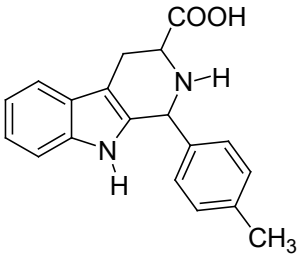
# Supporting Information

## Scheme 1-

**General procedure and spectroscopic data for the preparation of 1-(p-tolyl)-2, 3, 4, 9-tetrahydro-β-carboline-3-carboxylic acid (A-1; $C_{19}H_{18}N_2O_2$)**

A mixture of L-tryptophan (10.2 g, 50 mmol), acetic acid (200 ml) and aldehyde (55 mmol, p-tolualdehyde) was stirred at room temperature on magnetic stirrer for 2 hours. After stirring, it was refluxed for 5 hours on a water bath, then cooled and adjusted to pH 5 with ammonium hydroxide solution. The precipitated product was collected by filtration and washed well with water, then dried and completion of reaction was checked by TLC.

**A-1**

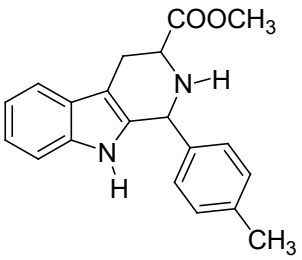



M.P.: 258-260ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3406.26 (O-H Str.), 3332.02 (N-H Str.), 3082.32 (Ar-C-H Str.), 2904.13 (C-H Str.), 1651.50 (C=O Str.), 1457.25 (C=C ring Str.), 1322.32 (C-N Str.), 1102.22 (C-C Str.), 790.52 (C-H out of plane bending vibration).

**General procedure for the preparation of Methyl 1-(*p*-tolyl)-2, 3, 4, 9-tetrahydro-β-carboline-3-carboxylate (A-2; $C_{20}H_{20}N_2O_2$)**

To a solution of the corresponding 1-(p-tolyl)-2, 3, 4, 9-tetrahydro-β-carboline-3-carboxylic acid (20 mmol) in methanol (500 ml), $SOCl_2$ (20 ml) was added drop wise with cooling and stirred at room temperature for 1 hour, then heated at reflux for 5 hours, evaporated in reduced pressure. The resulting mixture was poured onto water (200 ml), and extracted with ethyl acetate (3 × 200 ml). The completion of reaction was established by single spot by TLC on silica gel G plates using the solvent system n-hexane: ethyl acetate in the ratio of (9:1). The organic phase was washed with water and brine, then dried over anhydrous sodium sulfate, filtered and evaporated.

**A-2**

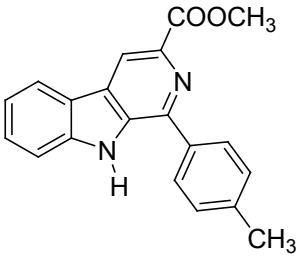



M.P. = 260-262ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3408.13, 3132.32 (N-H Str.), 3062.43 (Ar-C-H Str.), 2860.36 (C-H Str.), 1655.25 (C=O Str.), 1472.12 (C=C ring Str.), 1325.13 (C-N Str.), 1106.42 (C-C Str.), 798.15 (C-H out of plane bending vibration).

**General procedure for the preparation of Methyl 1-(p-tolyl)-β-carboline-3-carboxylate (A-3; $C_{20}H_{16}N_2O_2$)**

In a round bottom flask equipped with a reflux condenser, a suspension of the corresponding Methyl 1-(*p*-tolyl)-2, 3, 4, 9-tetrahydro-β-carboline-3-carboxylate (10 mmol) and sulfur (25 mmol) in xylene (200 ml) was heated at reflux on a water bath for 6 hours, then cooled and stored at 4 °C for 3 hours, and then filtered and washed generously with petroleum ether (40-60°C), the solid was dried and crystallized from ethyl acetate.

**A-3**



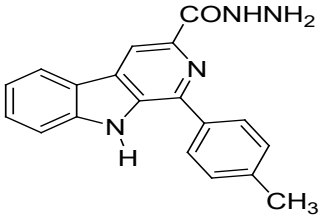

M.P. = 263-265ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3330.16 (N-H Str.), 3076.14 (Ar-C-H Str.), 2868.23 (C-H Str.), 1674.52 (C=O Str.), 1498.32 (C=C ring Str.), 1612.35 (Pyr-C=N str.), 1327.13 (C-N Str.), 794.15. (C-H out of plane bending vibration).

**General procedure for the preparation of 1-*p*-tolyl-β-carboline-3-carbohydrazide (A-4; $C_{19}H_{16}N_4O$)**

In a round bottom flask, intermediate compound (10 mmol) was dissolved in ethanol (100 ml) and hydrazine hydrate (15 ml) was added and the mixture was refluxed for 6 hours.

The reaction mixture was cooled and the precipitate was collected by filteration and washed with ethanol. The solid was recrystalized from ethanol.

**A-4**

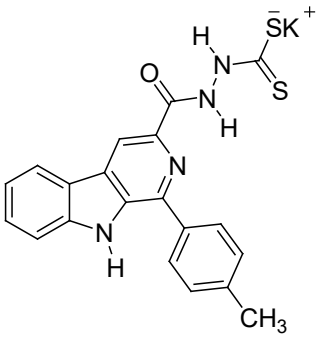



M.P. = 268-270ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3410.23, 3350.16 (N-H Str.), 3067.24 (Ar-C-H Str.), 2878.13 (C-H Str.), 1674.54 (C=O Str.), 1492.13 (C=C ring Str.), 1622.53 (Pyr-C=N str.), 1332.33 (C-N Str.), 802.61 (C-H out of plane bending vibration).

**General method for synthesis of 1-*p*-tolyl-β-carboline-3-potassiumdithiocarbohydrazide (A-5; $C_{20}H_{15}KN_4OS_2$)**

Potassium hydroxide (10 mmol) was dissolved in absolute ethanol (100 ml). The solution was cooled in ice bath and 1-*p*-tolyl-β-carboline-3-carbohydrazide (10 mmol) was added with stirring. To this carbon disulphide (10 mmol) was added in small portions with constant stirring. The reaction mixture was agitated continuously for 4 hours at room temperature. The mixture was refluxed for 8 hours and then cooled; the precipitated product was collected by filtration, washed with anhydrous ether (100 ml) and dried. The 1-*p*-tolyl-β-carboline-3-potassiumdithiocarbohydrazide was thus obtained.

**A-5**




M.P. = 325-327ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3412.52, 3180.14 (N-H Str.), 3069.72 (Ar-C-H Str.), 2875.61 (C-H Str.), 1654.55 (C=O Str.), 1490.61 (C=C ring Str.), 1624.75 (Pyr-C=N str.), 1322.63 (C-N Str.), 1346.24, 1235.46 (C=S Str.), 805.66 (C-H out of plane bending).

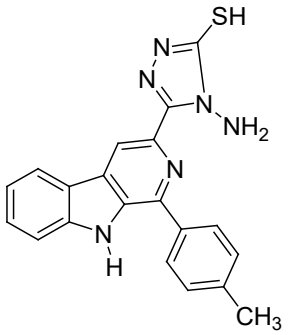
**General method for synthesis of 1-(p-tolyl)-3-(4-amino-5-thiol-1, 2, 4-triazol-3-yl) β-carboline (1; $C_{20}H_{16}N_6S$)**

In a round bottom flask equipped with a reflux condenser, a suspension of 1-*p*-tolyl-β-carboline-3-potassiumdithiocarbohydrazide (10 mmol) and hydrazine hydrate (99%, 20 ml) was refluxed for 18-20 hours with occasional shaking. The colour of the reaction mixture changed to green with the evolution of hydrogen sulfide gas. A homogenous reaction mixture was obtained during the reaction process. The reaction mixture was cooled to room temperature and diluted with cold water (20 ml). On acidification with concentrated hydrochloric acid the required 1-(p-tolyl)-3-(4-amino-5-thiol-1, 2, 4-triazol-3-yl) β-carboline was precipitated out. It was filtered, washed thoroughly with cold water, dried and recrystallized from ethanol. Purity of the compound was checked by TLC using silica gel-G coated plates by using toluene: ethyl acetate: formic acid in the ratio of (5:4:1) as solvent system, and observed in UV light.

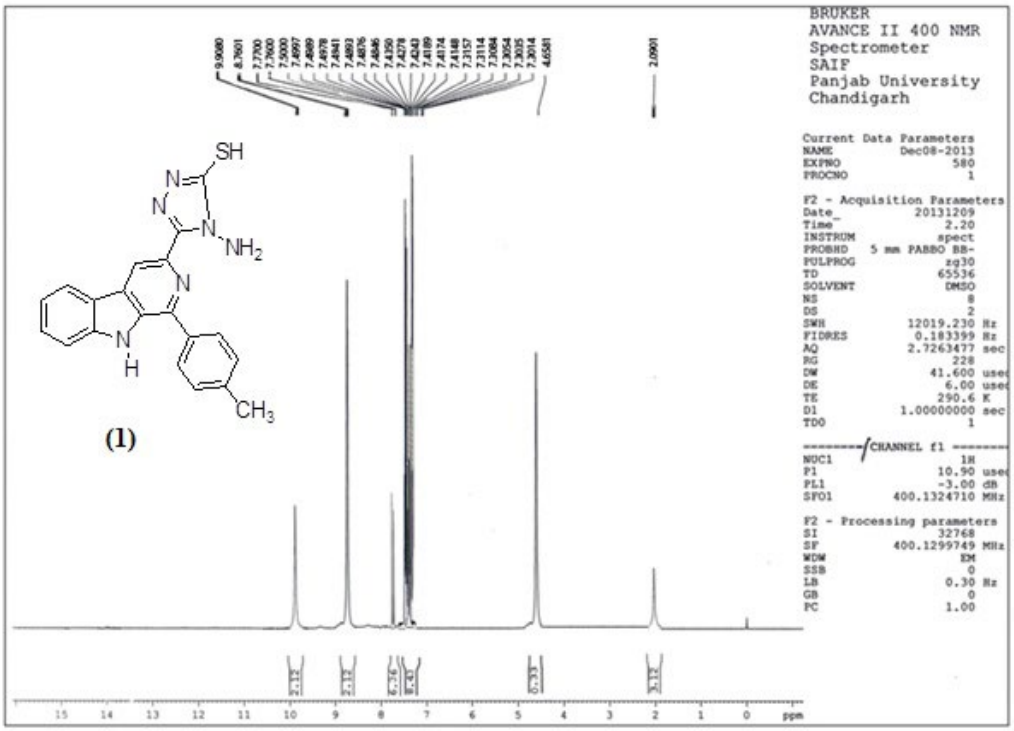
M.P. = 360-362ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3354.56, 3132.23 (N-H Str.), 3087.20 (Ar-C-H Str.), 2901.35 (C-H Str. Asym.), 2761.21 (C-H Str. sym.), 2551.10 (S-H str.), 1592.57, 1622.55 (1, 2, 4-triazole C=N; Pyr-C=N str.), 1518.98, 1454.56 (C=C ring str.), 1328.59 (C-N str.), 1248.90 (N-N str. of triazole), 731.55 (C-H out of plane bending); $^1$H NMR (400 MHz, DMSO-$d^6$): δ = 7.32-7.70 (m, ArH), 4.66 (s, 2H, $-NH_2$), 8.76 (s, N-H of pyrrole), 9.91 (s, H, S-H), 2.09 (s, $CH_3$) ppm; $^{13}$C NMR (100 MHz, DMSO-$d^6$): δ = 25.32 ($CH_3$ aliphatic), 123.15, 123.42, 124.40, 124.75, 125.21, 125.73, 126.29, 127.72, 128.48, 128.70, 128.92, 129.20, 129.60, 130.01, 130.12, 130.69, 157.91, 163.45, 172.94 (19 ArC's) ppm; MS (EI) m/z: 372.2 ($M^+$); CHN analysis: 64.43 (C), 4.22 (H), 22.48 (N).

**NMR and MS Spectra of Compound 1**

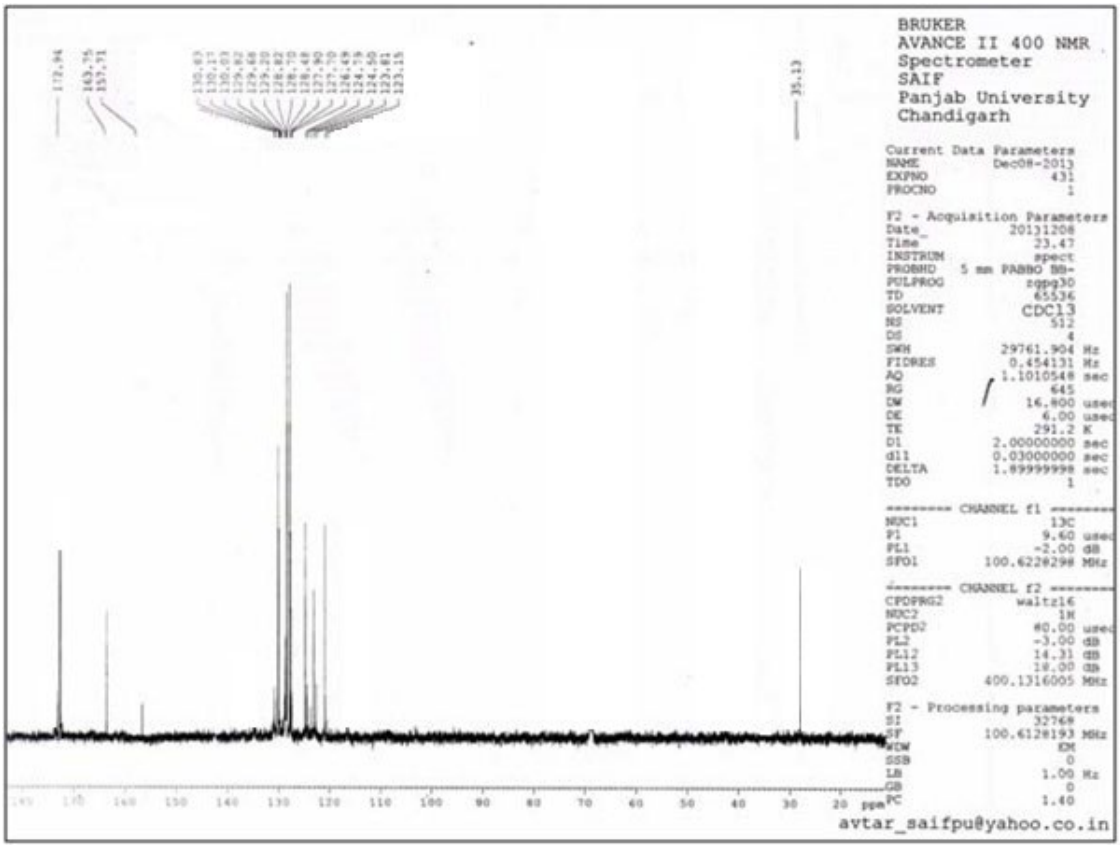
**1**



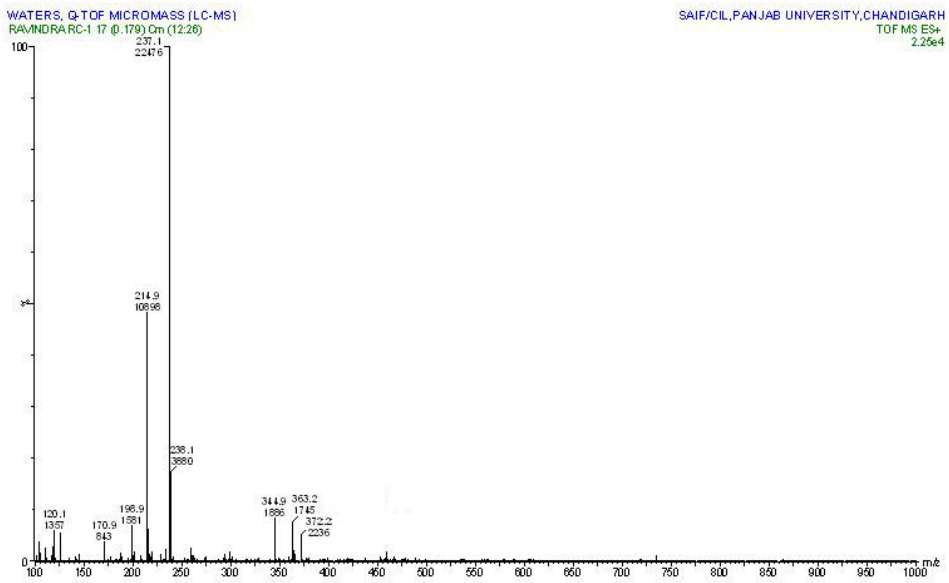
**$^{1}$HNMR**




**$^{13}$CNMR**



**MS**

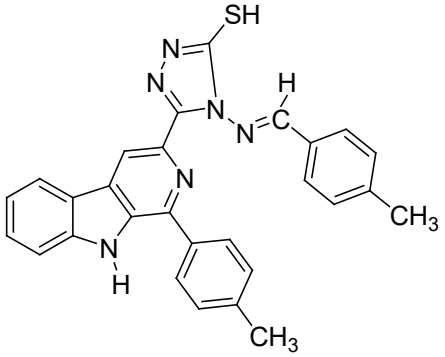



**General procedure for synthesizing Compounds 2-5 from compound 1**

A solution of 1-(p-tolyl)-3-(4-amino-5-thiol-1, 2, 4-triazol-3-yl) β-carboline (5 mmol) in glacial acetic acid (5 ml) was allowed to react with the appropriate aldehydes (5 mmol) under reflux for 5 hours. The reaction mixture was then cooled and the precipitated derivatives were filtered out, washed with water and dried. Completion of reaction was checked by TLC and recrystallized from ethanol to afford the desired compounds. The crude product was purified by column chromatography on silica gel using suitable solvent system.

