4

EXPERIMENTAL WORK

Melting points were determined in capillaries using Toshniwal melting point apparatus and are uncorrected. IR (in cm^{-1}) spectra in KBr pellets were taken on a Shimadzu 8300 instrument; and ^1H NMR spectra were recorded in $CDCl_3$ on a Brüker spectrometer (300 or 400 MHz), using tetramethylsilane as an internal standard. Chemical shift data are reported in parts per million (δ in ppm) where s, br, and m designate singlet, broad, and multiplet respectively. Elemental analyses were recorded on a Perkin-Elmer PE 2400 CHNS analyzer. Mass spectra were recorded on APISciEX mass spectrometer equipped with an electrospray ionisation (ESI) interface. Column chromatography was carried out using silica gel (100-200 mesh). Thin-layer chromatography (TLC) was performed on precoated silica gel Merck plates. Compounds were visualized by illuminating with UV light (254 nm) or by exposure to iodine vapors. Solvents were purified using standard methods.

The work carried out has been discussed under the following two main heads:

4.1 Chemical studies and

4.2 Biological studies

4.1 CHEMICAL STUDIES

The chemical studies are broadly described under the two heads:

4.1A 2,3-Diaryl-6,7-dihydro-5*H*-1,4-diazepines

4.1B 5,7-Diaryl-2,3-dihydro-1*H*-1,4-diazepines

4.1A 2,3-DIARYL-6,7-DIHYDRO-5*H*-1,4-DIAZEPINES

The synthetic work carried out has been discussed under sub heads:

4.1A.1 Synthesis of substituted phenylacetic acid derivatives

4.1A.2 Synthesis of 1,2-diaryl ethanone derivatives

4.1A.3 Synthesis of 1,2-diaryl-1,2-ethanedione derivatives

4.1A.4 Synthesis of 2,3-diaryl-1,4-diazepine derivatives

4.1A.1 Synthesis of substituted phenylacetic acid derivatives

3-Chlorophenylacetic acid (41c)

A dilute solution of sulphuric acid was prepared by adding conc. sulphuric acid (10 ml) cautiously to water (10 ml). Two thirds of the sulphuric acid was added into a round bottomed flask containing 3-chlorobenzylcyanide (2.5 g, 0.016 mol) and the nitrile adhering to the walls of the flask was washed down with the remaining acid. The reaction mixture was boiled under reflux for 15 min and then diluted with an equal volume of ice-cold water. The resulting white solid mass was filtered, washed and recrystallized from hot water to yield acid **(41c)** (1.94 g, 67.36%) m.p. 78-79 °C (78-79.5 °C)[174].

Anal:

R_f : 0.47 (chloroform)

IR (KBr) : 3026 and 1700 cm^{-1}

4-Methylphenylacetic acid (41e)

To a solution 4-methylacetophenone (20 ml, 0.15 mol) in morpholine (18 ml, 0.2 mol) precipitated sulphur (8 g, 0.25 mol) was added and the reaction mixture was refluxed for 18 hours. To this hot solution warm methanol (10 ml) was added and refrigerated for 3 hours to obtain a yellow crystalline thiomorpholide which was filtered and washed with cold methanol. The thiomorpholide (22 g) was taken into a 250 round-bottomed flask and 10% aqueous methanolic sodium hydroxide (150 ml) was added to it. The mixture was refluxed for 10 hours after which it was poured on to crushed ice. The resulting mixture was extracted thrice with successive volumes of chloroform (3x15 ml) and the aqueous layer acidified to get an off-white colored precipitate

of 4-methylphenylacetic acid **(41e)**. Recrystallization from hot water afforded the acid (17 g, 75.6%) m.p 90-92 °C (90-93 °C)[175].

Anal:

TLC : 0.5 [$CHCl_3$: CH_3OH (9.5:0.5)]

IR(KBr) : 3000 and 1700 cm^{-1}

4-Nitrobenzyl cyanide

A mixture of concentrated nitric acid (22 ml) and an equal volume of concentrated sulphuric acid was placed in a two necked flask fitted with a thermometer and a dropping funnel. The mixture was cooled to 10 °C with stirring in an ice bath and benzyl cyanide (14.7 ml, 0.126 mol) was run at such a rate (about 30 min) that the temperature was maintained around 10 °C and did not rise above 20 °C. The solution was further stirred for 1 hour at room temperature and then poured into crushed ice. The mass was filtered under vaccum and pressed well to remove as much oil as possible. Recrystallization from methanol afforded yellow needles of 4-nitrobenzyl cyanide (10.15 g, 49.9%) m.p. 115-116 °C (115-116 °C)[176].

4-Nitrophenylacetic acid (41f)

A dilute solution of sulphuric acid was prepared by adding concentrated sulphuric acid (25 ml) cautiously to water (25 ml). Two thirds of the sulphuric acid was added into a round bottomed flask containing 4-nitrobenzyl cyanide (7.45 g, 0.046 mol) and the nitrile adhering to the walls of the flask was washed down with the remaining acid. The contents were boiled under reflux for 15 min and diluted with 25 ml of ice-cold water. The resulting pale yellow solid mass was filtered, washed, decolorized and recrystallized from hot water to yield the acid **(41f)** (8.0 g, 96.0%) m.p. 151-152 °C (151-152 °C)[177].

Anal:

TLC : 0.5 [benzene: chloroform (1:1)]

IR(KBr) : 2900, 1700, 1511 and 1347 cm^{-1}

4.1A.2 Synthesis of 1,2-diaryl ethanone derivatives (42a-r)

1,2-Diphenyl-1-ethanone (42a)

To a solution of phenylacetic acid **(41a)** (5 g, 0.0367 mol) in dry benzene (5 ml) was added thionyl chloride (13 ml). The contents were refluxed for 3 hours under anhydrous condition. Excess of benzene and thionyl chloride were recovered under vacuum wherein phenylacetyl chloride was obtained as a reddish brown colored semisolid. Anhydrous aluminium chloride (10 g, 0.075 mol) was partially dissolved in dry benzene (10 ml) and stirred well. Phenylacetyl chloride in dry benzene (5 ml) was added dropwise to the above well stirred solution at 5 °C and stirring was continued for 2 hr at -5 to -10 °C. The reaction mixture was then poured over crushed ice containing conc. HCl and extracted with chloroform (3×30 ml) successively. The combined organic extract was washed with sodium bicarbonate solution twice, followed by water, dried, filtered and concentrated. The product so obtained was recrystallized from methanol to give **(42a)**, (5.0 g, 69.4%), m.p. 53-55 °C (55-56 °C)[202].

Anal:

TLC : 0.64 (benzene)

IR (KBr) : 1676, 1575, 1421, 1261, 1178, 1024, 813 and 770 cm^{-1}

2-Phenyl-1-(4-methylphenyl)-1-ethanone (42b)

Phenylacetyl chloride was prepared from phenylacetic acid (5 g, 0.0367 mol) by the above described method. Anhydrous aluminium chloride (10 g, 0.075 mol) was partially dissolved in dry toluene (10 ml) and stirred well. Phenylacetyl chloride in dry toluene (5 ml) was added dropwise to the above well stirred solution at -10 °C and allowed to stir for 2 hr at -5 to -10 °C. The rest of the experimental procedure was similar to that described for compound **(42a)**. The product so obtained was recrystallized from methanol to give **(42b)**, (4.5 g, 58.2%), m.p. 109-11 °C (109.6-111.1 °C)[203].

Anal:

TLC : 0.85 (benzene)

IR (KBr) : 1680, 1585, 1334, 1197, 813 and 732 cm^{-1}

2-Phenyl-1-(4-bromophenyl)-1-ethanone (42c)

Phenylacetic acid (8 g, 0.058 mol) was converted to the corresponding acid chloride by the procedure described for compound **(42a)**. The phenylacetyl chloride was reacted with anhydrous aluminium chloride (10 g, 0.075 mol) and dry bromobenzene (8 ml) in a similar manner as described for compound **(42a)**. Recrystallization from methanol gave compound **(42c)**, (9.6 g, 59.4%), m.p. 106-08 °C (114-115 °C)[181].

Anal:

TLC : 0.82 (benzene)

IR (KBr) : 1686, 1581, 1334, 1199, 821 and 744 cm^{-1}

2-Phenyl-1-(4-fluorophenyl)-1-ethanone (42d)

Phenylacetyl chloride was prepared as described for compound **(42a)**, from phenylacetic acid (8 g, 0.058 mol). The reaction of phenylacetyl chloride with anhydrous aluminium chloride (10 g, 0.075 mol) and dry fluorobenzene (10 ml) was then carried out in a similar manner as described for compound **(42a)**. The reaction mixture was extracted with chloroform (3 x 30 ml) successively. The combined extract was washed twice with sodium bicarbonate solution (10%), water and dried. Recovery of chloroform afforded a residue which was recrystallized from methanol to gives **(42d)**, (7.8 g, 62%), m.p. 71-73 °C.

Anal:

TLC : 0.55 (benzene: pet ether: 9:1)

IR (KBr) : 1685, 1600, 1506, 1153, 829 and 729 cm^{-1}

2-Phenyl-1-(4-methoxyphenyl)-1-ethanone (42e)

Phenylacetyl chloride was obtained by reacting phenylacetic acid (5 g, 0.0367 mol) with thionyl chloride (12 ml) in dry benzene (6 ml). The acid chloride was

reacted with anhydrous aluminum chloride (8 g, 0.06 mol) and anisole (8.0 ml) as described for compound **(42a)**. The work up of the reaction mixture and Recrystallization from methanol gives **(42e)**, (3.7 g, 44.5%), m.p. 130-31 °C (135 °C)[204].

Anal:

TLC : 0.6 (benzene)

IR (Kbr) : 1674, 1602, 1419, 1203, 1033 and 835 cm^{-1}

2-Phenyl-1-(4-methylsulfanylphenyl)-1-ethanone (42f)

Phenylacetyl chloride was obtained by reacting phenylacetic acid (10 g, 0.074 mol) in dry benzene (6.0 ml) with thionyl chloride (13 ml). Anhydrous aluminium chloride (14 g, 0.1 mol) was partially dissolved in a mixture of thioanisole (8.5 ml) and anhydrous dichloromethane with mechanical stirring. Phenylacetyl chloride was added into the above well stirred solution at -10 °C and allowed to stir for 2 hr at -5 to -10 °C. The reaction mixture was then poured over crushed ice containing conc. HCl and extracted with chloroform (3×30 ml). The combined organic extract was washed with sodium bicarbonate solution twice, followed by water, dried, filtered and concentrated. The product so obtained was recrystallized from methanol to give **(42f)**, (10.7g, 60.14%), m.p. 101-103 °C (99.4-99.8 °C)[205].

Anal:

TLC : 0.4 (n-Hexane: Ethyl acetate:: 9:1)

IR (KBr) : 1681, 1587, 1334, 1089, 813 and 746 cm^{-1}

2-(4-Chlorophenyl)-1-(4-methylphenyl)-1-ethanone (42g)

4-Chlorophenylacetyl chloride was synthesized by reacting 4-chlorophenylacetic acid **(41d)** (5 g, 0.0293 mol) with thionyl chloride (10 ml) in dry benzene (5 ml) by the procedure described in the preparation of **(42a)**. The acid chloride so prepared was then reacted with anhydrous aluminium chloride (8 g, 0.06 mol) and dry toluene (10 ml) in a similar manner as described for

compound **(42a)**. The work up followed by recrystallization from methanol gave the compound **(42g)**, (5.5 g, 76.7%), m.p. 116-18 °C.

Anal:

TLC : 0.86 (benzene)

IR (KBr) : 1676, 1612, 1312, 1080, 820 and 768 cm^{-1}

1,2-Bis-(4-chlorophenyl)-1-ethanone (42h)

4-Chlorophenylacetyl chloride was prepared as described for compound **(42a)**, from 4-chlorophenylacetic acid (8 g, 0.0469 mol). The reaction of phenylacetyl chloride with anhydrous aluminium chloride (10 g, 0.075mol) and dry chlorobenzene (10 ml) was then carried out in a similar manner as described for compound **(42a)**. The reaction mixture was extracted with chloroform (3 x 30 ml) successively. The combined extract was washed twice with sodium bicarbonate solution (10%), water and dried. Chloroform was recovered to afford a residue which was recrystallized from methanol to afford **(42h)**, (7.3 g, 58.7%), m.p. 115-17 °C (114 °C)[206].

Anal:

TLC : 0.52 (n-Hexane: Ethyl acetate:: 9:1)

IR (KBr) : 1690, 1586, 1339, 1075, 821 and 778 cm^{-1}

2-(4-Chlorophenyl)-1-(4-fluorophenyl)-1-ethanone (42i)

4-Chlorophenylacetyl chloride was prepared according to the procedure for **(42a)** from 4-chlorophenylacetic acid (10 g, 0.0586 mol) and thionyl chloride (12 ml). The acid chloride was then treated with anhydrous aluminium chloride (13 g, 0.0975 mol) and dry fluorobenzene (10 ml) followed by the workup procedure described for **(42a)**. The residue obtained was recrystallized from methanol to afford **(42i)**, (11.5 g, 79.3%), m.p. 124-26 °C.

Anal:

TLC : 0.61 (n-Hexane: Ethyl acetate:: 9:1)

IR (KBr) : 1683, 1600, 1327, 1245, 998, 834 and 810 cm^{-1}

2-(4-Chlorophenyl)-1-(4-methylsulfanylphenyl)-1-ethanone (42j)

4-Chlorophenylacetyl chloride was obtained by reacting 4-chlorophenylacetic acid **(42a)** (8 g, 0.047 mol) with thionyl chloride (12 ml) in dry benzene (5 ml). It was reacted with anhydrous aluminum chloride (10 g, 0.074 mol) and thioanisole (8.5 ml) in dichloromethane (10 ml) as described for compound **(42a)**. The work up of the reaction mixture and recrystallization from methanol afforded **(42j)** (3.7 g, 28.5%), m.p. 160-162 °C.

Anal:

TLC : 0.50 (n-Hexane: Ethyl acetate:: 9:1)

IR (KBr) : 1672, 1587, 1398, 1087 and 813 cm^{-1}

2-(4-Chlorophenyl)-1-phenyl-1-ethanone (42k)

4-Chlorophenylacetyl chloride was synthesized as per the procedure described in the preparation of the compound **(42a)** by taking 4-chlorophenylacetic acid (5 g, 0.0293 mol) as the starting material. The acid chloride so obtained was then treated with anhydrous aluminium chloride (8 g, 0.06 mol) and dry benzene in a similar manner as described for compound **(42a)**. The workup of the reaction mixture and recrystallization from methanol afforded the desired compound **(42k)**, (4.9 g, 72.4%), m.p. 137-39 °C (138 °C)[206].

