MedChemCom

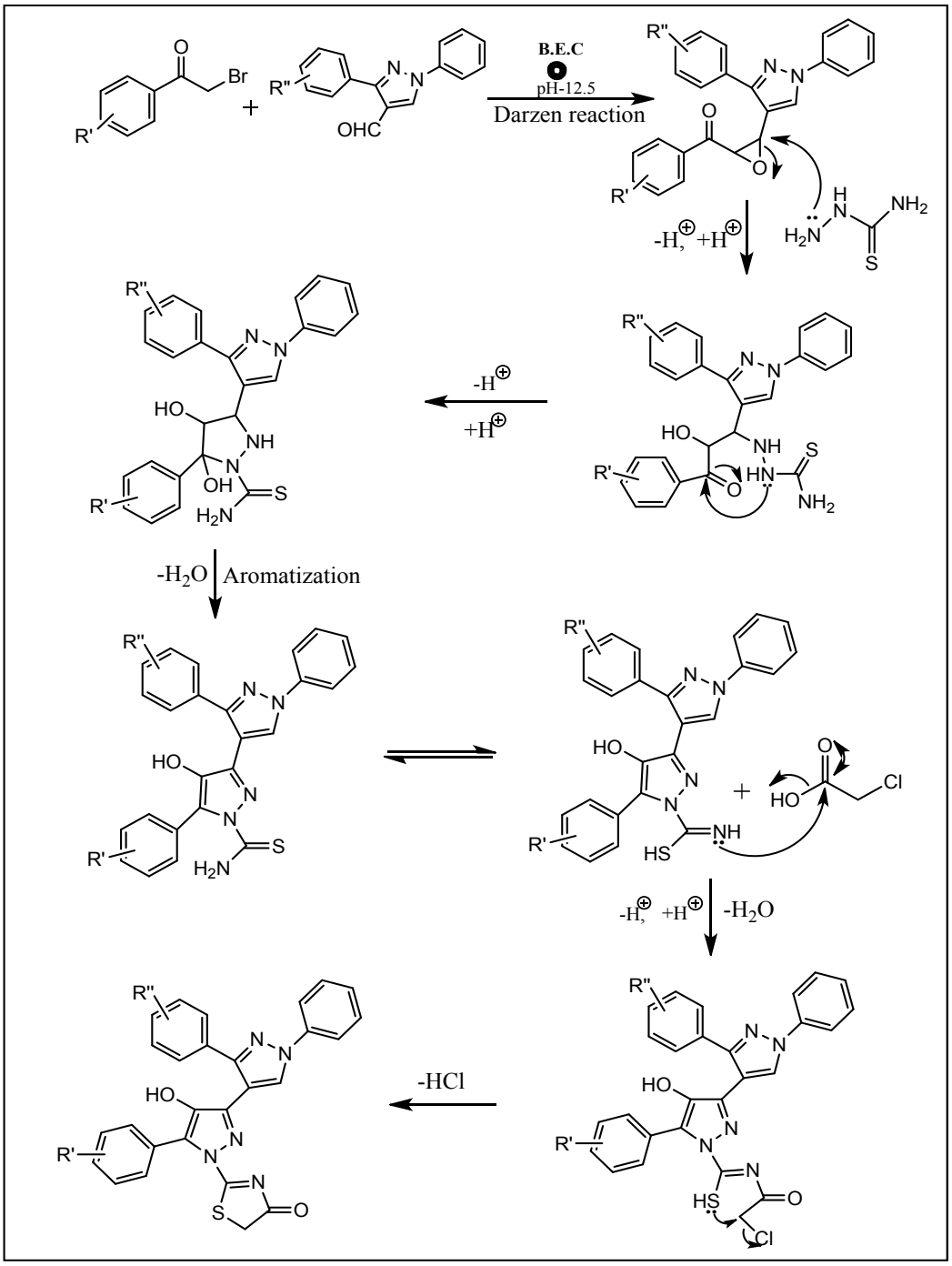
Synthesis and molecular docking studies of new series of bipyrazol-yl-thiazol-ylidene-hydrazinecarbothioamide derivatives as potential antitubercular agents

Pratima P. Mogle, Rohan J. Meshram, Shrikant V. Hese, Rahul D. Kamble, Sonali S. Kamble, Rajesh N. Gacche, Bhaskar S. Dawane*

a. *School of Chemical Sciences, Swami Ramanand Teerth Marathwada University, Nanded (MS), India 431606.*
b. *School of Life Sciences, Swami Ramanand Teerth Marathwada University, Nanded (MS), India.*

1. Chemistry

1.1 Probable mechanism for the BEC (pH-12.5) catalyzed synthesis of intermediate bipyrazol-yl-thiazol-one derivatives via Darzen reaction (**5a-r**).



1.2 Characterizations

1.2.1 2-(3'-(4-chlorophenyl)-4-hydroxy-5-(4-nitrophenyl)-1'-phenyl-1H,1'H-[3,4'-bipyrazol] -1-yl)thiazol-4(5H)-one **(5k)**

M.P. 163-165ºC; Yield, 89%; IR (KBr, cm^{-1}): 3462 (-OH), 3033 (Ar, C-H), 2855 (aliphatic, C-H), 1681 (>C=O, amidic), 1643 (-C=N), 1268 (C-S-C); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 11.32 (s, 1H, -OH), 9.18 (s, 1H, C_5-H of pyrazole), 8.48-7.42 (m, 13H, Ar-H), 4.56 (s, 2H, CH_2); EIMS: 556 [M+]; Elemental Analysis. Calculated (found) for $C_{27}H_{17}ClN_6O_4S$: % C, 58.22 (58.20); H, 3.08 (3.10); Cl, 6.37 (6.35), N, 15.09 (15.07); O, 11.49 (11.51), S, 5.76 (5.74).

1.2.2 2-(3'-(4-bromophenyl)-4-hydroxy-5-(4-nitrophenyl)-1'-phenyl-1H,1'H-[3,4'-bipyrazol]-1-yl)thiazol-4(5H)-one **(5l)**

M.P. 168-170ºC; Yield, 86%; IR (KBr, cm^{-1}): 3492 (-OH), 3013 (Ar, C-H), 2977 (aliphatic, C-H), 1686 (>C=O, amidic), 1626 (-C=N), 1265 (C-S-C); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 11.54 (s, 1H, -OH), 9.08 (s, 1H, C_5-H of pyrazole), 8.55-7.38 (m, 13H, Ar-H), 4.46 (s, 2H, CH_2); EIMS: 601 [M+]; Elemental Analysis. Calculated (found) for $C_{27}H_{17}BrN_6O_4S$: % C, 53.92 (53.90); H, 2.85 (2.83); Br, 13.29 (13.27), N, 13.97 (13.95); O, 10.64 (10.62), S, 5.33 (5.31).

