3.1 INTRODUCTION

The potential applications of phenothiazine analogues and the continued interest in development of phenothiazine based heterocycles, make the synthesis of imidazole ring system important in natural and synthetic Organic Chemistry as useful therapeutic and pharmacological agents (Bellina et al., 2007). When comparing to other five membered heterocycles 1H-imidazoles have some unique properties due to the presence of two nitrogens. The properties include its basicity, ability to form hydrogen bonds and leaving group ability. 1H-Imidazoles are present in a variety of natural products but are well known for defining structural features of the amino acid histidine (Jin et al., 2011). The clinically usefulazole families, the imidazoles have good antimicrobial activity. The most commonly prescribed drugs are miconazole, ketoconazole and clotrimazole.

![Figure 3.1 Clinically useful imidazole derivatives](image-url)
The azoles compounds act by inhibiting the P450 enzymes [14α-sterol demethylase (CYP51s)] responsible for the synthesis of ergosterol, which is the main sterol in fungal cell membrane. The depletion of ergosterol causes a loss in fluidity of the membrane thereby making it brittle which can fracture the membrane leading to leakage of cell contents and ultimately cell death. The imidazole ring is present in the nucleotides adenine and guanine in DNA as also in biotin (also known as Co-enzyme R), a member of the B group of vitamins. The emergence of powerful and elegant imidazole has stimulated major advances in chemotherapeutic agents of remarkable significance in medicine, biology and pharmacy.

Imidazoles are considered as important pharmacophores in medicinal chemistry showing wide range of biological activities such as antibacterial (Jain et al., 2010; Małgorzata et al., 2013), antirheumatoid (Sisko et al., 2002), antitubercular (Lu et al., 2012), antiviral (Sharma et al., 2009), antiepileptic (Puratchikody et al., 2005), anti-inflammatory (Navidpour et al., 2007; El-Araby et al., 2012) and anticancer (Sharma et al., 2010; Wittine et al., 2012). In recent years, there has been considerable amount of focus on imidazole chemistry due to the high therapeutic potential of imidazole based drugs and the importance of the imidazole structure in biological processes. The imidazole nucleus appears in a number of naturally occurring products like amino acids, purines and histidine, which comprise many of the most important bases in nucleic acids.

3.1.1 XANTHENE

Multi-component reactions (MCRs) have become important tools for building diverse and complex organic molecules through carbon-carbon and carbon-heteroatom bond formations taking place in tandem manner (Domling et al., 2000). A number of three and four-component reactions have been developed in the last thirty years (Bahador et al., 2012). It is well known for many years that dyes have been most widely used in dyeing, as well as high technology as such as lasers, liquid crystal displays, ink-jet printers and electro-optical devices (Hafez et al., 1987). Xanthene derivatives occupy an important position among different families of dyes, owing to a number of reasons related to their photochemical and photophysical properties (Chu et al., 2012). Eosin, Rose
Bengal and other xanthene dyes are the most frequently employed dye-sensitizer when a quantitative interpretation of the photodynamic effect is required (Kathiravan et al., 2009). Synthesis of xanthene derivatives continues to be a significant area because these moieties are privileged pharmacophores as well as valuable reactive intermediates in both synthetic and medicinal chemistry.

Several methods have been developed for the synthesis of xanthene derivatives, which in general can be obtained by the condensation of appropriate active methylene compounds with different aldehydes catalyzed by mineral acids (Esther et al., 2011). 1,8-dioxo-octahydroxanthenes are important class of oxygen heterocycles in which a phenyl substituted pyran ring is fused on either side with two cyclohexenone rings. Presence of conjugated bis-dienone functionality makes these compounds sensitive to attack by nucleophiles and light energy. Xanthene derivatives are used as biodegradable agrochemicals (Hafez et al., 1987), fluorescent materials (Callan et al., 2005), photodynamic therapy agents (Jaberi et al., 2008), cosmetics and pigments (Ellis 1997), luminescent sensors (Kazuya 2010) and in laser technology (Banerjee et al., 1981).

The synthesis of xanthenes, especially benzoxanthenes, is an important area in organic synthesis due to their wide range of biological and therapeutic properties such as antibacterial, antiviral and anti-inflammatory, anticancer (Song et al., 2013; Giri et al., 2010), antimicrobial (Omolo et al., 2011) and antidiabetic activities (Miura et al., 2001) as well as paralyzing action of zoxazolamine, a drug used especially as a skeletal muscle relaxant and uricosuric agent (Saint et al., 1975). Hence, these compounds have received lot of attention in synthetic chemistry.

3.1.2 PYRAN

Multifunctionalized 4H-pyrans are important structural units present in many natural or synthetic compounds with important biological or pharmacological activities such as anti-coagulant, anticancer, spasmylytic and anti-anaphylactic (Kang et al., 2009; Green et al., 1995; Rong et al., 2006). Some of these compounds also serve as useful intermediates for organic synthesis (Xiang et al., 2008). Pyrans are important core units in a number of natural products (Tang et al., 2006; Jung et al., 2010) and photochromic
materials (Kumar et al., 2010). The pyran-2-one ring is highly susceptible to nucleophilic attack at the electrophilic centers C-2, C-4 and C-6, and a variety of synthetic approaches for preparation of arenes and heteroarenes starting from pyran-2-ones have been developed (Ram et al., 2001). Reactions of 2H-pyran-2-ones with different dienophiles have been widely investigated and utilized for preparation of a variety of carbocyclic or heterocyclic products (Afarinkia et al., 1992). Moreover, 4H-pyran are useful intermediates for synthesis of various compounds such as polyazanaphthalenes (Adbel et al., 1989), pyranopyridine derivatives (Lei et al., 2011), pyridin-2-ones (Srivastava et al., 1996) and pyranopyrimidines (Quintela et al., 1995). Compounds with pyran ring system have many pharmacological properties and have an important role in biochemical processes (Hepworth et al., 2005). Preparation of this heterocyclic nucleus has gained more importance in organic synthesis because of these reasons.

The 4H-pyran derivatives are of the immense interest in synthesis of various drugs due to their pharmacological and biological activities such as antimicrobial (Hussain et al., 2011), mutagenicity (Smith et al., 1998), sex pheromone (Bianchi et al., 1987), antiproliferative (Venkatesham et al., 2012), antitumour (Hawas et al., 2011) and central nervous system (CNS) activity (Eiden et al., 1991). These privileged structures have since then been used extensively in medicinal chemistry programs to identify new ligands and are probably one of the most familiar structural units in naturally occurring compounds. Several methods have been reported for the synthesis of pyran derivatives through a three-component condensation of β-dicarbonyl compounds with aldehydes and malononitrile.
3.2 RESULTS AND DISCUSSION

The present work focuses on synthesis, characterization of some heterocyclic derivatives containing phenothiazine moiety. One pot three component reactions 10-alkyl-10H-phenothiazine-3-carbaldehyde with different reactants under conventional as well as ultrasonic irradiation were used to synthesize these compounds. The ultrasonic irradiation gave larger yields in lesser reaction time compared to conventional methods. These compounds were evaluated for antioxidant and antibacterial activities.

