5. EXPERIMENTAL

5.1 Chemical work

All the reagents and solvents required for synthesis of the compounds were purified by general laboratory [104] techniques before use. Melting points were determined using silicon oil bath type (Veego) and heating block type (Lab India) melting point apparatus and are uncorrected. Completion of the reactions was monitored by thin layer chromatography (TLC) using silica gel pre-coated plates (60 F_{254}, Merck, 0.25 mm thickness) visualizing in ultraviolet light (254 nm) or iodine vapours. Yields reported here are un-optimized. The IR spectra (wave numbers in cm^{-1}) were recorded on a BRUKER ALPHA-T (Germany) FT-IR spectrophotometer using potassium bromide discs. ^{1}H-NMR and ^{13}C-NMR spectra were recorded using Bruker Advance-II 400 MHz spectrometer in $CDCl_3$ or DMSO-d_6 solvents. Chemical shift has been expressed as δ ppm and coupling constant (*J*) in Hz. Mass spectra were recorded using a Thermo Fisher mass spectrometer with EI as ion source or Advion mass spectrometer with ESI as ion source and also using AB Sciex 3200 Q Trap mass analyzer for the compounds.

HPLC analysis was performed using Shimadzu prominence system (Kyoto, Japan) consisting of LC-20AT Pump, and SPD 20 A detector. The chromatographic column used was Phenomenex C-18, 250 mm length × 4.6 mm diameter with 0.5 μ particle sizes and the column temperature was maintained at 25-28 °C. Separation of analytes was performed under isocratic conditions at a flow-rate of 0.5-1.0 ml/min. The mobile phase consisted of acetonitrile/water (60:40). The purity of the compounds was found to be greater than 98%. Chromatographic separations were performed on columns using silica gel (100–200) or neutral alumina, activity grade I. All reagents used were of analytical reagent grade obtained from S. d. fine chemicals, Spectrochem, Qualigens or Sigma-Aldrich Avera chemicals.

5.1.1 2- Chlorophenylethylpropanamide[105] (4)

To a solution of 2-phenylethylamine **(1)** (2 gm, 1.65 mM) in chloroform (20 ml) aqueous solution of K_2CO_3 (6.8 gm, 5.61mM) was added and the reaction mixture was stirred at 0 ^{o}C for 15 min. 2- chloropropionyl chloride **(3)** (3.2 ml, 3.43mM) was diluted in $CHCl_3$ and added to the above reaction mixture dropwise in 30 min, while maintaining the temperature at 0°C. The reaction was monitored by TLC. The chloroform layer was separated

and recovered to afford a white solid product **(4),** (3.3gm, 98%); m.p. 65-70 ^{o}C. (Lit[106]. m.p. 64-65 ^{o}C).

Anal:

TLC : R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3285, 3089, 1655, 1555, 776.

MS (m/z) : 211.93 $(M)^+$.

5.1.2 *N*-(4-Chlorophenylethyl)-2-chloropropanamide[107] (5)

To a solution of 2-(4-chlorophenyl)ethylamine **(2)** (2 gm, 1.26 mM) in chloroform (20 ml) aqueous solution of K_2CO_3 (7.21 gm, 5.61 mM) was added and the reaction mixture was stirred at 0 ^{o}C for 15 min. 2-Chloropropionyl chloride **(3)** (3.2 ml, 3.43 mM) was diluted in $CHCl_3$ and added to the above reaction mixture drop-wise in 30 min while maintaining the temperature at 0 ^{o}C. The reaction was monitored by TLC. The chloroform layer was separated and recovered to afford a white solid product **(5),** (3,4 gm, 98 %); m.p. 70-75 ^{o}C.

Anal:

TLC : R_f 0.18 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3277, 3090, 2881, 1652, 1197, 835.

MS (m/z) : 247.74 $(M)^+$.

5.1.3 1-Methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one[107] (6)

2-Chloro-*N*-phenylethylpropanamide[105] **(4)** (2 g, 0.094 mmol) was melted to a tan oil with bubbling at 91°C, in a 100 ml RBF. Anhydrous aluminum chloride (6 g) was added to this and the reaction mixture was heated up to 180 ^{o}C for 10-15 min, cooling to room temperature and quenching with 10% HCl solution. Stirring was carried out for further 20 min. The resulting mixture was extracted with ethyl acetate (50 ml). The organic layer was dried over sodium sulphate and the solvent removed to get a semi solid compound which was purified by column chromatography using silica gel (100-200) as stationary phase and *n*-hexane-ethyl acetate (70 : 30 %) as eluent to get pure product **(6),** (1 g, 62%); m.p. 151-153 ^{o}C.

Anal:

TLC : R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3321, 3061, 2940, 1645, 1544, 753.

^{1}HNMR ($CDCl_3$) : 7.20-7.16 (m, 4H), 7.14 (bs, 1H), 4.24-4.22 (q, 1H, *J* = 6.9 Hz), 3.74 (m, 1H), 3.35 (m, 1H), 3.32 (m, 1H), 2.95 (m, 1H), 1.50-1.48 (d, 3H, *J* = 6.9 Hz).

MS (m/z) : 175.38 $(M)^+$.

5.1.4 8-Chloro-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one[107] (7)

Compounds **(7)** was prepared from *N*-(4-chlorophenylethyl)-2-chloropropanamide **(5)** using a procedure similar to that described for compound **(6)** to get a white solid **(7), (**1 gm, 50%); m.p. 155-160 ^oC.

Anal:

TLC : R_f 0.15 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3321, 3061, 2940, 1645, 1544, 753.

^{1}H-NMR ($CDCl_3$) : 7.44 (bs, 1H), 7.19-7-15 (m, 2H), 7.12 (s, 1H) 4.30-4.24 (q, 1H, *J* = 6.8 Hz), 3.78-3.72 (m, 1H), 3.25-3.12 (m, 2H), 3.01-2.94 (m, 1H), 1.38-1.36 (d, 3H, *J* = 6.8 Hz).

MS (m/z) : 209.41$(M)^+$.

5.1.5 General procedure (A) for preparation of 3-substitued 1-methyl-4,5-dihydro-1*H* benzo[*d*]azepin-2(3*H*)-one (8-43)

To a mixture of NaH (60% dispersion in mineral oil; 75 mg, 3.43 mM) in dry THF (9 ml) and DMF (1 ml) (4.5:0.5), 3-benzazepin-2-one **(6)** (500 mg, 2.85 mmol) was added in 100 ml two neck RBF and stirred for half an hour. Solution of the halide in dry THF (4.5 ml) and DMF (0.5 ml) was added drop wise to the above slurry and the resulting mixture was heated up to 60-80 ^oC in an oil bath in presence of dry N_2. On cooling to the room temperature, the reaction mixture was treated with ice-water (20 ml) and extracted with ethyl acetate (100 ml). The organic layer was dried over sodium sulphate and the solvent removed

to get a semi solid compound which was purified by column chromatography using silica gel as stationary phase and *n*-hexane-ethyl acetate as eluent.

5.1.6 3-Ethyl-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (8)

Synthesized as per the general procedure (A) using ethyl iodide (0.45 ml) to get a semi solid **(8),** (150 mg, 61 %).

Anal:

TLC : R_f 0.39 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3132, 2927, 1639, 1401, 727.

^{1}H-NMR ($CDCl_3$) : 7.17-7.09 (m, 4H), 4.41-4.36 (q, 1H, *J* = 6.9 Hz), 4.20-4.13 (m, 1H), 3.49-3.22 (m, 4H), 3.15-3.08 (m, 1H), 1.45-1.43 (d, 3H, *J* = 6.9 Hz), 1.07-1.03 (t, 3H, *J* = 7.1 Hz).

^{13}C-NMR ($CDCl_3$) : 175.58, 137.67, 129.62, 128.95, 127.61, 126.96, 125.85, 41.85, 40.89, 32.92, 18.35, 14.69.

MS (m/z) : 203.88 $(M)^+$.

5.1.7 3-Butyl-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (9)

Synthesized as per the general procedure (A) using butyl bromide (0.4 ml) to get a semi solid **(9),** (200 mg, 76%).

Anal:

TLC : R_f 0.42 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3130, 2932, 2871, 1658, 1401, 1097, 799.

^{1}H-NMR ($CDCl_3$) : 7.18-7.08 (m, 4H), 4.43-4.38 (q, 1H, *J* = 6.8 Hz), 4.22-4.16 (m, 1H), 3.43-3.41 (m, 2H), 3.38-3.36 (m, 1H), 3.32-3.28 (m, 1H), 3.27-3.25 (m, 1H), 1.44-1.43(d, 3H, *J* = 6.8 Hz), 1.41-140 (m, 2H), 1.26-1.16 (m, 2H), 0.88-0.85 (t, 3H, *J* = 7.3 Hz).

^{13}C-NMR ($CDCl_3$) : 175.63, 137.65, 137.13, 129.99, 128.95, 125.86, 47.60, 46.49, 41.47, 32.99, 30.33, 29.72, 20.10, 14.70.

