Chapter 4

EXPERIMENTAL WORK

4

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The melting points were taken in open capillaries and are uncorrected. The UV spectra were recorded on a Shimadzu UV-1601 spectrophotometer. The IR spectra were recorded on a Shimadzu-8300 FTTR instrument using KBr pellet/neat samples. The PMR spectra (on Varian 300 MHz) were recorded for solutions in $CDCl_3$ (unless specified) and the chemical shifts are reported in parts per million (δ) relative to TMS as internal standard. TLC plates were prepared with silica gel G, activated at 110 °C for about one hour and the spots were located by exposure to iodine vapors. Anhydrous sodium sulphate was used as drying agent.

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 work carried out has been described under the following heads:

4.1.1 Syntheses of benzil derivatives **(D)** through benzoin condensation

4.1.2 Syntheses of benzil derivatives **(D)** through Friedel-Crafts acylation

4.1.3 Syntheses of substituted benzil dioximes

4.1.4 Syntheses of 3,4-diaryl-1,2,5-oxadiazoles

4.1.5 Syntheses of 3,4-diaryl-1,2,5-oxadiazole N-oxides

4.1.1 SYNTHESES OF BENZIL DERIVATIVES (D) THROUGH BENZOIN CONDENSATION

1. SYNTHESES OF BENZOIN DERIVATIVES

Benzoin (58)

A 100 ml round-bottomed flask was charged with a solution of sodium cyanide (5.0 g, 0.102 mol) in water (20 ml), benzaldehyde (50.0 g, 0.47 mol) and ethanol (95 %, 65 ml). The reaction mixture was refluxed for 1 h and poured onto crushed ice. The yellow solid mass so obtained was filtered, washed with cold water, dried and recrystallized from methanol to yield **(58),** (42.0 g, 84 %), m.p. 136-137 °C (137 °C)[204].

Anal.:

TLC : Rf 0.7 ($CHCl_3$: MeOH :: 9.5 : 0.5)

Anisoin (59)

To a solution of sodium cyanide (8.0 g, 0.163 mol) in water (25 ml), anisaldehyde (61.5 g, 0.452 mol) and ethanol (95 %, 90 ml) were added and the reaction mixture was refluxed for 3 h. Excess of ethanol was recovered and the residue poured onto ice-cold water (300 ml). The mixture was extracted with chloroform (4 x 75 ml), washed with water once, dried and excess chloroform recovered. The reaction mixture was subjected to steam distillation. Water was decanted and residue was recrystallized from methanol to yield **(59),** (25.1 g, 45.6 %), m.p. 112-14 °C (110-12 °C)[204].

Anal.:

TLC : Rf 0.83 ($CHCl_3$: MeOH :: 9 : 1)

UV max (MeOH) : 275 nm (log ϵ 4.39)

IR (KBr) : 3463, 1664, 1596, 1265 and 1024 cm^{-1}

2'-Chloro-4-methoxybenzoin (60)

To a solution of 2-chlorobenzaldehyde (7.0 g, 49.82 mmol) in aqueous ethanol (75ml, 50 % v/v) was added sodium cyanide (4.0 g, 81.63 mmol) and anisaldehyde (6.8 g, 50 mmol). The reaction mixture was refluxed for 2 h and the resulting suspension was poured onto crushed ice. The yellow solid mass was filtered, washed and dried. The product **(60)** was obtained by recrystallization from methanol (6.95 g, 50.4 %), m.p. 80-82 °C (84 °C)[205].

Anal.:

TLC	: Rf 0.66 (Benzene)
UV max (MeOH)	: 283 nm (log ∈ 4.05)
IR (KBr)	: 3477, 1666, 1601, 1225, 1086 and 1030 cm^{-1}

2'-Chloro-3, 4-dimethoxybenzoin (61)

To a solution of veratraldehyde (16.6 g, 10 mmol) and 2-chlorobenzaldehyde (14.0 g, 10 mmol) in aqueous ethanol (100 ml, 50 %) was added sodium cyanide (8.0 g, 0.16 mmol) and the reaction mixture was refluxed for two and half hours and diluted with ice-cold water. The yellow solid mass obtained was filtered, dried and recrystallized from methanol to give **(61),** (17.1g, 69.8 %), m.p. 138-40 °C (142 °C)[205].

Anal.:

TLC	: Rf 0.62 ($CHCl_3$: MeOH :: 9.5 : 0.5)
UV max (MeOH)	: 231 nm (log ∈ 4.07), 280 nm (log ∈ 3.93) and 310 nm (log ∈ 3.9)
IR (KBr)	: 3439, 1662, 1582, 1269, 1085 and 1027 cm^{-1}

2'-Chloro-4-dimethylaminobenzoin (62)

A solution of 4-dimethylaminobenzaldehyde (7.5 g, 50.33 mmol), 2-chloro benzaldehyde (7.5 g, 53.38 mmol) and sodium cyanide (2.0 g, 40.82 mmol) in alcohol (45 ml, 65 %) was refluxed for 1 h. Crushed ice was added into the above reaction mixture to obtain a yellow precipitate which was filtered, dried and recrystallized from methanol to afford compound **(62),** (6.65 g, 43 %), m.p. 172-74 °C (166 °C)[206].

Anal..

TLC	: Rf 0.5 ($CHCl_3$: MeOH ·: 9.5.0.5)
UV max (MeOH)	: 346 nm (log ∈ 4.48)
IR (KBr)	: 3444, 1651, 1588, 1379, 1300 and 1081 cm^{-1}

ATTEMPTED SYNTHESIS OF 3,4-DIMETHOXY-6-NITROBENZOIN

3,4-Dimethoxy-6-nitrobenzoin was tried to be synthesized by cross benzoin condensation reaction between 6-nitroveratraldehyde and benzaldehyde.

6-Nitroveratraldehyde

A 100 ml round-bottomed flask was charged with concentrated nitric acid (35 ml), cooled up to 15 °C and stirred. Veratraldehyde (7.0 g, 0.042 mol) was slowly added in small portions to the acid by maintaining the internal temperature at 18 to 22 °C. The mixture was stirred for half an hour after the addition of the last portion of the aldehyde and poured onto crushed ice. Yellow precipitate so obtained was filtered, washed with cold water, dried and recrystallized from methanol to give 6-nitro-veratraldehyde, (5.5 g, 61 %), m.p. 131-32 °C (132-34 °C)[224].

Anal.:

TLC	: Rf 0.85 ($CHCl_3$: MeOH :: 9.5:0.5)
IR (KBr)	: 1574, 1521, 1338, 1063, 877 and 793 cm^{-1}

3,4-Dimethoxy-6-nitrobenzoin

A reaction mixture containing benzaldehyde (0.5 g, 4.71 mmol), 6-nitroveratraldehyde (1 0 g, 4.73 mmol) and sodium cyanide (0.05 g) in ethanol (20 ml, 60 %) was refluxed for 3 h. Crushed ice was added to the reaction mixture and yellow precipitate so obtained was filtered, dried and recrystallized from methanol. The compound was identified to be benzoin **(58)**, (0.3 g, 60 %), m.p. 137 °C (137 °C)[204].

Anal.:

TLC : Rf 0.7 ($CHCl_3$: MeOH :: 9.5.0.5)

SYNTHESIS OF BENZOIN (58) AS DEPICTED IN SCHEME-5

Desoxybenzoin (63)

A solution of phenylacetic acid (10.0 g, 0.074 mol) and thionyl chloride (8 ml, 0.15 mol) in dry benzene (25 ml) was refluxed for 3 h under anhydrous condition. Excess of benzene and thionyl chloride was recovered under vacuum wherein a reddish brown colored, semisolid phenyl acetyl chloride was obtained. Anhydrous aluminium chloride (11.0 g, 0.083 mol) was dissolved in dry benzene (10 ml) and stirred well. Phenylacetyl chloride in dry benzene (5 ml) was added dropwise to this stirred solution at 10-15 °C. The reaction mixture was further stirred for half an hour at room temperature followed by refluxing on a steam bath for 1 h under anhydrous conditions. The reaction mixture was quenched with ice-cold water containing concentrated hydrochloride acid (40 ml) and extracted with chloroform (3 x 150 ml) successively. The combined organic layers were washed with sodium bicarbonate solution (20 %) twice and then with water. Excess of chloroform and benzene were recovered. The brown residue so obtained was dried, dissolved in methanol and decolorized by refluxing with activated charcoal (0.05 g) for 10 min. The filtrate on concentration afforded **(63)**, (9.3 g, 64.6 %), m.p. 53-55 ° C (56-58 °C)[207].

Anal.:

TLC	: Rf 0.64 (Benzene)
IR (KBr)	: 1685, 1498, 1448, 1338, 1218 and 993 cm^{-1}

2-Bromodesoxybenzoin (64)

Method A

Desoxybenzoin **(63)** (5.0 g, 0.026 mol) was dissolved in dry carbontetrachloride (100 ml) in a 250 ml stoppered conical flask. N-Bromosuccinimide (7.0 g, 0.039 mol) and a few drops of bromine solution were added to this mixture and flask was exposed to a 500 watt tungsten lamp for half an hour to initiate bromination. The reaction mixture was refluxed for 2 h under the influence of visible irradiation and then for 4 h in absence of light. After 2 h, succinimide started to float and deposited on the wall of the flask. The reaction mixture was left overnight. Succinimide was filtered and excess of carbontetrachloride recovered. The residue so obtained was recrystallized from petroleum ether to afford a mixture of **(64)** and **(65).** Both the products **(64),** (1.7 g, 24 %), m.p. 49-51 °C and **(65),** (2,8 g, 31 %), m.p. 101-03 °C could be isolated in a pure form during recrystallization.

2-Bromodesoxybenzoin (64)

Anal.:

TLC	: Rf 0.57 (Benzene : Pet. Ether :: 1 : 1)
UV max (MeOH)	: 250 nm (log ϵ 4.18)
IR (KBr)	: 1690, 1447, 1175, 704 and 694 cm^{-1}
PMR	: δ 6.41 (s, 1H), 8.00-8.02 (d, 2H) and 7.37-7.56 (d, 8H)

1-(4-Bromophenyl)-2-bromo-2-phenylethanone (65)

Anal.:

TLC	: Rf 0.7 (Benzene : Pet. Ether :: 1 : 1)
UV max (MeOH)	: 255 nm (log ∈ 4.17)
IR (KBr)	: 1689, 1444, 1219, 1007 and 710 cm^{-1}
PMR	: δ 7.27-7.48 (m, 6H), 7.66-7.69 (d, 2H) and 7.75-7.78 (d, 8H)

Method B

In a 250 ml stoppered conical flask provided with a dropping funnel with guard tube, desoxybenzoin **(63)** and dry carbontetrachloride (50 ml) were charged. The flask was exposed to the rays of a 500 watt tungsten lamp. Bromine in carbon tetrachloride (1.16 g, 15 ml) was added dropwise over a period of 45 min with efficient stirring. The reaction mixture was further stirred for 15 min and solid sodium metabisulphite was added in small portions to neutralize unreacted bromine. The reaction mixture was filtered and excess carbontetrachloride recovered. The residue so obtained was recrystallized from petroleum ether to give compound **(64),** (1.8 g, 64 %), m.p. 49-51 °C (51-52 °C)[208-209].

Benzoin (58)

A reaction mixture containing 2-bromodesoxybenzoin **(64)** (0.5 g, 1.82 mmol), potassium hydroxide (1.0 g) in water (2 ml) and methanol (10 ml) was refluxed for 3 h and poured onto crushed ice. The precipitate so obtained was filtered, dried and recrystallized from methanol to give **(58),** (0.05 g, 14.7 %), m.p. 135-136 °C (137 °C)[204].

Anal.:

TLC	: Rf 0.7 ($CHCl_3$: MeOH :: 9.5 : 0.5)

1. SYNTHESES OF BENZIL DERIVATIVES

Benzil (66)

Benzoin **(58)** (2.0 g, 10.64 mmol), ammonium nitrate (1.0 g, 12.5 mmol), copper acetate (0.02 g, 0.16 mmol) and aqueous acetic acid (10 ml, 80 % v/v) were placed in a 100 ml round-bottomed flask fitted with an air condenser. The reaction mixture was heated at reflux for 90 min with occasional shaking and poured onto ice-cold water (200ml). The yellow precipitate so obtained was filtered, dried and recrystallized from methanol to give **(66),** (1.8 g, 91 %), m.p. 94-96 °C (94-96 °C)[204].

Anal.:

TLC : Rf 0.7 (Benzene)

Anisil (67)

A reaction mixture containing anisoin **(59)** (2.0 g, 7.35 mmol), ammonium nitrate (0.94 g, 11.74 mmol), copper acetate (0.02 g, 0.16 mmol) and aqueous acetic acid (6.6 ml, 80 % v/v) were placed in a 100 ml round-bottomed flask fitted with an air condenser. The reaction mixture was heated at reflux for 90 min with occasional shaking and processed as per the procedure described for compound **(66)** following recrystallization from methanol to afford **(67),** (1.6 g, 80 %), m.p. 131-32 °C (132-33 °C)[225-226].

Anal.:

TLC : Rf 0.44 ($CHCl_3$)

UV max (MeOH) : 298 nm (log ϵ 4.42)

IR (KBr) : 1654, 1598, 1261, 1161 and 1016 cm^{-1}

1-(2-Chlorophenyl)-2-(4-methoxyphenyl)ethanedione (68)

A mixture containing 2'-chloro-4-methoxy benzoin **(60)** (5.0 g, 18.07 mmol), ammonium nitrate (2.5 g, 31.23 mmol) and copper acetate (0.05 g, 0.41 mmol) in aqueous acetic acid (50 ml, 80 % v/v) was refluxed for 90 min. The resulting reaction mixture was processed as per the procedure described in the preparation of **(66)** followed by recrystallization from methanol to afford the compound **(68),** (4.2 g, 84.7 %), m.p. 106-08 °C (104 °C)[205].

Anal.:

TLC	: Rf 0.86 ($CHCl_3$: MeOH :: 9:1)
UV max (MeOH)	: 298 nm (log ∈ 4.20) and 260 nm (log ∈ 4.07)
IR (KBr)	: 1673, 1662, 1597, 1256, 1176 and 1071 cm^{-1}

1-(2-Chlorophenyl)-2-(3, 4-dimethoxyphenyl)ethanedione (69)

2'-Chloro-3,4-dimethoxy benzoin **(61)** (5.0 g, 16.3 mmol) was reacted with ammonium nitrate (2.5 g, 31.23 mmol), and copper acetate (0.05 g, 0.41 mmol) in aqueous acetic acid (30 ml, 80% v/v) as described for compound **(66)** to yield compound **(69)** (4.25 g, 85.6 %), m.p. 118-20 °C (117 °C)[205].

Anal.:

TLC	: Rf 0.75 ($CHCl_3$: MeOH :: 9.5 : 0.5)
UV max (MeOH)	: 262 nm (log ∈ 3.96) and 282 nm (log ∈ 3.99)
IR (KBr)	: 1663, 1647, 1579, 1260 and 1016 cm^{-1}

1-(2-Chlorophenyl)-2-(4-dimethylaminophenyl)ethanedione (70)

A benzil derivative **(70)** was synthesized by reacting 2'-chloro-4-dimethylamino benzoin **(62)** (0.5 g, 1.73 mmol), ammonium nitrate (0.25 g, 3.12 mmol) and copper acetate (0.02 g, 0.16 mmol) in aqueous acetic acid (5 ml, 80 % v/v) by the procedure described for compound **(66).** The

work up followed by recrystallization from methanol yielded the compound **(70),** (0.35 g, 70.4 %), m.p. 152-55 °C.

Anal.:

TLC	: Rf 0.67 ($CHCl_3$: MeOH :: 9.5:0.5)
UV max (MeOH)	: 250 nm (log ∈ 3.95) and 363 nm (log ∈ 4.22)
IR (KBr)	: 1679, 1577, 1386, 1176, 1068 and 745 cm^{-1}

4.1.2 SYNTHESES OF BENZIL DERIVATIVES (D) THROUGH FRIEDEL–CRAFTS ACYLATION

1. SYNTHESES OF DESOXYBENZOIN DERIVATIVES

Synthesis of substituted arylacetic acids

Substituted arylacetic acids required for performing Friedel-Crafts acylation reaction as depicted in **Scheme-2** were synthesized by the following procedures.

4-Nitrophenylacetic acid (73)

Method A

Phenylacetic acid (10.0 g, 0.074 mol) was dissolved in glacial acetic acid (20 ml) and concentrated sulphuric acid (50 ml) with stirring. The mixed acid reagent containing concentrated sulphuric acid (14 ml) and concentrated nitric acid (12 ml) was added to the stirred solution maintained at -5 to 0 °C. After the addition was complete, the white pasty mass was stirred for half an hour at room temperature and then diluted with ice-cold water. The pasty mass was filtered, dried and recrystallized from water to afford the desired acid **(73),** (7.5 g, 56.4 %), m.p. 145-46 °C (151-52 °C)[211].

Anal.:

TLC	: Rf 0.5 [Benzene : $CHCl_3$ (1:1) + 2 drops of AcOH]

Method B

4-Nitrobenzyl cyanide **(72)** was prepared by the following method, which on acid hydrolysis gave 4-nitrophenylacetic acid **(73)**.

