AN EXPERIMENTAL STUDY OF SPECIAL LEAVING GROUP BEHAVIOR IN THE REACTION OF ARYLIDENEBARBITURIC ACIDS WITH CARBON NUCLEOPHILES

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Abstract – The reaction of benzylidenebarbituric acid and 1,3-dimethylbenzylidenebarbituric acid with malononitrile as well as with dimedone in piperidine is investigated. In reaction with malononitrile, substituted pyridine-3,5-dicarbonitriles are obtained, while with dimedone, xanthenes and/or 6-hydroxy-5-((2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-enyl)(aryl)methyl)-1,3-dimethyl pyrimidine-2,4(1H,3H)-dione derivatives are isolated.

Benzylidenebarbituric acids which are potential organic oxidizers 1,2 are used in preparation of oxadeazaflavines, 3 unsymmetrical synthesis of disulphides, 4 synthesis of Merocyanine dyes 5 and as antibacterial agents. 6 Benzylidenebarbiturate derivatives such as benzylidene(thio)barbiturate-β-D-glycosides act as mushroom tyrosinase inhibitors. 7,8 Furthermore, benzylidenebarbituric acids are important building blocks in the synthesis of pyrazolo[3,4-d]pyrimidines and pyrido[2,3-d]pyrimidines, 9-11 which show a broad spectrum of biological activities. 12-14 Some of these compounds have also been studied as nonlinear optical materials. 15

The nucleophilic attack at the electron-deficient double bond of Michael acceptors has long been a field of great interest in physical organic chemistry. 16,17 Benzylidenebarbituric and thiobarbituric acids are characterized by their strongly polarized exocyclic double bond with a positive partial charge on the
The reaction of enones 1a-e with two equivalents of dimedone (2) in the presence of an excess piperidine in EtOH furnished xanthene derivatives 3a-e. Under the same conditions the N,N-dimethylderivatives 1f-j gave 6-hydroxy-5-((2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-enyl)(aryl)methyl)-1,3-dimethylpyrimidine-2,4-(1H,3H)-dione derivatives 4f-j, while the compounds 1k and 1l did not react at all (Scheme 1 and Table 1).

Along with the formation of products 3a-e, barbiturate salts precipitate from the reaction mixture. No such precipitations were observed in formation of 4f-j. To investigate further, the reaction of 1b,c,e with 1,3-indanedione was also carried out which lead to the corresponding 2-benzylidene-1,3-indanediones 5b,c,d containing no barbituric acid moiety.

The formation of xanthenes 3 could be rationalized by an initial Michael addition of 2, followed by a sequence involving concurrent retro-Michael elimination of the barbiturate moiety, followed by the second Michael addition of 2 and cyclization (Scheme 2).
The presence of hydrogens or nitrogen atoms is clearly a determining factor in the type of products formed. The reaction of enones 1a-f with two equivalent of malononitrile (6) in presence of an excess amount of piperidine in EtOH afforded pyridinedinitrile derivatives 7a-e in 45-65% yields, presumably through a similar addition-elimination-addition sequence as dimedone 2 and final cyclization as shown (Scheme 3 and Table 2).

**Table 2. Reaction of enones 1a-f with malononitrile**

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>Ar</th>
<th>product</th>
<th>Yield (%)</th>
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<tr>
<td>a</td>
<td>H</td>
<td>C₆H₅-</td>
<td>7a</td>
<td>60</td>
</tr>
<tr>
<td>b</td>
<td>H</td>
<td>4-MeOC₆H₅-</td>
<td>7b</td>
<td>45</td>
</tr>
<tr>
<td>c</td>
<td>H</td>
<td>4-ClC₆H₅-</td>
<td>7c</td>
<td>63</td>
</tr>
<tr>
<td>d</td>
<td>H</td>
<td>2-ClC₆H₅-</td>
<td>7d</td>
<td>65</td>
</tr>
<tr>
<td>e</td>
<td>H</td>
<td>4-MeC₆H₅-</td>
<td>7e</td>
<td>53</td>
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<tr>
<td>f</td>
<td>Me</td>
<td>C₆H₅-</td>
<td>7a</td>
<td>58</td>
</tr>
</tbody>
</table>

In products isolated from the reactions 1a-f with malononitrile, barbituric acid units are absent. A possible mechanism is shown in Scheme 3.
The reaction of aryldenebarbituric acids with dimedone was found to give two types of products depending upon the presence of N-H bonds or otherwise. Starting materials 1a-e gave xanthenes where as 1f-j gave substituted pyrimidinediones. Similar results were obtained from the reaction of malononitrile with aryldenebarbituric acids except for compound 1f.

