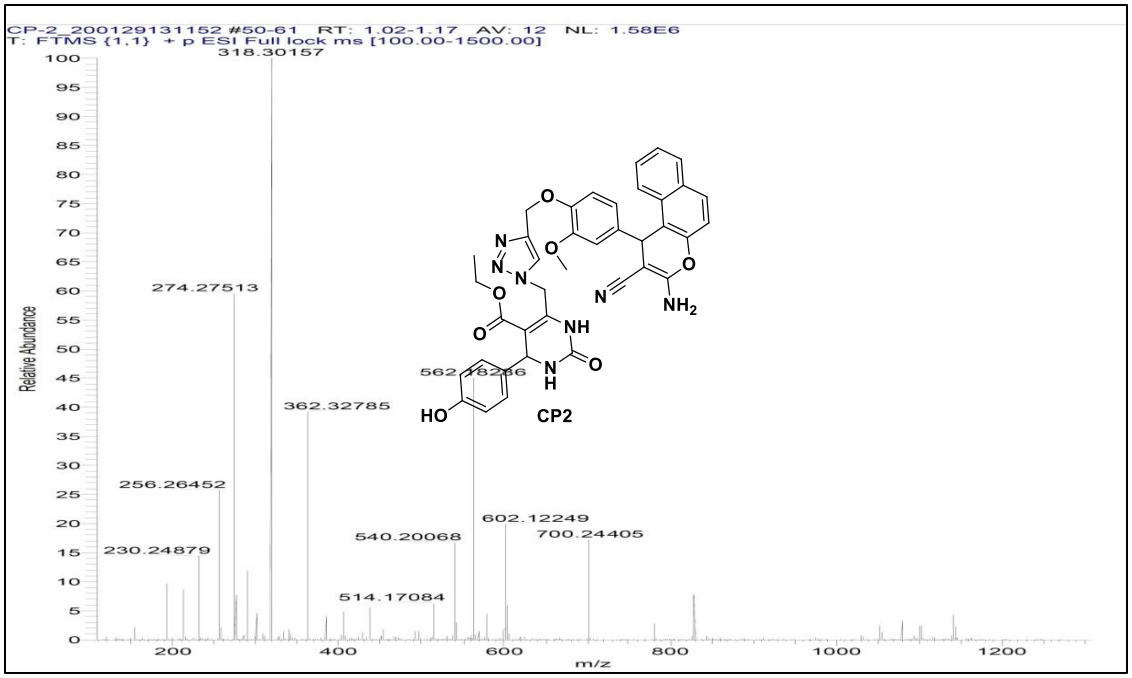

100
90
80
70
60
%T
4000
3000
2000
1000
400
Wavenumber [cm-1]
3383.01 cm-1
2928.38 cm-1
2207.89 cm-1
1697.53 cm-1
1652.7 cm-1
1604.97 cm-1
1512.4 cm-1
1487.33 cm-1
1457.92 cm-1
1369.21 cm-1
1307.98 cm-1
1227.47 cm-1
1175.4 cm-1
1097.78 cm-1
1030.28 cm-1
756.923 cm-1
CP1

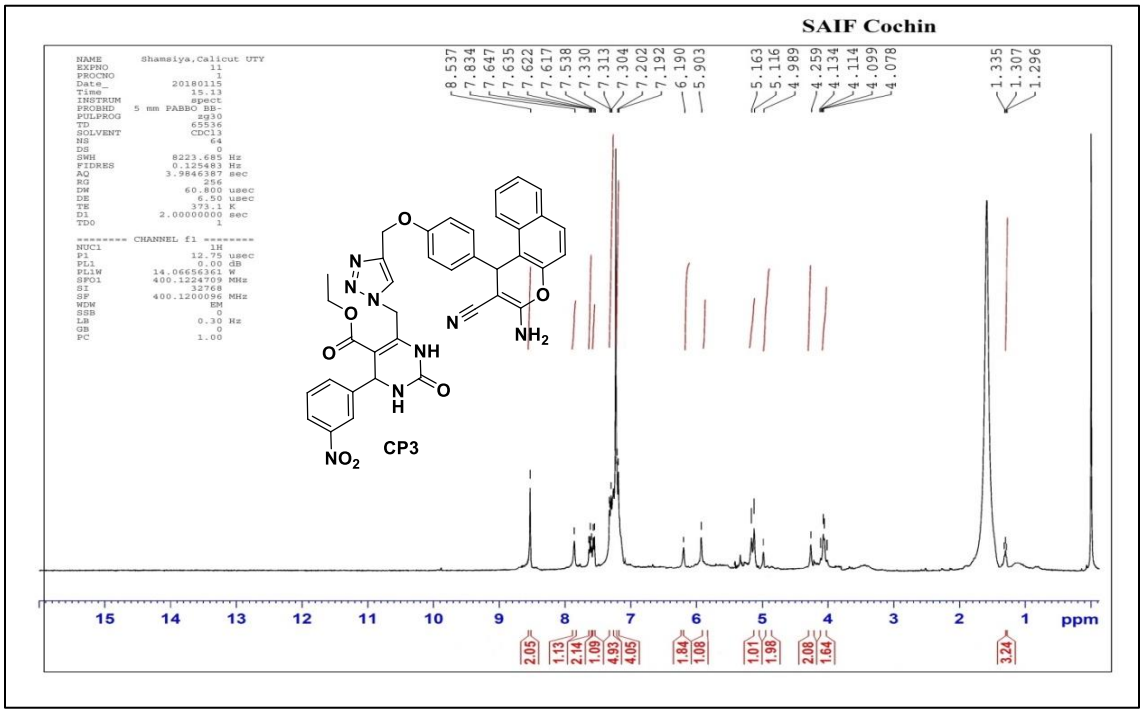

CP-1_200129131152 #50-61 RT: 1.02-1.17 AV: 12 NL: 1.58E6
T: FTMS {1,1} + p ESI Full lock ms [100.00-1500.00]
287.37152
246.62528
669.23352
517.26058
502.17840
602.16582
Relative Abundance
m/z
CP1

