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Few Novel Face -'d'- pyrido condensed benzazepines with 2-hetrylamino substitution:Synthesis and characterisations

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Abstract

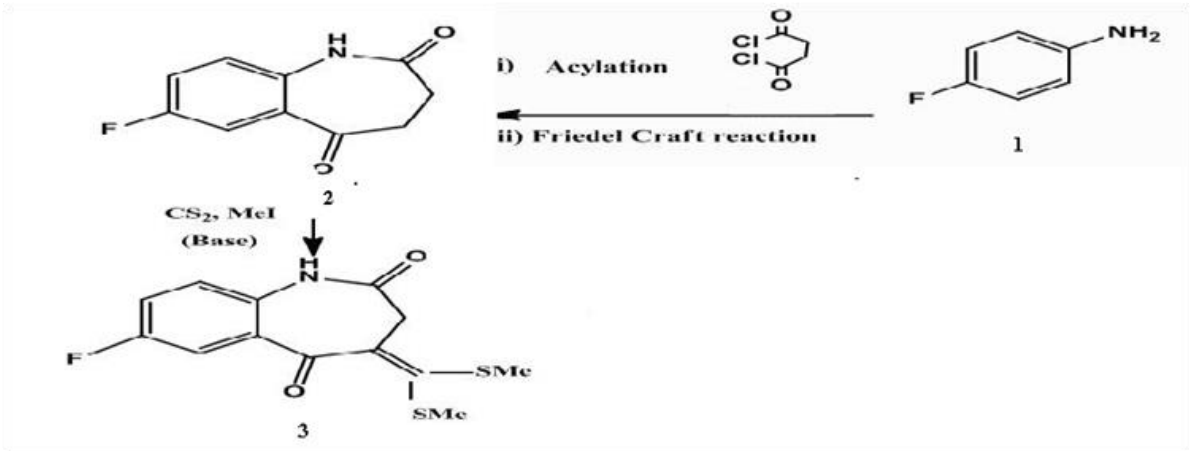
It has been observed that the incorporation of the bioactive pharmacophores such as pyrrolidine, piperidine, piperazines etc. in the existing drug molecules, exert a profound influence on the biological profiles of the parent molecules. Greatly encouraged by such a trend in the literature,it was planned in the present communication to incorporate in **6** , the structural features of pyrrolidine,piperidine,N-substituted piperazines (N-methyl, N-ethyl, N-benzyl, N-carboxyethyl, and N-acetylpiperazines) to afford the compounds **6.030**-**6.037** [Scheme-2] respectively, following the procedures described for their incorporation, other related substrates in the literature [1-3]

Keywords 10-fluoro-4-(methylamino)-6-(methylthio)-2-phenyl-5H-benzo[b]pyrido[2,3-d]azepin-1-oxide

Introduction

Literature is replete with wide variety of examples showing that one of the important tool for medicinal chemists in defining the potential activity of novel chemical entities, is to synthesize a large number of related compounds with diverse structures and then to study the role played by each part of the molecule in imparting the specific activity displayed by the molecules. These studies have allowed interesting revelations to emerge concerning to the structural requirements of the drugs and helped one to adopt a rational approach in the design of new drugs.

This communication has targeted to address the problems of tolerance of the drugs arising in the use of the combination therapy recently introduced in the treatment of HIV infections. We sought to utilize in the present work, the exceptional ability of iminothiomethyl ether function of benzazepines to undergo nucleophilic displacements and used it as a synthetic tool to exploit this property in the incorporation of hetryl amine bearing constituents on the 2-position of the benzazepines, on this premise that their presence in the same molecular framework could provide a significant impact on to the overall biological efficacy in the resulting molecules.