EXPERIMENTAL

1. Instruments and characterization
Melting points were measured on an Electrothermal 9200 apparatus and are uncorrected. $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker DRX-300 AVANCE spectrometer at 300.13 MHz. IR spectra were recorded on a Bomem MB-Series FTIR. Electrospray ionization (ESI) mass spectrometry (MS) experiments were performed on Finnigan-MAT-8430 mass spectrometer, at 70 eV, in m/z. Elemental analyses were carried out on a Heraeus CHN-O-Rapid analyzer.

2. General procedure for the preparation of 5-((aryl)(2-hydroxy-6-oxocyclohex-1-enyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (4f-j).
Piperidine (8 mmol) was added dropwise to a solution of enone 1 (2 mmol) and dimedone (2, 4 mmol) in absolute EtOH (15 mL) at room temperature. The reaction mixture was refluxed until the disappearance of the starting material (4-6 h), (monitored by TLC), solution was evaporated and was diluted with H$_2$SO$_4$ (10%) (15 mL), precipitate solid product was recrystallized from water/acetone.

2.1. 6-Hydroxy-5-((2-hydroxy-6-oxocyclohex-1-enyl)(phenyl)methyl)-1,3-dimethylpyrimidine-2,4-(1H,3H)-dione (4f).
Yield 70%. Mp 186-188°C. IR (KBr cm$^{-1}$) 2200-3383, 1700, 1631, 1616. $^1$H NMR (CDCl$_3$) $\delta$: 1.15 (s, 3H, Me), 1.28 (s, 3H, Me), 2.30-2.54 (m, 4H, 2CH$_2$), 3.36 (s, 3H, N-Me), 3.45 (s, 3H, N-Me), 5.58 (s, 1H, CH), 7.12-7.33 (m, 5H, aryl), 10.6 (br, 1H, OH), 12.85 (s, 1H, OH). $^{13}$C NMR (CDCl$_3$) $\delta$: 27.1, 28.9, 29.2, 29.7, 31.12, 33.6, 45.7, 47.0, 92.4, 116.4, 126.2, 126.5, 128.3, 137.2, 150.7, 162.3, 164.2, 190.6, 191.5. MS: m/z (%) = 384 (M$^+$, 68), 263 (8), 243 (26), 227 (100), 171 (14), 156 (22), 129 (12), 116 (19), 102 (27), 83 (13), 71 (9), 55 (14), 42 (33). Anal. Calcd for C$_{21}$H$_{24}$N$_2$O$_5$: C, 65.61; H, 6.29; N, 7.29. Found: C, 65.71; H, 6.32; N, 7.08.