**1-(p-tolyl)-3-(4-(p-tolylmethanimine)-5-thio-1, 2, 4-triazol-3-yl) β-carboline (2; $C_{28}H_{22}N_6S$)**

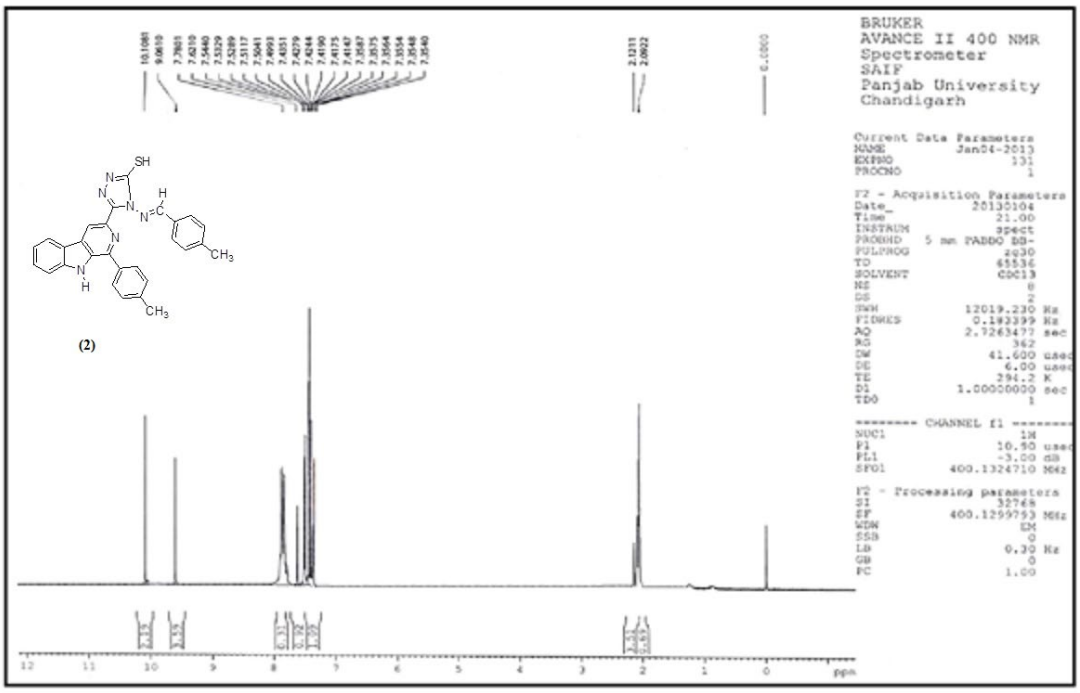
**2**



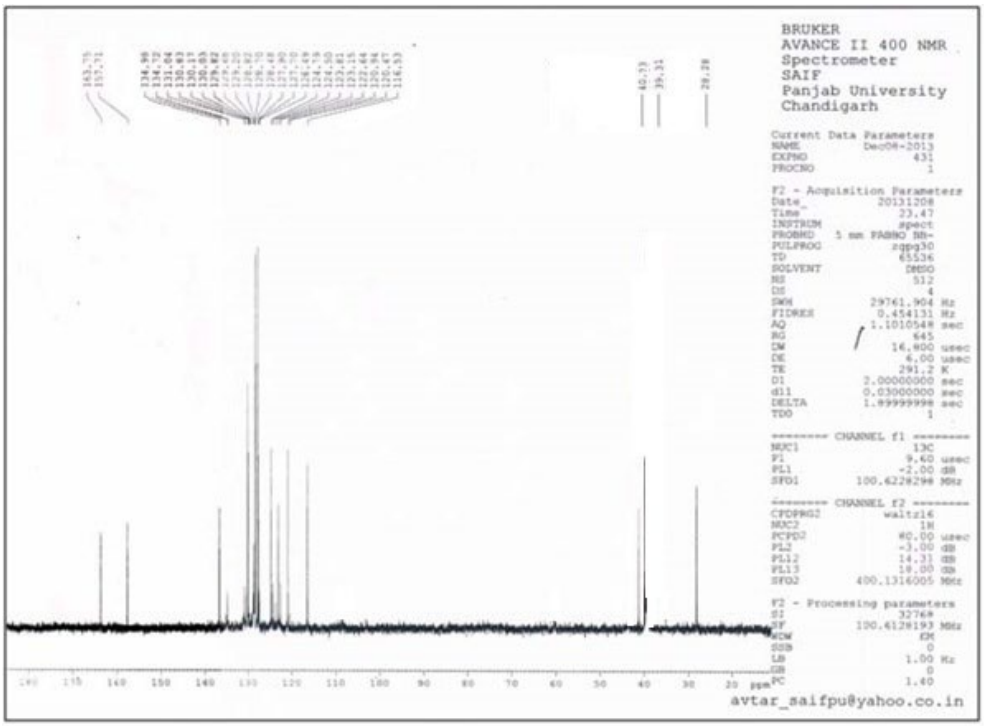
M.P. = 368-370ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3348.46 (N-H str.), 3085.32 (Ar-C-H str.), 2921.15 (C-H str. Asym.), 2841.28 (C-H str. Sym.), 2542.31 (S-H str.), 1587.46, 1628.67 (1, 2, 4-triazole C=N; Pyr-C=N str.), 1582 (N=CH str.), 1528.14, 1452.26 (C=C ring str.), 1308.59 (C-N str.), 1242.59 (N-N str. of triazole), 738.74 (C-H out of plane bending); $^{1}H$ NMR (400 MHz, DMSO-$d^6$): δ = 7.35-7.62 (m, ArH), 9.06 (s, N-H of pyrrole), 10.11 (s, H, S-H), 2.09 (s, $CH_3$), 2.12 (s, $CH_3$), 7.78 (s, H, -N=CH) ppm; $^{13}C$ NMR (100 MHz, DMSO-$d^6$): δ = 29.28 ($CH_3$ aliphatic), 39.31 ($CH_3$ aliphatic), 40.79 (CH aliphatic), 116.33, 120.47, 120.94, 121.79, 122.64, 123.06, 123.56, 124.15, 124.64, 124.79, 125.32, 126.69, 127.70, 127.90, 128.92, 129.02, 129.48, 129.93, 130.03, 130.47, 131.04, 134.72, 134.90, 157.71, 163.75 (25 ArC's) ppm; MS (EI) m/z: 474.8 ($M^+$); CHN analysis: 70.80 (C), 4.56 (H), 17.63 (N).

**NMR and MS Spectra of Compound 2**

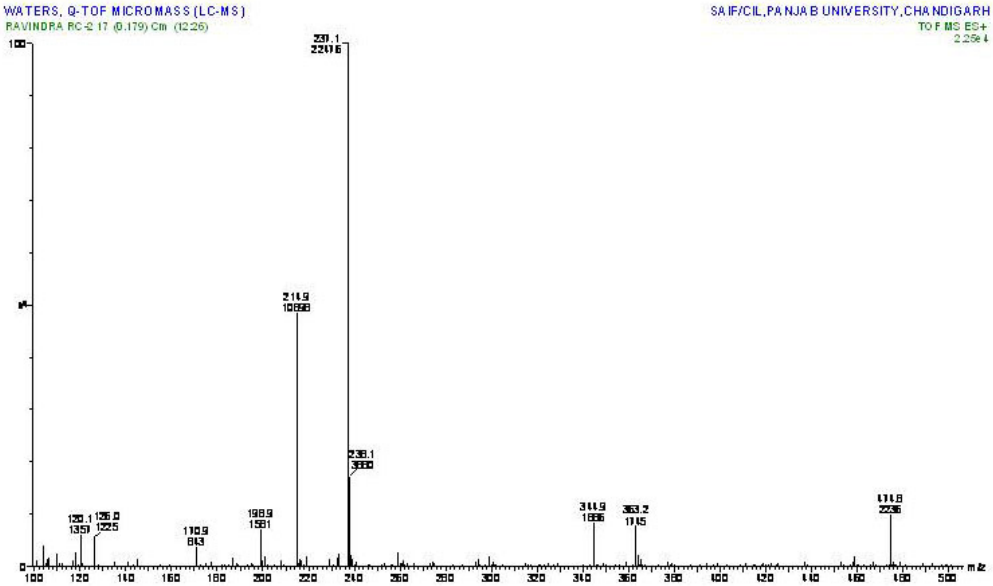
**$^{1}$HNMR**



## $^{13}$CNMR

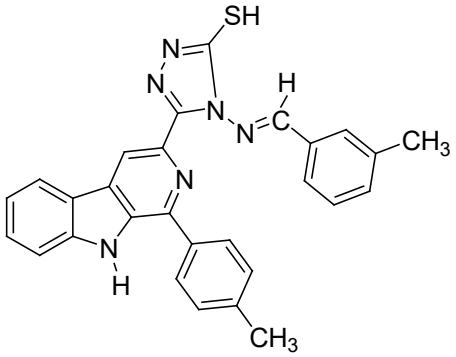

BRUKER
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh
avtar_saifpu@yahoo.co.in

## MS


WATERS, Q-TOF MICROMASS (LC-MS)
SAIF/CIL,PANJAB UNIVERSITY,CHANDIGARH
TOF MS ES+

**1-(p-tolyl)-3-(4-(m-tolylmethanimine)-5-thio-1, 2, 4-triazol-3-yl) β-carboline (3; $C_{28}H_{22}N_6S$)**

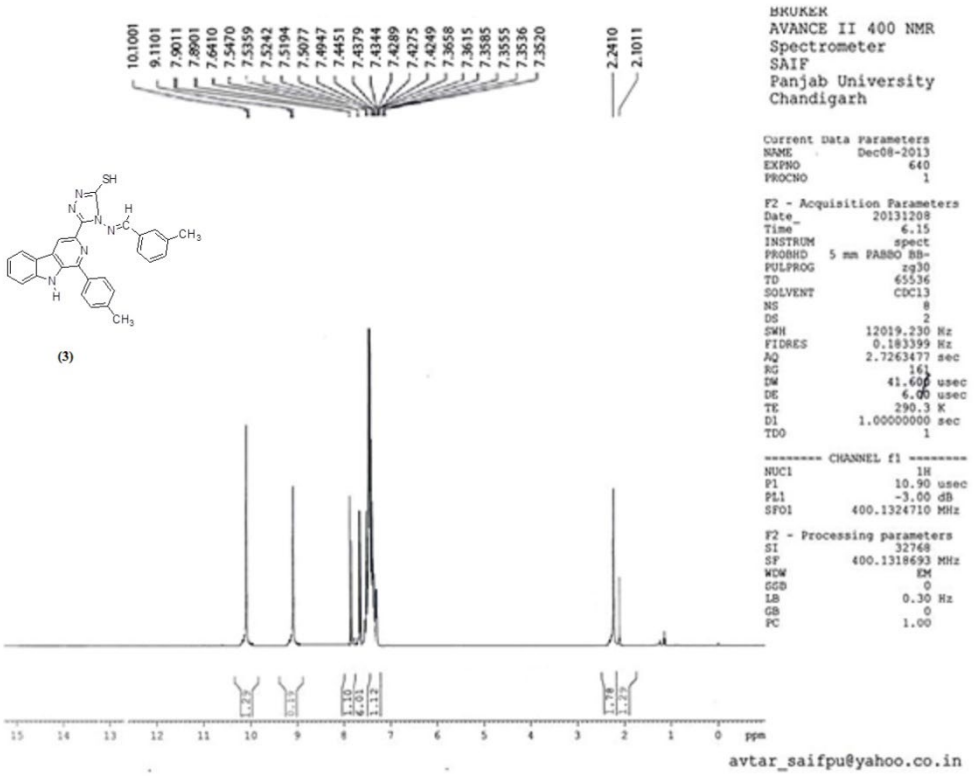
**3**



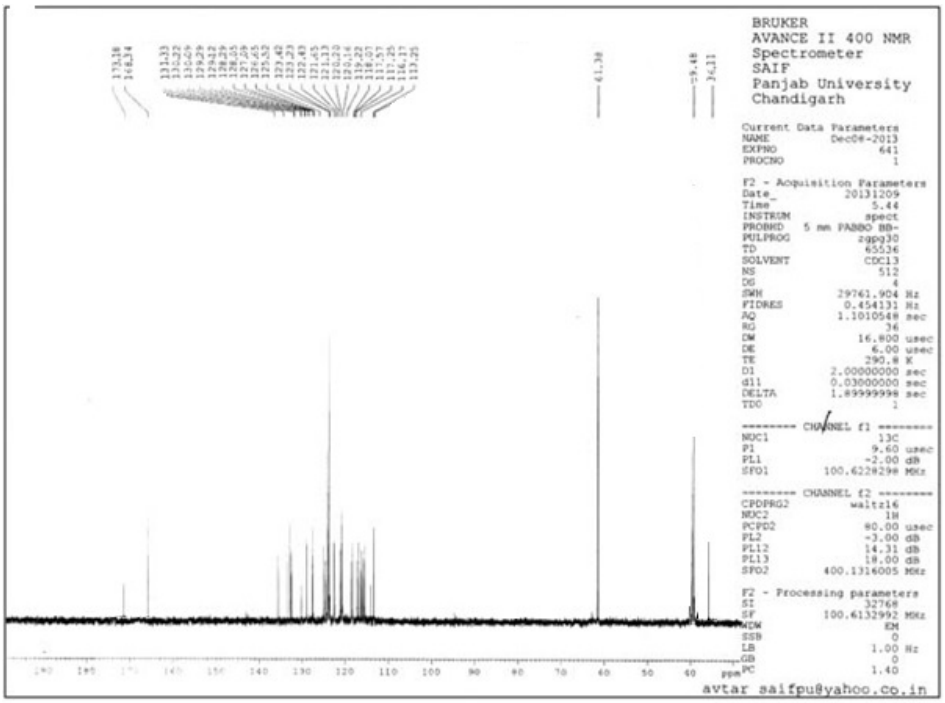

M.P. = 362-364ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3368.63 (N-H str.), 3065.22 (Ar-C-H str.), 2935.65 (C-H str. Asym.), 2843.83 (C-H str. Sym.), 2546.33 (S-H str.), 1568.61, 1638.17 (1, 2, 4-triazole C=N; Pyr-C=N str.), 1586 (N=CH str.), 1532.41, 1456.61 (C=C ring str.), 1309.66 (C-N str.), 1252.55 (N-N str. of triazole), 780.56 (C-H out of plane bending); $^1$H NMR (400 MHz, DMSO-$d^6$): δ = 7.35-7.89 (m, ArH), 9.11 (s, N-H of pyrrole), 10.10 (s, H, S-H), 2.10 (s, $CH_3$), 2.241 (s, $CH_3$), 7.90 (s, H, -N=CH) ppm; $^{13}$C NMR (100 MHz, DMSO-$d^6$): δ = 36.11 ($CH_3$ aliphatic), 39.49 ($CH_3$ aliphatic), 61.34 (CH aliphatic), 113.33 116.17, 117.23, 117.57, 118.01, 119.02, 119.22, 120.16, 120.33, 121.33, 121.45, 122.43, 123.23, 123.42, 125.52, 126.65, 127.05, 128.34, 129.41, 130.01, 130.32, 130.69, 131.31, 166.34, 170.18 (25 ArC's) ppm; MS (EI) m/z: 474.7 ($M^+$); CHN analysis: 70.81 (C), 4.58 (H), 17.62 (N).