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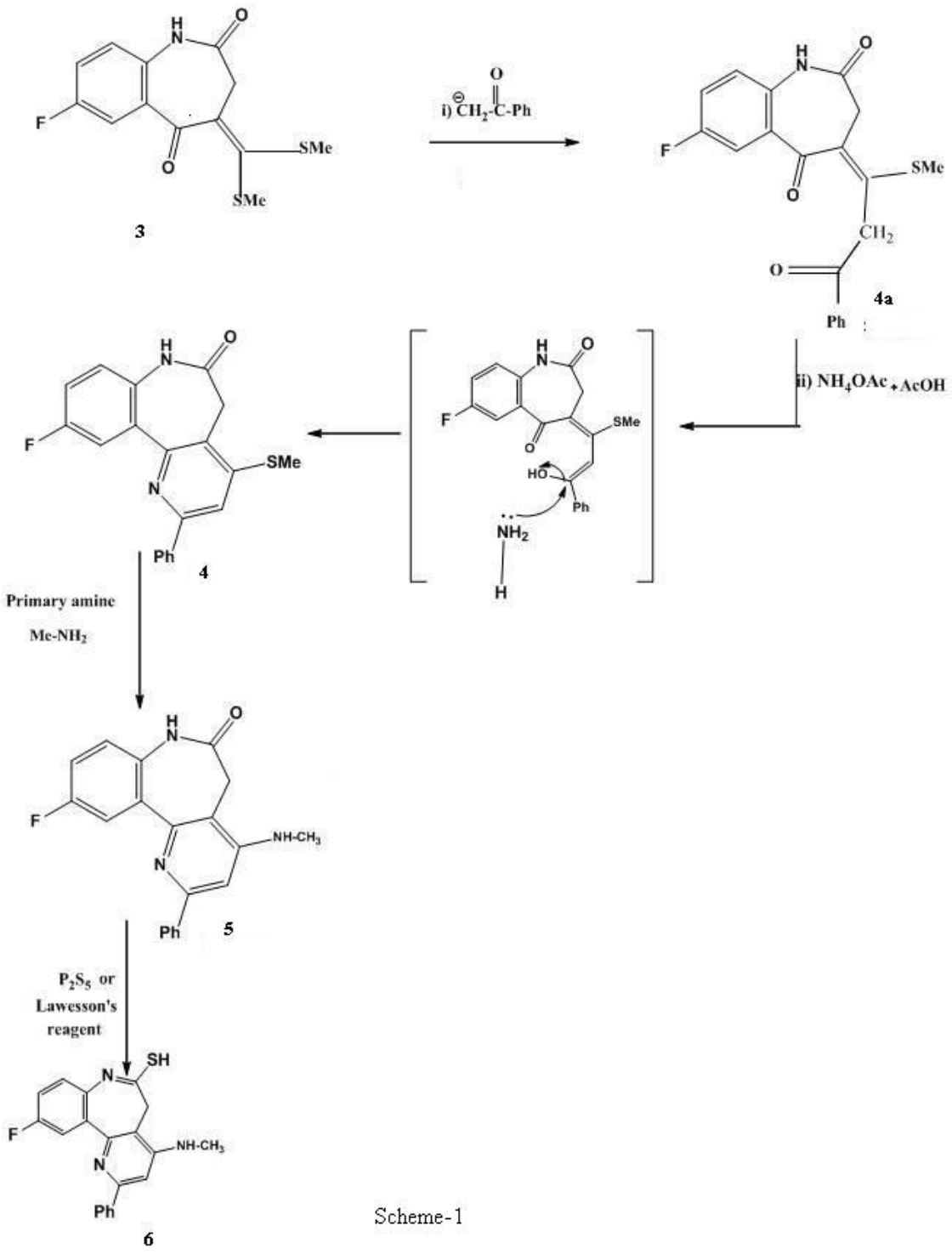

Scheme-1

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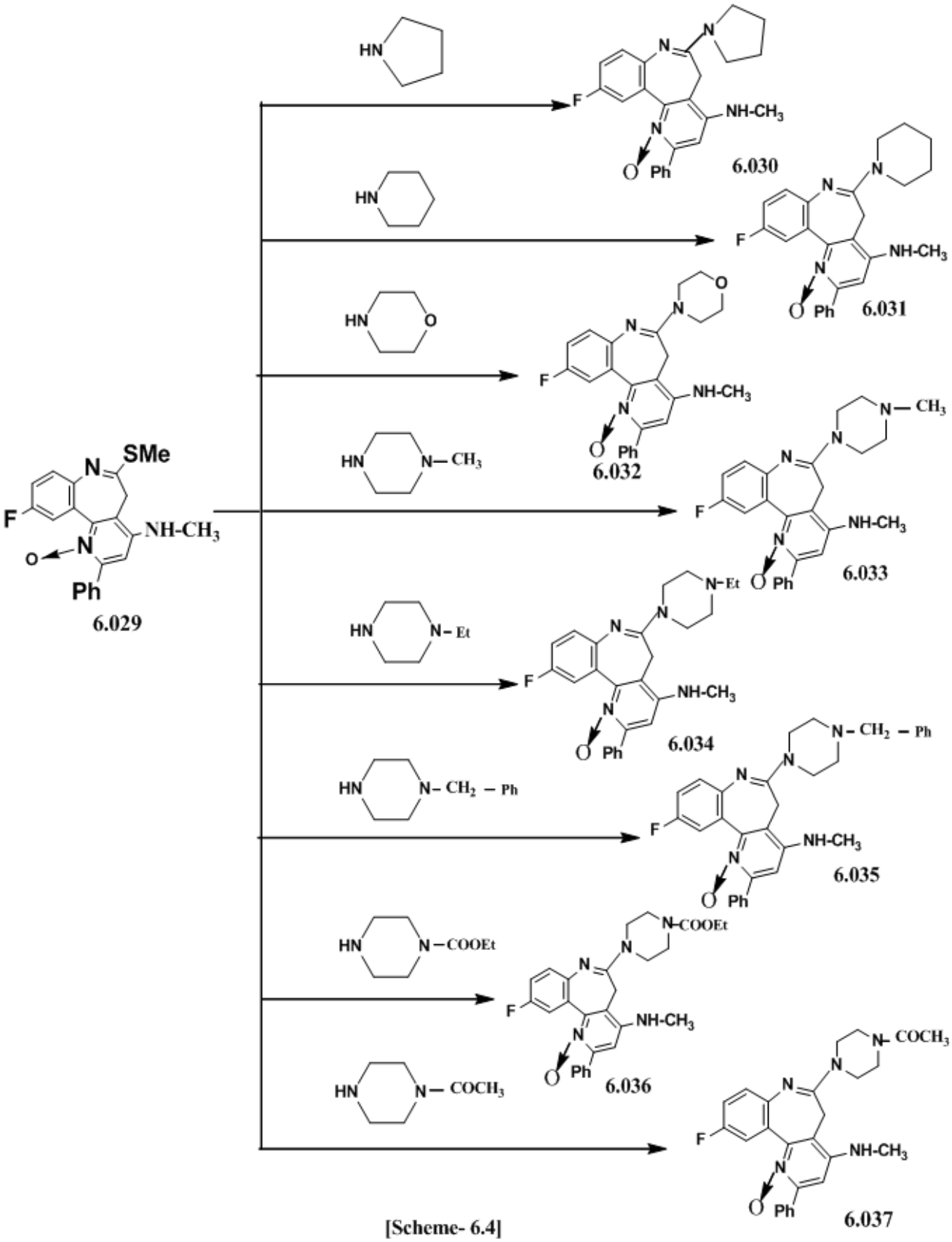