2.2. 6-Hydroxy-5-((2-hydroxy-6-oxocyclohex-1-enyl)(p-tolyl)methyl)-1,3-dimethylpyrimidine-2,4-(1H,3H)-dione (4g).
Yield 68%. Mp 176-179°C. IR (KBr cm$^{-1}$) 2200-3200, 1703, 1604. $^1$H NMR (CDCl$_3$) $\delta$: 1.10 (s, 3H, Me), 1.27 (s, 3H, Me), 2.32 (s, 3H, Me-aryl), 2.34-2.53 (m, 4H, 2CH$_2$), 3.35 (s, 3H, N-Me), 3.44 (s, 3H, N-Me), 5.53 (s, 1H, CH), 7.01 (d, $J$ = 7.7 Hz, 2H, aryl) 7.10 (d, $J$ = 8.1 Hz, 2H, aryl), 11.0 (br, 1H, OH), 12.8 (s, 1H, OH). $^{13}$C NMR (CDCl$_3$) $\delta$: 20.9, 27.1, 28.8, 29.2, 29.9, 31.2, 33.2,
2.3. 5-((4-Chlorophenyl) (2-hydroxy-6-oxocyclohex-1-enyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (4h). Yield 62%. Mp 176 °C. IR (KBr cm⁻¹) 2200-3385, 1703, 1604. ¹H NMR (CDCl₃) δ: 1.13 (s, 3H, Me), 1.26 (s, 3H, Me), 2.29-2.53 (m, 4H, 2CH₂), 3.35 (s, 3H, N-Me), 3.44 (s, 3H, N-Me), 5.50 (s, 1H, CH), 7.05 (d, J = 11.4 Hz, 2H, aryl) 7.25 (d, J = 11.4 Hz, 2H, aryl), 9.50 (br, 1H, OH), 12.79 (s, 1H, OH). ¹³C NMR (CDCl₃) δ: 27.1, 28.9, 29.1, 29.9, 31.2, 33.3, 46.0, 46.5, 47.0, 92.2, 116.1, 128.0, 128.4, 131.9, 135.8, 150.6, 162.3, 146.1, 191.1, 191.2. MS: m/z (%) = 418 (M⁺, 7), 400 (11), 289 (30), 207 (15), 186 (13), 167 (43), 149 (100), 80 (48), 64 (59), 41 (43). Anal. Calcd for C₂₁H₂₃N₂O₅Cl: C, 60.22; H, 5.53; N, 6.69. Found: C, 60.83; H, 5.43; N, 6.75.

2.4. 6-Hydroxy-5-((2-hydroxy-6-oxocyclohex-1-enyl)(3-nitrophenyl)methyl)-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (4i). Yield 59%. Mp 180-182 °C. IR (KBr cm⁻¹) 2200-3392, 1703, 1609. ¹H NMR (CDCl₃) δ: 1.16 (s, 3H, Me), 1.33 (s, 3H, Me), 2.32-2.58 (m, 4H, 2CH₂), 3.36 (s, 3H, N-Me), 3.47 (s, 3H, N-Me), 5.58 (s, 1H, CH), 7.47 (d, J = 4.5 Hz, 2H, aryl), 8.02 (d, J = 1.1 Hz, H, aryl), 8.09 (m, 1H, aryl), 9.80 (br, 1H, OH), 12.79 (s, 1H, OH). ¹³C NMR (CDCl₃) δ: 27.0, 28.9, 29.3, 29.9, 31.2, 33.72, 46.1, 46.9, 91.5, 115.7, 121.4, 122.4, 129.2, 132.7, 139.9, 148.5, 150.5, 162.4, 164.2, 191.4, 191.6. MS: m/z (%) = 429 (M⁺, 11), 378 (11), 289 (27), 273 (60), 256 (100), 242 (15), 226 (44), 189 (19), 156 (61), 129 (29), 115 (28), 101 (37), 69 (21), 55 (43), 42 (89). Anal. Calcd for C₂₁H₂₃N₃O₇: C, 58.71; H, 5.40; N, 9.79. Found: C, 58.94; H, 5.41; N, 9.56.

2.5. 5-((4-Bromophenyl) (2-hydroxy-6-oxocyclohex-1-enyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (4j). Yield 70%. Mp 193-195 °C. IR (KBr cm⁻¹) 2200-3391, 1705, 1607. ¹H NMR (CDCl₃) δ: 1.14 (s, 3H, Me), 1.26 (s, 3H, Me), 2.29-2.53 (m, 4H, 2CH₂), 3.35 (s, 3H, N-Me), 3.44 (s, 3H, N-Me), 5.48 (s, 1H, CH), 7.00 (d, J = 8.5 Hz, 2H, aryl) 7.41 (d, J = 8.5 Hz, 2H, aryl), 9.65 (br, 1H, OH), 12.70 (s, 1H, OH). ¹³C NMR (CDCl₃) δ: 27.1, 29.2, 29.5, 29.9, 31.2, 33.3, 46.0, 46.9, 92.1, 116.1, 120.0, 128.5, 131.2, 136.4, 150.6, 162.3, 164.1, 191.1, 191.2. MS: m/z (%) = 464 (M⁺, 33), 462 (33), 323 (20), 307 (53), 227 (100), 209 (7), 196 (10), 171 (26), 141 (11), 115 (23), 101 (16), 83 (16), 69 (10), 55 (20), 42 (40). Anal. Calcd for C₂₁H₂₃N₂O₅Br: C, 54.44; H, 5.40; N, 6.05. Found: C, 54.86; H, 5.44; N, 6.04.
3. General procedure for the preparation of 9-(aryl)-3,4,6,7-tetrahydro-3,3,6,6-tetramethylanthracene-1,8(2H,5H,9H,10H)-dione (3a-e).