4-Nitrobenzyl cyanide (72)

A mixture of concentrated nitric acid (22 ml) with 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 **(71)** (14.7 ml, 0.126 mol) was run at such a rate (about 30 min) that the temperature remained at about 10 °C and did not rise above 20 °C. The solution was further stirred for 1 h at room temperature and then poured onto crushed ice. A pasty mass that slowly separated contained 4-nitrobenzyl cyanide **(72)** and the oily 2-nitrobenzyl cyanide. The mass was filtered under vacuum and pressed well to remove as much oil as possible. Recrystallization from methanol afforded white needles **(72)** (10 15 g, 49.9 %) mp 105–6 °C (105–6 °C)[210].

Anal.:

TLC : Rf 0.5 (Benzene)

4-Nitrophenylacetic acid (73)

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 was added into a round-bottomed flask containing 4-nitrobenzyl cyanide **(72)** (7.45 g, 0.046 mol) and the nitrile adhering to the walls of the flask was washed down with the remainder of acid. The mixture was boiled under reflux for 15 min and then diluted with an equal volume of ice-cold water. The resulting yellow solid mass was filtered, washed, decolorized and recrystallized from water to yield the acid **(73)**, (8.0 g, 96 %), m.p. 154-55 °C (151-52 °C)[211]

Anal.:

TLC	: Rf 0.5 [Benzene : $CHCl_3$ (1:1) + 2 drops of AcOH]
UV max (MeOH)	: 264 nm (log ∈ 3.81)
IR (KBr)	: 2900, 1700, 1511, 1347, 1252 and 709 cm^{-1}

4-Tolylacetic acid (74)

Method A

To a solution of 4-methylacetophenone (20 ml, 0.15 mol) in morpholine (18 ml, 0.2 mol) was added precipitated sulphur (8.0 g, 0.25 mol) and the reaction mixture was refluxed for 18 h. To this hot solution, warm methanol (10 ml) was added and refrigerated for 3 h to obtain a yellow crystalline thiomorpholide. It was filtered and washed with cold methanol. Thiomorpholide (22.0 g) was taken in a 250 ml round-bottomed flask and aqueous sodium hydroxide (150 ml, 20 %) was added to it. The mixture was refluxed for 18 h and poured onto crushed ice. The resulting mixture was extracted thrice with small portions of chloroform (2 x 15 ml) and the aqueous layer acidified to get off-white colored precipitate of 4-tolylacetic acid **(74)**. Recrystallization from methanol afforded the acid **(74)**, (17.0 g, 75.6 %), m.p. 90-92 °C (90-93 °C)[227].

Anal.:

TLC	: Rf 0.5 ($CHCl_3$: MeOH :: 9.5 : 0.5)
IR (KBr)	: 3000, 1701, 1517, 1409, 1240 and 1170 cm^{-1}

Method B

A reaction mixture containing 4-methylacetophenone (20 ml, 0.15 mol), precipitated sulphur (8.0 g, 0.25 mol), morpholine (18 ml, 0.2 mol) was refluxed for 18 h. To this hot solution, warm methanol (10 ml) was added and refrigerated for 3 h to obtain yellow crystalline thiomorpholide. It was filtered and washed with cold methanol. Thiomorpholide (20.0 g) was taken in a 250 ml round-bottomed flask. A Phase transfer catalyst

(PTC) (Triethylbenzylammonium chloride [TEBA]) (2.0 g), and aqueous sodium hydroxide (150 ml, 20 %) was added to it. The mixture was refluxed for 18 h. Work up of the reaction mixture by the procedure as described in **(Method A)** followed by recrystallization from methanol afforded the acid **(74),** (16 0 g, 71 %), m.p. 90-92 °C (90-93 °C)[227].

4-Fluorophenylacetic acid (75)

4-Fluorophenylacetic acid **(75)** was synthesized by the reaction of 4-fluoroacetophenone (5 ml, 36.5 mmol), precipitated sulphur (2.0 g, 62.38 mmol) and morpholine (4.5 ml, 49.66 mmol) followed by hydrolysis of thiomorpholide (2.5 g) using aqueous sodium hydroxide (35 ml, 50 %) as per the method described for compound **(74).** Recrystallization from water gave the compound **(75),** (2.0 g, 35.6 %), m.p. 85-86 °C (86 °C)[228].

Anal.:

TLC	: Rf 0.6 ($CHCl_3$: MeOH :: 9.5 : 0.5)
IR (KBr)	. 3054, 1700, 1515, 1408 and 1229 cm^{-1}

Biphenylacetic acid (76)

4-Phenylacetophenone was prepared by the following method, which was then subjected to Willgerodt reaction to afford **(76).**

4-Phenylacetophenone

A 100 ml two-necked round bottomed flask provided with a dropping funnel and a reflux condenser with guard tube was charged with biphenyl (1.0 g, 6.48 mmol), anhydrous aluminium chloride (1.9 g, 14.34 mmol) and anhydrous carbon disulphide (10 ml). The mixture was refluxed on a steam bath for 20 min Acetic anhydride (7 ml, 7.62 mmol) in carbon disulphide (5 ml) was added dropwise over a period of 15 min with efficient stirring at 10-15 °C. The reaction mixture was further refluxed for 1 h and poured onto crushed ice containing concentrated hydrochloric acid (10 ml) and the residual carbon disulphide removed by

air bubbling. The precipitate so obtained was filtered, dried and recrystallized from methanol to yield 4-phenylacetophenone, (0.85 g, 76.1 %), m.p. 118-20 °C (120-21°C)[229].

Anal.:

TLC : Rf 0.6 (Benzene : Pet. Ether :: 9 : 1)

IR (KBr) : 1680, 1603, 1264 and 765 cm^{-1}

Biphenylacetic acid (76)

A mixture containing 4-phenylacetophenone (1.0 g, 5.81 mmol) morpholine (5 ml) and precipitated sulphur (0.5 g, 15.5 mmol) was refluxed for 18 h. Warm methanol (5 ml) was added to the mixture and refrigerated overnight to obtain thiomorpholide. Thiomorpholide so obtained was filtered and washed with cold methanol. Hydrolysis of thiomorpholide using an aqueous sodium hydroxide (10 ml, 20 %) was performed as described under **(74).** The work up of the reaction mixture by the procedure as described for **(74)** yielded crude buff colored product which was purified by recrystallization from methanol to yield the acid **(76),** (0.7 g, 64.1 %), m.p. 158-60 °C (164-65 °C)[213].

Anal.:

TLC : Rf 0.5 [$CHCl_3$: MeOH (9.5:0.5) + 1 drop of acetic acid]

UV max (MeOH) : 252 nm (log∈ 4.46)

IR (KBr) : 3400, 1690, 1489, 1257 and 764 cm^{-1}

PMR : δ 3.70 (s, 2H) and 7.25-7.66 (m, 9H).

2-Naphthylacetic acid (80)

2-Acetylnaphthalene **(77)** required for synthesizing 2-naphthyl-acetic acid **(80)** was prepared as per the following procedure.

2-Acetylnaphthalene (77)

Naphthalene (20.0 g, 0.156 mol) and aluminium chloride (23.0 g, 0.173 mol) were dissolved in nitrobenzene. Acetyl chloride (12 ml) was added with efficient stirring at –5 to 0 °C over a period of 30 min. The reaction mixture was further stirred for 1 h at –5 to 0 °C and poured onto crushed ice. The mixture was extracted with successive amounts of chloroform (3 x 100 ml), washed with water and excess chloroform and nitrobenzene recovered. The residue so obtained was vacuum distilled to afford **(77),** (11.3 g, 42.5 %), 52-53 °C (52 °C)[215].

Anal.:

TLC	: Rf 0.7 (Benzene)
UV max (MeOH)	: 246 nm (log∈ 4.68)
IR (KBr)	. 1678, 1465, 1361, 1280, 1193 and 833 cm^{-1}

2-Naphthylacetic acid (80)

A reaction mixture containing 2-acetylnaphthalene **(77)** (10.0 g, 58 82 mmol), precipitated sulphur (2.8 g, 87.5 mmol) and morpholine (10.0 ml) were refluxed for 18 h. To this hot solution, warm methanol (10 ml) was added and refrigerated for 3 h to obtain thiomorpholide. Thiomorpholide so obtained was filtered, washed with cold methanol and refluxed with sodium hydroxide solution (50 ml, 40 %) for 18 h. The work up of the reaction mixture by the procedure as described for **(74)** yielded the crude product which was purified by recrystallization from benzene to yield the acid **(80),** (6.8 g, 61.93 %), m.p. 141-42 °C (142-43 °C)[212]

Anal.:

TLC	: Rf 0.55 (Benzene)
UV max (MeOH)	: 275 nm (log∈ 3.78)
IR (KBr)	. 3039, 1701, 1415, 1238 and 831 cm^{-1}

6-Methoxy-2-naphthylacetic acid (81)

For the preparation of 6-Methoxy-2-naphthylacetic acid **(81),** required Nerolin **(78)** and 2-Acetyl-6-methoxynaphthalene **(79)** were synthesized by the following procedures.

Nerolin (78)

2-Naphthol (2.0 g, 0.013 mol) was dissolved in aqueous sodium hydroxide (10 ml, 10 %). Dimethylsulphate (1.75 g, 0.013 mol) was added to the mixture at 10 °C with continuous stirring. The reaction mixture was heated at 70-80 °C for 1 h with efficient stirring and poured onto crushed ice. Precipitate so obtained was filtered, dried and recrystallized from methanol to give **(78),** (1.8 g, 82 %), 69-71 °C (72 °C)[216].

Anal.:

TLC	: Rf 0.8 (Benzene)
IR (KBr)	: 1631, 1571, 1507, 1258, 1016 and 838 cm^{-1}

2-Acetyl-6-methoxynaphthalene (79)

Anhydrous aluminium chloride (12.0 g, 0.09 mol) was dissolved in nitrobenzene (50 ml) and the mixture was cooled to 10 °C. Nerolin **(78)** (10.0 g, 0.063 mol) was added to it in small portions with stirring followed by acetyl chloride (5 ml) maintaining the temperature between 10-13 °C. The reaction mixture was further stirred for 2 h at 10-13 °C and left overnight at room temperature. The mixture was poured onto crushed ice containing concentrated hydrochloric acid (30 ml), extracted with successive amounts of chloroform (4 x 50 ml), washed with water and chloroform recovered. The resulting mixture was steam-distilled until free from nitrobenzene, water decanted and the solid residue so obtained was distilled under high vacuum and fraction boiling between 165-185 °C was collected. The yellow distillate so obtained was recrystallized from methanol to give **(79),** (6.55 g, 47.9 %), m.p. 104-05 °C (104-05 °C)[217].

Anal.:

TLC : Rf 0.69 (Benzene : Pet. Ether :: 1 : 1)

UV max (MeOH) : 241 nm (log ∈ 4.79)

IR (KBr) : 1675, 1622, 1387, 1257 and 1200 cm^{-1}

6-Methoxy-2-naphthylacetic acid (81)

A mixture of 2-acetyl-6-methoxynaphthalene (79) (5.0 g, 0.023 mol), precipitated sulphur (1.5 g, 0.047 mol) and morpholine (8 ml) was refluxed for 18 h. Warm methanol (5 ml) was added to this hot mixture and refrigerated overnight. Thiomorpholide so obtained was filtered, washed with cold methanol and refluxed with aqueous sodium hydroxide (25 ml, 50 %) for 18 h. The work up of the reaction mixture by the procedure as described for **(74)** yielded crude buff colored product which was recrystallized from methanol to yield **(81),** (2.4 g, 44.7 %), m.p. 172-73 °C (172-73 °C)[217].

Anal.:

TLC : Rf 0.74 ($CHCl_3$: MeOH :: 9.5 : 0.5)

UV max (MeOH) : 226 nm (log ∈ 4.39)

IR (KBr) : 2957, 1696, 1269, 1224 and 1028 cm^{-1}

PMR : δ 3.78 (s, 2H), 3.91 (s, 3H), 7.11 (s, 1H),
7.11-7.15 (d, 1H), 7.34-7.39 (d, 1H) and
7.66-7.73 (m, 3H)

Synthesis of substituted benzenes

Thioanisole

Thioanisole required for the preparation of compounds (**87, 89** and **90**) was prepared by the following methods.

Method A

A 100 ml round-bottomed flask was charged with thiophenol (1 ml, 8.47 mmol), potassium hydroxide (1.0 g, 17.86 mmol) and dimethyl formamide (5 ml). Dimethylsulphate (2 ml, 21.11 mmol) was added to this well-stirred solution at 0-5 °C and the reaction mixture was kept on stirring overnight at room temperature. Potassium hydroxide (2.0 g) was added to destroy the excess of DMS. The mixture was quenched with ice-cold water and extracted with chloroform (3 x 30 ml). The combined organic layers was washed with water, dried, filtered and concentrated by vacuum to yield thioanisole, (1.1 ml, 97.6 %), b.p. 188 °C.

Method B

To a mixture of thiophenol (5 ml, 42.37 mmol) and anhydrous potassium carbonate (8.0 g, 57.97 mmol) was added methyl iodide (4 ml, 64.68 mmol) at 10-15 °C with stirring. After the addition was complete, the reaction mixture was stirred at room temperature for 24 h. The solution was diluted with ice-cold water and extracted with chloroform (3 x 25 ml). The combined chloroform extract was washed with water and concentrated to give thioanisole, (5.5 ml, 97.7 %), b.p. 188 °C (188 °C) [230].

SYNTHESIS OF DESOXYBENZOIN DERIVATIVES

2-Phenyl-1-(4-tolyl)ethanone (82)

To a solution of phenylacetic acid (10.0 g, 0 074 mol) in dry benzene (25 ml) was added thionyl chloride (8 ml, 0.15 mol). The contents were refluxed for 3 h under anhydrous conditions. Excess of benzene and thionyl chloride was recovered under vacuum wherein a reddish brown colored, semisolid phenylacetyl chloride was obtained. Anhydrous aluminium chloride (11.0 g, 0.083 mol) was dissolved in dry toluene (10 ml) and stirred well. Phenylacetyl chloride in dry toluene (5 ml) was added dropwise to this stirred solution at 10-15 °C. The reaction mixture was further stirred for half an hour at room temperature followed by heating on a steam bath for 1 h under anhydrous conditions. The reaction mixture was quenched with ice-cold water containing concentrated hydrochloride acid (40 ml) and extracted with chloroform (3 x 150 ml) successively. The combined organic layers were washed with sodium bicarbonate solution (20 %) twice and then with water. Excess of chloroform was recovered and toluene steam distilled. Water was decanted and the brown residue so obtained was dried, dissolved in methanol and decolorized by refluxing with activated charcoal (0.05 g) for 10 min. The filtrate on concentration afforded **(82),** (9.7 g, 62.8 %), m.p. 99–101 °C.

Anal.:

TLC	: Rf 0.7 (Benzene)
UV max (MeOH)	: 252 nm (log ∈ 4.26)
IR (KBr)	· 1681, 1604, 1334, 1222 and 815 cm^{-1}

2-(4-Methoxyphenyl)-1-phenylethanone (83)

Phenylacetyl chloride obtained by reacting phenylacetic acid (10.0 g, 0.074 mol) with thionyl chloride (8 ml, 0.15 mol) in dry benzene (10 ml) was reacted with anhydrous aluminium chloride (11.0 g, 0.083 mol) and dry anisole (15 ml) as described for compound **(82).** The

work up of the reaction mixture and recrystallization from methanol gave a white solid **(83),** (10.5 g, 63.1%), m.p. 72-74 °C.

Anal.:

TLC	· Rf 0.56 (Benzene)
UV max (MeOH)	: 280 nm (log ∈ 4.08) and 279 nm (log ∈ 3.62)
IR (KBr)	: 1670, 1600, 1264, 1172 and 1029 cm^{-1}

2-(4-Chlorophenyl)-1-phenylethanone (84)

Phenylacetyl chloride was synthesized as per the procedure described in the preparation of the compound **(82)** by taking phenylacetic acid (10.0 g, 0.074 mol) as the starting material. Phenylacetyl chloride so obtained was then treated with anhydrous aluminium chloride (11.0 g, 0.083 mol) and dry chlorobenzene (15 ml) in a similar manner as described for the compound **(82).** The work up of the reaction mixture and recrystallization from methanol afforded the desired compound **(84),** (9.3 g, 54.8 %), m.p. 103-04 °C (104-05 °C)[218].

Anal:

TLC	: Rf. 0.8 (Benzene, 1 drop of AcOH)
UV max (MeOH)	: 250 nm (log ∈ 4.087)
IR (KBr)	: 1684, 1453, 1399, 1332, 992 and 819 cm^{-1}

2-(4-Fluorophenyl)-1-phenylethanone (85)

Phenylacetyl chloride was prepared as described for the compound **(82),** from phenylacetic acid (10.0 g, 0.074 mmol). The reaction of phenylacetyl chloride with anhydrous aluminium chloride (11.0 g, 0.083 mol) and dry fluorobenzene (20 ml) was then carried out in a similar manner as described for compound **(82).** The reaction mixture was extracted with dichloromethane (DCM) (3 x 150 ml) successively. The

combined DCM extracts was washed twice with sodium bicarbonate solution (10 %), and with water and dried. Excess of DCM and fluorobenzene was recovered by fractional distillation. The residue so obtained was dissolved in methanol, decolorized and recrystallized from methanol to afford **(85),** (10.6 g, 67.3 %), m.p. 82-83 °C.