[Scheme- 6.4]

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Materials and method

p-Fluoroaniline and succinyl chloride were obtained from commercial sources. All the reagents were used of AR Grade. Melting points were determined in open glass capillaries and are uncorrected. The purity of the compounds was checked by TLC on silica gel (G) plates.IR spectra were recorded on CE (Schimatzu) FTIR-9050 S.^{1}H- NMR spectra and ^{13}C NMR spectra were recorded on Sea 400 (Bruker) using $CDCl_3$ as solvent and TMS as an internal reference. Chemical shift are expressed in δ ppm. Mass spectra were recorded on Bosch Tech.

Experimental

Preparation of 7-fluoro-3,4-dihydro-1H-benzo[b]azepine-2,5-dione (2)

p-Fluoroaniline **(1)** (3.60ml,0.03 mol) was mixed with succinyl chloride (4.92g, 0.03 mol) in dry pyridine (20.0 ml) and the mixture was refluxed for 15 min. Cold reaction mixture was poured slowly with stirring to 150-200ml ice cold water. The solid which settled was filtered, washed with cold water, recrystallized from methanol and water .PPA (25g) was mixed to 3.21 g (0.01 mol) of it and heated at 150-160^{o}C for 4h (the progress of the reaction was monitored by TLC).The reaction mixture was cooled to 20^{o}C and a concentrated aqueous solution of Na_2CO_3 was added to make it alkaline. The product was extracted with ethyl acetate (3x10 ml).The extract was dried over anhydrous Na_2SO_4 and concentrated in vaccum. The residue was purified by column chromatography on silica gel with $CHCl_3$ as an eluent to give **2** (2.85g, yield :79%); m.p.: 158-160 ^{o}C; IR (KBr) cm^{-} : 3240(N-H str.), 2990 (C-H str.), 2900, 1400 (-CH_2 next to C=O), 1712, 1704 (C=O), 1535 (C=Cstr.); ^{1}H-NMR (400MHz, $CDCl_3$) δ ppm: 8.0 (1H, s, NH), 7.26-7.78 (3H, m, Ar-H), 3.49 (4H, s, $(CH_2)_2$); ^{13}C-NMR (400MHz, $CDCl_3$) δ ppm: Ar-C [157.55 (CF), 120.24 (CH), 113.54 (CH), 112.44 (CH)], Ar-C [134.44 (C), 115.25 (C), azepinone], 27.6, 34.4 [$(CH_2)_2$ azepinone)], 176.75 (C of amide), 183.49 (C of carbonyl); MS: m/z 193.17(M^{+}); Anal. calcd. / found for $C_{10}H_8FNO_2$: C, 62.18 / 62.35; H, 4.17/4.11; N, 7.25/7.48.

