Synthesis of 1,3-Dimethylpyrimido[4,5-b]quinoline-2,4(1H,3H)-diones (1,3-Dimethyl-5-deazaalloxazines) and Related Compounds via the Intramolecular Cycloaddition of Azahexatrienes

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Heating of 6-arylamino-1,3-dimethyluracils (IIa→e) with one-carbon reagents (dimethylformamide dimethylacetal, dimethylformamide-phosphorus oxychloride, and triethyl orthoformate) afforded 1,3-dimethylpyrimido[4,5-b]quinoline-2,4(1H,3H)-diones (Va→e) via the intramolecular cycloaddition of azahexatrienes. Similarly, treatment of IIa with arylaldehydes provided 5-aryl-1,3-dimethylpyrimido[4,5-b]quinoline-2,4(1H,3H,5H,10H)-diones (VIIa→e), which were subsequently dehydrogenated with either thiayl chloride or diethyl azodicarboxylate to give 5-aryl-1,3-dimethylpyrimido[4,5-b]quinoline-2,4(1H,3H)-diones (Xa→e). The reaction of 6-arylamino-1,3-dimethyl-4-N-phenylcytosines (XIIa→c) with dimethylformamide dimethylacetal to give 4-arylimino-1,3-dimethylpyrimido[4,5-b]quinoline-2(1H,3H)-ones (XIIIa→c) is also described.

Keywords—6-arylamino-1,3-dimethyluracils; dimethylformamide dimethylacetal; dimethylformamide-phosphorus oxychloride; triethyl orthoformate; arylaldehydes; intramolecular cycloaddition of azahexatrienes; 1,3-dimethylpyrimido[4,5-b]quinoline-2,4(1H,3H)-diones; 6-arylamino-1,3-dimethyl-4-N-phenylcytosines; 4-arylimino-1,3-dimethylpyrimido[4,5-b]quinoline-2,4(1H,3H)-ones

The intramolecular cycloaddition of azahexatrienes has recently been shown to offer a useful synthetic route to various heterocyclic systems, e.g., purine, pyrazolo[3,4-d]pyrimidine, 6-azapteridine, pyrimido[4,5-e]-as-triazine (6-azapteridine), and pyrimido[4,5-c]-pyridazine. We now report a new synthesis of 1,3-dimethylpyrimido[4,5-b]quinoline-2,4(1H,3H)-diones (1,3-dimethyl-5-deazaalloxazines: Va→e and Xa→e) via the intramolecular cycloaddition of azahexatrienes by the reaction of 6-arylamino-1,3-dimethyluracils (IIa→e) with one-carbon reagents, i.e., dimethylformamide dimethylacetal (DMFDMA), dimethylformamide-phosphorus oxychloride (Vilsmeier reagent), triethyl orthoformate, and arylaldehydes. In addition, we report the synthesis of 4-arylimino-1,3-dimethylpyrimido[4,5-b]quinoline-2(1H,3H)-ones (XIIIa→c) by the reaction of 6-arylamino-1,3-dimethyl-4-N-phenylcytosines (XIIa→c) with DMFDMA, which also involves the intramolecular cycloaddition of azahexatrienes.

The requisite starting materials (IIa→e and XIIa→c) were prepared by the nucleophilic displacement of 6-chloro-1,3-dimethyluracil (I) or 6-chloro-1,3-dimethyl-4-N-phenylcytosine

1) A part of this work has been reported in a preliminary form: K. Senga, K. Shimizu, S. Nishigaki, and F. Yoneda, *Heterocycles*, 6, 1361 (1977).
2) Location: a) 35, Shinanomachi, Shinjuku-ku, Tokyo 160, Japan; b) 5-1, Os-honmachi, Kumanoto 862, Japan.
(XI), respectively, with the appropriate arylamines according to the reported procedures\(^8,9\) (Tables I and II).