Anal:

TLC : 0.77 (n-Hexane: Ethyl acetate:: 9:1)

IR (KBr) : 1684, 1578, 1332, 1016, 812 and 752 cm^{-1}

2-(4-Chlorophenyl)-1-(4-bromophenyl)-1-ethanone (42l)

4-Chlorophenylacetic acid (8 g, 0.0469 mol) was converted to the corresponding acid chloride by the procedure described for the compound **(42a)**. The acid chloride was reacted with anhydrous aluminium chloride (10 g, 0.075 mol) and dry bromobenzene (10 ml) in a similar manner as described for the compound **(42a)**. Recrystallization from methanol gave compound **(42l)**, (8.7g, 60%), m.p. 130-32 °C.

Anal:

TLC : 0.46 (n-Hexane: Ethyl acetate:: 9:1)

IR (KBr) : 1689, 1582, 1395, 1000, 813 and 772 cm^{-1}

2-(4-Nitrophenyl)-1-phenyl-1-ethanone (42m)

4-Nitrophenylacetyl chloride was synthesized by refluxing 4-nitrophenylacetic acid **(41f)** (5 g, 0.0276 mol) with phosphorous trichloride (5 ml) for 1 h. The solution was decanted from the residue of phosphorous acid into a dropping funnel containing dry benzene (5 ml) and added dropwise into a stirred solution of anhydrous aluminum chloride (6.2 g, 0.0465 mol) in dry benzene (10 ml) at 10-15 °C. The mixture was stirred further for 30 min at room temperature and subjected to reflux for 1 hour. The reaction mixture was worked up in the usual manner. Recrystallization from methanol affords the desired ethanone **(42m)**, (2.8 g, 42%), m.p. 135-37 °C (140-44 °C)[207].

Anal:

TLC : 0.62 (benzene)

IR (KBr) : 1685, 1600, 1514, 1353, 856 and 763 cm^{-1}

2-(4-Nitrophenyl)-1-(4-methylphenyl)-1-ethanone (42n)

4-Nitrophenylacetyl chloride was prepared as described for compound **(42m)** from 4-nitrophenylacetic acid (7 g, 0.0386 mol). The above acid chloride was reacted with anhydrous aluminium chloride (10 g, 0.075 mol) and dry toluene (12 ml) in a similar manner as described for the compound **(42a)**. Recrystallization from methanol gave compound **(42n)**, (8.2 g, 80.3%), m.p. 114-16 °C.

Anal:

TLC : 0.6 (benzene)

IR (KBr) : 1680, 1603, 1514, 1346, 857 and 773 cm^{-1}

2-(2-Chlorophenyl)-1-(4-chlorophenyl)-1-ethanone (42o)

2-Chlorophenylacetyl chloride was synthesized as per the procedure described in the preparation of the compound **(42a)** taking 2-chlorophenylacetic acid **(41b)** (10 g, 0.0586 mol) as the starting material. The acid chloride so obtained was then treated with anhydrous aluminium chloride (12 g, 0.09 mol) and dry chlorobenzene in a similar manner as described for the compound **(42a)**. The workup of the reaction mixture and recrystallization from methanol afforded the desired compound **(42o)**, (12 g, 77.2%), m.p. 93-95 °C (108.5 °C)[206].

Anal:

TLC : 0.87 (benzene)

IR (KBr) : 1691, 1581, 1437, 1197, 815 and 758 cm^{-1}

2-(2-Chlorophenyl)-1-(4-methylsulfanylphenyl)-1-ethanone (42p)

2-Chlorophenylacetyl chloride obtained by reacting 2-chlorophenylacetic acid (7 g, 0.041 mol) with thionyl chloride (12 ml) in dry benzene (6 ml). 2-chlorophenylacetyl chloride was reacted with anhydrous aluminum chloride (10 g, 0.075 mol) and thioanisole (8 ml) in dichloromethane (10 ml) as described for compound **(42a)**. The usual work up and recrystallization from methanol afforded **(42p)** (3.2 g, 28.19%), m.p. 89-92 °C.

Anal:

TLC : 0.35 (n-Hexane: Ethyl acetate:: 9:1)

IR (KBr) : 1670, 1591, 1190, 1089 and 815 and 750 cm^{-1}

1,2-Bis-(4-methylphenyl)-1-ethanone (42q)

4-Methylphenylacetyl chloride was prepared from 4-methylphenylacetic acid **(41e)** (8.8 g, 0.0586 mol) and thionyl chloride (12 ml) by the method described for the compound **(42a)**. 4-Methylphenylacetyl chloride was treated with anhydrous aluminium chloride (13 g, 0.975 mol) and dry toluene (12 ml) by the procedure described for compound **(42a)**. Recrystallization from methanol gave the compound **(42q)**, (7.1 g, 54%), m.p. 106-09 °C.

Anal:

TLC : 0.64 (benzene)

IR (KBr) : 1685, 1600, 1300, 1195, 813 and 768 cm^{-1}

2-(3-Chlorophenyl)-1-(4-methylphenyl)-1-ethanone (42r)

3-Chlorophenylacetyl chloride was synthesized by reacting 3-chlorophenylacetic acid **(41c)** (8 g, 0.0468 mol) with thionyl chloride (10 ml) in dry benzene (5 ml) by the procedure described in the preparation of **(42a)**. The acid chloride so prepared was then reacted with anhydrous aluminium chloride (13 g, 0975 mol) and dry toluene (10 ml) in a similar manner as described for compound **(42a)**. The work up followed by recrystallization from methanol gave the compound **(42r)**, (7.5 g, 66%), m.p. 84-85 °C.

Anal:

TLC : 0.37 (n-Hexane: Ethyl acetate:: 9:1)

IR (KBr) : 1685, 1602, 1330, 1089, 812 and 760 cm^{-1}

4.1A.3 Synthesis of 1,2-diaryl-1,2-ethanedione derivatives (43a-r)

1,2-Diphenyl-1,2-ethanedione (43a)

A mixture of 1,2-diphenyl-1-ethanone **(42a)** (5 g, 0.0237 mol), selenium dioxide (5 g, 0.045 mol) and dimethylsulphoxide (DMSO) (20 ml) in a loosely stoppered conical flask was exposed to microwave radiations for 30 sec intermittently. The hot reaction mixture was filtered to remove selenium metal and washed with hot dioxane. The filtrate was poured over crushed ice; the precipitated solid filtered and washed with excess of water. Recrystallization from methanol afforded **(43a)**, (4.5 g, 84.1%), m.p. 93-94 °C (94-95 °C)[208].

Anal:

TLC : 0.82 (benzene)

IR (KBr) : 1654, 1577, 1450, 1211, 1174, 875, 794 and 717 cm^{-1}

2-Phenyl-1-(4-methylphenyl)-1,2-ethanedione (43b)

A mixture of 2-phenyl-1-(4-methylphenyl)-1-ethanone **(42b)** (5 g, 0.0237 mol), selenium dioxide (5 g, 0.045 mol) and dimethylsulphoxide (DMSO) (20 ml) in a loosely stoppered conical flask was exposed to microwave radiations for 30 sec intermittently. The reaction mixture was processed by the procedure as described for compound **(43a)** and a precipitated sticky solid was obtained[209]. The crude product **(43b)** was used in the next step without any purification (4.1 g, 76.9%).

Anal:

TLC : 0.9 (benzene)

IR (KBr) : 1652, 1570, 1267, 1166, 879, 850 and 771 cm^{-1}

2-Phenyl-1-(4-bromophenyl)-1,2-ethanedione (43c)

A mixture of 2-phenyl-1-(4-bromophenyl)-1-ethanone **(42c)** (8 g, 0.029 mol), selenium dioxide (6 g, 0.054 mol) and dimethylsulphoxide (DMSO) (20 ml) in a loosely stoppered conical flask was exposed to microwave radiations for 95 sec intermittently. The reaction mixture was processed by the procedure as described for compound **(43a)** followed by recrystallization from methanol to yield **(43c)**, (4.75 g, 56.5%), m.p. 85-87 °C (84-95 °C)[210].

Anal:

TLC : 0.71(benzene: pet ether: 9:1)

IR (KBr) : 1668, 1579, 1211, 1174, 873 and 752 cm^{-1}

2-Phenyl-1-(4-fluorophenyl)-1,2-ethanedione (43d)

A mixture of 2-phenyl-1-(4-fluorophenyl)-1-ethanone **(42d)** (5.4 g, 0.025 mol), selenium dioxide (4.5 g, 0.04 mol) and dimethylsulphoxide (DMSO) (15 ml) in a loosely stoppered conical flask was exposed to microwave radiations for 80 sec intermittently. The workup of the reaction mixture was similar as described for compound **(43a)** followed by recrystallization from methanol to afford **(43d)**, (4.3 g, 74.7%), m.p. 66-68 °C.

Anal:

TLC : 0.76(benzene: pet ether: 9:1)

IR (KBr) : 1664, 1596, 1207, 875 and 722 cm^{-1}

2-Phenyl-1-(4-methoxyphenyl)-1,2-ethanedione (43e)

A mixture of 2-phenyl-1-(4-methoxyphenyl)-1-ethanone **(42e)** (3 g, 0.0132 mol) and selenium dioxide (2.5 g, 0.022 mol) and DMSO (10 ml) in a loosely stoppered conical flask was exposed to microwave radiation for 35 seconds intermittently. The work up of the reaction mixture is as described for the compound **(43a)**. The product obtained was sticky in nature and could not be recrystallized from any solvent **(43e)** (2.7 g, 84.9%).

Anal:

TLC : 0.62 (benzene)

IR (KBr) : 1668, 1215, 1020, 877, 840and 731 cm^{-1}

2-Phenyl-1-(4-methylsulfanylphenyl)-1,2-ethanedione (43f)

A mixture of 2-phenyl-1-(4-methylsulfanylphenyl)-1-ethanone **(42f)** (2 g, 0.0082 mol), selenium dioxide (1.7 g, 0.015 mol) and DMSO (10 ml) in a loosely stoppered conical flask was exposed to microwave radiation for 35 seconds intermittently. The work up of the reaction mixture followed by recrystallization as described for compound **(43a)** yielded compound **(43f)**, (1.7 g, 80.56%), m.p. 61-63 °C.

Anal:

TLC : 0.63 (10% EtOAc in hexane)

IR (KBr) : 1666, 1215, 1174, 873, 831and 796 cm^{-1}

2-(4-Chlorophenyl)-1-(4-methylphenyl)-1,2-ethanedione(43g)

A mixture of 2-(4-chlorophenyl)-1-(4-methylphenyl)ethanone **(42g)** (1.5 g, 0.0061 mol), selenium dioxide (1 g, 0.009 mol) and DMSO (8 ml) in a loosely stoppered conical flask was exposed to microwave radiation for 50 seconds intermittently.

The work up followed by recrystallization as described for compound **(43a)** yielded compound **(43g)**, (0.85 g, 80.9%), m.p. 126-28 °C.

Anal:

TLC : 0.8 (10% EtOAc in hexane)

IR (KBr) : 1666, 1605, 1174, 880, 831and 753 cm^{-1}

1,2-Bis-(4-chlorophenyl)-1,2-ethanedione (43h)

A mixture of 1,2-bis(4-chlorophenyl)-1-ethanone **(42h)** (6 g, 0.0226 mol), selenium dioxide (5 g, 0.045 mol) and dimethylsulphoxide (DMSO) (15 ml) in a loosely stoppered conical flask was exposed to microwave radiations for 100 sec intermittently. The workup of the reaction mixture was similar as described for compound **(43a)** followed by recrystallization from methanol to afford **(43h)**, (3.2 g, 50.7%), m.p. 196-98 °C (194-95 °C)[210].

Anal:

TLC : 0.65 (10% EtOAc in hexane)

IR (KBr) : 1658, 1586, 1209, 1173, 870, 831and 763 cm^{-1}

2-(4-Chlorophenyl)-1-(4-fluorophenyl)-1,2-ethanedione (43i)

To a solution of 2-(4-chlorophenyl)-1-(4-fluorophenyl)-1-ethanone **(42i)** (6 g, 0.0241 mol) in dimethylsulphoxide (DMSO) (18 ml), selenium dioxide (5 g, 0.045 mol) was added and exposed to microwave radiations for 80 sec. intermittently. The work up of the reaction mixture followed by recrystallization as described for compound **(43a)** yielded **(43i)**, (4.6 g, 73%), m.p. 144-46 °C.

Anal:

TLC : 0.81 (10% EtOAc in hexane)

IR (KBr) : 1663, 1588, 1150, 890, 838and 770 cm^{-1}

2-(4-Chlorophenyl)-1-(4-methylsulfanylphenyl)-1,2-ethanedione (43j)

Selenium dioxide (2.2 g, 0.0198 mol) was added into a solution of 2-(4-chlorophenyl)-1-(4-methylsulfanylphenyl)-1-ethanone **(42j)** (3.4 g, 0.0122 mol) in dimethylsulphoxide (10 ml). The mixture was exposed to microwave radiations

for 115 sec. intermittently. The reaction mixture was processed as described for compound **(43a)** followed by recrystallization from methanol to yield **(43j)**, (2.8 g, 74%), m.p. 134-36 °C.

Anal:

TLC : 0.69 (50% benzene in pet ether)

IR (KBr) : 1652, 1585, 1321, 1225, 1175, 877, 833 and 765 cm^{-1}

2-(4-Chlorophenyl)-1-phenyl-1,2-ethanedione (43k)

To a solution of 2-(4-chlorophenyl)-1-phenyl-1-ethanone **(42k)** (6 g, 0.026 mol) in dimethylsulphoxide (DMSO) (18 ml), selenium dioxide (5 g, 0.045 mol) was added and exposed to microwave radiations for 55 sec. intermittently. The work up of the reaction mixture followed by recrystallization as described for compound **(43a)** yielded **(43k)**, (5.7 g, 89.6%), m.p. 79-81 °C (73-74 °C)[210].

Anal:

TLC : 0.86 (10% EtOAc in hexane)

IR (KBr) : 1667, 1585, 1210, 870, 825and 738 cm^{-1}

2-(4-Chlorophenyl)-1-(4-bromophenyl)-1,2-ethanedione (43l)

A mixture of 2-(4-chlorophenyl)-1-(4-bromophenyl)-1-ethanone **(42l)** (7 g, 0.0226 mol), selenium dioxide (9 g, 0.081 mol) and dimethylsulphoxide (DMSO) (22 ml) in a loosely stoppered conical flask was exposed to microwave radiations for 155 sec. intermittently. The workup of the reaction mixture was similar as described for compound **(43a)** followed by recrystallization from methanol to afford **(43l)**, (5 g, 68%), m.p. 206-08 °C (203-04 °C)[210].

Anal:

TLC : 0.66(10% EtOAc in hexane)

IR (KBr) : 1664, 1586, 1217, 1183, 875, 825and 765 cm^{-1}

2-(4-Nitrophenyl)-1-phenyl-1,2-ethanedione (43m)

Selenium dioxide (2.5 g, 0.0225 mol) was added into a solution of 2-(4-nitrophenyl)-1-phenyl-1-ethanone **(42m)** (3 g, 0.0124 mol) in

dimethylsulphoxide (10 ml). The mixture was exposed to microwave radiations for 20 sec. intermittently. The reaction mixture was processed as described for compound **(43a)** followed by recrystallization from methanol to yield **(43m)** (2.4 g, 75.7%), m.p. 142-44 °C (140-41 °C)[210].