Preparation of 4-(bis (methylthio) methylene) - 7-fluoro-3, 4-dihydro-1H-benzo [b]azepine-2, 5-dione (3)

A mixture of 7-fluoro-3,4-dihydro-1H-benzo[b]azepine-2,5-dione **(2)** (2.82g, 0.01 mol) and CS_2 (1.6 ml,0.01mol) was added to a well stirred and cold suspension of t-BuOK (2.23g,0.02 mol) in dry benzene (7.0ml) and DMF (3.0ml) and the reaction mixture was allowed to stand for 4h. Methyl iodide (3.3ml, 0.02mol) was gradually added with stirring and external cooling (exothermic reaction) and the reaction mixture was allowed to stand for 4 h. at room temperature with occasional shaking and then refluxed on a water bath for 3 h. The mixture was poured on crushed ice and the benzene layer was separated. The aqueous portion was extracted with benzene and the combined extracts were washed with water, dried over anhydrous sodium sulphate and the solvent was removed by distillation. The product thus obtained was purified by crystallization with ethanol to give **3** (1.7g, yield: 60%); m.p.:155-157^{o}C ; IR (KBr) cm^{-}: 3240 (N-H str.), 3000 (C-H str.), 2900, 1400 (-CH_2 next to C=O), 1640, 1685 (C=O), 1620 (C=C of α, β–unsaturated ketone), 1535 (C=C str.), 680 (C-S str.); ^{1}H- NMR (400 MHz, $CDCl_3$) δ ppm: 8.0(1H, s, NH), 7.45-7.98 (3H, m, Ar-H), 3.53 (2H, s, CH_2), 2.80 (6H, s, $(CH_3)_2$ of $(SMe)_2$); ^{13}C-NMR (400MHz, $CDCl_3$) δ ppm : Ar-C [164.5 (CF), 121.5 (CH), 113.1 (CH), 112.6 (CH)] , Ar-C [136.8 (C), 136.0 (C), 108.7 (C), azepinone] ,28.60 (CH_2 azepinone), 168.7 (C of amide), 187.0 (C of carbonyl),155.3 [-C-$(SMe)_2$] , 18.0 [2C of $(CH_3)_2$]; MS: m/z 297.37 (M^{+}); Anal. calcd. / found for $C_{13}H_{12}FNO_2S_2$: C, 52.51/ 52.32; H, 4.07/4.01; N, 14.71/14.48; S, 21.57/ 21.38

Preparation of 10-fluoro-4- (methylthio)-2 -phenyl- 5H-benzo[b]pyrido[2,3-d]azepin- 6(7H)-one (4)

To a mixture of **(3)** (3.95g, 0.01mol) in dry THF was added a solution of acetophenone (1.2g,0.01mol) and potassium t-BuOK (2.2g,0.02mol) in dry THF (15 ml).The solution was stirred at room temperature overnight, then glacial acetic acid (15ml) and ammonium acetate (1.6g,0.02mol) were added to the above solution which was then refluxed for 4h with constant removal of THF. The solution was then cooled to 20^{o}C, poured in ice (50 g), neutralized the excess acetic acid with NH_4OH and allowed to stand for 1 h, water was added and the precipitate was collected and recrystallized with petroleum ether to give **4** (3.50g, yield: 89%); m.p.:145-147^{o}C; IR (KBr) cm^{-} : 3180 (N-H str.),3010(C-H str.),2990,1400(-CH_2 next to C=O),1660(C=O),1580 (C=C str.),685(C-S str.); ^{1}H-NMR (400MHz, $CDCl_3$) δ ppm: 8.01(1H,s,NH),7.43-8.48 (5H,m,Ar-H),7.24-8.34(3H,m,Ar-H),6.97(1H,s,CH), 3.49(2H,s,CH_2) ,2.53 (3H,s,CH_3); ^{13}C-NMR (400MHz, $CDCl_3$) δ ppm: Ar-C[157.62(CF),123.71(CH), 116.22(CH), 114.31(CH)],Ar-C[158.94 (C), 134.72(C), 125. 13(C), 122.22(C),a zepinone], 168.23(C of amide) ,41.44 (CH_2 azepinone),152.64 (pyridine C,-CPh),153.15 (pyridine C,-CSMe),109.11(pyridine C),15.12 (C of CH_3),Ar-C[139.24(C), 129.23 (two CH), 127.64(two CH), 127.32 (CH), phenyl];MS,m/z:350.24(M^{+}60.0%), 338.09 (13.2%),

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294.58(100%), 232.10 (22.3%);Anal. calcd. / found for $C_{20}H_{15}FN_2OS$:C, 68.55 / 68.38; H, 4.31/4.24; N, 7.99/7.74;S,9.15/9.32.