**NMR and MS Spectra of Compound 3**

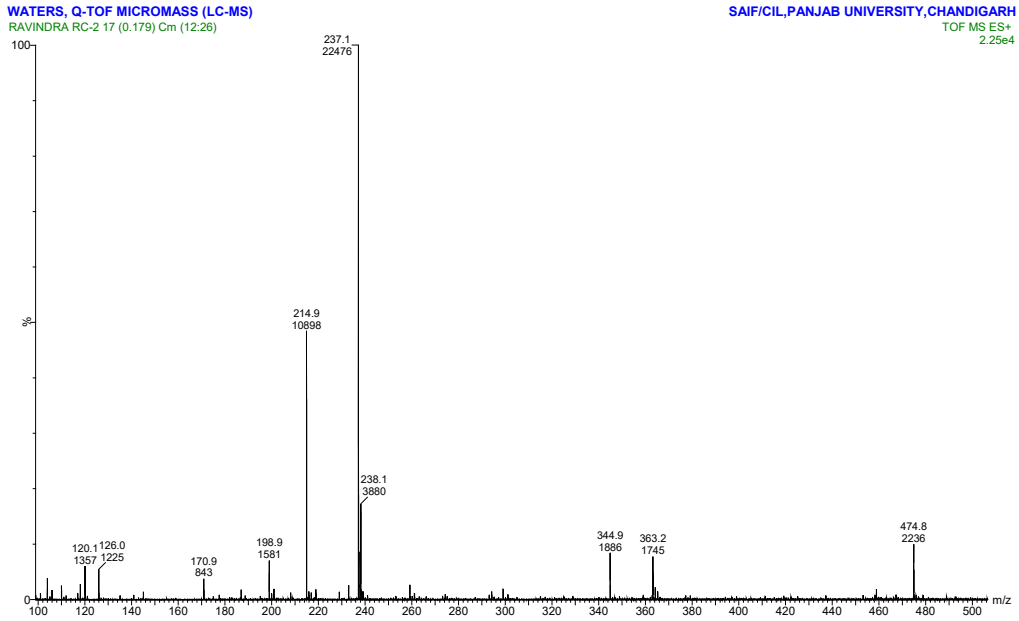
**$^{1}$HNMR**




**$^{13}$CNMR**

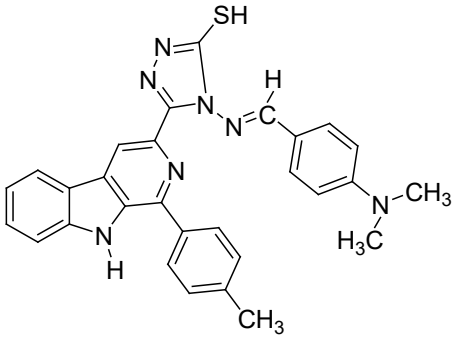


**MS**




**1-(p-tolyl)-3-(4-(p-(iminomethyl)-*N*, *N*-dimethylbenzenamine) -5-thio-1, 2, 4-triazol-3-yl) β-carboline (4; $C_{29}H_{25}N_7S$)**

**4**

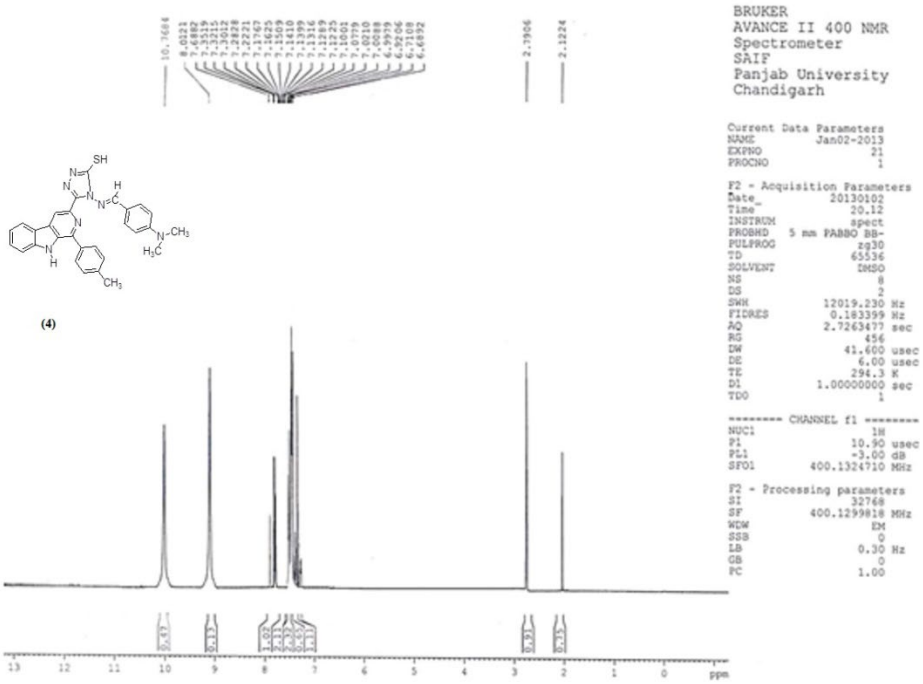



M.P. = 374-376ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3412.12 (N-H str.), 3088.27 (Ar-C-H str.), 2912.46 (C-H str. Asym.), 2843.83 (C-H str. Sym.), 2554.23 (S-H str.), 1548.26, 1629.12 (1, 2, 4-triazole C=N; Pyr-C=N str.), 1581 (N=CH str.), 1530.21, 1426.46 (C=C ring str.), 1312.46 (C-N str.), 1258.58 (N-N str. of triazole), 784.25 (C-H out of plane bending); $^1$H NMR (400 MHz, DMSO-$d^6$): δ = 6.68-7.68 (m, ArH), 8.02 (s, N-H of pyrrole), 10.16 (s, H, S-H), 2.12 (s, $CH_3$), 2.39 (s, N-$(CH_3)_2$), 7.68 (s, H, -N=CH) ppm; $^{13}$C NMR (100 MHz, DMSO-$d^6$): δ = 44.04 ($CH_3$ aliphatic), 46.48 ($CH_3$ aliphatic), 60.78 ($CH_3$ aliphatic), 78.28 (CH aliphatic),

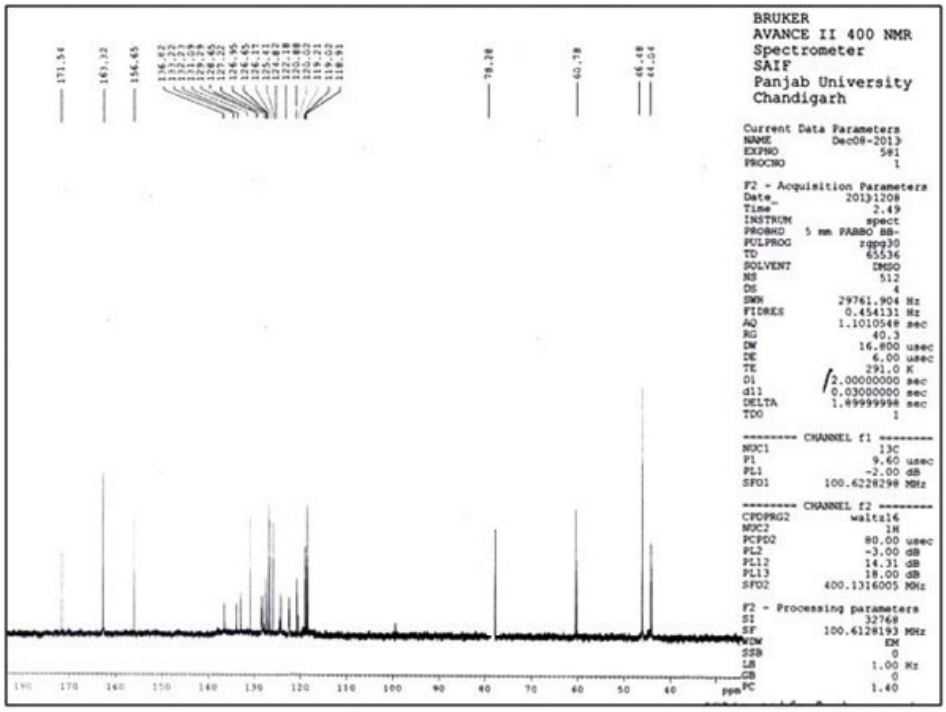
118.91, 119.02, 119.21, 120.02, 120.78, 122.18, 124.02, 125.41, 126.17, 126.63, 126.95, 127.21, 128.65, 129.29, 131.51, 132.23, 133.32, 134.42, 156.65, 133.32, 171.54, 157.8 (22 ArC's); MS (EI) m/z: 503.5 ($M^+$); CHN analysis: 69.12 (C), 4.92 (H), 19.42 (N).

**NMR and MS Spectra of Compound 4**

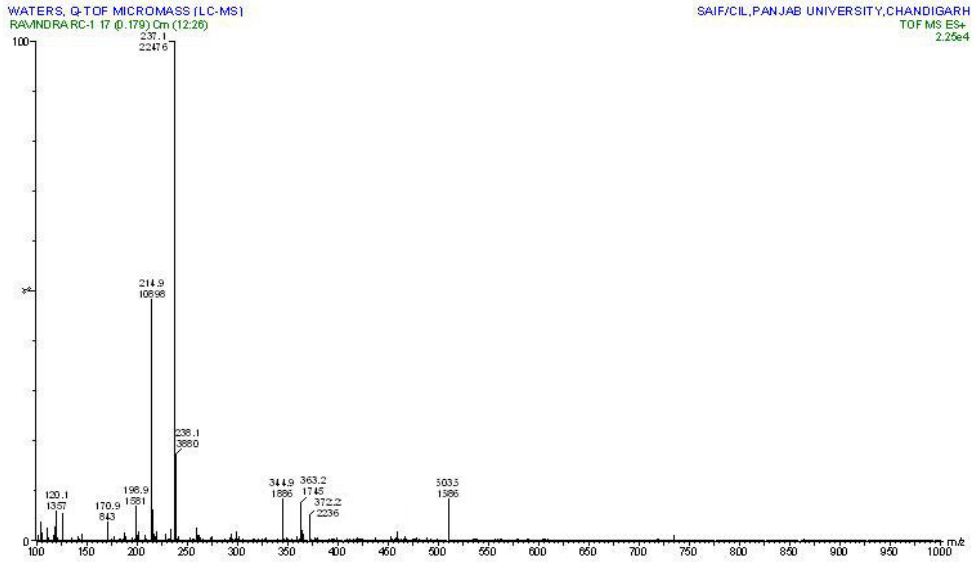
**$^1$HNMR**




**$^{13}$CNMR**

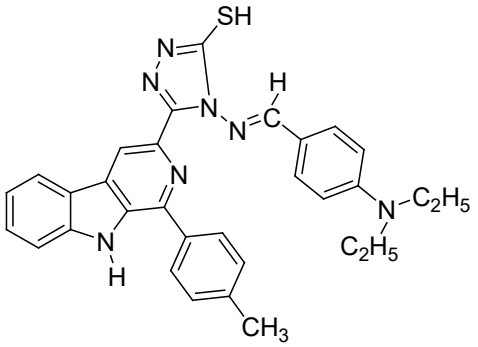


**MS**




**1-(p-tolyl)-3-(4-(p-(iminomethyl)-*N*,*N*-diethylbenzenamine)-5-thio-1,2,4-triazol-3-yl) β-carboline (5; $C_{31}H_{29}N_7S$)**

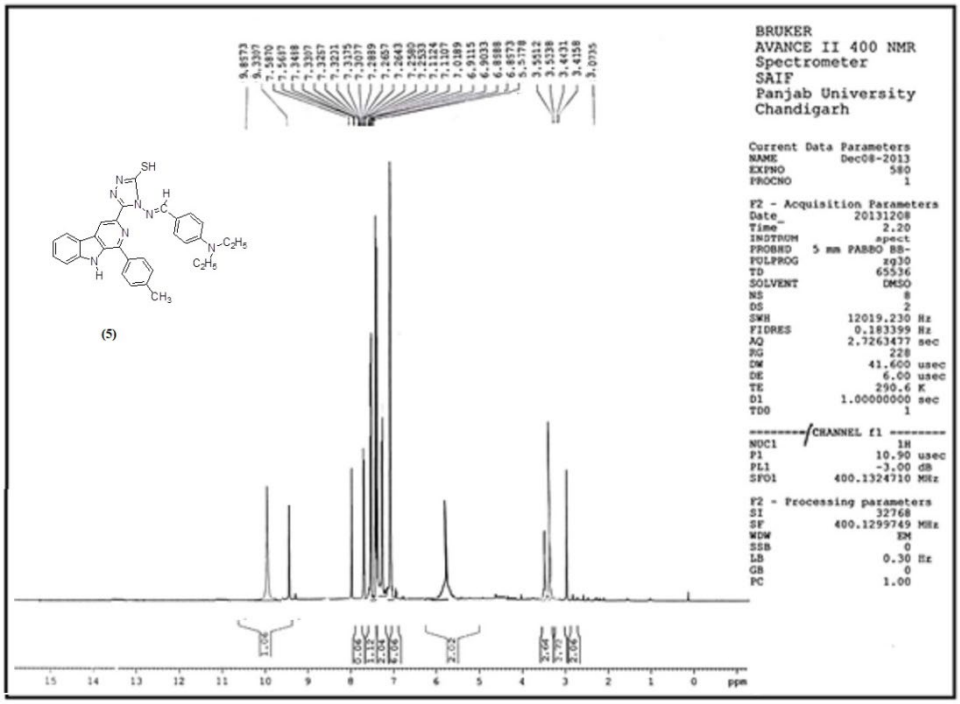
**5**



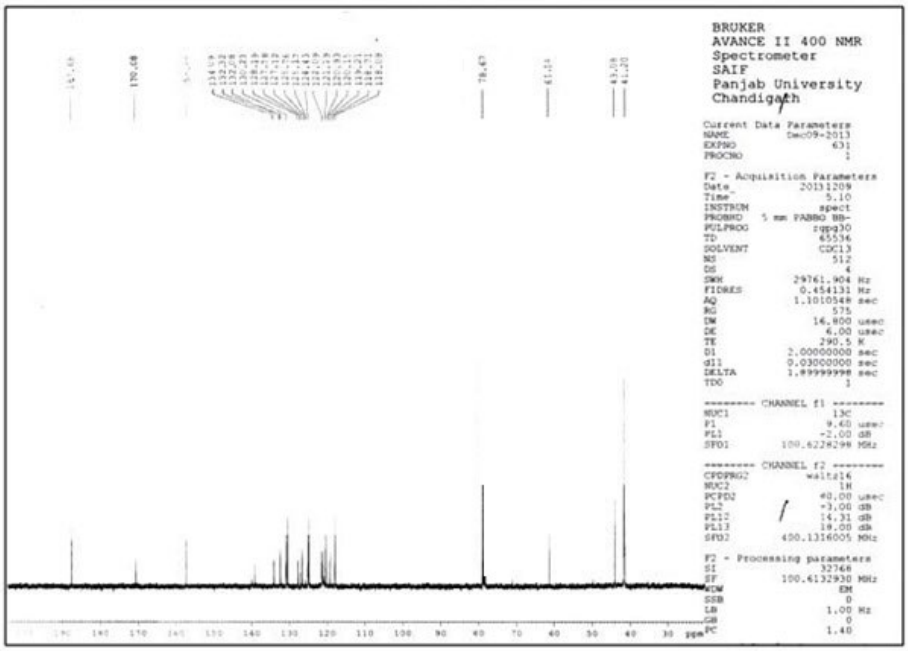

M.P. = 378-380ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3382.42 (N-H str.), 3092.36 (Ar-C-H str.), 2918.62 (C-H str. Asym.), 2811.35 (C-H str. Sym.), 2534.37 (S-H str.), 1578.46, 1632.72 (1, 2, 4-triazole C=N; Pyr-C=N str.), 1588 (N=CH str.), 1539.32, 1429.62 (C=C ring str.), 1317.84 (C-N str.), 1265.82 (N-N str. of triazole); $^1$H NMR (400 MHz, DMSO-$d^6$): δ = 6.51-7.34 (m, ArH), 9.33 (s, N-H of pyrrole), 9.85 (s, H, S-H), 3.07 (s, 3H, $CH_3$), 3.41 (t, N-$CH_2$), 3.44 (q, N-$CH_3$), 7.58 (s, H, -N=CH), 7.56 (d, H, C-H); $^{13}$C NMR (100 MHz, DMSO-$d^6$): δ = 42.20 ($CH_3$ aliphatic), 43.02 ($CH_3$ aliphatic), 61.2 ($CH_2$ aliphatic), 78.47 (CH aliphatic), 118.08, 118.31, 119.21, 120.15, 120.33, 121.32, 122.6, 124.43, 125.13, 125.75, 127.13, 128.14, 129.33, 130.03, 132.31, 134.34, 155.68, 156.3, 157.9, 170.24, 185.58, (21 ArC's); MS (EI) m/z: 531.2 ($M^+$); CHN analysis: 69.12 (C), 5.34 (H), 18.34 (N).

## NMR and MS Spectra of Compound 5

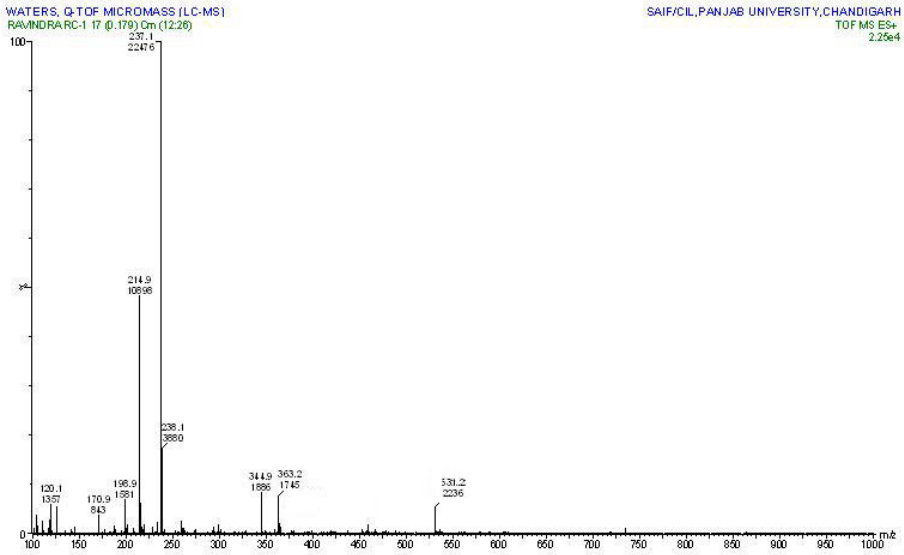
### $^{1}$HNMR




### $^{13}$CNMR



**MS**

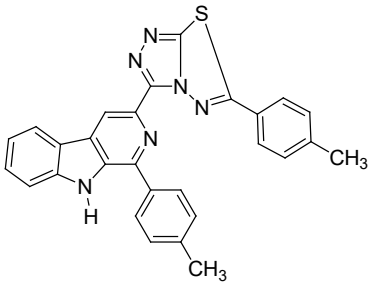



**General method for the synthesis of Compounds 6-7 from compound 1**

An equimolar mixture (5 mmol) of 1-(p-tolyl)-3-(4-amino-5-thiol-1, 2, 4-triazol-3-yl) β-carboline and appropriate aromatic acids in phosphorus oxychloride (5 ml) was refluxed for 5 hours. The reaction mixture was cooled to room temperature and then gradually poured onto crushed ice with stirring. The mixture was allowed to stand overnight and the separated out solid was filtered, treated with dilute sodium hydroxide solution and washed thoroughly with cold water. The compound so obtained was dried and crystallized from ethanol.