Anal:

TLC : 0.73 (benzene)

IR (KBr) : 1662, 1527, 1348, 1205, 885, 872and 798 cm^{-1}

2-(4-Nitrophenyl)-1-(4-methylphenyl)-1,2-ethanedione (43n)

To a solution of 2-(4-nitrophenyl)-1-(4-methylphenyl)-1-ethanone **(42n)** (8 g, 0.0313 mol) in dimethylsulphoxide (DMSO) (20 ml), selenium dioxide (7 g, 0.063 mol) was added and exposed to microwave radiations for 35 sec. intermittently. The work up of the reaction mixture followed by recrystallization as described for compound **(43a)** yielded **(43n)** (6.25 g, 74%), m.p. 185-86 °C.

Anal:

TLC : 0.56 (50% pet ether in benzene)

IR (KBr) : 1661, 1602, 1521, 1348 and 846 cm^{-1}

2-(2-Chlorophenyl)-1-(4-chlorophenyl)-1,2-ethanedione (43o)

A mixture of 2-(2-chlorophenyl)-1-(4-chlorophenyl)-1-ethanone **(42o)** (3 g, 0.0113 mol), selenium dioxide (2.5 g, 0.0225 mol) and dimethylsulphoxide (DMSO) (10 ml) in a loosely stoppered conical flask was exposed to microwave radiations for 40 sec. intermittently. The workup of the reaction mixture was similar to compound **(43a)**. Recrystallization from methanol afforded **(43o)**, (1.6 g, 50.7%), m.p. 103-05 °C.

Anal:

TLC : 0.8 (50% pet ether in benzene)

IR (KBr) : 1674, 1580, 1200, 1176, 867, 825and 766 cm^{-1}

2-(2-Chlorophenyl)-1-(4-methylsulfanylphenyl)-1,2-ethanedione (43p)

Selenium dioxide (3.5 g, 0.0315 mol) was added into a solution of 2-(2-chlorophenyl)-1-(4-methylsulfanylphenyl)-1-ethanone **(42p)** (3.1 g, 0.0112 mol) in dimethylsulphoxide (14 ml). The mixture was exposed to microwave radiations for 40 sec. intermittently. The reaction mixture was processed as described for compound **(43a)** and followed by recrystallization from methanol to yield **(43p)** (1.7 g, 52.3%), m.p. 101-03 °C.

Anal:

TLC : 0.37 (10% EtOAc in hexane)

IR (KBr) : 1659, 1589, 1253, 1099, 877, 862and 769 cm^{-1}

1,2-Bis-(4-methylphenyl)-1,2-ethanedione (43q)

A mixture of 1,2-bis(4-methylphenyl)-1-ethanone **(42q)** (0.5 g, 0.0022 mol), selenium dioxide (1 g, 0.009 mol) and dimethylsulphoxide (DMSO) (5 ml) in a loosely stoppered conical flask was exposed to microwave radiations for 40 sec intermittently. The workup of the reaction mixture was similar to that as described for compound **(43a)**. Recrystallization from methanol afforded **(43q)** (0.5 g, 94.33%), m.p. 101-03 °C (102-04)[211].

Anal:

TLC : 0.85 (benzene)

IR (KBr) : 1660, 1604, 1172, 885, 829and 748 cm^{-1}

2-(3-chlorophenyl)-1-(4-methylphenyl)-1,2-ethanedione (43r)

To a solution of 2-(3-chlorophenyl)-1-(4-methylphenyl)-1-ethanone **(42r)** (6.3 g, 0.0257 mol) in dimethylsulphoxide (DMSO) (20 ml), selenium dioxide (6 g, 0.054 mol) was added and exposed to microwave radiations for 55 sec. intermittently. The work up of the reaction mixture was similar as described for compound **(43a)**. The product obtained was sticky in nature and could not recrystallize from any solvent (4.2 g, 63%).

Anal:

TLC : 0.85 (benzene)

IR (KBr) : 1677, 1604, 1201, 898, 808and 769 cm^{-1}

4.1A.4 Synthesis of 2,3-diaryl-1,4-diazepine derivatives

2,3-Diphenyl-6,7-dihydro-5*H*-1,4-diazepine (44a)

An equimolar mixture of 1,2-diphenyl-1,2-ethanedione **(43a)** (3.0 g, 0.014 mol), 1,3-propanediamine (1.2 ml, 0.14 mol) and glacial acetic acid (0.8 ml, 0.014 mol) in ethanol (30 ml) was allowed to reflux for 24 hrs. The reaction was monitored throughout by TLC. After removal of solvent under vaccum, the resulting solid was recrystallized from methanol to yield the product **(44a)**, (0.35 g, 10%), 115-18 °C (114-16 °C)[115].

Anal:

TLC : 0.32 (n-hexane)

IR (KBr) : 1605 (C=N), 1510, 1332, 1272, 825 and 780 cm^{-1}

PMR : δ 2.31-2.40 (m, 2H, N-CH_2-$C\underline{H}_2$-), 3.47 (br, 4H, N-$C\underline{H}_2$-CH_2-), 7.2-7.6 (m, 10H, ArH)

MS : m/z 249 (M+1).

2-Phenyl-3-(4-methylphenyl)-6,7-dihydro-5*H*-1,4-diazepine (44b)

2-Phenyl-1-(4-methylphenyl)-1,2-ethanedione **(43b)** (4.1 g, 0.0182 mol) was dissolved in a mixture of 1,3-propanediamine (1.36 g, 0.0183 mol) and glacial acetic acid (1.1 g, 0.0183 mol) in ethanol (30 ml). The mixture was refluxed for 34 hrs. After removal of solvent in vaccum, the resulting sticky compound was subjected to silica gel column chromatography (eluent-benzene) to obtain a syrupy compound. The syrup was thoroughly triturated with petroleum ether to get a solid compound which was filtered off. The crude product so obtained was further purified by recrystallization from methanol to yield **(44b)**, (1.1 g, 23%), 82-84 °C.

Anal:

TLC	: 0.31 (benzene)
IR (KBr)	: 1608, 1592 (C=N), 1510, 1332, 1272, 825 and 780 cm^{-1}
PMR	: δ 2.32 (s, 3H, CH_3), 2.34-2.41(m, 2H, N-CH_2-$C\underline{H}_2$-), 3.5 (br, 4H, N-$C\underline{H}_2$-CH_2-), 7.11-7.64 (m, 9H, ArH)
MS	: m/z 263 (M+1).

2-Phenyl-3-(4-bromophenyl)-6,7-dihydro-5*H*-1,4-diazepine (44c)

An equimolar mixture of 2-phenyl-1-(4-bromophenyl)-1,2-ethanedione **(43c)** (4 g, 0.014 mol), 1,3-propanediamine (1.025g, 0.014 mol) and glacial acetic acid (0.79 ml, 0.014 mol) in ethanol (30 ml) was refluxed for 30 hrs. The workup of the reaction mixture was similar to that described for compound **(44b)**. Column chromatography on silica gel using benzene as eluent afforded a crude product which on recrystallization from petroleum ether afforded the pure compound **(44c)**, (0.275 g, 6%), 93-95 °C.

Anal:

TLC	: 0.51 (5% MeOH in benzene)
IR (KBr)	: 1598 (C=N), 1585, 1392, 1272, 1068, 945 and 825 cm^{-1}
PMR	: δ 2.33-2.41(m, 2H, N-CH_2-$C\underline{H}_2$-), 3.5 (br, 4H, N-$C\underline{H}_2$-CH_2-), 7.1-7.6 (m, 9H, ArH)
MS	: m/z 329 (M+2)

2-Phenyl-3-(4-fluorophenyl)-6,7-dihydro-5*H*-1,4-diazepine (44d)

1,3-Propanediamine (1.33 g, 0.0179 mol) was added to the refluxing mixture of 2-phenyl-1-(4-fluorophenyl)-1,2-ethanedione **(43d)** (4.1 g, 0.0179 mol) and glacial acetic acid (1.07 g, 0.0179 mol) in ethanol (30 ml). After refluxing for 28 hrs and removal of solvent a sticky compound was obtained. The remaining experimental procedure was similar to that as described for compound **(44b)**. Recrystallization from petroleum ether yielded **(44d)**, (0.6 g, 12.5%), 77-78 °C.

Anal:

TLC : 0.61 (5% MeOH in benzene)

IR (KBr) :1598 (C=N), 1587, 1506, 1288, 1159, 1080, 943 and 850 cm^{-1}

PMR : δ 2.31-2.4 (m, 2H, N-CH_2-CH_2-), 3.5 (br, 4H, N-CH_2-CH_2-), 6.9-7.6 (m, 9H, ArH)

2-Phenyl-3-(4-methoxyphenyl)-6,7-dihydro-5*H*-1,4-diazepine (44e)

2-Phenyl-1-(4-methoxyphenyl)-1,2-ethanedione **(43e)** (2.7 g, 0.011 mol) was dissolved into a mixture of 1,3-propanediamine (0.83 g, 0.011 mol) and glacial acetic acid (0.67 g, 0.011 mol) in ethanol (30 ml). The mixture was refluxed for 25 hrs. The rest of the experimental procedure was similar to that described for compound **(44b)**. The crude product so obtained was further purified by recrystallization from methanol to yield **(44e)**, (0.42 g, 13.46%), 106-08 °C.

Anal:

TLC : 0.3 (5%MeOH in benzene)

IR (KBr) : 1600 (C=N), 1570, 1508, 1247, 1029, 945, 813 and 786 cm^{-1}

PMR : δ 3.77 (s, 3H, OCH_3), 2.31-2.38 (m, 2H, N-CH_2-CH_2-), 3.2 (br, 4H, N-CH_2-CH_2-), 6.8-7.3 (m, 9H, ArH)

MS : m/z 279 (M+1)

2-Phenyl-3-(4-methylsulfanylphenyl)-6,7-dihydro-5*H*-1,4-diazepine (44f)

An equimolar mixture of 1,3-propanediamine (0.87 g, 0.0117 mol), 2-phenyl-1-(4-methylsulfanylphenyl)-1,2-ethanedione **(43f)** (3 g, 0.0117 mol) and glacial acetic acid (0.7 g, 0.0117 mol) in ethanol (30 ml) was refluxed for 30 hrs. The workup of the reaction mixture was similar to that described for compound **(44b)**. Elution from column chromatography on silica gel using benzene as eluent gave a product which on recrystallization from petroleum ether afford the pure compound **(44f)**, (1.0 g, 29.06%), 115-117 °C.

Anal:

TLC : 0.52 (5%MeOH in benzene)

IR (KBr) : 1600, 1593 (C=N), 1247, 1180, 1097, 960, 823 and 785 cm^{-1}

PMR : δ 2.4 (s, 3H, SCH_3), 2.34-2.37 (m, 2H, N-CH_2-$C\underline{H}_2$-), 3.5 (br, 4H, N-$C\underline{H}_2$-CH_2-), 7.1-7.5 (m, 9H, ArH)

MS : m/z 295 (M+1)

2-(4-Chlorophenyl)-3-(4-methylphenyl)-6,7-dihydro-5*H*-1,4-diazepine (44g)

2-(4-Chlorophenyl)-1-(4-methylphenyl)-1,2-ethanedione **(43g)** (3.2 g, 0.0123 mol) was dissolved into a mixture of 1,3-propanediamine (0.917 g, 0.0123 mol) and glacial acetic acid (0.7 g, 0.0123 mol) in ethanol (30 ml). The mixture was refluxed for 24 hrs. A viscous oily compound was obtained after the usual experimental procedure as described for compound **(44b)**. Scratching of the oily compound induced the formation of a crude solid material. The crude product obtained was further purified by recrystallization from methanol to yield **(44g)**, (1.25 g, 34%), 102-04 °C.

Anal:

TLC : 0.65 (5%MeOH in benzene)

IR (KBr) : 1610 (C=N), 1600, 1593, 1400, 840, 821and 761 cm^{-1}

PMR : δ 2.3 (s, 3H, CH_3), 2.32-2.39 (m, 2H, N-CH_2-$C\underline{H}_2$-), 3.4 (br, 4H, N-$C\underline{H}_2$-CH_2-), 7.1-7.5 (m, 8H, ArH)

Cald for $C_{18}H_{17}ClN_2$: C, 72.84; H, 5.77; N, 9.44 %

Found : C, 72.83; H, 5.62; N, 9.49 %

2,3-Bis(4-chlorophenyl)-6,7-dihydro-5*H*-1,4-diazepine (44h)

1,3-Propanediamine (0.64 g, 0.0086 mol) was added to the refluxing mixture of 1,2-bis(4-chlorophenyl)-1,2-ethanedione **(43h)** (2.4 g, 0.0086 mol) and glacial acetic acid (0.52 g, 0.0086 mol) in ethanol (30 ml). After refluxing for 24 hrs and removal of solvent a sticky compound was obtained. The remaining experimental procedure was similar to that as described for compound **(44b)** to afford a crude compound. Further purification was effected by recrystallization from petroleum ether to yield **(44h)** (0.45 g, 16.5%), m.p. 111-13 °C.

Anal:

TLC : 0.32 (benzene)

IR (KBr) : 1614 (C=N), 1591, 1467, 1398, 1080, 840, 769 cm^{-1}

PMR : δ 2.31-2.40 (m, 2H, N-CH_2-$C\underline{H}_2$-), 3.5 (br, 4H, N-$C\underline{H}_2$-CH_2-), 7.2-7.5 (m, 8H, ArH)

Cald for $C_{17}H_{14}Cl_2N_2$: C, 64.37; H, 4.45; N, 8.83 %

Found : C, 64.24; H, 3.97; N, 8.98 %

2-(4-Chlorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-5*H*-1,4-diazepine (44i)

An equimolar mixture of 1,3-propanediamine (1.13 g, 0.0152 mol), 2-(4-chlorophenyl)-1-(4-fluorophenyl)-1,2-ethanedione **(43i)** (4 g, 0.0152 mol) and glacial acetic acid (0.92 g, 0.0152 mol) in ethanol (30 ml) was refluxed for 30 hrs. The remaining experimental procedure was similar to that described for compound **(44b)** which was followed by column chromatography on silica gel using benzene as eluent to afford a crude compound. Recrystallization from methanol yielded the pure compound **(44i)**, (1.9 g, 41%), 104-06 °C.