Piperidine (8 mmol) was added dropwise to a solution of enone 1 (2 mmol) and dimedone (2, 4 mmol) in absolute EtOH (15 mL) at room temperature. The reaction mixture was refluxed until the disappearance of the starting material (3.5-5 h), (monitored by TLC) and barbituric acid salt was filtered off. The filtrate was evaporated and was diluted with H$_2$SO$_4$ (10%) (15 mL), precipitate solid product was recrystallized from water/acetone.

3.1. 3,4,6,7-Tetrahydro-3,3,6,6-tetramethyl-9-phenyl-2H-xanthene-1,8(5H,9H)-dione (3a). Yield 75%. Mp 199-203 °C. IR (KBr cm$^{-1}$) 2958, 1677, 1662, 1623. $^1$H NMR (acetone) δ: 0.96 (s, 6H, CH(Me)$_2$), 1.08 (s, 6H, CH(Me)$_2$), 2.02-2.55 (m, 8H, 4CH$_2$), 4.64 (s, 1H, CH), 7.04-7.26 (m, 5H, aryl). $^{13}$C NMR (acetone) δ: 27.1, 32.5, 32.6, 41.0, 51.1, 115.9, 126.9, 128.5, 129.3, 145.6, 163.4, 196.2. Anal. Calcd for C$_{23}$H$_{26}$O$_3$: C, 78.85; H, 7.42; N, 0.00. Found: C, 78.30; H, 7.60; N, 0.21.

3.2. 3,4,6,7-Tetrahydro-9-(4-methoxyphenyl)-3,3,6,6-tetramethyl-2H-xanthene-1,8(5H,9H)-dione (3b). Yield 45%. Mp 245-247 °C. IR (KBr cm$^{-1}$) 2953, 1679, 1678, 1659, 1619. $^1$H NMR (DMSO-d$_6$) δ: 0.88 (s, 6H, CH(Me)$_2$), 1.02 (s, 6H, CH(Me)$_2$), 2.02-2.52 (m, 8H, 4CH$_2$), 3.66 (s, 3H, OMe), 4.44 (s, 1H, CH), 6.75 (d, $J = 8.6$ Hz, 2H, aryl), 7.05 (d, $J = 8.6$ Hz, 2H, aryl). $^{13}$C NMR (DMSO-d$_6$) δ: 26.4, 28.6, 30.2, 31.8, 48.3, 50.0, 113.2, 114.6, 128.9, 136.4, 162.6, 196.0. Anal. Calcd for C$_{24}$H$_{28}$O$_4$: C, 75.79; H, 7.37; N, 0.00. Found: C, 75.60; H, 7.30; N, 0.15.

3.3. 9-(4-Chlorophenyl)-3,4,6,7-tetrahydro-3,3,6,6-tetramethyl-2H-xanthene-1,8(5H,9H)-dione (3c). Yield 79%. Mp 214-217 °C. IR (KBr cm$^{-1}$) 2951, 1679, 1662, 1624. $^1$H NMR (DMSO-d$_6$) δ: 0.88 (s, 6H, CH(Me)$_2$), 0.97 (s, 6H, CH(Me)$_2$), 2.09-2.59 (m, 8H, 4CH$_2$), 4.48 (s, 1H, CH), 7.16 (d, $J = 8.5$ Hz, 2H, aryl), 7.26 (d, $J = 8.5$ Hz, 2H, aryl). $^{13}$C NMR (DMSO-d$_6$) δ: 26.5, 28.6, 30.9, 31.8, 49.9, 113.9, 127.8, 129.9, 130.7, 143.2, 163.0, 196.0. Anal. Calcd for C$_{23}$H$_{25}$O$_3$Cl: C, 71.78; H, 6.50; N, 0.00. Found: C, 72.2; H, 6.47; N, 0.09.