**1-(p-tolyl)-3-(6-p-tolyl-(1, 2, 4 triazolo (3, 4-*b*) 1, 3, 4-thiadiazole-3-yl) β-carboline (6; $C_{28}H_{20}N_6S$)**

**6**

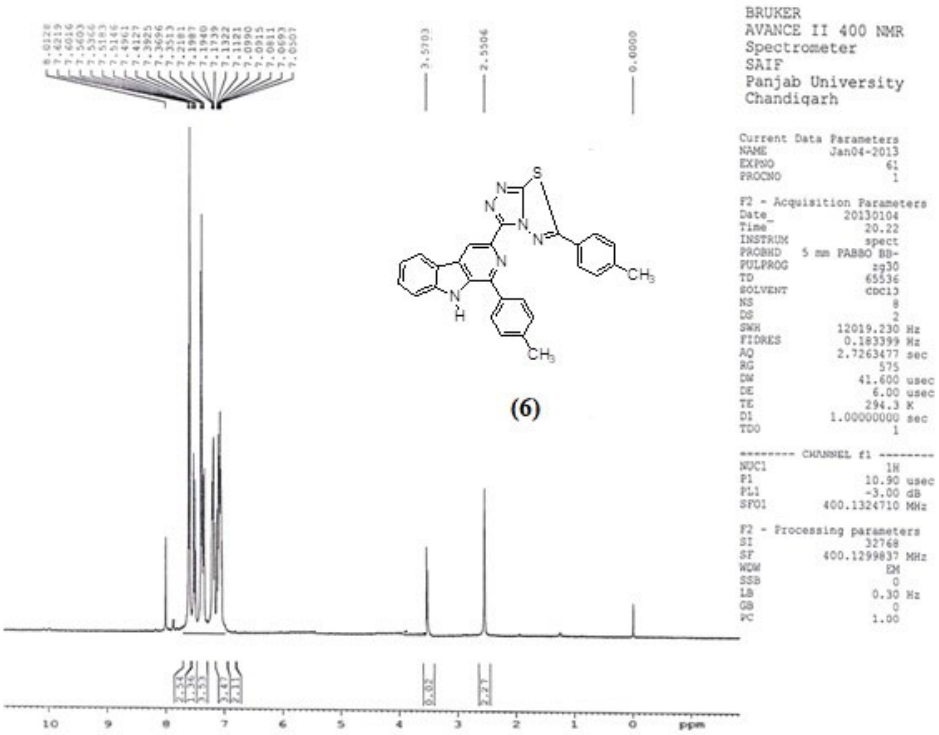



M.P. = 384-386ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3378.24 (N-H str.), 3094.62 (Ar-C-H str.), 2920.18 (C-H str. Asym.), 2813.25 (C-H str. Sym.), 1574.62, 1638.27 (1, 2, 4-triazole C=N; Pyr-C=N

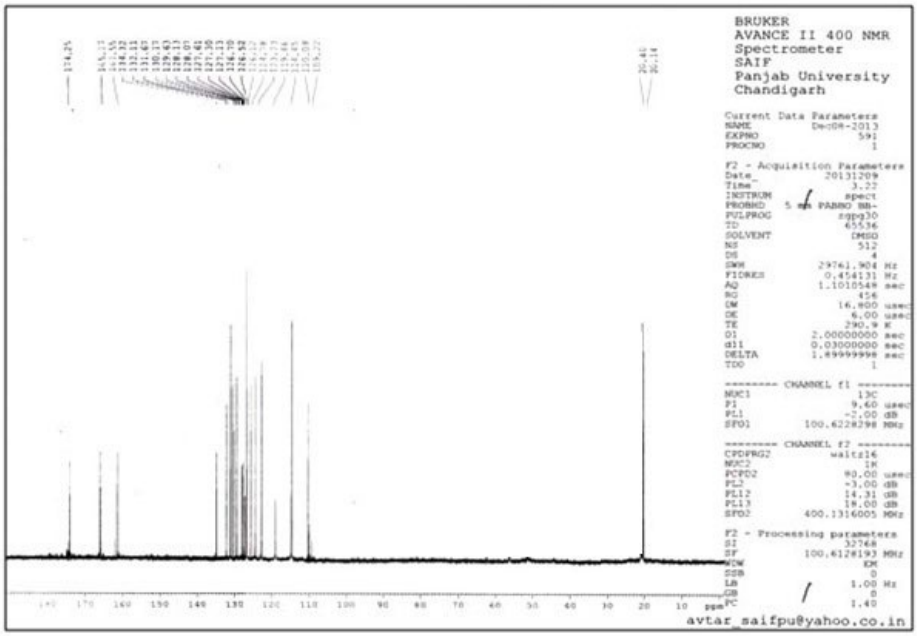
str.), 1537.93, 1427.36 (C=C ring str.), 1315.48 (C-N str.), 1266.48 (N-N str. of triazole), 786.61 (C-H out of plane bending); $^{1}$H NMR (400 MHz, DMSO-d$^{6}$): δ = 7.05-7.62 (m, ArH), 8.08 (s, N-H of pyrrole), 3.57 (s, 3H, $CH_3$), 2.55 (s, 3H, $CH_3$); $^{13}$C NMR (100 MHz, DMSO-d$^{6}$): δ =20.11 ($CH_3$ aliphatic), 20.49 ($CH_3$ aliphatic), 112.27, 113.01, 113.45, 119.11, 122.19, 124.74, 125.15, 126.70, 127.13, 127.30, 127.41, 128.03, 128.13, 129.43, 130.17, 130.63, 131.67, 132.13, 148.6, 162.13, 167.15, 174.63 (22 ArC's); MS (EI) m/z: 472.2 ($M^{+}$); CHN analysis: 71.12 (C), 4.23 (H), 17.71 (N).

**NMR and MS Spectra of Compound 6**

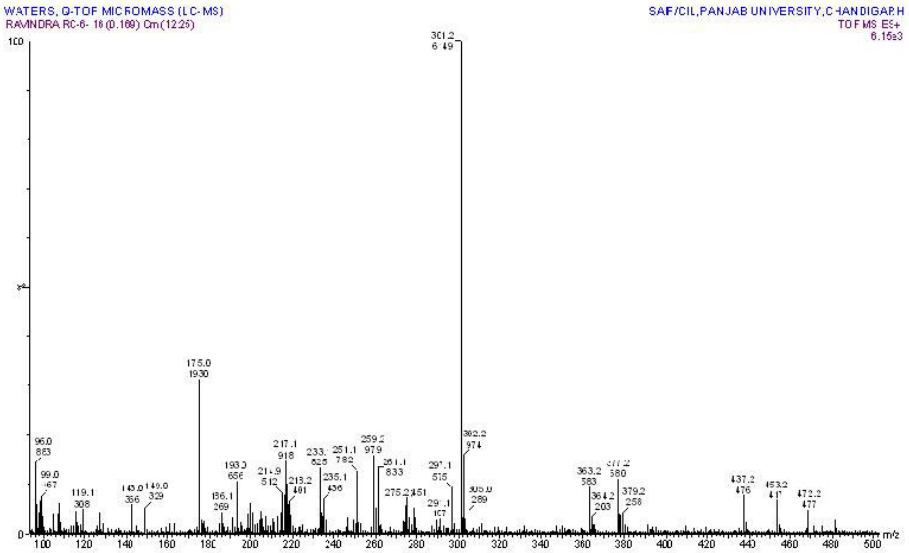
**$^{1}$HNMR**



**$^{13}$CNMR**

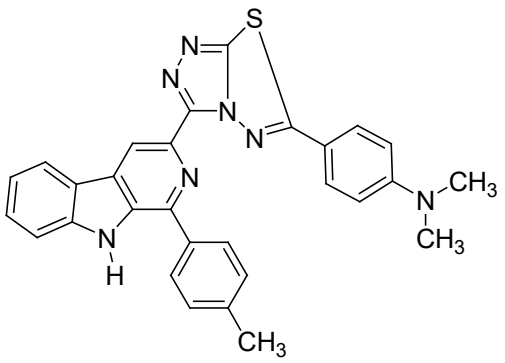



**MS**




**1-(p-tolyl)-3-(6- *N*, *N*-dimethylbenzenamine-(1, 2, 4 triazolo (3, 4-*b*) 1, 3, 4-thiadiazole-3-yl) β-carboline (7; $C_{29}H_{23}N_7S$)**

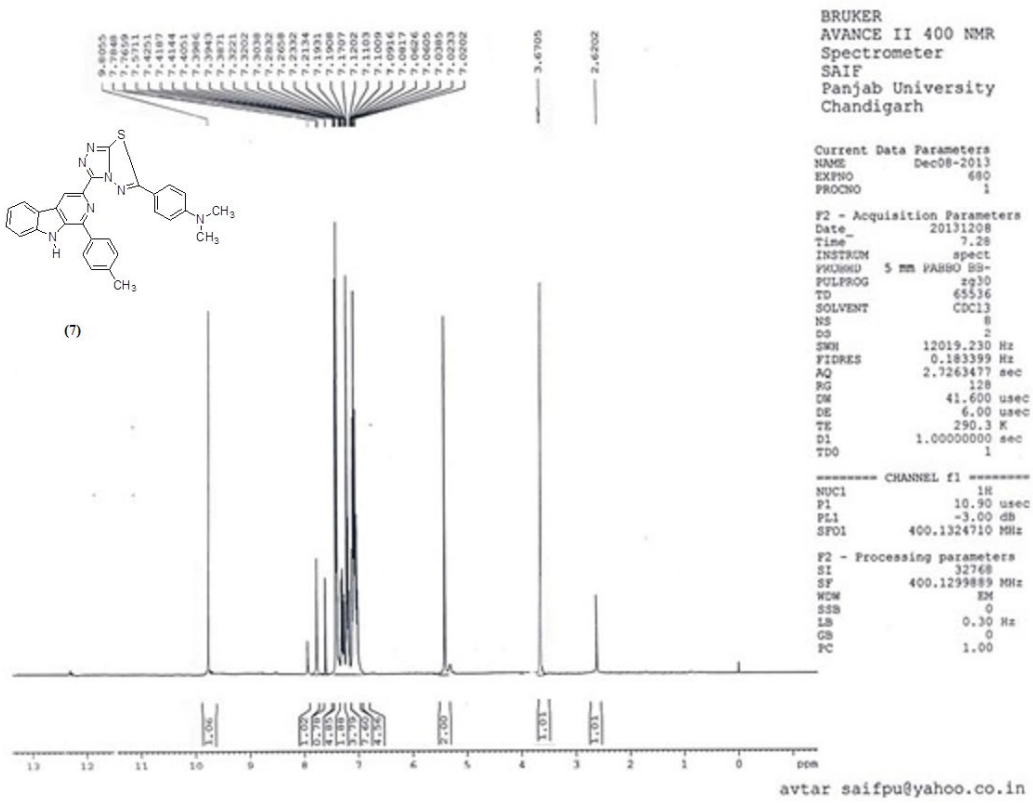
**7**



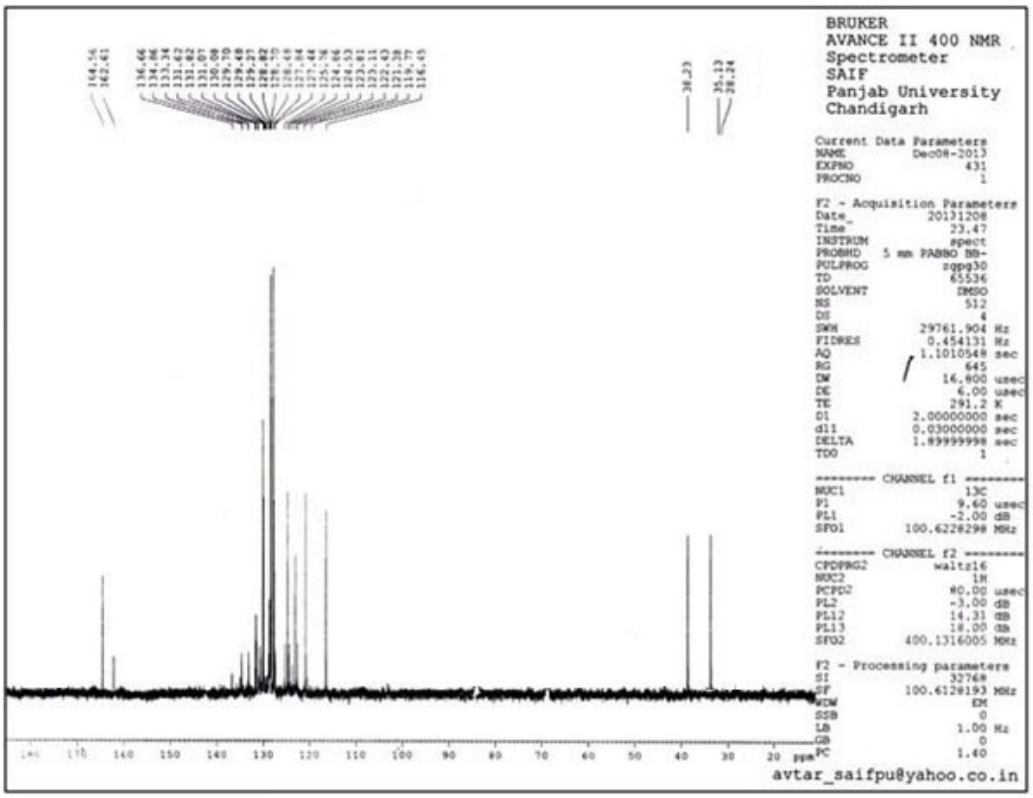
M.P. = 378-380ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3368.48 (N-H str.), 3097.64 (Ar-C-H str.), 2938.56 (C-H str. Asym.), 2815.65 (C-H str. Sym.), 1575.63, 1636.87 (1, 2, 4-triazole C=N; Pyr-C=N str.), 1540.26, 1427.76 (C=C ring str.), 1319.88 (C-N str.), 1268.38 (N-N str. of triazole), 790.51 (C-H out of plane bending); $^{1}H$ NMR (400 MHz, DMSO-$d^6$): δ =7.223-7.588 (m, ArH), 9.60 (s, N-H of pyrrole), 2.62 (s, 3H, $CH_3$), 3.67 (s, N-$(CH_3)_2$); $^{13}C$ NMR (100 MHz, DMSO-$d^6$): δ = 33.24 ($CH_3$ aliphatic), 33.33 ($CH_3$ aliphatic), 38.22 ($CH_3$ aliphatic), 116.15, 119.77, 121.20, 122.43, 123.11, 123.91, 124.53, 124.66, 125.76, 126.08, 126.76, 127.46, 128.40, 128.70, 129.03, 130.01, 131.07, 131.47, 131.80, 132.44, 133.07, 133.34, 134.04, 136.44, 162.61, 164.14 (26 ArC's); MS (EI) m/z: 501.7 ($M^+$); CHN analysis: 69.38 (C), 4.56 (H), 19.48 (N).

**NMR and MS Spectra of Compound 7**

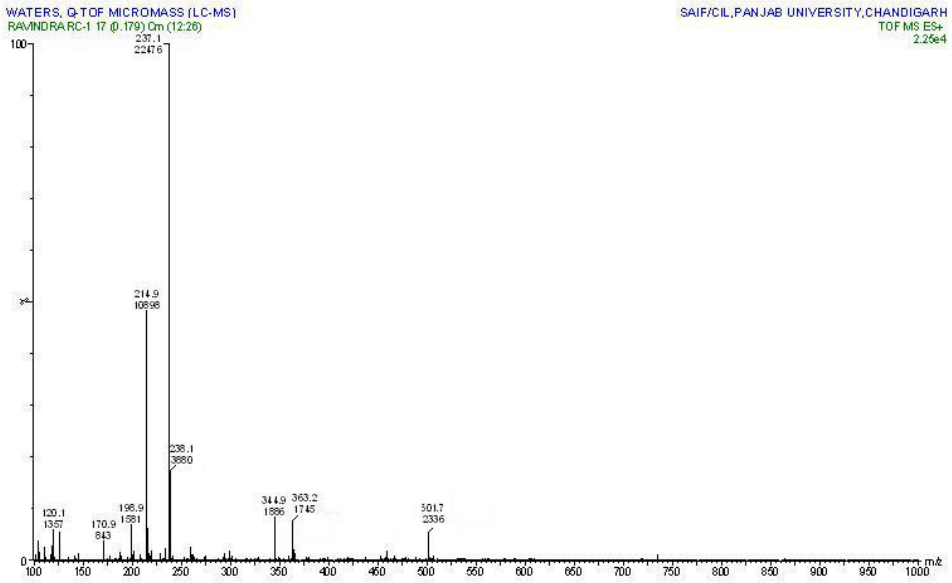
**$^{1}$HNMR**


BRUKER
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh
(7)
avtar saifpu@yahoo.co.in

**$^{13}$CNMR**


BRUKER
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh
avtar_saifpu@yahoo.co.in

**MS**

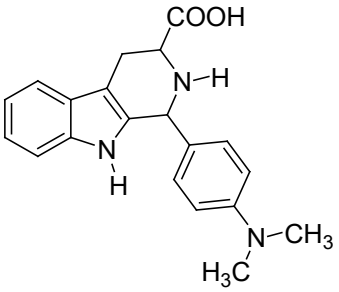

WATERS, Q-TOF MICROMASS (LC-MS)
RAVINDRA RC-1 17 (0.179) Cm (12:26)
SAIF/CIL,PANJAB UNIVERSITY,CHANDIGARH
TOF MS ES+
2.25e4
237.1
22476
214.9
10898
238.1
3880
120.1
1357
170.9
843
195.9
1581
344.9
1886
363.2
1745
501.2
2336
m/z

# Scheme 2-

**General procedure for the preparation of 1-(4-(dimethylamino) phenyl)-2, 3, 4, 9-tetrahydro-β-carboline-3-carboxylic acid (B-1; $C_{20}H_{21}N_3O_2$)**

A mixture of L-tryptophan (10.2 g, 50 mmol), acetic acid (200 ml) and aldehyde (55 mmol, p-dimethylaminobenzyldehyde) was stirred at room temperature on magnetic stirrer for 2 hours. After stirring it was refluxed for 5 hours, then cooled and adjusted to pH 5 with ammonium hydroxide solution, the precipitated product was collected by filtration and washed well with water, then dried. The progress of reaction was monitored by TLC.