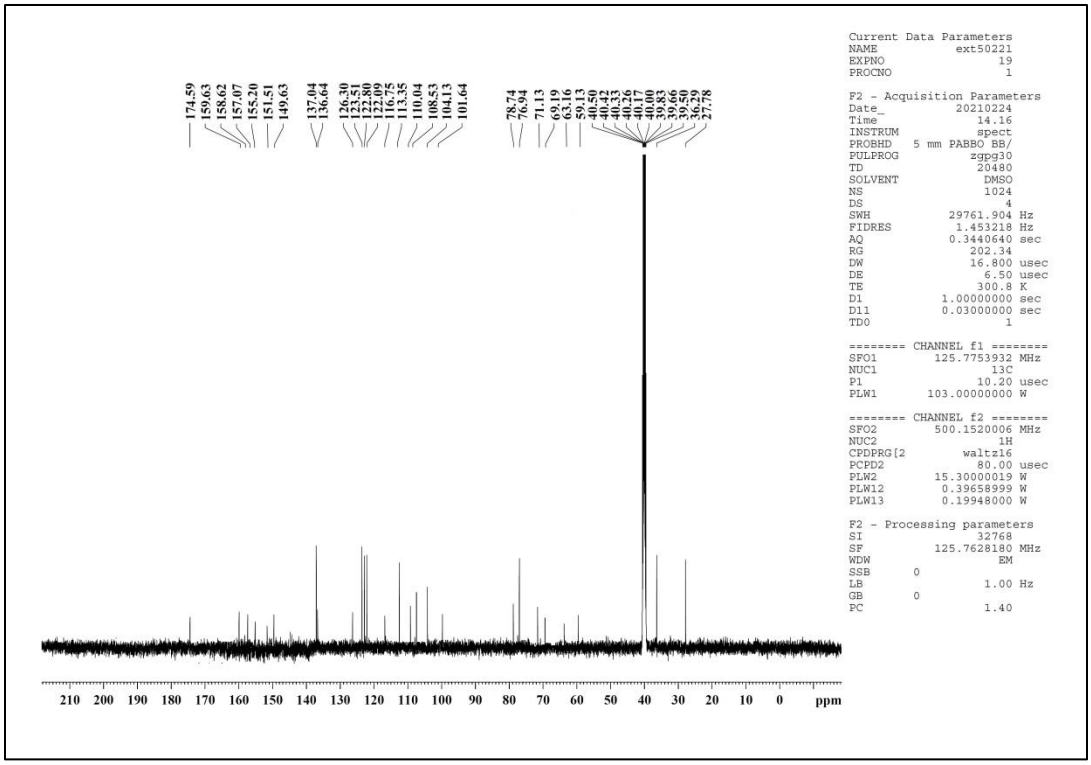

SAIF Cochin
CP2
ppm

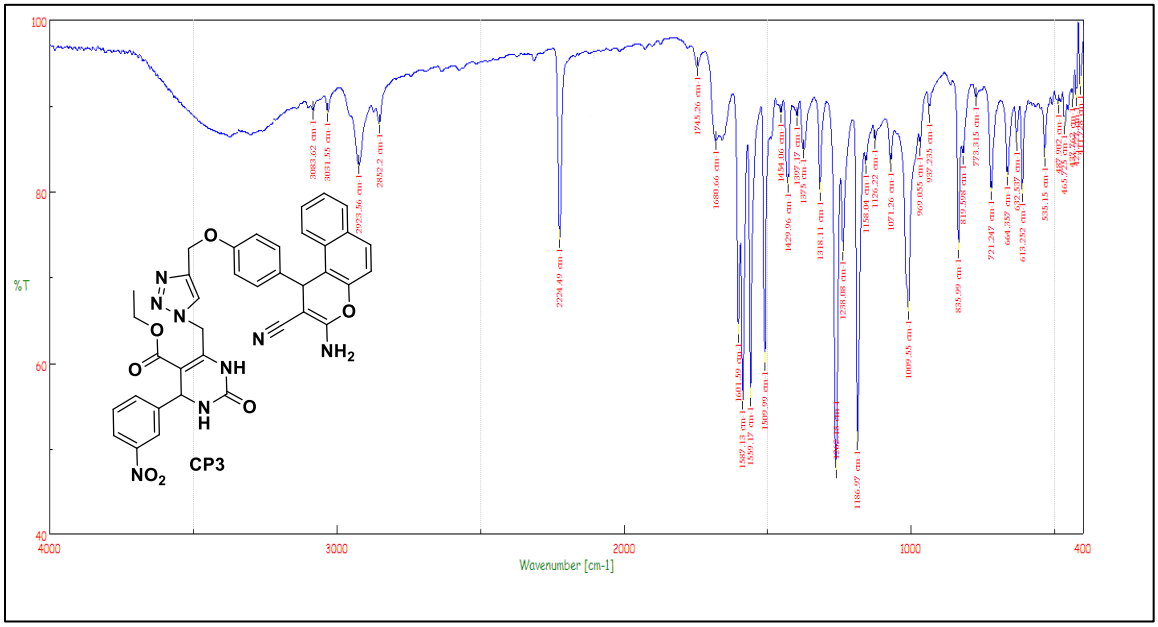

173.03
165.01
156.08
154.53
152.60
133.13
131.62
130.27
128.87
125.01
122.94
121.73
116.93
113.64
103.70
79.31
78.25
68.05
57.13
56.53
40.51
40.43
40.34
40.27
40.17
40.01
39.84
39.67
39.51
34.05
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Current Data Parameters
NAME ext50221
EXPNO 18
PROCNO 1
F2 - Acquisition Parameters
Date_ 20210224
Time 13.49
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 20480
SOLVENT DMSO
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 1.453218 Hz
AQ 0.3440640 sec
RG 202.34
DW 16.800 usec
DE 6.50 usec
TE 300.7 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7753932 MHz
NUC1 13C
P1 10.20 usec
PLW1 103.00000000 W
======== CHANNEL f2 ========
SFO2 500.1520006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 15.30000019 W
PLW12 0.39658999 W
PLW13 0.19948000 W
F2 - Processing parameters
SI 32768
SF 125.7628180 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

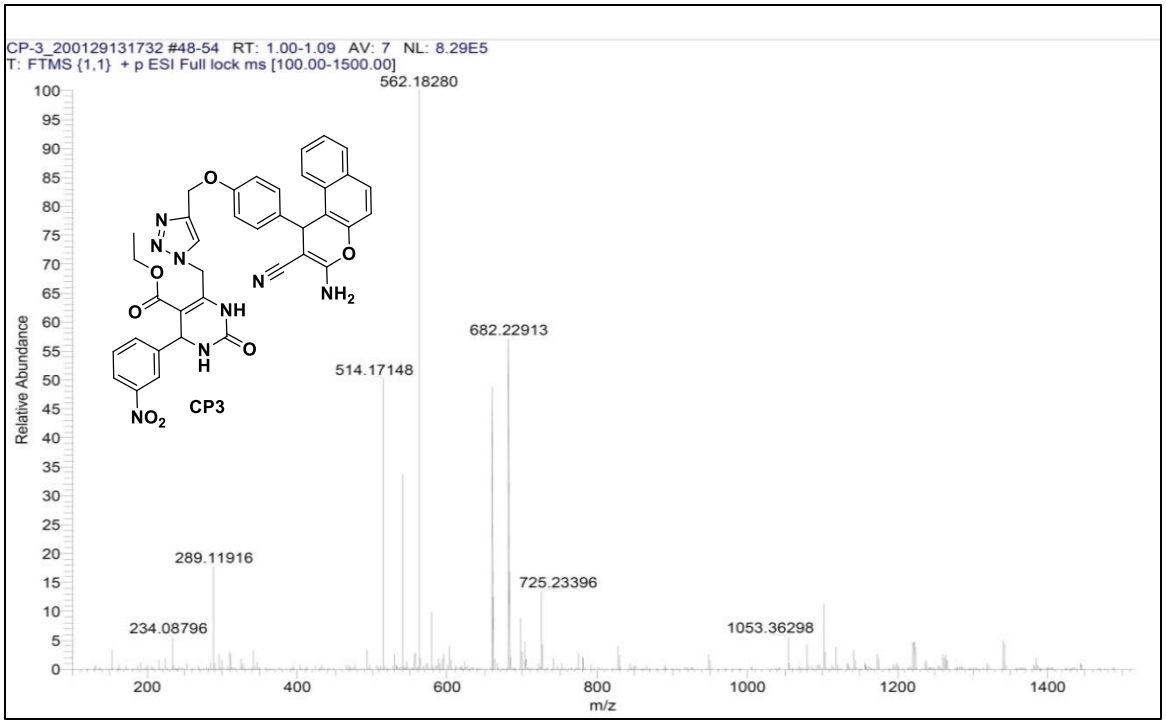

%T
Wavenumber [cm-1]
3403.26 cm-1
2920.18 cm-1
2223.52 cm-1
1696.09 cm-1
1585.2 cm-1
1510.95 cm-1
1461.78 cm-1
1425.14 cm-1
1341.25 cm-1
1274.72 cm-1
1145.99 cm-1
1097.3 cm-1
1016.3 cm-1
804.171 cm-1
624.823 cm-1
CP2

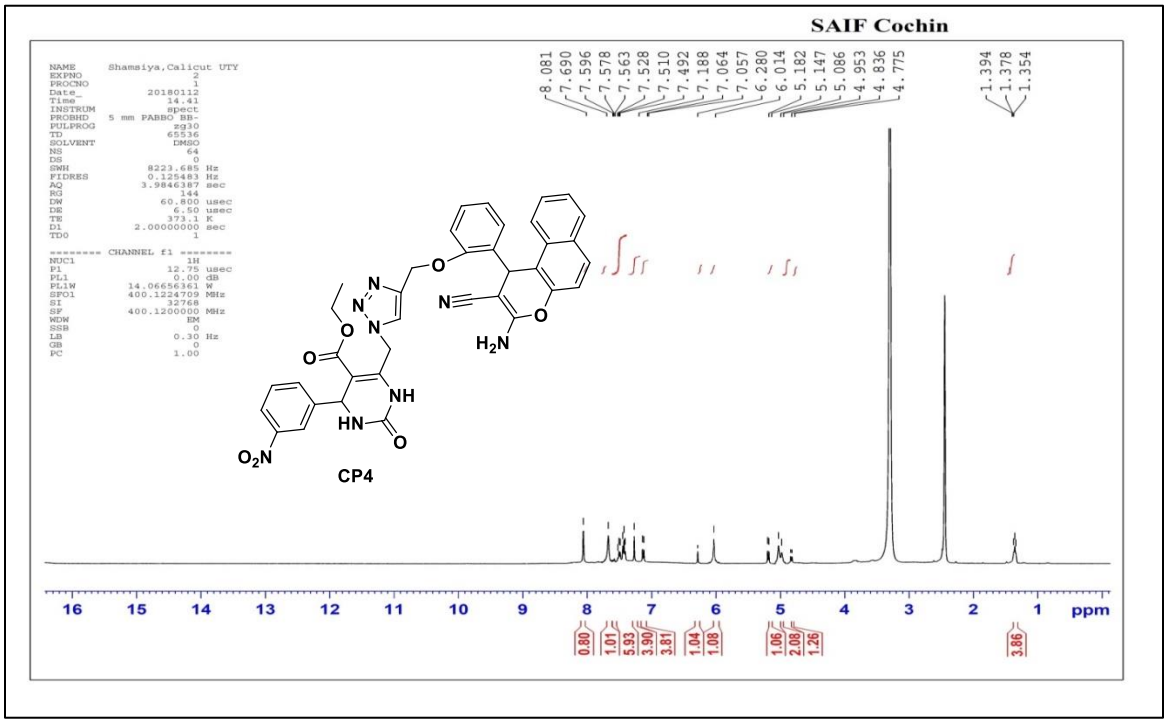

CP-2_200129131152 #50-61 RT: 1.02-1.17 AV: 12 NL: 1.58E6
T: FTMS {1,1} + p ESI Full lock ms [100.00-1500.00]
318.30157
274.27513
362.32785
256.26452
230.24879
540.20068
602.12249
700.24405
514.17084
562.78286
Relative Abundance
m/z
CP2