3.4. 9-(2-Chlorophenyl)-3,4,6,7-tetrahydro-3,3,6,6-tetramethyl-2H-xanthene-1,8(5H,9H)-dione (3d). Yield 80%. Mp 217-218 °C. IR (KBr cm$^{-1}$) 2959, 1680, 1655, 1625. $^1$H NMR (DMSO-d$_6$) δ: 0.9 (s, 6H, CH(Me)$_2$), 1.03 (s, 6H, CH(Me)$_2$), 2.06-2.6 (m, 8H, 4CH$_2$), 4.82 (s, 1H, CH), 7.08-7.26 (m, 4H, aryl). $^{13}$C NMR (DMSO-d$_6$) δ: 26.3, 28.6, 30.5, 31.6, 50.0, 113.1, 126.4, 127.7, 129.4, 131.9, 132.8, 140.7, 168.2, 195.8. Anal. Calcd for C$_{22}$H$_{25}$O$_3$Cl: C, 71.78; H, 6.50; N, 0.00. Found: C, 71.30; H, 6.61; N, 0.07.
3.5. 3,4,6,7-Tetrahydro-9-(4-methylphenyl)-3,3,6,6-tetramethyl-2H-xanthene-1,8(5H,9H)-dione (3e). Yield 45%. Mp 222-225°C. IR (KBr cm\(^{-1}\)) 2950, 1677, 1676, 1660, 1617. \(^1\)H NMR (DMSO-d\(_6\)) \(\delta\): 1.00 (s, 6H, C(Me)\(_2\)), 1.11 (s, 6H, C(Me)\(_2\)), 1.99-2.22 (m, 8H, 4CH\(_2\)), 2.44 (s, 3H, Me), 4.6 (s, 1H, CH), 6.69 (d, \(J = 8.6\) Hz, 2H, aryl), 7.13 (d, \(J = 8.6\) Hz, 2H, aryl). \(^1\)C NMR (DMSO-d\(_6\)) \(\delta\): 22.5, 26.4, 28.5, 30.2, 31.8, 50.1, 113.0, 114.6, 128.7, 136.2, 163.6, 197.0. Anal. Calcd for C\(_{24}\)H\(_{28}\)O\(_3\): C, 79.09; H, 7.74; N, 0.00. Found: C, 78.73; H, 7.65; N, 0.09.

4. General procedure for the preparation 2-(benzyliden)-2H-indene-1,3-dione (5b,c,e)

Piperidine (8 mmol) was added dropwise to a solution of enone 1 (2 mmol) and 2H-indene-1,3-dione (2 mmol) in absolute EtOH (15 mL) at room temperature. The reaction mixture was refluxed until the disappearance of the starting material (5-7 h), (monitored by TLC) and barbituric acid salt was filtered off. The filtrate was evaporated and was diluted with H\(_2\)SO\(_4\) (10%) (15 mL), precipitate solid product was recrystallized from hot EtOH.

4.1. 2-(4-Methoxybenzylidene)-2H-indene-1,3-dione (5b). Yield 68%. Mp 156-157°C. IR (KBr cm\(^{-1}\)) 1725, 1680. \(^1\)H NMR (CDCl\(_3\)) \(\delta\): 3.9 (s, 3H, OMe), 7.02 (d, \(J = 8.9\) Hz, 2H, aryl), 7.58 (s, 1H, =CH), 7.79 (m, 2H, aryl), 7.98 (m, 2H, aryl), 8.55 (d, \(J = 8.9\) Hz, 2H, aryl), \(^1\)C NMR (CDCl\(_3\)) \(\delta\): 55.6, 123.1, 123.5, 126.4, 126.5, 134.8, 135.1, 137.2, 139.9, 142.3, 146.8, 188.3, 190.8. Anal. Calcd for C\(_{17}\)H\(_{12}\)O\(_3\): C, 77.26; H, 4.58; N, 0.00. Found: C, 77.73; H, 4.65; N, 0.06.