Anal:

TLC : 0.5 (5%MeOH in benzene)

IR (KBr) : 1614 (C=N), 1587, 1272, 1090, 945, 850, 763 cm^{-1}

PMR : δ 2.32-2.39 (m, 2H, N-CH_2-$C\underline{H}_2$-), 3.5 (br, 4H, N-$C\underline{H}_2$-CH_2-), 6.98-7.31 (m, 8H, ArH)

Cald for $C_{17}H_{14}ClFN_2$: C, 67.89; H, 4.69; N, 9.31 %

Found : C, 68.12; H, 4.16; N, 9.54 %

2-(4-Chlorophenyl)-3-(4-methylsulfanylphenyl)-6,7-dihydro-5*H*-1,4-diazepine (44j)

2-(4-chlorophenyl)-1-(4-methylsulfanylphenyl)-1,2-ethanedione **(43j)** (2.6 g, 0.0089 mol) was dissolved into a mixture of 1,3-propanediamine (0.66g, 0.0089 mol) and glacial acetic acid (0.53 g, 0.008 mol) in ethanol (30 ml). The mixture was refluxed for 30 hrs. A viscous oily compound was obtained after the normal

experimental procedure as described for compound **(44b)**. Trituration of the oily compound with petroleum ether yielded a crude solid material which was washed with excess of petroleum ether and filtered to afford a pure compound **(44j)**, (0.35 g, 12.7%), m.p. 120-22 °C.

Anal:

TLC : 0.51 (5%MeOH in benzene)

IR (KBr) : 1610 (C=N), 1589, 1396, 1274, 1095, 941, 835, 815 cm^{-1}

PMR : δ 2.45 (s, 3H, SCH_3), 2.28-2.43 (m, 2H, N-CH_2-CH_2-), 3.51 (br, 4H, N-CH_2-CH_2-), 7.1-7.7 (m, 8H, ArH)

Cald for $C_{18}H_{17}ClN_2S$: C, 65.74; H, 5.21; N, 8.52 %

Found : C, 65.91; H, 4.72; N, 8.82 %

2-(4-Chlorophenyl)-3-phenyl-6,7-dihydro-5*H*-1,4-diazepine (44k)

1,3-Propanediamine (0.91 g, 0.012 mol) was added to the refluxing mixture of 2-(4-chlorophenyl)-1-phenyl-1,2-ethanedione **(43k)** (3 g, 0.012 mol) and glacial acetic acid (0.74 g, 0.012 mol) in ethanol (30 ml). After refluxing for 24 hrs and removal of solvent a sticky compound was resulted. The remaining experimental procedure was similar to that described for compound **(44b)** to afford a crude compound. Further purification was effected by recrystallization from methanol to yield **(44k)** (1.3 g, 37.5%), 72-74 °C.

Anal:

TLC : 0.42 (5%MeOH in benzene)

IR (KBr) : 1611, 1592 (C=N), 1456, 1338, 1272, 1092, 835, 786 cm^{-1}

PMR : δ 2.32-2.41(m, 2H, N-CH_2-CH_2-), 3.5 (br, 4H, N-CH_2-CH_2-), 7.2-7.6 (m, 9H, ArH)

MS : m/z 283 (M+1)

2-(4-Chlorophenyl)-3-(4-bromophenyl)-6,7-dihydro-5*H*-1,4-diazepine (44l)

An equimolar mixture of 1,3-propanediamine (1.14g, 0.0154 mol), 2-(4-chlorophenyl)-1-(4-bromophenyl)-1,2-ethanedione **(43l)** (5 g, 0.0154 mol) and

glacial acetic acid (0.93 g, 0.0154 mol) in ethanol (30 ml) was refluxed for 26 hrs. The remaining experimental procedure was similar to that described for compound **(44b)** which was followed by column chromatography on silica gel using benzene as eluent to afford a crude compound. Recrystallization from methanol affords the pure compound **(44l)**, (0.9 g, 16%), 140-42 °C.

Anal:

TLC : 0.65 (5%MeOH in benzene)

IR (KBr) : 1612 (C=N), 1585, 1490, 1310, 1068, 943, 827, 769 cm^{-1}

PMR : δ 2.3-2.4 (m, 2H, N-CH_2-$C\underline{H}_2$-), 3.5 (br, 4H, N-$C\underline{H}_2$-CH_2-), 7.2-7.5 (m, 8H, ArH)

Cald for $C_{17}H_{14}BrClN_2$: C, 56.46; H, 3.9; N, 7.75 %

Found : C, 57.05; H, 3.33; N, 8.19 %

2-(4-Nitrophenyl)-3-phenyl-6,7-dihydro-5*H*-1,4-diazepine (44m)

1,3-Propanediamine (0.7 g 0.0094 mol) was added to the refluxing mixture of 2-(4-nitrophenyl)-1-phenylethanedione **(43m)** (2.4 g, 0.0094 mol) and glacial acetic acid (0.56 g, 0.0094 mol) in ethanol (30 ml). After refluxing for 24 hrs and removal of solvent a sticky compound was obtained. The remaining experimental procedure was similar to that described for compound **(44b)** to yield a crude compound. Further purification was effected by recrystallization from methanol to yield **(44m)** (0.3 g, 10.9%), m.p. 99-101 °C.

Anal:

TLC : 0.5 (5%MeOH in benzene)

IR (KBr) : 1608, 1600 (C=N), 1574, 1520, 1347, 854, 794 cm^{-1}

PMR : δ 2.3-2.4 (m, 2H, N-CH_2-$C\underline{H}_2$-), 3.5 (br, 4H, N-$C\underline{H}_2$-CH_2-), 7.2-8.1 (m, 9H, ArH)

MS : m/z 293 (M^+)

2-(4-Nitrophenyl)-3-(4-methylphenyl)-6,7-dihydro-5*H*-1,4-diazepine (44n)

2-(4-Nitrophenyl)-1-(4-methylphenyl)-1,2-ethanedione **(43n)** (5 g, 0.085 mol) was dissolved into a mixture of 1,3-propanediamine (1.37 g, 0.0185 mol) and glacial acetic acid (1.11g, 0.0185 mol) in dioxane (30 ml). The mixture was refluxed for 30 hrs. A viscous oily compound was obtained after the usual experimental procedure as described for that compound **(44b)**. Trituration of the oily compound with petroleum ether afforded a crude solid material which was washed with excess of petroleum ether and filtered to yield the pure compound **(44n)**, (1.05 g, 17.4%), m.p. 161-63 °C.

Anal:

TLC	: 0.48 (5%MeOH in benzene)
IR (KBr)	: 1595 (C=N), 1514, 1344, 1259, 1160, 1090, 973, 850 cm^{-1}
PMR	:δ 2.33 (s, 3H, CH_3), 2.34-2.4 (m, 2H, N-CH_2-$C\underline{H}_2$-), 3.58 (br, 4H, N-$C\underline{H}_2$-CH_2-), 7.1-8.1 (m, 8H, ArH)

2-(2-Chlorophenyl)-3-(4-chlorophenyl)-6,7-dihydro-5*H*-1,4-diazepine (44o)

The equimolar mixture of 1,3-propanediamine (0.8 g, 0.0107 mol), 2-(2-chlorophenyl)-1-(4-chlorophenyl)-1,2-ethanedione **(43o)** (3 g, 0.0107 mol) and glacial acetic acid (0.64 g, 0.0107 mol) in ethanol (30 ml) was refluxed for 24 hrs. The remaining experimental procedure was similar to that described for compound **(44b)** followed by column chromatography on silica gel using benzene as eluent to afford crude compound. Recrystallization from methanol afforded the title compound **(44o)**, (0.26 g, 7.6%), m.p. 115-116 °C.

Anal:

TLC	: 0.54 (5%MeOH in benzene)
IR (KBr)	: 1608 (C=N), 1589, 1490, 1320, 1100, 945, 850, 775 cm^{-1}
PMR	: δ 2.43-2.52 (m, 2H, N-CH_2-$C\underline{H}_2$-), 3.58-3.62 (t, 2H, J =12 Hz, N-$C\underline{H}_2$-CH_2-), 3.70-3.74 (t, 2H, J = 12 Hz, N-$C\underline{H}_2$-CH_2-), 7.22-7.68 (m, 8H, ArH)

Cald for $C_{17}H_{14}Cl_2N_2$: C, 64.37; H, 4.45; N, 8.83 %

Found : C, 64.75; H, 3.95; N, 9.12 %

2-(2-Chlorophenyl)-3-(4-methylsulfanylphenyl)-6,7-dihydro-5*H*-1,4-diazepine (44p)

2-(2-Chlorophenyl)-1-(4-methylsulfanylphenyl)-1,2-ethanedione **(43p)** (1.7 g, 0.0058 mol) was dissolved into a mixture of 1,3-propanediamine (0.43 g, 0.0058 mol) and glacial acetic acid (0.35 g, 0.0058 mol) in ethanol (30 ml). The mixture was refluxed for 30 hrs. A viscous oily compound was obtained after usual experimental procedure as described for that compound **(44b)**. Trituration of the oily compound with petroleum ether affords the crude solid material which was washed with excess of petroleum ether and filtered to afford the pure compound **(44p)**, (0.22 g, 11.45%), 119-21°C.

Anal:

TLC : 0.6 (5%MeOH in benzene)

IR (KBr) : 1610 (C=N), 1309, 1274, 1184, 1097, 943, 856, 750 cm^{-1}

PMR : δ 2.43 (s, 3H, SCH_3), 2.46-2.49 (m, 2H, N-CH_2-CH_2-), 3.60- 3.63 (t, 2H, J = 12 Hz, N-CH_2-CH_2-), 3.70-3.73 (t, 2H, J =12 Hz, N-CH_2-CH_2-), 7.1-7.3 (m, 8H, ArH)

MS : m/z 329 (M+1)

2,3-Bis(4-methylphenyl)-6,7-dihydro-5*H*-1,4-diazepine (44q)

1,3-Propanediamine (0.65 g, 0.0088 mol) was added to the refluxing mixture of 1,2-bis(4-methylphenyl)-1,2-ethanedione **(43q)** (2.1 g, 0.0088 mol) and glacial acetic acid (0.52 g, 0.0088 mol) in ethanol (30 ml). After refluxing for 25 hrs and removal of solvent a sticky compound was resulted. The rest of the experimental procedure was similar to that described for compound **(44b)** to get the crude compound. Further purification was effected by recrystallization from petroleum ether to yield **(44q)** (0.4 g, 16.46%), 94-95 °C.

Anal:

TLC	: 0.57 (5%MeOH in benzene)
IR (KBr)	: 1608 (C=N), 1593, 1319, 1278, 1083, 945, 852, 800 cm^{-1}
PMR	: δ 2.32 (s, 6H, $(CH_3)_2$), 2.34-2.37 (m, 2H, N-CH_2-CH_2-), 3.5 (br, 4H, N-CH_2-CH_2-), 7.11-7.52 (m, 8H, ArH)
MS	: m/z 277 (M+1)

2-(3-Chlorophenyl)-3-(4-methylphenyl)-6,7-dihydro-5*H*-1,4-diazepine (44r)

2-(3-Chlorophenyl)-1-(4-methylphenyl)-1,2-ethanedione **(43r)** (3 g, 0.011 mol) was dissolved into a mixture of 1,3-propanediamine (0.86 g, 0.011 mol) and glacial acetic acid (0.7 g, 0.011 mol) in ethanol (30 ml). The mixture was refluxed for 25 hrs. A viscous oily compound was obtained after the usual experimental procedure as described for compound **(44b)**. Scratching of the oily compound with petroleum ether affords a crude solid material. Purification was further effected by recrystallization from petroleum ether to yield **(44r)**, (1.3 g, 38%), 119-21 °C.

Anal:

TLC	: 0.47 (5%MeOH in benzene)
IR (KBr)	: 1608 (C=N), 1595, 1471, 1255, 1091, 943, 829, 761 cm^{-1}
PMR	: δ 2.33 (s, 3H, CH_3), 2.35-2.40 (m, 2H, N-CH_2-CH_2-), 3.53 (br, 4H, N-CH_2-CH_2-), 7.1-7.7 (m, 8H, ArH)
MS	: m/z 297 (M+1)

4.1B 5,7-DIARYL-2,3-DIHYDRO-1*H*-1,4-DIAZEPINE

The synthetic work carried out has been discussed under following sub heads:

4.1B.1 Synthesis of substituted 2-hydroxyacetophenone derivatives

4.1B.2 Synthesis of 2-acetyl-1-(substituted benzoyloxy)benzene derivtives

4.1B.3 Synthesis of 1,3-substituted diphenyl-1,3-propanedione derivatives

4.1B.4 Synthesis of 2-(substituted phenyl)chromen-4-one derivatives

4.1B.5 Synthesis of 5,7-substituted diphenyl-1*H*-1,4-diazepine derivatives

4.1B.1 Synthesis of substituted 2-hydroxyacetophenone derivative

5-Methoxy-2-hydroxyacetophenone (45b)

Hydroquinone acetate

One drop of sulphuric acid was added to a mixture of hydroquinone (10 g) and acetic anhydride (20 ml). The mixture was occasionally stirred for 10 minutes to obtain a clear solution. The clear solution was poured into crushed ice and filtered. The white crystalline solid obtained was dried. The crude diacetate was pure enough and used in the next step without further purification. The yield is 16 g (90.7%) and m.p. 119-20 °C (121-22 °C)[190].

2,5-Dihydroxyacetophenone

A mixture of dry hydroquinone acetate (10 g) and anhydrous aluminium hydrochloride (15 g) was powdered finely in a mortar and transferred into a 250 ml of round-bottomed flask. The mixture was heated on oil bath at 160-165 °C for 3 hours until the complete evolution of hydrogen chloride gas. After 3 hours the mixture was poured into a mixture of ice containing con. HCl. The dark green solid obtained was filtered and washed with water. Recrystallization from hot water yielded 5.2 g (66.4%) and melts at 198-200 °C (202-03 °C)[189].

5-Methoxy-2-hydroxyacetophenone (45b)

Methyl iodide (3 ml) and potassium carbonate (4 g) was added to a solution of 2,5-dihydroxyacetophenone (5 g) in acetone (30 ml) . The mixture was allowed

to reflux on a water bath for 6 hours. Maximum amount of the acetone was recovered and the residual dark-colored liquid was cooled and acidified with 5% dil. H_2SO_4. The resulting mixture was steam distilled until no oily drops were seen in the condenser. The distillate was allowed to stand overnight at room temperature, and the yellowish brown colour crystals were filtered and dried to yield **(45b)** (3.1 g, 56.7%), m.p. 48 °C (48-50 °C)[188].

Anal:

R_f : 0.62 (chloroform)

IR (KBr) : 3066, 1640, 1218, 1037, 850 and 769 cm^{-1}

4.1B.2 Synthesis of 2-acetyl-1-(substituted benzoyloxy)benzene

2-Acetyl-1-benzoyloxybenzene (46a)

To a cold solution of 2-hydroxyacetophenone **(45a)** (6.78 g, 0.0497 mol) and benzoic acid (6.08 g, 0.0497 mol) in pyridine (30 ml), $POCl_3$ (6 ml) was added slowly. The reaction mixture was stirred at room temperature for 3 hours and poured into a mixture of crushed ice and Con. HCl. The precipitated solid was filtered, washed with water and dried. Recrystallization from methanol gave the compound **(46a)** (8 g, 66.8%) m.p 88-90 °C (87-88 °C)[212].