1.2.3 2-(3'-(4-bromophenyl)-4-hydroxy-5-(3-nitrophenyl)-1'-phenyl-1H,1'H-[3,4'-bipyrazol]-1-yl)thiazol-4(5H)-one **(5m)**

M.P. 168-170ºC; Yield, 84%; IR (KBr, cm^{-1}): 3490 (-OH), 3010 (Ar, C-H), 2970 (aliphatic, C-H), 1688 (>C=O, amidic), 1649 (-C=N), 1246 (C-S-C); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 11.51 (s, 1H, -OH), 9.13 (s, 1H, C_5-H of pyrazole), 8.53-7.35 (m, 13H, Ar-H), 4.49 (s, 2H, CH_2); EIMS: 601 [M+]; Elemental Analysis. Calculated (found) for $C_{27}H_{17}BrN_6O_4S$: % C, 53.92 (53.90); H, 2.85 (2.83); Br, 13.29 (13.27), N, 13.97 (13.95); O, 10.64 (10.62), S, 5.33 (5.31).

1.2.4 2-(4-hydroxy-3',5-bis(4-nitrophenyl)-1'-phenyl-1H,1'H-[3,4'-bipyrazol]-1-yl) thiazol-4(5H)-one **(5n)**

M.P. 163-165ºC; Yield, 88%; IR (KBr, cm^{-1}): 3495 (-OH), 3014 (Ar, C-H), 2957 (aliphatic, C-H), 1689 (>C=O, amidic), 1637 (-C=N), 1271 (C-S-C); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 11.51 (s, 1H, -OH), 9.04 (s, 1H, C_5-H of pyrazole), 8.54-7.46 (m, 13H, Ar-H), 4.47 (s, 2H, CH_2); EIMS: 567 [M+]; Elemental Analysis. Calculated (found) for $C_{27}H_{17}N_7O_6S$: % C, 57.14 (57.12); H, 3.02 (3.00); N, 17.28 (17.30); O, 16.91 (16.93); S, 5.65 (5.63).

1.2.5 2-(4-hydroxy-3'-(3-nitrophenyl)-5-(4-nitrophenyl)-1'-phenyl-1H,1'H-[3,4'-bipyrazol]-1-yl) thiazol-4(5H)-one **(5o)**

M.P. 167-169ºC; Yield, 88%; IR (KBr, cm^{-1}): 3491 (-OH), 3011 (Ar, C-H), 2952 (aliphatic, C-H), 1687 (>C=O, amidic), 1640 (-C=N), 1256 (C-S-C); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 11.48 (s, 1H, -OH), 9.16 (s, 1H, C_5-H of pyrazole), 8.51-7.45 (m, 13H, Ar-H), 4.48 (s, 2H, CH_2); EIMS: 567 [M+]; Elemental Analysis. Calculated (found) for $C_{27}H_{17}N_7O_6S$: % C, 57.14 (57.12); H, 3.02 (3.00); N, 17.28 (17.30); O, 16.91 (16.93); S, 5.65 (5.63).

1.2.6 2-(4-hydroxy-3',5-bis(3-nitrophenyl)-1'-phenyl-1H,1'H-[3,4'-bipyrazol]-1-yl) thiazol-4(5H)-one **(5p)**

M.P. 169-171ºC; Yield, 89%; IR (KBr, cm^{-1}): 3493 (-OH), 3013 (Ar, C-H), 2955 (aliphatic, C-H), 1691 (>C=O, amidic), 1635 (-C=N), 1260 (C-S-C); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 11.56 (s, 1H, -OH), 9.18 (s, 1H, C_5-H of pyrazole), 8.57-7.50 (m, 13H, Ar-H), 4.45 (s, 2H, CH_2); EIMS: 567 [M+]; Elemental Analysis. Calculated (found) for $C_{27}H_{17}N_7O_6S$: % C, 57.14 (57.12); H, 3.02 (3.00); N, 17.28 (17.30); O, 16.91 (16.93); S, 5.65 (5.63).

1.2.7 2-(4-hydroxy-5-(3-nitrophenyl)-3'-(4-nitrophenyl)-1'-phenyl-1H,1'H-[3,4'-bipyrazol]-1-yl) thiazol-4(5H)-one **(5q)**

M.P. 171-173ºC; Yield, 88%; IR (KBr, cm^{-1}): 3489 (-OH), 3017 (Ar, C-H), 2963 (aliphatic, C-H), 1689 (>C=O, amidic), 1629 (-C=N),1250 (C-S-C); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm):

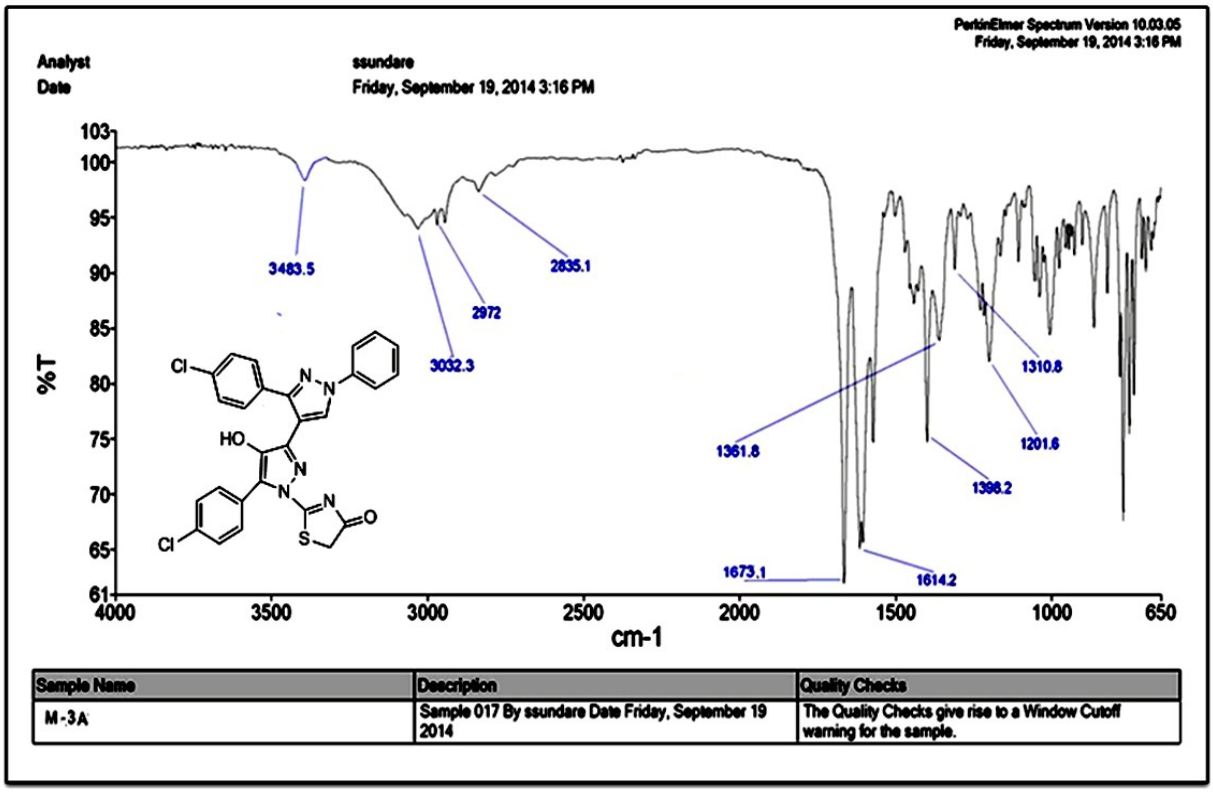
11.59 (s, 1H, -OH), 9.28 (s, 1H, C_5-H of pyrazole), 8.55-7.50 (m, 13H, Ar-H), 4.41 (s, 2H, CH_2); EIMS: 567 [M+]; Elemental Analysis. Calculated (found) for $C_{27}H_{17}N_7O_6S$: % C, 57.14 (57.12); H, 3.02 (3.00); N, 17.28 (17.30); O, 16.91 (16.93); S, 5.65 (5.63).