3.2.1 CHEMISTRY

3-phenothiazine substituted-4,5-diphenylimidazoles 8(a-d) were synthesized by reacting benzil with 10-alkyl-10H-phenothiazine-3-carbaldehyde 3(a-b) in the presence of ammonium acetate with glacial acetic acid as solvent under reflux and ultrasonic irradiation methods (Scheme 3.1).

\[
\text{NH} + \text{R}_1 \text{CO} \rightarrow \text{NH}_2 \text{OAC} \rightarrow \text{R}_1 \text{N} \text{H} \text{N} \text{R} \\
8(a-d)
\]

Scheme 3.1 Synthetic protocol of compound 8a-d.

The IR spectrum of compound 8a showed absorption frequency at 3421 cm\(^{-1}\) corresponding to -NH group which evidenced the formation of compound 8a and the disappearance of carbonyl group at 1678 cm\(^{-1}\) in compound 3a supports the formation of imidazole. In the \(^1\)H NMR spectrum of compound of 8a, the peak at \(\delta\) 12.56 ppm corresponds to -NH proton and the disappearance of formyl proton at \(\delta\) 9.76 ppm in compound 3a also confirms to the formation of compound 8a.

The Compounds 9(a-d) were synthesized by the reaction of dimedone with 3(a-b) in presence of p-TSA at 100°C in methanol for 3 hours to yield of 74-86%. The reaction was also carried out under ultrasonic irradiation to get higher yield of the product (Scheme 3.2).
The IR absorption band at 1664 cm\(^{-1}\) is due to \(\alpha, \beta\)-unsaturated carbonyl group which is present in the compound 9a. The \(^1\)H NMR spectrum of compound 9a shows singlet at \(\delta 1.01\) and 1.08 ppm which corresponds to two methyl protons of dimedone unit and two methylene protons resonating at \(\delta 2.45\) and 2.19 ppm also support the formation of compound 9a. The peak at \(\delta 4.64\) ppm corresponds to CH proton present in the cyclic ring supports the formation of cyclization of xanthenes unit.

The compound 10(a-d) were synthesized by one pot three component reaction of malononitrile, dimedone and 3(a-b) in the presence of potassium phosphate (K\(_3\)PO\(_4\)) catalyst at 100°C with ethanol-water (1:1 ratio) as a solvent for 3 hours (Scheme 3.3) and the same reaction was carried using ultrasonic irradiation method. IR spectrum of compound 10a shows absorption bands at 3442 and 3257 cm\(^{-1}\) due to primary amine, at 2189 cm\(^{-1}\) due to nitrile group and at 1687 cm\(^{-1}\) (Fig. 3.2) due to \(\alpha, \beta\)-unsaturated carbonyl group which is clearly indicating formation of compound 10a. The \(^1\)H NMR spectrum of compound 10a the exhibited peaks at \(\delta 1.03, 0.97\) ppm as two singlets corresponding to two methyl groups of dimedone, while methylene protons of dimedone appeared at \(\delta 2.14, 2.37\) as quartet, methyl group protons attached to phenothiazine ring appeared at \(\delta 3.27\) as singlet.
SCHEME 3.3 Synthetic protocol of compound 10a-d.

The singlet observed at $\delta$ 4.49 ppm corresponds to $-\text{NH}_2$ protons and the peak at $\delta$ 4.25 ppm corresponds to benzylic methine proton confirming the formation of compound 10a. The structures of newly synthesized phenothiazine derivatives confirmed through characterization through IR, $^1$H NMR, $^{13}$C NMR and HR-MS spectra. The physical data of all the synthesized compounds are presented in Table 3.1.

Fig.3.2 IR spectrum of compound 10a
Table 3.1 Physical data of synthesized compounds

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
<th>R₁</th>
<th>Reaction Time(^a) (min)</th>
<th>Yield(^{a,b}) (%)</th>
<th>m.p. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8a</td>
<td>CH₃</td>
<td></td>
<td>480/15</td>
<td>75/79</td>
<td>252-254</td>
</tr>
<tr>
<td>8b</td>
<td>CH₂-CH₃</td>
<td></td>
<td>490/16</td>
<td>73/77</td>
<td>235-237</td>
</tr>
<tr>
<td>8c</td>
<td>CH₃</td>
<td>CH₃</td>
<td>400/12</td>
<td>78/81</td>
<td>232-234</td>
</tr>
<tr>
<td>8d</td>
<td>CH₂-CH₃</td>
<td>CH₃</td>
<td>410/13</td>
<td>76/80</td>
<td>226-228</td>
</tr>
<tr>
<td>9a</td>
<td>CH₃</td>
<td>CH₃</td>
<td>150/8</td>
<td>82/86</td>
<td>225-227</td>
</tr>
<tr>
<td>9b</td>
<td>CH₂-CH₃</td>
<td>CH₃</td>
<td>165/9</td>
<td>80/84</td>
<td>213-215</td>
</tr>
<tr>
<td>9c</td>
<td>CH₃</td>
<td>H</td>
<td>175/10</td>
<td>78/83</td>
<td>198-200</td>
</tr>
<tr>
<td>9d</td>
<td>CH₂-CH₃</td>
<td>H</td>
<td>180/10</td>
<td>74/79</td>
<td>192-194</td>
</tr>
<tr>
<td>10a</td>
<td>CH₃</td>
<td>CH₃</td>
<td>165/7</td>
<td>85/87</td>
<td>195-197</td>
</tr>
<tr>
<td>10b</td>
<td>CH₂-CH₃</td>
<td>CH₃</td>
<td>170/8</td>
<td>83/86</td>
<td>160-162</td>
</tr>
<tr>
<td>10c</td>
<td>CH₃</td>
<td>H</td>
<td>175/8</td>
<td>84/86</td>
<td>152-155</td>
</tr>
<tr>
<td>10d</td>
<td>CH₂-CH₃</td>
<td>H</td>
<td>180/9</td>
<td>81/83</td>
<td>145-147</td>
</tr>
</tbody>
</table>

\(^a\)At reflux temperature/ultrasonic irradiation; \(^b\)Isolated yields

3.2.2 BIOLOGICAL ACTIVITY STUDIES

3.2.2.1 SCREENING OF ANTIOXIDANT ACTIVITY

The free radical activity of all the synthesized compounds was determined using the standard procedure given in Annexure I.
All the newly synthesized compounds were subjected to antioxidant activity using DPPH free radical scavenging assay method. The antioxidant studies indicate that compounds 10a and 10b showed moderate radical scavenging activity (25.50% and 28.14% respectively) comparable to that of BHT and ascorbic acid (100%), while compounds 10c and 10d showed lower activity. The compounds 8a, 8b, 9a, 9b, 9c and 9d showed least activity even at 100 µg/mL concentrations at 30 minutes incubation time. Free radical scavenging capacities of the synthesized phenothiazine compounds, ascorbic acid and BHT at 100 µg/mL concentration after half an hour incubation time in dark at room temperature, measured by DPPH assay are shown in Fig 3.3.