**B-1**

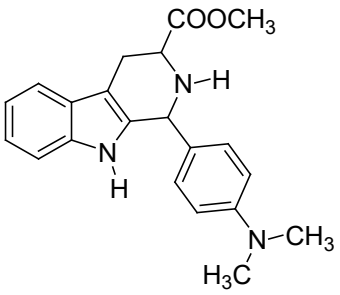



M.P. = 259-261ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3408.32 (O-H str.), 3342.62, 3356.1 (N-H str.), 3088.62 (Ar-C-H str.), 2924.21 (C-H str. Asym.), 2843.52 (C-H str. Sym.), 1655.45 (C=O str.), 1528.29, 1452.42 (C=C ring str.), 1325.53 (C-N str.), 1106.62 (C-C str.),789.65 (C-H out of plane bending).

**General procedure for the preparation of Methyl 1-(4-(dimethylamino) phenyl)-2, 3, 4, 9-tetrahydro-β-carboline-3-carboxylate (B-2; $C_{21}H_{23}N_3O_2$)**

To a solution of corresponding 1-(4-(dimethylamino) phenyl)-2, 3, 4, 9-tetrahydro-β-carboline-3-carboxylic acid (20 mmol) in methanol (500 ml), $SOCl_2$ (20 ml) was added drop wise with cooling and stirred at room temperature for 1 hour then heated at reflux for 5 hours and evaporated in reduced pressure. The resulting mixture was poured onto water (200 ml), and extracted with ethyl acetate (3 × 200 ml). The completion of reaction was established by single spot by TLC on silica gel G plates using the solvent system n-hexane: ethyl acetate in the ratio of (9:1). The organic phase was washed with water and brine, then dried over anhydrous sodium sulfate, filtered and evaporated.

**B-2**

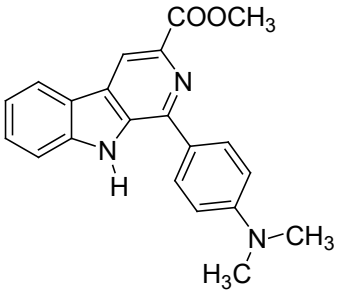



M.P. = 261-263ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3488.38, 3138.43 (N-H str.), 3068.74 (Ar-C-H str.), 2910.23 (C-H str.), 1684.32 (C=O str.), 1625.42, 1475.15 (C=C ring str.), 1328.61 (C-N str.), 1108.54 (C-C str.), 807.61 (C-H out of plane bending).

**General procedure for the preparation of Methyl 1-(4-(dimethylamino) phenyl)-β-carboline-3-carboxylate (B-3; $C_{21}H_{19}N_3O_2$)**

A suspension of the corresponding Methyl 1-(4-(dimethylamino) phenyl)-2, 3, 4, 9-tetrahydro-β-carboline-3-carboxylate (10 mmol) and sulfur (25 mmol) in xylene (200 ml) was heated at reflux for 6 hours, then cooled and stored at 4 °C for 3 hours and then filtered and washed generously with petroleum ether (40-60°C), the solid was dried and crystallized from ethyl acetate.

**B-3**



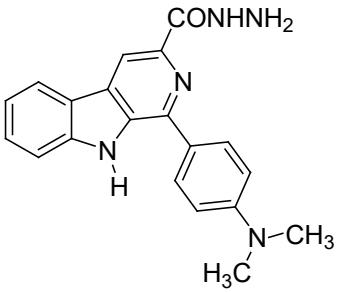

M.P. = 264-266ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ =3325.41 (N-H str.), 3068.51 (C-H str.), 2936.45 (C-H str. Asym.), 2838.83 (C-H str. Sym.), 1685.45 (C=O str.), 1650.42, 1492.34 (C=C ring str.), 1618.63 (Pyr-C=N str.), 1324.14 (C-N str.), 798.17 (C-H out of plane bending).

**General procedure for the preparation of 1-(4-dimethylamino) phenyl-β-carboline-3-carbohydrazide (B-4; $C_{20}H_{19}N_5O$)**

Intermediate compound (10 mmol) was dissolved in ethanol (100 ml) and hydrazine hydrate (15 ml) was added and the mixture was refluxed for 6 hours. The reaction mixture was cooled

and the precipitate was collected by filteration and washed with ethanol. The solid was recrystalized from ethanol.

**B-4**

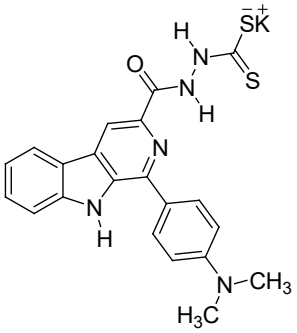



M.P. = 269-271ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3340.71 (N-H str.), 3065.72 (Ar-C-H str.), 2870.21 (C-H str.), 1678.25 (C=O str.), 1490.01 (C=C ring str.), 1612.65 (Pyr-C=N str.), 1334.53 (C-N Str.), 806.46 (C-H out of plane bending).

**General method for synthesis of 1-(4-dimethylamino) phenyl-β-carboline-3-potassiumdithiocarbohydrazide (B-5; $C_{21}H_{18}KN_5OS_2$)**

Potassium hydroxide (10 mmol) was dissolved in absolute ethanol (100 ml). The solution was cooled in ice bath and 1-(4-dimethylamino) phenyl-β-carboline-3-carbohydrazide (10 mmol) was added with stirring. To this carbon disulphide (10 mmol) was added in small portions with constant stirring. The reaction mixture was agitated continuously for 4 hours at room temperature. The mixture was refluxed for 8 hours and cooled. The precipitated product was collected by filtration, washed with anhydrous ether (100 ml) and dried. The 1-(4-dimethylamino) phenyl-β-carboline-3-potassiumdithiocarbohydrazide was thus obtained.

**B-5**



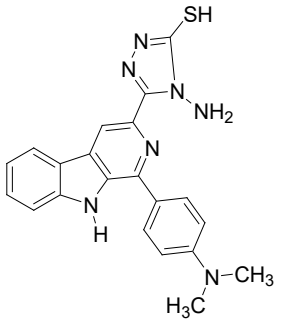

M.P. = 326-328ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3422.15, 3321.98, 3155.04 (N-H str.), 3071.02 (Ar-C-H str.), 2872.71 (C-H str.), 1652.65 (C=O str.), 1488.91 (C=C ring str.), 1628.07 (Pyr-C=N str.), 1324.23 (C-N str.), 1342.32, 1238.34 (C=S str.), 806.76 (C-H out of plane bending).

**General method for synthesis of 1-(p- *N*, *N*-dimethylbenzenamine)-3-(4-amino-5-thiol-1, 2, 4-triazol-3-yl) β-carboline (8)**

A suspension of 1-(4-dimethylamino) phenyl-β-carboline-3-potassiumdithiocarbohydrazide (10 mmol) and hydrazine hydrate (99%, 20 ml) was refluxed for 18-20 hours with occasional shaking. The colour of the reaction mixture changed to green with the evolution of hydrogen sulfide gas. A homogenous reaction mixture was obtained during the reaction process. The reaction mixture was cooled to room temperature and diluted with cold water (20 ml). On acidification with concentrated hydrochloric acid the required 1-(p- *N*, *N*-dimethylbenzenamine)-3-(4-amino-5-thiol-1, 2, 4-triazol-3-yl) β-carboline was precipitated out. It was filtered, washed thoroughly with cold water, dried and recrystallised from ethanol. Purity of the compound was checked by TLC using silica gel-G coated plates by using toluene: ethyl acetate: formic acid (T: E: F); (5:4:1) as solvent system, and observed in UV light.

**1-(p- *N*, *N*-dimethylbenzenamine)-3-(4-amino-5-thiol-1, 2, 4-triazol-3-yl) β-carboline (8; $C_{21}H_{19}N_7S$)**

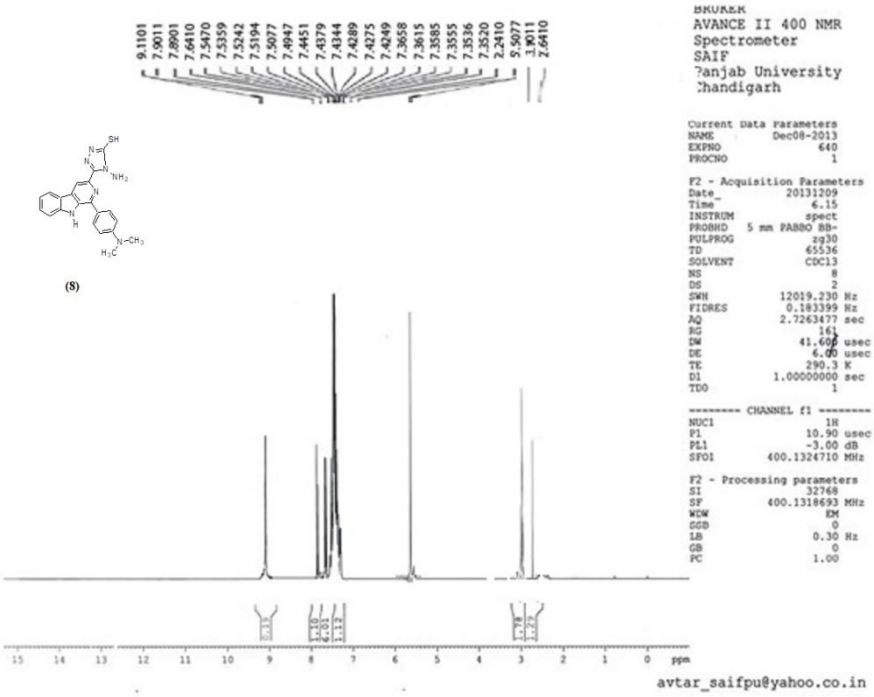
**8**



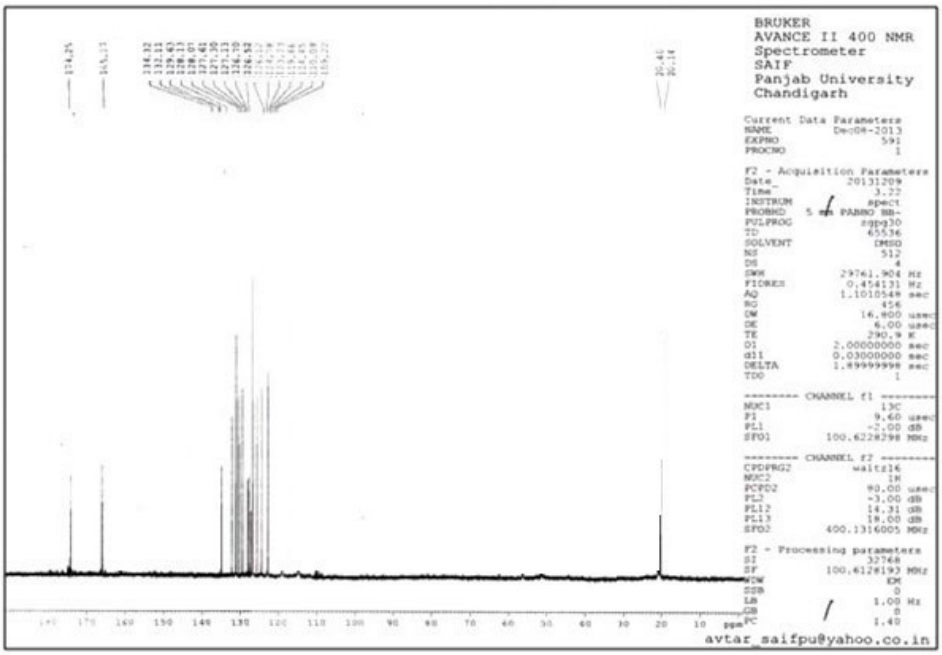

M.P. = 361-363ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3411.25, 3130.03 (N-H str.), 3084.32 (Ar-C-H str.), 2912.23 (C-H str. Asym.), 2765.32 (C-H str. Sym.), 2555.41 (S-H str.), 1590.25, 1627.25 (1, 2, 4-triazole C=N; Pyr-C=N str.), 1522.29, 1452.25 (C=C ring str.), 1325.15 (C-N str.), 1242.03 (N-N str. of triazole), 734.15 (C-H out of plane bending). $^1$H NMR (400 MHz, DMSO-$d^6$): δ =7.24-7.90 (m, ArH), 9.11 (s, N-H of pyrrole), 5.50 (s, H, S-H), 3.01 (s, $NH_2$), 2.64 (s, N-$(CH_3)_2$); $^{13}$C NMR (100 MHz, DMSO-$d^6$): δ = 20.14 ($CH_3$ aliphatic), 20.46 ($CH_3$ aliphatic), 120.17, 121.23, 122.56, 123.16, 123.85, 124.24, 125.27, 125.98, 126.62, 127.20, 127.79, 128.55, 128.97, 130.51, 131.37, 132.12, 133.03, 165.17, 174.37 (19 ArC's); MS (EI) m/z: 401.1 ($M^+$); CHN analysis: 62.84 (C), 4.73 (H), 24.43 (N), 7.98 (S).

## NMR and MS Spectra of Compound 8

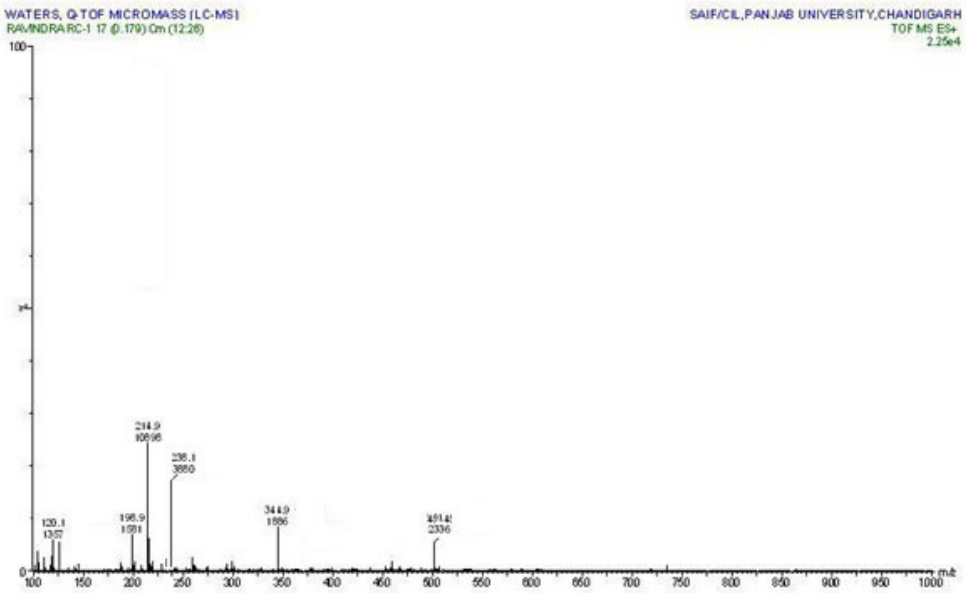
### $^{1}$HNMR




### $^{13}$CNMR



**MS**

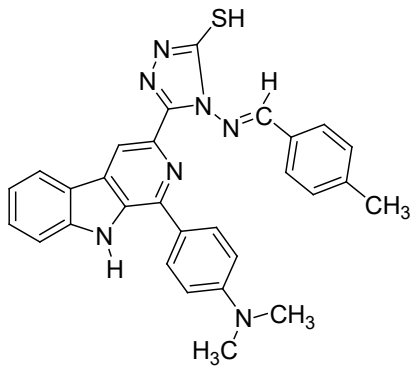



**General procedure for synthesizing Compounds 9-12 from compound 8**

A solution of 1-(p- *N*, *N*-dimethylbenzenamine)-3-(4-amino-5-thiol-1, 2, 4-triazol-3-yl) β-carboline (5 mmol) in glacial acetic acid (5 ml) was allowed to react with the appropriate aldehydes (5 mmol) under reflux for 5 hours. The reaction mixture was then cooled and the precipitated derivatives were filtered off, washed with water, dried, completion of reaction was checked by TLC and recrystallized from ethanol to afford the title compounds. The crude product was purified by column chromatography on silica gel using suitable solvent system.