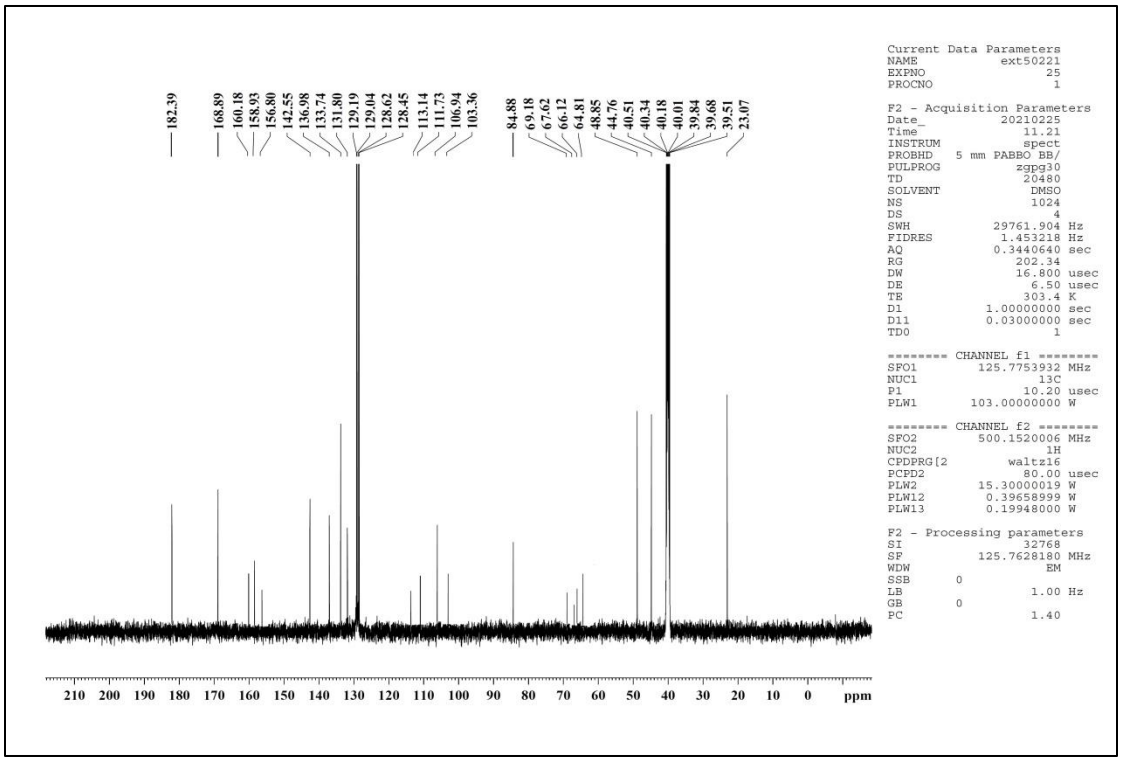

SAIF Cochin
CP3

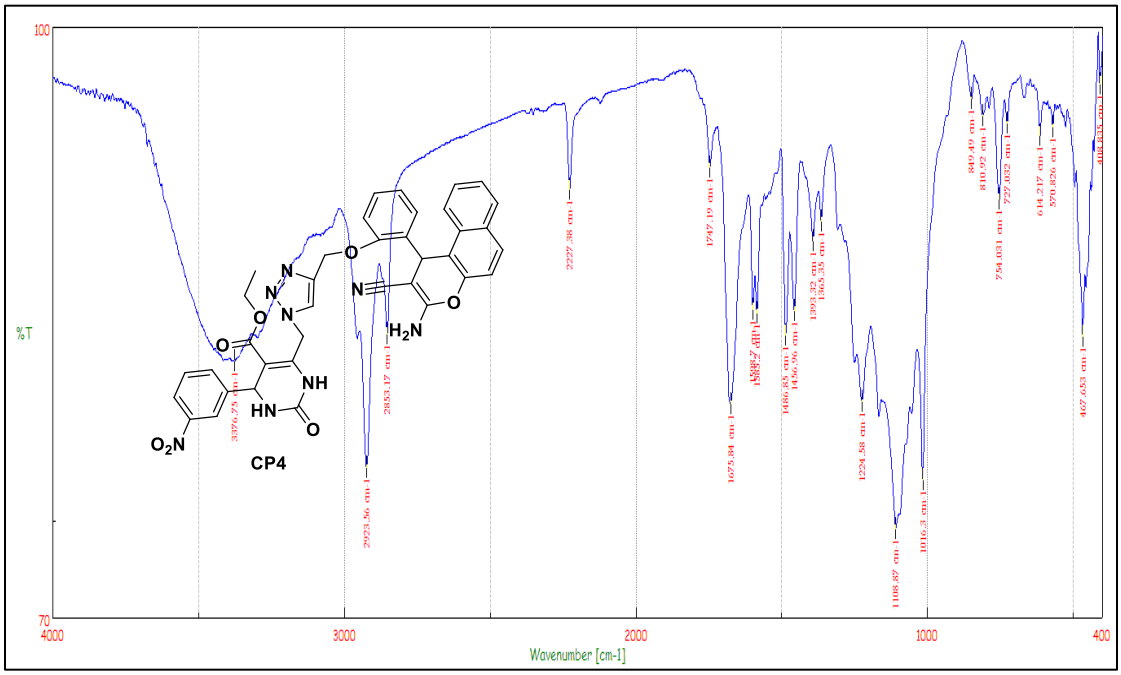

174.59
159.63
158.62
157.07
155.20
151.51
149.63
137.04
136.64
126.30
125.51
122.80
122.09
116.75
113.35
110.04
108.53
104.13
101.64
78.74
76.94
71.13
69.19
63.16
59.13
40.50
40.42
40.33
40.26
40.17
40.00
39.83
39.66
39.50
36.29
27.78
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Current Data Parameters
NAME ext50221
EXPNO 19
PROCNO 1
F2 - Acquisition Parameters
Date_ 20210224
Time 14.16
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 20480
SOLVENT DMSO
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 1.453218 Hz
AQ 0.3440640 sec
RG 202.34
DW 16.800 usec
DE 6.50 usec
TE 300.8 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7753932 MHz
NUC1 13C
P1 10.20 usec
PLW1 103.00000000 W
======== CHANNEL f2 ========
SFO2 500.1520006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 15.30000019 W
PLW12 0.39658999 W
PLW13 0.19948000 W
F2 - Processing parameters
SI 32768
SF 125.7628180 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