Table 3.2 Antioxidant activity of synthesized compounds 8a-d, 9a-d, and 10a-d using DPPH radical scavenging method

<table>
<thead>
<tr>
<th>Compound</th>
<th>Absorbance</th>
<th>%Antioxidant activity</th>
<th>Compound</th>
<th>Absorbance</th>
<th>%Antioxidant activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>8a</td>
<td>1.5930</td>
<td>13.83</td>
<td>9d</td>
<td>1.6458</td>
<td>10.98</td>
</tr>
<tr>
<td>8b</td>
<td>1.6355</td>
<td>11.50</td>
<td>10a</td>
<td>1.3772</td>
<td>25.50</td>
</tr>
<tr>
<td>9a</td>
<td>1.7655</td>
<td>4.50</td>
<td>10b</td>
<td>1.3285</td>
<td>28.14</td>
</tr>
<tr>
<td>9b</td>
<td>1.7575</td>
<td>4.93</td>
<td>10c</td>
<td>1.5311</td>
<td>17.18</td>
</tr>
<tr>
<td>9c</td>
<td>1.7465</td>
<td>5.53</td>
<td>10d</td>
<td>1.4956</td>
<td>19.10</td>
</tr>
<tr>
<td>Control*</td>
<td>1.8488</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*At 100 µg/mL concentration and BHT and ascorbic acid was used as a standard antioxidant.

The radical scavenging activity (RSA) for methanolic solutions of synthesized compounds are presented in (Table 3.2) and compared with those of standards BHT and ascorbic acid.
3.2.2.2 SCREENING OF ANTIBACTERIAL ACTIVITY

The synthesized different substituted phenothiazine derivatives 8(a-d), 9(a-d) and 10(a-d) were screened for their *in vitro* antibacterial activity against three “Gram +ve” bacterial strains, *S. aureus* (MTCC 3381), *P. aeruginosa* (MTCC 2295) and *B. cereus* (MTCC 8372) and two “Gram -ve” bacterial strains, *E. coli* (MTCC 1302), *K. pneumonia* (MTCC 3384) at 25, 50 μg/mL concentration in Mueller-Hinton agar medium using the standard procedure given in Annexure II. Tetracycline was used as standard drugs for antibacterial activity. The MIC (μg/mL) was determined for the *in vitro* assays for compounds 8(a-d), 9(a-d) and 10(a-d).

The synthesized compounds 10a, 10b and 8d showed good activity against *S. aureus, E. coli, P. aeruginosa, B. cereus* and *K. pneumonia*, whereas, compounds 8b, 8c, 9a and 9b shows good activity against *S. aureus* and *E. coli* and moderate activity against *P. aeruginosa, B. cereus* and *K. pneumonia*. Compounds 9a, 9c, 10c and 10d showed low activity against *K. pneumonia* and compound 9d showed low activity against *S. aureus* and compound 8a showed low activity against all the organisms. Zone of inhibition was determined for all the compounds and results are summarized in Table 3.3.

![Antioxidant activity of synthesized compounds and BHT, ascorbic acid using DPPH free radical scavenging method after 30 min. of incubation.](image-url)
Table 3.3 Antibacterial activities of the synthesized compounds 8a-d, 9a-d, and 10a-d.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Zone of bacterial inhibition in(^a) (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E. coli</td>
</tr>
<tr>
<td></td>
<td>25 µg/mL</td>
</tr>
<tr>
<td>8a</td>
<td>9</td>
</tr>
<tr>
<td>8b</td>
<td>10</td>
</tr>
<tr>
<td>8c</td>
<td>11</td>
</tr>
<tr>
<td>8d</td>
<td>12</td>
</tr>
<tr>
<td>9a</td>
<td>10</td>
</tr>
<tr>
<td>9b</td>
<td>11</td>
</tr>
<tr>
<td>9c</td>
<td>11</td>
</tr>
<tr>
<td>9d</td>
<td>10</td>
</tr>
<tr>
<td>10a</td>
<td>12</td>
</tr>
<tr>
<td>10b</td>
<td>13</td>
</tr>
<tr>
<td>10c</td>
<td>11</td>
</tr>
<tr>
<td>10d</td>
<td>10</td>
</tr>
</tbody>
</table>

(Ampicillin\(^b\) 25 µg/mL)

\(^a\)zone of inhibition in mm; \(^b\)Standard antibacterial drug;

3.3 CONCLUSIONS

Synthesis and characterization of a series of phenothiazine incorporated imidazole, xanthene dione and pyran derivatives are reported using conventional as well as ultrasonic irradiation methods. All the synthesized phenothiazine derivatives have been verified for their in vitro antioxidant activity using DPPH free radical scavenging method and data presented. Compounds 8(a-d), 9(a-d) and 10 (a-d) were screened for their in vitro antibacterial activity using agar well diffusion method. It could be seen that the phenothiazine incorporated pyran and imidazole derivatives exhibit a good antibacterial activity.
3.4 EXPERIMENTAL PROCEDURE

3.4.1 GENERAL

The chemicals used were obtained from SD Fine, Sisco Research Laboratory and Aldrich. All chemicals and solvents used for the synthesis were of analytical reagent grade. Melting points were determined by open capillary method and were uncorrected. IR spectra (umax in cm\(^{-1}\)) were recorded on a Shimadzu FT-IR 8300 spectrophotometer using KBr pellet. \(^1\)H and \(^{13}\)CNMR spectra were recorded on an Bruker Spectrospin DPX 400 MHz spectrometer in CDCl\(_3\) and DMSO-\(d_6\) used as a solvent and chemical shift values are recorded in units \(\delta\) (ppm) relative to tetramethylsilane (Me\(_4\)Si) as an internal standard. UV spectra were recorded on UV/Vis-spectrophotometer (Model V-670, JASCO UVVISNIR) under thermostatic conditions at 25\(^\circ\)C. Sonication reaction was performed by SONICS, Vibra Cell, VC 130 ultrasonic processor equipped with a 3 mm wide and 140 mm long probe, which was immersed directly into the reaction mixture. Mass spectra were recorded using high resolution mass spectrometer (JEOL 1600 HRMS) and the samples were dried under vacuum before analysis.