1.2.8 2-(3',5-bis(4-bromophenyl)-4-hydroxy-1'-phenyl-1H,1'H-[3,4'-bipyrazol]-1-yl) thiazol-4(5H)-one **(5r)**

M.P. 173-175ºC; Yield, 80%; IR (KBr, cm^{-1}): 3478 (-OH), 3038 (Ar, C-H), 2966 (aliphatic, C-H), 1690 (>C=O, amidic), 1620 (-C=N), 1277 (C-S-C); ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 11.40 (s, 1H, -OH), 9.21 (s, 1H, C_5-H of pyrazole), 8.58-7.45 (m, 13H, Ar-H), 4.51 (s, 2H, CH_2); EIMS: 635 [M+]; Elemental Analysis. Calculated (found) for $C_{27}H_{17}Br_2N_5O_2S$: % C, 51.04 (51.02); H, 2.70 (2.68); Br, 25.15(25.17); N, 11.02 (11.00); O, 5.04 (5.02), S, 5.05 (5.03).

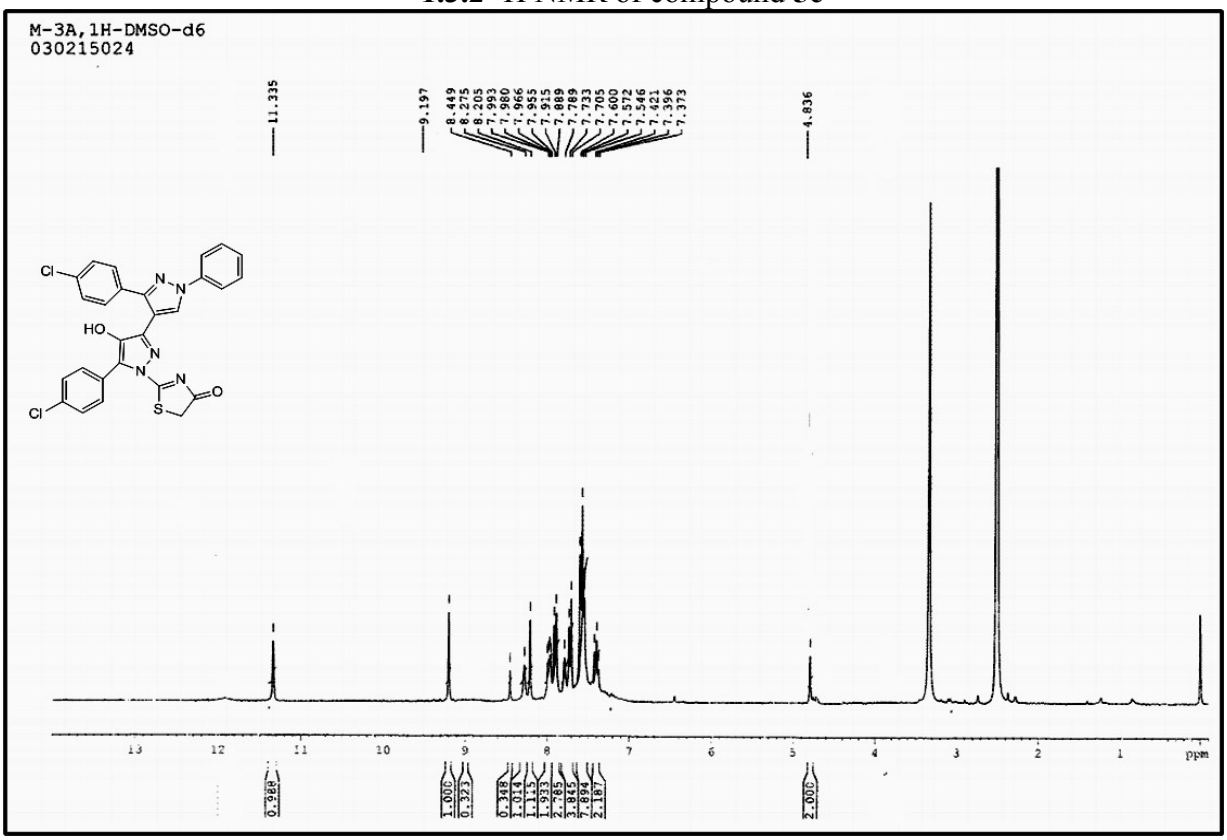
1.3 IR, ^{1}H NMR, ^{13}C NMR, Mass spectrum of synthesized derivatives