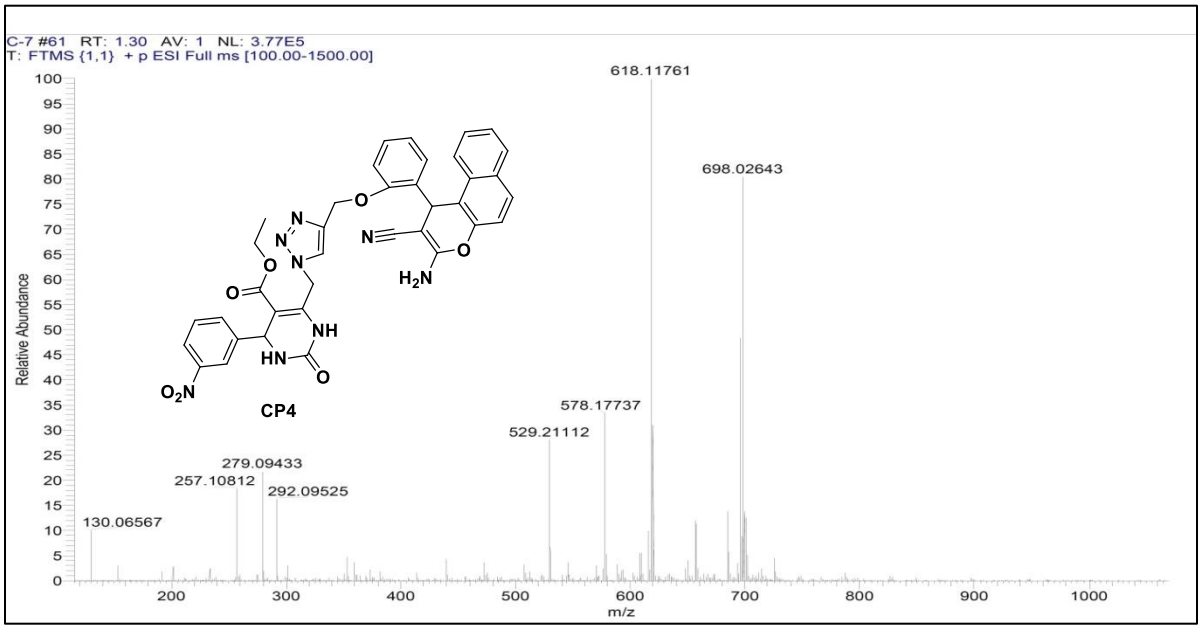

100
80
60
40
%T
4000
3000
2000
1000
400
Wavenumber [cm-1]
3883.62 cm-1
3831.55 cm-1
2923.56 cm-1
2852.2 cm-1
2224.49 cm-1
1745.26 cm-1
1689.66 cm-1
1587.13 cm-1
1559.17 cm-1
1454.06 cm-1
1429.96 cm-1
1397.17 cm-1
1375 cm-1
1318.11 cm-1
1238.68 cm-1
1186.97 cm-1
1158.00 cm-1
1126.22 cm-1
1071.26 cm-1
1009.55 cm-1
969.055 cm-1
907.255 cm-1
835.99 cm-1
819.598 cm-1
773.315 cm-1
721.247 cm-1
664.357 cm-1
613.252 cm-1
592.857 cm-1
535.15 cm-1
465.397 cm-1
O
N
N
N
O
O
NH
N
H
O
NH2
NO2
CP3

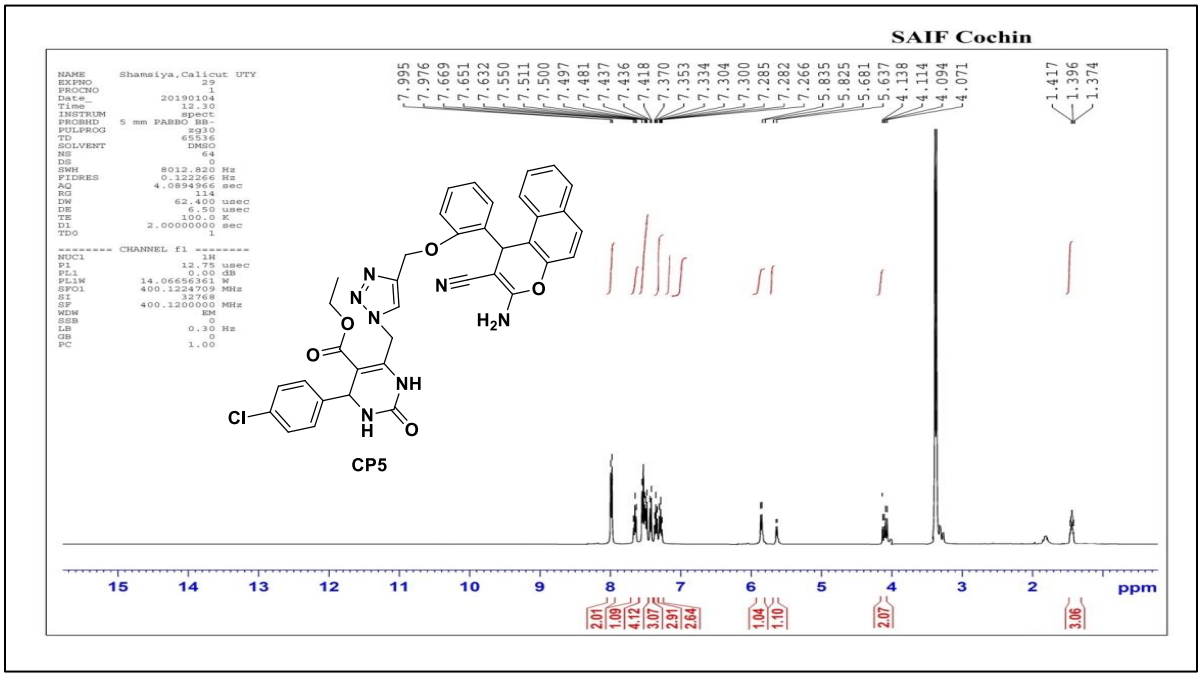

CP-3_200129131732 #48-54 RT: 1.00-1.09 AV: 7 NL: 8.29E5
T: FTMS {1,1} + p ESI Full lock ms [100.00-1500.00]
562.18280
682.22913
514.17148
289.11916
725.23396
234.08796
1053.36298
Relative Abundance
m/z
CP3

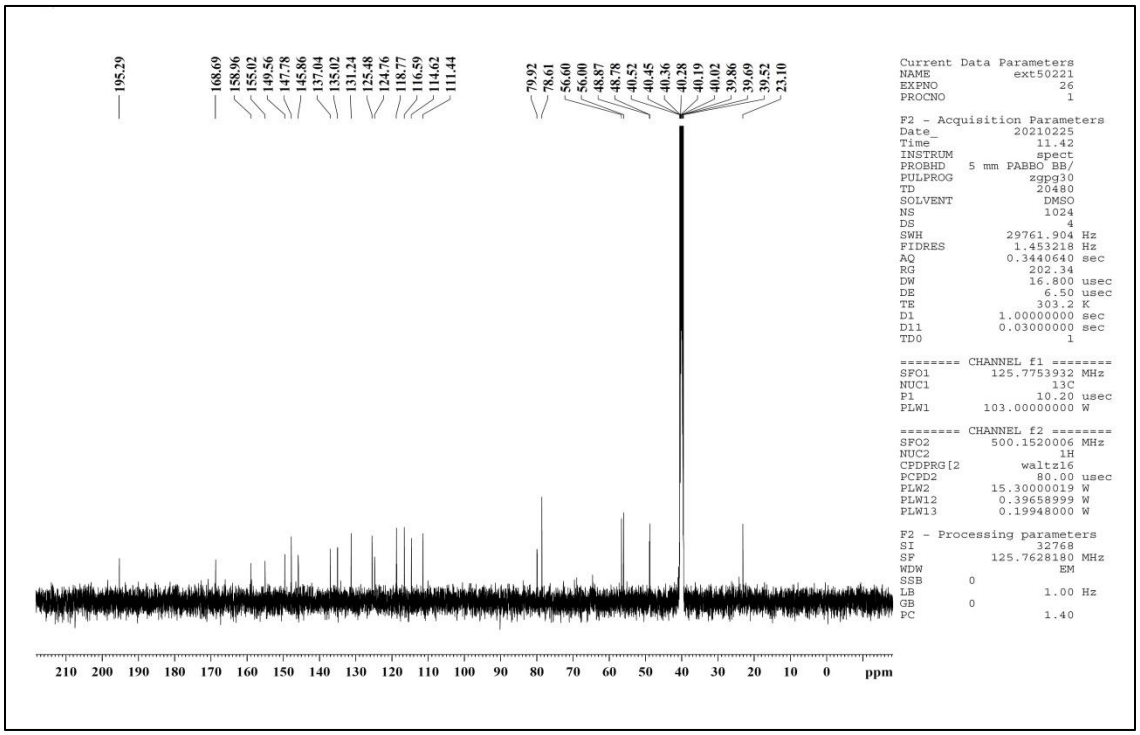

SAIF Cochin
8.081
7.690
7.596
7.578
7.563
7.528
7.510
7.492
7.188
7.064
7.057
6.280
6.014
5.182
5.147
5.086
4.953
4.836
4.775
1.394
1.378
1.354
CP4
ppm