Heating of IIa with excess DMFDMA at 95° for 1 hr afforded a 60% yield of 1,3-dimethylpyrimido[4,5-\(b\)]quinoline-2,4(1H,3H)-dione (V\(a\)), which was isolated by concentration of the reaction mixture and addition of ethanol. The structure of V\(a\) was readily established from the analytical and spectral data. In particular, the nuclear magnetic resonance (NMR)

**Table I. 6-Arylamino-1,3-dimethyluracils**

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>R</th>
<th>mp (°C)</th>
<th>Yield (%)</th>
<th>Formula</th>
<th>Analysis (%) (Found)</th>
<th>IR (Nujol) cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>H</td>
<td>190—192(^{a, b})</td>
<td>87</td>
<td>C(<em>{12})H(</em>{13})N(<em>{2})O(</em>{2})</td>
<td>62.32 5.67 18.17</td>
<td>1700 3270</td>
</tr>
<tr>
<td>IIb</td>
<td>OMe</td>
<td>188—190(^{a, c})</td>
<td>91</td>
<td>C(<em>{12})H(</em>{13})N(<em>{2})O(</em>{3})</td>
<td>59.76 5.79 16.08</td>
<td>1690 3210</td>
</tr>
<tr>
<td>IIc</td>
<td>Br</td>
<td>217—219(^{d})</td>
<td>97</td>
<td>C(<em>{12})H(</em>{13})BrN(<em>{2})O(</em>{2})</td>
<td>46.46 3.90 13.55</td>
<td>1710 3240</td>
</tr>
<tr>
<td>IId</td>
<td>Cl</td>
<td>210—212(^{a, e})</td>
<td>81</td>
<td>C(<em>{12})H(</em>{13})ClN(<em>{2})O(</em>{3})</td>
<td>54.24 4.56 15.82</td>
<td>1705 3210</td>
</tr>
<tr>
<td>IIe</td>
<td>NO(_{2})</td>
<td>270—272(^{c})</td>
<td>48</td>
<td>C(<em>{12})H(</em>{13})N(<em>{2})O(</em>{4})</td>
<td>52.17 4.38 20.28</td>
<td>1690 3220</td>
</tr>
</tbody>
</table>

\(^{a}\) Recrystallized from EtOH.
\(^{b}\) Lit.\(^{9}\) mp 196.5—197°.
\(^{d}\) Lit.\(^{9}\) mp 212—214°.
\(^{e}\) Recrystallized from DMF.

**Table II. 6-Arylamino-1,3-dimethyl-4-N-phenylcytosines**

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>R(^{1})</th>
<th>R(^{2})</th>
<th>mp (°C)(^{a})</th>
<th>Yield (%)</th>
<th>Formula</th>
<th>Analysis (%) (Found)</th>
<th>IR (Nujol) cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>XIIa</td>
<td>H</td>
<td>H</td>
<td>179—181</td>
<td>52</td>
<td>C(<em>{18})H(</em>{24})N(_{4})O</td>
<td>70.56 5.92 18.29</td>
<td>1655 3290</td>
</tr>
<tr>
<td>XIIb</td>
<td>H</td>
<td>OMe</td>
<td>151—151.5</td>
<td>60</td>
<td>C(<em>{18})H(</em>{24})N(<em>{3})O(</em>{2})</td>
<td>67.84 5.99 16.66</td>
<td>1655 3280</td>
</tr>
<tr>
<td>XIIc</td>
<td>H</td>
<td>Br</td>
<td>155—155.5</td>
<td>46</td>
<td>C(<em>{18})H(</em>{17})BrN(_{4})O</td>
<td>56.11 4.46 14.54</td>
<td>1655 3300</td>
</tr>
</tbody>
</table>

\(^{a}\) All compounds were recrystallized from EtOH-H\(_{2}\)O.