3.4.2 Procedure for the preparation of 10-alkyl phenothiazine 2(a-b):

Phenothiazine (1.0 mmol), iodoethane or iodomethane (3.0 mmol) and DMF (30 mL) were added in a 50 mL two-necked round bottom flask, solution was warmed to 75\(^\circ\)C, treated portion-wise with potassium tert-butoxide (1.5 mmol) and then stirred at 80\(^\circ\)C for 24 h. After the reaction was completed (monitored through TLC), it was cooled to room temperature and poured into ice water, the reaction mixture was extracted with chloroform (75 mL) and dried over Na\(_2\)SO\(_4\). Crude products obtained by removing the solvent were purified by column chromatography hexane/ethyl acetate (4:1) to give 2 (a-b) as a white solid (yield: 80-84%).

10-methyl-10H-phenothiazine (2a): mp. 95-97 \(^\circ\)C; IR (KBr) \(\nu_{max}\): 3053, 2981, 2937, 2826, 1899, 1788, 1591, 1570, 1483, 1456, 1440, 1384, 1327, 1280, 1232, 1130, 1109, 1033 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl\(_3\), ppm), \(\delta_H = 6.95-7.28\) (m, 6H, Ar-H of phenothiazine ring), 6.84 (d, 2H, J = 8.0Hz, C3 & C6-Ar-H of phenothiazine ring), 3.40
(s, 3H, CH₃); ¹³C NMR (125.757 MHz, CDCl₃, ppm), δC = 145.8, 127.4, 123.4, 122.4, 114.0, 35.3; HRMS (EI): m/z [M⁺] calcd. for C₁₃H₁₂NS: 213.0612; found: 212.2038.

10-ethyl-10H-phenothiazine (2b): mp. 101-103ºC; IR (KBr) νmax: 3055, 2960, 2879, 2816, 1568, 1489, 1456, 1446, 1330, 1286, 1259, 1163, 1136, 1107, 1039 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, ppm), δH = 6.90-7.28 (m, 8H, Ar-H of phenothiazine ring), 3.96 (d, 2H, J = 5.6Hz, CH₂), 1.46 (t, 3H, J = 5.4Hz, CH₃); ¹³C NMR (125.757 MHz, CDCl₃, ppm), δC = 145.0, 127.3, 127.2, 124.5, 122.3, 115.1, 41.7, 13.7; HRMS (EI): m/z [M⁺] calcd. for C₁₄H₁₃NS: 227.0769; found: 227.1685.

3.4.3 Procedure for the preparation of 10-alkyl-3-formylphenotheizine 3(a-b):

Phosphorus oxychloride (POCl₃) (4.1 mmol) was taken in a two necked round bottom flask and 4.7 mmol of freshly distilled N,N-dimethylformamide was added dropwise at 0°C to this under nitrogen atmosphere. A solution of (1.0 mmol) N-alkylphenothiazine 2(a-b) dissolved in dichloroethane 30 mL was added dropwise to POCl₃/DMF complex at 30°C. The reaction mixture was stirred at 80°C for 16 h. After the reaction was completed (through TLC monitoring), it was cooled to room temperature and poured into ice water. The obtained mixture was neutralized with NaHCO₃ extracted with chloroform (75 mL), dried over Na₂SO₄ and the solvent was removed by vacuum distillation. The crude product was purified by column chromatography using petroleum ether/ethylacetate solvent; yield (78-81%).

10-methyl-10H-phenothiazine-3-carbaldehyde (3a): mp. 105-107 ºC; IR (KBr) νmax: 3056, 2986, 2884, 2819, 2735, 1678, 1641, 1595, 1566, 1327, 1288, 1252, 1144, 1036 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm), δH = 9.79 (s, 1H, CHO), 7.00-7.74 (m, 7H, Ar-H of phenothiazine ring), 3.37 (s, 3H, CH₃); ¹³C NMR (100.612 MHz, CDCl₃, ppm),
δ_C = 190.6, 150.4, 143.6, 130.8, 130.4, 128.0, 127.2, 126.9, 123.5, 122.3, 121.1, 115.4, 114.5, 35.6; HRMS (EI): m/z [M^+] calcd. for C_{14}H_{11}NOS: 241.0561; found: 241.0069.

10-ethyl-3-formylphenothiazine (3b): mp. 110-112 °C; IR (KBr) _ν_ max: 3057, 2977, 2931, 2827, 2738, 1669, 1598, 1572, 1525, 1466, 1368, 1310, 1238, 1199, 1135, 1102, 1042 cm⁻¹; _¹_H NMR (400 MHz, CDCl₃, ppm), δ_H = 9.78 (s, 1H, CHO), 7.62 (d, 1H, _J_ = 8.4Hz, C7-Ar-H of phenothiazine ring), 7.56 (s, 1H, C8-Ar-H of phenothiazine ring), 6.89-7.26 (m, 5H, Ar-H of phenothiazine ring), 3.97 (d, 2H, _J_ = 6.4Hz, CH₂), 1.45 (d, 3H, _J_ = 6.4Hz, CH₃); _¹³_C NMR (100.612 MHz, CDCl₃, ppm), δ_C = 190.0, 150.3, 143.0, 130.9, 130.2, 128.2, 127.6, 127.5, 124.4, 123.5, 123.2, 115.6, 114.4, 42.4, 12.8; HRMS (EI): m/z [M^+] calcd. for C_{15}H_{13}NOS: 255.0718; found: 255.2485.

3.4.4 Procedure for the preparation of 3-(4,5-diphenyl-1H-imidazol-2-yl)-10-alkyl-10H-phenothiazine 8(a-d):

**Conventional method**

A mixture of 10-alkyl-10H-phenothiazine-3-carbaldehyde (1 mmol), benzil (1 mmol), ammonium acetate (5 mmol) and glacial acetic acid (10 mL) was refluxed for 6 hours. The progress of reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature, poured into cold water (200 mL) and neutralized with NH₄OH. The solid obtained was filtered, washed with excess of water and recrystallized from ethanol.
Ultrasonic irradiation method

A mixture of benzil (1 mmol), 10-alkyl-10H-phenothiazine-3-carbaldehyde (1 mmol) and ammonium acetate (5 mmol) in 5 mL of glacial acetic acid was taken in a 10 mL beaker. The ultrasound probe was immersed into the reaction mixture and irradiated for duration as indicated in Table 3.1. Sonication was performed at frequencies of 18 kHz and the progress of reaction was monitored by TLC. After completion of reaction, the mixture was poured into ice cooled water, the solid separated was filtered off, dried at room temperature and recrystallized from ethanol to get the corresponding imidazole derivatives.