MS (m/z) : 231.28 $(M)^+$.

5.1.8 3-Allyl-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (10)

Synthesized as per the general procedure (A) using allyl bromide (0.37 ml) to get a semi solid **(10)**, (200 mg, 73%).

Anal:

TLC : R_f 0.36 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3129, 2935, 1657, 1404, 797.

^{1}H-NMR ($CDCl_3$) : 7.20-7.09 (m, 4H), 5.74-5.55 (m, 1H), 5.07-5.06 (d, 2H), 4.46-4.41 (q, 1H, *J* = 6.8 Hz), 4.16-4.09 (m, 1H), 4.04-4.00 (m, 1H), 3.90-3.89 (m, 1H), 3.37-3.28 (m, 1H), 3.20-3.10 (m, 1H), 3.08-3.05 (m, 1H), 1.46-1.44 (d, 3H, *J* = 6.8Hz).

MS (m/z) : 215.79 $(M)^+$.

5.1.9 3-Propyl-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (11)

Synthesized as per the general procedure (A) using *n*-propyl bromide (0.33 ml) to get a semi solid **(11),** (195 mg, 79%).

Anal:

TLC : R_f 0.32 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3130, 2968, 2933, 1655, 1401,745.

^{1}H-NMR ($CDCl_3$) : 7.19-7.08 (m, 4H), 4.40-4.38 (q, 1H, *J* = 6.8 Hz), 4.21-4.17 (m, 1H), 3.44-3.41 (m, 2H), 3.31-3.29 (m, 2H), 3.22-3.21 (m, 1H), 1.52-1.48 (m, 2H), 1.46-1.43 (d, 3H, *J* = 6.8 Hz), 0.82-0.78 (t, 3H, *J* = 7.3 Hz).

^{13}C-NMR ($CDCl_3$) : 173.79, 137.29, 136.13, 130.02, 126.70, 126.71, 125.95, 49.48, 46.57, 40.49, 33.05, 21.47, 14.84, 11.32.

MS (m/z) : 217.66 $(M)^+$.

5.1.10 3-Dodecyl-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (12)

Synthesized as per the general procedure (A) using 1-bromododecane (0.83 ml) to get a semi solid **(12)**, (200 mg, 78%).

Anal:

TLC : R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3111, 2923, 1641, 1463, 1402, 945, 732.

^{1}H-NMR ($CDCl_3$) : 7.26-7.23 (d, 1H, *J* = 8.7 Hz), 7.20-7.13 (m, 2H), 7.09-7.06 (d, 1H, J = 8.7 Hz), 4.36-4.30 (q, 1H, *J* = 6.9 Hz), 4.13-4.06 (m, 1H), 3.45-3.32 (m, 3H), 3.22-3.17 (m, 1H), 3.13-3.10 (m, 1H), 1.55-1.52 (d, 3H, *J* = 6.9 Hz), 1.50-1.47 (m, 2H), 1.31-1.22 (m, 18H), 0.84-0.86 (t, 3H, *J* = 7.2 Hz).

^{13}C-NMR ($CDCl_3$) : 173.70, 137.30, 130.14, 129.99, 126.69, 125.92, 47.94, 46.56, 40.49, 33.06, 31.97, 29.68, 29.61, 29.59, 29.46, 29.40, 28.27, 26.91, 22.74, 14.81, 14.17.

MS (m/z) : 343.14 $(M)^+$.

5.1.11 3-(4-Bromobenzyl)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (13)

Synthesized as per the general procedure (A) using 4-bromobenzyl bromide (0.85 g) to get a white solid **(13)**, (210 mg, 81%); m.p. 90-92 ^oC.

Anal:

TLC : R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3129, 1647, 1401, 791.

^{1}H-NMR (DMSO-d_6): 7.40-7.37 (d, 2H, *J* = 8.3 Hz), 7.22-7.13 (m, 3H), 7.07-7.05 (m, 3H), 4.58-4.43 (m, 3H), 4.18-4.10 (m, 1H), 3.33-3.31 (m, 1H), 3.20-3.15 (m, 1H), 2.99-2.93 (m, 1H), 1.48-1.47 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 174.01, 137.12, 136.86, 136.12, 131.64, 129.87, 129.70, 126.90, 126.81, 125.67, 121.22, 50.24, 46.39, 40.30, 32.45, 14.59.

MS (m/z) : 343.22 $(M)^+$.

Calcd for $C_{18}H_{18}BrNO$: C, 62.80; H, 5.27; N, 4.07. Found: C, 62.65; H, 5.01; N, 3.72 %.

5.1.12 3-(2,6-Difluorobenzyl)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (14)

Synthesized as per the general procedure (A) using 2,6-difluorobenzyl bromide (0.70 g) to get a white solid **(14)**, (290 mg, 85%); m.p. 133-135 ^oC.

Anal:

TLC : R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3116, 2984, 2944, 1662, 1401, 1033, 836.

^{1}H-NMR (DMSO-d_6) : 7.35-7.31 (m, 1H), 7.18-7.10 (m, 3H), 7.03-7.01 (d, 1H, *J* = 6.6 Hz), 6.97-6.93 (m, 2H), 4.79-4.76 (d, 1H, *J* = 14.1 Hz), 4.54-4.45 (d, 1H, *J* = 14.1 Hz), 4.45-4.43 (q, 1H, *J* = 6.8 Hz), 4.20-4.12 (m, 1H), 3.41-3.37 (m, 1H), 3.17-3.12 (m, 1H), 2.99-2.92 (m, 1H) 1.45-1.43 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 172.55, 162.16, 159.68, 135.74, 135.01, 128.88, 128.55, 125.66, 124.82, 112.34, 110.46, 44.57, 39.29, 37.28, 31.43, 13.67.

MS (m/z) : 301.64 $(M)^+$.

Calcd for $C_{18}H_{17}F_2NO$: C, 71.75; H, 5.69; N, 4.65. Found: C, 71.52; H, 5.45; N, 4.41 %.

5.1.13 3-Isopropyl-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (15)

Synthesized as per the general procedure (A) using isopropyl iodide (0.54 ml) to get a semi solid **(15)**, (145 mg, 59%).

Anal:

TLC : R_f 0.40 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3276, 3129, 1639, 1548, 1401, 1262, 763.

^{1}H-NMR (DMSO-d_6): 7.46-7.43 (m, 2H), 7.36-7.34 (m, 1H), 7.24-7.22 (m, 1H), 7.18-7.16 (m, 1H), 7.13-7.7.09 (m, 1H), 5.65-5.60 (m, 1H), 5.32-5.29 (m, 1H), 3.94-3.83 (m, 2H), 1.32-1.30 (d, 3H, *J* = 7.0 Hz), 1.09-1.07 (d, 3H, *J* = 6.6 Hz), 1.02-1.01 (d, 3H, *J* = 6.6 Hz).

MS (m/z) : 216.46 $(M)^+$.

5.1.14 1-Methyl-3-pentyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3H)-one (16)

Synthesized as per the general procedure (A) using iodopentane (0.45 ml) to get a semi solid **(16)**, (210 mg, 73%).

Anal:

TLC : R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3128, 3024, 2932, 1641, 1401, 733.

^{1}H-NMR ($CDCl_3$) : 7.26-7.24 (d, 1H, *J* = 8.3 Hz), 7.20-7.13 (m, 2H), 7.09-7.07 (d, 1H, *J* = 8.3 Hz), 4.36-4.31 (q, 1H, *J* = 6.8 Hz), 4.14-4.06 (m, 1H), 3.45-3.27 (m, 4H), 3.17- 3.10 (m, 1H), 1.56-1.50 (d, 3H, *J* = 6.8 Hz), 1.48-1.46 (m, 2H), 1.31-1.16 (m, 4H), 0.86-0.83 (t, 3H, *J* = 7.1 Hz).

^{13}C-NMR ($CDCl_3$) : 173.66, 137.29, 136.12, 129.96, 126.66, 126.58, 125.88, 47.85, 46.51, 40.43, 33.02, 29.02, 27.89, 22.14, 14.77, 14.01.

MS (m/z) : 245.79 $(M)^+$.

5.1.15 3-Isopentyl-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepine-2(3*H*)-one (17)

Synthesized as per the general procedure (A) using 1-bromo-3-methylbutane (0.42 ml) to get a semi solid **(17)**, (200 mg, 71%).

Anal:

TLC : R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3133, 2960, 2873, 1645, 1401, 735.

^{1}H-NMR (DMSO-d_6) : 7.19-7.18 (d, 1H, *J* = 8.4 Hz), 7.13-7.06 (m, 2H), 7.02-7.00 (d, 1H, *J* = 8.4 Hz), 4.28-4.23 (q, 1H, *J* = 6.8 Hz), 4.06-3.99

(m, 1H), 3.40-3.27 (m, 3H), 3.22-3.15 (m, 1H), 3.07-3.01 (m, 1H), 1.48-1.44 (d, 3H, *J* = 6.8 Hz), 1.40-1.36 (m, 1H), 1.32-1.27 (m, 2H), 0.82-0.80 (d, 6H, *J* = 6.6 Hz).