spectrum (DMSO-\textit{d}_6) showed three sharp singlets at $\delta$ 3.33 (N–Me), 3.63 (N–Me), and 9.40 (C^9–H) as well as a multiplet at $\delta$ 7.33–8.33 (C^8–9–H). In accord with the above result, the reactions of other 6-arylamino-1,3-dimethyluracils (IIb–e) with DMFDMA provided 35–63% yields of the corresponding 1,3-dimethylpyrimidino[4,5-\textit{b}]quinoline-2,4(1H,3H)-diones (Vb–e). The compounds Va–d could also be obtained in 43–91% yields by refluxing IIa–d with the Vilsmeier reagent in benzene for 30 min. Alternatively, refluxing IIa–e with triethyl orthoformate in dimethylformamide for 1 hr gave 42–87% yields of Va–e; however, attempted cyclization of IIa with triethyl orthoacetate or triethyl orthopropionate under the same conditions to give 5-alkyl-1,3-dimethylpyrimido[4,5-\textit{b}]quinoline-2,4(1H,3H)-diones resulted in the recovery of the starting material (Table III).

TABLE III. 1,3-Dimethylpyrimido[4,5-\textit{b}]quinoline-2,4-(1H, 3H)-diones

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>R</th>
<th>mp (°C)a</th>
<th>Yield (%)</th>
<th>Formula</th>
<th>Analysis (%)</th>
<th>IR (Nujol) cm(^{-1}) (CO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Va</td>
<td>H</td>
<td>211–212</td>
<td>60 91 68</td>
<td>C\textsubscript{18}H\textsubscript{14}N\textsubscript{5}O\textsubscript{4}</td>
<td>64.72 4.60 17.42</td>
<td>1650 1705</td>
</tr>
<tr>
<td>Vb</td>
<td>OMe</td>
<td>273–274</td>
<td>63 43 65</td>
<td>C\textsubscript{14}H\textsubscript{16}N\textsubscript{4}O\textsubscript{4}</td>
<td>61.98 4.83 15.49</td>
<td>1650 1705</td>
</tr>
<tr>
<td>Vc</td>
<td>Br</td>
<td>275</td>
<td>56 50 69</td>
<td>C\textsubscript{18}H\textsubscript{16}BrN\textsubscript{4}O\textsubscript{3}</td>
<td>48.77 3.15 13.15</td>
<td>1655 1715</td>
</tr>
<tr>
<td>Vd</td>
<td>Cl</td>
<td>270</td>
<td>62 81 42</td>
<td>C\textsubscript{18}H\textsubscript{16}ClN\textsubscript{4}O\textsubscript{2}</td>
<td>56.62 3.66 15.24</td>
<td>1655 1710</td>
</tr>
<tr>
<td>Ve</td>
<td>NO\textsubscript{2}</td>
<td>300</td>
<td>35 87</td>
<td>C\textsubscript{18}H\textsubscript{16}N\textsubscript{5}O\textsubscript{4}</td>
<td>54.58 3.58 19.86</td>
<td>1675 1730</td>
</tr>
</tbody>
</table>

a) All compounds were recrystallized from DMF.
b) Cyclization with dimethylformamide dimethylacetal.
c) Cyclization with the Vilsmeier reagent.
d) Cyclization with triethyl orthoformate.

The reaction of IIa–e with DMFDMA or the Vilsmeier reagent leading to Va–e was presumably initiated by the formation of a 5-N,N-dimethylaminomethylene intermediate (III), which possesses an azahexatriene-type structure. This could undergo intramolecular cyclization through valence isomerization and subsequent aromatization of IV by the loss of dimethylaniline. Analogously, the reaction of IIa–e with triethyl orthoformate can be explained in the same way (the N,N-dimethylamino groups of the intermediates (III and IV) are replaced by ethoxy groups). In this case, the aromatization of IV to Va–e proceeds by the elimination of ethanol (Chart 1).