3.4.4.1 3-(4,5-diphenyl-1H-imidazol-2-yl)-10-methyl-10H-phenothiazine (8a):

10-methyl-10H-phenothiazine-3-carbaldehyde (1 mmol), benzil (1 mmol) and ammonium acetate (5 mmol) were mixed in glacial acetic acid (10 mL) and the reaction was carried out as per general procedure given at 3.4.4. Title compound was obtained by recrystallization with ethanol; mp. 252-254 °C; IR (KBr) ν_max: 3421, 3057, 2962, 1602, 1462, 1450, 1334, 1257, 1139, 1072 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆, ppm), δ_H = 12.56 (s, 1H, NH), 7.92 (d, 1H, J = 8.0Hz, Ar-H of phenyl ring), 7.87 (s, 1H, Ar-H of phenyl ring), 6.98-7.55 (m, 15H, Ar-H of phenothiazine and phenyl ring), 3.35 (s, 3H, CH₃); ¹³C NMR (100.612 MHz, DMSO-d₆, ppm), δ_C = 145.1, 144.8, 144.7, 136.9, 135.1, 131.0, 128.6, 128.2, 123.2, 122.6, 122.3, 121.5, 114.7, 114.7, 35.2; HRMS (EI): m/z [M⁺] calcd. for C₂₈H₂₁N₃S: 431.1456; found: 431.1456.

3.4.4.2 3-(4,5-diphenyl-1H-imidazol-2-yl)-10-ethyl-10H-phenothiazine(8b):

10-ethyl-10H-phenothiazine-3-carbaldehyde (1 mmol), benzil (1 mmol) and ammonium acetate (5 mmol) were mixed in glacial acetic acid (10 mL) and the reaction was carried out as per general procedure given at 3.4.4. Title compound was obtained by
recrystallization with ethanol; mp. 235-237 °C; IR (KBr) ν<sub>max</sub>: 3421, 3132, 2987, 2935, 1604, 1462, 1382, 1328, 1251, 1136, 1072 cm<sup>-1</sup>; ¹H NMR (400 MHz, DMSO-<em>d</em><sub>6</sub>, ppm), δ<sub>H</sub> = 12.61 (s, 1H, NH), 7.89 (d, 1H, <em>J</em> = 8.4Hz, Ar-H of phenyl ring), 7.84 (s, 1H, o-Ar-H of phenyl ring), 6.93-7.52 (m, 15H, Ar-H of phenothiazine and phenyl ring), 3.95 (d, 2H, <em>J</em> = 6.0Hz, CH<sub>2</sub>), 1.32 (t, 3H, <em>J</em> = 5.4Hz, CH<sub>3</sub>); ¹³C NMR (100.612 MHz, DMSO-<em>d</em><sub>6</sub>, ppm), δ<sub>C</sub> = 144.7, 144.2, 143.8, 128.3, 127.7, 127.6, 127.0, 124.7, 124.6, 123.4, 123.0, 122.5, 122.2, 115.5, 115.4, 41.2, 12.6; HRMS (EI): m/z [M<sup>+</sup>] calcd. for C<sub>29</sub>H<sub>23</sub>N<sub>3</sub>S: 445.1613; found: 445.1617.

3.4.4.3 3-(4,5-dimethyl-1H-imidazol-2-yl)-10-methyl-10H-phenothiazine(8c):

10-methyl-10H-phenothiazine-3-carbaldehyde (1 mmol), biacetyl (1 mmol) and ammonium acetate (5 mmol) were mixed in glacial acetic acid (10 mL) and the reaction was carried out as per general procedure given at 3.4.4. Title compound was obtained by recrystallization with ethanol; mp. 232-234 °C; IR (KBr) ν<sub>max</sub>: 3401, 3138, 2977, 2930, 1598, 1478, 1368, 1332, 1259, 1130, 1095 cm<sup>-1</sup>; ¹H NMR (400 MHz, CDCl<sub>3</sub>, ppm), δ<sub>H</sub> = 7.98 (s, 1H, NH), 6.97-7.78 (m, 7H, Ar-H of phenothiazine ring), 3.35 (s, 3H, N-CH<sub>3</sub>) 2.11 (s, 6H, 2xCH<sub>3</sub>); ¹³C NMR (100.612 MHz, CDCl<sub>3</sub>, ppm), δ<sub>C</sub> = 144.7, 143.8, 141.6, 128.7, 127.6, 1264, 124.7, 123.0, 122.5, 121.3, 115.9, 114.9, 34.3, 10.3; HRMS (EI): m/z [M<sup>+</sup>] calcd. for C<sub>18</sub>H<sub>17</sub>N<sub>3</sub>S: 307.1143; found: 307.1148.

3.4.4.4 3-(4,5-dimethyl-1H-imidazol-2-yl)-10-ethyl-10H-phenothiazine(8d):

10-ethyl-10H-phenothiazine-3-carbaldehyde (1 mmol), biacetyl (1 mmol) and ammonium acetate (5 mmol) were mixed in glacial acetic acid (10 mL) and the reaction
was carried out as per general procedure given at 3.4.4. Title compound was obtained by recrystallization with ethanol; mp. 226-228 °C; IR (KBr) $\nu_{\text{max}}$: 3394, 3126, 2966, 2825, 1610, 1465, 1388, 1334, 1250, 1123, 1085 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$, ppm), $\delta_{\text{H}} = 7.70$ (d, 1H, $J = 7.6$Hz, NH), 6.95-7.64 (m, 7H, Ar-H of phenothiazine ring), 3.95 (d, 2H, $J = 6.4$Hz, N-CH$_2$), 2.16 (s, 6H, 2xCH$_3$), 1.31 (d, 3H, $J = 5.6$Hz, CH$_3$); $^{13}$C NMR (100.612 MHz, CDCl$_3$, ppm), $\delta_{\text{C}} = 144.9, 143.5, 141.2, 127.9, 127.1, 126.2, 124.5, 123.2, 122.8, 121.9, 115.7, 115.5, 41.2, 12.5, 9.8; HRMS (EI): m/z [M$^+$] calcd. for C$_{19}$H$_{19}$N$_3$S: 321.1300; found: 321.1295.

3.4.5 Procedure for the preparation of 3,3,6,6-tetramethyl-9-(10-methyl-10H-phenothiazin-3-yl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (9a-d).

**Conventional method**

A mixture of Dimedone (2 mmol), 10-alkyl-10H-phenothiazine-3-carbaldehyde (1 mmol), $p$-TSA (15 mol%), ethanol (10 mL) were taken in a 50 mL round bottomed flask and the reaction mixture was stirred at 80°C for time periods as given in Table 3.1. The reaction was monitored by TLC. After completion, the reaction mixture was poured in to ice cooled water, the solid separated was filtered off, washed with excess amount of water (15 mL) and residue recrystallized from ethanol to get the pure product.