1.3.1 IR of compound **5c**

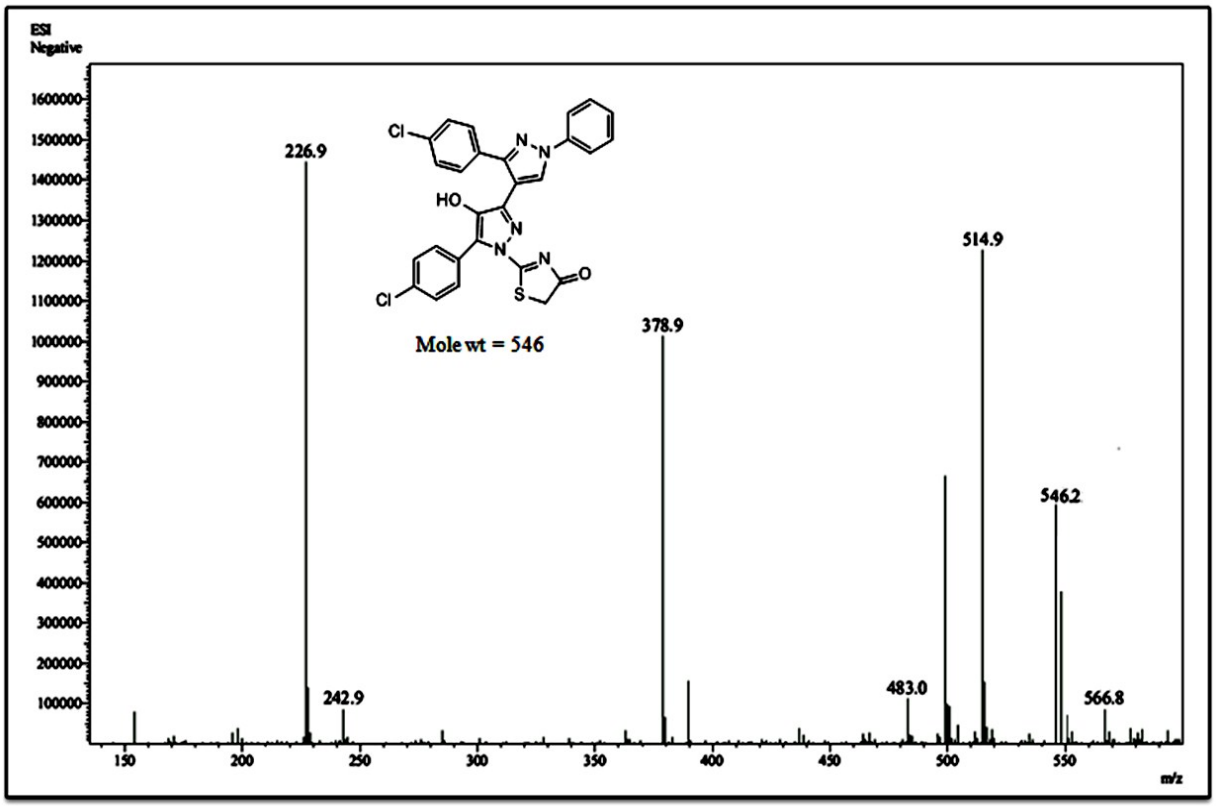


Sample Name	Description	Quality Checks
M-3A	Sample 017 By ssundare Date Friday, September 19 2014	The Quality Checks give rise to a Window Cutoff warning for the sample.