Preparation of 10-fluoro-4-(methylamino)-2-phenyl-5H-benzo[b]pyrido[2,3-d]azepin-6(7H) -one (5)

To the solution of 10-fluoro-4-(methylthio)- 2-phenyl-5H-benzo [b]pyrido [2,3-d] azepin-6 (7H)-one **(4)** (3.50g,0.01 mol), the aqueous solution of methyl amine (0.04 mol) was added and the mixture was stirred at room temperature for 15h. The solvent was then evaporated to afford a viscous crude product which was purified by column chromatography (silica gel: EtOAc), (1:1) to give **5** (2.54g, yield:73%); m.p.:152-154^oC; IR (KBr) cm^- : 3170 (N-H str.),2990(C-Hstr.), 2980,1400(-CH_2 next to C=O),2950(C-H str.in CH_3) ,1660(C=O),1590(C=N imine),1580(C=C str.); ^{1}H-NMR (400MHz, $CDCl_3$) δ ppm: 8.01(1H,s,NH), 7.43-8.48 (5H,m ,Ar-H),7.24-8.34(3H,m, Ar-H),6.31(1H,s,CH) ,4.0(1H,m,NH),3.49(2H,s,CH_2),2.63(3H,d,CH_3); ^{13}C-NMR (400MHz, $CDCl_3$) δ ppm: Ar-C[157.62(CF),123.71CH), 116.22(CH),114.31(CH)],Ar-C[159.74(C),134.72(C), 122.21(C),114.52(C), azepinone], 168.23 (C of amide),39.92 (CH_2 azepinone),157.92(pyridine C,-CPh),153.43 (pyridine C,-CNH-),105.92(pyridine C),34.70 (C of CH_3),Ar-C[139.24(C),129.23(two CH),127.64(two CH), 127.32 (CH),phenyl]; MS,m/Z: 333.16(M^+40.0%),320.12(11.1%)278.33(100%),235.13(15.5%);Anal. calcd. / found for $C_{20}H_{16}FN_3O$: C, 72.06/72.23; H, 4.84/4.89; N, 12.61/12.48.

Preparation of (E)-10-fluoro-4-(methylamino)-6-(methylthio)-2-phenyl-5H-benzo[b] pyrido [2,3-d] azepin-1-oxide (6)

In a 100ml single-necked,round bottomed flask equipped with a magnetic stirrer, 10-fluoro-4-(methylamino)-2-phenyl-5H-benzo[b]pyrido[2,3-d]azepin-6(7H)-one**(5)**(2.52g,0.007mol) ,m-chloroperoxybenzoic acid (670mg,3 mmol),$CHCl_3$ (5ml) and EtOH (5 ml) were added. The reaction mixture was refluxed until there was no starting material left (monitored by TLC), then cooled to room temperatutre. NaOH (0.28 g,0.007mol) was added and stirring was continued for 30 min.The aqueous phase was extracted with $CHCl_3$,(2x25ml),and the combined organic phases were dried over anhydrous magnesium sulphate and concentrated in vacuo. The residue was purified by column chromatography using an eluent MeOH-$CHCl_3$.A suspension of it (2.15g,0.006) and Lawesson's reagent (2.10g,0.006 mol) in CH_2Cl_2 /toulene (1:1) (20ml) was heated under reflux for 25h.After this,the reaction mixture was concenterated to dryness under reduced pressure and the residue was recrystallized from ethanol. A mixture of above isolated compound (2.01g,0.005 mol) and methyl iodide (2.25ml,0.01 mol) in ethyl acetate (80 ml) was stirred at room temperature for15h.The precipitate formed was filtered and recrystallized from ethanol to afford **6** (1.92g, yield:76%); m.p.202-204^oC; IR (KBr) cm^- : 3180 (N-H str.),2980(C-Hstr.),2950(C-H str.in CH_3) ,1580,1615(C=N), 1570(C=C str.),685(C-S); ^{1}H-NMR (400MHz, $CDCl_3$) δ ppm:7.43-8.48 (5H,m,Ar-H), 7.24-8.34(3H,m,ArH), 6.24(1H,s,CH), 4.0(1H,m,NH),2.60(2H,s,CH_2),2.63(3H,d,CH_3),2.55(3H,s,CH_3 of SMe); ^{13}C-NMR (400MHz, $CDCl_3$) δ ppm: Ar-C[160.50(CF),124.42(CH), 116.21(CH), 115.42(CH)], Ar-C[159.72(C), 143.22(C) ,128.41 (C),114.52 (C),azepine] ,29.43(CH_2 azepine), 167.72(azepine C,-CSMe) ,15.50 (C of CH_3 ,-SMe),157.92(pyridine C,-CPh),153.43 (pyridine C,-CNH-),105.92 (pyridine C),34.70 (C of CH_3,-NH-CH_3),Ar-C[130.32 (twoCH), 129.72 (CH),129.2 3(twoCH), 127.52(C),phenyl]; MS,m/z:379.02(M^+60.0%),357.11(13.9%),323.32(100%),251.11(24.5%);
Anal. calcd. / found for $C_{21}H_{18}FN_3OS$: C,66.47/66.25; H, 4.78/4.70; N, 11.07/11.22;S,8.45/8.22.