^{13}C-NMR ($CDCl_3$) : 172.52, 136.15, 135.06, 128.90, 125.61, 125.53, 124.78, 45.42, 45.28, 39.26, 35.92, 31.95, 25.01, 21.54, 13.66.

MS (m/z) : 245.39 $(M)^+$.

5.1.16 1-Methyl-3-(3-propargyl)-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (18)

Synthesized as per the general procedure (A) using 3-bromo-1-propyne (0.30 ml) to get a white solid **(18)**, (180 mg, 74%), m.p. 122-124 ^oC.

Anal:

TLC : R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3129, 1664, 1401, 800.

^{1}H-NMR ($CDCl_3$) : 7.24-7.23 (m, 1H), 7.22-7.15 (m, 2H), 7.13-7.10 (m, 1H), 4.41-4.36 (dd, 2H, J_1 = 2.5 Hz and J_2 = 17.4 Hz), 4.34-4.30 (q, 1H, *J* = 6.6 Hz), 4.16-4.11 (m, 1H), 3.65-3.58 (m, 1H), 3.36-3.29 (m, 1H), 3.24-3.16 (m, 1H), 2.19-2.18 (t, 1H, *J* = 2.5 Hz), 1.58-1.56 (d, 3H, *J* = 6.6 Hz).

^{13}C-NMR ($CDCl_3$) : 173.21, 136.96, 136.42, 129.77, 126.91, 126.79, 125.79, 79.26, 71.78, 46.31, 40.50, 36.25, 32.49, 14.05.

MS (m/z) : 213.46 $(M)^+$.

Calcd for $C_{14}H_{14}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.58; H, 6.93; N, 6.48 %.

5.1.17 1-Methyl-3-(1-naphthylmethyl)-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (19)

Synthesized as per the general procedure (A) using 1-chloromethylnaphthalene (0.34 ml) to get a semi solid **(19)**, (300 mg, 87%).

Anal:

TLC : R_f 0.37 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3116, 2984, 2944, 1662, 1401, 1032, 836.

^{1}H-NMR (DMSO-d_6) : 7.81-7.80 (d, 1H, *J* = 8.2 Hz), 7.74-7.69 (dd, 2H, *J* = 8.2 Hz), 7.36-7.15 (m, 5H), 7.12-7.08 (m, 1H), 7.00-6.96 (m, 1H), 6.71-6.69 (d, 1H, *J* = 8.0 Hz), 5.03-5.00 (d, 1H, *J* = 14.8 Hz), 4.98-4.94 (d, 1H, *J* = 14.8 Hz) 4.35-4.30 (q, 1H, *J* = 6.8 Hz), 3.88-3.81 (m, 1H), 3.30-3.24 (m, 1H), 2.94-2.88 (m, 1H), 2.61-2.53 (m, 1H), 1.56-1.54 (d, 3H, J = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 173.88, 136.75, 136.03, 133.73, 133.07, 131.80, 129.99, 128.52, 128.45, 127.10, 126.75, 126.55, 126.38, 125.97, 125.68, 125.12, 123.87, 48.07, 44.60, 40.38, 32.19, 14.67.

MS (m/z) : 315.67 $(M)^+$.

5.1.18 3-(2-Chloro-4-fluoro)benzyl-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (20)

Synthesized as per the general procedure (A) using 2-chloro-4-fluorobenzyl bromide (0.8 g) to get a semi solid **(20)**, (240 mg, 66%).

Anal:

TLC : R_f 0.39 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3130, 2930, 1658, 1400, 1041, 903.

^{1}H-NMR ($CDCl_3$) : 7.30-7.28 (d, 1H, *J* = 7.5 Hz), 7.24-7.19 (m, 2H), 7.11-6.99 (m, 3H), 6.85-6.83 (d, 1H, *J* = 8.2 Hz), 4.74-4.64 (dd, 2H, J_1 = 15.5 Hz, and J_2 = 21.44 Hz), 4.43-4.38 (q, 1H, *J* = 6.8 Hz), 4.11-4.03 (m, 1H), 3.44-3.38 (m, 1H), 3.27-3.20 (m, 1H), 3.01-2.94 (m, 1H), 1.61-1.59 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 174.21, 162.91, 137.18, 136.81, 134.05, 133.95, 131.21, 130.67, 129.92, 127.00, 125.76, 116.88, 114.52, 47.60, 46.93, 40.41, 32.55, 14.59.

MS (m/z) : 317.73 $(M)^+$.

5.1.19 3-(*sec*. Butyl)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (21)

Synthesized as per the general procedure (A) using 2-bromobutane (0.38 ml) to get semi solid **(21)**, (210 mg, 82%).

Anal:

TLC : R_f 0.39 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3122, 2965, 1637, 1453, 802.

^{1}H-NMR ($CDCl_3$) : 7.44-7.41 (m, 1H), 7.26-7.17 (m, 3H), 6.94-6.86 (m, H), 5.59-5.54 (m, 1H), 5.30-5.27 (m, 1H), 3.82-3.73 (m, 2H), 1.45-144 (d, 3H, *J* = 7.2 Hz), 1.34-1.10 (m, 3H), 0.99-0.88 (d, 3H, *J* = 6.6 Hz), 0.75-0.63 (t, 3H, *J* = 7.4 Hz).

5.1.20 1-Methyl-3-(4-methylbenzyl)-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (22)

Synthesized as per the general procedure (A) using 4-methylbenzyl bromide (0.49 ml) to get a white solid **(22)**, (290 mg, 88%); m.p. 93-95 ^oC.

Anal:

TLC : R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3122, 2965, 1672, 1453, 802.

^{1}H-NMR ($CDCl_3$) : 7.28-7.26 (d, 1H, *J* = 7.6 Hz), 7.22-7.20 (d, 1H, *J* = 7.5 Hz), 7.16-7.12 (d, 1H, *J* = 7.5 Hz), 7.07-7.00 (m, 5H), 4.63-4.59 (d, 1H, *J* = 14.6 Hz), 4.53-4.49 (d, 1H, *J* = 14.6 Hz), 4.40-4.35 (q, 1H, *J* = 6.8 Hz), 4.01-3.93 (m, 1H), 3.39-3.33 (m, 1H), 3.16-3.11 (m, 1H), 2.95-2.86 (m, 1H), 2.30 (s, 3H), 1.69-1.59 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 173.95, 137.19, 136.99, 136.31, 134.71, 129.93, 129.23, 128.08, 126.75, 126.65, 125.78, 50.33, 45.90, 40.41, 32.51, 21.13, 14.78.

MS (m/z) : 279.26 $(M)^+$.

Calcd for $C_{19}H_{21}NO$: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.42; H, 7.44; N, 4.83%.

5.1.21 3-(4-Isopropylbenzyl)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (23)

Synthesized as per the general procedure (A) using 4-isopropylbenzyl bromide (0.60 ml) to get a white solid **(23)**, (300 mg, 81%); m.p. 75-77 ^{o}C.

Anal:

TLC : R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3131, 3013, 2961, 1644, 1403, 1097, 800.

^{1}H-NMR ($CDCl_3$) : 7.30-7.28 (d, 1H, *J* = 7.6 Hz), 7.23-7.12 (m, 4H), 7.09-7.07 (d, 2H, *J* = 8.2 Hz), 7.03-7.01 (d, 1H, *J* = 7.2 Hz), 4.69-4.65 (d, 1H, *J* = 14.7 Hz), 4.51-4.47 (d, 1H, *J* = 14.7 Hz), 4.40-4.39 (q, 1H, *J* = 6.9 Hz), 4.00-3.96 (m, 1H), 3.41-3.35 (m, 1H), 3.18-3.13(m, 1H), 2.93-2.86 (m, 2H) 1.62-1.61 (d, 3H, *J* = 6.9 Hz), 1.24-1.22 (d, 6H, *J* = 6.9 Hz).

^{13}C-NMR ($CDCl_3$) : 172.86, 146.94, 136.16, 135.26, 133.99, 128.86, 126.98, 125.69, 125.63, 125.53, 124.71, 49.29, 44.94, 39.34, 32.73, 31.41, 22.97 13.71.

MS (m/z) : 307.65 $(M)^{+}$.

Calcd for $C_{21}H_{25}NO$: C, 82.04; H, 8.20; N, 4.56. Found: C, 81.72; H, 7.92; N, 4.44 %.

5.1.22 3-(4-Trifluoromethylbenzyl)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (24)

Synthesized as per the general procedure (A) using 4-trifluoromethylbenzyl bromide (1.55 ml) to get a white solid **(24)**, (300 mg, 79%); m.p. 79-81 ^{o}C.

Anal:

TLC : R_f 0.22 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3130, 2931, 1658, 1326, 1117, 817.