Anal.:

TLC	: Rf. 0.8 (Benzene)
UV max (MeOH)	: 244 nm (log ∈ 4.14)
IR (KBr)	: 1684, 1599, 1452, 1332 and 828 cm^{-1}

2-(4-Bromophenyl)-1-phenylethanone (86)

Phenylacetic acid (10.0 g, 0.072 mol) was converted to the corresponding acetyl chloride by the procedure as described for the compound **(82).** The phenylacetyl chloride was reacted with anhydrous aluminium chloride (15.0 g, 0.113 mol) and dry bromobenzene (15 ml) in a similar manner as described for the compound **(82).** Recrystallization from methanol gave compound **(86)**, (10.5 g, 51.9 %), m.p. 102–04 °C (114-15 °C)[218].

Anal.:

TLC	: Rf 0.7 (Benzene: Pet. Ether :: 1 : 1)
UV max (MeOH)	: 258 nm (log ∈ 4.06)
IR(KBr)	: 1684, 1575, 1217, 990 and 703 cm^{-1}

2-(4-Methylthiophenyl)-1-phenylethanone (87)

Phenylacetic acid (5 0 g, 36.76 mmol) was reacted with thionyl chloride (4 ml, 74.94 mmol) by the procedure as described for compound **(82)** to afford semisolid phenylacetyl chloride. Anhydrous aluminum chloride (6.0 g, 45.28 mmol) was dissolved partially in carbon disulphide with mechanical stirring. Phenylacetyl chloride was added into this well-stirred solution slowly at 0 °C. Thioanisole (5 ml) in carbon disulphide

(5 ml) was added to this reaction mixture maintained at –10 °C and allowed to stir for 1 h at –5 to –10 °C. The mixture was quenched with ice-cold water containing concentrated hydrochloric acid (20 ml) and extracted with chloroform (3 x 100 ml). The combined organic extract was washed with sodium bicarbonate solution twice, followed by water, dried, filtered and concentrated. The residue so obtained was recrystallized from methanol to afford **(87),** (6.3 g, 70.8 %), m.p. 104-06°C.

Anal.:

TLC	: Rf 0.73 (Benzene)
UV max (MeOH)	308 nm (log∈ 4.36) and 230 nm (log∈ 3.94)
IR (KBr)	: 1680, 1586, 1395, 1333, 1088 and 813 cm^{-1}

2-(4-Nitrophenyl)-1-phenylethanone (88)

4-Nitrophenylacetyl chloride was prepared using two different reagents, thionyl chloride **(Method A)** and phosphorous trichloride **(Method B).**

Method A

4-Nitrophenylacetyl chloride was synthesized following the procedure as described for **(82),** taking 4-nitrophenylacetic acid **(73)** (1.0 g, 5.52 mmol) and thionyl chloride (1 ml, 18.73 mmol) in dry benzene (5 ml). 4-Nitrophenylacetyl chloride was then reacted with anhydrous aluminium chloride (1.1 g, 8.3 mmol) and dry benzene (10 ml) following the procedure as described for **(82).** The work up followed by recrystallization from methanol yielded the compound **(88),** (0.55 g, 41.3 %), m.p. 132-34 °C.

Method-B

4-Nitrophenylacetyl chloride was prepared by refluxing 4-nitrophenylacetic acid **(73)** (2.0 g, 11 05 mmol) with phosphorous trichloride (1 ml, 11.74 mmol) for 1 h. The solution was decanted from the

residue of phosphorous acid into a dropping funnel containing dry benzene (10 ml) and added slowly to a stirred solution of anhydrous aluminium chloride (2.0 g, 15.04 mmol) in dry benzene (10 ml) at 10-15 °C. The mixture was stirred for 30 min at room temperature, refluxed for 1 h. The reaction mixture was worked up in the usual manner. Recrystallization from methanol resulted in the desired ketone **(88),** (1.9 g, 71.2 %), m.p. 136-39 °C (140-44 °C)[231].

Anal.:

TLC	: Rf 0.63 (Benzene and 2 drops of AcOH)
UVmax (MeOH)	: 248 nm (log ∈ 4.29)
IR (KBr)	. 1686, 1514, 1352 and 1324 cm^{-1}

1-(4-Methylthiophenyl)-2-(4-tolyl)ethanone (89)

4-Methylphenylacetyl chloride was prepared from 4-methylphenyl-acetic acid **(74)** (3.0 g, 19.98 mmol) and thionyl chloride (4 ml, 74.94 mmol) by the method described for the compound **(82).** 4-Methylphenylacetyl chloride was treated with anhydrous aluminium chloride (4.0 g, 30.19 mmol) and thioanisole (1.5 ml) by the procedure as described for compound **(87).** Recrystallization from methanol gave the compound **(89),** (2.6 g, 50.8 %), m.p. 98-99 °C.

Anal :

TLC	: Rf 0.7 (Benzene)
UV max (MeOH)	: 308 nm (log ∈ 4.30)
IR (KBr)	: 1679, 1588, 1340, 1091 and 688 cm^{-1}

2-(4-Fluorophenyl)-1-(4-methylthiophenyl)ethanone (90)

4-Fluorophenylacetic acid **(75)** (1.0 g, 6.49 mmol) and phosphorous trichloride (1.0 ml, 10.92 mmol) were refluxed for 3 h to get 4-fluorophenylacetyl chloride, which was decanted by adding carbon disulphide. 4-Fluorophenylacetyl chloride was then reacted with

anhydrous aluminium chloride (1.0 g, 7.55 mmol) and thioanisole (0.5 ml) by the procedure described for compound **(87).** Recrystallization from methanol afforded the ketone **(90),** (0.3 g, 17.8 %), m.p. 136-38 °C.

Anal.:

TLC	: Rf 0.7 (Benzene)
UV max (MeOH)	: 308 nm (log ∈ 4.34)
IR (KBr)	: 1675, 1585, 1333, 1222, 1156 and 1091 cm^{-1}

2-(4-Chlorophenyl)-1-(4-tolyl)ethanone (91)

4-Chlorophenylacetyl chloride was synthesized by reacting 4-chlorophenylacetic acid (10.0 g, 0.059 mol) with thionyl chloride (7 ml, 0.131 mol) in dry benzene (20 ml) by the procedure described in a preparation of **(82).** The acetyl chloride so prepared was then treated with anhydrous aluminium chloride (15.0 g, 0.113 mol) and dry toluene (15 ml) in a similar manner as described for compound **(82).** The work up followed by recrystallization from methanol gave the compound **(91),** (11.4 g, 79.4 %), m.p. 112-14 °C.

Anal.:

TLC	: Rf 0.84 (Benzene)
UV max (MeOH)	: 254 nm (log ∈ 4.27)
IR (KBr)	: 1677, 1494, 1410, 1330, 1015 and 801 cm^{-1}

2-(4-Chlorophenyl)-1-(4-methoxyphenyl)ethanone (92)

4-Chlorophenylacetyl chloride, which was prepared from 4-chlorophenylacetic acid (10.0 g, 0.059 mol) was reacted with anhydrous aluminium trichloride (15.0 g, 0.113 mol) and dry anisole (15 ml) following the procedure described for **(82).** The work up of the reaction mixture and recrystallization from methanol yielded the ketone **(92),** (9.7 g, 63.5 %), m.p. 137-39 °C.

Anal.:

TLC : Rf 0.7 (Benzene)

UV max (MeOH) : 275 nm (log ∈ 4.29)

IR (KBr) : 1675, 1601, 1260, 1024 and 805 cm^{-1}

2-(4-Chlorophenyl)-1-(4-fluorophenyl)ethanone (93)

4-Chlorophenylacetyl chloride was prepared according to the procedure described for **(82)** from 4-chlorophenylacetic acid (10.0 g, 0.059 mol) and thionyl chloride (7 ml, 0.131 mol). 4-Chlorophenylacetyl chloride was then treated with anhydrous aluminium chloride (15.0 g, 0.113 mol) and dry fluorobenzene (15 ml) following the procedure described for **(82).** The work up followed by recrystallization from methanol afforded **(93),** (8.6 g, 59 %), m.p 122-24°C.

Anal.:

TLC : Rf 0.8 (Benzene)

UV max (MeOH) : 244 nm (log ∈ 4.18)

IR (KBr) : 1683, 1597, 1409, 1327, 1245 and 835 cm^{-1}

2-(2-Chlorophenyl)-1-phenylethanone (94)

2-Chlorophenylacetic acid (10.0 g, 0.0758 mol) was converted to the corresponding acetyl chloride by the procedure as described for the compound **(82).** 2-Chlorophenylacetyl chloride was reacted with anhydrous aluminium chloride (12.0 g, 0 09 mol) and dry benzene (15 ml) in a similar manner as described for the compound **(82).** Work up of the reaction mixture followed by recrystallization from methanol gave the ketone **(94),** (10.5 g, 77.6 %), m.p. 68-69 °C.

Anal.:

TLC : Rf 0.5 (Benzene: Pet. Ether :: 1 : 1)

UV max (MeOH) : 243 nm (log ∈ 3.54)

IR (KBr) : 1692, 1595, 1331, 1219, 1050 and 703 cm^{-1}

2-(2-Chlorophenyl)-1-(4-tolyl)ethanone (95)

2-Chlorophenylacetyl chloride was synthesized by reacting 2-chlorophenylacetic acid (10.0 g, 0.058 mol) with thionyl chloride (8 ml, 0.15 mol) in dry benzene (20 ml) by the procedure described in a preparation of **(82).** The acetyl chloride so prepared was then treated with anhydrous aluminium chloride (12.0 g, 0.09 mol) and dry toluene (10 ml) in a similar manner as described for compound **(82).** The workup followed by recrystallization from methanol gave the compound **(95),** (10.1 g, 70.4 %), m.p. 79-80 ^{o}C.

Anal.:

TLC	: Rf 0.6 (Benzene : Pet. Ether :: 1 : 1)
UV max (MeOH)	: 256 nm (log $\in$ 4.00)
IR (KBr)	: 1680, 1604, 1328, 1225, 1060 and 747 cm^{-1}

2-(1-Biphenyl)-1-phenylethanone (96)

Biphenylacetic acid **(76)** (1.0 g, 5.31 mmol) and thionyl chloride (1.5 ml, 28.1 mmol) was refluxed in benzene for 4 h to obtain biphenylacetyl chloride. Biphenylacetyl chloride was then reacted with anhydrous aluminium chloride (2 0 g, 15.0 mmol) and dry benzene (5 ml) by the method described for **(82).** The work up of the reaction mixture and recrystallization from methanol afforded the ketone **(96),** (1.0 g, 69.2 %), m.p. 157-58 °C.

Anal :

TLC	: Rf 0.53 (Benzene : Pet. Ether :: 1 : 1)
IR (KBr)	: 252 nm (log$\in$ 4.27)
UV max (MeOH)	: 1684, 1488, 1332, 1209 and 752 cm^{-1}

2-(1-Biphenyl)-1-(4-tolyl)ethanone (97)

4-Biphenylacetyl chloride was synthesized by reacting 4-biphenylacetic acid **(76)** (1.0 g, 5.31 mmol) with thionyl chloride (1.5 ml, 28.1 mmol) in dry benzene (5 ml) by the procedure described in preparation of **(82).** 4-Biphenylacetyl chloride was then treated with anhydrous aluminium chloride (2.0 g, 15 mol) and dry toluene (5 ml) in a similar manner as described for compound **(82).** The workup followed by recrystallization from methanol afforded the compound **(97),** (0.8 g, 52.6 %), m.p. 164-66 °C.

Anal.:

TLC	: Rf 0.76 (Benzene : Pet. Ether :: 1 : 1)
UV max (MeOH)	: 253 nm (log∈ 4.16)
IR (KBr)	: 1687, 1605, 1488, 1197 and 813 cm^{-1}

1-(6-Methoxy-2-naphthyl)-2-phenylethanone (98)

A reaction mixture containing phenylacetic acid (20.0 g, 0.147 mol) and phosphorous trichloride (12 ml, 0.14 mol) was refluxed for 2 h. Phenylacetyl chloride so obtained was decanted from the reaction mixture to a dropping funnel containing nitrobenzene (20 ml) and added to the stirred solution of anhydrous aluminium chloride (21.0 g, 0.13 mol), nerolin **(78)** (17.0 g, 0.1. mol) and nitrobenzene (100 ml) at 12-14 °C over a period of 1 h. The reaction mixture was further stirred for 3 h at room temperature. The work up was done following the procedure as described for compound **(82).** The residue so obtained was distilled under vacuum to afford compound **(98),** (8.0 g, 27 %), 111-13 °C.

Anal.:

TLC	: Rf 0.54 (Benzene)
UV max (MeOH)	: 242 nm (log∈ 4.82)
IR (KBr)	: 1681, 1624, 1483, 1225, 1031 and 738 cm^{-1}

2-(1-Naphthyl)-1-phenylethanone (99)

1-Naphthylacetic acid (2.0 g, 0.01 mol) was refluxed with thionyl chloride (3 ml, 0.04 mol) for 3 h to afford the corresponding acetyl chloride. 1-Naphthylacetyl chloride was reacted with aluminium chloride (3.5 g, 0.026 mol) and dry benzene (10 ml) in a similar manner as described for the compound **(82).** The reaction mixture was processed in the usual manner to afford a brownish residue. The residue was chromatographed over a column of silica gel G (100-200 mesh) and eluted with benzene to afford a pale yellow colored compound **(99),** (1.4 g, 52.9 %), m.p. 119-21 °C.

Anal.:

TLC	: Rf 0.6 (Benzene)
UV max (MeOH)	: 250 nm (log ∈ 4.54)
IR (KBr)	· 1712, 1490, 1263, 1016, 821 and 775 cm^{-1}

2-(2-Naphthyl)-1-phenylethanone (100)

2-Naphthylacetic acid **(80)** (2.0 g, 10.75 mmol) and thionyl chloride (3.0 ml, 40.6 mmol) was refluxed in benzene for 3 h to obtain 2-naphthylacetyl chloride 2-Naphthylacetyl chloride was then reacted with anhydrous aluminium chloride (3.5 g, 26.4 mmol) and dry benzene (10 ml) by the method described for **(82).** The work up of the reaction mixture and recrystallization from methanol afforded the ketone **(100),** (1.5 g, 56.8 %), m.p. 118-19 °C.

Anal.:

TLC	: Rf 0.82 (Benzene : Pet. Ether ·. 7 : 3)
IR (KBr)	: 223 nm (log ∈ 4.77)
UV max (MeOH)	: 1685, 1595, 1446, 1330, 1209 and 999 cm^{-1}

2. SYNTHESIS OF BENZIL DERIVATIVES

Attempted synthesis of benzil (66)

Method A

Compound **(58)** (0.5 g, 2.66 mmol) was dissolved in dioxane (3 ml) and water (1 ml). Selenium dioxide (1.0 g, 9.01 mmol) was added to it. The reaction mixture was refluxed for 4 h and poured on to crushed ice. The precipitate so obtained was filtered, dried and recrystallized from methanol. The product so obtained was characterized to be the benzoin **(58),** (0.3 g), 135-37 °C (137 °C)[204].

Anal.:

TLC . Rf 0.7 ($CHCl_3$: MeOH :: 9.5 : 0.5)

Method B

A reaction mixture containing the compound **(58)** (0.5 g, 2.66 mmol), selenium dioxide (1.0 g, 9.01 mmol) and acetic acid (5 ml) was refluxed for 12 h. The work up of the reaction mixture in the usual manner offered a solid mass. The compound so obtained was identified to be a mixture of benzoin **(58)** and benzil **(66).**

Anal.:

TLC : Rf 0.4 and 0.7 (Benzene)

Benzil (66)

A reaction mixture containing benzoin **(58)** (1.0 g, 5.32 mmol) and selenium dioxide (2.0 g, 18.02 mmol) in acetic anhydride (5 ml) was refluxed on an oil-bath for 8 h with continuous stirring. The reaction was monitored by TLC. The resulting hot reaction mixture was filtered to remove insoluble selenium and the filtrate poured onto crushed ice. The yellow solid mass so obtained was filtered, dried and recrystallized from methanol to give benzil **(66),** (0.9 g, 91 %) m.p. 94-96 °C (94-96 °C)[204].

Anal.:

TLC : 0.7 (Benzene)

1-Phenyl-2-(4-tolyl)ethanedione (101)

A reaction mixture containing 2-phenyl-1-(4-tolyl)ethanone **(82)** (1.0 g, 4.76 mmol) and selenium dioxide (2.0 g, 18.02 mmol) in acetic anhydride (5 ml) was refluxed on an oil-bath for 8 h with continuous stirring. The work up of the reaction mixture as described for compound **(66)** afforded the yellow sticky mass. It was extracted with chloroform (3 x 40) successively. The chloroform extract was washed with sodium bicarbonate (10 %) and water and the solvent recovered. The product **(101)** obtained was oily in nature and didn't crystallize from any solvent. The yield was (0.9 g, 84.4 %) m.p. 31 °C[232] up on purification on silica gel G (100-200 mesh) (Benzene).

Anal.:

TLC	: 0.68 (Benzene)
UV max (MeOH)	: 264 nm (log∈ 4.34)
IR (KBr)	: 1668, 1604, 1450, 1208 and 1174 cm^{-1}

1-(4-Methoxyphenyl)-2-phenylethanedione (102)

To a solution of 2-(4-methoxyphenyl)-1-phenylethanone **(83)** (5.0 g, 20.63 mmol) in acetic anhydride (10 ml), selenium dioxide (10.0 g, 90.12 mmol) was added. The reaction mixture was refluxed for 6 h on an oil-bath with continuous stirring. The reaction mixture was processed as per the procedure described for the compound **(66)** to obtain a yellow sticky residue (4.5 g, 90.73 %), which was utilized for the next step without further purification.