Although the introduction of an alkyl substituent at the 5 position of Va was unsuccessful, heating of IIA with excess benzaldehyde at 180° for 5 hr, followed by dilution with ethanol caused the separation of 1,3-dimethyl-5-phenylpyrimidino[4,5-\textit{b}]quinoline-2,4(1H,3H, 5H,10H)-dione (VIIa) in 50% yield. The characterization of VIIa was based on the following evidence. The analytical and mass spectral data established the molecular formula as C\textsubscript{19}H\textsubscript{17}N\textsubscript{5}O\textsubscript{2}. The infrared (IR) spectrum exhibited a secondary amino absorption band at 3240 cm\(^{-1}\), while the NMR spectrum (DMSO-\textit{d}_6) showed three sharp singlets at $\delta$ 3.13 (N–Me), 3.53 (N–Me), and 5.17 (C\textsuperscript{5–H}), a multiplet at $\delta$ 6.77–7.50 (C\textsubscript{6}H\textsubscript{5} and C\textsuperscript{6–9–H}), and a deuterium oxide-exchangeable broad singlet at $\delta$ 9.17 (NH). Similarly, the reaction of IIa with other
Chart 1

Table IV. 5-Aryl-1,3-dimethylpyrimido[4,5-b]quinoline-2,4(1H,3H,5H,10H)-diones

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>R</th>
<th>mp (°C)</th>
<th>Yield (%)</th>
<th>Formula</th>
<th>Analysis (%)</th>
<th>IR (Nujol) cm⁻¹</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Calcd (Found)</td>
<td>(CO) (NH)</td>
</tr>
<tr>
<td>VIIa</td>
<td>H</td>
<td>&gt;300a)</td>
<td>50</td>
<td>C₁₅H₁₂N₂O₂</td>
<td>71.45 5.37 13.16</td>
<td>1690 3240</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(71.27 5.36 13.36)</td>
<td></td>
</tr>
<tr>
<td>VIIb</td>
<td>Me</td>
<td>228—231b)</td>
<td>24</td>
<td>C₁₅H₁₂N₂O₂</td>
<td>72.05 5.74 12.61</td>
<td>1690 3240</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(71.91 5.44 12.39)</td>
<td></td>
</tr>
<tr>
<td>VIIc</td>
<td>OMe</td>
<td>254—256a)</td>
<td>49</td>
<td>C₁₅H₁₂N₂O₃</td>
<td>68.75 5.48 12.03</td>
<td>1690 3240</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(68.56 5.32 11.86)</td>
<td></td>
</tr>
<tr>
<td>VIIId</td>
<td>Br</td>
<td>&gt;300a)</td>
<td>37</td>
<td>C₁₅H₁₄BrN₂O₂</td>
<td>57.30 4.05 10.55</td>
<td>1700 3260</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(57.31 4.02 10.55)</td>
<td></td>
</tr>
<tr>
<td>VIIe</td>
<td>Cl</td>
<td>299—300a)</td>
<td>34</td>
<td>C₁₅H₁₄ClN₂O₂</td>
<td>64.50 4.56 11.88</td>
<td>1695 3240</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(64.30 4.56 11.97)</td>
<td></td>
</tr>
</tbody>
</table>

a) Recrystallized from EtOH-DMF.
b) Recrystallized from EtOH.
arylaldehydes yielded 24—49% yields of the corresponding 5-aryl-1,3-dimethylpyrimido[4,5-b]quinoline-2,4(1H,3H,5H,10H)-diones (VIIb—e) (Table IV). The dehydrogenation of VIIa—e to 5-aryl-1,3-dimethylpyrimido[4,5-b]quinoline-2,4(1H,3H)-diones (Xa—e) was achieved in 61—89% yields by refluxing with thionyl chloride for 15 min. Alternatively, heating of the appropriate VIIa—e with diethyl azodicarboxylate at 160° for 15 min furnished 70—90% yields of the corresponding Xa—e (Table V).