^{1}H-NMR ($CDCl_3$) : 7.51-7.49 (d, 2H, *J* = 8.1 Hz), 7.31-7.29 (d, 1H, *J* = 7.6 Hz), 7.25-7.16 (m, 4H), 7.05-7.03 (d, 1H, *J* = 7.6 Hz), 4.70-4.60 (dd, 2H, J_1 = 15.2 Hz and J_2 = 13.1), 4.42-4.37 (q, 1H, *J* = 6.8 Hz),

4.07-4.00 (m, 1H), 3.40-3.33 (m, 1H), 3.25-3.18 (m, 1H), 2.98-2.90 (m, 1H), 1.63-1.61 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 174.08, 141.96, 137.23, 136.12, 129.83, 129.48, 128.22, 126.92, 125.68, 125.58, 125.47, 122.81, 50.62, 46.83, 40.41, 32.44, 14.56.

MS (m/z) : 333.78 $(M)^+$

Calcd for $C_{19}H_{18}F_3NO$: C, 68.46; H, 5.44; N, 4.20. Found: C, 68.19; H, 5.25; N, 3.96%.

5.1.23 3-(3,5-Difluorobenzyl)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (25)

Synthesized as per the general procedure (A) using 3,5-difluorobenzyl bromide (0.44 ml) to get a semi solid **(25)**, (280 mg, 82%).

Anal:

TLC : R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3129, 2984, 1657, 1446, 1596, 1116, 761.

^{1}H-NMR ($CDCl_3$) : 7.31-7.29 (d, 1H, *J* = 7.3 Hz), 7.26-7.24 (d, 1H, *J* = 7.3 Hz), 7.19-7.17 (m, 1H), 7.08-7.06 (d, 1H, *J* = 7.3 Hz), 6.69-6.60 (m, 3H), 4.62-4.58 (d, 1H, *J* = 15.3 Hz), 4.54-4.50 (d, 1H, *J* = 15.3 Hz), 4.42-4.37 (q, 1H, *J* = 6.8 Hz), 4.07-4.00 (m, 1H), 3.39-3.33 (m, 1H), 3.28-3.23 (m, 1H), 3.03-2.94 (m, 1H), 1.62-1.61 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 174.06, 164.41, 161.93, 141.96, 141.78, 137.15, 129.79, 127.04, 125.62, 110.57, 103.01, 50.30, 46.86, 40.30, 32.32, 14.48.

MS (m/z) : 301.23 $(M)^+$.

5.1.24 3-(2-Chloro-6-fluoro)benzyl-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (26)

Synthesized as per the general procedure (A) using 2-chloro-6-fluorobenzyl bromide (0.48 ml) to get a white solid **(26)**, (290 mg, 80%); m.p. 147-149 ^{o}C.

Anal:

TLC : R_f 0.28 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3140, 2933, 1663, 1531, 1402, 781.

^{1}H-NMR ($CDCl_3$) : 7.27-7.12 (m, 5H), 7.00-6.96 (m, 2H), 5.02-4.98 (d, 1H, *J* = 14.3 Hz) 4.73-4.69 (d, 1H, *J* = 14.3 Hz), 4.40-4.35 (q, 1H, *J* = 6.8 Hz), 4.01-3.93 (m, 1H), 3.37-3.31 (m, 1H), 3.15-3.09 (m, 1H), 2.96-2.88 (m, 1H), 1.59-1.57 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 172.66, 162.47, 135.67, 135.17, 135.02, 128.96, 128.58, 125.65, 124.83, 124.52, 122.06, 121.89, 113.29, 43.61, 39.95, 39.33, 31.45, 13.72

MS (m/z) : 317.03 $(M)^{+}$.

Calcd for $C_{18}H_{17}FClNO$: C, 68.03; H, 5.39; N, 4.41. Found: C, 67.79; H, 5.14; N, 4.18 %.

5.1.25 3-(2,5-(Bistrifluoro)benzyl-1-methy-4,5-dihydro-1-benzo[*d*]azepin-2(3*H*)-one (27)

Synthesized as per the general procedure (A) using 2,5-bistrifluoromethylbenzyl bromide (0.65 ml) to get a white solid **(27)**, (300 mg, 66%); m.p. 110-112 ^{o}C.

Anal:

TLC : R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 2981, 2932, 1657, 1491, 1286, 1117, 706.

^{1}H-NMR ($CDCl_3$) : 7.73 (s, 1H), 7.48 (s, 2H), 7.32-7.30 (d, 1H, *J* = 7.3 Hz), 7.26-7.24 (d, 1H, *J* = 7.4 Hz), 7.20-7.18 (d, 1H, *J* = 7.4 Hz), 7.07-7.05 (d, 1H, *J* = 7.3 Hz), 4.84-4.80 (d, 1H, *J* = 15.5 Hz), 4.60-

4.56 (d, 1H, *J* = 15.5 Hz), 4.43- 4.38 (q, 1H, *J* = 6.8 Hz), 4.12-4.06 (m, 1H), 3.40-3.35 (m, 2H), 3.00-2.92 (m, 1H), 1.63-1.55 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 174.25, 140.67, 137.26, 135.77, 132.41, 131.75, 129.73, 127.65, 127.23, 125.40, 124.55, 121.43, 121.39, 121.35, 121.31, 50.42, 47.37, 40.24, 32.27, 14.16.

Calcd for $C_{18}H_{17}FClNO$: C, 68.03; H, 5.39; N, 4.41. Found: C, 67.79; H, 5.14; N, 4.18 %.

5.1.26 3-(2-Cyanobenzyl)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (28)

Synthesized as per the general procedure (A) using 2-bromomethylbenzonitrile (0.68 g) to get a white solid **(28)**, (290 mg, 80%); m.p. 141-143 ^{o}C.

Anal:

TLC : R_f 0.33 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3143, 2978, 2225, 1650, 1490, 1357, 1165, 770.

^{1}H-NMR ($CDCl_3$) : 7.67-7.61 (m, 1H), 7.45-7.41 (m, 1H), 7.34-7.30 (m, 2H), 7.21-7.17 (m, 3H), 7.06-7.04 (d, 1H), 4.87-4.77 (dd, 2H, J_1 = 15.6 Hz and J_2 = 19.08 Hz), 4.45-4.39 (q, 1H, *J* = 6.8 Hz), 4.14-4.08 (m, 1H), 3.52-3.42 (m, 1H), 3.30-3.23 (m, 1H), 3.02-2.93 (m, 1H), 1.65-1.60 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 174.16, 141.72, 137.02, 136.08, 133.19, 132.71, 129.82, 128.88, 127.79, 126.97, 125.62, 117.64, 111.67, 49.11, 47.37, 40.24, 32.41, 14.45.

MS (m/z) : 291.1 $(M+1)^+$.

Calcd for Calcd for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.65. Found: C, 78.22; H, 5.98; N, 9.32 %.

5.1.27 3-(3-Nitrobenzyl)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (29)

Synthesized as per the general procedure (A) using 3-nitrobenzyl bromide (0.73 g) to get a white solid **(29)**, (250 mg, 80%); m.p. 120-122 ^{o}C.

Anal:

TLC : R_f 0.24 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3130, 2979, 2930, 1655, 1525, 1348, 1091, 811.

^{1}H-NMR ($CDCl_3$) : 8.10-8.07 (d, 1H, *J* = 7.3 Hz), 7.96 (s, 1H), 7.43-7.41 (m, 2H), 7.31-7.29 (d, 1H, *J* = 7.2 Hz), 7.26-7.24 (m, 1H), 7.21-7.19 (d, 1H, *J* = 7.2 Hz), 7.06-7.04 (d, 1H, *J* = 7.2 Hz), 4.71-4.69 (d, 1H, *J* = 14.9 Hz), 4.68-4.66 (d, 1H, *J* = 14.9 Hz), 4.42-4.40 (q, 1H, *J* = 6.8 Hz), 4.09-4.07 (m, 1H), 3.42-3.38 (m, 1H), 3.24-3.20 (m, 1H), 2.97-2.87 (m, 1H), 1.63-1.61 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 173.08, 147.30, 139.00, 136.07, 134.88, 132.94, 128.75, 128.59, 126.03, 125.95, 124.55, 121.40, 121.38 49.42, 46.08, 39.22, 31.30, 13.36.

MS (m/z) : 311.00 $(M+1)^{+}$.

Calcd for $C_{18}H_{18}N_2O_2$: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.45; H, 5.58; N, 8.78 %.

5.1.28 3-(4-Chlorobenzyl)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (30)

Synthesized as per the general procedure (A) using 4-chlorobenzyl bromide (0.45 ml) to get a white solid **(30)**, (290 mg, 82%); m.p. 102-104 ^{o}C.

Anal:

TLC : R_f 0.24 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3133, 3028, 2977, 1649, 1403, 1093, 816.

^{1}H-NMR ($CDCl_3$) : 7.20-7.14 (m, 5H), 7.05-7.00 (m, 3H), 4.62-4.50 (dd, 2H, J_1 = 14.9 Hz and J_2 = 21.26 Hz), 4.40-4.38 (q, 1H, *J* = 6.8 Hz),

4.00-3.96 (m, 1H), 3.37-3.30 (m, 1H), 3.19-3.12 (m, 1H), 2.94-2.85 (m, 1H), 1.60-1.59 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 173.98, 137.16, 136.12, 133.14, 129.84, 128.68, 126.87, 125.69, 50.21, 46.37, 40.40, 32.46, 14.60.