Preparation of 10-fluoro-4-(methylamino)-2-phenyl-6-(pyrrolidin-1-yl)-5H-benzo[b] pyrido[2,3-d]azepine-1-oxide (6.030):

To the solution of compound (**6)** (1.9 g,0.005moles) in dry acetone (10mL) an equimolar amount of triethylamine (0.78mL,0.005 mol) was added .The solution was cooled to 0^oC ,and the pyrollidine (5ml) was added dropwise. Reaction mixture was stirred for 2h.The precipitated triethylamine hydrochloride was filtered off, the solvent was removed by distillation and the crude product was recrystallized from acetonitrile to give **6.030** ,1.60g,yield (84%),m.p.135-137^oC.

In a similar manner other compounds **6.031**-**6.037** were prepared by changing the reaction time and reagents and completion of reaction was checked by TLC.

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Table-6.1: Physical and analytical & Spectal data for compounds 6.030-6.037

S. No. I	Compound II	Mol.wt. III	Mol.formula IV	M.P. (°C) V	Yield (%) VI	C Calcd./ found	H Calcd./ found	N Calcd./ found	S Calcd./ found
1	6.030	402.46	$C_{24}H_{23}FN_4O$	135-137	84	71.62/ 71.78	5.76/ 5.70	13.92/ 13.79	_
2	6.031	416.49	$C_{25}H_{25}FN_4O$	140-142	75	72.09/ 72.23	6.05/ 6.01	13.45/13.31	_
3	6.032	418.46	$C_{24}H_{23}FN_4O_2$	152-154	70	68.88/ 68.69	5.54/ 5.48	13.39/13.23	_
4	6.033	431.51	$C_{25}H_{26}FN_5O$	155-157	65	69.59/ 69.43	6.07/ 6.01	16.23/16.39	_
5	6.034	445.53	$C_{26}H_{28}FN_5O$	100-102	78	70.09/ 70.26	6.63/ 6.58	15.72/15.59	_
6	6.035	507.60	$C_{31}H_{30}FN_5O$	99-101	76	73.35/ 73.53	5.96/ 5.92	13.80/13.72	_
7	6.036	489.54	$C_{27}H_{28}FN_5O_3$	115-117	73	66.24/ 66.42	5.77/ 5.72	14.31/14.18	_
8	6.037	459.52	$C_{26}H_{26}FN_5O_2$	105-108	69	67.96/ 67.64	5.70/ 5.64	15.24/15.46	_

S. No. I	Compound II	IR(KBr) cm^{-1} III	^{1}HNMR($CDCl_3$)δ(ppm) and MS;m/z (relative abundance) IV	^{13}C NMR ($CDCl_3$) δ(ppm) V
1	6.030	3250(N-H str.) 3000(C-Hstr.) 1615,1410(C=N) 1575(C=C str.)	7.44-8.48 (5H,m,Ar-H) 7.22-8.34 (3H,m,Ar-H) 6.24(1H,s,CH) 4.02(1H,m,NH)	Ar-C[160.23(CF),124.63(CH), 116.02 (CH), 114.62 (CH)] Ar-C[163.45(C),159.86(C), 144.25(C), 128.77(C),119.32(C), azepine] 23.52(CH_2 azepine) 157.85(pyridine C,-CPh)