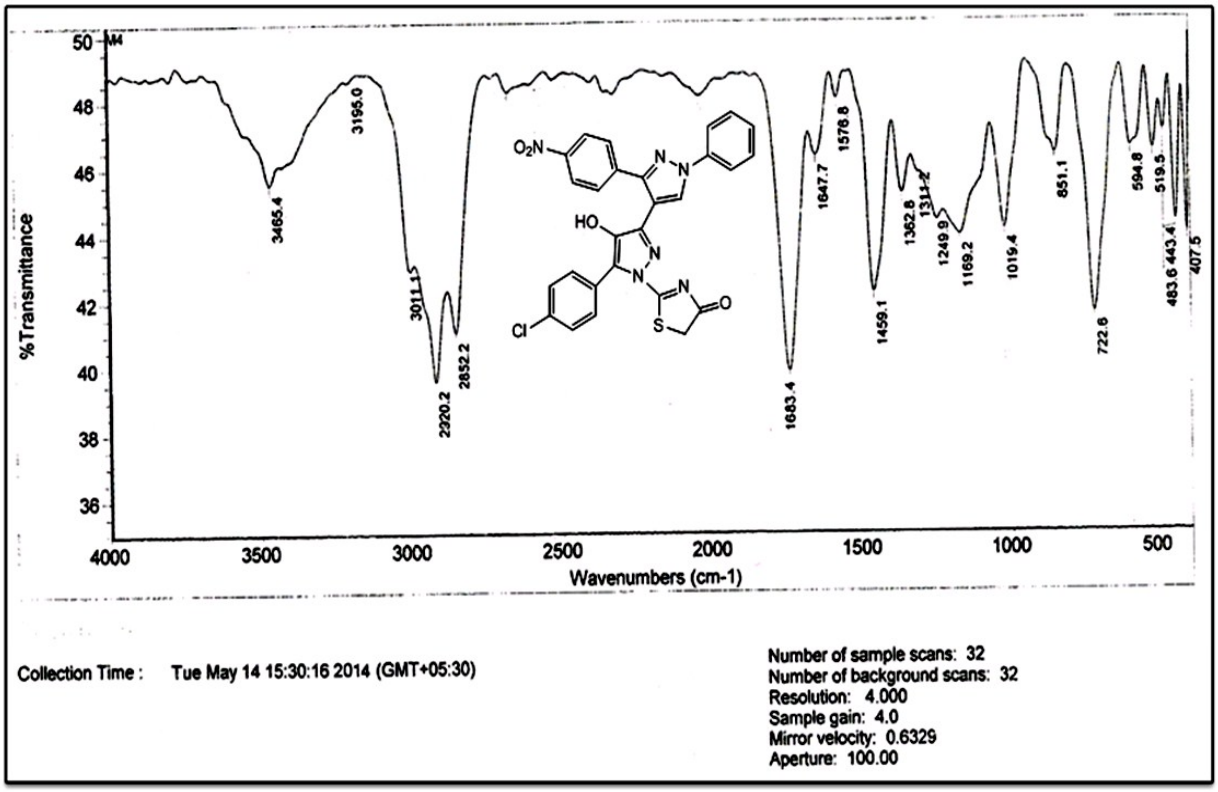
1.3.2 ^{1}H NMR of compound **5c**



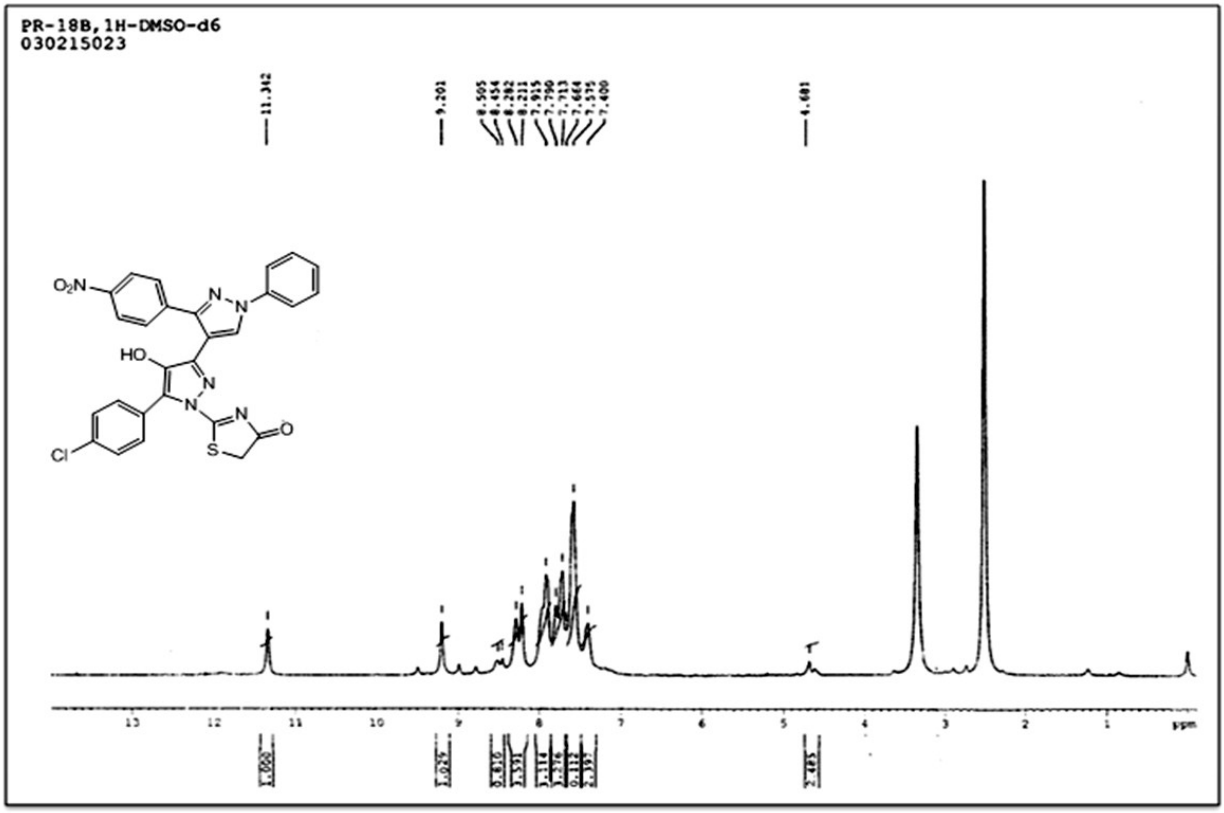
1.3.3 Mass of compound **5c**



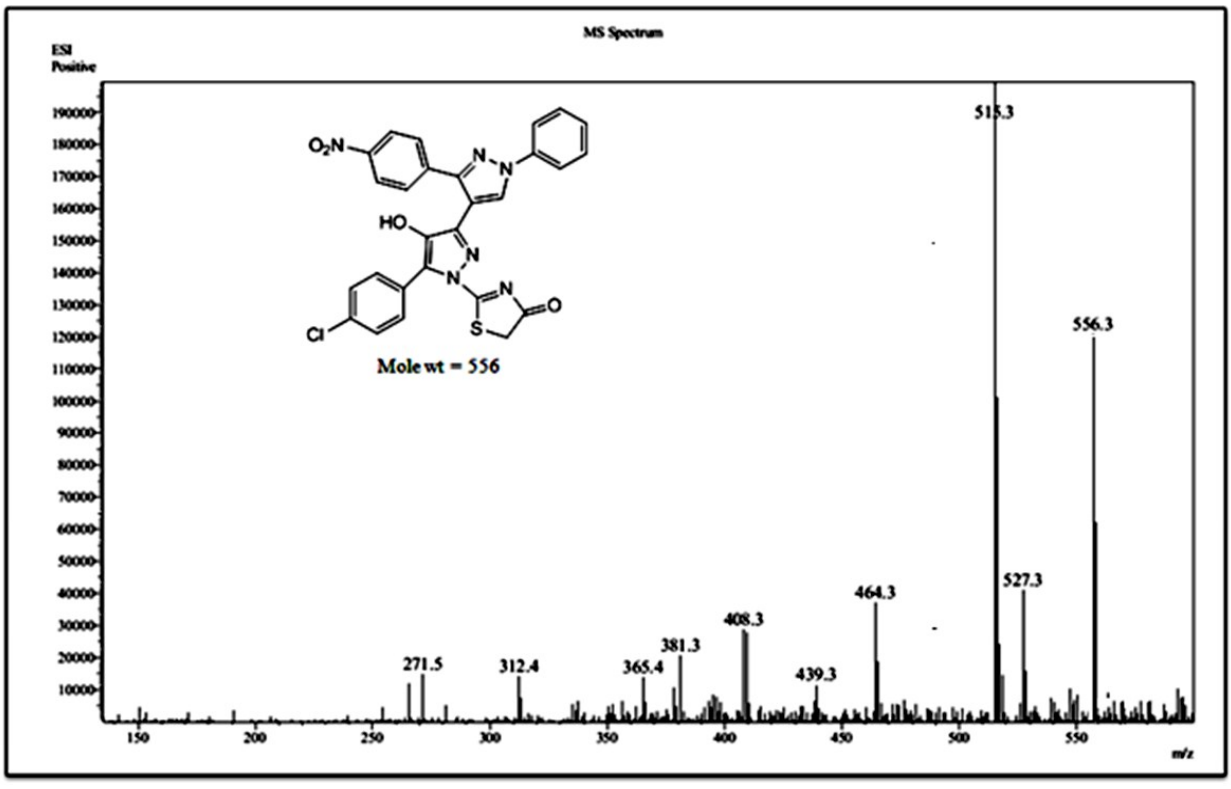
1.3.4 IR of compound **5e**