MS (m/z) : 300.01 $(M+1)^+$.

Calcd for $C_{18}H_{18}ClNO$: C, 72.11; H, 6.05; N, 4.67. Found: C, 71.85; H, 5.85; N, 4.35%.

5.1.29 3-(4-Methoxybenzyl)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (31)

Synthesized as per the general procedure (A) using 4-methoxybenzyl bromide (0.47 ml) to get a semi solid **(31)**, (290 mg, 82%).

Anal:

TLC : R_f 0.24 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3108, 3065, 2935, 1649, 1247, 1034, 821.

^{1}H-NMR ($CDCl_3$) : 7.23-7.18 (m, 1H), 7.15-7.11 (d, 1H, *J* = 7.2 Hz), 7.09- 7.06 (d, 1H, *J* = 7.2 Hz), 7.00-6.99 (m, 2H), 6.94-6.92 (d, 1H, *J* = 7.3 Hz), 6.74-6.71 (m, 2H), 4.55-4.52 (d, 1H, *J* = 14.6 Hz), 4.48-4.42 (d, 1H, *J* = 14.6 Hz), 4.32-4.30 (q, 1H, *J* = 6.8 Hz), 3.95-3.88 (m, 1H), 3.70 (s, 3H), 3.33-3.27 (m, 1H), 3.20-3.08 (m, 1H), 2.86-2.82 (m, 1H), 1.65-1.60 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 173.92, 158.91, 137.14, 136.27, 129.93, 129.87, 129.41, 126.73, 126.64, 125.76, 113.91, 55.28, 50.01, 45.78, 40.40, 32.52, 14.74.

MS (m/z) : 296.01 $(M+1)^+$.

5.1.30 3-(4-Fluorobenzyl)-1-methyl- 4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (32)

Synthesized as per the general procedure (A) using 4-fluorobenzyl bromide (0.42 ml) to get semi solid **(32)**, (240 mg, 70%).

Anal:

TLC : R_f 0.24 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3130, 2964, 2928, 1653, 1403, 1262, 798.

^{1}H-NMR ($CDCl_3$) : 7.29-7.14 (m, 3H), 7.12-7.08 (m, 2H), 7.03-7.02 (m, 1H), 6.96-6.91 (m, 2H), 4.60-4.52 (dd, 2H, J_1 = 14.8 Hz and J_2 = 18.14 Hz), 4.40-4.35 (q, 1H, J = 6.8 Hz), 4.04-3.96 (m, 1H), 3.39-3.32 (m, 1H), 3.19-3.12 (m, 1H), 2.85-2.29 (m, 1H), 1.61-1.59 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 174.03, 163.44, 137.22, 136.21, 133.65, 130.07, 129.93, 127.69, 126.82, 125.77, 115.69, 50.16, 46.27, 40.48, 32.60, 14.69.

MS (m/z) : 284.01 $(M+1)^+$.

5.1.31 3-Cyclopropylmethyl-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (33)

Synthesized as per the general procedure (A) using bromomethylcyclopropane (0.34 ml) to get a semi solid **(33)**, (110 mg, 70%).

Anal:

TLC : R_f 0.29 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3128, 3010, 1650, 1401.

^{1}H-NMR ($CDCl_3$) : 7.26-7.24 (m, 1H,), 7.19-7.15 (m, 2H), 7.08-7.07 (m, 1H), 4.39-4.34 (q, 1H, *J* = 6.8 Hz), 4.21-4.13 (m, 1H), 3.57-3.50 (m, 1H), 3.37-3.16 (m, 4H), 1.57- 1.51 (d, 3H, *J* = 6.8 Hz), 0.98-0.91 (m, 1H), 0.49-0.41 (m, 2H), 0.26-0.17 (m, 2H).

^{13}C-NMR ($CDCl_3$) : 173.80, 137.06, 136.20, 130.03, 126.64, 126.52, 125.93, 51.72, 46.32, 40.33, 33.02, 14.81, 9.96, 3.56.

MS (m/z) : 230.00 $(M+1)^+$.

5.1.32 3-(4-*t*.Butylbenzyl)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (34)

Synthesized as per the general procedure (A) using 4-*t*.butylbenzyl bromide (0.64 ml) to get a white solid **(34)**, (310 mg, 87%); m.p. 101-103 ^{o}C.

Anal:

TLC : R_f 0.28 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3133, 2961, 2869, 1645, 1407, 1038, 813.

^{1}H-NMR ($CDCl_3$) : 7.20-7.18 (m, 3H), 7.13-7.04 (m, 2H), 7.00-6.98 (d, 2H, *J* = 8.2 Hz), 6.93-6.91 (d, 1H, *J* = 7.3 Hz), 4.59-4.53 (d, 1H, *J* = 14.7 Hz), 4.39-4.36 (d, 1H, *J* = 14.7 Hz) 4.31-4.26 (q, 1H, *J* = 6.8 Hz), 3.93-3.85 (m, 1H), 3.31-3.25 (m, 1H), 3.08-3.01 (m, 1H), 2.97-2.87 (m, 1H), 1.52-1.50 (d, 3H, *J* = 6.8 Hz), 1.20 (s, 9H).

^{13}C-NMR ($CDCl_3$) : 172.85, 149.19, 136.16, 135.27, 133.60, 128.86, 126.68, 125.69, 125.60, 124.71, 124.39, 49.22, 44.99, 39.35, 33.44, 31.40, 30.32, 13.72.

MS (m/z) : 322.1 $(M+1)^{+}$.

Calcd for $C_{22}H_{27}NO$: C, 82.20; H, 8.47; N, 4.36. Found: C, 81.89; H, 8.25; N, 4.11 %.

5.1.33 3-Cyclohexylmethyl-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (35)

Synthesized as per the general procedure (A) using cyclohexyl bromide (0.50 ml) to get a white solid **(35)**, (289 mg, 76%), m.p. 92-94 ^{o}C.

Anal:

TLC : R_f 0.32 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 2926, 2851, 1637, 1439, 770.

^{1}H-NMR ($CDCl_3$) : 7.92-7.85 (m, 1H), 7.23-7.08 (m, 2H), 6.99-6.94 (m, 1H), 5.67-5.62 (m, 1H), 4.15-4.05 (q, 1H), 3.74-3.65 (m, 1H), 3.35-3.28

(m, 1H), 3.06-3.00 (m, 3H), 1.75-1.74 (d, 3H), 1.62-1.54 (m, 6H), 1.51-1.38 (m, 4H), 0.96-0.87 (m, 1H).

^{13}C-NMR ($CDCl_3$) : 176.00, 141.45, 134.39, 130.01, 128.11, 127.22, 126.89, 56.53, 47.56, 36.73, 33.97, 32.74, 30.96, 30.96, 30.67, 26.36, 25.88.

MS (m/z) : 272.1 $(M+1)^+$.

Calcd for $C_{18}H_{25}NO$: C, 79.66; H, 9.28; N, 5.16. Found: C, 79.46; H, 9.12; N, 4.93 %.

5.1.34 3-(2-Cyano-4-biphenyl)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (36)

Synthesized as per the general procedure (A) using 4-bromomethyl-2-biphenylcarbonitrile (0.93 g) to get a semi solid **(36)**, (310 mg, 86%).

Anal:

TLC : R_f 0.29 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3063, 2961, 2855, 2220, 1647, 1360, 1102, 846.

^{1}H-NMR ($CDCl_3$) : 7.77-7.74 (d, 1H, *J* = 7.9 Hz), 7.65-7.61 (d, 1H, *J* = 7.9 Hz), 7.49-7.41 (m, 5H), 7.31-7.29 (d, 1H, *J* = 7.4 Hz), 7.24-7.20 (m, 2H), 7.17-1.15 (m, 1H), 7.07-7.05 (d, 1H, *J* = 7.4 Hz), 4.73-4.70 (d, 1H, *J* = 15.1 Hz), 4.65-4.61 (d, 1H, *J* = 15.1 Hz) 4.45-4.40 (q, 1H, *J* = 6.8 Hz), 4.11-4.03 (m, 1H), 3.46-3.40 (m, 1H), 3.24-3.18 (m, 1H), 2.99-2.94 (m, 1H), 1.64-1.62 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 173.10, 144.08,, 136.15, 135.19, 132.72, 131.82, 129.01, 128.95, 127.93, 127.21, 126.53, 125.85, 125.70, 124.60, 117.71, 110.12, 49.42, 45.41, 39.25, 31.36, 28.67, 13.56.

MS (m/z) : 367.01 $(M+1)^+$.