**1-(*N*, *N*-dimethylbenzenamine)-3-(4-(p-tolylmethanimine)-5-thio-1, 2, 4-triazol-3-yl) β-carboline (9; $C_{29}H_{25}N_7S$)**

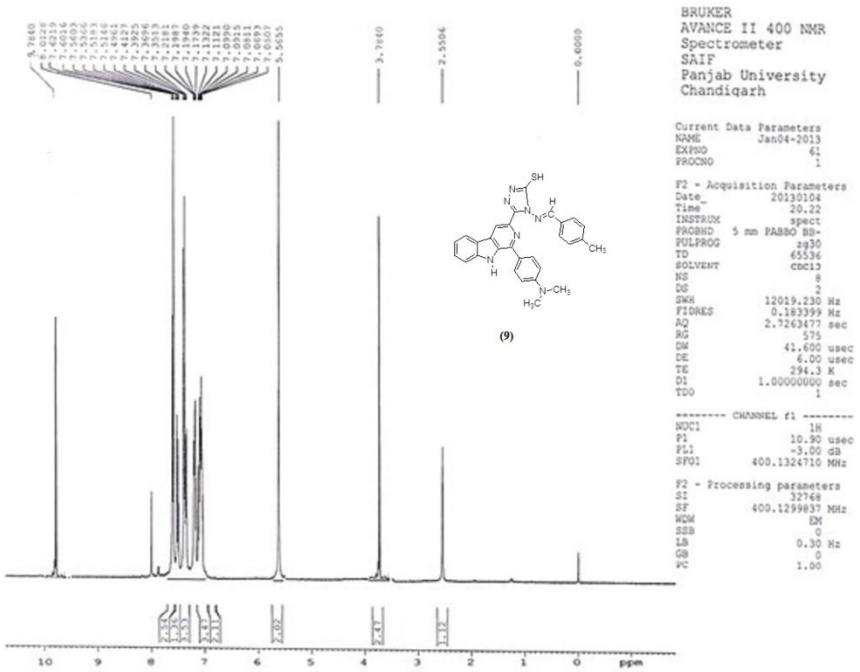
**9**



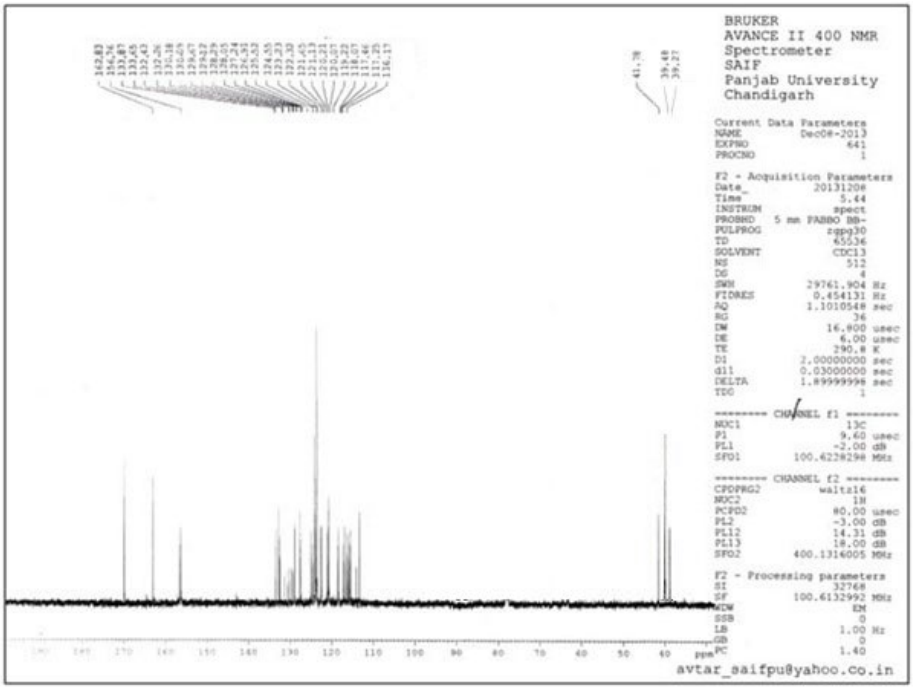

M.P. = 361-363ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3344.64 (N-H str.), 3089.63 (Ar-C-H str.), 2925.25 (C-H str. Asym.), 2844.24 (C-H str. Sym.), 2544.33 (S-H str.), 1588.44, 1623.71 (1, 2, 4-triazole C=N; Pyr-C=N str.), 1584 (N=CH str.), 1527.43, 1455.61 (C=C ring str.), 1311.52 (C-N str.), 1241.53 (N-N str. of triazole), 735.71 (C-H out of plane bending); $^{1}H$ NMR (400 MHz, DMSO-$d^6$): δ =7.05-7.62 (m, ArH), 9.26 (s, N-H of pyrrole), 5.56 (s, H, S-H), 2.55 (s, $CH_3$), 3.74 (s, N-$(CH_3)_2$), 8.01 (s, H, -N=CH); $^{13}C$ NMR (100 MHz, DMSO-$d^6$): δ = 39.27 ($CH_3$ aliphatic), 39.44 ($CH_3$ aliphatic), 41.30 (CH aliphatic), 116.17, 116.33, 117.44, 118.07, 118.33, 120.02, 121.13, 121.45, 122.20, 122.70, 122.73, 124.55, 125.37, 126.31, 127.24, 128.05, 128.29, 129.17, 129.47, 130.0.6, 130.34, 132.24, 133.45, 133.87, 154.74, 162.03 (26 ArC's); MS (EI) m/z: 503.2 ($M^+$); CHN analysis: 69.08 (C), 4.84 (H), 19.38 (N).

**NMR and MS Spectra of Compound 9**

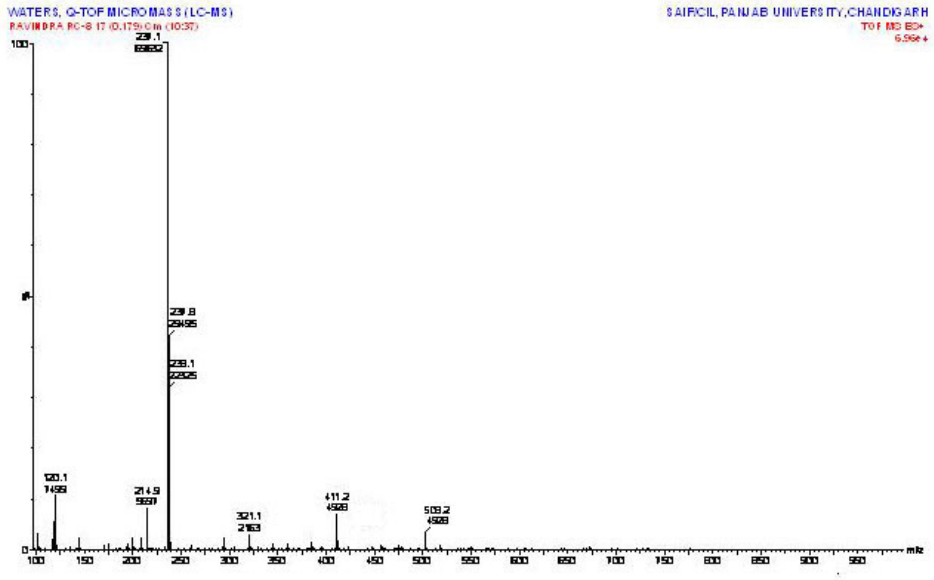
**$^{1}$HNMR**




**$^{13}$CNMR**

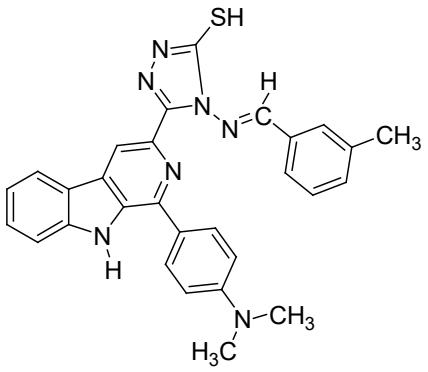


**MS**




**1-(*N*, *N*-dimethylbenzenamine)-3-(4-(m-tolylmethanimine)-5-thio-1, 2, 4-triazol-3-yl) β-carboline (10; $C_{29}H_{25}N_7S$)**

**10**

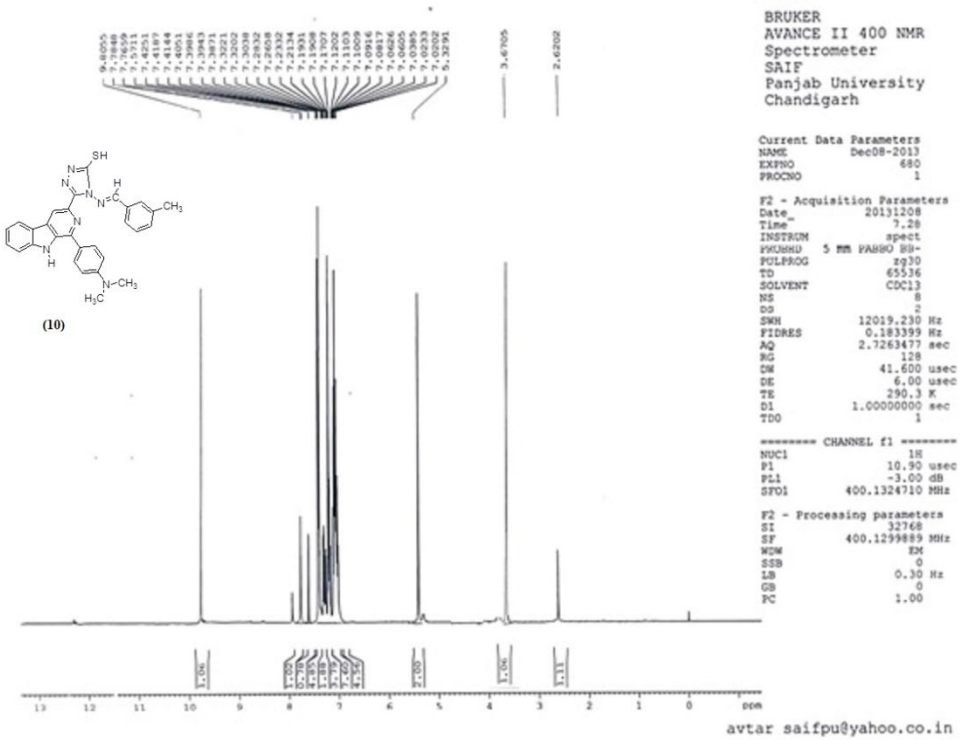



M.P. = 361-363ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3362.46 (N-H str.), 3068.24 (Ar-C-H Str.), 2939.56 (C-H str. Asym.), 2844.84 (C-H str. Sym.), 2556.31 (S-H str.), 1569.46, 1648.71 (1, 2, 4-triazole C=N; Pyr-C=N str.), 1582 (N=CH str.), 1534.42, 1455.64 (C=C ring str.), 1310.36 (C-N str.), 1254.57 (N-N str. of triazole), 787.36 (C-H out of plane bending); $^1$H NMR (400 MHz, DMSO-$d^6$): δ =. 7.02-7.54 (m, ArH), 9.80 (s, N-H of pyrrole), 5.32 (s, H, S-H), 2.62 (s, $CH_3$), 3.67 (s, N-$(CH_3)_2$), 7.78 (s, H, -N=CH), $^{13}$C NMR (100 MHz, DMSO-$d^6$): δ = 28.33 ($CH_3$ aliphatic), 37.38 ($CH_3$ aliphatic), 43.78 ($CH_3$ aliphatic), 66.33 (CH aliphatic), 109.26, 111.16, 107.23, 110.56, 119.13, 120.68, 122.52, 126.76, 127.32, 129.62, 131.72, 132.09, 132.73, 133.28, 135.58, 138.79, 140.97, 141.51, 144.16, 147.67, 148.61, 158.25, 159.16,

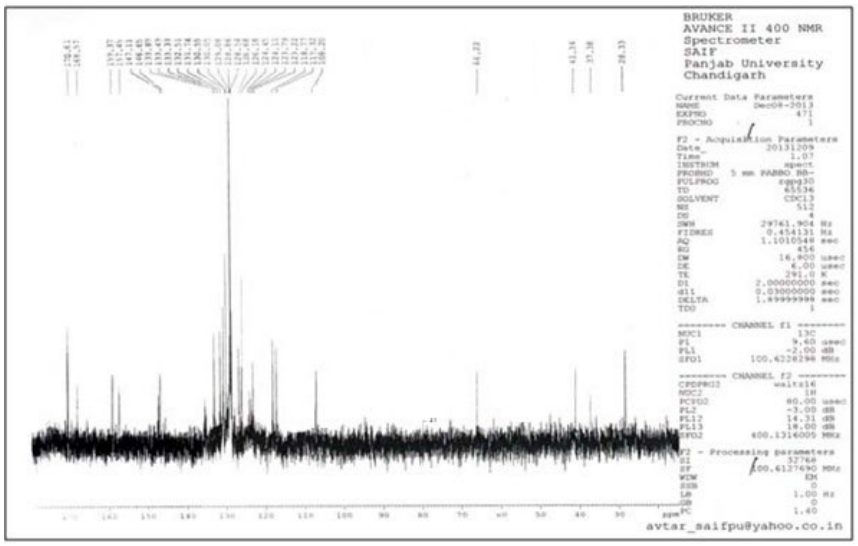
168.10, 170.73 (25 ArC's); MS (EI) m/z: 503.1 ($M^+$); CHN analysis: 69.14 (C), 4.59 (H), 19.22 (N).

**NMR and MS Spectra of Compound 10**

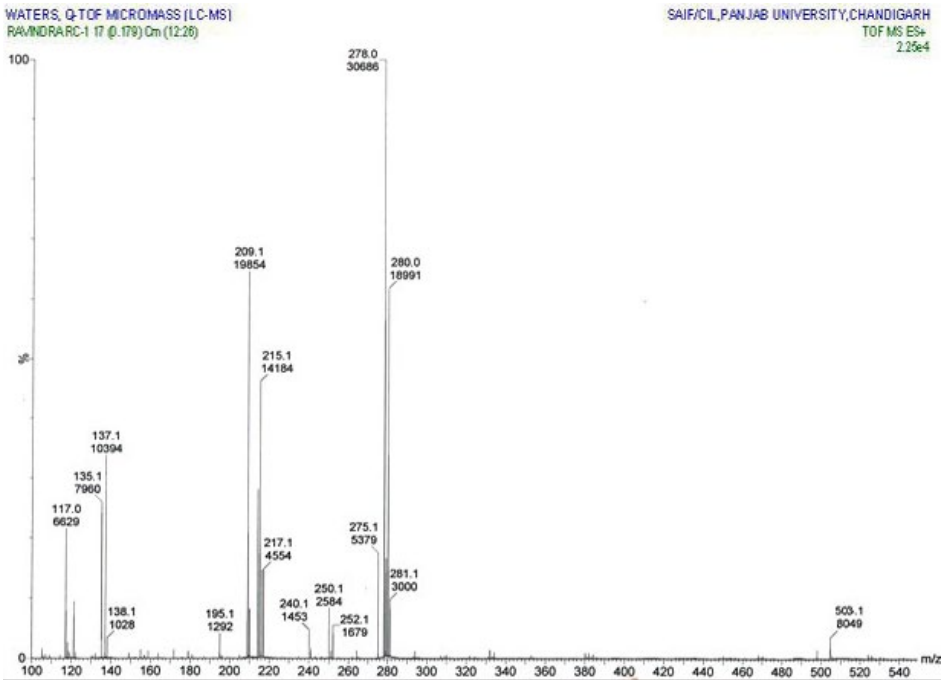
**$^1$HNMR**




**$^{13}$CNMR**

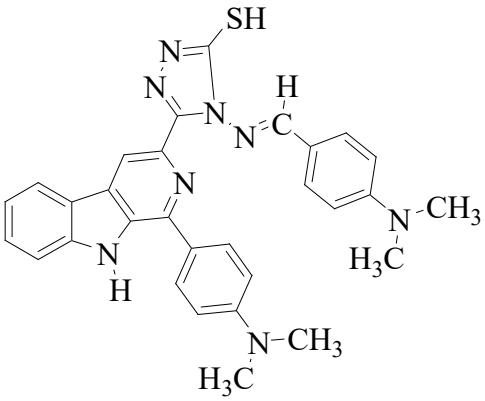


**MS**




**1-(*N*, *N*-dimethylbenzenamine)-3-(4-(p-(iminomethyl)-*N*, *N*-dimethylbenzenamine)- 5-thio-1, 2, 4-triazol-3-yl) β-carboline (11; $C_{30}H_{28}N_8S$)**