Anal:

TLC : 0.63 (benzene)

IR (KBr) : 1735, 1680, 1484, 1063, 849, and 765 cm^{-1}

2-Acetyl-1-(4-methylbenzoyloxy)benzene (46b)

$POCl_3$ (6 ml) was added slowly to a cold solution of 2-hydroxyacetophenone **(45a)** (6 g, 0.044 mol) and 4-methylbenzoic acid (6 g, 0.044 mol) in pyridine (30 ml). The reaction mixture was stirred for 3 hours at room temperature. The workup of the reaction mixture was on similar lines as described for compound **(46a)**. The solid compound **(46b)** obtained was used in the next step without further purification, (9.2 g, 82.1%) m.p. 99-102 °C.

Anal:

TLC : 0.52 (benzene)

IR (KBr) : 1735, 1683, 1267, 1178, 765, and 750 cm^{-1}

2-Acetyl-1-(3-methylbenzoyloxy)benzene (46c)

In synthesis of **46b**, 4-methylbenzoic acid was substituted by 3-methylbenzoic acid to afford the compound **(46c)**, (8.3 g, 74.1%) m.p. 60-62 °C.

Anal:

TLC : 0.57 (benzene)

IR (KBr) : 1732, 1683, 1271, 1184, 842, and 769 cm^{-1}

2-Acetyl-1-(4-methoxybenzoyloxy)benzene (46d)

To a cold solution of 2-hydroxyacetophenone **(45a)** (6 g, 0.044 mol) and 4-methoxybenzoic acid (6.7 g, 0.044 mol) in pyridine (30 ml), $POCl_3$ (6 ml) was added slowly. The reaction mixture was stirred at room temperature for 3 hours and poured into crushed ice-Con. HCl mixture. The precipitated solid was filtered, washed with excess of water and dried to yield the compound **(46d)**. Compound **(46d)** was used in the next step without further purification, (11.6 g, 97.39%) m.p. 116-18 °C.

Anal:

TLC : 0.59 (benzene)

IR (KBr) : 1724, 1683, 1610, 1199, 1070, 844 and 765 cm^{-1}

2-Acetyl-1-(3-methoxybenzoyloxy)benzene (46e)

In synthesis of **46d**, 4-methoxybenzoic acid was substituted by 3-methoxybenzoic acid and stirred at room temperature for 3 hours. The reaction mixture was then poured over crushed ice containing Conc. HCl and extracted with chloroform (3×30 ml) successively. The combined organic extract was washed with sodium bicarbonate solution twice, followed by water, dried, filtered and concentrated to afford a yellow color syrupy liquid **(46e)**, (9.6 g, 80.6%). Compound **(46e)** was used in the next step without further purification.

Anal:

TLC : 0.63 (benzene)

IR (KBr) : 1741, 1679, 1242, 1082, 837 and 754 cm^{-1}

2-Acetyl-1-(3,4-dimethoxybenzoyloxy)benzene (46f)

$POCl_3$ (6 ml) was added slowly to a cold solution of 2-hydroxyacetophenone **(45a)** (3.73 g, 0.0274 mol) and 3,4-dimethoxybenzoic acid (5 g, 0.0274 mol) in pyridine (30 ml). The reaction mixture was stirred for 3 hours at room temperature. The workup of the reaction mixture was similar to that described for compound **(46a)**. The solid compound **(46f)** obtained was used in the next step without further purification, (3.6 g, 43.9%) m.p. 129-31 °C.

Anal:

TLC : 0.41 (benzene)

IR (KBr) : 1732, 1681, 1519, 1234, 1026, 918 and 760 cm^{-1}

2-Acetyl-1-(4-chlorobenzoyloxy)benzene (46g)

To a cold solution of 2-hydroxyacetophenone **(45a)** (4.34 g, 0.0318 mol) and 4-chlorobenzoic acid (5 g, 0.0319 mol) in pyridine (30 ml), $POCl_3$ (6 ml) was added slowly. The reaction mixture was stirred at room temperature for 3 hours and poured into crushed ice-Con. HCl mixture. The precipitated solid was filtered, washed with excess of water and dried to yield the compound **(46g)**. Compound **(46g)** was used in the next step without further purification, (6.5 g, 74.2%) m.p. 60-62 °C.

Anal:

TLC : 0.63 (benzene)

IR (KBr) : 1739, 1681, 1602, 1197, 1070, 842 and 765 cm^{-1}

2-Acetyl-1-(3-chlorobenzoyloxy)benzene (46h)

In synthesis of **46g**, 4-chlorobenzoic acid was substituted by 3-chlorobenzoic acid and worked as above to afford the compound **(46h)**, (7 g, 80.0%) m.p. 86-88 °C.

Anal:

TLC : 0.51 (benzene)

IR (KBr) : 1739, 1685, 1602, 1255, and 750 cm^{-1}

2-Acetyl-1-(2-chlorobenzoyloxy)benzene (46i)

In the synthesis of **46g**, 4-chlorobenzoic acid was substituted by 2-chlorobenzoic acid to obtain the compound **(46i)**, (8.5 g, 97.1%) m.p. 68-70 °C.

Anal:

TLC : 0.51 (benzene)

IR (KBr) : 1743, 1683, 1604, 1245, 1099 and 767 cm^{-1}

2-Acetyl-1-(2,4-dichlorobenzoyloxy)benzene (46j)

In synthesis of **46g**, 4-chlorobenzoic acid was substituted by 2,4-dichlorobenzoic acid to give the compound **(46j)**, (11.0 g, 96.9%) m.p. 62-64 °C.

Anal:

TLC : 0.8 (benzene)

IR (KBr) : 1751, 1681, 1600, 1245, 1027, 898 and 756 cm^{-1}

2-Acetyl-1-(4-bromobenzoyloxy)benzene (46k)

To a cold solution of 2-hydroxyacetophenone **(45a)** (5 g, 0.0367 mol) and 4-bromobenzoic acid (7.38 g, 0.0367 mol) in pyridine (30 ml), $POCl_3$ (8 ml) was added slowly. The reaction mixture was stirred at room temperature for 3 hours and poured into crushed ice-Con. HCl mixture. The precipitated solid was filtered, washed with excess of water and dried to obtain the compound **(46k)**. Compound **(46k)** was used in the next step without further purification, (7.5 g, 64.0%) m.p 130-32 °C.

Anal:

TLC : 0.67 (benzene)

IR (KBr) : 1739, 1681, 1600, 1487, 1072, 960, and 747 cm^{-1}

2-Acetyl-1-(4-fluorobenzoyloxy)benzene (46l)

$POCl_3$ (6 ml) was added slowly to a cold solution of 2-hydroxyacetophenone **(45a)** (5 g, 0.0367 mol) and 4-fluorobenzoic acid (5.14 g, 0.0366 mol) in pyridine (30 ml). The reaction mixture was stirred for 3 hours at room temperature. The workup of the reaction mixture was similar to that described for the compound **(46a)**. The solid compound **(46l)** obtained was used in the next step without further purification, (8.2 g, 86.4%) m.p. 95-97 °C.

Anal:

TLC : 0.74 (benzene)

IR (KBr) : 1741, 1685, 1600, 1251, 1178, 850 and 750 cm^{-1}

2-Acetyl-1-(2-furoyloxy)benzene (46m)

To a cold solution of 2-hydroxyacetophenone **(45a)** (6 g, 0.044 mol) and 2-furoic acid (4.93 g, 0.0439 mol) in pyridine (30 ml), $POCl_3$ (6 ml) was added slowly. The reaction mixture was stirred at room temperature for 3 hours and poured into crushed ice-Con. HCl mixture. The precipitated solid was filtered, washed with excess of water and dried. Compound **(46m)** was used in the next step without further purification, (7 g, 69.0%) m.p 94-96 °C (80 °C)[213].

Anal:

TLC : 0.5 (benzene)

IR (KBr) : 1732, 1689, 1604, 1469, 1203, 1093, 788 and 747 cm^{-1}

2-Acetyl-1-(2-thienoyloxy)benzene (46n)

$POCl_3$ (6 ml) was added slowly to a cold mixture of 2-hydroxyacetophenone **(45a)** (5.31 g, 0.039 mol) and 2-thienoic acid (5 g, 0.039 mol) in pyridine (30 ml). The reaction mixture was stirred at room temperature for 3 hours and poured into crushed ice-Con. HCl mixture. The precipitated solid was filtered, washed with excess of water and dried. Compound **(46n)** was used in the next step without further purification, (9.6 g, 100%) m.p 112-15 °C.

Anal:

TLC : 0.58 (benzene)

IR (KBr) : 1732, 1681, 1602, 1413, 1245, 1062, 858 and 763 cm^{-1}

2-Acetyl-1-benzoyloxy-4-methoxybenzene (46o)

To a cold mixture of 2-hydroxy-5-methoxyacetophenone **(45b)** (3.57 g, 0.0214 mol) and benzoic acid (2.62 g, 0.0214 mol) in pyridine (20 ml) $POCl_3$ (4 ml) was added slowly. The reaction mixture was stirred at room temperature for 3 hours and poured into crushed ice-Con. HCl mixture. The precipitated solid was filtered, washed with excess of water and dried to obtain compound **(46o)**. Compound **(46o)** was used in the next step without further purification, (5 g, 86.2%) m.p 52-53 °C.

Anal:

TLC : 0.65 (benzene)

IR (KBr) : 1738, 1687, 1604, 1469, 1203, 1093, 788 and 747 cm^{-1}

2-Acetyl-1-(4-methylbenzoyloxy)-4-methoxybenzene (46p)

$POCl_3$ (6 ml) was added slowly to a cold mixture of 2-hydroxy-5-methoxy acetophenone **(45b)** (5 g, 0.03 mol) and 4-methylbenzoic acid (4.1g, 0.03 mol) in pyridine (30 ml). The reaction mixture was stirred for 3 hours at room temperature. The workup of the reaction mixture was similar to that described for the compound **(46a)**. The solid compound **(46p)** obtained was used in the next step without further purification, (5.2 g, 60.8%).

Anal:

TLC : 0.52 (benzene)

IR (KBr) : 1724, 1683, 1199, 1070, 964, 850, and 769 cm^{-1}

2-Acetyl-1-(4-chlorobenzoyloxy)-4-methoxybenzene (46q)

To a cold mixture of 2-hydroxy-5-methoxyacetophenone **(45b)** (3.0 g, 0.018mol) and 4-chlorobenzoic acid (2.82 g, 0.018 mol) in pyridine (20 ml), $POCl_3$ (5 ml)

was added slowly. The reaction mixture was stirred at room temperature for 3 hrs and poured into crushed ice-Con. HCl mixture. The precipitated solid was filtered, washed with excess of water and dried to obtain the compound **(46q)**. Compound **(46q)** was used in the next step without further purification, (4.2 g, 76.3%).

Anal:

TLC : 0.76 (benzene)

IR (KBr) : 1726, 1699, 1593, 1274, 1205, 1093, 846 and 750 cm^{-1}

2-Acetyl-1-(3-chlorobenzoyloxy)-4-methoxybenzene (46r)

In synthesis of **46q**, 4-chlorobenzoic acid was substituted by 3-chlorobenzoic acid to afford the compound **(46r)**, (4 g, 72.7%).

Anal:

TLC : 0.53 (benzene)

IR (KBr) : 1737, 1683, 1255, 1038, 842, and 769 cm^{-1}

2-Acetyl-1-(4-methoxybenzoyloxy)-4-methoxybenzene (46s)

$POCl_3$ (6 ml) was added slowly to a cold mixture of 2-hydroxy-5-methoxy acetophenone **(45b)** (3.5 g, 0.021 mol) and 4-methoxybenzoic acid (3.2 g, 0.021 mol) in pyridine (20 ml). The reaction mixture was stirred for 3 hours at room temperature. The workup of the reaction mixture was similar to that described for compound **(46a)**. The solid compound **(46s)** obtained was used in the next step without further purification, (1.8 g, 28.48%) m.p. 95-96 °C.

Anal:

TLC : 0.54 (chloroform)

IR (KBr) : 1735, 1681, 1604, 1186, 1053, 850, and 761 cm^{-1}

4.1B.3 Synthesis of 1,3-substituted diphenyl-1,3-propanedione derivatives (47a-s)

1-(2-Hydroxyphenyl)-3-phenyl-1,3-propanedione (47a)

2-Acetyl-1-benzoyloxybenzene **(46a)** (6 g) was dissolved in 25 ml of pyridine and heated to 50 °C. To the warm solution finely powdered potassium hydroxide (1 g) was added in small portions over a period of 10 min. and stirring was continued for an additional 30 min at room temperature. 30 ml of 10% acetic acid in water was added to the reaction mixture. The precipitate formed was filtered, washed and dried. Recrystallization from methanol afforded **(47a)**, (5.2 g, 86.7%) m.p. 115-17 °C (117-20 °C)[206].

Anal:

TLC : 0.83 (benzene)

IR (KBr) : 1614, 1454, 1273, 1161, 1018, 815 and 750 cm^{-1}

1-(2-Hydroxyphenyl)-3-(4-methylphenyl)-1,3-propanedione (47b)

Finely powdered potassium hydroxide (1 g) was added in portions to the warm solution of 2-acetyl-1-(4-methylbenzoyloxy)benzene **(46b)** (3 g) in pyridine (25 ml). The reaction mixture was stirred at room temperature for 30 min. The workup of the reaction mixture was similar to that described for compound **(47a)**, wherein a yellow solid compound **(47b)** was obtained. The solid compound **(47b)** obtained was used in the next step without further purification, (2.3 g, 76.6%) m.p. 109-11 °C.

Anal:

TLC : 0.85 (benzene)

IR (KBr) : 1616, 1579, 1487, 1299, 1182, 1031, 800 and 750 cm^{-1}

1-(2-Hydroxyphenyl)-3-(3-methylphenyl)-1,3-propanedione (47c)

To a warm mixture of 2-acetyl-1-(3-methylbenzoyloxy)benzene **(46c)** (4 g) in pyridine (1 g) powdered potassium hydroxide was added in portions and the reaction mixture was stirred at room temperature for 30 min. The reaction

mixture was worked up in a similar manner as described for the compound **(47a)** to afford **(47c)**, (3.3 g, 82.5%).

Anal:

TLC : 0.8 (benzene)

IR (KBr) : 1612, 1488, 1299, 1047, 900 and 750 cm^{-1}

1-(2-Hydroxyphenyl)-3-(4-methoxyphenyl)-1,3-propanedione (47d)

2-Acetyl-1-(4-methoxybenzoyloxy)benzene **(46d)** (5 g) was dissolved in 25 ml of pyridine and heated to 50 °C. To the warm solution finely powdered potassium hydroxide (1.5 g) was added in small portions over a period of 10 min. and stirring was continued for an additional 30 min at room temperature. The workup of the reaction mixture was similar to that described for the compound **(47a)** to afford a yellow solid compound **(47d)**. The solid compound **(47d)** obtained was used in the next step without further purification, (4.1 g, 82%), m.p. 111-13 °C.