5.1.35 General procedure (B) for the preparation of 3-substitued 8-chloro-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (37-42)

To a stirred suspension of 8-chloro-3-benzazepin-2-one **(6)** (500 mg, 2.38 mmol) and NaH (63.00 mg, 2.61 mmol) in a mixture (2 ml) of dry THF and DMF (4.5:0.5) was added a solution of desired halide in dry THF and DMF (2 ml) and the mixture was heated under a stream of dry N_2 at 60-80 ^oC on an oil bath. The reaction mixture on cooling to room temperature was treated with cold water and extracted with ethyl acetate. The organic layer was dried over sodium sulphate, filtered and concentrated to get semi solid of the compound which was further purified by column chromatography using silica gel as stationary phase and *n*-hexane: ethyl acetate as eluent.

5.1.36 8-Chloro-3-ethyl-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (37)

Prepared according to general procedure (B) using ethyl iodide (0.24 ml) to get a white solid **(37)**, (120 mg, 65%) ; m.p. 74-76 ^oC.

Anal:

TLC : R_f 0.29 (20% EtOAc in *n*-hexane)

IR (KBr, cm^{-1}) : 3130, 2977, 2933, 1643, 1429, 812.

^{1}H-NMR ($CDCl_3$) : 7.26-7.21 (m, 1H), 7.16-7.11 (m, 1H), 7.08-7.00 (m, 1H), 4.31-4.26 (q, 1H, *J* = 6.8 Hz), 4.12-4.04 (m, 1H), 3.53-3.36 (m, 3H), 3.25-3.11 (m, 1H), 3.09-3.05 (m, 1H), 1.54-1.52 (d, 3H, *J* = 6.8 Hz), 1.12-1.08 (t, 3H).

^{13}C-NMR ($CDCl_3$) : 172.94, 139.19, 135.90, 132.49, 129.80, 127.48, 126.60, 46.00, 42.66, 40.14, 33.02, 14.78, 13.29

MS (m/z) : 238.10 $(M+1)^+$.

Calcd for $C_{13}H_{16}ClNO$: C, 65.68; H, 6.78; N, 5.89. Found: C, 65.39; H, 6.54; N, 5.68 %.

5.1.37 3-Butyl-8-chloro-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (38)

Prepared according to general procedure (B) *n*-butyl iodide (3.3 ml) to get a semi solid **(38),** (210.10 mg, 73%).

Anal:

TLC : R_f 0.36 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3136, 2960, 2869, 1656, 1402, 1107, 805.

^{1}H-NMR ($CDCl_3$) : 7.21-6.91 (m, 3H), 4.31-4.25 (q, 1H, J = 6.8 Hz), 4.15-4.06 (m, 1H), 3.44-3.31 (m, 3H), 3.24-3.16 (m, 1H), 3.08-3.05 (m, 1H), 1.55-1.53 (d, 3H), 1.48-1.44 (m, 2H), 1.33-1.20 (m, 2H), 0.93-0.86 (t, 3H).

^{13}C-NMR ($CDCl_3$) : 173.26, 139.08, 135.78, 132.40, 129.80, 127.43, 126.75, 47.65, 46.25, 40.00, 32.92, 30.38, 20.12, 14.74, 13.89.

MS (m/z) : $266.1(M+1)^+$.

5.1.38 3-Allyl-8-chloro-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (39)

Prepared according to general procedure (B) using allyl bromide (0.25 ml) to get a semi solid **(39)**, (150.10 mg, 78%).

Anal:

TLC : R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3081, 2980, 2934, 1658, 1409, 1368, 1054, 927.

^{1}H-NMR ($CDCl_3$) : 7.19-6.92 (m, 3H), 5.74-7.55 (m, 1H), 5.70-5.60 (m, 1H), 5.07-5.00 (m, 2H), 4.26-4.20 (q, 1H, *J* = 6.8 Hz), 3.99-3.92 (m, 3H), 3.35-3.27 (m, 1H), 3.16-3.08 (m, 1H), 3.03-2.95 (m, 1H), 1.48-1.45 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 173.15, 138.03, 135.07, 133.49, 132.41, 131.20, 129.70, 127.33, 126.81, 117.49, 50.01, 45.70, 39.81, 32.55, 14.64.

MS (m/z) : $250.10\ (M+1)^+$.

5.1.39 8-Chloro-3-propyl-1-methyl-4,5-dihydro-1H-benzo[d]azepin-2(3H)-one (40)

Prepared according to general procedure (B) using *n*-propyl bromide (0.28 ml) to get a pale yellow solid **(40),** (190 mg, 68%), Mp = 83-85 ^{o}C.

Anal:

TLC : R_f 0.39 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 2965, 2930, 1646, 1455, 803.

^{1}H-NMR ($CDCl_3$) : 7.26-6.99 (m, 3H), 4.31-4.26 (q, 1H, *J* = 6.8 Hz), 4.15-4.07 (m, 1H), 3.44-3.28 (m, 3H), 3.25-3.05 (m, 2H), 1.53-1.51 (d, 3H, *J* = 6.8 Hz), 1.50-1.48 (m, 2H), 0.94-0.81 (t, 3H).

^{13}C-NMR ($CDCl_3$) : 173.42, 139.36, 135.78, 134.49, 132.34, 129.03, 126.74, 50.63, 46.26, 39.89, 32.51, 21.06, 20.03, 14.74.

MS (m/z) : 252.10 $(M+1)^{+}$.

5.1.40 8-Chloro-3-dodecyl-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (41)

Prepared according to general procedure (B) using a solution of 1-bromododecane (0.7 ml) to get a semi-solid **(41)**, (170.10 mg, 66%).

Anal:

TLC : R_f 0.38 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3136, 2960, 1655, 1402, 1191, 855.

^{1}H-NMR ($CDCl_3$) : 7.18-7.15 (m, 2H), 7.07 (s, 1H), 4.29-4.27 (q, 1H, *J* = 6.8 Hz), 4.11-4.08 (m, 1H), 3.48-3.35 (m, 3H), 3.20-3.19 (m, 1H), 3.13-3.09 (m, 1H), 1.53-1.46 (m, 3H), 1.48-1.46 (m, 2H), 1.31-1.22 (m, 18H), 0.89-0.83 (t, 3H).

^{13}C-NMR ($CDCl_3$) : 173.27, 137.98, 135.85, 132.41, 129.83, 127.46, 126.65, 47.97, 46.19, 39.95, 32.98, 32.00, 29.71, 29.63, 29.49, 29.43, 28.43, 26.93, 22.77, 14.75, 14.19.

MS (m/z) : 378.30 $(M+1)^{+}$.

5.1.41 3-(4-Bromobenzyl)-8-chloro-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (42)

Prepared according to general procedure (B) using 4-bromobenzyl bromide (0.78 g) to get a semi solid **(42)**, (220.20 mg, 76%).

Anal:

TLC : R_f 0.32 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3130, 2980, 1657, 1402, 1011, 760.

^{1}H-NMR ($CDCl_3$) : 7.40-7.37 (m, 2H), 7.22-7.13 (d, 1H), 7.19-7.17 (m, 1H), 7.15-7.11 (m, 1H), 7.02-6.98 (m, 1H), 6.94-6.92 (d, 1H), 4.58-4.43 (m, 2H), 4.37-4.30 (q, 1H), 4.06-3.97(m, 1H), 3.36-3.29 (m, 1H), 3.15-3.07 (m, 1H), 2.99-2.93 (m, 1H), 1.58-1.56 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 173.57, 138.89, 137.95, 136.71, 135.59, 134.51, 132.59, 131.73, 129.74, 126.94, 121.40, 50.27, 46.05, 39.96, 32.36, 14.62.

MS (m/z) : 380.00 $(M+1)^+$.

5.1.42 8-Chloro-3-(2,6-difluorobenzyl)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (43)

Prepared according to general procedure (B) using 2,6-difluorobenzyl bromide (0.60 g) to get a white solid **(43)**, (210 mg, 88%), m.p. 98-101 ^oC.

Anal:

TLC : R_f 0.36 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3130, 2977, 1643, 1429, 812.

^{1}H-NMR ($CDCl_3$) : 7.28-7.20 (m, 2H), 7.16-7.09 (m, 1H), 6.98 (s, 1H), 6.91-6.83 (m, 2H), 4.94-4.82 (m, 1H), 4.63-4.56 (m, 1H), 4.32-4.27 (q, 1H), 4.15-4.02 (m, 1H), 3.50-3.39 (m, 1H), 3.14-3.08 (m, 1H), 2.96-2.86 (m, 1H) 1.45-1.43 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 173.17, 163.18, 160.70, 138.74, 135.36, 132.39, 131.23, 129.70, 128.03, 127.35, 126.75, 113.21, 111.53, 45.34, 39.98, 32.37, 30.53, 14.81.

MS (m/z) : 336.10 $(M+1)^+$.