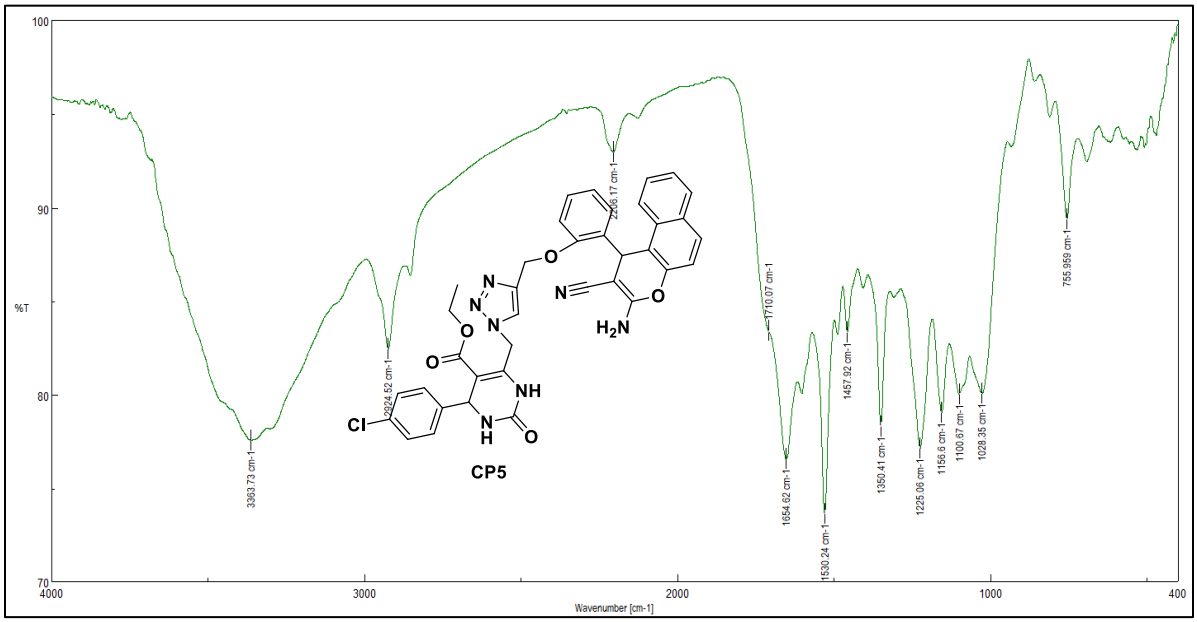

182.39
168.89
160.18
158.93
156.80
142.55
136.98
133.74
131.80
129.19
129.04
128.62
128.45
113.14
111.73
106.94
103.36
84.88
69.18
67.62
66.12
64.81
48.85
44.76
40.51
40.34
40.18
40.01
39.84
39.68
39.51
23.07
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Current Data Parameters
NAME ext50221
EXPNO 25
PROCNO 1
F2 - Acquisition Parameters
Date_ 20210225
Time 11.21
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 20480
SOLVENT DMSO
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 1.453218 Hz
AQ 0.3440640 sec
RG 202.34
DW 16.800 usec
DE 6.50 usec
TE 303.4 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7753932 MHz
NUC1 13C
P1 10.20 usec
PLW1 103.00000000 W
======== CHANNEL f2 ========
SFO2 500.1520006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 15.30000019 W
PLW12 0.39658999 W
PLW13 0.19948000 W
F2 - Processing parameters
SI 32768
SP 125.7628180 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

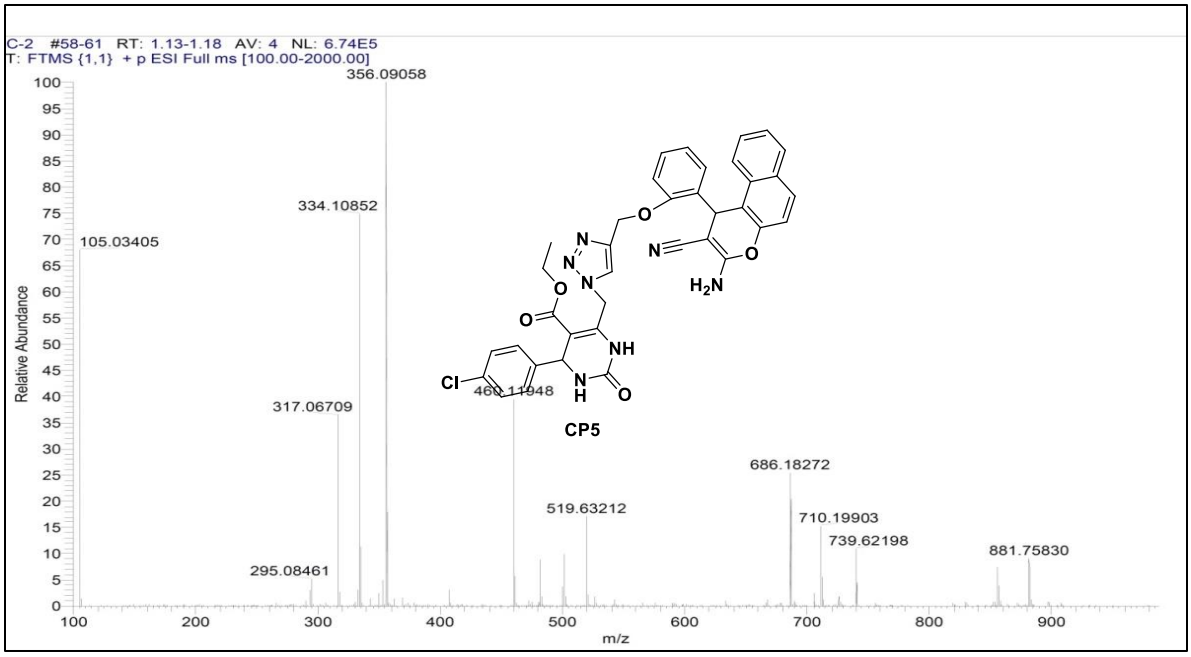

100
%T
70
4000
3000
2000
1000
400
Wavenumber [cm-1]
3376.75 cm-1
2923.56 cm-1
2853.17 cm-1
2227.38 cm-1
1747.19 cm-1
1675.84 cm-1
1588.7 cm-1
1486.85 cm-1
1456.96 cm-1
1393.32 cm-1
1365.35 cm-1
1254.58 cm-1
1108.87 cm-1
1016.3 cm-1
849.49 cm-1
810.92 cm-1
754.031 cm-1
727.032 cm-1
614.217 cm-1
570.826 cm-1
467.653 cm-1
408.833 cm-1
CP4

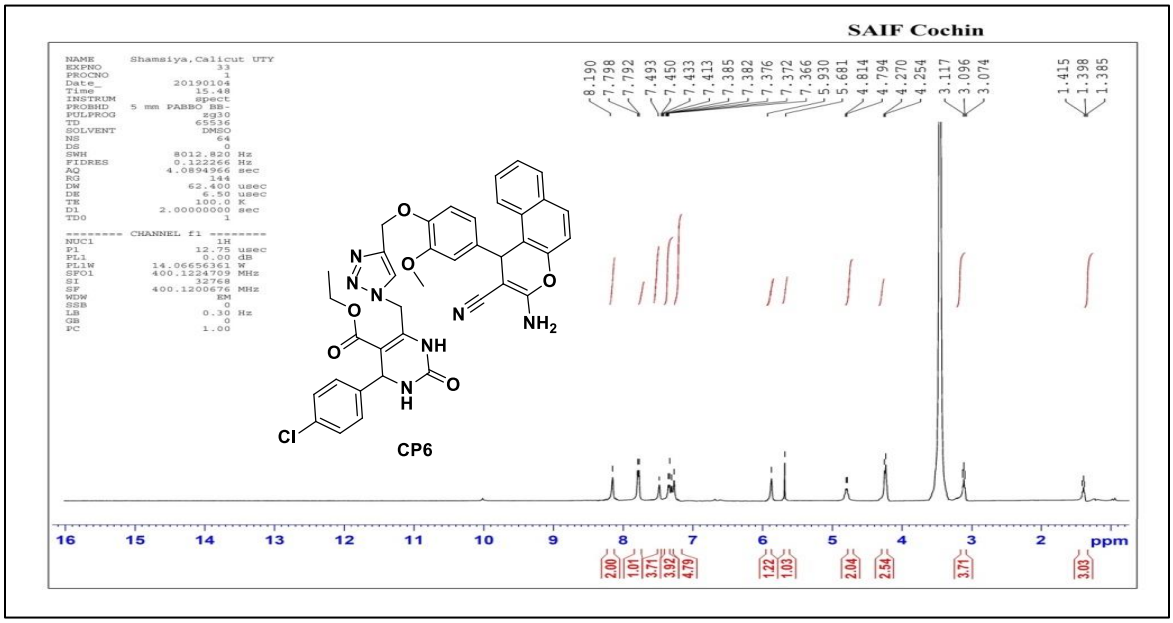

C-7 #61 RT: 1.30 AV: 1 NL: 3.77E5
T: FTMS {1,1} + p ESI Full ms [100.00-1500.00]
Relative Abundance
m/z
618.11761
698.02643
578.17737
529.21112
279.09433
257.10812
292.09525
130.06567
CP4