**Ultrasonic irradiation method**

A mixture of 10-alkyl-10H-phenothiazine-3-carbaldehyde (1 mmol), dimerdone (2 mmol) and $p$-TSA (15 mol%) in 10 mL EtOH was taken in a 25 mL beaker and irradiated using ultrasonic probe at frequencies of 22 kHz at 60°C for the required reaction time (Table 2). After the completion of the reaction (indicated by TLC), the reaction mixture was poured into ice water, the precipitated solid was collected by filtration, washed with water and dried. The resulting solid products were recrystallized from ethanol.
3.4.5.1 3,3,6,6-tetramethyl-9-(10-methyl-10H-phenothiazin-3-yl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (9a):

Dimedone (2 mmol), 10-methyl-10H-phenothiazine-3-carbaldehyde (1 mmol), p-TSA (15 mol%) were mixed with 10 mL of ethanol and the reaction was carried out as per general procedure given at 3.4.5. Title compound was obtained by recrystallization with ethanol; mp. 225-227 ºC; IR (KBr) \( \nu_{\text{max}} \): 3178, 2958, 2872, 1664, 1622, 1577, 1465, 1359, 1328, 1199, 1165, 1138 cm\(^{-1}\); \(^{1}\)H NMR (400 MHz, CDCl\(_3\), ppm), \( \delta_H = 7.18 \) (d, 2H, \( J = 8.0 \)Hz, C7 & C8-Ar-H of phenothiazine ring), 6.66-7.14 (m, 5H, Ar-H of phenothiazine ring), 4.65 (s, 1H, CH), 3.29 (s, 3H, N-CH\(_3\)), 2.45 (q, 4H, \( J = 16.0 \)Hz, 2xCH\(_2\)), 2.18 (q, 4H, \( J = 16.2 \)Hz, 2xCH\(_2\)), 1.08 (s, 6H, 2xCH\(_3\)), 1.00 (s, 6H, 2xCH\(_3\)); \(^{13}\)C NMR (100.612 MHz, CDCl\(_3\), ppm), \( \delta_C = 196.5, 162.3, 145.9, 144.2, 138.7, 128.2, 127.4, 127.1, 126.6, 123.4, 122.8, 122.2, 115.4, 114.0, 113.7, 50.8, 40.9, 35.3, 32.3, 31.0, 29.2, 27.7; HRMS (EI): m/z [M\(^+\)] calcd. for C\(_{30}\)H\(_{31}\)NO\(_3\)S: 485.2025; found: 485.2020.

3.4.5.2 9-(10-ethyl-10H-phenothiazin-3-yl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (9b):

Dimedone (2 mmol), 10-ethyl-10H-phenothiazine-3-carbaldehyde (1 mmol), p-TSA (15 mol%) were mixed with 10 mL of ethanol and the reaction was carried out as per general procedure given at 3.4.5. Title compound was obtained by recrystallization with ethanol; mp. 213-215 ºC; IR (KBr) \( \nu_{\text{max}} \): 2949, 2868, 1656, 1618, 1573, 1463, 1359, 1327, 1203, 1138 cm\(^{-1}\); \(^{1}\)H NMR (400 MHz, CDCl\(_3\), ppm), \( \delta_H = 7.15 \) (d, 1H, \( J = 8.0 \)Hz, C7-Ar-H of phenothiazine ring), 7.04-7.11 (m, 2H, Ar-H of phenothiazine ring), 6.91 (s, 1H, C6-Ar-H of phenothiazine ring), 6.76-6.86 (m, 3H, Ar-H of phenothiazine ring), 4.64 (s, 1H, CH), 3.84 (q, 2H, \( J = 7.6 \)Hz, N-CH\(_2\)), 2.45 (q, 4H, \( J = 16.0 \)Hz, 2xCH\(_2\)), 2.19 (q, 4H, \( J = 17.2 \)Hz, 2xCH\(_2\)), 1.35 (t, 3H, \( J = 6.6 \)Hz, CH\(_3\)), 1.08 (s, 6H, 2xCH\(_3\)), 1.01
(s, 6H, 2xCH₃); ¹³C NMR (100.612 MHz, CDCl₃, ppm), δC = 196.5, 162.3, 144.9, 143.4, 138.5, 128.0, 127.3, 127.1, 126.7, 124.3, 123.6, 122.0, 115.4, 114.9, 114.5, 50.8, 41.7, 40.9, 32.3, 30.9, 29.1, 27.7, 13.0; HRMS (EI): m/z [M⁺] calcd. for C₃₁H₃₃NO₃S: 499.2181; found: 499.2175.

3.4.5.3 9-(10-methyl-10H-phenothiazin-3-yl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (9c):
Cyclohexane-1,3-dione (2 mmol), 10-methyl-10H-phenothiazine-3-carbaldehyde (1 mmol), p-TSA (15 mol%) were mixed with 10 mL of ethanol and the reaction was carried out as per general procedure given at 3.4.5. Title compound was obtained by recrystallization with ethanol; mp. 198-200 °C; IR (KBr) νmax: 2923, 2786, 1659, 1612, 1568, 1452, 1349, 1307, 1213, 1129 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm), δH = 7.24 (d, 1H, J = 8.4Hz, C7-Ar-H of phenothiazine ring), 7.09-7.12 (m, 2H, Ar-H of phenothiazine ring), 6.90 (s, 1H, C6-Ar-H of phenothiazine ring), 4.70 (s, 1H, CH), 3.30 (s, 3H, N-CH₃), 2.51-2.67 (m, 4H, 2xCH₂), 2.25-2.38 (m, 4H, 2xCH₂), 1.99-2.01 (m, 4H, 2xCH₂); ¹³C NMR (100.612 MHz, CDCl₃, ppm), δC = 196.7, 164.0, 146.0, 144.3, 139.0, 128.4, 127.4, 127.1, 126.5, 123.4, 122.9, 122.3, 116.7, 114.0, 113.7, 37.0, 36.8, 35.3, 30.9, 27.2, 20.3; HRMS (EI): m/z [M⁺] calcd. for C₂₆H₂₃NO₃S: 429.1399; found: 429.1392.
3.4.5.4 9-(10-ethyl-10H-phenothiazin-3-yl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (9d):