Calcd for $C_{18}H_{16}ClF_2NO$: C, 64.39; H, 4.80; N, 4.17. Found: C, 64.18; H, 4.56; N, 3.95 %

5.1.43 Methyl 4-(1-methyl-2-oxo-1,3,4,5-tetrahydrobenzo[*d*]azepinyl)methylbenzoate (44)

To a mixture of NaH (60% dispersion in mineral oil; 75 mg, 3.43 mM) in dry THF (9 ml) and DMF (1 ml) (4.5:0.5), 3-benzazepin-2-one **(6)** (500 mg, 2.85 mmol) was added in a 100 ml two neck RBF and stirred for half an hour. Solution of methyl (4-bromomethyl)benzoate (0.78 g) in dry THF (4.5 ml) and DMF (0.5 ml) was added drop wise to the above slurry and the resulting mixture was heated up to 60-80 ^oC in an oil bath in presence of dry N_2. On cooling to the room temperature, the reaction mixture was treated with ice-water (20 ml) and extracted with ethyl acetate (100 ml). The organic layer was dried over sodium sulphate and the solvent removed to get a semi solid compound which was purified by column chromatography using silica gel as stationary phase and *n*-hexane-ethyl acetate as eluent and to get a white solid **(44)**, (240 mg, 70%); m. p. 92-95^oC

Anal:

TLC : R_f 0.28 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3126, 2928, 2854, 1707, 1678, 1402, 1289, 738.

^{1}H-NMR ($CDCl_3$) : 7.85-7.83 (d, 2H, *J* = 7.9 Hz), 7.23-7.21(d, 1H, *J* =.7.9 Hz), 7.18-7.14 (m, 1H), 7.12-7.09 (m, 3H), 6.96-6.94 (d, 1H, *J* = 7.4 Hz), 4.64-4.60 (d, 1H, *J* = 15.2 Hz), 4.56-4.52 (d, 1H, *J* = 15.2 Hz) 4.36-4.30 (q, 1H, *J* = 6.8 Hz), 4.00-3.92 (m, 1H), 3.83 (s, 3H), 3.31-3.25 (m, 1H), 3.15-3.08 (m, 1H), 2.88-2.80 (m, 1H), 1.55-1.53 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 174.07, 166.89, 143.10, 137.12, 136.09, 129.87, 129.85, 129.29, 127.76, 126.93, 126.83, 125.65, 52.11, 50.01, 46.59, 40.28, 32.41, 14.55.

MS (m/z) : 337.7 $(M+1)^+$.

Calcd for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. Found: C, 73.88; H, 6.36; N, 4.05%.

5.1.44 4-(1-Methyl-2-oxo-1,3,4,5-tetrahydrobenzo[d]azepinyl)methylbenzoic acid (45)

Compound **(44)** (50 mg) was taken in a two neck round bottom flask. To this 5 % solution of KOH (5 ml) and methanol (4 ml) was added. The reaction got completed in half an hour which was confirmed by TLC. The reaction mixture was poured into ice-cold water (50 ml), acidified with dil HCl and extracted with dichloromethane. The solvent was removed and the compound was purified over a column of silica gel using *n*-hexane and ethyl-acetate to get a white solid **(45)**, (45 mg, 98%); m.p. 197-200 ^oC.

Anal:

TLC : R_f 0.36 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3069, 2969, 2854, 1700, 1652, 1486, 1297, 750.

^{1}H-NMR ($CDCl_3$) : 8.00-7.97 (d, 2H, *J* = 7.8 Hz), 7.31-7.21 (d, 1H, *J* = 7.8 Hz), 7.26-7.16 (m, 4H), 7.05-7.03 (d, 1H, *J* = 7.2 Hz), 4.74-4.70 (d, 1H, *J* = 15.3 Hz), 4.67-4.63 (d, 1H, *J* = 15.3 Hz) 4.44-4.39 (q, 1H, *J* = 6.8 Hz), 4.09-4.01 (m, 1H), 3.41-3.34 (m, 1H), 3.25-2.18 (m, 1H), 2.98-2.90 (m, 1H), 1.64-1.62 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 174.19, 170.99, 143.96, 137.14, 136.07, 130.50, 129.83, 128.43, 127.82, 126.97, 126.88, 125.71, 50.77, 46.70, 40.43, 32.41, 14.59

MS (m/z) : 310.00 $(M+1)^+$.

Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 5.53. Found: C, 73.65; H, 5.99; N, 5.42 %.

5.1.45 General procedure (C) for preparation of 1,3-disubstitued 1-methyl-4,5-dihydro-1*H* benzo[*d*]azepin-2(3*H*)-one (46, 47)

To a mixture of NaH (60% dispersion in mineral oil; 102 mg, 7.12 mM) in dry THF (9 ml) and DMF (1 ml) (4.5:0.5), 3-benzazepin-2-one **(6)** (500 mg, 2.85 mmol) was added in 100 ml two neck RBF and stirred for half an hour. Solution of the halide in dry THF (4.5 ml) and DMF (0.5 ml) was added drop wise to the above slurry and the resulting mixture was heated up to 60-80 ^{o}C in an oil bath in presence of dry N_2. On cooling to the room temperature, the reaction mixture was treated with ice-water (20 ml) and extracted with ethyl acetate (100 ml). The organic layer was dried over sodium sulphate and the solvent removed to get a semi solid compound which was purified by column chromatography using silica gel as stationary phase and *n*-hexane-ethyl acetate as eluent.

5.1.46 1,3-Dibenzyl-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (46)

Prepared according to general procedure (C) using a solution of benzyl bromide (254 µl) to get a semi solid **(46)**, (170 mg, 74.04%).

Anal:

TLC	: R_f 0.35 (20% EtOAc in *n*-hexane).
IR (KBr, cm^{-1})	: 3129, 1611, 1490, 1005, 765, 700.
^{1}H-NMR ($CDCl_3$)	: 7.51-7.49 (d, 1H), 7.30-7.17 (m, 6H), 7.10-7.05 (m, 4H), 6.91-6.90 (m, 1H), 6.74-6.72 (q, 2H), 4.68-4.14 (d, 1H), 4.54-4.51 (d, 1H), 3.68-3.65 (m, 1H), 3.37-3.30 (m, 2H), 3.13-3.10 (d, 1H), 2.7-2.6 (m, 1H), 2.56-2.48 (m, 1H), 1.78 (s, 3H).
MS (m/z)	: 355.24 $(M+1)^+$.

5.1.47 1,3-Bis(3-fluorobenzyl)-4,5-dihydro-1-methyl-1*H*-benzo[*d*]azepin-2(3*H*)-one (47)

Prepared according to general procedure (C) using a solution of 3-flurobenzyl bromide (261.43 µl) to get a semi solid **(47)**, (300 mg, 67.24 %).

Anal:

TLC	: R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3126, 2931, 1616, 1587, 1401, 1018, 693.

^{1}H-NMR ($CDCl_3$) : 7.44-7.42 (d, 1H, *J* = 8.08Hz), 7.21-7.15 (m, 2H), 7.07-7.04 (m, 1H), 6.97-6.92 (m, 2H,) 6.83-6.75 (m, 2H), 6.73 (m, 1H), 6.71-6.70 (m, 1H), 6.48-6.46 (d, 1H, *J* = 7.64 Hz), 6.33-6.29 (m, 1H), 4.68-4.60 (m, 1H), 4.45- 4.41 (m, 1H), 3.78-3.74 (m, 1H), 3.32-3.25 (m, 1H), 3.18- 3.16 (m, 1H), 2.97-2.93 (m, 1H), 2.59-2.53 (m, 1H), 2.36-2.32 (m, 1H), 1.81-1.79 (s, 3H).

MS (m/z) : 391.00 $(M+1)^+$.

5.1.48 3-(2-Acatamido)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepin-2(3*H*)-one (51)

Step-*I: 2-Bromo-N-tritylacetamide* (49)

2-Bromo-*N*-tritylacetamide **(49)** was synthesized from 2-bromoacetamide **(48)**. A solution of the amide **(48)** (0.864 mmol), triphenylmethanol (0.576 mmol, 0.67 equiv.) and *p*-toluene-sulphonic acid (0.288 mmol) in dry toluene (15 ml) was refluxed under nitrogen with the help of Dean Stark apparatus.[108] The reaction was monitored by TLC using ethyl acetate and *n*-hexane. The reaction mixture was cooled to room temperature, quenching with 2 % aqueous sodium bicarbonate solution, and extracted with ethyl acetate (3×5 ml). The organic layer was washed with water, brine and dried to get a pure white solid **(49)**, (1 gm, 88%); m.p.. 197-199 ^oC (literature m.p. 204-211 ^oC)[109].

Anal:

TLC : R_f 0.35 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3265, 3052, 2852, 1664, 1491, 736.

Step-II: 3-(2-Acatamido)-1-methyl-4,5-dihydro-1*H*-benzo[*d*]azepine-2(3*H*)-one (51)

To a stirred suspension of 3-benzazepin-2-one **(6)** (200 mg) and NaH (60% dispersion in mineral oil; 68.46 mg) in a mixture (2 ml) of dry THF and DMF (4.5:0.5), a solution of the 2-bromo-*N*-tritylacetamide **(49)** (228.74 mg) in the same solvent (2 ml) as mentioned above was added. The reaction mixture was heated in a stream of dry N_2 at 60-80 ^oC in an oil bath. The reaction mixture was cooled to room temperature and treated with cold water and extracted with ethyl acetate. The resulting organic layer was dried over sodium sulphate to

get an intermediate **(50)** which was stirred with trifluroacetic acid : DCM (70:30) for half an hour. As soon as the reaction got completed, the resulting mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulphate to a get a compound which was purified by column chromatography using silica gel as stationary phase and *n*-hexane: ethyl acetate as solvent and to get white solid (**50**) (210 mg, 67.40 %); m.p. 138-140 ^{o}C.