**Table V. 5-Aryl-1,3-dimethylpyrimido[4,5-b]quinoline-2,4(1H,3H)-diones**

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>R</th>
<th>mp (°C)</th>
<th>Yield (%)</th>
<th>mp (°C)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>A</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Xa</td>
<td>H</td>
<td>261—264</td>
<td>89</td>
<td>90</td>
<td>C&lt;sub&gt;15&lt;/sub&gt;H&lt;sub&gt;12&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>71.91</td>
<td>4.76</td>
<td>13.24</td>
</tr>
<tr>
<td>Xb</td>
<td>Me</td>
<td>236—237</td>
<td>73</td>
<td>70</td>
<td>C&lt;sub&gt;16&lt;/sub&gt;H&lt;sub&gt;14&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>72.49</td>
<td>5.17</td>
<td>12.68</td>
</tr>
<tr>
<td>Xc</td>
<td>OMe</td>
<td>262—264</td>
<td>70</td>
<td>75</td>
<td>C&lt;sub&gt;16&lt;/sub&gt;H&lt;sub&gt;14&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>69.15</td>
<td>4.93</td>
<td>12.10</td>
</tr>
<tr>
<td>Xd</td>
<td>Br</td>
<td>255—256</td>
<td>61</td>
<td>87</td>
<td>C&lt;sub&gt;15&lt;/sub&gt;H&lt;sub&gt;14&lt;/sub&gt;BrN&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>57.55</td>
<td>3.54</td>
<td>10.61</td>
</tr>
<tr>
<td>Xe</td>
<td>Cl</td>
<td>286</td>
<td>62</td>
<td>70</td>
<td>C&lt;sub&gt;15&lt;/sub&gt;H&lt;sub&gt;14&lt;/sub&gt;CIN&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;</td>
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<td></td>
<td></td>
<td>64.87</td>
<td>4.01</td>
<td>11.94</td>
</tr>
</tbody>
</table>

The reaction of IIa with arylaldehydes to give VIIa—e can be rationalized by assuming the initial formation of the 5-benzylidene intermediate (VI), followed by intramolecular cyclization via valence isomerization. The dehydrogenation of VIIa—e with thionyl chloride<sup>10</sup> to Xa—e probably proceeds through the N-sulfinyl chloride intermediate (VIII) and subsequent aromatization accompanied by the loss of hydrogen chloride and sulfur monoxide. On the other hand, the dehydrogenation of VIIa—e with diethyl azodicarboxylate<sup>11</sup> to give Xa—e would involve the intermediacy of the N-(1,2-dicarboethoxyhydradino) derivative (IX), which undergoes aromatization by the elimination of diethyl hydrazodicarboxylate (Chart 2).

In connection with the successful synthesis of Va—e by the reactions of IIa—e with DMFDMA, we also investigated the following reactions. Thus, treatment of XIIa or XIIc with excess DMFDMA at 160° for 1.5 hr gave 15 and 10% yields of 1,3-dimethyl-4-phenyliminopyrimido[4,5-b]quinoline-2(1H,3H)-one (XIIIa) and 4-(p-bromophenyl)iminono-1,3-dimethylpyrimido[4,5-b]quinoline-2(1H,3H)-one (XIIIc), respectively, as the only isolatable products. The structures of XIIIa and XIIIc were readily confirmed by their quantitative conversion

<sup>10</sup> Thionyl chloride is known to be a strong dehydrogenation agent: For example, K. Senga, Y. Kanamori, and S. Nishigaki, *Chem. Pharm. Bull.*, 26, 3240 (1978).

to Va using hot concentrated hydrochloric acid. In contrast, the reaction of XIIb with DMFDMA under the same conditions afforded a 5% yield of 7-methoxy-1,3-dimethyl-4-phenyliminopyrimido[4,5-b]quinoline-2(1H,3H)-one (XIIIb), which, upon heating with concentrated hydrochloric acid, yielded Vb quantitatively (Table VI). In addition, refluxing of 3-methyl-6-(N-methylanilino)uracil (XIV)\textsuperscript{12} with DMFDMA at 160° for 30 min provided a 55% yield of 1,3-dimethyl-6-(N-methylanilino)uracil (XV), and none of the expected 3,10-dimethylpyrimido[4,5-b]quinoline-2,4(3H,10H)-dione could be isolated (Chart 3).