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			2.79(3H,d,CH_3) 2.62(2H,s,CH_2) 1.74[4H,m,$(CH_2)_2$ of pyrrolidine] 2.67[4H,m,$(CH_2)_2$ of pyrrolidine] **MS,m/z:**402.19(M^+47%),379.36(100%),329.37(34.9%),269.83(48.9%)	147.58(pyridine C,-CNH-) 105.36(pyridine C) Ar-C[136.16(C), 129.32(two CH), ,127.72(two CH),127.52(CH),phenyl] 32.13(C of CH_3) 49.87[$(CH_2)_2$ of pyrrolidine] 36.32[$(CH_2)_2$ of pyrrolidine]
2	6.031	3250(N-H str.) 3000(C-H str.) 1615,1410(C=N) 1575(C=C str.)	7.44-8.48(5H,m,Ar-H) 7.22-8.34(3H,m,Ar-H) 6.24(1H,s,CH) 4.0(1H,m,NH) 3.17[4H,m,$(CH_2)_2$of piperidine] 2.60(2H,s,CH_2) 2.74(3H,d,CH_3) 1.59[2H,m, CH_2 of piperidine] 1.53[4H,m,$(CH_2)_2$ of piperidine] **MS,m/z:**416.29(M^+55%),406.20(28.5%),378.29 (38.9%),346.21(100.0%),	Ar-C[160.23(CF),124.63(CH), 116.02 (CH), 114.62 (CH)] Ar-C[163.45(C),159.86(C), 144.26(C), 128.77(C),119.32(C), azepine] 23.52(CH_2 azepine) 157.85(pyridine C,-CPh) 147.58(pyridine C,-CNH-) 105.36(pyridine C) Ar-C[136.16(C), 129.32(two CH), ,127.72(two CH),127.52(CH),phenyl] 32.13(C of CH_3) 48.9[$(CH_2)_2$ piperidine] 26.1(CH_2 piperidine) 24.2[$(CH_2)_2$ piperidine]
3	6.032	3250(N-H str.) 3000(C-Hstr.) 1615,1410(C=N) 1575(C=C str.)	7.44-8.48(5H,m,Ar-H) 7.22-8.34(3H,m,Ar-H) 6.24(1H,s,CH) 4.0(1H,m,NH) 3.65[4H,m,$(CH_2)_2$of morpholine] , 3.15[4H,m, $(CH_2)_2$ of morpholine] 2.60(2H,s,CH_2) 2.74(3H,d,CH_3) **MS,m/z:**418.26(M^+65.0%),4	Ar-C[160.23(CF),124.63(CH), 116.02 (CH), 114.62 (CH)] Ar-C[163.45(C),159.86 (C), 144.26(C), 128.77(C),119.32(C), azepine] 23.52(CH_2 azepine) 157.85(pyridine C,-CPh) 147.58(pyridine C,-CNH-) 105.36(pyridine C) Ar-C[136.16(C), 129.32(two CH), ,127.72(two CH),127.52(CH),phenyl] 32.13(C of CH_3)

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			07.18(27.5%),395.19(100.0%),302.34 (39.7%)	26.0 [$(CH_2)_2$of morpholine] 48.9 [$(CH_2)_2$of morpholine]
4	6.033	3270(N-H str.) 3010(C-H str.) 1625,1415(C=N) 1575(C=C str.) 2906(CH_3,CH)	7.44-8.48(5H,m,Ar-H) 7.22-8.34(3H,m,Ar-H) 6.24(1H,s,CH) 4.0(1H,m,NH) 2.60(2H,s,CH_2) 2.74(3H,d,CH_3) 2.26(3H,s,CH_3) 2.13(4H,m,$(CH_2)_2$of methylpiperazine ring) 2.79(4H,m,$(CH_2)_2$of methylpiperazine ring) **MS,m/z:**431.39(M^+45..0%),418.21(100%),368.22 (27.4%)	Ar-C[160.23(CF),124.63(CH), 116.02 (CH), 114.62 (CH)] Ar-C[163.45(C),159.86 (C), 144.26(C), 128.77(C),119.32(C), azepine] 23.52(CH_2 azepine) 157.85(pyridine C,-CPh) 147.58(pyridine C,-CNH-) 105.36(pyridine C) Ar-C[136.16(C), 129.32(two CH), ,127.72(two CH),127.52(CH),phenyl] 32.13(C of CH_3) 50.2[$(CH_2)_2$ methylpiperazine] 52.1[$(CH_2)_2$ methylpiperazine] 46.6(C of CH_3 ,methylpiperazine)
5	6.034	3270(N-H str.) 3010(C-H str.) 1625,1415(C=N) 1575(C=C str.) 2906(CH_3,CH_2,CH)	7.44-8.48(5H,m,Ar-H) 7.22-8.34(3H,m,Ar-H) 6.24(1H,s,CH) 4.0(1H,m,NH) 2.60(2H,s,CH_2) 2.79[4H,t,$(CH_2)_2$ of N-ethylpiperazine], 2.74(3H,d,CH_3) 2.38(2H,q,CH_2,ethylpiperazine) 2.37[4H,t,$(CH_2)_2$of N-ethylpierazine]	Ar-C[160.23(CF),124.63(CH), 116.02 (CH), 114.62 (CH)] Ar-C[163.45(C),159.86(C), 144.26(C), 128.77(C),119.32(C), azepine] 23.52(CH_2 azepine) 157.85(pyridine C,-CPh) 147.58(pyridine C,-CNH-) 105.36(pyridine C) Ar-C[136.16(C), 129.32(two CH), ,127.72(two CH),127.52(CH),phenyl] 32.13(C of CH_3) 50.9 [$(CH_2)_2$ ethylpiperazine]