4.2. 2-(4-Chlorobenzylidene)-2H-indene-1,3-dione (5c). Yield 72%. Mp 172-174°C. IR (KBr cm\(^{-1}\)) 1727, 1690. \(^1\)H NMR (CDCl\(_3\)) \(\delta\): 7.47 (d, \(J = 8.5\) Hz, 2H, aryl), 7.81 (s, 1H, =CH), 7.83 (m, 2H, aryl), 8.01 (m, 2H, aryl), 8.41 (d, \(J = 8.5\) Hz, 2H, aryl), \(^1\)C NMR (CDCl\(_3\)) \(\delta\): 123.3, 123.4, 129.1, 129.4, 135.3, 135.5, 139.5, 140.1, 142.5, 145.1, 188.9, 189.9. Anal. Calcd for C\(_{16}\)H\(_9\)ClO\(_2\): C, 71.52; H, 3.38; N, 0.00. Found: C, 71.67; H, 3.15; N, 0.08.

4.3. 2-(4-Methylbenzylidene)-2H-indene-1,3-dione (5e). Yield 80%. Mp 146-147°C. IR (KBr cm\(^{-1}\)) 1726, 1683. \(^1\)H NMR (CDCl\(_3\)) \(\delta\): 2.46 (s, 3H, Me), 7.32 (d, \(J = 8.1\) Hz, 2H, aryl), 7.81(m, 2H, aryl), 7.88 (s, 1H, =CH), 8.01 (m, 2H, aryl), 8.40 (d, \(J = 8.2\) Hz, 2H, aryl). \(^1\)C NMR (CDCl\(_3\)) \(\delta\): 22.09, 123.2, 128.2, 129.6, 130.6, 134.5, 135.0, 135.2, 140.0, 142.5, 144.6, 147.1, 189.2, 190.5. Anal. Calcd for C\(_{17}\)H\(_{12}\)O\(_2\): C, 82.24; H, 4.87; N, 0.00. Found: C, 81.89; H, 4.70; N, 0.04.

5. General procedure for the preparation of 2-amino-4-(2-aryl)-6-(piperidinyl)pyridine-3,5-dicarbonitriles (7a-e).
Piperidine (8 mmol) was added dropwise to a solution of enone 1 (2 mmol) and malononitrile (6, 4 mmol) in absolute EtOH (15 mL) at room temperature. The reaction mixture was refluxed until the disappearance of the starting material (8-10 h), (monitored by TLC) and barbituric acid salt was filtered off. The filtrate was evaporated and was diluted with water (15 mL), precipitate solid product was recrystallized from water/acetone. In some cases column chromatography was used using ethylacetate/chloroform mixture as eluent.

5.1. 2-Amino-4-phenyl-6-(piperidin-1-yl)pyridine-3,5-dicarbonitrile (7a). Yield 60%. Mp 203-205 °C. IR (KBr cm\(^{-1}\)) 3474, 3325, 3222, 2202, 1624, 1583, 1567. \(^1\)H NMR (DMSO-d\(_6\)) \(\delta\): 1.61 (m, 6H, piperidine), 3.71 (m, 4H, piperidine), 7.44-7.53 (m, 7H, aryl and NH2). \(^13\)C NMR (DMSO-d\(_6\)) \(\delta\): 24.9, 26.6, 49.4, 81.8, 82.5, 117.2, 118.8, 129.5, 129.7, 130.9, 136.3, 160.8, 161.7, 162.8. MS: m/z (%) = 303 (M\(^+\), 1), 302 (3), 277 (4), 238 (100), 213 (3), 183 (3), 162 (24), 145 (3), 127 (19), 103 (15), 84 (17), 56 (8), 41 (9). Anal. Calcd for C\(_{18}\)H\(_{17}\)N\(_5\): C, 71.28; H, 5.65; N, 23.09. Found: C, 71.78; H, 6.01; N, 22.76.

5.2. 2-Amino-4-(4-methoxyphenyl)-6-(piperidin-1-yl)pyridine-3,5-dicarbonitrile (7b). Yield 45%. Mp 198-200 °C. IR (KBr cm\(^{-1}\)) 3512, 3401, 2196, 1602, 1580, 1554. \(^1\)H NMR (acetone) \(\delta\): 1.65 (m, 6H, piperidine), 3.76 (m, 4H, piperidine), 3.87 (s, 3H, OMe), 6.71 (s, 2H, NH\(_2\)), 7.06 (d, \(J = 6.8\) Hz, 2H, aryl), 7.49 (d, \(J = 6.8\) Hz, 2H, aryl). \(^13\)C NMR (acetone) \(\delta\): 25.1, 26.7, 49.7, 55.7, 81.7, 83.8, 114.7, 116.9, 118.4, 128.5, 131.4, 161.1, 162.1, 162.4, 162.5. MS: m/z (%) = 333 (M\(^+\), 68), 332 (100), 318 (23), 304 (9), 182 (14), 125 (23), 84 (8), 55 (7), 41 (5). Anal. Calcd for C\(_{19}\)H\(_{19}\)N\(_5\)O: C, 68.45; H, 5.74; N, 21.01. Found: C, 67.92; H, 5.69; N, 21.50.