Table VI. 4-Arylimino-1,3-dimethylpyrimido[4,5-b]quinoline-2(1H,3H)-ones

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
<th>mp (°C)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Yield (%)</th>
<th>Formula</th>
<th>Analysis (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>IR (Nujol) cm&lt;sup&gt;-1&lt;/sup&gt; (&gt;CO)</th>
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</thead>
<tbody>
<tr>
<td>XIIa</td>
<td>H</td>
<td>H</td>
<td>224–225</td>
<td>15</td>
<td>C&lt;sub&gt;19&lt;/sub&gt;H&lt;sub&gt;16&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>72.13 (71.84)</td>
<td>1690</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.10 (5.07)</td>
<td>17.71 (17.64)</td>
</tr>
<tr>
<td>XIIb</td>
<td>H</td>
<td>OMe</td>
<td>243–244</td>
<td>5</td>
<td>C&lt;sub&gt;20&lt;/sub&gt;H&lt;sub&gt;18&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;</td>
<td>69.35 (69.06)</td>
<td>1685</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.24 (5.20)</td>
<td>16.18 (15.97)</td>
</tr>
<tr>
<td>XIIc</td>
<td>Br</td>
<td>H</td>
<td>230–231</td>
<td>10</td>
<td>C&lt;sub&gt;19&lt;/sub&gt;H&lt;sub&gt;15&lt;/sub&gt;BrN&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>57.73 (57.46)</td>
<td>1690</td>
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<td></td>
<td></td>
<td></td>
<td>3.83 (3.79)</td>
<td>14.14 (13.92)</td>
</tr>
</tbody>
</table>

<sup>a</sup> All compounds were recrystallized from EtOH.

Chart 3

Experimental<sup>13a</sup>

6-Arylamino-1,3-dimethyluracils (IIa–c) (Table I) — A mixture of 6-chloro-1,3-dimethyluracil (I)<sup>7</sup> (0.87 g, 0.005 mol) and an appropriate arylamine (0.01 mol) was heated at 180° for 3 hr. The reaction mixture was triturated with a mixture of ether and H<sub>2</sub>O. The insoluble material was filtered and recrystallized to give the corresponding IIa–c.

6-Arylamino-1,3-dimethyl-4-N-phenylcytosines (XIIa–c) (Table II) — A mixture of 6-chloro-1,3-dimethyl-4-N-phenylcytosine (XI)<sup>9</sup> (1.25 g, 0.005 mol) and an appropriate arylamine (0.01 mol) was heated at 180° for 3 hr. The reaction mixture was dissolved in EtOH and made basic with 28% NH<sub>3</sub>. The precipitates were filtered, washed with H<sub>2</sub>O, dried, and recrystallized to give the corresponding XIIa–c.

<sup>13</sup> Melting points were taken on a YANACO micro hot-stage melting point apparatus and are uncorrected. IR spectra were recorded on a JASCO IR-E spectrophotometer from samples milled in Nujol. NMR spectra were determined at 60 MHz with a Varian T-60 spectrometer using tetramethylsilane as internal standard. Mass spectra were obtained on a JEOL JMS-D 300 spectrometer with a direct inlet system at 70 eV.
1,3-Dimethylpyrimido[4,5-\(b\)]quinoline-2,4(1H,3H)-diones (Va–e) (Table III)—Method A: A mixture of the appropriate IIa–e (0.001 mol) and dimethylformamide dimethylacetal (DMF DMA: 0.357 g, 0.003 mol) was heated at 95° for 1.5 hr. The reaction mixture was concentrated in vacuo and the residue was covered with EtOH. The insoluble material was filtered, washed with EtOH, and recrystallized to give the corresponding Va–e.