Cyclohexane-1,3-dione (2 mmol), 10-methyl-10H-phenothiazine-3-carbaldehyde (1 mmol), p-TSA (15 mol%) were mixed with 10 mL of ethanol and the reaction was carried out as per general procedure given at 3.4.5. Title compound was obtained by recrystallization with ethanol; mp. 192-194 °C; IR (KBr) \( \nu_{\text{max}} \): 2935, 2872, 1660, 1625, 1494, 1463, 1359, 1327, 1130 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm), \( \delta_H = 7.20 \) (d, 2H, J = 8.0Hz, C7-Ar-H of phenothiazine ring), 6.71-7.07 (m, 5H, Ar-H of phenothiazine ring), 4.69 (s, 1H, CH), 3.65 (q, 2H, J = 7.2Hz, N-CH\(_2\)), 2.51-2.66 (m, 4H, 2xCH\(_2\)), 2.30-2.38 (m, 4H, 2xCH\(_2\)), 1.72-2.20 (m, 4H, 2xCH\(_2\)); \(^{13}\)C NMR (100.612 MHz, CDCl\(_3\), ppm), \( \delta_C = 196.8, 164.0, 145.1, 143.5, 138.7, 128.3, 127.3, 127.2, 126.6, 124.3, 123.7, 122.1, 116.7, 115.0, 114.6, 41.7, 37.0, 30.7, 27.2, 20.3, 13.1; HRMS (EI): m/z [M\(^+\)] calcd. for C\(_{27}\)H\(_{25}\)NO\(_3\)S: 443.1555; found: 443.1550.

3.4.6 Procedure for the preparation of 2-amino-7,7-dimethyl-4-(10-methyl-10Hphenothiazin-3-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (10 a-d).

**Conventional method**

A mixture of 10-alkyl-10H-phenothiazine-3-carbaldehyde (1 mmol), malononitrile (1 mmol), 1,3-diketone (1 mmol) and K\(_3\)PO\(_4\) (21 mg, 15 mol%) in 20% ethanol (5 mL) was refluxed with stirring at 80°C for the time given in Table 3.1 (progress of reaction being monitored by TLC using hexane/ethyl acetate as eluent). The crude product got precipitated from the reaction mixture by cooling, the solid was filtered and recrystallized with ethanol to get pure product.
Ultrasonic irradiation method

A mixture of malononitrile (1.0 mmol), 10-alkyl-10H-phenothiazine-3-carbaldehyde (1.0 mmol), 1,3-diketones (1.0 mmol) in the presence of a catalytic amount of K$_3$PO$_4$ (21 mg, 15 mol%) in 20% ethanol (5 mL) as a mixture was irradiated using ultrasound probe at frequencies of 22 kHz for the time periods given in Table.3.1. After completion of the reaction as indicated by TLC, the reaction mixture was filtered; the precipitate was washed with water and purified by recrystallization from hot ethanol.

3.4.6.1 2-amino-7,7-dimethyl-4-(10-methyl-10H-phenothiazin-3-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (10a):
A mixture of 10-methyl-10H-phenothiazine-3-carbaldehyde (1 mmol), malononitrile (1 mmol), dimedone (1 mmol) and K$_3$PO$_4$ (21 mg, 15 mol %) were mixed with 50 mL of 20% ethanol and the reaction was carried out as per general procedure given at 3.4.6. Title compound was obtained by recrystallization with ethanol; mp. 195-197 °C; IR (KBr) $\nu_{\text{max}}$: 3442, 3257, 2958, 2891, 2189, 1687, 1672, 1598, 1467, 1402, 1361, 1330, 1249, 1203, 1139, 1103, 1037 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$, ppm), $\delta$H = 6.84-7.20 (m, 5H, Ar-H of phenothiazine ring), 6.71 (d, 1H, $J = 7.6$Hz, C2-Ar-H of phenothiazine ring), 6.66 (d, 1H, $J = 7.6$Hz, C4-Ar-H of phenothiazine ring), 4.49 (s, 2H, NH$_2$), 4.25 (s, 1H, CH), 3.27 (s, 3H, N-CH$_3$), 2.37 (q, 2H, $J = 17.8$Hz, CH$_2$), 2.14 (q, 2H, $J = 16.6$Hz, CH$_2$), 1.03 (s, 3H, CH$_3$), 0.97 (s, 3H, CH$_3$); $^{13}$C NMR (100.612 MHz, CDCl$_3$, ppm), $\delta$C = 195.8, 161.3, 157.4, 145.7, 144.8, 137.5, 127.4, 127.2, 125.8, 123.5, 123.0, 122.3, 118.5, 113.9, 113.8, 63.2, 50.6, 40.6, 35.2, 34.6, 32.2, 28.6, 27.8; HRMS (EI): m/z [M$^+$] calcd. for C$_{25}$H$_{23}$N$_3$O$_2$S: 429.1511; found: 429.1514.
3.4.6.2 2-amino-4-(10-ethyl-10H-phenothiazin-3-yl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (10b):

A mixture of 10-methyl-10H-phenothiazine-3-carbaldehyde (1 mmol), malononitrile (1 mmol), dimedone (1 mmol) and K$_3$PO$_4$ (21 mg, 15 mol %) were mixed with 50 mL of 20% ethanol and the reaction was carried out as per general procedure given at 3.4.6. Title compound was obtained by recrystallization with ethanol; mp. 160-162 °C; IR (KBr) $\nu_{\text{max}}$: 3352, 3255, 3170, 2958, 2933, 2191, 1680, 1651, 1606, 1485, 1385, 1251, 1215, 1138, 1035 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$, ppm), $\delta_H$ = 6.83-7.20 (m, 5H, Ar-H of phenothiazine ring), 6.76 (d, 1H, $J = 6.8$Hz, C2-Ar-H of phenothiazine ring), 6.71 (d, 1H, $J = 7.2$Hz, C2-Ar-H of phenothiazine ring), 4.45 (s, 2H, NH$_2$), 4.24 (s, 1H, CH), 3.82 (s, 2H, N-CH$_2$), 2.37 (q, 2H, $J = 17.6$Hz, CH$_2$), 2.15 (s, 2H, CH$_2$), 1.32 (s, 3H, CH$_3$), 1.03 (s, 3H, CH$_3$), 0.99 (s, 3H, CH$_3$); $^{13}$C NMR (100.612 MHz, CDCl$_3$, ppm), $\delta_C$ = 195.8, 161.3, 157.3, 144.7, 144.0, 137.3, 127.2, 127.1, 126.9, 126.0, 124.4, 124.0, 122.1, 118.5, 114.9, 114.8, 113.8, 63.4, 50.6, 41.7, 40.6, 34.5, 32.2, 28.6, 27.9, 12.9; HRMS (EI): m/z [M$^+$] calcd. for C$_{26}$H$_{25}$N$_3$O$_2$S: 443.1667; found: 443.1663.