Anal:

TLC : 0.85 (benzene)

IR (KBr) : 1616, 1508, 1242, 1176, 1035, 839 and 750 cm^{-1}

1-(2-Hydroxyphenyl)-3-(3-methoxyphenyl)-1,3-propanedione (47e)

Finely powdered potassium hydroxide (2 g) was added in portions to a warm solution of 2-acetyl-1-(3-methoxybenzoyloxy)benzene **(46e)** (8 g) in pyridine (40 ml). The reaction mixture was stirred at room temperature for 30 min. The workup of the reaction mixture was similar to that described for the compound **(47a)**. The yellow solid compound **(47e)** obtained was used in the next step without further purification, (6.2 g, 77.5%).

Anal:

TLC : 0.9 (benzene)

IR (KBr) : 1621, 1500, 1236, 1154, 1035, 848 and 750 cm^{-1}

1-(2-Hydroxyphenyl)-3-(3,4-dimethoxyphenyl)-1,3-propanedione (47f)

To a mixture of 2-acetyl-1-(3,4-dimethoxybenzoyloxy)benzene **(46f)** (3.5 g) in pyridine (20 ml) powdered potassium hydroxide (1 g) was added in portions and the reaction mixture was stirred at room temperature for 30 min. The reaction mixture was worked up in a similar manner as described for the compound **(47a)** to afford (**47f**), (2 g, 57.1%).

Anal:

TLC : 0.67 (benzene)

IR (KBr) : 3400, 1604, 1517, 1199, 1018, 887 and 750 cm^{-1}

1-(2-Hydroxyphenyl)-3-(4-chlorophenyl)-1,3-propanedione (47g)

2-Acetyl-1-(4-chlorobenzoyloxy)benzene **(46g)** (4 g) was dissolved in 25 ml of pyridine and heated to 50 °C. To the warm solution finely powdered potassium hydroxide (1 g) was added in small portions over a period of 10 min. and stirring was continued for an additional 30 min at room temperature. The workup of the reaction mixture was on similar lines to compound **(47a)**. The yellow solid obtained **(47g)** was used in the next step without further purification, (3.9 g, 97.5%).

Anal:

TLC : 0.8 (benzene)

IR (KBr) : 3436, 1625, 1583, 1201, 1163, 842 and 734 cm^{-1}

1-(2-Hydroxyphenyl)-3-(3-chlorophenyl)-1,3-propanedione (47h)

Finely powdered potassium hydroxide (1 g) was added in portions to a warm solution of 2-acetyl-1-(3-chlorobenzoyloxy)benzene **(46h)** (6 g) in pyridine (30 ml). The reaction mixture was stirred at room for 30 min. The workup of the reaction mixture was similar to that described for the compound **(47a)**. The yellow solid compound **(47h)** obtained was used in the next step without further purification, (5.1 g, 85%) m.p. 116-18 °C.

Anal:

TLC : 0.8 (benzene)

IR (KBr) : 3419, 1618, 1581, 1232, 1046, 792 and 740 cm^{-1}

1-(2-Hydroxyphenyl)-3-(2-chlorophenyl)-1,3-propanedione (47i)

To a mixture of 2-acetyl-1-(2-chlorobenzoyloxy)benzene **(46i)** (8.2 g) in pyridine (30 ml) powdered potassium hydroxide (2 g) was added in portions and the reaction mixture was stirred at room temperature for 30 min. The reaction mixture was worked up in a similar manner as described for the compound **(47a)** to afford **(47i)**, (6.6 g, 80.4%).

Anal:

TLC : 0.61 (benzene)

IR (KBr) : 3421, 1608, 1560, 1252, 1026, 860 and 768 cm^{-1}

1-(2-Hydroxyphenyl)-3-(2,4-dichlorophenyl)-1,3-propanedione (47j)

2-Acetyl-1-(2,4-dichlorobenzoyloxy)benzene **(46j)** (11 g) was dissolved in 40 ml of pyridine and heated to 50 °C. To the warm solution finely powdered potassium hydroxide (3 g) was added in small portions over a period of 10 min. and stirring was continued for an additional 30 min at room temperature. The workup of the reaction mixture was similar to that described for the compound **(47a)** which afforded a yellow solid compound **(47j)**. The solid compound **(47j)** was used in the next step without further purification, (9.8 g, 89%).

Anal:

TLC : 0.74 ($CHCl_3$)

IR (KBr) : 1620, 1488, 1197, 1020, 873 and 763 cm^{-1}

1-(2-Hydroxyphenyl)-3-(4-bromophenyl)-1,3-propanedione (47k)

Finely powdered potassium hydroxide (1.5 g) was added in portions to the warm solution of 2-acetyl-1-(4-bromobenzoyloxy)benzene **(46k)** (7.4 g) in pyridine (30 ml). The reaction mixture was stirred at room for 30 min. The workup of the reaction mixture was similar to that described for the compound

(47a). The solid compound **(47k)** was used in the next step without further purification, (6.5 g, 87.8%) m.p. 134-36 °C.

Anal:

TLC : 0.74 ($CHCl_3$)

IR (KBr) : 1614, 1488, 1239, 1026, 894, 800 and 750 cm^{-1}

1-(2-Hydroxyphenyl)-3-(4-fluorophenyl)-1,3-propanedione (47l)

To a mixture of 2-acetyl-1-(4-fluorobenzoyloxy)benzene **(46l)** (8.1 g) in pyridine (30 ml) powdered potassium hydroxide (1.5 g) was added in portions and the reaction mixture was stirred at room temperature for 30 min. The reaction mixture was worked up in a similar manner as described for the compound **(47a)** to afford (47l), (7.8 g, 96.2%).

Anal:

TLC : 0.8 (benzene)

IR (KBr) : 3436, 1625, 1490, 1201, 1163, 842 and 734 cm^{-1}

1-(2-Hydroxyphenyl)-3-(2-furyl)-1,3-propanedione (47m)

2-Acetyl-1-(2-furoyloxy)benzene **(46m)** (6.5 g) was dissolved in 30 ml of pyridine and heated to 50 °C. To the warm solution finely powdered potassium hydroxide (1.5 g) was added in small portions over a period of 10 min. and stirring was continued for an additional 30 min at room temperature. The workup of the reaction mixture was on similar lines as described for the compound **(47a)**. The solid compound **(47m)** obtained was used in the next step without further purification, (5.5 g, 84.6%) m.p. 79-81 °C (82 °C)[213].

Anal:

TLC : 0.75 (benzene)

IR (KBr) : 3423, 1616, 1541, 1200, 1012, 883 and 750 cm^{-1}

1-(2-Hydroxyphenyl)-3-(2-thienyl)-1,3-propanedione (47n)

Finely powdered potassium hydroxide (2 g) was added in portions to the warm solution of 2-acetyl-1-(2-thienoyloxy)benzene **(46n)** (9 g) in pyridine (40 ml). The

reaction mixture was stirred at room for 30 min. The workup of the reaction mixture was similar to that described for the compound **(47a)**. The solid compound **(47n)** obtained was used in the next step without further purification, (7.2 g, 80%).

Anal:

TLC : 0.84 (benzene)

IR (KBr) : 1620, 1507, 1241, 1075, 817 and 778 cm^{-1}

1-(2-Hydroxy-5-methoxyphenyl)-3-phenyl-1,3-propanedione (47o)

To a mixture of 2-acetyl-1-benzoyloxy-4-methoxybenzene **(46o)** (5 g) in pyridine (25 ml) powdered potassium hydroxide (1 g) was added in portions and the reaction mixture was stirred at room temperature for 40 min. The reaction mixture was worked up in a similar manner as described for the compound **(47a)** to afford (**47o**), (4.3 g, 86%), m. p. 80-82 °C.

Anal:

TLC : 0.85 ($CHCl_3$)

IR (KBr) : 3423, 1627, 1186, 1033, 823 and 780 cm^{-1}

1-(2-Hydroxy-5-methoxyphenyl)-3-(4-methylphenyl)-1,3-propanedione (47p)

2-Acetyl-1-(4-methylbenzoyloxy)-4-methoxybenzene **(46p)** (6 g) was dissolved in 25.0 ml of pyridine and heated to 50 °C. To the warm solution finely powdered potassium hydroxide (1.5 g) was added in small portions over a period of 10 min. and stirring was continued for an additional 30 min at room temperature. The workup of the reaction mixture was on similar lines as described for the compound **(47a)** and afforded a yellow solid compound **(47p)**. The solid compound **(47p)** obtained was used in the next step without further purification, (4.8 g, 80%).

Anal:

TLC : 0.75 (benzene)

IR (KBr) : 1614, 1506, 1186, 1043, 833 and 750 cm^{-1}

1-(2-Hydroxy-5-methoxyphenyl)-3-(4-chlorophenyl)-1,3-propanedione (47q)

Finely powdered potassium hydroxide (1 g) was added in portions to a warm solution of 2-acetyl-1-(4-chlorobenzoyloxy)-4-methoxybenzene **(46q)** (2.5 g) in pyridine (20 ml). The reaction mixture was stirred at room for 40 min. The workup of the reaction mixture was similar to that described for the compound **(47a)** and afforded a yellow solid compound **(47q)**. The solid compound **(47q)** obtained was used in the next step without further purification, (2 g, 80%).

Anal:

TLC : 0.8 ($CHCl_3$)

IR (KBr) : 3450, 1608, 1488, 1203, 1035, 819 and 794 cm^{-1}

1-(2-Hydroxy-5-methoxyphenyl)-3-(3-chlorophenyl)-1,3-propanedione (47r)

2-Acetyl-1-(3-chlorobenzoyloxy)-4-methoxybenzene **(46r)** (3 g) was dissolved in 25.0 ml of pyridine and heated to 50 °C. To the warm solution finely powdered potassium hydroxide (1.5 g) was added in small portions over a period of 10 min. and stirring was continued for an additional 30 min at room temperature. The workup of the reaction mixture was as similar described for compound **(47a)** to afford a yellow solid compound **(47r)**. The solid compound **(47r)** was used in the next step without further purification, (2.5 g, 83.3%).

Anal:

TLC : 0.75 (benzene)

IR (KBr) : 1617, 1500, 1255, 1186, 1043, 833 and 750 cm^{-1}

1-(2-Hydroxy-5-methoxyphenyl)-3-(4-methoxyphenyl)-1,3-propanedione (47s)

To a mixture of 2-acetyl-1-(4-methoxybenzoyloxy)-4-methoxybenzene **(46s)** (1.5 g) in pyridine (20 ml) powdered potassium hydroxide (1 g) was added in portions and the reaction mixture was stirred at room temperature for 40 min. The reaction mixture was worked up by similar manner as described for the compound **(47a)** to afford **(47r)**, (1 g, 66.6%).

Anal:

TLC : 0.82 (benzene)

IR (KBr) : 1612, 1500, 1252, 1026, 860 and 768 cm^{-1}

4.1B.4 Synthesis of 2-(substituted phenyl)chromen-4-one derivatives (48a-r)

2-Phenyl-chromen-4-one (48a)

Con. H_2SO_4 (1 ml) was added to a suspension of 1-(2-hydroxyphenyl)-3-phenyl-1,3-propanedione **(47a)** (3 g) in 25 ml of glacial acetic acid and refluxed for 2 hrs. The reaction mixture was poured into crushed ice; the precipitated solid was filtered and washed with excess of water. Recrystallization from methanol afforded **(48a)**, (2.6 g, 93.5%) m.p. 98-100 °C (95-97 °C)[206].

Anal:

TLC : 0.34 ($CHCl_3$)

IR (KBr) : 1645, 1569, 1464, 1376, 1128, 900 and 770 cm^{-1}

2-(4-Methylphenyl)chromen-4-one (48b)

To a mixture of 1-(2-hydroxyphenyl)-3-(4-methylphenyl)-1,3-propanedione **(47b)** (2 g) in glacial acetic acid (20 ml), Con. sulphuric acid (1ml) was added and refluxed for 2 hrs. The remaining experimental procedure is same as described for compound **(48a).** Recrystallization from methanol afforded **(48b),** (1.6 g, 95.8%) m.p. 115-17 °C.

Anal:

TLC : 0.42 (benzene)

IR (KBr) : 1637, 1568, 1465, 1373, 1124, 825 and 750 cm^{-1}

2-(3-Methylphenyl)chromen-4-one (48c)

A mixture of 1-(2-hydroxyphenyl)-3-(3-methylphenyl)-1,3-propanedione **(47c)** (3.1 g) in glacial acetic acid (25 ml) and Con. sulphuric acid (1ml) was refluxed for 2 hrs. The reaction mixture was processed as described for the compound

(48a) followed by recrystallization from methanol to afford **(48c)**, (2 g, 69.4%), m.p. 110-12 °C.

Anal:

TLC : 0.38 (benzene)

IR (KBr) : 1637, 1569, 1487, 1367, 1224, 1051, 869 and 775 cm^{-1}

2-(4-Methoxyphenyl)chromen-4-one (48d)

Con. H_2SO_4 (1 ml) was added to a suspension of 1-(2-hydroxyphenyl)-3-(4-methoxyphenyl)-1,3-propanedione **(47d)** (4 g) in 30 ml of glacial acetic acid and refluxed for 2 hrs. The usual work up of the reaction mixture followed by recrystallization from methanol gave the compound **(48d)**, (3.5 g, 94.5%), m.p. 158-61 °C.

Anal:

TLC : 0.5 (benzene)

IR (KBr) : 1649, 1608, 1515, 1269, 1195, 1026, 825 and 767 cm^{-1}

2-(3-Methoxyphenyl)chromen-4-one (48e)

To a mixture of 1-(2-hydroxyphenyl)-3-(3-methoxyphenyl)-1,3-propanedione **(47e)** (6.2 g) in glacial acetic acid (30 ml)., Con. sulphuric acid (1 ml) was added and refluxed for 2 hrs. The remaining experimental procedure was same as described for the compound **(48a)**. Recrystallization from methanol afforded **(48e)**, (2.6 g, 45%), m.p. 134-36 °C.

Anal:

TLC : 0.43 ($CHCl_3$)

IR (KBr) : 1652, 1606, 1569, 1272, 1082, 1003, 873 and 769 cm^{-1}

2-(3,4-Dimethoxyphenyl)chromen-4-one (48f)

A mixture of 1-(2-hydroxyphenyl)-3-(3,4-dimethoxyphenyl)-1,3-propanedione **(47f)** (1.1 g) in glacial acetic acid (15 ml) and Con. sulphuric acid (0.5 ml) was refluxed for 2 hrs. The reaction mixture was processed as described for

compound **(48a)** followed by recrystallization from methanol to afford **(48f)**, (0.9 g, 87.37%), m.p. 145-47 °C.