Anal:

TLC : R_f 0.28 (20% EtOAc in *n*-hexane).

IR (KBr, cm^{-1}) : 3397, 3197, 1682, 1642, 1394, 742.

^{1}H-NMR ($CDCl_3$) : 77.28-7.13 (m, 4H), 6.08 (s, 1H), 5.24 (s, 1H), 4.40-4.35(q, 1H, *J* = 6.8 Hz), 4.23-4.17 (m, 1H), 4.09-4.03 (d, 1H, *J* = 15.5 Hz), 3.99-3.90 (d, 1H, *J* = 15.5 Hz), 3.55-3.49 (m, 1H), 3.37-3.30 (m, 1H), 3.21-3.13 (m, 1H), 1.59-1.57 (d, 3H, *J* = 6.8 Hz).

^{13}C-NMR ($CDCl_3$) : 174.56, 171.62, 136.90, 129.88, 127.22, 127.04, 125.52, 52.51, 48.98, 40.11, 32.15, 14.20.

MS (m/z) : 255.1$(M+Na)^+$.

Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 66.99; H, 6.84; N, 11.97%.

5.2 Biological work

(All biological work has been carried out by the researchers of pharmacology section and not by the candidate himself)

5.2.1 Materials: 5-Hydroxytryptamine creatinine sulphate was purchased from Hi-Media. *m*-CPP and RS-102221 were procured from Sigma Aldrich.

5.2.2 Animals: Male Wistar rats (200-250 gm) and female Swiss Albino mice (25-30 gm) were used for the studies with free access of food and water *ad libitum* during the course of the study. Animals were maintained on 12 hr light/dark cycle. After 15 days acclimatization, animals were used for the studies. All the protocols were approved by the Institutional Animal Ethics Committee (IAEC) and were conducted as per the guidelines of CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals) with approval no: MSU/PHARM/IAEC/2013/02.

5.2.3 *In vitro* 5-HT_{2A} bioassay using isolated rat thoracic aorta strip: Wister rats (200-250 g) were used for the study. The animals were sacrificed by an overdose of sodium pentobarbital (50 mg/kg). After dissecting the thoracic aorta, the helical strips were mounted as described earlier in the Kreb's solution aerated with 95% O_2 and 5% CO_2 at 37 °C under 1 g of resting tension.[110] For each determination at least six arterial strips were utilized. Isometric contractions were recorded using a force transducer (UGO BASILE, Italy) coupled to a Gemini 7070 recorder (UGO BASILE, Italy). All the test compounds were checked for their 5-HT_{2A} receptor agonist and antagonist actions at a single concentration of 2×10^{-5} M before determining their pA_2 or pD_2 values. 5-HT (10^{-8} to 10^{-5} M) was used as standard agonist to determine 5-HT_{2A} antagonism by the test compounds.

5.2.4 *In vitro* 5-HT_{2B} bioassay using an isolated rat fundus preparation: Wistar rats weighing 200-250 gm, fasted for 48 hr, were sacrificed by an overdose of sodium pentobarbital (50 mg/kg). The fundus strips were prepared as described earlier[111] and mounted in a 25 ml organ tube containing Kerb's solution at 37 °C, well aerated with 95% O_2 and 5% CO_2 with initial resting tension of 2 g. At least 6 longitudinal and 6 horizontal strip preparations were used for each test substance. The contractile responses were recorded on a 2-channel recorder using a force transducer coupled to a Gemini 7070 recorder (UGO Basile, Italy). Initially the test compounds were assessed to check their 5-HT_{2B} receptor activity at 2×10^{-5} M concentration. The compounds showing contractile responses were further evaluated (at 10^{-6} to 10^{-4} M) in the presence of SB-206553 (10^{-6} and 10^{-7} M) (5H_{2B} receptor antagonist) to confirm their 5-HT_{2B} agonism which was evident by their pD_2 values. Similar to the previous experiment, the antagonistic activity of the selected compounds was determined using 5-HT (10^{-8} to 10^{-5} M) as agonist.

5.2.5 *In vivo* rodent models for 5-HT_{2C} receptor agonistic activity: After the *in vitro* screening of the compounds for evaluating 5-HT_{2A} and 5-HT_{2B} receptor agonist/antagonist actions, the inactive compounds in both the studies were further evaluated using different *in vivo* rodent models as described below for their 5-HT_{2C} receptor agonistic potentials. *m*-CPP (2 mg/kg, p.o.) was used as standard, while the test compounds were administered at a dose of 10 mg/kg, p.o. Dose of the test compounds were decided after dose-deciding pilot study (data not shown). For all *in vivo* experiments, six animals per group were utilized.

5.2.5.1 Despair swim test: Swiss Albino mice were forced to swim inside a vertical Plexiglas cylinder (45 cm height × 20 cm diameter) filled with water up to 30 cm height and maintained at 25 °C to assess their depression state. After the 15 min training period, animals

were randomly divided into different experimental groups. Next day, 1 hr after the drug administration, the animals were again placed in the cylinder and total duration of immobility was measured during a 5 min test period .[112]

5.2.5.2 Elevated plus maze test: Anxiety was assessed on elevated plus maze apparatus using Swiss Albino mice. Animals were acclimatized to the apparatus for 10 min before performing the experiment. One hour after the drug treatment, animals were individually placed at the centre of the maze facing their heads towards open arm and allowed to explore all the arms for 5 min. Number of entries and time spent in open arms were recorded .[113]

5.2.5.3 Hypophagic response: Food deprived Wistar rats were housed individually for 24 hr. Next day, after the treatment, animals were supplemented with weighed amounts of the normal food pellets. Amount of food remaining after 2 hr was measured. 5-HT_{2C} receptor selectivity was also assessed by the administration of RS-10222 **(VII)** (selective 5-HT_{2C} receptor antagonist) (2 mg/kg, i.p.) [114, 115] to the animals 30 min prior to administration of the test compounds .[116]

5.2.5.4 Penile erection model: Immediately after the treatment, rats were placed in Plexiglas observation cages. A mirror was placed behind the cages to observe penile erection over a 2 hour period. To assess the 5-HT_{2C} receptor selectivity, the animals were administered with RS-102221 (2 mg/kg, i.p.), 30 min prior to the test compound. Number of lickings of the penis were observed .[117]

5.2.5.5 Estimation of monoamines: 5-HT_{2C} receptor agonists negatively regulate the monoamine firing in the brain. [118-120]It was confirmed by the estimation of DA and 5-HT levels in the rat brain using HPLC. After demonstrating the hypophagic response of compounds (**8, 13-15, 25, 31,** and **37**), their 5-HT_{2C} selectivity was confirmed in the presence of RS-102221 **(VII)**. At the end of the study, all the rats were sacrificed by an overdose of sodium pentobarbital (50 mg/kg). The brains were dissected out, weighed and homogenized in 10% w/v 0.17 M perchloric acid to extract the monoamines. Homogenates were allowed to stand for 15 min and the supernatants were decanted in separate Eppendorf tubes and were centrifuged at 4 °C for 20 min at 15,000 rpm. After centrifugation, the supernatants were separated and analyzed immediately or stored at -70 °C until assayed. Brain concentrations of DA and 5-HT were assessed by RP-HPLC coupled with electrochemical detector (Model No. Waters 2465) (Waters Corporation, Milford, USA). Estimation was performed as per previously described method with minor modifications.[121] Briefly, a Sunfire® C18 column

(4.6 mm×150 mm, particle size 5µm) was used and separation was carried out using mobile phase containing methanol (15% v/v) in a solution (*p*H 4.2) of 32 mM citric acid, 12.5 mM disodium hydrogen orthophosphate, 0.5 mM sodium octyl sulphate, 0.5 mM EDTA and 2 mM KCl, at a flow rate of 1.2 ml/min, an operating pressure of 3000 psi and an operating potential of 0.61 V. The internal standards were prepared by spiking known amounts of mixed standards (10, 20, 40, 80 and 160 ng/ml of each 5-HT and DA) in 1 ml of pooled brain homogenates. The standard curves were used to quantify the amount of 5-HT and DA in each sample by calculating the area under the curve (AUC). The limit of detection (LOD) for 5-HT and DA were found 0.83±0.06 ng/ml and 0.11±0.03 ng/ml, respectively while the limit of quantification (LOQ) was found to be 2.53±0.12 ng/ml and 0.34 ± 0.03 ng/ml respectively.

5.2.5.6 Statistical analysis: All the observed data were analyzed using GraphPad Prizm-5. Comparison within groups was made by repeated measures ANOVA and comparison among groups was made by factorial ANOVA followed by Bonferroni test. Data were expressed as mean ± SEM. A value of $p<0.05$ was considered significant.