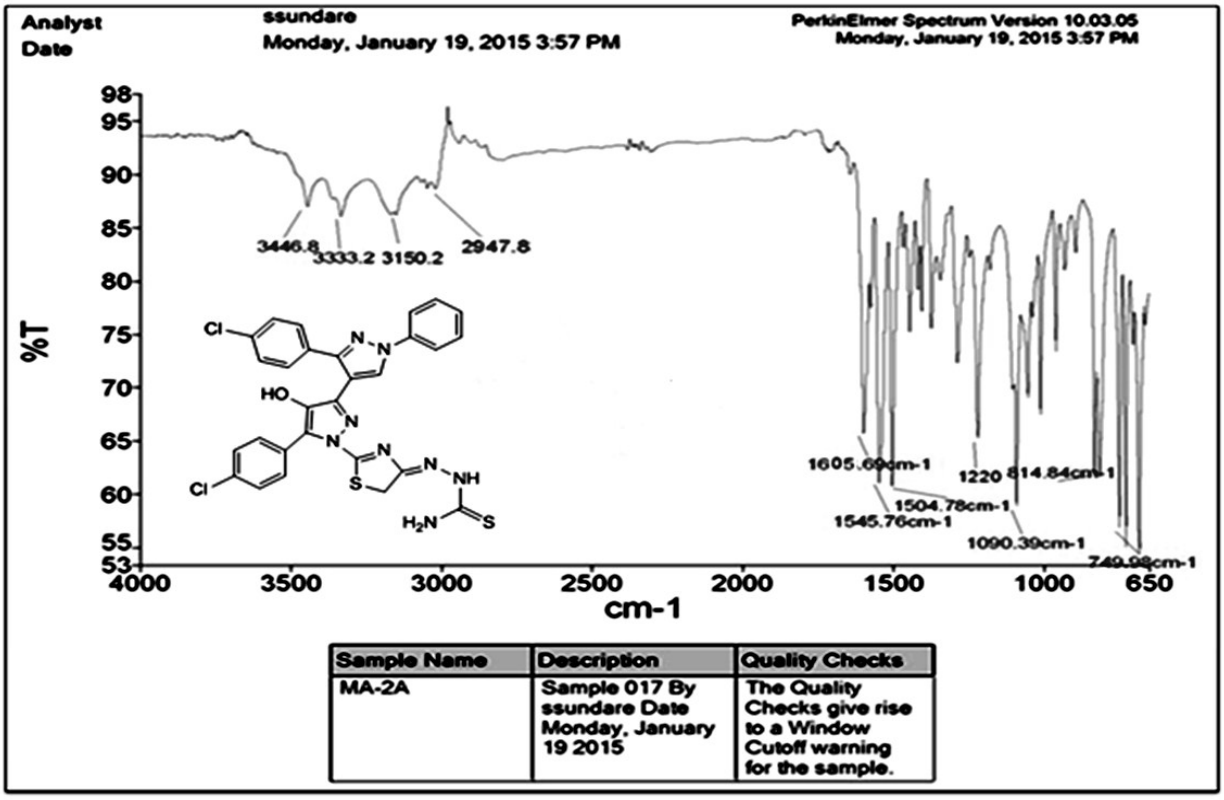
1.3.5 ^{1}H NMR of compound **5e**



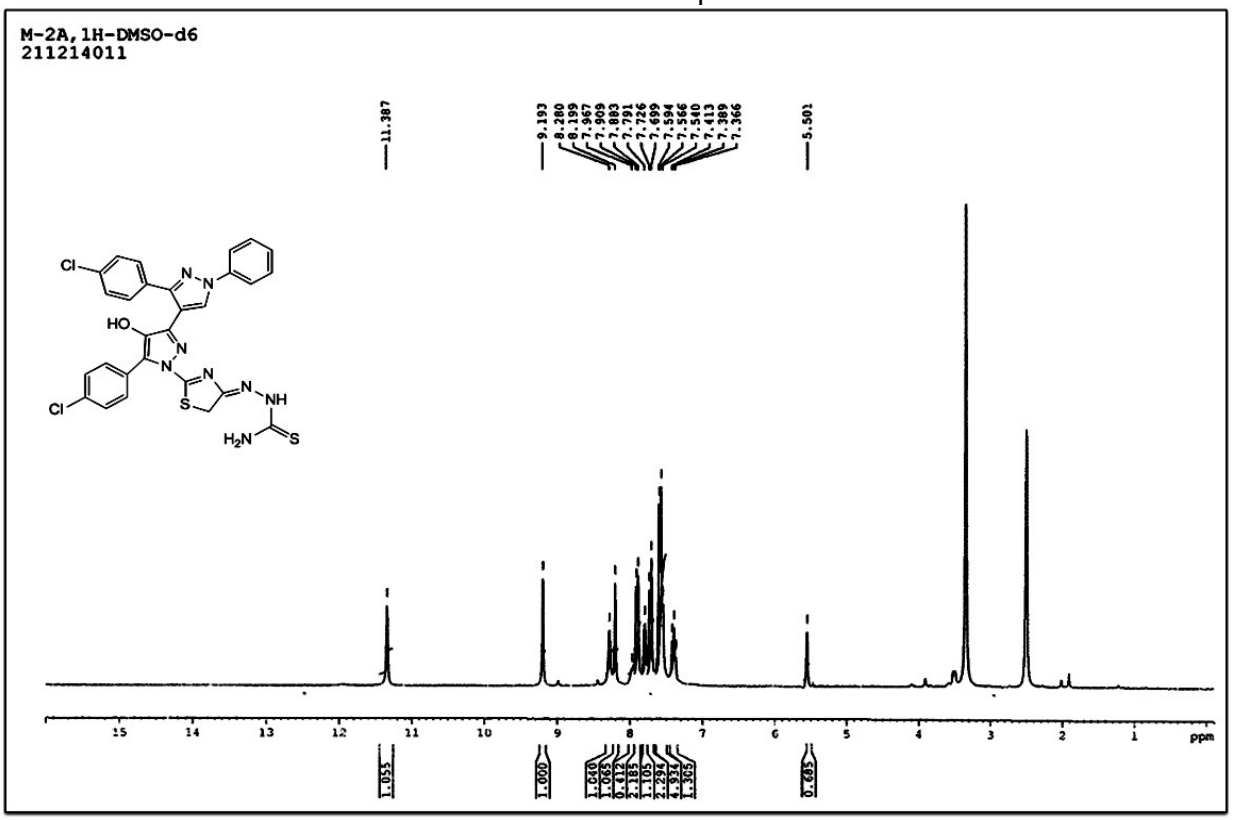
1.3.6 Mass of compound **5e**



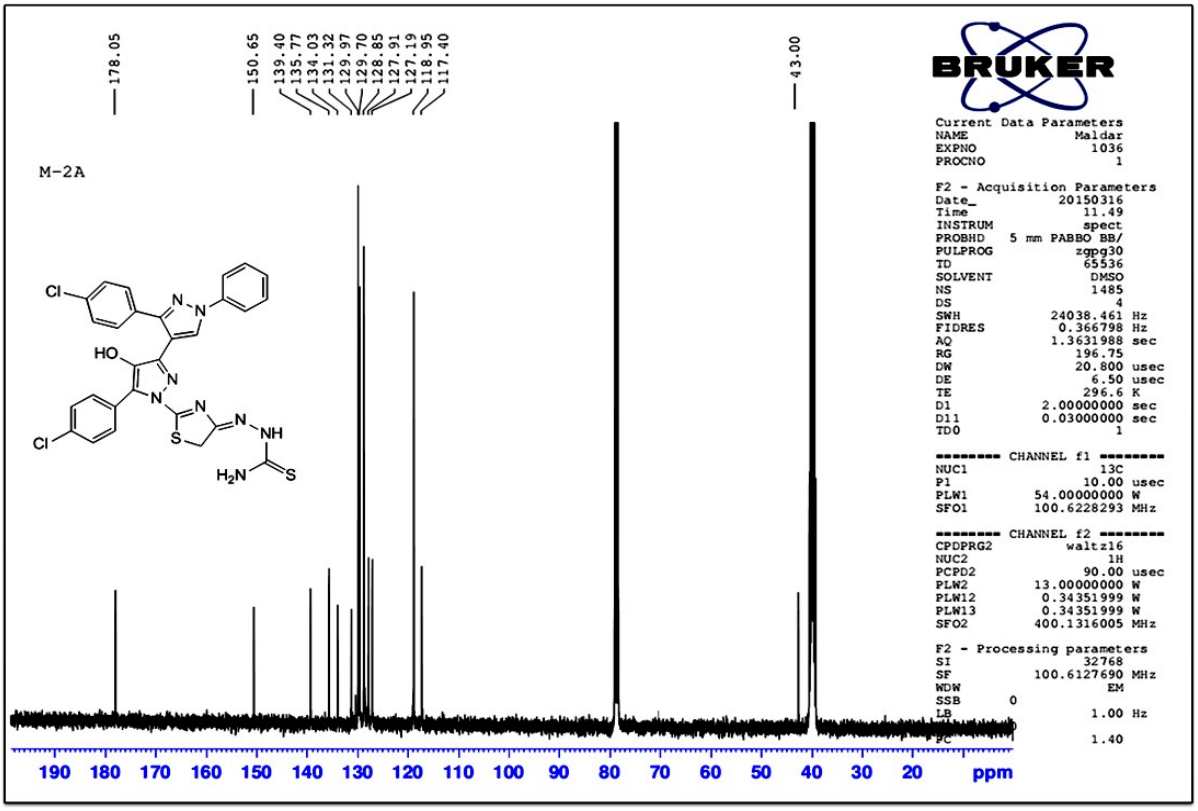