Anal :

TLC	: Rf 0.6 (Benzene)
UV max (MeOH)	· 293 nm (log∈ 4.14) and 256 nm (log∈ 4.01)
IR (KBr)	: 1675, 1651, 1597, 1270, 1166 and 1020 cm^{-1}

1-(4-Chlorophenyl)-2-phenylethanedione (103)

A reaction mixture containing 2-(4-chlorophenyl)-1-phenylethanone **(84)** (5.0 g, 21.68 mmol) and selenium dioxide (10 g, 90.12 mmol) in acetic anhydride (10 ml) was refluxed in an oil-bath for 6 h, with continuous vigorous stirring. The work up of the reaction mixture and recrystallization from methanol afforded the compound **(103)**, (2.8 g, 52.8 %), m.p. 72-73 °C (73 °C)[218].

Anal:

TLC	: Rf 0.6 (Benzene : Pet. Ether :: 1 : 1)
UV max (MeOH)	: 266 nm (log∈ 4.63)
IR (KBr)	: 1666, 1586, 1450, 1211 and 876 cm^{-1}

1-(4-Fluorophenyl)-2-phenylethanedione (104)

Compound **(104)** was prepared according to the method described for the compound **(66)** taking 1-(4-fluorophenyl)-2-phenylethanone **(85)** (3.0 g, 14 mmol) and selenium dioxide (6.0 g, 54.07 mmol). Recrystallization from petroleum ether gave the compound **(104),** (2.6 g, 81.4 %), m.p. 63-65 °C.

Anal :

TLC	: Rf 0 88 (Benzene)
UV max (MeOH)	: 260 nm (log∈ 4.31)
IR (KBr)	: 1668, 1600, 1505, 1239, 1207 and 1157 cm^{-1}

1-(4-Bromophenyl)-2-phenylethanedione (105)

A reaction mixture of 1-(4-bromophenyl)-2-phenylethanone **(86)** (5.0 g, 18.24 mmol) and selenium dioxide (10.0 g, 90.12 mmol) in acetic anhydride (10 ml) was refluxed for 6 h on an oil-bath with continuous vigorous stirring. The work up similar to that of compound **(66)** followed

by recrystallization from methanol afforded **(105),** (4.6 g, 87.6 %), m.p. 84-86 °C (86-87 °C)[218]

Anal.:

TLC	: Rf. 0.85 (Benzene : Pet. Ether :: 1 : 1)
UV max (MeOH)	: 271 nm (log∈ 4.25)
IR(KBr)	: 1665, 1575, 1211, 1068, 873 cm^{-1}

1-(4-Methylthiophenyl)-2-phenylethanedione (106)

A solution of 1-(4-methylthiophenyl)-2-phenylethanone **(87)** (1.0 g, 4.13 mmol) in acetic anhydride (5 ml) was refluxed with selenium dioxide (2.0 g, 18.02 mmol) in an oil-bath for 1 h with continuous stirring. The work up of the reaction mixture as described for compound **(66)** followed by recrystallization from methanol yielded **(106),** (0.85 g, 80.4 %), m.p. 78-80 °C

Anal.:

TLC	: Rf 0.53 (Benzene : Pet. Ether :: 1 : 1)
UV max (MeOH)	: 248 nm (log∈ 4.12)
IR (KBr)	: 1662, 1583, 1216, 1174, 1097 and 873 cm^{-1}

1-(4-Nitrophenyl)-2-phenylethanedione (107)

2-(4-Nitrophenyl)-1-phenylethanone **(88)** (1.0 g, 4.15 mmol) and selenium dioxide (2.0 g, 18.02 mmol) was refluxed with acetic anhydride (5 ml) for 5 h with continuous vigorous stirring. The reaction mixture was processed by the procedure described for compound **(66).** Recrystallization from methanol gave the benzil derivative **(107),** (0.8 g, 75.7 %), m.p. 140-42 °C (142 °C)[233].

Anal.:

TLC	: Rf 0.7 (Benzene : $CHCl_3$ :: 1 : 1)
UV max (MeOH)	: 253 nm (log ∈ 4.69) and 230 nm (log ∈ 4.74)
IR (KBr)	: 1662, 1527, 1348, 1206 and 842 cm^{-1}

1-(4-Methylthiophenyl)-2-(4-tolyl)ethanedione (108)

A solution of 1-(4-methylthiophenyl)-2-(4-tolyl)ethanone **(89)** (1.5 g, 5.85 mmol) in acetic anhydride (5 ml) was refluxed with selenium dioxide (3.0 g, 27.03 mmol) on an oil-bath for 7 h with continuous stirring. The work up as described for compound **(66)** followed by recrystallization from methanol yielded **(108)**, (1.3 g, 82.2 %), m.p. 82-83 °C.

Anal.:

TLC	: Rf 0.72 (Benzene)
UV max (MeOH)	: 325 nm (log ∈ 4.35) and 266 nm (log ∈ 4.13)
IR (KBr)	: 1654, 1585, 1172 and 1097 cm^{-1}

1-(4-Fluorophenyl)-2-(4-methylthiophenyl)ethanedione (109)

Compound **(109)** was prepared according to the method described for compound **(66)** from 2-(4-fluorophenyl)-1-(4-methylthiophenyl)-ethanone **(90)** (1.3 g, 4.99 mmol) and selenium dioxide (3.0 g, 27.04 mmol). Recrystallization from methanol gave the compound **(109),** (0.95 g, 69.4 %), m.p. 96-98 °C.

Anal.:

TLC	: Rf 0.8 (Benzene)
UV max (MeOH)	: 327 nm (log ∈ 4.35) and 251 nm (log ∈ 4.09)
IR (KBr)	: 1667, 1652, 1587, 1215 and 1157 cm^{-1}

1-(4-Chlorophenyl)-2-(4-tolyl)ethanedione (110)

To a solution of 2-(4-chlorophenyl)-1-(4-tolyl)ethanone **(91)** (5.0 g, 20.43 mmol) in acetic anhydride (10 ml) was added selenium dioxide (10.0 g, 90.12 mmol) and the reaction mixture was refluxed for 7 h with continuous vigorous stirring. The work up was performed as per the compound **(66).** Recrystallization from methanol gave **(110),** (4.8 g, 90.7 %), m.p. 118-20 °C.

Anal.:

TLC	: Rf 0.86 (Benzene)
UV max (MeOH)	: 269 nm (log ∈ 4.4)
IR (KBr)	: 1661, 1604, 1206, 1172, 1011 and 827 cm^{-1}

1-(4-Chlorophenyl)-2-(4-methoxyphenyl)ethanedione (111)

Compound **(111)** was prepared according to the method described for the compound **(66)** from 2-(4-chlorophenyl)-1-(4-methoxyphenyl)-ethanone **(92)** (1.0 g, 3.84 mmol) and selenium dioxide (2.0 g, 18.02 mmol). The crude product obtained was recrystallized from methanol to give the desired compound **(111),** (1.0 g, 95 %), m p. 128-30 °C.

Anal.:

TLC	: Rf 0.88 (Benzene)
UV max (MeOH)	: 292 nm (log ∈ 4.37) and 268 nm (log ∈ 4.35)
IR (KBr)	: 1675, 1653, 1600, 1267, 1029 and 836 cm^{-1}

1-(4-Chlorophenyl)-2-(4-fluorophenyl)ethanedione (112)

A mixture of 2-(4-chlorophenyl)-1-(4-fluorophenyl)ethanone **(93)** (10.0 g, 0.04 mol) and selenium dioxide (20.0 g, 0.18 mol) in acetic anhydride (10 ml) was refluxed for 6 h on an oil-bath with continuous vigorous stirring. The reaction mixture was processed as described for **(66).** The resulting yellow precipitate was recrystallized from methanol to give **(112),** (9.7 g, 91.9 %), m.p. 145-46 °C.

Anal.:

TLC	: Rf 0.87 (Benzene)
UV max (MeOH)	. 267 nm (log ∈ 4.37)
IR (KBr)	: 1662, 1588, 1230, 1178 and 839 cm^{-1}

1-(2-Chlorophenyl)-2-phenylethanedione (113)

A reaction mixture of 2-(2-chlorophenyl)-1-phenylethanone **(94)** (10.0 g, 43.34 mmol) and selenium dioxide (20.0 g, 180.2 mmol) in acetic anhydride (15 ml) was refluxed for 6 h on an oil-bath with continuous vigorous stirring. The work up of the reaction mixture similar to that of compound **(66)** afforded the sticky product **(113),** (10.2 g, 96.2 %) and used for the next step without further purification.

Anal:

TLC · Rf. 0.89 (Benzene)

1-(2-Chlorophenyl)-2-(4-tolyl)ethanedione (114)

To a solution of 2-(2-chlorophenyl)-1-(4-tolyl)ethanone **(95)** (7.0 g, 28.60 mmol) in acetic anhydride (10 ml) was added selenium dioxide (12.0 g, 108 mmol) and the reaction mixture was refluxed for 4 h with continuous vigorous stirring. The workup was performed as for compound **(66).** Recrystallization from methanol yielded **(114),** (6.8 g, 91.9 %), m.p. 92-93 °C.

Anal.:

TLC : Rf 0.7 (Benzene : Pet. Ether :: 1 : 1)

UV max (MeOH) : 265 nm (log ϵ 4.26)

IR (KBr) : 1671, 1602, 1209, 1172, 1041 and 866 cm^{-1}

1-(1-Biphenyl)-2-phenylethanedione (115)

Compound **(96)** (0.9 g, 3.3 mmol) was reacted with selenium dioxide (2.0 g, 18.02 mmol) and acetic anhydride (5 ml) as per the procedure described for **(66).** The work up of the reaction mixture followed by recrystallization from methanol afforded a pale yellow product **(115),** (0.9 g, 94.7 %), m.p. 95-96 °C.

Anal.:

TLC	: Rf 0.63 (Benzene : Pet. Ether :: 1 : 1)
UV max (MeOH)	: 303 nm (log∈ 4.32)
IR (KBr)	: 1675, 1594, 1215 and 887 cm^{-1}

1-(1-Biphenyl)-2-(4-tolyl)ethanedione (116)

To a solution of 2-(1-biphenyl)-1-(4-tolyl)ethanone **(97)** (0.7 g, 2.44 mmol) in acetic anhydride (5 ml), selenium dioxide (1.5 g, 13.52 mmol) was added and the reaction mixture was refluxed for 6 h with continuous vigorous stirring. The work up was performed as for compound **(66).** The yellow precipitate obtained was recrystallized from methanol gave **(116),** (0.6 g, 60.7 %), m.p. 137-38 °C.

Anal.:

TLC	: Rf 0.87 (Benzene : Pet. Ether :: 1 : 1)
UV max (MeOH)	: 299 nm (log∈ 4.44)
IR (KBr)	: 1674, 1600, 1407, 1220, 1173 and 888 cm^{-1}

ATTEMPTED SYNTHESIS OF 1-(4-METHANESULPHONYLPHENYL)-2-PHENYLETHANEDIONE (117)

Method A

A reaction mixture containing 1-(4-methylthiophenyl)-2-phenylethanedione **(106)** (1.0 g, 3.9 mmol), hydrogen peroxide solution (20 ml, 30 %) and acetic acid (15 ml) was refluxed for 3 h. Crushed ice was added to this mixture and white precipitate so obtained was filtered, washed and dried to afford a white solid which was identified to be sulphoxide and not the desired sulphone (0.75 g, 70.8 %), m.p. 99-101 °C.

Anal.:

TLC	: Rf 0.65 ($CHCl_3$: MeOH :: 9 : 1)
IR (KBr)	: 1660, 1580, 1215, 1175, 1050 and 872 cm^{-1}

Method B

A solution of 1-(4-methylthiophenyl)-2-phenylethanedione **(106)** (0.5 g, 1.95 mmol), hydrogen peroxide solution (10 ml, 30 %) and sodium hydroxide solution (5 ml, 4 N) (15 ml) was stirred at room temperature for 3 h and then refluxed for 1 h. The mixture was poured onto crushed ice and white precipitate so obtained was filtered, washed and dried to afford a white compound which was again identified to be undesired sulphoxide (0.24 g, 45.3 %), m.p. 98-100 °C.

Anal.:

TLC	: Rf 0.65 ($CHCl_3$: MeOH :: 9 : 1)
IR (KBr)	: 1660, 1580, 1215, 1175, 1050 and 872 cm^{-1}

1-(4-Methanesulphonylphenyl)-2-phenylethanedione (117)

To a stirred solution of 1-(4-methylthiophenyl)-2-phenyl-ethanedione **(106)** (4.0 g, 15.6 mmol) in dry DCM (25 ml) was added m-chloroperbenzoic acid (MCPBA) (15.0 g, 37 mmol) in portions at –10 to 0 °C over a period of 30 min. The resulting mixture was stirred overnight at room temperature. The suspension so obtained was filtered and to the filtrate sodium metabisulphite (6.0 g) was added to destroy excess of MCPBA. The reaction mixture was stirred further for 1 h at room temperature. The mixture was quenched with ice-cold water and subjected to successive extractions with DCM (4 x 30 ml). The combined organic fractions were repeatedly washed with sodium bicarbonate solution (10 %) to remove 3-chloro benzoic acid and then with water. The organic phase was dried, recovered and the residue obtained was recrystallized from methanol to yield **(117),** (4.1 g, 91.1 %), m.p. 129-31°C.

Anal.:

TLC	: Rf 0.9 ($CHCl_3$: MeOH :: 9 : 1)
UV max (MeOH)	: 255 nm (log ϵ 4.2)
IR (KBr)	: 1682, 1668, 1595, 1325, 1146 and 960 cm^{-1}

1-(4-Methanesulphonylphenyl)-2-(4-tolyl)ethanedione (118)

Compound **(118)** was synthesized following the procedure described for the compound **(117)** by treating 1-(4-methylthiophenyl)-2-(4-tolyl)ethanedione **(108)** (0.8 g, 2.96 mmol) in dry DCM (20 ml) with MCPBA (3.0 g, 7.4 mmol). Recrystallization from methanol gave the white product **(118)**, (0.85 g, 95.5%), m.p. 129-30 °C.

Anal.:

TLC	: Rf 0.3 (Chloroform)
UV max (MeOH)	: 261 nm (log ∈ 4.27)
IR (KBr)	: 1683, 1670, 1604, 1298 and 1147 cm^{-1}

1-(4-Fluorophenyl)-2-(4-methanesulphonylphenyl)ethanedione (119)

To a stirred solution of 1-(4-methythiophenyl)-2-(4-fluorophenyl)-ethanedione **(109)** (0.7 g, 2.55 mmol) in dry DCM (25 ml), MCPBA was added (3.0 g, 7.4 mmol) in portions at -5 to –10 °C over a period of 30 min. The reaction mixture was further stirred at room temperature overnight, worked up as for the compound **(117)** and recrystallized from methanol to yield compound **(119),** (0.7 g, 97.3 %), m.p. 172-74°C.

Anal.:

TLC	: Rf 0.3 ($CHCl_3$)
UV max (MeOH)	: 256 nm (log ∈ 4.24)
IR (KBr)	: 1666, 1596, 1310, 1234 and 1151 cm^{-1}

1-(6-Methoxy-2-naphthyl)-2-phenylethanedione (120)

A mixture of 1-(6-methoxy-2-naphthyl)-2-phenylethanone **(98)** (2.5 g, 9.0 mmol), selenium dioxide (1.7 g, 15.32 mmol) and dimethylsulphoxide (DMSO) (10 ml) in a loosely stoppered conical flask was exposed to microwave radiations for 30 sec intermittently. The work up of the

reaction mixture as described for compound **(66)** and recrystallization from methanol afforded the benzil **(120)**, (1.5 g, 95 %), 87-89 °C.

Anal.:

TLC	: Rf 0.66 (Benzene)
UV max (MeOH)	: 245 nm (log ∈ 4.61)
IR (KBr)	: 1675, 1652, 1618, 1263, 1029 and 711 cm^{-1}

1-(1-Naphthyl)-2-phenylethanedione (121)

A mixture of 2-(1-naphthyl)-1-phenylethanone **(99)** (2.0 g, 8.13 mmol), selenium dioxide (1.4 g, 12.61 mmol) and dimethylsulphoxide (DMSO) (10 ml) in a loosely stoppered conical flask was exposed to microwave radiations for 30 sec intermittently The work up of the reaction mixture as described for compound **(66)** followed by recrystallization from methanol gave **(121)**, (1.0 g, 47.4 %), 220-22 °C.

Anal.:

TLC	: Rf 0.4 (Benzene)
UV max (MeOH)	: 224 nm (log ∈ 4.77)
IR (KBr)	: 1718, 1602, 1276, 1014 and 829 cm^{-1}

1-(2-Naphthyl)-2-phenylethanedione (122)

A reaction mixture containing 2-(2-naphthyl)-1-phenylethanone **(100)** (2.0 g, 8.13 mmol), selenium dioxide (1.4 g, 12.61 mmol) and dimethylsulphoxide (DMSO) (10 ml) was exposed to microwave radiations for 30 sec intermittently. The reaction mixture was processed by the procedure as described for compound **(66)** followed by recrystallization from methanol yielded **(122)**, (1.2 g, 56.9 %), 92-94 °C.