5.3. 2-Amino-4-(4-chlorophenyl)-6-(piperidin-1-yl)pyridine-3,5-dicarbonitrile (7c). Yield 63%. Mp 218-220 °C. IR (KBr cm\(^{-1}\)) 3470, 3331, 3326, 2209, 1628, 1576, 1530. \(^1\)H NMR (acetone) \(\delta\): 1.65 (m, 6H, piperidine), 3.79 (m, 4H, piperidine), 6.82 (s, 2H, NH\(_2\)), 7.54-7.61 (m, 4H, aryl). \(^13\)C NMR (acetone) \(\delta\): 25.0, 26.6, 49.6, 81.3, 83.3, 116.4, 118.0, 129.6, 131.5, 132.1, 135.4, 136.4, 160.9, 161.5, 161.9. MS: m/z (%) = 337 (M\(^+\), 46), 336 (100), 308 (10), 294 (41), 281 (5), 219 (5), 84 (7), 69 (8), 55 (7), 41 (8). Anal. Calcd for C\(_{18}\)H\(_{16}\)N\(_5\)Cl: C, 64.00; H, 4.77; N, 20.73. Found: C, 63.90; H, 4.71; N, 20.47.

5.4. 2-Amino-4-(2-chlorophenyl)-6-(piperidin-1-yl)pyridine-3,5-dicarbonitrile (7d). Yield 65%. Mp 188-189 °C. IR (KBr cm\(^{-1}\)) 3467, 3327, 3221, 2207, 1622, 1572, 1531. \(^1\)H NMR (acetone) \(\delta\): 1.65 (m, 6H, piperidine), 3.80 (m, 4H, piperidine), 6.85 (s, 2H, NH\(_2\)), 7.47-7.61 (m, 4H, aryl). \(^13\)C NMR (acetone) \(\delta\): 25.0, 26.6, 49.4, 83.0, 84.1, 115.8, 117.4, 128.3, 130.6, 131.1, 132.0, 132.6, 135.8, 160.3, 160.6, 161.2. MS: m/z (%) = 337 (M\(^+\), 75), 308 (33), 302 (100), 294 (9), 281 (9), 260 (15), 247 (19), 219 (20), 165 (13),
84 (21), 55 (12), 41 (15). Anal. Calcd for C$_{18}$H$_{16}$N$_5$Cl: C, 64.00; H, 4.77; N, 20.73. Found: C, 64.06; H, 4.71; N, 20.77.

5.5. 2-Amino-6-(piperidin-1-yl)-4-p-tolylpyridine-3,5-dicarbonitrile (7e). Yield 53%. Mp 198 °C. IR (KBr cm$^{-1}$) 3479, 3327, 3221, 2201, 1623, 1579, 1556, 1535. $^1$H NMR (CDCl$_3$) $\delta$: 1.69 (m, 6H, piperidine), 2.41 (s, 3H, Me) 3.79 (m, 4H, piperidine), 5.35 (s, 2H, NH$_2$), 7.30 (d, $J = 8.1$ Hz, 2H, aryl), 7.39 (d, $J = 8.1$ Hz, 2H, aryl). $^{13}$C NMR (CDCl$_3$) $\delta$: 21.5, 24.4, 25.9, 49.2, 81.5, 83.5, 116.7, 117.8, 128.6, 129.5, 131.8, 140.7, 159.4, 161.2, 162.4. MS: m/z (%) = 317 (M$^+$, 56), 316 (100), 302 (17), 288 (9), 219 (4), 179 (4), 84 (8), 69 (8), 55 (5), 41 (7). Anal. Calcd for C$_{19}$H$_{19}$N$_5$: C, 71.90; H, 6.03; N, 22.07. Found: C, 72.09; H, 6.20; N, 21.69.

REFERENCES