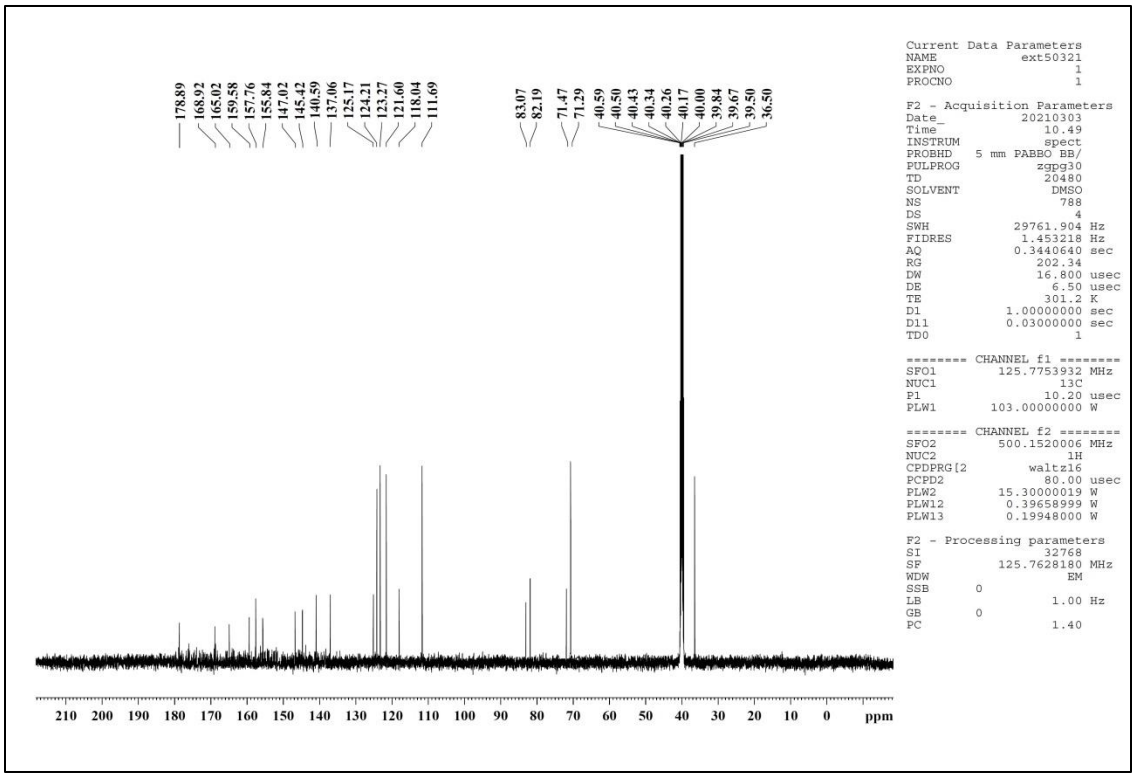

SAIF Cochin
CP5
ppm

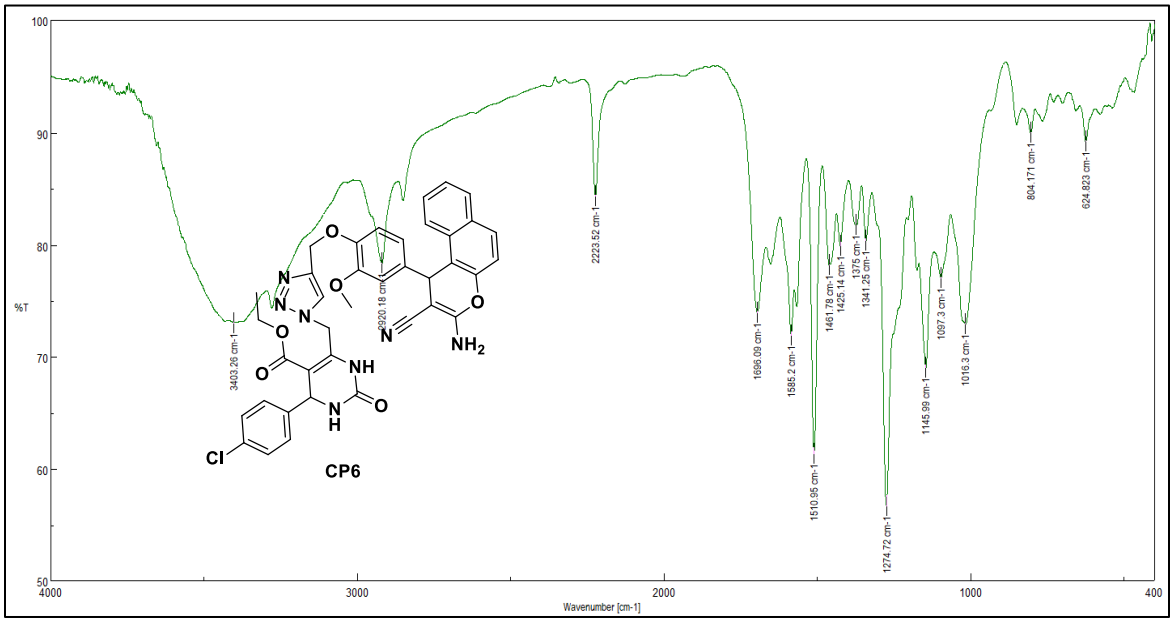

195.29
168.69
158.96
155.02
149.56
147.78
145.86
137.04
135.02
131.24
125.48
124.76
118.77
116.59
114.62
111.44
79.92
78.61
56.60
56.00
48.87
48.78
40.52
40.45
40.36
40.28
40.19
40.02
39.86
39.69
39.52
23.10
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Current Data Parameters
NAME ext50221
EXPNO 26
PROCNO 1
F2 - Acquisition Parameters
Date_ 20210225
Time 11.42
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 20480
SOLVENT DMSO
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 1.453218 Hz
AQ 0.3440640 sec
RG 202.34
DW 16.800 usec
DE 6.50 usec
TE 303.2 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7753932 MHz
NUC1 13C
P1 10.20 usec
PLW1 103.00000000 W
======== CHANNEL f2 ========
SFO2 500.1520006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 15.30000019 W
PLW12 0.39658999 W
PLW13 0.19948000 W
F2 - Processing parameters
SI 32768
SF 125.7628180 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