Anal.:

TLC	: Rf 0.7 (Benzene)
IR (KBr)	: 1668, 1625, 1596, 1450, 1174 and 759 cm^{-1}

4.1.3 SYNTHESES OF SUBSTITUED BENZIL DIOXIMES

Benzil dioxime (123)

Benzil **(66)** (0.5 g, 2.38 mmol), hydroxylamine hydrochloride (0.4 g, 5.76 mmol) and dry pyridine (2 ml) were refluxed on an oil-bath for 4 h. The reaction mixture was poured onto crushed ice containing concentrated hydrochloric acid (5 ml) and the pink precipitate so obtained was filtered, washed and dried. The residue was crystallized from methanol to give **(123),** (0.4 g, 70.2 %), m.p. 180-82 °C (243-44 °C, 212-16 °C)[234-235] which appeared to be a mixture of α and β- isomers of dioxime and used in the next reaction without further purification.

Anal.:

TLC : Rf 0.3 (Benzene)

IR (KBr) : 3279,1443,1399, 986 and 711 cm^{-1}

Anisil dioxime (124)

Anisil **(67)** (2.0 g, 7 4 mmol) and hydroxylamine hydrochloride (2.0 g, 28.78 mmol) were dissolved in anhydrous pyridine (10 ml). The reaction mixture was refluxed for 3 h. The work up of the reaction mixture followed by recrystallization as described for compound **(123)** yielded compound **(124),** (0.5 g, 25 %), m.p. 205-10 °C.

Anal.:

TLC : Rf 0.29 ($CHCl_3$)

UV max (MeOH) : 269 nm (log ∈ 4.52)

(Alk. MeOH): 285 nm (log ∈ 4.67)

IR (KBr) : 3275, 1607, 1513, 1247, 1029 and 820 cm^{-1}

1-(2-Chlorophenyl)-2-(4-methoxyphenyl)ethanedione dioxime (125)

1-(2-Chlorophenyl)-2-(4-methoxyphenyl)ethanedione **(68)** (1.0 g, 3.64 mmol), hydroxylamine hydrochloride (2.0 g, 28.78 mmol) and dry

pyridine (5 ml) were refluxed for 7 h. The workup of the reaction mixture was similar to that of compound **(123)** followed by recrystallization from methanol to give **(125),** (0.5 g, 45 %), m.p. 240-43 °C.

Anal.:

TLC	: Rf 0.6 ($CHCl_3$: MeOH :: 9:1)
UVmax (MeOH)	: 228 nm (log ∈ 4.22)
IR (KBr)	: 3241, 1605, 1511, 1248, 1057 and 1080 cm^{-1}

1-(2-Chlorophenyl)-2-(3,4-dimethoxyphenyl)ethanedione dioxime (126)

Compound **(126)** was synthesized by refluxing a mixture of 1-(2-chlorophenyl)-2-(3,4-dimethoxyphenyl)ethanedione **(69)** (5.0 g, 16.4 mmol), hydroxylamine hydrochloride (7.0 g, 100.7 mmol) and dry pyridine (10 ml) for 8 h. The work up of the reaction mixture similar to that of compound **(123)** followed by recrystallization from methanol afforded the compound **(126),** (1.85 g, 33.7 %), m.p. 238-40 °C.

Anal.:

TLC	: Rf 0.56 ($CHCl_3$: MeOH :: 9:1)
UV max (MeOH)	: 231 nm (log ∈ 4.29)
IR (KBr)	: 3245, 1603, 1589, 1515, 1240 and 1060 cm^{-1}

1-(2-Chlorophenyl)-2-(4-dimethylaminophenyl)ethanedione dioxime (127)

1-(2-Chlorophenyl)-2-(4-dimethylaminophenyl)ethanedione **(70)** (8.0 g, 27.8 mmol) and hydroxylamine hydrochloride (10.0 g, 143 mmol) in dry pyridine (20 ml) were refluxed for 8 h and then poured onto crushed ice containing concentrated hydrochloric acid (30 ml). The resulting buff colored precipitate was filtered and dried to give the dioxime **(127),** (7.0 g, 95.4 %).

Anal.:

TLC	: Rf 0.3 ($CHCl_3$: MeOH :: 9:1)

1-Phenyl-2-(4-tolyl)ethanedione dioxime (128)

Compound **(101)** (5.0 g, 22 mmol) was dissolved in ethylene glycol (20 ml). Hydroxylamine hydrochloride (8.0 g, 115 mmol), sodium acetate (5.0 g, 72 mmol) and a few drops of water were added to it. The mixture was refluxed for 8 h and then poured onto crushed ice containing concentrate hydrochloric acid (20 ml). The pink solid mass obtained was filtered, washed and dried to give compound **(128),** (4 g, 70.6 %), m.p. 165-70 °C.

Anal.:

TLC	: Rf 0.5 ($CHCl_3$: MeOH :: 9:1)
IR	: 3184, 1610, 1541, 1409, 1242 and 1072 cm^{-1}

1-(4-Methoxyphenyl)-2-phenylethanedione dioxime (129)

1-(4-Methoxyphenyl)-2-phenylethanedione **(102)** (0.5 g, 2.08 mmol) and hydroxylamine hydrochloride (0.8 g, 11.5 mmol) was dissolved in dry pyridine (5 ml). The contents were heated to reflux for 6 h. Work up of the reaction mixture similar to that for compound **(123)** afforded pinkish white precipitate which was recrystallized from methanol to give the compound **(129),** (0.2 g, 35.7 %), m.p. 175-77 °C.

Anal.:

TLC	: Rf 0.35 ($CHCl_3$: MeOH :: 9:1)
UV max (MeOH)	: 259 nm (log∈ 4.44)
IR (KBr)	· 3326, 1602, 1514, 1250 and 1025cm^{-1}

1-(4-Chlorophenyl)-2-phenylethanedione dioxime (130)

Method A

A solution containing 1-(4-chlorophenyl)-2-phenylethanedione **(103)** (2 g, 8.17 mmol), hydroxylamine hydrochloride (2.8 g, 40.28 mmol), sodium acetate (3.5 g, 42 68 mmol) in ethylene glycol (10 ml) and

a few drops of water was refluxed for 4.5 h and poured onto crushed ice containing concentrated hydrochloric acid (20 ml). The brown precipitate so obtained was filtered, dried and recrystallized from methanol to give the dioxime **(103),** (1.8 g, 35.6 %), m.p. 185-87 °C.

Anal.:

TLC	: Rf 0.5 ($CHCl_3$: MeOH :: 9.5 : 0.5)
IR (KBr)	. 3190, 1611, 1540, 1251 and 958 cm^{-1}

Method B

To a solution of 1-(4-chlorophenyl)-2-phenylethanedione **(103)** (2.1 g, 8.58 mmol) in pyridine (10 ml) was added hydroxylamine hydrochloride (5.0 g, 71.94 mmol). The reaction mixture was refluxed for 6 h. It was processed as described for compound **(123).** Recrystallization from methanol gave the dioxime **(130),** (1.4 g, 59.3 %), m.p. 186-89 °C.

Anal.:

TLC	. Rf 0.5 ($CHCl_3$: MeOH :: 9.5 : 0.5)

1-(4-Fluorophenyl)-2-phenylethanedione dioxime (131)

Preparation of the compound **(131)** was done as per the procedure described for compound **(123)** by reacting 1-(4-fluorophenyl)-2-phenylethanedione **(104)** (2.0 g, 8.76 mmol) with hydroxylamine hydrochloride (3.7 g, 53.24 mmol) in dry pyridine (10 ml). Purification was effected by recrystallization from acetone to yield a white solid **(131),** (1.4 g, 62 %), m.p. 170-73 °C.

Anal.:

TLC	: Rf 0.5 ($CHCl_3$: MeOH :: 9.5 : 0.5)
UV max (MeOH)	: 250 nm (log$\in$ 4.28)
IR (KBr)	: 3231, 1638, 1506, 1235, 1154 and 955 cm^{-1}

1-(4-Bromophenyl)-2-phenylethanedione dioxime (132)

To a solution of 1-(4-bromophenyl)-2-phenylethanedione **(105)** (1.0 g, 3.46 mmol) in pyridine (5 ml) was added hydroxylamine hydrochloride (2.0 g, 28.78 mmol) and the reaction mixture was refluxed for 6 h. The work up of the reaction mixture similar to that of compound **(123)** yielded the pink colored dioxime **(132),** (1.0 g, 90.9 %), m.p. 206-09 °C.

Anal.:

TLC	: Rf 0.8 ($CHCl_3$: MeOH :: 9 : 1)
IR (KBr)	: 3190, 1488, 1390, 1245, 1068 and 987 cm^{-1}

1-(4-Methylthiophenyl)-2-phenylethanedione dioxime (133)

To a solution of 1-(4-methylthiophenyl)-2-phenylethanedione **(106)** (2.0 g, 7.8 mmol) in pyridine (10 ml), hydroxylamine hydrochloride (4.0 g, 57.55 mmol) was added and the reaction mixture was refluxed for 7 h. The work up of the reaction mixture as per the compound **(123)** afforded the pink product **(133),** (2.15 g, 96.4 %), m.p. 175-79°C.

Anal.:

TLC	: Rf 0.4 ($CHCl_3$: MeOH :: 9 : 1)
UV max (MeOH)	: 288 nm (logϵ 4.3) and 275 nm (logϵ 4.22)
IR (KBr)	: 3332, 1592, 1493, 1247, 1070 and 912 cm^{-1}

1-(4-Nitrophenyl)-2-phenylethanedione dioxime (134)

A reaction mixture of 1-(4-nitrophenyl)-2-phenylethanedione **(107)** (3.45 g, 13.53 mmol), hydroxylamine hydrochloride (3.7 g, 53.23 mmol) and aqueous sodium acetate (4.4 g in 3 ml, 53.65 mmol) in ethylene glycol (10 ml) was refluxed for 3 h and processed in the usual manner. Purification by recrystallization from methanol provided the dioxime **(134),** (1.0 g, 25.9 %), m.p. 187-90 °C.

Anal.:

TLC	: Rf 0.5 ($CHCl_3$: MeOH :: 9.5 : 0.5)
IR (KBr)	: 3275, 1527, 1350 and 714 cm^{-1}

1-(4-Chlorophenyl)-2-(4-tolyl)ethanedione dioxime (135)

A solution containing 1-(4-chlorophenyl)-2-(4-tolyl)ethanedione **(110)** (1.0 g, 3.87 mmol) and hydroxylamine hydrochloride (1.5 g, 21.58 mmol) in pyridine (5 ml) was refluxed for 7 h. Processing of the reaction mixture in the usual manner followed by recrystallization from methanol gave the dioxime **(135)**, (0 8 g, 71.4 %), m.p. 219-22 °C.

Anal.:

TLC	: Rf 0.72 ($CHCl_3$: MeOH :: 1:1)
UV max (MeOH)	: 231 nm (log ϵ 4.32)
IR (KBr)	: 3289, 1490, 1088 and 981 cm^{-1}

1-(4-Chlorophenyl)-2-(4-methoxyphenyl)ethanedione dioxime (136)

1-(4-Chlorophenyl)-2-(4-methoxyphenyl)ethanedione **(111)** (5.0 g, 18.21 mmol) was subjected to oximation as described for compound **(123)** using hydroxylamine hydrochloride (12.0 g, 172 mmol) and pyridine (15 ml). The crude product **(136)** (5.2 g, 93.7 %) was utilized for the next step without further purification, m.p. 206-08 °C.

Anal.:

TLC	: Rf 0.54 ($CHCl_3$: MeOH :: 9:1)
UV max (MeOH)	: 258 nm (log ϵ 4.01)
IR (KBr)	: 3272, 1606, 1513, 1250, 1022 and 982 cm^{-1}

1-(4-Chlorophenyl)-2-(4-fluorophenyl)ethanedione dioxime (137)

The compound **(137)** was prepared as per the procedure described for compound **(123)** by reacting 1-(4-chlorophenyl)-2-(4-fluorophenyl)-ethanedione **(112)** (5.0 g, 19.04 mmol) with hydroxylamine hydrochloride

(10.0 g, 143.88 mmol) in dry pyridine (15 ml). After work up, the crude product obtained was used for the next step without further purification. The yield of compound **(137)** was 4.6 g (82 6 %), m.p 168-71 °C.

Anal.:

TLC	· Rf 0.56 ($CHCl_3$: MeOH :: 9:1)
UV max (MeOH)	: 254 nm (log ∈ 4.46)
IR (KBr)	: 3408, 1608, 1510, 1239 and 921 cm^{-1}

1-(2-Chlorophenyl)-2-phenylethanedione dioxime (138)

To a solution of 1-(2-chlorophenyl)-2-phenylethanedione **(113)** (10.0 g, 40.86 mmol) in pyridine (15 ml) was added hydroxylamine hydrochloride (20.0 g, 287.8 mmol) and the reaction mixture was refluxed for 6 h. The work up of the reaction mixture similar to that for **(123)** gave the dioxime **(138),** (6.7 g, 58.8 %), m p. 170-73 °C.

Anal.:

TLC	: Rf 0.48 ($CHCl_3$: MeOH :: 9 : 1)
IR (KBr)	: 3365, 1642, 1373, 1245, 1007 and 885 cm^{-1}

1-(2-Chlorophenyl)-2-(4-tolyl)ethanedione dioxime (139)

A reaction mixture containing 1-(2-chlorophenyl)-2-phenylethanedione **(114)** (5.0 g, 19.32 mmol) and hydroxylamine hydrochloride (8.0 g, 115 mmol) in pyridine (10 ml) was refluxed for 9 h. Work up of the reaction mixture in the usual manner afforded the dioxime **(139),** (5.4 g, 96.8 %), m.p. 245-48 °C.

Anal.:

TLC	: Rf 0.5 ($CHCl_3$: MeOH :: 1:1)
IR (KBr)	: 3268, 1512, 1405, 1056 and 988 cm^{-1}

1-(1-Biphenyl)-2-phenylethanedione dioxime (140)

A solution of 1-(1-biphenyl)-2-phenylethanedione **(115)** (1.0 g, 3.49 mmol), hydroxylamine hydrochloride (2.0 g, 28.78 mmol) and pyridine (10 ml) was refluxed for 7 h. The reaction mixture was processed in the usual manner to afford the desired product **(140),** (0.9 g, 90.9 %), m.p. 207-10 °C.

Anal.:

TLC	: Rf 0.74 ($CHCl_3$ · MeOH :: 1 : 1)
UV max (MeOH)	: 284 nm (log∈ 4.42)
IR (KBr)	: 3341, 1603, 1488, 1245 and 913 cm^{-1}

1-(1-Biphenyl)-2-(4-tolyl)ethanedione dioxime (141)

1-(1-Biphenyl)-2-(4-tolyl)ethanedione **(116)** (1.0 g, 3.33 mmol) in dry pyridine (10 ml) was treated with hydroxylamine hydrochloride (2.0 g, 28.78 mmol) followed by the work up of the reaction mixture similar to that for **(123)** to yield the white dioxime **(141),** (1.0 g, 90.9 %), m.p. 182-85°C.

Anal.:

TLC	: Rf 0.49 ($CHCl_3$: MeOH :: 9 : 1)
IR (KBr)	: 3231, 1601, 1487, 1233 and 945 cm^{-1}

1-(4-Methanesulphonylphenyl)-2-phenylethanedione dioxime (142)

A reaction mixture containing 1-(4-methanesulphonylphenyl)-2-phenylethanedione **(117)** (0.5 g, 1.73 mmol and hydroxylamine hydrochloride (1.0 g, 14.38 mmol) in pyridine (5 ml) was refluxed for 4 h. Work up of the reaction mixture as per the procedure described for **(123)** gave the compound **(142),** (0.4 g, 72.8 %), m.p. 249-52 °C.

Anal.:

TLC	: Rf 0.7 ($CHCl_3$: MeOH :: 9 : 1)
UV max (MeOH)	: 256 nm (log∈ 4.42)
IR (KBr)	: 3378, 1591, 1398, 1310, 1276 and 1143 cm^{-1}

1-(4-Methanesulphonylphenyl)-2-(4-tolyl)ethanedione dioxime (143)

1-(4-Methanesulphonylphenyl)-2-(4-tolyl)ethanedione **(118)** (0.8 g, 2.65 mmol) was subjected to oximation by refluxing with hydroxylamine hydrochloride (2.0 g, 28.78 mmol) in pyridine (5 ml) as per the method described for **(123).** The crude product obtained was utilized for the next step without further purification. The yield was 0.5 g (56.9 %), m.p. 210-13 °C.

Anal.:

TLC	: Rf 0.7 ($CHCl_3$: MeOH :: 9:1)
UV max (MeOH)	: 261 nm (log ∈ 4.52)
IR (KBr)	: 3377, 1696, 1575, 1302 and 1142 cm^{-1}

1-(4-Fluorophenyl)-2-(4-methanesulphonylphenyl)ethanedione dioxime (144)

A reaction mixture of 1-(4-fluorophenyl)-2-(4-methanesulphonyl-phenyl)ethanedione **(119)** (0.8 g, 2.75 mmol) and hydroxylamine hydrochloride (2.0 g, 28.78 mmol) in pyridine (5 ml) was refluxed for 7 h. It was processed in the usual manner to afford the dioxime **(144),** (0.7 g, 92.4 %), m.p. 245-47 °C.