**11**

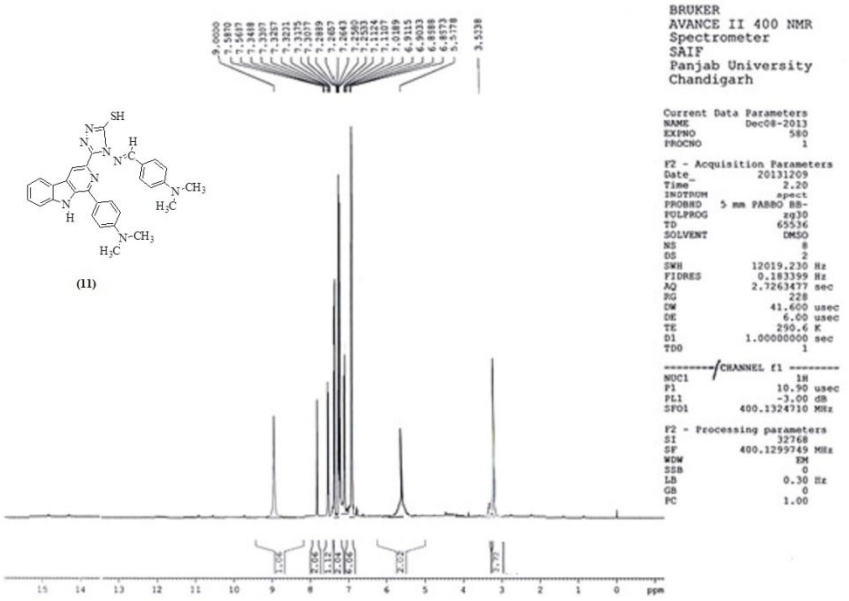


M.P. = 375-377ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3422.72 (N-H str.), 3086.22 (Ar-C-H Str.), 2918.45 (C-H str. Asym.), 2845.18 (C-H str. Sym.), 2555.32 (S-H str.), 1544.65, 1632.22 (1, 2, 4-triazole C=N; Pyr-C=N str.), 1584 (N=CH str.), 1532.24, 1428.14 (C=C ring str.), 1315.44 (C-N str.), 1255.56 (N-N str. of triazole), 780.42 (C-H out of plane bending); $^1$H NMR (400 MHz, DMSO-$d^6$): δ = 6.51-7.56 (m, ArH), 9.00 (s, N-H of pyrrole), 5.51 (s, H, S-H), 3.53 (s, N-$(CH_3)_2$), 7.58 (s, H, -N=CH); $^{13}$C NMR (100 MHz, DMSO-$d^6$): δ = 24.33 ($CH_3$ aliphatic), 27.57 ($CH_3$ aliphatic), 35.78($CH_3$ aliphatic), 37.70 ($CH_3$ aliphatic), 64.76 (CH aliphatic), 117.95, 122.01, 123.02, 123.15, 124.31, 124.74, 126.06, 127.97, 128.11, 128.55, 129.07,

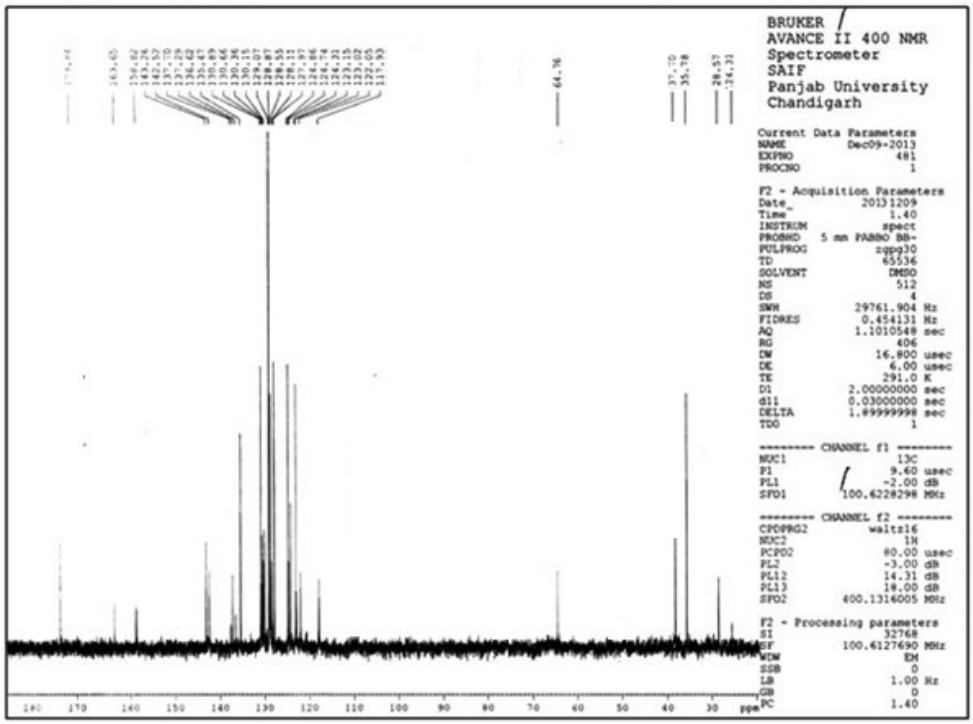
130.05, 130.15, 130.16, 130.46, 130.98, 135.47.6, 136.42, 137.26, 137.70, 142.57, 143.26, 159.23, 163.68, 174.28 (25 ArC's); MS (EI) m/z: 532.1 ($M^+$); CHN analysis: 67.55 (C), 5.25 (H), 21.01 (N).

**NMR and MS Spectra of Compound 11**

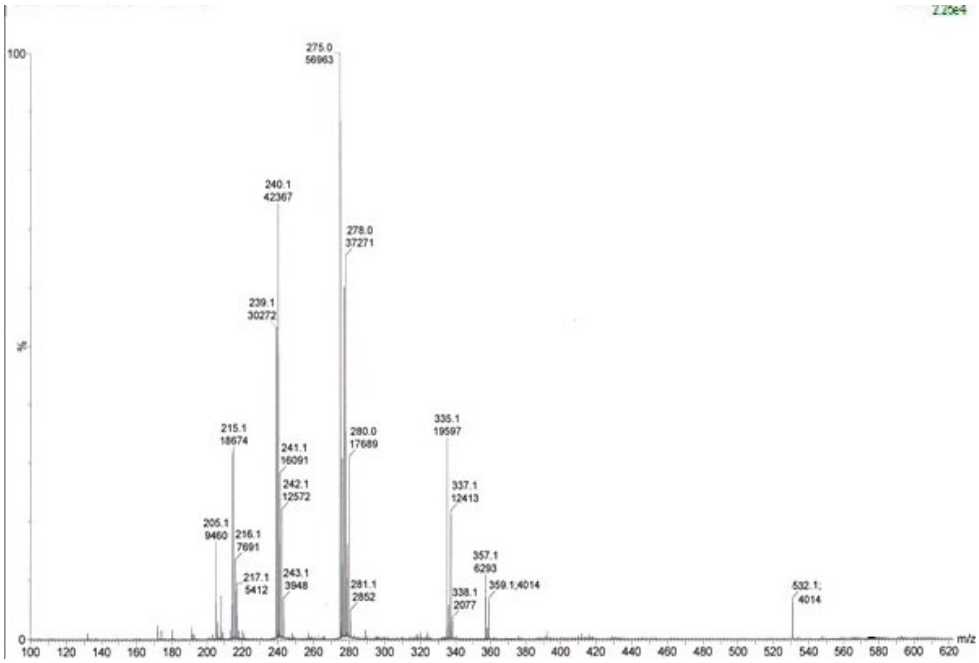
**$^1$HNMR**




**$^{13}$CNMR**

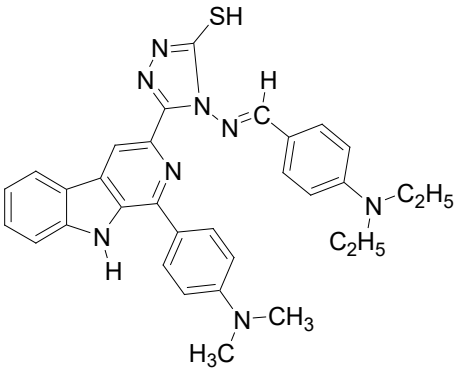


**MS**




**1-(*N*,*N*-dimethylbenzenamine)-3-(4-(p-(iminomethyl)-*N*,*N*-diethylbenzenamine)-5-thio-1, 2, 4-triazol-3-yl) β-carboline (12; $C_{32}H_{32}N_8S$)**

**12**

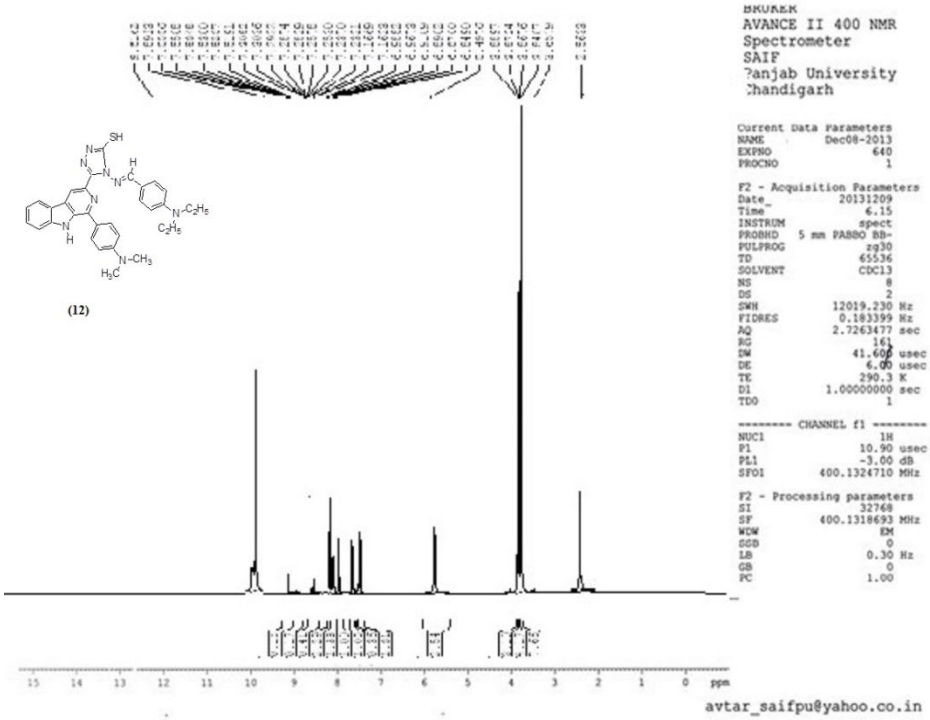



M.P. = 379-381ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3358.43 (N-H str.), 3069.63 (Ar-C-H str.), 2912.66 (C-H str. Asym.), 2817.63 (C-H str. Sym.), 2548.36 (S-H str.), 1577.64, 1638.17 (1, 2, 4-triazole C=N; Pyr-C=N str.), 1582 (N=CH str.), 1532.62, 1425.36 (C=C ring str.), 1312.58 (C-N Str.), 1262.85 (N-N str. of triazole), 782.62 (C-H out of plane bending); $^1$H NMR (400 MHz, DMSO-$d^6$): δ = 6.84-7.55 (m, ArH), 9.11 (s, N-H of pyrrole), 5.49 (s, H, S-H), 3.64-3.68 (q, N-$CH_2$), 2.56 (t, -$CH_3$), 3.46 (s, N-$(CH_3)_2$), 7.89 (s, H, -N=CH); $^{13}$C NMR (100 MHz, DMSO-$d^6$): δ =38.12 ($CH_2$ aliphatic), 38.32 ($CH_2$ aliphatic), 38.62($CH_3$ aliphatic), 39.04 ($CH_3$ aliphatic), 39.63 ($CH_3$ aliphatic), 39.91 ($CH_3$ aliphatic), 65.01 (CH aliphatic), 109.04,

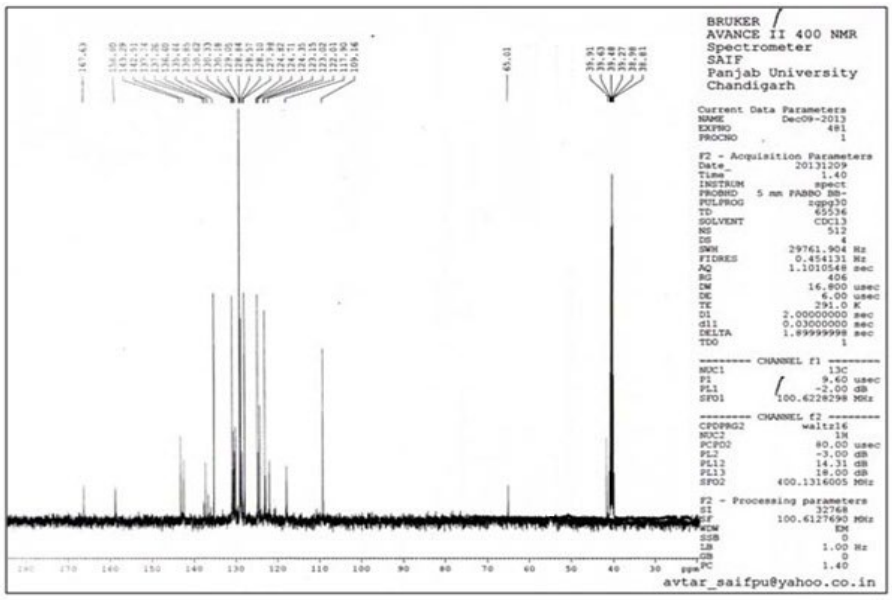
117.15, 120.13, 122.14, 123.94, 124.07, 124.74, 124.91, 127.35, 128.07, 128.48, 128.87, 129.09, 130.17, 130.47, 130.65, 130.99, 136.26, 136.40, 137.23, 137.57, 142.43, 143.29, 158.10, 167.73 (25 ArC's); MS (EI) m/z: 560.2 ($M^+$); CHN analysis: 68.46 (C), 5.68 (H), 19.87 (N).

**NMR and MS Spectra of Compound 12**

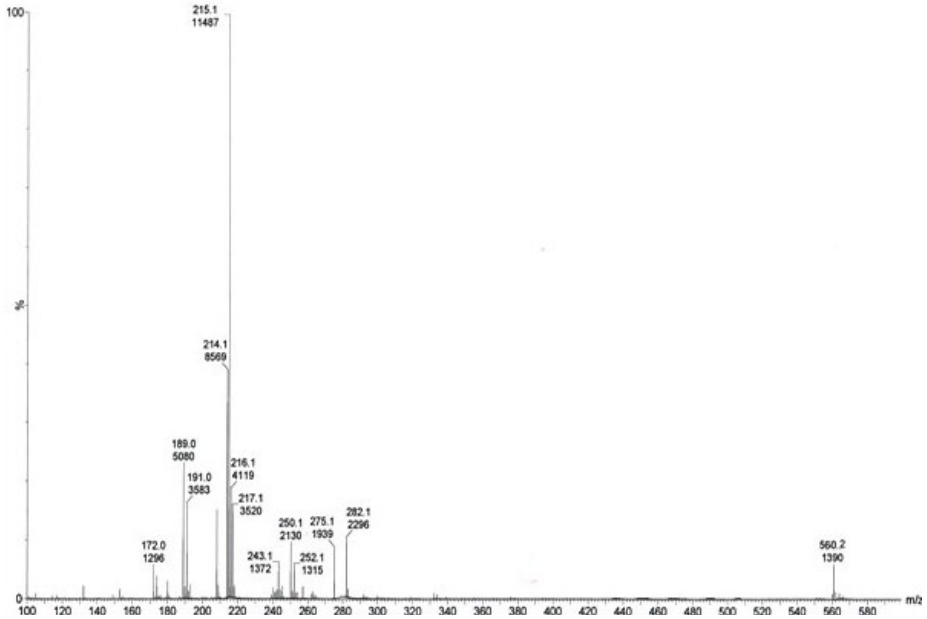
**$^1$HNMR**




**$^{13}$CNMR**



**MS**

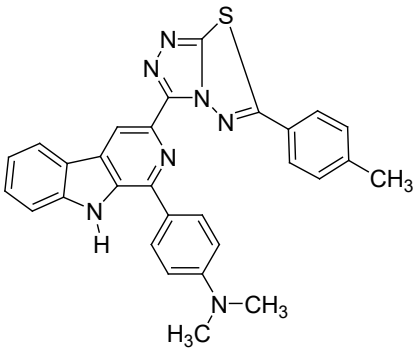



**General method for the synthesis of Compounds 13-14 from compound 8**

An equimolar mixture (5 mmol) of 1-(p- *N*, *N*-dimethylbenzenamine)-3-(4-amino-5-thiol-1, 2, 4-triazol-3-yl) β-carboline and appropriate aromatic acids in phosphorus oxychloride (5 ml) was refluxed for 5 hours. The reaction mixture was cooled to room temperature and then gradually poured onto crushed ice with stirring. The mixture was allowed to stand overnight and the separated out solid was filtered, treated with dilute sodium hydroxide solution and washed thoroughly with cold water. The compound so obtained was dried and crystallized from ethanol.