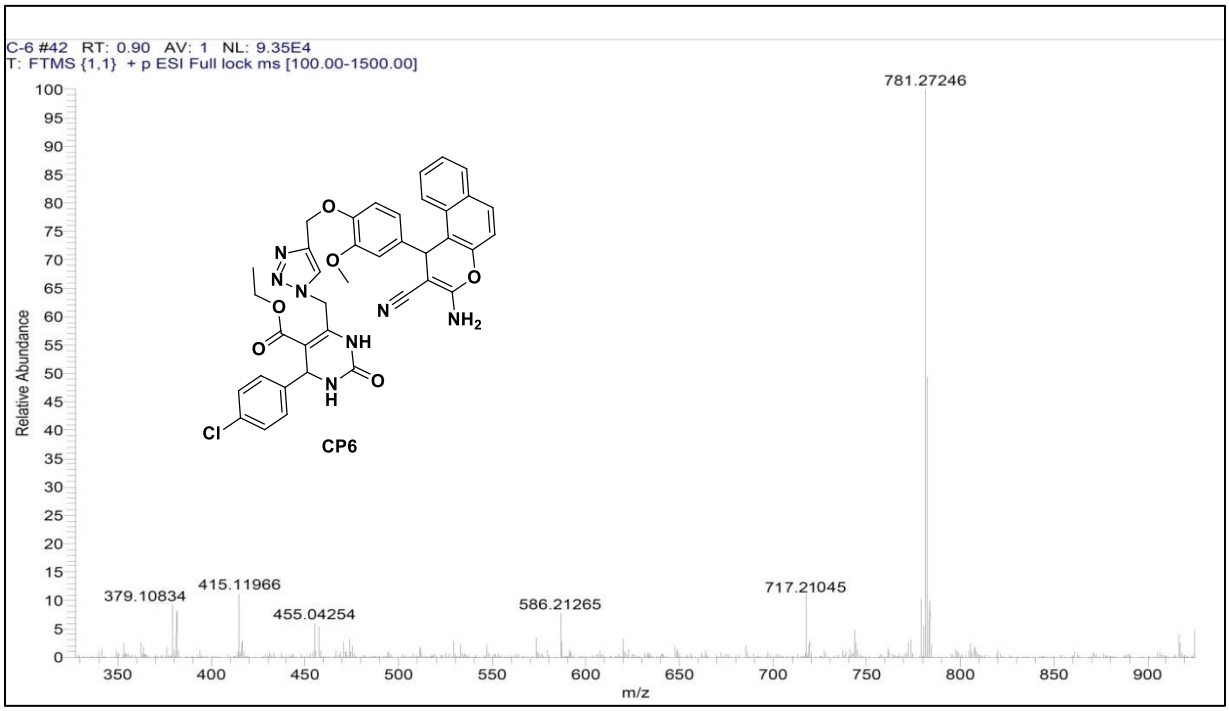

100
90
80
70
%T
4000
3000
2000
1000
400
Wavenumber [cm-1]
3383.73 cm-1
2924.82 cm-1
2456.17 cm-1
1710.07 cm-1
1654.62 cm-1
1530.24 cm-1
1457.92 cm-1
1350.41 cm-1
1225.06 cm-1
1156.6 cm-1
1100.67 cm-1
1028.35 cm-1
755.959 cm-1
CP5

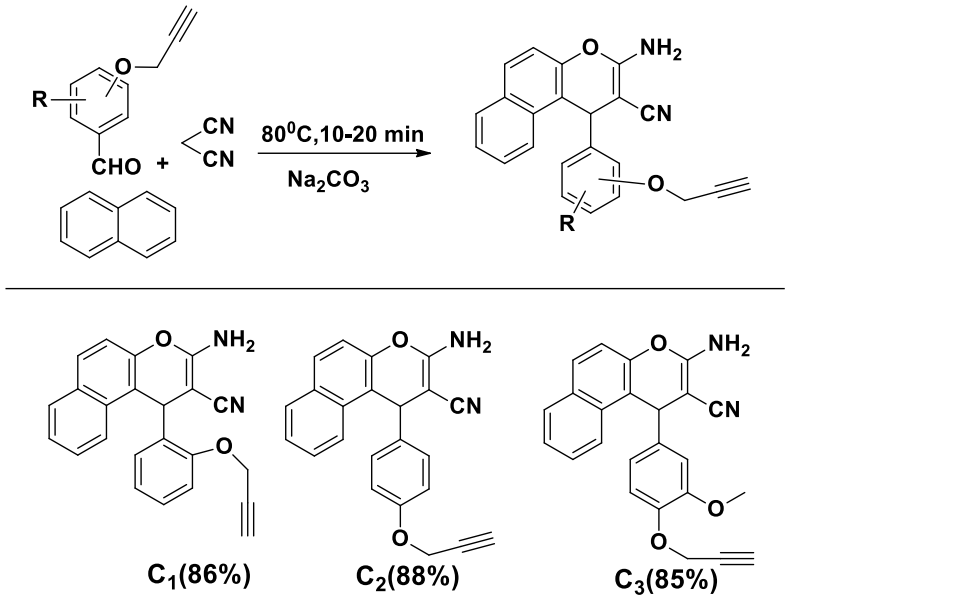

C-2 #58-61 RT: 1.13-1.18 AV: 4 NL: 6.74E5
T: FTMS {1,1} + p ESI Full ms [100.00-2000.00]
356.09058
334.10852
105.03405
317.06709
460.11948
519.63212
686.18272
710.19903
739.62198
881.75830
295.08461
Relative Abundance
m/z
CP5


SAIF Cochin
CP6
ppm

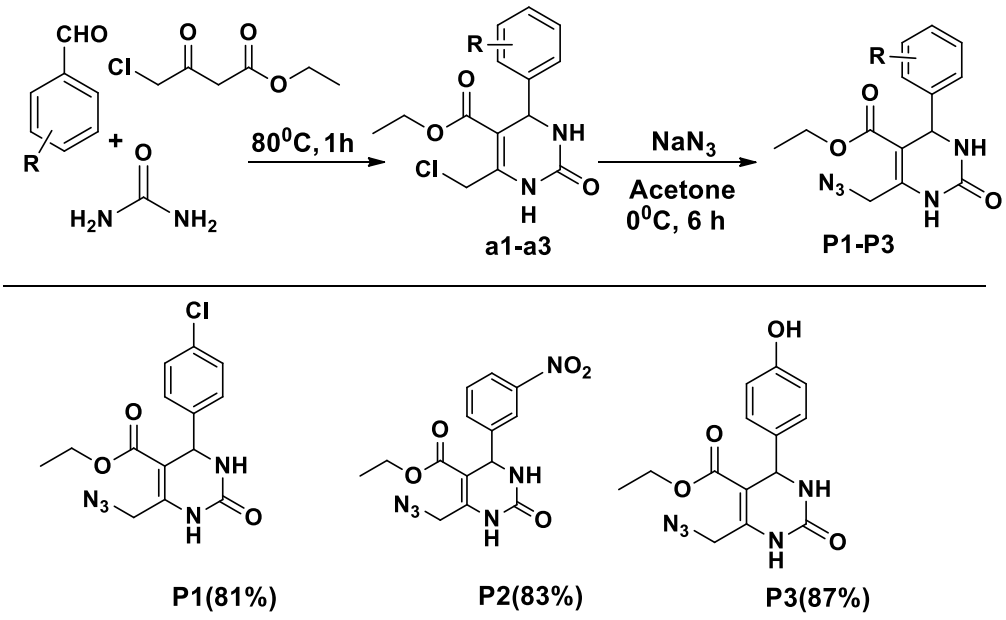

178.89
168.92
165.02
159.58
157.76
155.84
147.02
145.42
140.59
137.06
125.17
124.21
123.27
121.60
118.04
111.69
83.07
82.19
71.47
71.29
40.59
40.50
40.43
40.34
40.26
40.17
40.00
39.84
39.67
39.50
36.50
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Current Data Parameters
NAME ext50321
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20210303
Time 10.49
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 20480
SOLVENT DMSO
NS 788
DS 4
SWH 29761.904 Hz
FIDRES 1.453218 Hz
AQ 0.3440640 sec
RG 202.34
DW 16.800 usec
DE 6.50 usec
TE 301.2 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7753932 MHz
NUC1 13C
P1 10.20 usec
PLW1 103.00000000 W
======== CHANNEL f2 ========
SFO2 500.1520006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 15.30000019 W
PLW12 0.39658999 W
PLW13 0.19948000 W
F2 - Processing parameters
SI 32768
SF 125.7628180 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40


%T
100
90
80
70
60
50
4000
3000
2000
1000
400
Wavenumber [cm-1]
3403.26 cm-1
2920.18 cm-1
2223.52 cm-1
1696.09 cm-1
1585.2 cm-1
1510.95 cm-1
1461.78 cm-1
1425.14 cm-1
1375 cm-1
1341.25 cm-1
1274.72 cm-1
1145.99 cm-1
1097.3 cm-1
1016.3 cm-1
804.171 cm-1
624.823 cm-1
CP6


C-6 #42 RT: 0.90 AV: 1 NL: 9.35E4
T: FTMS {1,1} + p ESI Full lock ms [100.00-1500.00]
781.27246
379.10834
415.11966
455.04254
586.21265
717.21045
Relative Abundance
m/z
CP6



Scheme S1: Three component MCR synthesis of Chromene alkynes



Scheme S2: Biginelli multicomponent synthesis of dihydropyrimidinone azides

Table S1: Cheminformatics descriptors of CP1-CP6

Entry	MW	TPSA	miLog P	Number of rotatable bonds	Number of Violations
CP1	669.70	186.66	4.91	10	2
CP2	699.72	195.89	4.50	11	2
CP3	698.70	212.25	5.35	11	3
CP4	698.70	212.25	5.30	11	3
CP5	688.14	166.43	6.02	10	3
CP6	718.17	175. 66	5.66	11	3

Table S2: Docking scores were obtained for CP1-CP6 with CDK2

Compound	Docking score/Binding affinity(kcalmol^{-1})	Interaction with receptor
CP1	-9.8	ASN132(HB),ASP145,GLN131,GLY13,GLY11,GLU12,ILE10,LEU83, LEU134,LYS88,LYS89,LYS129,LYS33,THR14,PHE80,VAL18
CP2	-9.6	ASP145,ALA144,GLN131,ILE10,LEU134,LYS89,LYS33,PHE80,VAL8
CP3	-9.4	ALA31,GLN131, LEU134, LYS129,LYS89,HIS84,PHE80,VAL18
CP4	-9.6	ALA31,ALA144,ASP145,GLU12,GLY11,GLY13,ILE10,LEU134,LYS88 ,LYS89, PHE80, PHE82,VAL18,VAL64
CP5	-9.6	ALA31,ASP145(HB),GLN131,HIS84,ILE10,LEU134,LYS89,PHE80,VA L18
CP6	-9.5	ALA144,ASP145,GLU12,GLY13,ILE10,LYS89,PHE80,THR14(HB),VA L18, VAL64