Anal:

TLC : 0.63 ($CHCl_3$)

IR (KBr) : 1652, 1602, 1465, 1267, 1141, 1028, 875 and 756 cm^{-1}

2-(4-Chlorophenyl)chromen-4-one (48g)

Con. H_2SO_4 (1 ml) was added to a suspension of 1-(2-hydroxyphenyl)-3-(4-chlorophenyl)-1,3-propanedione **(47g)** (3.8 g) in 25 ml of glacial acetic acid and refluxed for 2 hrs. The usual work up of the reaction mixture followed by recrystallization from methanol gave the compound **(48g)**, (1.5 g, 42.3%), m.p. 188-90 °C.

Anal:

TLC : 0.5 (benzene)

IR (KBr) : 1662, 1606, 1407, 1375, 1050, 827 and 769 cm^{-1}

2-(3-Chlorophenyl)chromen-4-one (48h)

To a mixture of 1-(2-hydroxyphenyl)-3-(3-chlorophenyl)-1,3-propanedione **(47h)** (5 g) in glacial acetic acid (30 ml), Con. sulphuric acid (1 ml) was added and refluxed for 2 hrs. The remaining experimental procedure is same as described for compound **(48a)**. Recrystallization from methanol afforded **(48h)**, (4.3 g, 93.4%), m.p. 123-25 °C.

Anal:

TLC : 0.8 ($CHCl_3$)

IR (KBr) : 1641, 1565, 1373, 1261, 1047, 853 and 777 cm^{-1}

2-(2-Chlorophenyl)chromen-4-one (48i)

A mixture of 1-(2-hydroxyphenyl)-3-(2-chlorophenyl)-1,3-propanedione **(47i)** (6.5 g) in glacial acetic acid (30 ml) and Con. sulphuric acid (1 ml) was refluxed for 2 hrs. The reaction mixture was processed as described for compound **(48a)**

followed by recrystallization from methanol to afford **(48i)**, (4.5 g, 74%), m.p. 137-39 °C.

Anal:

TLC : 0.41 ($CHCl_3$)

IR (KBr) : 1652, 1604, 1467, 1369, 1126, 1031, 850 and 754 cm^{-1}

2-(2,4-Dichlorophenyl)chromen-4-one (48j)

Con. H_2SO_4 (2 ml) was added to a suspension of 1-(2-hydroxyphenyl)-3-(2,4-dichlorophenyl)-1,3-propanedione **(47j)** (9.7 g) in 40 ml of glacial acetic acid and refluxed for 2 hrs. The usual work up of the reaction mixture gave the compound **(48j)** and used in the next step without further purification, (8.1 g, 89%).

Anal:

TLC : 0.68 ($CHCl_3$)

IR (KBr) : 1650, 1606, 1469, 1365, 1110, 1035, 823 and 775 cm^{-1}

2-(4-Bromophenyl)chromen-4-one (48k)

To a mixture of 1-(2-hydroxyphenyl)-3-(4-bromophenyl)-1,3-propanedione **(47k)** (6 g) in glacial acetic acid (30 ml) , Con. sulphuric acid (1 ml) was added and refluxed for 2 hrs. The remaining experimental procedure is same as described for compound **(48a)**. Recrystallization from methanol to afford **(48k)**, (4.75 g, 84%), m.p. 162-64 °C.

Anal:

TLC : 0.65 ($CHCl_3$)

IR (KBr) : 1666, 1490, 1373, 1130, 1072, 906, 850 and 775 cm^{-1}

2-(4-Fluorophenyl)chromen-4-one (48l)

A mixture of 1-(2-hydroxyphenyl)-3-(4-fluorophenyl)-1,3-propanedione **(47l)** (7.7 g) in glacial acetic acid (40 ml) and Con. sulphuric acid (1 ml) was refluxed for 2 hrs. The reaction mixture was processed as described for the compound

(48a) which was followed by recrystallization from methanol to afford **(48l)**, (6 g, 83.8%), m.p. 145-48 °C.

Anal:

TLC : 0.51 ($CHCl_3$)

IR (KBr) : 1639, 1510, 1380, 1234, 1164, 1045, 908, 835 and 750 cm^{-1}

2-(2-Furyl)chromen-4-one (48m)

Con. H_2SO_4 (1 ml) was added to a suspension of 1-(2-hydroxyphenyl)-3-(2-furyl)-1,3-propanedione **(47m)** (5 g) in 30 ml of glacial acetic acid and refluxed for 2 hrs. The usual work up of the reaction mixture followed by recrystallization from methanol gave the compound **(48m)**, (4.3 g, 93.4%), m.p. 136-38 °C (137 °C)[213].

Anal:

TLC : 0.41 ($CHCl_3$)

IR (KBr) : 1662, 1458, 1240, 1127, 1008, 850 and 760 cm^{-1}

2-(2-Thienyl)chromen-4-one (48n)

To a mixture of 1-(2-hydroxyphenyl)-3-(2-thienyl)-1,3-propanedione **(47n)** (8 g) in glacial acetic acid (40 ml) Con. sulphuric acid (1 ml) was added and refluxed for 2 hrs. The remaining experimental procedure is same as described for compound **(48a)**. Recrystallization from methanol afforded **(48n)**, (6.8 g, 91.8%), m.p. 92-94 °C.

Anal:

TLC : 0.8 ($CHCl_3$)

IR (KBr) : 1639, 1566, 1255, 1126, 1031, 850 and 750 cm^{-1}

2-Phenyl-6-methoxy-chromen-4-one (48o)

A mixture of 1-(2-hydroxy-5-methoxyphenyl)-3-phenyl-1,3-propanedione **(47o)** (4 g) in glacial acetic acid (20 ml) and Con. sulphuric acid (1 ml) was refluxed for 2 hrs. The reaction mixture was processed as described for compound **(48a)**

followed by recrystallization from methanol to afford (**48o**), (3.34 g, 89.5%), m.p. 163-65 °C.

Anal:

TLC : 0.38 ($CHCl_3$)

IR (KBr) : 1641, 1487, 1205, 1126, 1076, 845 and 787 cm^{-1}

2-(4-Methylphenyl)-6-methoxy-chromen-4-one (48p)

Con. H_2SO_4 (1 ml) was added to a suspension of 1-(2-hydroxy-5-methoxyphenyl)-3-(4-methylphenyl)-1,3-propanedione (**47p**) (3 g) in 30 ml of glacial acetic acid and refluxed for 2 hrs. The usual work up of the reaction gave the compound (**48p**) which was used in the next step without further purification (2.1 g, 75%).

Anal:

TLC : 0.41 ($CHCl_3$)

IR (KBr) : 1647, 1514, 1363, 1267, 1195, 1026, 827 and 780 cm^{-1}

2-(4-Chlorophenyl)-6-methoxy-chromen-4-one (48q)

To a mixture of 1-(2-hydroxyphenyl)-3-(4-chlorophenyl)-1,3-propanedione (**47q**) (2 g) in glacial acetic acid (20 ml) Con. sulphuric acid (0.5 ml) was added and refluxed for 2 hrs. The remaining experimental procedure is same as described for compound (**48a**) which was followed by recrystallization from methanol to afford (**48q**), (1.2 g, 63.8%), m.p. 181-83 °C.

Anal:

TLC : 0.48 ($CHCl_3$)

IR (KBr) : 1635, 1485, 1249, 1080, 910 and 823 cm^{-1}

2-(3-Chlorophenyl)-6-methoxy-chromen-4-one (48r)

Con. H_2SO_4 (1 ml) was added to a suspension of 1-(2-hydroxy-5-methoxyphenyl)-3-(4-methylphenyl)-1,3-propanedione (**47r**) (2 g) in 30 ml of glacial acetic acid and refluxed for 2 hrs. The usual work up of the reaction gave

the compound **(48r)** and used in the next step without further purification, (1.3 g, 69.1%).

Anal:

TLC : 0.5 ($CHCl_3$)

IR (KBr) : 1642, 1505, 1344, 1257, 1080, 1026, 818 and 750 cm^{-1}

2-(4-Methoxyphenyl)-6-methoxy-chromen-4-one (48s)

A mixture of 1-(2-hydroxyphenyl)-3-(4-methoxyphenyl)-1,3-propanedione **(47s)** (1.5 g) in glacial acetic acid (20 ml) and Con. sulphuric acid (0.5 ml) was refluxed for 2 hrs. The reaction mixture was processed as described for the compound **(48a)** and followed by recrystallization from methanol to afford **(48s)**, (1.1 g, 78.5%), m.p. 193-96 °C.

Anal:

TLC : 0.5 (benzene)

IR (KBr) : 1647, 1487, 1363, 1267, 1195, 1026, 910 and 827 cm^{-1}

4.1B.5 Synthesis of 5,7-substituted diphenyl-1*H*-1,4-diazepine derivatives (49a-s)

5-(2-Hydroxyphenyl)-7-phenyl-2,3-dihydro-1*H*-1,4-diazepine (49a)

A mixture of 2-phenylchromen-4-one **(48a)** (1 g) and 70% aqueous ethylenediamine (20 ml) was refluxed for 1hr on an oil bath. After 2 hrs the reaction mixture was cooled and 25 ml of cold water was added to the cooled reaction mixture. The solid obtained was filtered, dried and recrystallized from methanol to afford **(49a)**, (0.55 g, 46.6%), m.p. 208-10 °C.

Anal:

TLC : 0.51 (50%MeOH in $CHCl_3$)

IR (KBr) : 3231, 3000, 1605, 1531, 1260, 1180 and 750 cm^{-1}

PMR : δ 3.65 (br, 2H, CH_2), 3.9 (br, 2H, CH_2), 5.71(s, 1H, CH), 8.35 (br, 1H, NH), 6.45-7.74 (m, 9H, ArH)

MS : m/z 264 (M^+)

5-(2-Hydroxyphenyl)-7-(4-methylphenyl)-2,3-dihydro-1*H*-1,4-diazepine (49b)

A suspension of 2-(4-methylphenyl)chromen-4-one **(48b)** (1 g) in 20 ml of 70% aqueous ethylenediamine was refluxed for 2 hrs on an oil bath. The rest of the experimental procedure was similar to that described compound **(49a)** which was followed by recrystallization from methanol to yield **(49b)**, (0.3 g, 25.6%), m.p. 235-37 °C.

Anal:

TLC : 0.51 (50%MeOH in $CHCl_3$)

IR (KBr) : 3176, 2916, 1595, 1510, 1321, 1255, 1150 and 742 cm^{-1}

PMR : δ 2.39 (s, 3H, CH_3), 3.72 (br, 2H, CH_2), 3.82 (br, 2H, CH_2), 5.8 (s, 1H, CH), 9.8 (br, 1H, NH), 6.53-7.62 (m, 8H, ArH)

5-(2-Hydroxyphenyl)-7-(3-methylphenyl)-2,3-dihydro-1*H*-1,4-diazepine (49c)

2-(3-methylphenyl)chromen-4-one **(48c)** (1.1g) was dissolved in 70% aqueous ethylenediamine (20 ml) and refluxed for 2 hrs on an oil bath. The work up of the reaction mixture was similar to that described for compound **(49a)**. Recrystallization from methanol yields **(49c)**, (0.65 g, 50.38%), m.p. 206-08 °C.

Anal:

TLC : 0.55 (50%MeOH in $CHCl_3$)

IR (KBr) : 3232, 3000, 1608, 1433, 1319, 1259, 1139 and 752 cm^{-1}

PMR : δ 2.45 (s, 3H, CH_3), 3.62 (br, 2H, CH_2), 3.9 (br, 2H, CH_2), 5.7 (s, 1H, CH), 8.27 (br, 1H, NH), 6.48-7.65 (m, 9H, ArH)

MS : m/z 279 (M+1)

5-(2-Hydroxyphenyl)-7-(4-methoxyphenyl)-2,3-dihydro-1*H*-1,4-diazepine (49d)

A mixture of 2-(4-methoxyphenyl)chromen-4-one **(48d)** (1g) and 20 ml of 70% aqueous ethylenediamine was refluxed for 2 hrs on an oil bath. After the usual experimental procedure followed by recrystallization from methanol **(49d),** (0.5 g, 42.7%), m.p. 228-30 °C, was obtained.

Anal:

TLC	: 0.46 (50%MeOH in $CHCl_3$)
IR (KBr)	: 3200, 3000, 1604, 1508, 1255, 1172, 1031 and 752 cm^{-1}
PMR	: δ 3.63 (br, 2H, CH_2), 3.88 (bs, 5H, CH_2 &OCH_3), 5.7 (s, 1H, CH), 8.25 (br, 1H, NH), 6.45-7.65 (m, 8H, ArH)
Cald for $C_{18}H_{18}N_2O_2$	: C, 73.45; H, 6.16; N, 9.52 %
Found	: C, 73.49; H, 6.13; N, 9.64 %

5-(2-Hydroxyphenyl)-7-(3-methoxyphenyl)-2,3-dihydro-1*H*-1,4-diazepine (49e)

A suspension of 2-(3-methoxyphenyl)chromen-4-one **(48e)** (1 g) in 20 ml of 70% aqueous ethylenediamine was refluxed for 2 hrs on an oil bath. The rest of the experimental procedure was similar to that described compound for **(49a).** Recrystallization from methanol yielded **(49e),** (0.3 g, 31%), m.p. 185-88 °C.

Anal:

TLC	: 0.35 (50%MeOH in $CHCl_3$)
IR (KBr)	: 3200, 2985, 1600, 1508, 1230, 1178, 1048 and 760 cm^{-1}
PMR	: δ 3.63 (br, 2H, CH_2), 3.9 (bs, 5H, CH_2 & OCH_3), 5.72 (s, 1H, CH), 8.25 (br, 1H, NH), 6.45-7.66 (m, 8H, ArH)
MS	: m/z 295 (M+1)

5-(2-Hydroxyphenyl)-7-(3,4-dimethoxyphenyl)-2,3-dihydro-1*H*-1,4-diazepine (49f)

2-(3,4-dimethoxyphenyl)chromen-4-one **(48f)** (0.6 g) was dissolved in 70% aqueous ethylenediamine (20 ml) and refluxed for 2 hrs on an oil bath. The

work up of the reaction mixture was similar to that described for compound **(49a)**. Recrystallization from methanol yielded **(49f)**, (0.23 g, 31%), m.p. 238-39 °C.

Anal:

TLC : 0.72 (50%MeOH in $CHCl_3$)

IR (KBr) : 3217, 2929, 1602, 1500, 1251, 1141, 1024, 837 and 750 cm^{-1}

PMR : δ 3.63 (br, 2H, CH_2), 3.9 (bs, 2H, CH_2), 3.88 (s, 3H, OCH_3), 5.73 (s, 1H, CH), 8.25 (br, 1H, NH), 6.5-7.6 (m, 7H, ArH)

5-(2-Hydroxyphenyl)-7-(4-chlorophenyl)-2,3-dihydro-1*H*-1,4-diazepine (49g)

A mixture of 2-(4-chlorophenyl)chromen-4-one **(48g)** (1 g) and 20 ml of 70% aqueous ethylenediamine was refluxed for 2 hrs on oil bath. After the usual experimental procedure followed by recrystallization from methanol the desired compound **(49g)**, (0.25 g, 21.5%), m.p. 243-45 °C, was obtained.