**1-(*N*, *N*-dimethylbenzenamine)-3-(6-p-tolyl-(1, 2, 4 triazolo (3, 4-*b*) 1, 3, 4-thiadiazole-3-yl) β-carboline (13; $C_{29}H_{23}N_7S$)**

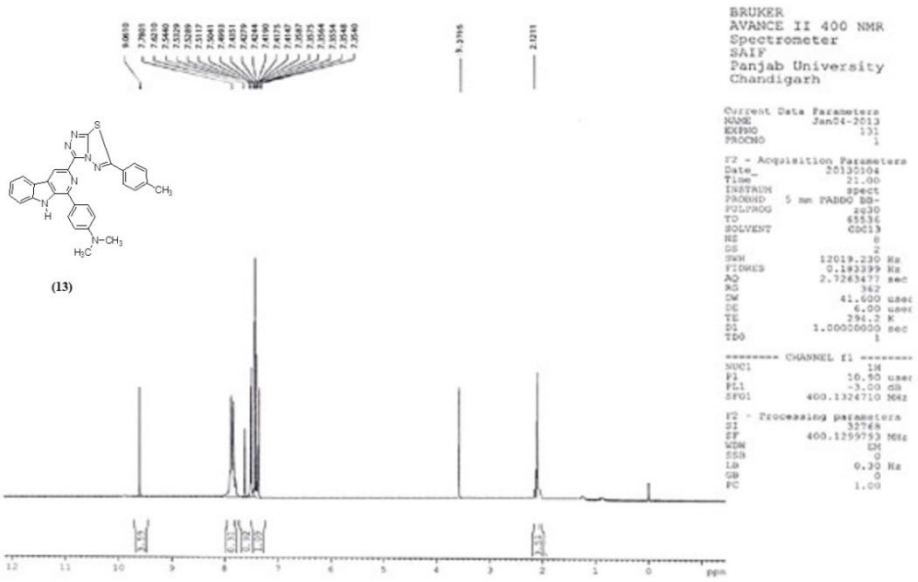
**13**



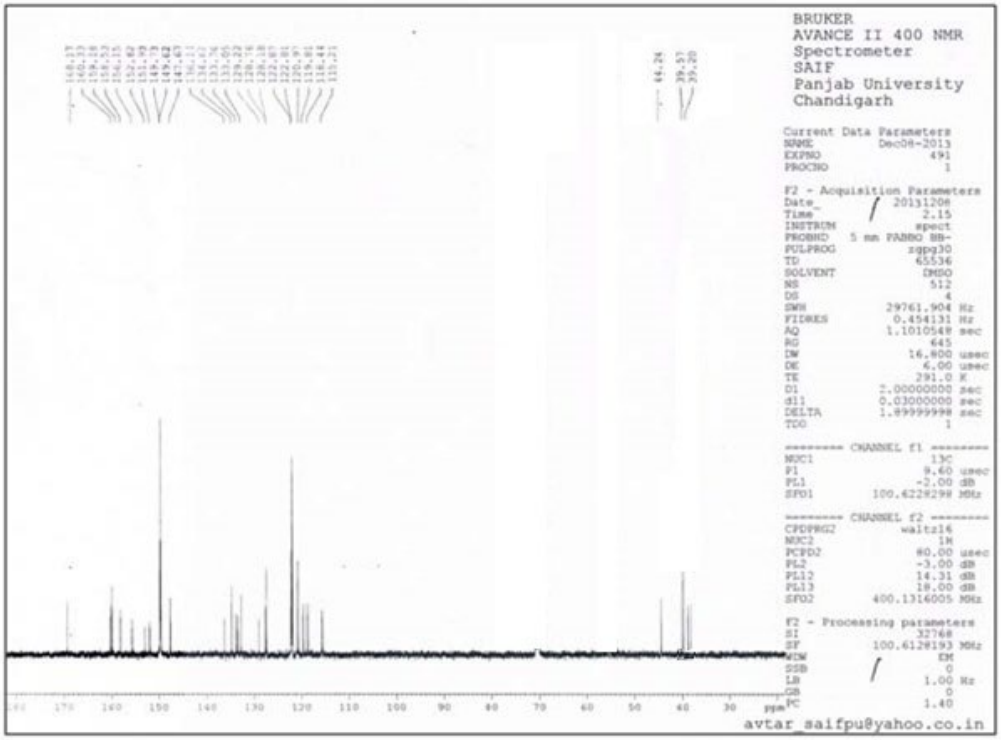

M.P. = 385-387ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3378.24 (N-H str.), 3094.86 (Ar-C-H str.), 2916.69 (C-H str. Asym.), 2818.39 (C-H str. Sym.), 1571.43, 1638.74 (1, 2, 4-triazole C=N; Pyr-C=N str.), 1532.93, 1432.96 (C=C ring str.), 1318.82 (C-N str.), 1266.84 (N-N str. of triazole), 782.91 (C-H out of plane bending); $^1$H NMR (400 MHz, DMSO-$d^6$): δ =7.20-7.68 (m, ArH), 9.52 (s, N-H of pyrrole), 2.12 (s, $CH_3$), 3.54 (s, N-$(CH_3)_2$); $^{13}$C NMR (100 MHz, DMSO-$d^6$): δ = 39.20 ($CH_3$ aliphatic), 39.57 ($CH_3$ aliphatic), 44.24 ($CH_3$ aliphatic), 115.42, 118.83, 119.22, 120.56, 122.23, 122.35, 128.26, 128.88, 129.28, 132.48, 133.16, 134.66, 136.11, 147.21 149.17, 149.56, 151.87, 152.73, 152.93, 154.29, 158.81, 159.91, 160.16, 1685.7, (23 ArC's); MS (EI) m/z: 500.1 ($M^+$); CHN analysis: 69.38 (C), 4.56 (H), 19.48 (N).

**NMR and MS Spectra of Compound 13**

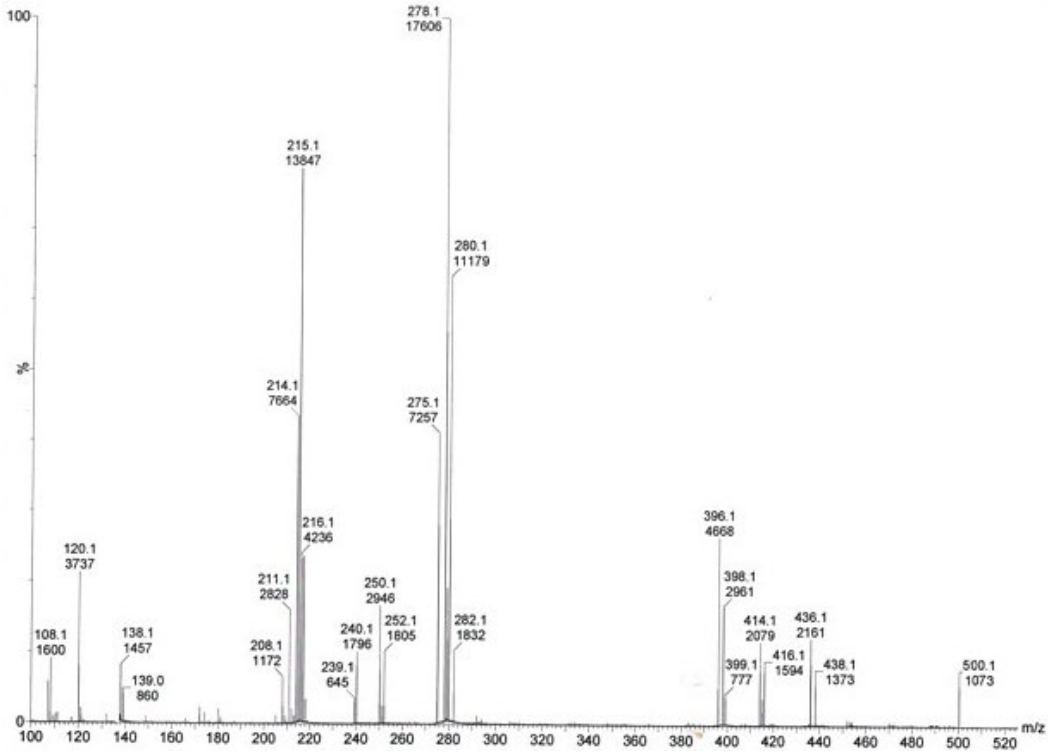
**$^1$HNMR**



## $^{13}$CNMR


BRUKER
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh
avtar_saifpu@yahoo.co.in

## MS


278.1
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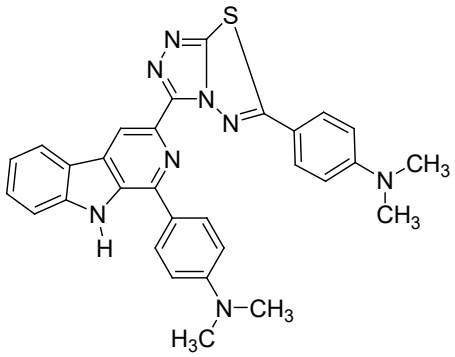
280.1
11179
214.1
7664
275.1
7257
216.1
4236
396.1
4668
120.1
3737
211.1
2828
250.1
2946
398.1
2961
108.1
1600
138.1
1457
240.1
1796
252.1
1805
282.1
1832
414.1
2079
436.1
2161
208.1
1172
239.1
645
399.1
777
416.1
1594
438.1
1373
500.1
1073
139.0
860
m/z

**1-(*N*, *N*-dimethylbenzenamine)-3-(6- *N*, *N*-dimethylbenzenamine -(1, 2, 4 triazolo (3, 4-*b*) 1, 3, 4-thiadiazole-3-yl) β-carboline (14; $C_{30}H_{26}N_8S$)**

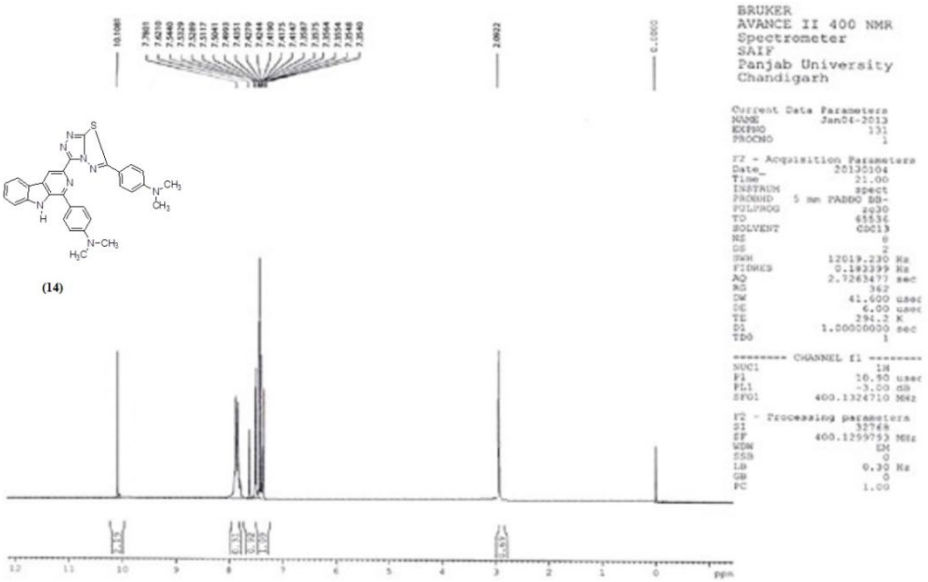
**14**



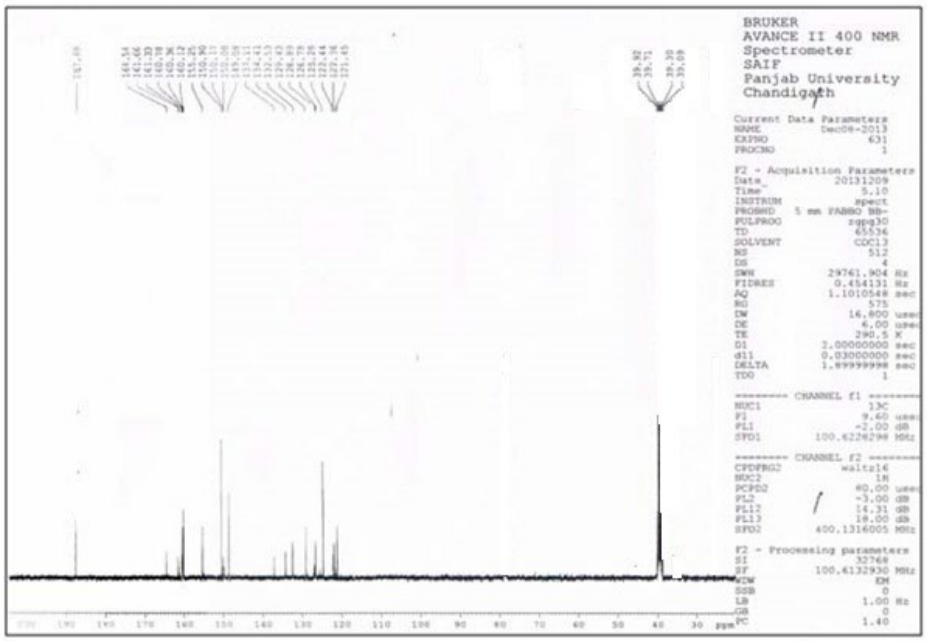
M.P. = 387-389ºC; IR (KBr, $cm^{-1}$): $\bar{\nu}$ = 3386.14 (N-H str.), 3088.73 (Ar-C-H str.), 2911.16 (C-H str. Asym.), 2816.23 (C-H str. Sym.), 1572.34, 1637.76 (1, 2, 4-triazole C=N; Pyr-C=N str.), 1536.31, 1422.16 (C=C ring str.), 1318.81 (C-N Str.), 1266.18 (N-N str. of triazole), 790.52 (C-H out of plane bending); $^1$H NMR (400 MHz, DMSO-$d^6$): δ = 7.12-7.72 (m, ArH), 10.16 (s, N-H of pyrrole), 3.06 (s, N-$(CH_3)_2$); $^{13}$C NMR (100 MHz, DMSO-$d^6$): δ =.): 39.09 ($CH_3$ aliphatic), 39.35 ($CH_3$ aliphatic), 39.72 ($CH_3$ aliphatic), 39.92 ($CH_3$ aliphatic), 121.13, 122.25, 122.85, 125.32, 126.32, 126.74, 129.03, 132.26, 134.74, 136.62, 148.26, 150.02, 150.65, 150.94, 155.27, 160.27, 160.33, 160.84, 161.36, 161.75, 164.63, 187.62 (22 ArC's); MS (EI) m/z: 530.1 ($M^+$); CHN analysis: 67.85 (C), 4.90 (H), 20.82 (N).

**NMR and MS Spectra of Compound 14**

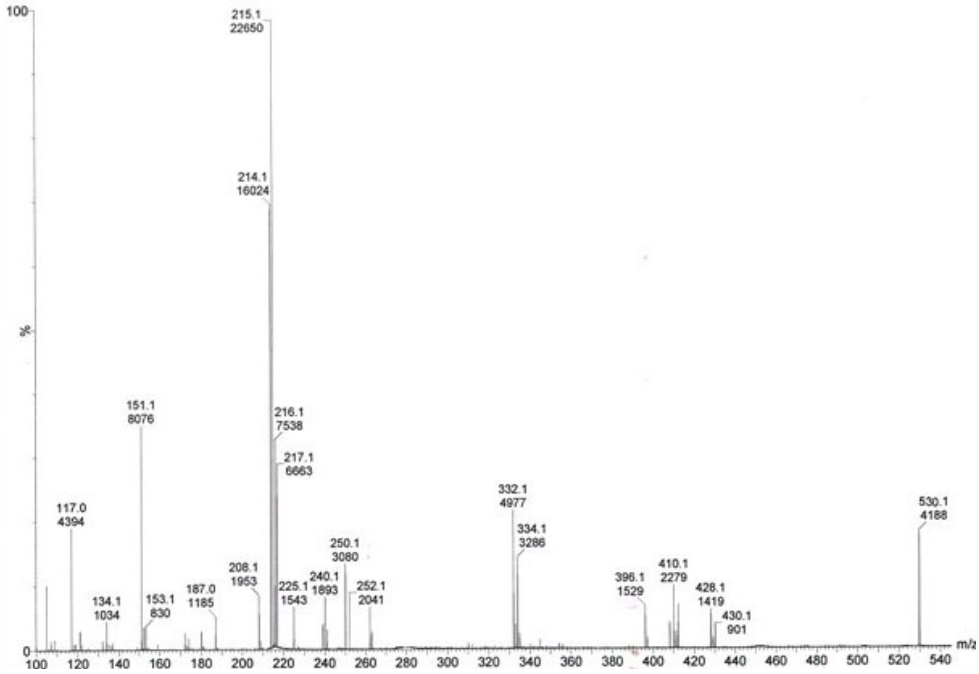
**$^1$HNMR**



**13CNMR**


BRUKER
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh

**MS**


215.1
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4394
134.1
1034
153.1
830
187.0
1185
208.1
1953
225.1
1543
240.1
1893
250.1
3080
252.1
2041
332.1
4977
334.1
3286
396.1
1529
410.1
2279
428.1
1419
430.1
901
530.1
4188
%
m/z

**Docking studies of designed compounds**

*Selection of the CDK2 structures*

Cyclin-Dependent Kinases (CDKs) are one of the most extensively studied Ser/Thr kinases. Cell division cycle 2 (Cdc2) was the first identified member of the CDKs and was originally isolated from *Saccharomyces cerevisiae*. CDK2/cyclin E functions during the cell cycle transition between gap phase I (G1) and DNA synthesis (S) phase, while CDK2/cyclin A is required throughout the progression of S phase. In previous reports CDK2 [1AQ1] have been widely used for the docking studies of β-carboline derivatives.

*Preparation of protein*

The PDB structures (www.rcsb.org) [1AQ1] were downloaded, refined and prepared using Schrodinger protein preparation wizard tool (Glide).

*Preparation of ligands*

Structures of the new designed β-carboline ligands were sketched using built panel of Maestro and taken in .mae format. Molecular Mechanics Force Fields (OPLS_2005) with default settings were used for the ligand minimization.

*Docking methodology*

Docking study was performed on Glide running on XP and previously reported methods.