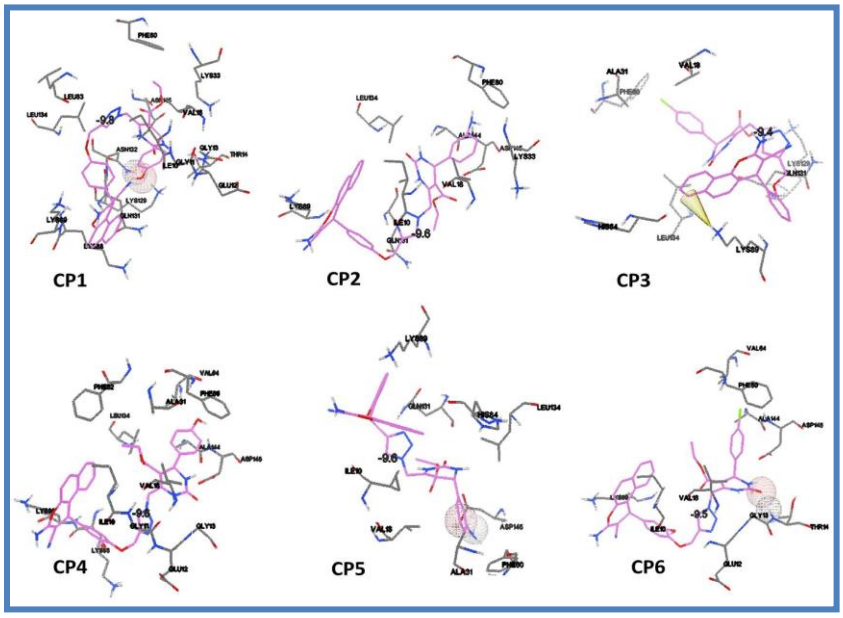


Figure S1. Docking interaction of CP1-CP6 with CDK2 protein

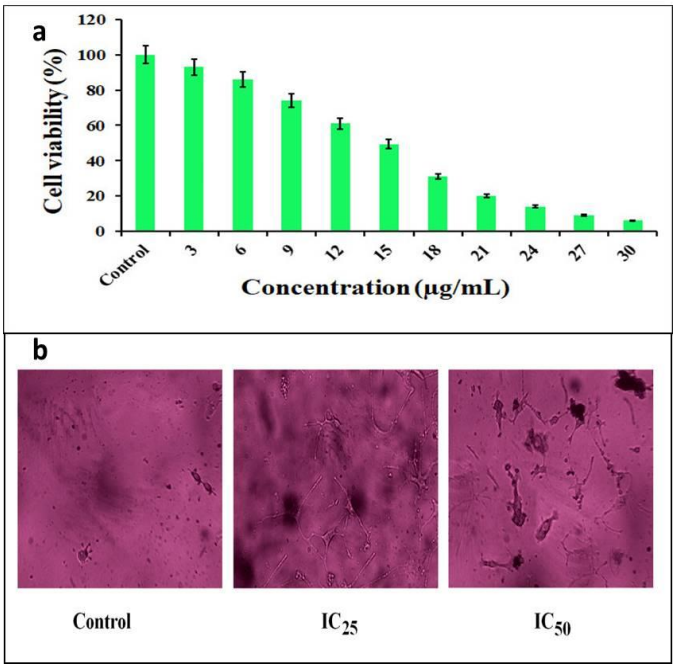


Figure S2. a, In vitro cytotoxicity assay results with the CP1 against Human cervical cancer cell line HeLa cells (IC50, 15 µg/mL). b, Bright field inverted light microscopy images of CP1 against HeLa cells

Table S3: Determination of Fe^{3+} in tap water

Sample	Added amount (µM)	Found (µM)	Recovery (%)	Error (%)
Tap Water	0.243	0.232	95.4	4.7
	0.476	0.453	95.1	5.0
	0.697	0.678	97.2	2.8
	0.909	0.978	107.5	7
	1.111	1.082	97.3	2.6
	1.304	1.275	97.7	2.9

Sample	Added amount (µM)	Found (µM)	Recovery (%)	Error (%)
Tap Water	0.243	0.229	94.2	6.1
	0.476	0.458	96.2	3.9
	0.697	0.682	97.8	2.1
	0.909	0.992	109.1	8.3
	1.111	1.091	98.1	1.8
	1.304	1.276	97.8	2.1

Sample	Added amount (μM)	Found (μM)	Recovery (%)	Error (%)
Tap water	0.243	0.229	94.2	6.1
	0.476	0.439	92.2	8.4
	0.697	0.652	93.5	6.9
	0.909	0.962	105.8	5.5
	1.111	1.098	98.8	1.1
	1.304	1.281	98.2	1.7

Error(%) is in the range 1.1-8.4

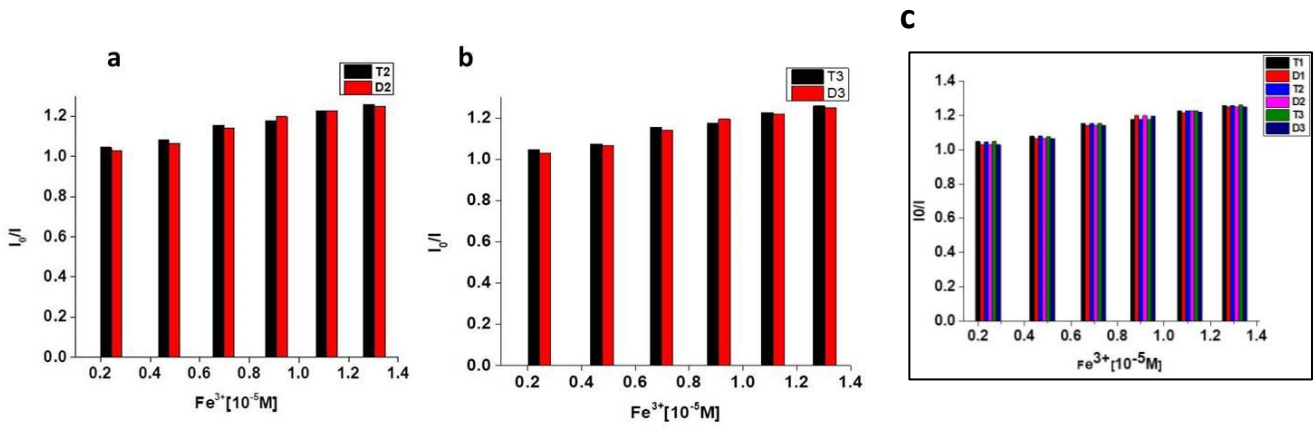


Figure S3. Repeat experiments for Fluorescence signaling of Fe^{3+} ions by **CP1** in distilled water and tap water for finding out the error range.

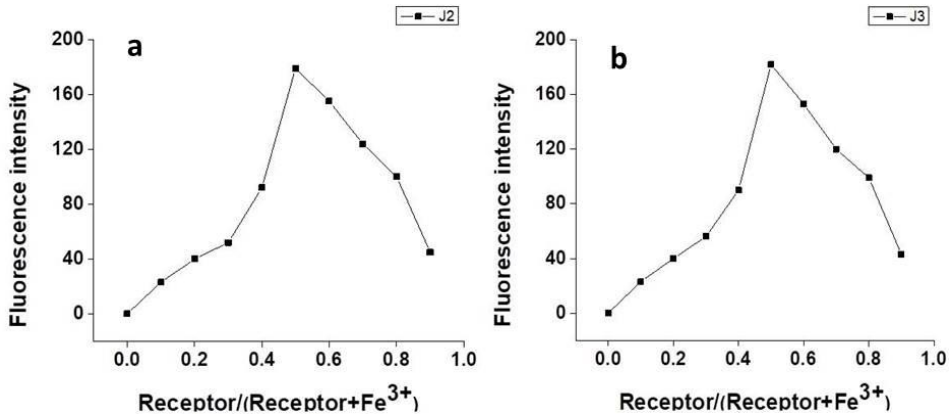


Figure S4: Repeat experiments for Job's plot for receptor Fe^{3+}