Anal.:

TLC	: Rf 0.6 ($CHCl_3$: MeOH :: 9:1)
UV max (MeOH)	: 255 nm (log ∈ 4.44)
IR (KBr)	: 3380, 1590, 1510, 1397, 1300 and 1141 cm^{-1}

1-(6-Methoxy-2-naphthyl)-2-phenylethanedione dioxime (145)

1-(6-Methoxy-2-naphthyl)-2-phenylethanedione **(120)** (1.0 g, 3.45 mmol) in pyridine (5 ml) was reacted with hydroxylamine hydrochloride (1.0 g, 14.38 mmol) as described for compound **(123).** Work up of the reaction mixture similar to that for compound **(123)** afforded the dioxime **(145),** (0.9 g, 81.8 %), m.p. 157-59 °C.

Anal.:

TLC	: Rf 0.41 ($CHCl_3$: MeOH :: 9:1)
UV max (MeOH)	: 244 nm (log ∈ 4.73)
IR (KBr)	: 3340, 1267, 1203 and 1025 cm^{-1}

1-(1-Naphthyl)-2-phenylethanedione dioxime (146)

1-(1-Naphthyl)-2-phenylethanedione **(121)** (1.5 g, 5.77 mmol) was subjected to oximation as described for compound **(123)** using hydroxylamine hydrochloride (2.0 g, 28.7 mmol) and pyridine (5 ml). The reaction mixture was processed in the usual manner to yield **(146),** (1.1 g, 65.9 %), m.p. 206-08 °C.

Anal.:

TLC	: Rf 0.55 ($CHCl_3$: MeOH :: 9:1)
IR (KBr)	: 3259, 1608, 1487, 1288, 1110 and 987 cm^{-1}

1-(2-Naphthyl)-2-phenylethanedione dioxime (147)

1-(2-naphthyl)-2-phenylethanedione **(122)** (1.5 g, 5.77 mmol) in pyridine (5 ml) was reacted with hydroxylamine hydrochloride (2.0 g, 28.7 mmol) as described for compound **(123).** Work up of the reaction mixture similar to that for compound **(123)** gave the crude product **(147),** (1.0 g, 59.9 %), m.p. 162-65 °C.

Anal.:

TLC	: Rf 0.5 ($CHCl_3$: MeOH :: 9:1)
UV max (MeOH)	: 247 nm (log ∈ 4.57)
IR (KBr)	: 3217, 1596, 1494, 1446, 1193 and 927 cm^{-1}

4.1.4 SYNTHESES OF 3,4-DIARYL-1,2,5-OXADIAZOLES

ATTEMPTED SYNTHESES OF 3,4-DIPHENYL-1,2,5-OXADIAZOLE (148)

The cyclization of benzil dioxime **(123)** to afford **(148)** was tried by following different methods:

Method A

The dioxime **(123)** (1.0 g, 4.16 mmol) was dissolved in dry pyridine (10 ml). Thionyl chloride (3 ml) was added and the reaction mixture was heated for 5 to 6 h. The reaction mixture was poured onto crushed ice. Precipitate so obtained was filtered and dried. The dioxime **(123)** was degraded to some unknown compound and could not characterize.

Method B

The dioxime **(123)** (1.0 g, 4.16 mmol) was refluxed with acetic anhydride (10 ml) for 12 h. The reaction mixture was poured onto crushed ice. Precipitate so obtained was filtered and dried. The product so obtained was characterized to be a diacetate derivative of **(123)** was obtained instead of the desired cyclized product **(98).**

Anal.:

TLC	: Rf 0.54 ($CHCl_3$: MeOH :: 9.5 : 0.5)
IR (KBr)	: 1745, 1442, 1367, 1074 and 893 cm^{-1}

3,4-Diphenyl-1,2,5-oxadiazole (148)

Benzil dioxime **(123)** (5.0 g, 20.81 mmol) and succinic anhydride (10.0 g, 100.0 mmol) were taken in a dry mortar and triturated. The

powder was heated for 15 min on an oil-bath at 180-200 °C. The molten product was cooled and a sufficient quantity of sodium bicarbonate solution (20 %) was added to make it alkaline. The mixture was heated for 1 h at 60-70 °C and poured onto ice-cold water (400 ml). The resulting mixture was extracted with chloroform (3 x 100 ml) successively. The combined organic extract was washed with water, dried and the solvent recovered. The residue was recrystallized from methanol to afford **(148),** (2.3 g, 49.7 %), m.p. 93-96 °C.

Anal.:

TLC	: Rf 0.64 (Benzene)
UV max (MeOH)	: 239 nm (log ∈ 4.02)
IR (KBr)	: 1577, 1442, 1367, 1074 and 893 cm^{-1}
PMR	: δ 7.37-7.56 (m, 10H)
MS	: m/z 223 (M + H), 192, 119, 103, 89 and 30
Calculated for $C_{14}H_{10}N_2O$	: C,75.66; H,4.54; N,12.61 %
Found	: C,75.86; H,4.38; N,12.45 %

3,4-Di(4-methoxyphenyl)-1,2,5-oxadiazole (149)

1,2-Di(4-methoxyphenyl)ethanedione dioxime **(124)** (0.5 g, 1.66 mmol) was reacted with succinic anhydride (1.0 g, 10 mmol) as described for compound **(148).** The work up of the reaction mixture and recrystallization from methanol yielded the cyclized compound **(149),** (0.025 g, 5 %), m.p. 123-25 °C.

Anal.:

TLC	: Rf 0.55 (Benzene)
UV max (MeOH)	: 268 nm (log ∈ 4.12)
IR (KBr)	: 1612, 1444, 1305, 1257, 1026 and 833 cm^{-1}

PMR : δ 3.86 (s, 6H), 6.92-6.96 (d, 4H) and 7.45-7.50 (d, 4H)

MS : m/z 283 (M^+), 252, 149, 133 and 119

Calculated for $C_{16}H_{14}N_2O_3$· C, 68.07; H, 5.00; N, 9.93 %

Found : C, 68.07; H, 4.68; N, 10.11 %

3-(2-Chlorophenyl)-4-(4-methoxyphenyl)-1,2,5-oxadiazole (150)

A powder mixture containing 1-(2-chlorophenyl)-2-(4-methoxyphenyl)ethanedione dioxime **(125)** (1.4 g, 4.57 mmol) and succinic anhydride (3.0 g, 30 mmol) was fused at 180-85 °C for 15 min in an oil-bath. The desired compound **(150)** was obtained by work up of the molten mixture as described for the compound **(148)** followed by recrystallization from methanol gave the needles **(150),** (0.5 g, 38.2 %), m.p. 107-08 °C.

Anal..

TLC : Rf 0.67 (Benzene : Pet. Ether :: 1:1)

UV max (MeOH) : 272 nm (log ∈ 4.40)

IR (KBr) : 1611, 1526, 1437, 1253, 1029 and 891 cm^{-1}

PMR : δ 3.80 (s, 3H), 6.84-6.87 (d, 2H), 7.41-7.44 (d, 2H) and 7.44-7.51 (m, 4H)

MS : m/z 287 (M^+)

3-(2-Chlorophenyl)-4-(3,4-dimethoxyphenyl)-1,2,5-oxadiazole (151)

The compound **(151)** was prepared by reacting 1-(2-chlorophenyl)-4-(3,4-dimethoxyphenyl)ethanedione dioxime **(126)** (3.9 g, 11.65 mmol) and succinic anhydride (7.0 g, 70 mmol) as described for compound **(148).** The work up of the reaction mixture followed by recrystallization from methanol yielded the title compound as cubic crystals **(151),** (2.2 g, 59.6 %), m.p. 77-79 °C.

Anal.:

TLC	: Rf 0.83 (Benzene)
UV max (MeOH)	: 295 nm (log ∈ 3.97)
IR (KBr)	: 1605, 1527, 1489, 1368, 1256, 1019 cm^{-1}
PMR	: δ 3.71 and 3.87 (s, 3H), 6.78-6.81 (d, 1H), 6.98-7.02 (dd, 1H), 7.08-7.087 (d, 1H) and 7.43-7.52 (m, 4H).
MS	: m/z 316 (M^+), 286, 179, 163 and 137

3-(2-Chlorophenyl)-4-(4-dimethylaminophenyl)-1,2,5-oxadiazole (152)

The oxadiazole derivative **(152)** was obtained by the reaction of 1-(2-chlorophenyl)-2-(4-dimethylaminophenyl)ethanedione dioxime **(127)** (8.0 g, 26.51 mmol) with succinic anhydride (15.0 g, 150 mmol) at 185 °C for 20 min. The reaction mixture was processed as per the compound **(148)** to afford a brownish residue. The residue was chromatographed over a column of silica gel G (100-200 mesh) and eluted with benzene to afford a pale yellow colored compound **(152)**, (0.2 g, 2.5 %), m.p. 84-85 °C.

Anal.:

TLC	· Rf 0.82 (Benzene)
UV max (MeOH)	: 310 nm (log ∈ 4.14) and 276 nm (log ∈ 4.00)
IR (KBr)	: 2902, 2820, 1619, 1430, 1371 and 1059 cm^{-1}
PMR	: δ 2.97 (s, 6H), 6.60-6.63 (d, 2H), 7.34-7.37 (d, 2H) and 7.38-7.51 (m, 4H).
MS	: m/z 300 (M+H)

3-Phenyl-4-(4-tolyl)-1,2,5-oxadiazole (153)

A uniform powder mixture of 1-phenyl-2-(4-tolyl)ethanedione dioxime **(128)** (4.0 g, 16 mmol) and succinic anhydride (8.0 g, 80 mmol) was heated at 180-85 °C for 15 min and processed on similar lines as for compound **(148).** The product was subjected to vacuum distillation followed by recrystallization from methanol to afford the title product **(153),** (0.45 g, 12.1 %), m.p. 57-59 °C.

Anal.:

TLC	: Rf 0.8 (Benzene : Pet. Ether :: 7 : 3)
UV max (MeOH)	: 242 nm (log∈ 4.24)
IR (KBr)	: 1605, 1527, 1450, 1368, 1256, 1019 cm^{-1}
PMR	: δ 2.40 (s, 3H) and 7.20-7.54 (m, 9H)
MS	· m/z 236 (M^+), 206, 133, 119, 103 and 89

3-(4-Methoxyphenyl)-4-phenyl-1,2,5-oxadiazole (154)

A mixture of 1-(4-Methoxyphenyl)-2-phenylethanedione dioxime **(129)** (5.0 g, 18.5 mmol) and succinic anhydride (10.0 g, 100 mmol) was heated on an oil-bath at 185-90 °C for 20 min. The work up of the reaction mixture was carried out as described for the compound **(148)** followed by decolorization and recrystallization from methanol to afford the title compound **(154),** (1.65 g, 35.4 %), m.p. 67-69 °C.

Anal.:

TLC	: Rf 0.8 (Benzene)
UV max (MeOH)	: 250 nm (log∈ 4.11)
IR (KBr)	: 1613, 1525, 1456, 1250, 1025 and 841 cm^{-1}
PMR	: δ 3.82 (s, 3H), 6.88-6.91 (d, 2H) and 7.37-7.55 (m, 7H)
MS	: m/z 252 (M^+), 222, 149, 133, 119, 103 and 89

3-(4-Chlorophenyl)-4-phenyl-1,2,5-oxadiazole (155)

1-(4-Chlorophenyl)-2-phenylethanedione dioxime **(130)** (2.9 g, 10.56 mmol) was reacted with succinic anhydride (6.0 g, 60 mmol) (the reaction temperature was maintained at 180-85 °C and the reaction time given was 15 min.) as described for compound **(148)** to obtain a crude product, which was purified by column chromatography (silica gel) using benzene as an eluent to yield the compound **(155),** (0.55 g, 20.3 %), m.p. 83-84 °C.

Anal.:

TLC	: Rf 0.9 (Benzene)
UV max (MeOH)	: 248 nm (log∈ 4.04)
IR(KBr)	: 1597, 1447, 1410, 1091, 987 and 772 cm^{-1}
PMR	: δ 7.42-7.49 (m, 9H)
MS	: m/z 256 (M^+), 226, 153, 137, 119, 103 and 89

3-(4-Fluorophenyl)-4-phenyl-1,2,5-oxadiazole (156)

A mixture of 1-(4-fluorophenyl)-2-phenylethanedione dioxime **(131)** (0.5 g, 1.94 mmol) and succinic anhydride (1.0 g, 10 mmol) was heated at 185–90 °C for 15 min. The work up by the procedure described in the preparation of compound **(148)** followed by recrystallization from methanol gave the title compound **(156),** (0.15 g, 32.3 %), m.p. 85-87 °C.

Anal.:

TLC	: Rf 0 9 (Benzene)
UV max (MeOH)	: 237 nm (log∈ 3.87)
IR (KBr)	: 1605, 1495, 1454, 1227, 1026, and 841 cm^{-1}
PMR	: δ 7.12 (m, 2H) and 7.40-7.56 (m, 7H)
MS	: m/z 240 (M^+), 210, 137, 119, 107, 95 and 89

3-(4-Bromophenyl)-4-phenyl-1,2,5-oxadiazole (157)

A uniform powder mixture of 1-(4-bromophenyl)-2-phenylethanedione dioxime **(132)** (5.0 g, 15.67 mmol) and succinic anhydride (10 g, 100 mmol) was heated in an oil-bath at 190 °C for 15 min. The work up in a similar fashion as described for **(148)** gave a crude product. Purification was effected by column chromatography (Silica gel G), elution with benzene and subsequent recrystallization from petroleum ether afforded the title compound as a pale yellow solid **(157),** (0.35 g, 7.4 %), m.p. 111-13°C.

Anal.:

TLC	: Rf 0.8 (Benzene : Pet. Ether :: 1 : 1)
UV max (MeOH)	: 248 nm (log ∈ 4.08)
IR (KBr)	: 1596, 1446, 1407, 1071, 986, 896 and 565 cm^{-1}
PMR	: δ 7.39-7.42 (d, 2H), 7.45-7.52 (m, 4H) and 7.55-7.56 (d, 2H)
MS	: m/z 302 (M^+), 272, 199, 169, 119 and 89

3-(4-Methylthiophenyl)-4-phenyl-1,2,5-oxadiazole (158)

The title compound **(158)** was prepared by reaction of 1-(4-methylthiophenyl)-2-phenylethanedione dioxime **(133)** (3.5 g, 12.22 mmol) with succinic anhydride (10.0 g, 100 mmol) at 180-85 °C for 12 min. The work up was performed by the procedure as described for compound **(148).** Recrystallization from methanol gave the desired compound **(158),** (0.55 g, 16.8 %), m.p. 83-84 °C.

Anal.:

TLC	: Rf 0.7 (Benzene : Pet. Ether :: 1 : 1)
UV max (MeOH)	: 288 nm (log ∈ 4.16)
IR (KBr)	: 1602, 1490, 1435, 1087, 816 and 693 cm^{-1}
PMR	: δ 2.50 (s, 3H), 7.24-7.26 (d, 2H) and 7.40-7.54 (m, 7H)
MS	: m/z 269 (M+H)

3-(4-Nitrophenyl)-4-phenyl-1,2,5-oxadiazole (159)

The compound **(159)** was synthesized following the procedure described for the compound **(148)** by reacting 1-(4-nitrophenyl)-2-phenylethanedione dioxime **(134)** (0.5 g, 1.73 mmol) and succinic anhydride (1.0 g, 10 mmol) at 180 °C for 10 min. Recrystallization from methanol gave a pale yellow solid **(159),** (0.1 g, 21.3 %), m.p. 139-42 °C.

Anal.:

TLC	: Rf 0.8 (Benzene)
UV max (MeOH)	: 266 nm (log ∈ 4.13)
IR (KBr)	: 1600, 1520, 1447, 1349, 859 and 760 cm^{-1}
PMR	: δ 7.47-7.50 (m, 5H), 7.74-7.77 (d, 2H) and 8.28-8.31 (d, 2H)
MS	: m/z 267 (M^+)

3-(4-Chlorophenyl)-4-(4-tolyl)-1,2,5-oxadiazole (160)

A uniform powder mixture of 1-(4-chlorophenyl)-2-(4-tolyl)-ethanedione dioxime **(135)** (4.0 g, 13.85 mmol) and succinic anhydride (8.0 g, 80 mmol) was heated at 180–85 °C for 15 min and processed on similar lines as described for the compound **(148).** The product **(160)** was purified by recrystallization from methanol in a yield of 0.7 g (18.7 %), m.p. 137-39 °C.

Anal.:

TLC	: Rf 0.7 (Benzene : Pet. Ether :: 1:1)
UV max (MeOH)	: 255.2 nm (log ∈ 4.68)
IR (KBr)	: 1612, 1516, 1408, 1091 and 754 cm^{-1}
PMR	. δ 2.46 (s, 3H), 7.34-7.37 (d, 2H), 7.47-7.50 (d, 2H), 8.08-8.11(d, 2H) and 8.10-8.13 (d, 2H)
MS	: m/z 270 (M^+)

3-(4-Chlorophenyl)-4-(4-methoxyphenyl)-1,2,5-oxadiazole (161)

The compound **(161)** was prepared by heating 1-(4-chlorophenyl)-2-(4-methoxyphenyl)ethanedione dioxime **(136)** (3.7 g, 12.15 mmol) and succinic anhydride (7.0 g, 70 mmol) at 180 °C for 13 min as described for compound **(148).** Recrystallization from methanol provided the compound **(161),** (0.9 g, 25.9 %), m.p. 98-100 °C.