1.3.7 IR of compound **6c**



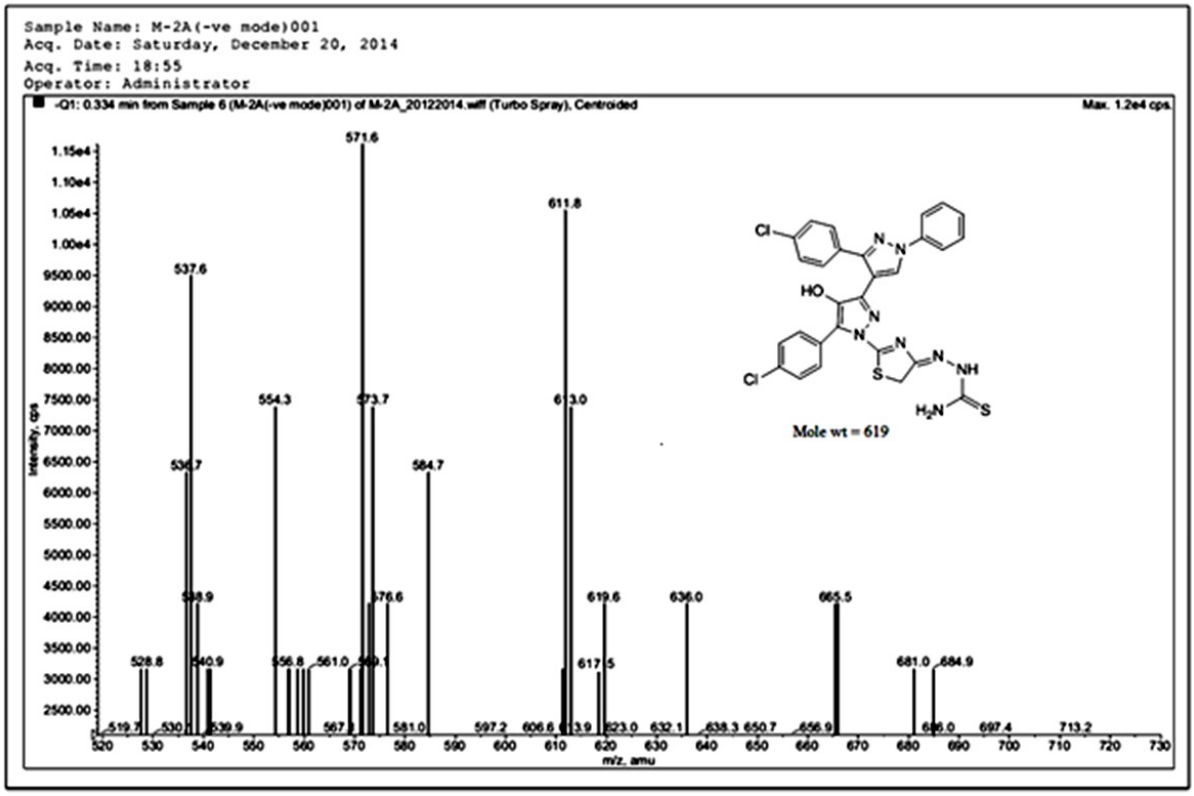
1.3.8 ^{1}H NMR of compound **6c**



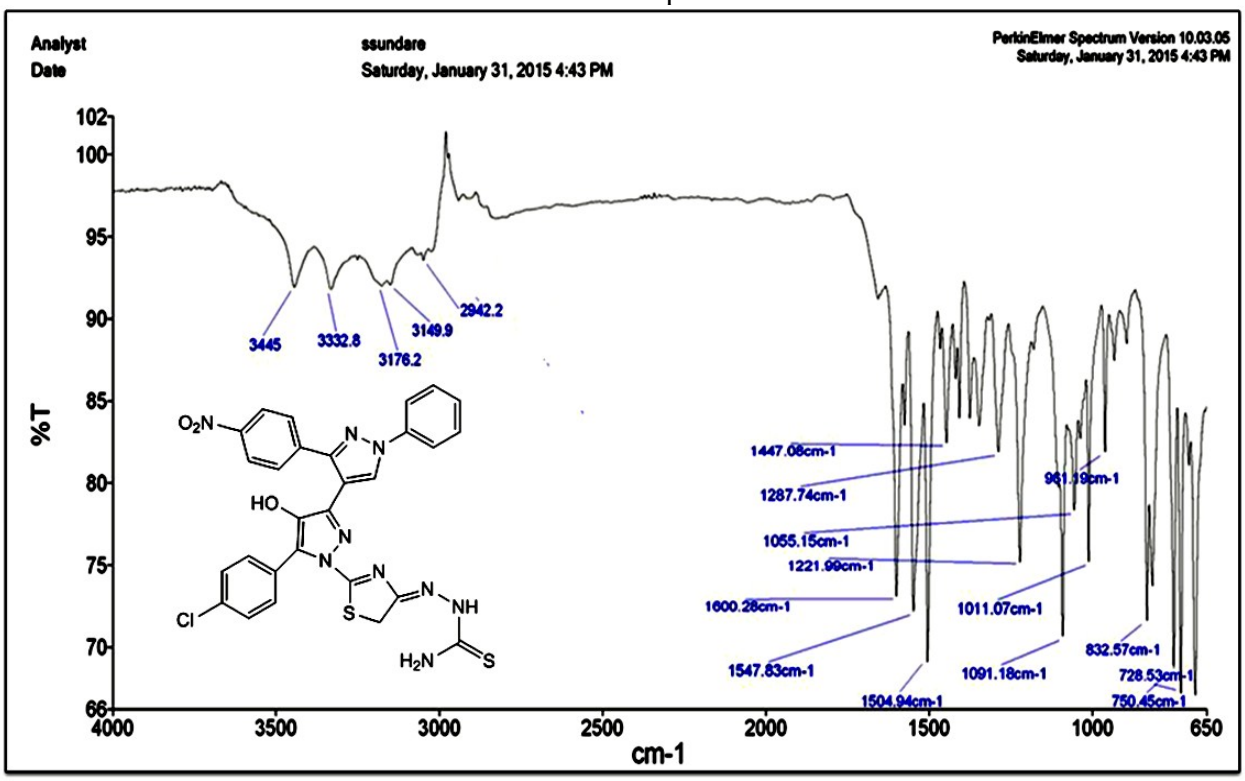
1.3.9 ^{13}C NMR of compound **6c**



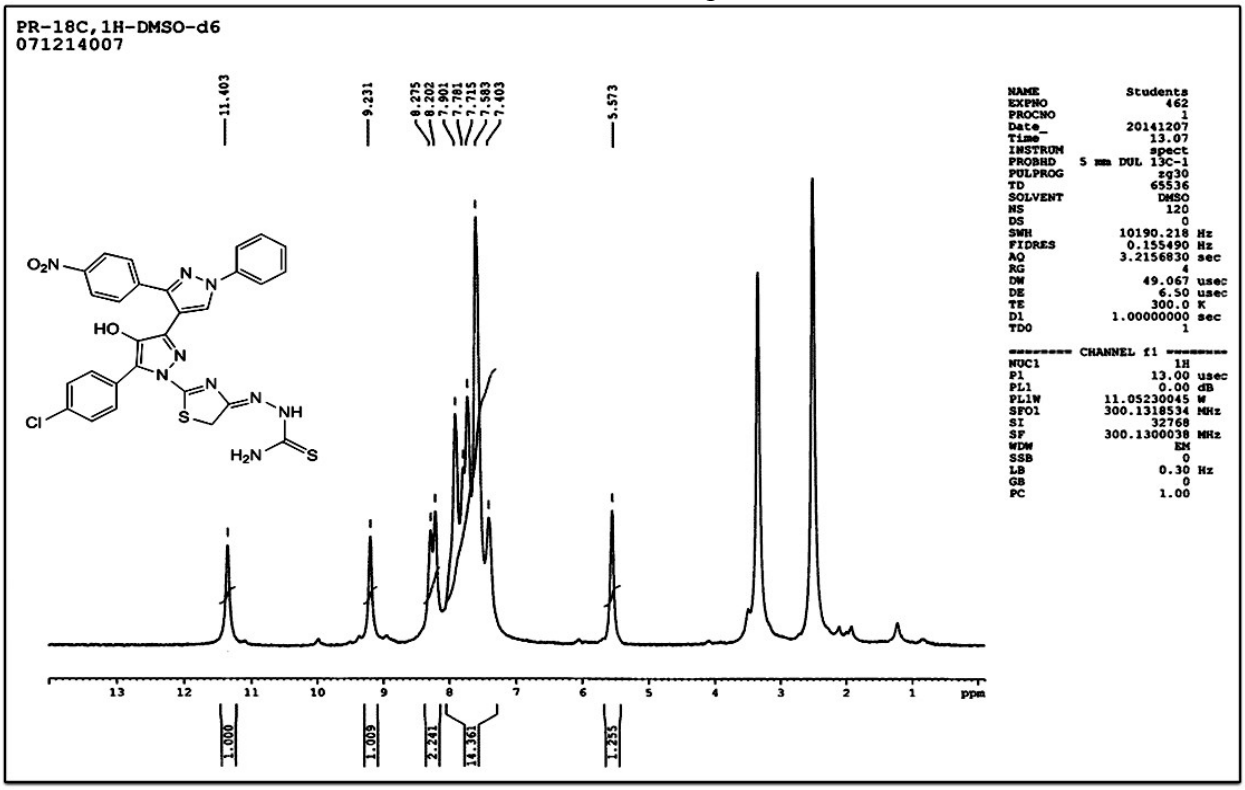