Anal:

TLC : 0.45 (50%MeOH in $CHCl_3$)

IR (KBr) : 3203, 3000, 1598, 1319, 1255, 1143, 1087, 850 and 756 cm^{-1}

PMR : δ 3.75 (br, 2H, CH_2), 3.85 (br, 2H, CH_2), 5.74 (s, 1H, CH), 7.74 (br, 1H, NH), 6.61-7.59 (m, 8H, ArH)

5-(2-Hydroxyphenyl)-7-(3-chlorophenyl)-2,3-dihydro-1*H*-1,4-diazepine (49h)

A suspension of 2-(3-chlorophenyl)chromen-4-one **(48h)** (1.1 g) in 20 ml of 70% aqueous ethylenediamine was refluxed for 2 hrs on an oil bath. The rest of the experimental procedure was similar to that described for compound **(49a)**. Recrystallization from methanol yielded **(49h)**, (0.65 g, 50.7%), m.p. 208-10 °C.

Anal:

TLC : 0.5 (50%MeOH in $CHCl_3$)

IR (KBr) : 3200, 2916, 1610, 1500, 1319, 1143, 1087, 862 and 775 cm^{-1}

PMR : δ 3.62 (br, 2H, CH_2), 3.92 (br, 2H, CH_2), 5.7 (s, 1H, CH), 8.28 (br, 1H, NH), 6.5-7.7 (m, 8H, ArH)

MS : m/z 298 (M^+)

5-(2-Hydroxyphenyl)-7-(2-chlorophenyl)-2,3-dihydro-1*H*-1,4-diazepine (49i)

2-(2-chlorophenyl)chromen-4-one **(48i)** (1 g) was dissolved in 70% aqueous ethylenediamine (20 ml) and refluxed for 2 hrs on an oil bath. The work up of the reaction mixture was similar to that described compound **(49a)**. Recrystallization from methanol yielded **(49i)**, (0.3 g, 25.9%), m.p. 210-12 °C.

Anal:

TLC : 0.8 (50%MeOH in $CHCl_3$)

IR (KBr) : 3232, 2916, 1598, 1506, 1321, 1263, 1141 and 754 cm^{-1}

PMR : δ 3.63 (br, 2H, CH_2), 4.0 (br, 2H, CH_2), 5.37 (s, 1H, CH), 8.3 (br, 1H, NH), 6.49-7.64 (m, 8H, ArH)

MS : m/z 298 (M^+)

5-(2-Hydroxyphenyl)-7-(2,4-dichlorophenyl)-2,3-dihydro-1*H*-1,4-diazepine (49j)

A mixture of 2-(2,4-dichlorophenyl)chromen-4-one **(48j)** (1 g) and 20 ml of 70% aqueous ethylenediamine was refluxed for 2hrs on an oil bath. After the usual experimental procedure followed by recrystallization from methanol **(49j)**, (0.46 g, 40.4%), m.p. 218-20 °C, was obtained.

Anal:

TLC : 0.4 (50%MeOH in $CHCl_3$)

IR (KBr) : 3087, 3000, 1598, 1506, 1321, 1263, 1141 and 754 cm^{-1}

PMR : δ 3.71 (br, 2H, CH_2), 3.97 (br, 2H, CH_2), 5.41 (s, 1H, CH), 7.54 (br, 1H, NH), 6.46-7.45 (m, 7H, ArH)

MS : m/z 333 (M^+)

5-(2-Hydroxyphenyl)-7-(4-bromophenyl)-2,3-dihydro-1*H*-1,4-diazepine (49k)

A suspension of 2-(4-bromophenyl)chromen-4-one **(48k)** (1.0 g) in 20 ml of 70% aqueous ethylenediamine was refluxed for 2 hrs on an oil bath. The rest of the experimental procedure was similar to that described for compound **(49a)**. Recrystallization from methanol yielded **(49k)**, (0.5 g, 54.5%), m.p. 252-56 °C.

Anal:

TLC	: 0.33 (50%MeOH in $CHCl_3$)
IR (KBr)	: 3064, 3000, 1635, 1492, 1330, 1089, 823 and 750 cm^{-1}
PMR	: δ 3.69 (br, 2H, CH_2), 3.89 (br, 2H, CH_2), 5.65 (s, 1H, CH), 8.11(br, 1H, NH), 6.46-7.54 (m, 8H, ArH)
MS	: m/z 345 (M+2)

5-(2-Hydroxyphenyl)-7-(4-fluorophenyl)-2,3-dihydro-1*H*-1,4-diazepine (49l)

2-(4-fluorophenyl)chromen-4-one **(48l)** (1.3 g) was dissolved in 70% aqueous ethylenediamine (20 ml) and refluxed for 2 hrs on an oil bath. The work up of the reaction mixture was similar to that described for compound **(49a)**. Recrystallization from methanol yielded **(49l)**, (0.4 g, 26.6%), m.p. 234-36 °C.

Anal:

TLC	: 0.52 (50%MeOH in $CHCl_3$)
IR (KBr)	: 3203, 3000, 1604, 1506, 1321, 1163, 850 and 750 cm^{-1}
PMR	: δ 3.65 (br, 2H, CH_2), 3.9 (br, 2H, CH_2), 5.68 (s, 1H, CH), 8.38 (br, 1H, NH), 6.5-7.8 (m, 8H, ArH)
MS	: m/z 282 (M^+)

5-(2-Hydroxyphenyl)-7-(2-furyl)-2,3-dihydro-1*H*-1,4-diazepine (49m)

A mixture of 2-(2-furyl)chromen-4-one **(48m)** (1.1 g) and 20 ml of 70% aqueous ethylenediamine was refluxed for 2 hrs on an oil bath. After the usual experimental procedure followed by recrystallization from methanol the desired compound **(49m)**, (0.6 g, 45.8%), m.p. 168-70 °C, was obtained.

Anal:

TLC : 0.31 (50%MeOH in $CHCl_3$)

IR (KBr) : 3286, 3000, 1608, 1508, 1332, 1150, 1020 and 750 cm^{-1}

PMR : δ 3.65 (br, 2H, CH_2), 3.9 (br, 2H, CH_2), 6.1 (s, 1H, CH), 8.28 (br, 1H, NH), 6.53-7.96 (m, 7H, ArH)

MS : m/z 254 (M^+)

5-(2-Hydroxyphenyl)-7-(2-thienyl)-2,3-dihydro-1*H*-1,4-diazepine (49n)

A suspension of 2-(2-thienyl)chromen-4-one **(48n)** (1.6 g) in 20 ml of 70% aqueous ethylenediamine was refluxed for 2 hrs on an oil bath. The rest of the experimental procedure was similar to that described for compound **(49a)**. Recrystallization from methanol yielded the desired compound **(49n)**, (1.1 g, 58.2%), m.p. 232-35 °C.

Anal:

TLC : 0.42 (50%MeOH in $CHCl_3$)

IR (KBr) : 3203, 3000, 1595, 1514, 1261, 1141, 840 and 750 cm^{-1}

PMR : δ 3.6 (br, 2H, CH_2), 3.9 (br, 2H, CH_2), 5.92 (s, 1H, CH), 8.3 (br, 1H, NH), 6.5-7.8 (m, 7H, ArH)

5-(2-Hydroxy-5-methoxyphenyl)-7-phenyl-2,3-dihydro-1*H*-1,4-diazepine (49o)

2-phenyl-6-methoxychromen-4-one **(48o)** (1 g) was dissolved in 70% aqueous ethylenediamine (20 ml) and refluxed for 2 hrs on an oil bath. The work up of the reaction mixture was similar to that described for compound **(49a)**. Recrystallization from methanol yielded **(49o)**, (0.6 g, 54.5%), m.p. 183 °C.

Anal:

TLC : 0.53 (50%MeOH in $CHCl_3$)

IR (KBr) : 3423, 3100, 1633, 1255, 1064, 823 and 744 cm^{-1}

PMR : δ 3.65 (br, 2H, CH_2), 3.8 (br, 2H, CH_2), 3.71 (s, 3H, OCH_3), 5.68 (s, 1H, CH), 7.57 (br, 1H, NH), 6.7-7.55 (m, 8H, ArH)

MS : m/z 295 (M+1)

5-(2-Hydroxy-5-methoxyphenyl)-7-(4-methylphenyl)-2,3-dihydro-1*H*-1,4-diazepine (49p)

A mixture of 2-(4-methylphenyl)-6-methoxychromen-4-one **(48p)** (0.5 g) and 20 ml of 70% aqueous ethylenediamine was refluxed for 2 hrs on an oil bath. After the usual experimental procedure followed by recrystallization from methanol the desired compound **(49p)**, (0.3 g, 52.6%), m.p. 194-96 °C, was obtained.

Anal:

TLC	: 0.45 (50%MeOH in $CHCl_3$)
IR (KBr)	: 3288, 3000, 1608, 1218, 1149, 1040, 831 and 776 cm^{-1}
PMR	: δ 2.38 (s, 3H, CH_3), 3.69 (br, 2H, CH_2), 3.78 (br, 2H, CH_2), 3.71(s, 3H, OCH_3), 5.68 (s, 1H, CH), 7.49 (br, 1H, NH), 6.75-7.47 (m, 7H, ArH)
MS	: m/z 309 (M+1)

5-(2-Hydroxy-5-methoxyphenyl)-7-(4-chlorophenyl)-2,3-dihydro-1*H*-1,4-diazepine (49q)

A suspension of 2-(4-chlorophenyl)-6-methoxychromene-4-one **(48q)** (1 g) in 20 ml of 70% aqueous ethylenediamine was refluxed for 2 hrs on an oil bath. The rest of the experimental procedure was similar to that described for compound **(49a)**. Recrystallization from methanol yielded the desired compound **(49q)**, (0.1 g, 18%), m.p. 187-89 °C.

Anal:

TLC	: 0.43 (50%MeOH in $CHCl_3$)
IR (KBr)	: 3299, 3000, 1595, 1494, 1271, 1153, 1095, 837 and 775 cm^{-1}
PMR	: δ 3.69 (br, 2H, CH_2), 3.92 (br, 2H, CH_2), 3.73 (s, 3H, OCH_3), 5.65 (s, 1H, CH), 7.87 (br, 1H, NH), 6.77-7.58 (m, 7H, ArH)

5-(2-Hydroxy-5-methoxyphenyl)-7-(3-chlorophenyl)-2,3-dihydro-1*H*-1,4-diazepine (49r)

2-(3-chlorophenyl)-6-methoxychromen-4-one **(48r)** (0.5 g) was dissolved in 70% aqueous ethylenediamine (20 ml) and refluxed for 2 hrs on an oil bath. The work up of the reaction mixture was similar to that described for compound **(49a)**. Recrystallization from methanol yielded **(49r)**, (0.24 g, 42.1%), m.p. 190-92 °C.

Anal:

TLC : 0.53 (50%MeOH in $CHCl_3$)

IR (KBr) : 3257, 3000, 1612, 1321, 1218, 1040, 850 and 750 cm^{-1}

5-(2-Hydroxy-5-methoxyphenyl)-7-(4-methoxyphenyl)-2,3-dihydro-1*H*-1,4-diazepine (49s)

A mixture of 2-(4-methoxyphenyl)-6-methoxychromen-4-one **(48s)** (0.32 g) and 20 ml of 70% aqueous ethylenediamine was refluxed for 2 hrs on oil bath. After the usual experimental procedure followed by recrystallization from methanol the desired compound **(49s)**, (0.1 g, 27.7%), m.p. 260 °C (dec), was obtained.

Anal:

TLC : 0. 52 (50%MeOH in $CHCl_3$)

IR (KBr) : 3222, 3000, 1604, 1257, 1143, 1033, 820 and 777 cm^{-1}

PMR : δ 3.66 (br, 2H, CH_2), 3.90 (br, 2H, CH_2), 3.72 (s, 6H, OCH_3), 5.69 (s, 1H, CH), 7.88 (br, 1H, NH), 6.75-7.47 (m, 7H, ArH)

MS : m/z 325 (M+1)

4.2 Biological studies

The compounds syntheiszed were screened for the following activities:

A. Antiproliferative activity

B. Antiplatelet activity

A. Antiproliferative activity

The results of the cytotoxic potencies of the synthesized compounds tested *in vitro* against five leukemic cell lines Jurkat, HL60-DS, Molt-3, NCEB-1 and K562 are summarized in **Table 4 and 5**. The synthesized compounds were dissolved in DMSO (5 µl of each compound at 10 µM final concentration) and dispensed into an assay plate using accustom built low volume 384-well head tool. The assay plates are then loaded with 45 µl of cells and allowed to incubate for 48 hours at 37 °C. Then, 5 µl of alamar blue reagent was added to the assay plate and incubated for 24 hours at 37 °C. Alamar blue reduction[196] was measured on CCD-based optical imaging reader.

For initial screening, 1% DMSO was utilized as the high control to represent maximum reduction of alamar blue from cellular metabolism. The cytotoxic agent staurosporine is utilized at 50 µM to represent minimal reduction of alamar blue as a result of total cellular killing. These controls are used to calculate Z' as a test of the functionality of the assay and to determine its range, robustness and reliability. For these cell lines, the controls gave a Z' factor of 0.598 or better and a good signal to noise ratio indicating a broad dynamic range making the study reliable in our initial screening.

B. Antiplatelet activity

Preparation of Platelet Rich Plasma (PRP) and Platelet Poor Plasma (PPP)

The blood was collected from healthy female Sprague-Dawley rats in tubes containing 4% trisodium citrate solution. Samples were centrifuged at 250g for 15 min to obtain (PRP. After separation of PRP, the samples were centrifuged at 1500g for 10 min to obtain PPP. PRP was diluted with PPP to a platelet count of 3×10^8 /ml.

Platelet aggregation study

Platelet aggregation was monitored by the turbidimetric method[201]. PRP (400 µl) was incubated at 37 °C for 1 minute with continuous stirring at 900 rpm and then stimulated with arachidonic acid solution (5 µl in ethanaol, 200 µM). The standard drug aspirin and diazepine derivatives **(44a-r)** and the vehicle (0.5% DMSO, 2 µl) were added to the PRP samples, 5 minutes before addition of aggregating agent. The change in optical density was monitored continuously every 30 seconds for 5 min at 560nm using microplate reader. The whole study was completed within 3 hours after blood withdrawal.

Calculation

Aggregation was recorded as change in light transmission and quantified as peak height (area under curve, (AUC)), in centimeters after 5 minutes of stimulation. Data are reported as percent of platelet aggregation with respect to samples stimulated in the presence of the same volume of solvent. Area under the aggregation curve (AUC) over 5 min was calculated using Graph pad software programmer. The results of the antiplatelet activity are presented in **Table 6** and 7. Percentage inhibition was calculated using the following formula:

% inhibition = AUC (control) - AUC (treatment)/ AUC (control) x100