Anal.:

TLC : Rf 0.79 (Benzene)

UV max (MeOH) : 252.6 nm (log ∈ 4.20)

IR (KBr) : 1614, 1451, 1253, 1090 and 1027 cm^{-1}

PMR : δ 3.86 (s, 3H), 6.94-6.97 (d, 2H), 7.40-7.43 (d, 2H), 7.43-7.46 (d, 2H) and 7.48-7.51 (d, 2H)

Calculated for $C_{15}H_{11}N_2O_2Cl$. C, 62.83; H, 3.84; N, 9.77 %

Found : C, 62.71; H, 3.82; N, 9.61 %

3-(4-Chlorophenyl)-4-(4-fluorophenyl)-1,2,5-oxadiazole (162)

1-(4-Chlorophenyl)-2-(4-fluorophenyl)ethanedione dioxime **(137)** (3.0 g, 10.26 mmol) and succinic anhydride (6.0 g, 60 mmol) was heated on an oil-bath at 180 °C for 13 mın. The work up of the reaction mixture was performed as described for the compound **(148).** The pure needle shaped crystalline product **(162)** was obtained after recrystallization from methanol in a yield of 0.47 g (16.7 %), m.p. 101-03 °C.

Anal :

TLC : Rf 0.85 (Benzene)

UV max (MeOH) : 244 nm (log ∈ 4.19)

IR (KBr) : 1601, 1447, 1225, 1090 and 833 cm^{-1}

PMR : δ 7.12-7.18 (dd, 2H), 7.44-7.46 (m, 4H) and 7.49-7.54 (m, 2H)

Calculated for $C_{14}H_8N_2OClF$: C, 61.22; H, 2.93; N, 10.20 %

Found · C, 60.98; H, 2.68; N, 10.07 %

3-(2-Chlorophenyl)-4-phenyl-1,2,5-oxadiazole (163)

A uniform powder mixture of 1-(2-chlorophenyl)-2-phenylethanedione dioxime **(138)** (3.0 g, 10.76 mmol) and succinic anhydride (6.0 g, 60 mmol) was heated in an oil-bath at 185-90 °C for 15 min. The work up in a similar fashion as described for **(148)** gave a crude product. Recrystallization from methanol afforded the title compound **(163),** (0.15 g, 5.4 %), m.p. 59-60 °C.

Anal.:

TLC	: Rf 0.8 (Benzene : Pet. Ether :: 1 : 1)
UV max (MeOH)	: 240 nm (log ∈ 3.88)
IR (KBr)	: 1600, 1434, 1366, 1062 and 762 cm^{-1}
PMR	: δ 7.34-7.51 (m, 9H)

3-(2-Chlorophenyl)-4-(4-tolyl)-1,2,5-oxadiazole (164)

A uniform powder mixture of 1-(2-chlorophenyl)-2-(4-tolyl)ethanedione dioxime **(139)** (1.0 g, 3.46 mmol) and succinic anhydride (3.0 g, 30 mmol) was heated at 180 °C for 8 min and processed on similar lines as described for the compound **(148).** The product was purified by recrystallization from methanol in a yield of 0.35 g (37.3 %), m.p. 117-18 °C.

Anal.:

TLC	: Rf 0 8 (Benzene : Pet. Ether :: 1:1)
UV max (MeOH)	: 246 nm (log ∈ 3.92)
IR (KBr)	: 1613, 1435, 1299, 1060 and 988 cm^{-1}
PMR	: δ 2.35 (s, 3H), 7.13-7.16 (d, 2H), 7.33-7.36 (d, 2H) and 7.39-7.51 (m, 4H)

3-(1-Biphenyl)-4-phenyl-1,2,5-oxadiazole (166)

1-(1-Biphenyl)-2-phenylethanedione dioxime **(140)** (0.7 g, 2.21 mmol) and succinic acid (1.5 g, 15 mmol) was heated at 185 °C for 15

min. The reaction mixture was processed by the method described for the compound **(148)** followed by recrystallization from methanol to afford the desired oxadiazole **(166),** (0.25 g, 37.9 %), m.p. 93-94 °C.

Anal.:

TLC	: Rf 0 86 (Benzene : Pet. Ether :: 1 : 1)
UV max (MeOH)	: 269 nm (log ∈ 4.29)
IR (KBr)	: 1612, 1485, 1450, 1411, 1074 and 987 cm^{-1}
PMR	: δ 7.36-7.62 (m, 14H)

3-(1-Biphenyl)-4-(4-tolyl)-1,2,5-oxadiazole (167)

A uniform powder mixture of 1-(1-biphenyl)-2-(4-tolyl)ethanedione dioxime **(141)** (0.5 g, 1.51 mmol) and succinic anhydride (1.0 g, 10 mmol) was heated in an oil-bath at 195-200 °C for 15 min. The work up in a similar manner as described for **(148)** gave a crude product. The compound was recrystallized from methanol to afford the title compound **(167),** (0.2 g, 42.3 %), m.p. 90-91°C.

Anal.:

TLC	: Rf 0.9 (Benzene : Pet. Ether :: 1 : 1)
UV max (MeOH)	: 267 nm (log ∈ 4.40)
IR (KBr)	: 1614, 1453, 1401, 988 and 825 cm^{-1}
PMR	: δ 2.42 (s, 3H) and 7.22-7.63 (m, 13H)

3-(4-Methanesulphonylphenyl)-4-phenyl-1,2,5-oxadiazole (168)

The compound **(168)** was prepared by reacting 1-(4-methanesulphonyl-phenyl)-2-phenylethanedione dioxime **(142)** (1.8 g, 5.65 mmol) with succinic anhydride (4 0 g, 40 mmol) at 185°C for 15 min, as per the procedure described in the preparation of **(148).** Purification was effected by recrystallization from methanol to afford the compound **(168),** (0.8 g, 47 1 %), m.p. 142-43 °C.

Anal.:

TLC	: Rf 0.8 ($CHCl_3$: MeOH :: 9.5 : 0.5)
UV max (MeOH)	: 242 nm (log ∈ 4.29)
IR (KBr)	: 1600, 1448, 1408, 1308, 1149 and 844 cm^{-1}
PMR	: δ 3.11 (s, 3H), 7.47-7.50 (m, 5H), 7.76-7.78 (d, 2H) and 8.00-8.03 (d, 2H).

Calculated for $C_{15}H_{12}N_2O_3S$: C, 59.99; H, 4.02; N, 9.32 %

Found : C, 59.84; H, 4.02, N, 9.26 %

3-(4-Methanesulphonylphenyl)-4-(4-tolyl)-1,2,5-oxadiazole (169)

1-(4-methanesulphonylphenyl)-2-(4-tolyl)ethanedione dioxime **(143)** (0.5 g, 1.5 mmol) was fused with succinic anhydride (1.0 g, 10 mmol) at 185–90 °C for 15 min in an oil-bath. The fusion mixture was processed as per the procedure for compound **(148).** The pure product **(169)** was obtained by recrystallization from methanol in a yield of 0.2 g (42.6 %), m.p. 141-42 °C.

Anal.:

TLC	: Rf 0 8 ($CHCl_3$: MeOH :: 9.5 : 0.5)
UV max (MeOH)	: 243 nm (log ∈ 4.28)
IR (KBr)	: 1610, 1451, 1407, 1307 and 1150 cm^{-1}
PMR	: δ 2.43 (s, 3H), 3.10 (s, 3H), 7.25-7.28 (d, 2H), 7.37-7.39 (d, 2H), 7.76-7.78 (d, 2H) and 8.00-8.02 (d, 2H)

3-(4-Fluorophenyl)-4-(4-methanesulphonylphenyl)-1,2,5-oxadiazole (170)

1-(4-Fluorophenyl)-2-(4-methanesulphonylphenyl)ethanedione dioxime **(144)** (0.5 g, 1.49 mmol) and succinic anhydride (1.0 g, 10 mmol) was heated at 180-85 °C for 15 min. The reaction mixture was worked up following the procedure described for compound **(148).** Recrystallization from methanol gave the oxadiazole **(170),** (0.15 g, 31.9 %), m.p. 155-57 °C.

Anal.:

TLC	: Rf 0.8 ($CHCl_3$: MeOH .: 9.5 : 0.5)
UV max (MeOH)	: 242 nm (log ∈ 4.26)
IR (KBr)	: 1606, 1524, 1402, 1310, 1225 and 1151 cm^{-1}
PMR	: δ 3.12 (s, 3H), 7.15-7.20 (dd, 2H), 7.49-7.53 (m, 2H),7.75-7.77 (d, 2H) and 8.02-8.05 d, 2H)

3-(6-Methoxy-2-naphthyl)-4-phenyl-1,2,5-oxadiazole (172)

Compound **(172)** was prepared by reacting 1-(6-methoxy-2-naphthyl)-2-phenylethanedione dioxime **(145)** (0.8 g, 25 mmol) with succinic anhydride (2.0 g, 100 mmol) at 185°C for 15 min, as per the procedure described in the preparation of **(148).** The work up in a similar fashion as described for **(148)** gave a crude product. Purification was effected by column chromatography (Silica gel G). Elution with benzene and subsequent recrystallization from petroleum ether afforded the title compound as a pale yellow solid **(172),** (0.35 g, 46.4 %), m.p. 124-25 °C.

Anal.:

TLC	: Rf 0.89 (Benzene)
UV max (MeOH)	: 235 nm (log ∈ 4.74)
IR (KBr)	. 1627, 1610, 1488, 1388, 1213 and 1031 cm^{-1}
PMR	δ 3 93 (s, 3H), 7.16 (s, 1H), 7.16-7.19 (m, 1H), 7.39-7.58 (m, 6H), 7.66-7.68 (d, 1H), 7.75- 7.78 (d, 1H) and 7.96 (s, 1H)
MS	: m/z 303 (M+H)

Attempted synthesis of 3-(1-naphthyl)-4-phenyl-1,2,5-oxadiazole (173)

1-(1-Naphthyl)-2-phenylethanedione dioxime **(146)** (3.0 g, 10.34 mmol) and succinic anhydride (6.0 g, 60 mmol) was heated at 180-85 °C for 15 min. The reaction mixture was worked up following the

procedure described for compound **(148)** to afford the crude product. It was chromatographed over a column of silica gel G (100-200 mesh) and eluted with benzene to afford a pale yellow solid. The compound so obtained was characterized to be **(174),** (0.25 g, 8.9 %), m.p. 298-300 °C.

Anal.:

TLC	: Rf 0.5 ($CHCl_3$. MeOH :: 9.5 : 0.5)
UV max (MeOH)	: 231 nm (log ∈ 4.83)
IR (KBr)	: 1701, 1676, 1587, 1375, 1280 and 779 cm^{-1}
MS	: m/z 395.1

Attempted synthesis of 3-(2-naphthyl)-4-phenyl-1,2,5-oxadiazole (175)

1-(2-Naphthyl)-2-phenylethanedione dioxime **(147)** (3.0 g, 10.34 mmol) and succinic anhydride (6 0 g, 60 mmol) was heated at 180-85 °C for 15 min. The reaction mixture was worked up following the procedure described for compound **(148)** to afford the mixture of products and a pure compound was tried to isolate through column chromatography (silica gel) using benzene as an eluent. A sticky material was obtained that did not crystallize from any solvent.

Anal.:

TLC	: Rf 0.8 (Benzene)
IR (KBr)	: 3058, 2225, 1596, 1448, 1272 and 968 cm^{-1}

3,4-Di(4-nitrophenyl)-1,2,5-oxadiazole (176) and

3-(3-Nitrophenyl)-4-(4-nitrophenyl)-1,2,5-oxadiazole (177)

Benzil oxadiazole **(148)** (1.0 g, 4.50 mmol) was dissolved in concentrated sulphuric acid (4 ml) with stirring at 10-15 °C. Fuming nitric acid (2 ml) was added to it dropwise. The reaction mixture was stirred for half an hour in cold condition and then 3 h at room temperature. It was left as such overnight. The reaction mixture was poured onto ice-cold water. A light yellow precipitate so obtained was filtered, dried and recrystallized

from methanol. Compound **(176)** (0.25 g, 17.85 %) separated, m.p. 221- 23 °C as first crop. Compound **(177)** was isolated as second crop in a yield of (0.4 g, 32.1 %), m.p. 119-21 °C.

3,4-Di(4-nitrophenyl)-1,2,5-oxadiazole (176)

Anal.:

TLC : 0.74 (Benzene)

UV max (MeOH) : 264 nm (log ∈ 4.46)

IR (KBr) . 1601, 1527, 1346, 990, 852 and 694 cm^{-1}

PMR : δ 7.72-7.75 (d, 4H) and 8.33-8.36 (d, 4H)

Calculated for $C_{14}H_{10}N_2O_2$: C, 53.85; H, 2.58; N, 17.94 %

Found : C, 53.89; H, 2.45; N, 17.76 %

3-(3-Nitrophenyl)-4-(4-nitrophenyl)-1,2,5-oxadiazole (177)

Anal.:

TLC : 0.7 (Benzene)

UV max (MeOH) : 259 nm (log ∈ 4.22)

IR (KBr) : 1540, 1530, 1349 and 988 cm^{-1}

PMR : δ 8.41-8.45 (m, 2H), 8.32-8.37 (d, 2H), 7.84-7.87 (m, 1H), 7.75-7.78 (d, 2H) and 7.70-7.79 (m, 1H)

MS : m/z 312 (M^+), 282, 164 and 134

3-Phenyl-4-(4-sulphamoylphenyl)-1,2,5-oxadiazole (178)

To a solution of benzil oxadiazole **(148)** (0.5 g, 2.25 mmol) in dry chloroform (10 ml) was added distilled chlorosulphonic acid (0.3 ml, 4.51 mmol) at 0 °C during 10 min and the reaction mixture was stirred at 0 °C for 15 min after addition of chlorosulphonic acid and refluxed on a water bath for 3 h. The reaction mixture was poured onto crushed ice and extracted with successive amounts of chloroform (3 x 20ml). To the dry chloroform extract, strong ammonia solution (8 ml) was added at 0-5 °C

during 5 min and stirred for 1 h at 0-10 °C. It was kept overnight in a freezer. A white solid product obtained was filtered and recrystallized from benzene to afford the compound **(178),** (0.2 g, 29.5 %), m.p. 84-86 °C.

Anal.:

TLC . Rf 0.65 ($CHCl_3$: MeOH :: 9:1)

IR (KBr) : 3368, 3177, 1354, 1149 and 874 cm^{-1}

PMR ($CDCl_3$ + DMSO-d_6): δ 7.37 (b, 2H), 7.47-7.55 (m, 5H), 7.65-7.68 (d, 2H) and 7.99-8.01 (d, 2H)

3,4-Di(4-sulphamoylphenyl)-1,2,5-oxadiazole (179)

A mixture containing benzil oxadiazole **(148)** (1.0 g, 4.5 mmol) in dry chloroform (15 ml) and chlorosulphonic acid (2.0 ml, 0.03 mol) was refluxed on a waterbath for 3 h under anhydrous conditions. After 3 h, the mixture was poured onto crushed ice to remove excess of chlorosulphonic acid. The organic layer was separated, washed with cold water once and dried. Strong ammonia solution (15 ml) was added into it dropwise at 0-2 °C during 30 min. The reaction mixture was stirred further for 90 min at room temperature and refrigerated overnight. It was poured onto ice-cold water. The white precipitate so obtained was filtered, dried and recrystallized from acetone to give the compound **(179),** (0.25 g, 58.1%), m.p. 258-60 °C.

Anal.:

TLC : Rf 0.67 ($CHCl_3$: MeOH :: 9:1)

UV max (MeOH) : 247 nm (log ∈ 4.25) and 228 nm (log ∈ 4.18)

IR (KBr) : 3355, 3266, 1332, 1159 and 901cm^{-1}

PMR ($CDCl_3$ + DMSO-d_6) : 7.34 (b, 2H), 7.64-7.67 (d, 4H) and 7.98-8.00 (d, 4H)

MS : m/z 380 (M^+), 350 and 198

4.1.5 SYNTHESIS OF 3,4-DIARYL-1,2,5-OXADIAZOLE N-OXIDES

3,4-Diphenyl-1,2,5-oxadiazole N-oxide (180)

Benzil dioxime **(123)** (5.0 g, 20.81 mmol) was dissolved in sodium hydroxide solution (20 %, 20 ml). The chilled sodium hypochlorite solution (20 ml) prepared by passing chlorine gas through 20 % sodium hydroxide solution was added to the above solution at 0-5 °C with stirring during 30 min. After the completion of addition, the reaction was further stirred for 1 h at 5-10 °C and refrigerated overnight. The mixture was diluted with ice-cold water and the white solid so obtained was filtered, dried and recrystallized from methanol to yield the product **(180),** (3.2 g, 64.5 %), m.p. 114-17 °C.