1.3.10 Mass of compound **6c**



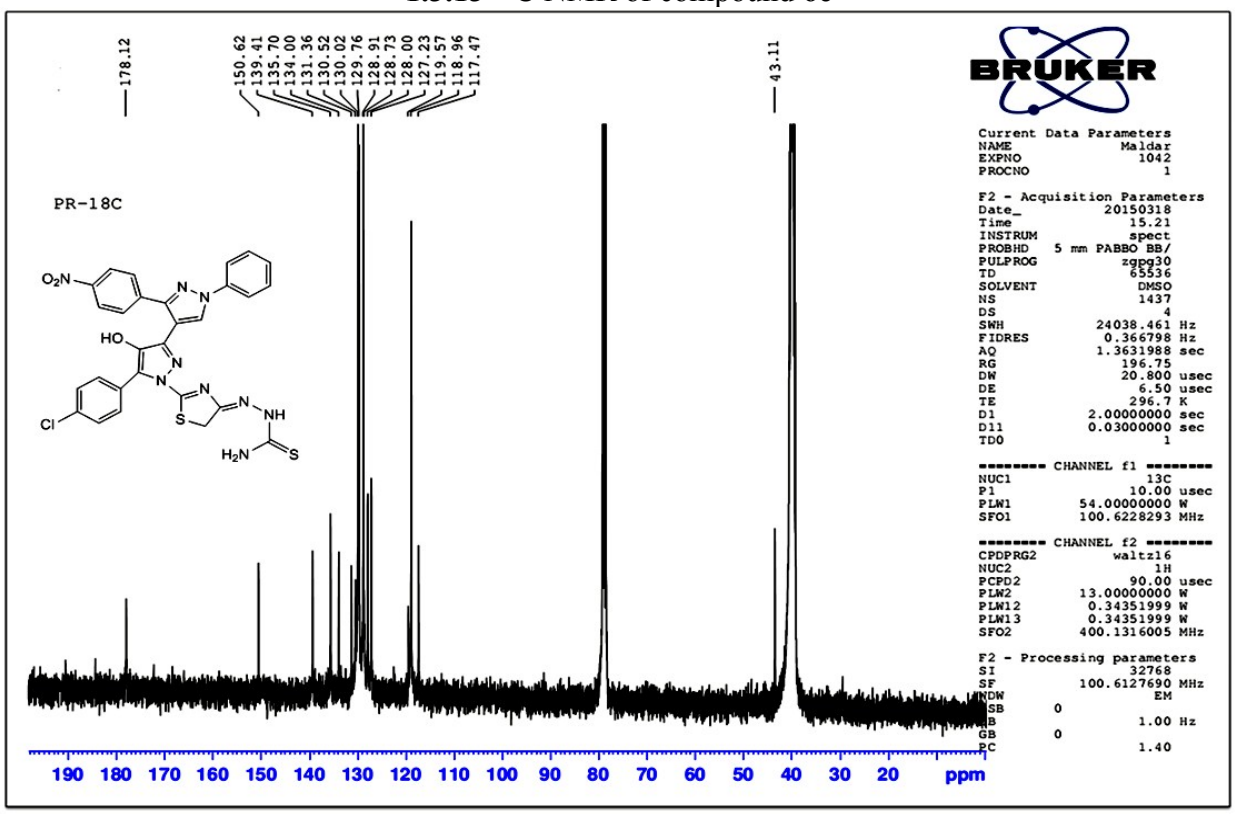
1.3.11 IR of compound **6e**



1.3.12 ^{1}H NMR of compound **6e**



1.3.13 ^{13}C NMR of compound **6e**



1.3.14 MASS of compound **6e**