3.4.6.3 2-amino-4-(10-methyl-10H-phenothiazin-3-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (10c):

A mixture of 10-methyl-10H-phenothiazine-3-carbaldehyde (1 mmol), malononitrile (1 mmol), cyclohexane-1,3-dione (1 mmol) and K$_3$PO$_4$ (21 mg, 15 mol %) were mixed with 50 mL of 20% ethanol and the reaction was carried out as per general procedure given at 3.4.6. Title compound was obtained by recrystallization with ethanol; mp. 152-155 °C; IR (KBr) $\nu_{\text{max}}$: 3360, 3325, 2922, 2203, 2191, 1680, 1647, 1606, 1566, 1485, 1365, 1334, 1261, 1126 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$, ppm), $\delta_H$ = 6.91-7.23 (m, 5H, Ar-H of phenothiazine ring), 6.86 (d, 1H, $J = 7.6$Hz, C2-Ar-H of phenothiazine ring), 6.75 (d, 1H, $J = 7.2$ Hz, 4-Ar-H of phenothiazine ring), 4.52 (s, 2H, NH$_2$), 4.34 (s, 1H,
3.32 (s, 3H, N-CH₃), 2.40-2.59 (m, 2H, CH₂), 2.28-2.35 (m, 2H, CH₂), 2.02-2.20 (m, 2H, CH₂); ¹³C NMR (100.612 MHz, CDCl₃, ppm), δC = 194.2, 157.4, 151.2, 143.2, 131.6, 129.0, 127.9, 127.3, 125.8, 125.3, 124.3, 124.1, 122.3, 121.9, 115.0, 114.3, 114.0, 60.5, 40.1, 36.7, 35.8, 26.9, 20.0; HRMS (EI): m/z [M⁺] calcd. for C₂₃H₁₉N₅O₂S: 401.1198; found: 401.1192.

3.4.6.4 2-amino-4-(10-ethyl-10H-phenothiazin-3-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (10d):
A mixture of 10-ethyl-10H-phenothiazine-3-carbaldehyde (1 mmol), malononitrile (1 mmol), cyclohexane-1,3-dione (1 mmol) and K₃PO₄ (21 mg, 15 mol %) were mixed with 50 mL of 20% ethanol and the reaction was carried out as per general procedure given at 3.4.6. Title compound was obtained by recrystallization with ethanol; mp. 145-147 ºC; IR (KBr) νmax: 3382, 3268, 2922, 2190, 1679, 1648, 1600, 1576, 1483, 1365, 1334, 1271, 1120 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm), δH = 6.90-7.25 (m, 5H, Ar-H of phenothiazine ring), 6.82 (d, 1H, J = 8.0Hz, C2-Ar-H of phenothiazine ring), 6.73 (d, 1H, J = 8.0Hz, C4-Ar-H of phenothiazine ring), 4.50 (s, 2H, NH₂), 4.33 (s, 1H, CH), 3.48 (s, 2H, N-CH₃), 2.57 (q, 2H, J = 6.6Hz, CH₂), 2.02 (m, 2H, CH₂), 1.45-1.55 (m, 2H, CH₂), 1.25 (s, 3H, CH₃); ¹³C NMR (100.612 MHz, CDCl₃, ppm), δC = 194.4, 157.5, 150.4, 144.2, 131.6, 129.4, 127.9, 127.6, 127.3, 124.2, 122.3, 115.3, 115.1, 114.9, 114.5, 59.8, 42.8, 41.8, 36.9, 27.1, 20.2, 13.1; HRMS (EI): m/z [M⁺] calcd. for C₂₄H₂₁N₃O₂S: 415.1354; found: 415.1350.
3.5 SPECTRAL DATA

$^1$H NMR, $^{13}$C NMR and Mass Spectra of compound 8a, 8b, 9b, 10a & 10b
3.5.1 $^1H$ NMR spectrum of 3-(4,5-diphenyl-1H-imidazol-2-yl)-10-methyl-10H-phenothiazine (8a):

3.5.2 $^{13}C$ NMR spectrum of 3-(4,5-diphenyl-1H-imidazol-2-yl)-10-methyl-10H-phenothiazine (8a):
3.5.3 *Mass spectrum* of 3-(4,5-diphenyl-1H-imidazol-2-yl)-10-methyl-10H-phenothiazine (8a):

![Mass spectrum of 3-(4,5-diphenyl-1H-imidazol-2-yl)-10-methyl-10H-phenothiazine (8a)](image)

3.5.4 $^1$H NMR spectrum of 3-(4,5-diphenyl-1H-imidazol-2-yl)-10-ethyl-10H-phenothiazine (8b):

![$^1$H NMR spectrum of 3-(4,5-diphenyl-1H-imidazol-2-yl)-10-ethyl-10H-phenothiazine (8b)](image)
3.5.5 $^{13}$C NMR spectrum of 3-(4,5-diphenyl-1H-imidazol-2-yl)-10-ethyl-10H-phenothiazine (8b):

![C NMR spectrum](image)

3.5.6 Mass spectrum of 3-(4,5-diphenyl-1H-imidazol-2-yl)-10-ethyl-10H-phenothiazine (8b):

![Mass spectrum](image)
3.5.7 $^1H$ NMR spectrum of 9-(10-ethyl-10H-phenothiazin-3-yl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (9b):

![NMR Spectrum Image]

3.5.8 $^{13}C$ NMR spectrum of 9-(10-ethyl-10H-phenothiazin-3-yl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (9b):

![NMR Spectrum Image]
3.5.9 *Mass spectrum of* 9-(10-ethyl-10H-phenothiazin-3-yl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (*9b*):

3.5.10 *FT IR spectrum of* 2-amino-7,7-dimethyl-4-(10-methyl-10H-phenothiazin-3-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (*10a*):
3.5.11 $^1$H NMR spectrum of 2-amino-7,7-dimethyl-4-(10-methyl-10H-phenothiazin-3-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (10a):

![H NMR spectrum of 2-amino-7,7-dimethyl-4-(10-methyl-10H-phenothiazin-3-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (10a)](image)

3.5.12 $^{13}$C NMR spectrum of 2-amino-7,7-dimethyl-4-(10-methyl-10H-phenothiazin-3-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (10a):

![C NMR spectrum of 2-amino-7,7-dimethyl-4-(10-methyl-10H-phenothiazin-3-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (10a)](image)
3.5.13 Mass spectrum of 2-amino-7,7-dimethyl-4-(10-methyl-10H-phenothiazin-3-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (10a):

![Mass spectrum diagram]

3.5.14 FT IR spectrum of 2-amino-4-(10-ethyl-10H-phenothiazin-3-yl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (10b):

![FT IR spectrum diagram]
3.5.15 $^1H$ NMR spectrum of 2-amino-4-(10-ethyl-10H-phenothiazin-3-yl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (10b):

3.5.16 $^{13}C$ NMR spectrum of 2-amino-4-(10-ethyl-10H-phenothiazin-3-yl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (10b):
3.5.17 Mass spectrum of 2-amino-4-(10-ethyl-10H-phenothiazin-3-yl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (10b):