Anal.:

TLC : Rf 0.85 (Benzene · $CHCl_3$ :: 1:1)

UV max (MeOH) : 278 nm (log ∈ 3.82) and 235 nm (log ∈ 4.34)

IR (KBr) : 1592, 1419, 1309, 1002 and 835 cm^{-1}

PMR : δ 7.35–7.55 (m, 10H)

MS . m/z 239 (M + H), 222, 208, 178 and 119

Calculated for $C_{14}H_{10}N_2O_2$: C, 70.48; H, 4.23; N, 11.76 %

Found : C, 70.17; H, 4.09; N, 11.50 %

3,4-Di(4-methoxyphenyl)-1,2,5-oxadiazole N-oxide (181)

The reaction of anisil dioxime **(124)** (5.0 g, 1.66 mmol) in aqueous sodium hydroxide (20 %, 20 ml) with freshly prepared sodium hypochlorite (20 ml) as depicted for compound **(180)** followed by recrystallization from methanol afforded the desired compound **(181),** (2.8 g, 56 %), m.p. 110-14 °C.

Anal.:

TLC : Rf 0.8 ($CHCl_3$)

UV max (MeOH) : 253 nm (log ∈ 4.35)

IR (KBr) : 1600, 1443, 1299, 1261, 1022 and 832 cm^{-1}

PMR : δ 3.84 and 3.85 (s, 6H), 6.93-6.96 (d, 2H), 6 94-6.97 (d, 2H), 7.44-7.47 (d, 2H) and 7.46-7.49 (d, 2H)

MS : m/z 299 (M+H), 282, 238 and 119

Calculated for $C_{16}H_{14}N_2O_2$: C,64.42; H,4.73; N,9.39 %

Found : C,64.83; H,4.48; N,9.16 %

3-(2-Chlorophenyl)-4-(4-methoxyphenyl)-1,2,5-oxadiazole N-oxide (182)

To a solution of compound **(125)** (1.6 g, 5.22 mmol) in sodium hydroxide solution (20 %, 20 ml) was added freshly prepared sodium hypochlorite solution (20 ml) dropwise with continuous stirring at 10-15 °C during 30 min. After the addition was complete, the reaction was allowed to stir at room temperature for 1 h and left overnight in a freeze (10-15 °C). The work up was performed by the method as described for the compound **(180)** followed by recrystallization from methanol to yield the product **(182),** (0.83 g, 52.5 %), m.p. 114-17 °C.

Anal.:

TLC : Rf 0.65 (Benzene : Pet. Ether :: 1·1)

UV max (MeOH) : 252 nm (log ∈ 3.79)

IR (KBr) : 1590, 1512, 1426, 1302, 1253, 1177, 1029 and 830 cm^{-1}

PMR : δ 3.80 and 3.81 (s, 3H), 6.85-6.86 (d, 2H), 7.37-7.57 (m, 4H) and 7.43-7.46 (d, 2H)

Calculated for $C_{15}H_{11}N_2O_3Cl$: C, 59.41; H, 2.36; N, 9.14 %

Found : C, 59.52; H, 2.46; N, 9.25 %

3-(2-Chlorophenyl)-4-(3,4-dimethoxyphenyl)-1,2,5-oxadiazole N-oxide (183)

To a solution of the dioxime **(126)** (2.5 g, 7.47 mmol) in sodium hydroxide solution (20 ml, 20 %) was added freshly prepared sodium hypochlorite solution (20 ml) in a cold condition during 30 min. After completion of addition, the reaction mixture was stirred for 1 h. 30 min. at room temperature and then poured onto crushed ice. The white precipitate so obtained was filtered, dried and recrystallized from methanol to give the title compound **(183)**, (0.85 g, 34.3 %), m.p. 110-11 °C.

Anal.:

TLC	: Rf 0.73 (Benzene : Pet. Ether :: 1:1)
UV max (MeOH)	: 256 nm (log ∈ 4.64)
IR (KBr)	: 1601, 1524, 1488, 1329, 1264 and 1025 cm^{-1}
PMR	: δ 3.63, 3.72 and 3.87 (s, 6H), 6.78-6.84 (m, 1H), 7.04-7.07 (m, 1H), 7.14-7.17 (m, 1H) and 7.42-7.59 (m, 4H)

Calculated for $C_{16}H_{13}N_2O_4Cl$: C, 57.76; H, 3.94; N, 8.42 %

Found : C, 57.38; H, 3.63; N, 8.38 %

3-Phenyl-4-(4-tolyl)-1,2,5-oxadiazole N-oxide (184)

The compound **(184)** was prepared as described for compound **(180)** by treating 1-phenyl-2-(4-tolyl)ethanedione dioxime **(128)** (4.0 g, 15.7 mmol) in sodium hydroxide solution (20 ml, 20 %) with freshly prepared sodium hypochlorite solution (20 ml). Recrystallization from methanol yielded the compound **(184)**, (2.1 g, 53.1 %), m.p. 104-06 °C.

Anal :

TLC	: Rf 0.7 (Benzene: Pet. Ether :: 1:1)
UV max (MeOH)	: 238 nm (log ∈ 4.07) and 279 nm (log ∈ 3.62)
IR (KBr)	: 1600,1429,1309, 1109 and 821 cm^{-1}

PMR : δ 2.40 and 2.42 (s, 3H), 7.21-7.24 (d, 2H) and 7.38-7.51 (m, 7H)

MS : m/z 252 (M^+) and 196

3-(4-Methoxyphenyl)-4-phenyl-1,2,5-oxadiazole N-oxide (185)

The compound **(185)** was obtained by reacting 1-phenyl-2-(4-methoxyphenyl)ethanedione dioxime **(129)** (5.0 g, 18.50 mmol) in aqueous sodium hydroxide (20 ml, 20 %) with freshly prepared sodium hypochlorite solution (20 ml) as described for the compound **(180)** to yield the N-oxide **(185),** (2.4 g, 48.4 %), m.p. 103-05 °C.

Anal.:

TLC : Rf 0.78 (Benzene)

UV max (MeOH) : 240 nm (log ∈ 4.33)

IR (KBr) : 1591, 1525, 1425, 1252 and 1026 cm^{-1}

PMR . δ 3.83 and 3.84 (s, 3H), 6.90-6.93 (d, 2H) and 7.40-7.54 (m, 7H)

Calculated for $C_{15}H_{12}N_2O_3$: C, 67.15; H, 4.51; N, 10.44 %

Found : C, 67.42; H, 4.39; N, 10.16 %

3-(4-Chlorophenyl)-4-phenyl-1,2,5-oxadiazole N-oxide (186)

The compound **(186)** was obtained by the reaction of 1-(4-chlorophenyl)-2-phenylethanedione dioxime **(130)** (2.0 g, 7.28 mmol) and freshly prepared sodium hypochlorite solution (10 ml) in sodium hydroxide solution (10 ml, 20 %) using the method described for compound **(180)** as a white solid **(186),** (0.65 g, 32.7 %), m p. 104-05 °C.

Anal.:

TLC : Rf 0.87 (Benzene)

UV max (MeOH) : 238 nm (log ∈ 4.42) and 278 nm (log ∈ 3.98)

IR (KBr) : 1591, 1569, 1434,1399,1093 and 831 cm^{-1}

PMR : δ 7.42- 7.49 (m, 9H)

Calculated for $C_{14}H_9N_2O_2Cl$: C, 61.96; H, 3.33; N, 10.28 %

Found : C, 62.14; H, 3.04; N, 9.90 %

3-(4-Fluorophenyl)-4-phenyl-1,2,5-oxadiazole N-oxide (187)

1-(4-Fluorophenyl)-2-phenylethanedione dioxime **(131)** (1.0 g, 3.87 mmol) was reacted with freshly prepared sodium hypochlorite solution (10 ml) as per the procedure for the compound **(180).** Recrystallization from methanol gave the title compound **(187),** (0.55 g, 55.3 %), m.p. 113-15 °C.

Anal.:

TLC	: Rf 0.9 (Benzene)
UV max (MeOH)	: 236 nm (log ∈ 4.24)
IR (KBr)	: 1588, 1429, 1228, 988 and 844 cm^{-1}
PMR	: δ 7.10-7.15 (dd, 2H) and 7.44-7.55 (m, 7H)
MS	: m/z 256 (M^+) and 196.

3-(4-Chlorophenyl)-4-(4-tolyl)-1,2,5-oxadiazole N-oxide (188)

The compound **(188)** was similarly prepared as for the compound **(180)** by treating 1-(4-chlorophenyl)-2-(4-tolyl)ethanedione dioxime **(135)** (4.0 g, 13.85 mmol) in sodium hydroxide solution (20 ml, 20 %) with freshly prepared sodium hypochlorite solution (20 ml). Purification was effected by recrystallization from methanol to afford the N-oxide **(188),** (1.47 g, 37 %), m.p. 121-23 °C.

Anal.:

TLC	: Rf 0.7 (Benzene : Pet. Ether :: 1:1)
UV max (MeOH)	: 242.4 nm (log ∈ 4.45)
IR (KBr)	: 1589,1436,1091 and 823 cm^{-1}
PMR	. δ 2.40 and 2.42 (s, 3H) and 7.24-7.27 (d, 2H) and 7 37-7.47 (m, 6H)
MS	: m/z 286 (M^+) and 226

3-(4-Chlorophenyl)-4-(4-methoxyphenyl)-1,2,5-oxadiazole N-oxide (189)

1-(4-Chlorophenyl)-2-(4-methoxyphenyl)ethanedione dioxime **(136)** (5.0 g, 16.42 mmol) was reacted with freshly prepared sodium hypochlorite solution (25 ml) by the procedure described for the compound **(180).** The compound was recrystallized from methanol to afford a crystalline white solid **(189),** (2.6 g, 52.27 %), m.p. 142-44 °C.

Anal.:

TLC	: Rf 0.67 (Benzene)
UV max (MeOH)	: 244.4 nm (log ∈ 4.41)
IR (KBr)	: 1591, 1450, 1254, 1088, 1025 and 825cm^{-1}
PMR	: δ 3.85 and 3.86 (s, 3H), 6.94-6.97 (d, 2H) and 7.40-7.51(m, 6H)

Calculated for $C_{15}H_{11}N_2O_3Cl$: C, 59.50; H, 3.64; N, 9.26 %

Found : C, 59.67, H, 3.35; N, 9.06 %

3-(4-Chlorophenyl)-4-(4-fluorophenyl)-1,2,5-oxadiazole N-oxide (190)

The compound **(190)** was obtained when 1-(4-chlorophenyl)-2-(4-fluorophenyl)ethanedione dioxime **(137)** (3.5 g, 11.97 mmol) in aqueous sodium hydroxide (20 ml, 20 %) was reacted with freshly prepared sodium hypochlorite solution (20 ml) as described for the compound **(180).** Recrystallization from methanol afforded the compound **(190),** (1.8 g, 51.8 %), m.p. 113-15 °C

Anal.:

TLC	: Rf 0.78 (Benzene)
UV max (MeOH)	: 239nm (log ∈ 4.72)
IR (KBr)	:1605, 1400, 1234, 1091, 993 and 849 cm^{-1}
PMR	: δ 7.16 (dd, 2H), 7.44-7.46 (m, 4H) and 7.48-7.54 (m, 2H)
MS	: m/z 290 (M^+) and 230

3-(2-Chlorophenyl)-4-(4-tolyl)-1,2,5-oxadiazole N-oxide (191)

The compound **(191)** was similarly prepared as the compound **(180)** by treating 1-(2-chlorophenyl)-2-(4-tolyl)ethanedione dioxime **(139)** (2.0 g, 6.93 mmol) in sodium hydroxide solution (20 ml, 20 %) with freshly prepared sodium hypochlorite solution (20 ml). Purification was effected by recrystallization from methanol to afford the N-oxide **(191),** (1.30 g, 65.5 %), m.p. 139-40 °C.

Anal.:

TLC	: Rf 0.8 (Benzene · Pet. Ether :: 1:1)
UV max (MeOH)	: 238 nm (log ∈ 4.28) and 267 nm (log ∈ 3.90)
IR (KBr)	: 1592, 1568, 1423, 1306, 1056 and 765 cm^{-1}
PMR	: δ 2 34 and 2.36 (s, 3H) and 7.12-7.52(m, 8H)

3-(4-Methanesulphonylphenyl)-4-phenyl-1,2,5-oxadiazole N-oxide (192)

To a stirred solution of 3-(4-methylthiophenyl)-4-phenyl-1,2,5-oxadiazole **(158)** (0.25 g, 0 93 mmol) in glacial acetic acid (10 ml) was added a potassium permanganate solution (25 ml, 3 %) at 60 °C dropwise. The reaction mixture was stirred further for 30 min at 60 °C. The mixture was cooled and excess of potassium permanganate was destroyed by adding sodium metabisulphite solution (10 %) to the stirred solution. The contents were extracted with successive amounts of chloroform (3 x 20 ml). The combined organic layers were washed with sodium metabisulphite solution (10 %) followed by washing with water, dried and concentrated. Purification by recrystallization from methanol provided the desired N-oxide **(192),** (0.1 g, 34.48 %), m.p. 125-27°C.

Anal:

TLC	: Rf 0.75 ($CHCl_3$: MeOH :: 9.5 : 0.5)
UV max (MeOH)	: 241 nm (log ∈ 4.33)
IR (KBr)	: 1594, 1572, 1448, 1307, 1150 and 955 cm^{-1}

PMR · δ 3.09 and 3.11 (s, 3H), 7.47-7.58 (m, 5H), 7.75-7.78 (d, 2H) and 8.00-8.03 (d, 2H)

MS . m/z 316 (M^+), 300, 256, 119 and 89

ATTEMPTED SYNTHESIS OF 3,4-DIPHENYL-1,2,5-OXADIAZOLE (148)

Compound **(148)** was tried to synthesize by deoxygenation of N-oxide **(180)** using different reagents like phosphorous trichloride and triphenylphosphite as described in the following procedures. The desired compound **(98)** could not be obtained by any of these methods.

Method A

A solution containing the compound **(180)** (0.05 g, 0.28 mmol) was heated with phosphorous trichloride (2 ml) at 70 °C for 4 h. The reaction mixture was poured on to crushed ice. Precipitate so obtained was filtered and dried to afford a white solid, m.p. 113-16 °C. The compound so obtained was identified to be starting material **(180)**.

Anal.:

TLC : Rf 0.85 (Benzene : $CHCl_3$ :: 1 : 1)

Method B

A reaction mixture containing the compound **(180)** (0.05 g, 0.28 mmol) and triphenylphosphite (5 ml) was heated at 150 °C for 2 h and poured on to crushed ice. Precipitate so obtained was filtered and dried to afford the solid, m.p. 114-17°C.

Anal.:

TLC : Rf 0 85 (Benzene : $CHCl_3$ :: 1:1)

4.2 BIOLOGICAL STUDIES

COX-I AND COX-II INHIBITION ASSAYS

MATERIALS

Cayman COX-I and COX-II colorimetric screening kit (Cayman Chemical company, MI, USA)

The kit includes assay buffer (0.1 M Tris-HCl buffer, pH 8), A solution of heme in DMSO, COX-I (ovine), COX-II (ovine), A solution of arachidonic acid in ethanol, potassium hydroxide (0.1 M), colorimetric substrate (A solution of N,N,N',N'-tetramethyl-*p*-phenylenediamine [TMPD]), 96 well plate and plate cover.

Test solution: Synthesized drugs were dissolved in DMSO and diluted in the assay buffer before use.

Procedure:

Synthesized drugs to inhibit COX-I and COX-II enzyme activity were examined using the Cayman COX-I and COX-II colorimetric screening kit (Cayman Chemical company, MI, USA). Indomethacin was used as the positive control for COX-I inhibition and Valdecoxib was used as the positive control for COX-II inhibition. Test drugs were dissolved in DMSO and diluted in the assay buffer before running the assays. COX-I and COX-II inhibition assays were performed according to the manufacturer's instructions as described below:

Preparation of Wells

Background Wells, 100 % Initial Activity Wells and Inhibitor Wells were prepared as per the following procedure.

Background Wells: Assay buffer (160 µl) and heme (10 µl) were added to three wells.

100 % Initial Activity Wells: Assay buffer (150 µl), heme (10 µl) and enzyme (either COX-I or COX-II) (10 µl) were added to three wells.

Inhibitor Wells: Assay buffer (150 µl), heme (10 µl) and enzyme (either COX-I or COX-II) (10 µl) were added to three wells.

A test solution (22 µg, 10 µl) prepared in DMSO was added to the Inhibitor wells. DMSO (10 µl) was added to the 100 % Initial Activity Wells and background wells. The plate was carefully shaken for a few seconds and incubated for 5 min at 25 °C. The colorimetric substrate solution (TMPD solution) (20 µl) followed by arachidonic acid solution (20 µl) was added to all the wells. The plate was shaken carefully for a few seconds and incubated for 5 min at 25 °C. The absorbance at 590 nm was noted using a plate reader. The average absorbance was determined for all the samples. The % inhibition of (COX-I or COX-II) were calculated by the formula as given below:

Calculation:

1. The average absorbance of all the samples was determined.
2. The absorbance of the background wells (blank reading) was subtracted from the 100 % Initial Activity (control reading) and the inhibitor wells (test reading).
3. The absorbance of each Inhibitor sample (test reading) was subtracted from the absorbance of 100 % Initial Activity sample (control reading), and multiplied by 100 to give the % inhibition.

Mathematically it is expressed as:

$$\% \text{ Inhibition} = \frac{(\text{Mean absorbance of control} - \text{Mean absorbance of test}) \times 100}{(\text{Mean absorbance of Control})}$$