Method B: Vilsmeier reagent prepared from dimethylformamide (0.11 g, 0.0015 mol) and phosphorus oxychloride (0.23 g, 0.0015 mol) was added dropwise to a suspension of the appropriate IIa–d (0.0005 mol) in dry benzene (2 ml). The mixture was refluxed for 30 min. The resulting solution was concentrated in vacuo and the residue was triturated with 5% NH₄OH. The insoluble material was filtered, washed well with H₂O, dried, and recrystallized to give the corresponding Va–d, identical in all respects with the compounds prepared by Method A.

Method C: A solution of the appropriate IIa–e (0.0005 mol) in a mixture of triethyl orthoformate (0.3 g, 0.002 mol) and dimethylformamide (1.5 ml) was refluxed for 1 hr. The reaction mixture was concentrated in vacuo and the residue was covered with EtOH. The insoluble material was filtered, washed with EtOH, and recrystallized to give the corresponding Va–c, identical in all respects with the compounds obtained by Method A.

5-Aryl-1,3-dimethylpyrimido[4,5-\(b\)]quinoline-2,4(1H,3H,5H,10H)-diones (VIIa–e) (Table IV)—A mixture of IIa (0.12 g, 0.0005 mol) and an appropriate arylaldehyde (0.0015 mol) was heated at 180° for 5 hr and the reaction mixture was triturated with EtOH. The insoluble material was filtered, washed with EtOH, and recrystallized to give the corresponding VIIa–e.

5-Aryl-1,3-dimethylpyrimido[4,5-\(b\)]quinoline-2,4(1H,3H)-diones (Xa–e) (Table V)—Method A: A suspension of the appropriate VIIa–e (0.0005 mol) in thionyl chloride (3 ml) was refluxed for 15 min. The reaction mixture was concentrated in vacuo and the residue was triturated with 5% NH₄OH. The insoluble material was filtered, washed well with H₂O, dried, and recrystallized to give the corresponding Xa–e.

Method B: A mixture of the appropriate VIIa–e (0.0003 mol) and diethyl azodicarboxylate (0.21 g, 0.0012 mol) was heated at 160° for 15 min and the reaction mixture was triturated with EtOH. The insoluble material was filtered, washed with hot EtOH, and recrystallized to give the corresponding Xa–c, identical in all respects with the compounds prepared by Method A.

4-Arylimino-1,3-dimethylpyrimido[4,5-\(b\)]quinoline-2(1H,3H)-ones (XIIa–c) (Table VI)—A mixture of the appropriate XIIa–c (0.001 mol) and DMF DMA (0.6 g, 0.005 mol) was heated at 160° for 1.5 hr. The reaction mixture was concentrated in vacuo and the residue was covered with EtOH. The insoluble material was filtered, washed with EtOH, and recrystallized to give the corresponding XIIa–c.

Acid Hydrolysis of XIIa–c—A suspension of the appropriate XIIa–c (0.0005 mol) in 35% HCl (3 ml) was heated at 95° for 30 min. The precipitates were filtered, washed well with H₂O, dried, and recrystallized from dimethylformamide to give Va or Vb, identical in all respects with the compounds prepared by the reaction of IIa or IIb with DMF DMA.

1,3-Dimethyl-6-(N-methylanilino)uracil (XV)—A mixture of 3-methyl-6-(N-methylanilino)uracil (XIV)¹₅ (0.462 g, 0.002 mol) and DMF DMA (0.36 g, 0.003 mol) was refluxed at 160° for 30 min. The reaction mixture was concentrated in vacuo and the residue was covered with ether. The insoluble material was filtered and recrystallized from H₂O to give XV (0.269 g, 55%), mp 104°. Anal. Calcd. for C₁₅H₁₄N₂O₂: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.40; H, 6.12; N, 17.34. IR cm⁻¹: 1645, 1690 (CO). NMR (CDCl₃) δ: 3.23 (s, 3H, N–Me), 3.36 (s, 3H, N–Me), 5.50 (s, 1H, C–H), 5.66–7.66 (m, 5H, C₉H₅). MS m/z: 245 (M⁺).

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