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			1.02(3H,t,CH_3) **MS,m/z:**445.35(M^+60%),423.22(100%),373.23 (37.5%)	52.1 [(CH_2)$_2$ ethylpiperazine] 49.6,13.3(CH_2,CH_3 ethyl)
6	6.035	3270(N-H str.) 3010(C-H str.) 1625,1415(C=N) 1575(C=C str.) 2851(CH_2,CH)	7.44-8.48(5H,m,Ar-H) 7.23-7.33(5H,m,Ar-H) 7.22-8.34(3H,m,Ar-H) 6.24(1H,s,CH) 4.0(1H,m,NH) 3.66(2H,s,N-CH_2-C linkage) 2.60(2H,s,CH_2) 2.79[4H,t,,(CH_2)$_2$of pierazine] 2.74(3H,d,CH_3) 2.37[4H,t,,(CH_2)$_2$of pierazine],) **MS,m/z:**507.48(M^+70.0%),484.24(100%),391.25(23.9%),434.25(15.8%)	Ar-C[160.23(CF),124.63(CH), 116.02 (CH), 114.62 (CH)] Ar-C[163.45(C),159.86(C), 144.26(C), 128.77(C),119.32(C), azepine] 23.52(CH_2 azepine) 157.85(pyridine C,-CPh) 147.58(pyridine C,-CNH-) 105.36(pyridine C) Ar-C[136.16(C), 129.32(two CH), ,127.72(two CH),127.52(CH),phenyl] 32.13(C of CH_3) 50.5[(CH_2)$_2$ piperazine] 55.1[(CH_2)$_2$ piperazine] Ar-C[138.16(C), 128.32(two CH), ,126.72(two CH),125.52(CH),phenyl] 64.4 (CH_2 ,-N-CH_2-C linkage)
7	6.036	3270(N-H str.) 3010(C-H str.) 1625,1415(C=N) 1575(C=C str.) 2995,2925,2855(CH_3,CH_2,CH)	7.44-8.48(5H,m,Ar-H) 7.22-8.34(3H,s,Ar-H) 6.24(1H,s,CH) 4.0(1H,m,NH) 4.13(2H,q,CH_2) 3.22[4H,t,(CH_2)$_2$of pierazine] 2.95[4H,t,(CH_2)$_2$ofpierazine] 2.60(2H,s,CH_2) 2.74(3H,d,CH_3) 1.29(3H,t,CH_3) **MS,m/z:**489.35(M^+54%),465.21(100%),415.22(100%),375	Ar-C[160.23(CF),124.63(CH), 116.02 (CH), 114.62 (CH)] Ar-C[163.45(C),159.86(C), 144.26(C), 128.77(C),119.32(C), azepine] 23.52(CH_2 azepine) 157.85(pyridine C,-CPh) 147.58(pyridine C,-CNH-) 105.36(pyridine C) Ar-C[136.16(C), 129.32(two CH), ,127.72(two CH),127.52(CH),phenyl] 32.13(C of CH_3) 51.5[(CH_2)$_2$ piperazine] 49.9[(CH_2)$_2$ piperazine]

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			.22(15.3%)	156.3(C=O ,COOEt) 62.0(CH_2 , -COOEt) 13.8(CH_3 ,- COOEt)
8	6.037	3270(N-H str.) 3010(C-Hstr.) 1625,1415(C=N) 1575(C=C) 2954(CH_3,CH)	7.44-8.48(5H,m,Ar-H) 7.22-8.34(3H,m,Ar-H) 6.24(1H,s,CH) 4.0(1H,m,NH) 3.46[4H,t,,$(CH_2)_2$of N-ethylpierazine] 2.95[(4H,t,$(CH_2)_2$of pierazine], 2.60(2H,s,CH_2) 2.74(3H,d,CH_3) 2.32(3H,s,CH_3) **MS,m/z:**459.36(M^+65%),436.20(100%),386.21(22.8%)	Ar-C[160.23(CF),124.63(CH), 116.02 (CH), 114.62 (CH)] Ar-C[163.45(C),159.86(C), 144.26(C), 128.77(C),119.32(C), azepine] 23.52(CH_2 azepine) 157.85(pyridine C,-CPh) 147.58(pyridine C,-CNH-) 105.36(pyridine C) Ar-C[136.16(C), 129.32(two CH), ,127.72(two CH),127.52(CH),phenyl] 32.13(C of CH_3) 50.0[$(CH_2)_2$ piperazine] 49.7[$(CH_2)_2$ piperazine] 168.9(C=O ,-COOMe) 21.0(CH_3 ,-COOMe)

Results and discussion

Bioactive heterocyclic scaffolds embellished with pharmacophores such as pyrrolidine, piperidine, piperazine etc. have been subject of several reports on account of the positive impact which they showed by their presence in these molecules. In view of impressive biological activities shown by hetrylamine substituted derivatives, it was thought in the present work to synthesize molecules which carried the hetrylamine bearing substituents on the 2-position of benzazepine nucleus[4-5] as shown in **[Scheme-2]** to give compounds **6.030-6.037**.

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