

SYNTHESIS OF FUSED AZOLES: SYNTHESIS OF SEVERAL NEW PYRROLO-  
[2,3:4',5']PYRROLO[2,1-b]THIAZOLES AND THIAZOLO[2,3-a]PYRIDINE  
DERIVATIVES

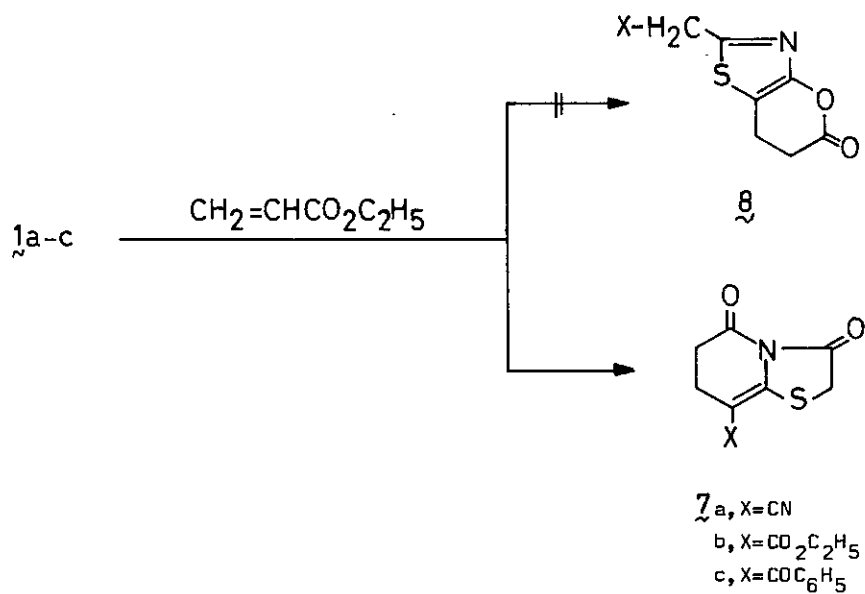
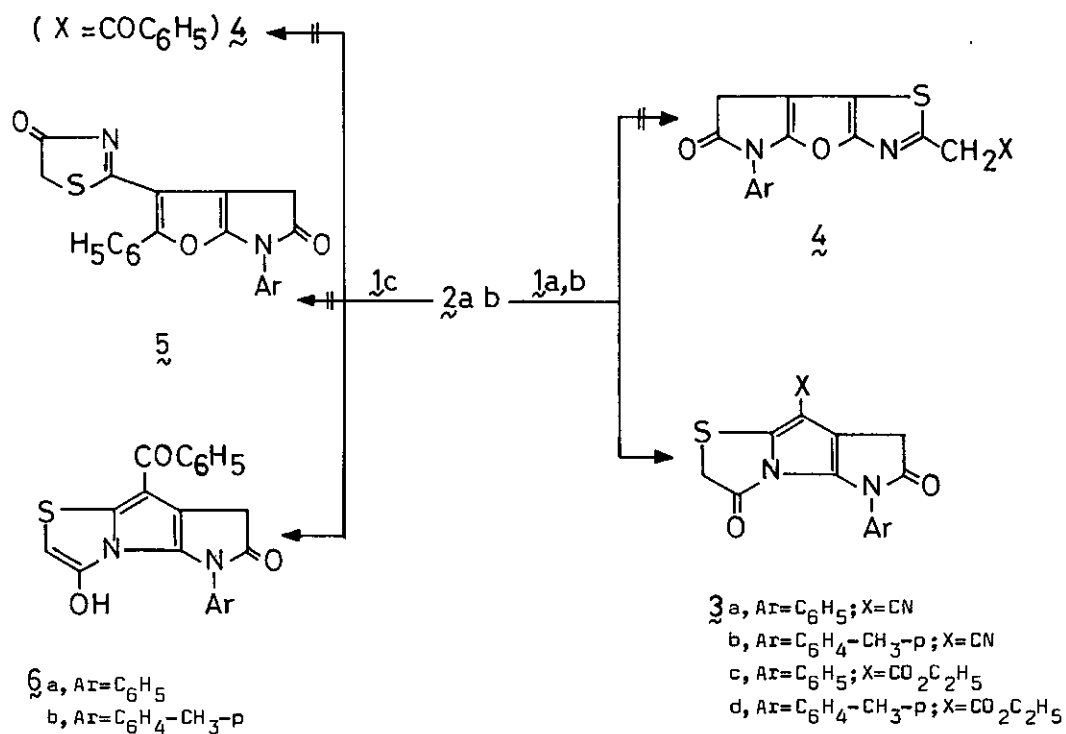
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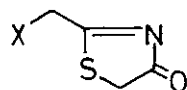
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**Abstract** - The reactions of the 2-functionally substituted methylthiazol-4-one derivatives (1a-c) with N-arylmaleimides (2a,b) and ethyl acrylate have resulted in the synthesis of several new pyrrolo[2,3:4',5']pyrrolo[2,1-b]thiazoles and thiazolo[2,3-a]pyridine derivatives. The structures of the synthesised compounds were assigned based on analytical and spectral data.

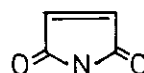
As a part of the program aiming to develop new efficient procedures for the synthesis of azoles<sup>1</sup>, azines<sup>2</sup> and azoloazines<sup>3,4</sup> we have recently reported a novel synthesis of thiazolo[2,3-a]pyridine derivatives via the addition of 2-functionally substituted methylthiazoles to cinnamionitrile derivatives<sup>5</sup>. We have been interested to see if reactions of this type can be extended to constitute a new general approach for the synthesis of azolothiazoles and thiazoloazine derivatives. The work has resulted in development of a new route for synthesis of pyrrolo[2,3:4',5']pyrrolo[2,1-b]thiazoles and thiazolo[2,3-a]pyridines bearing functional substituents that make them interesting for further chemical transformations.

Thus, it has been found that the 2-functionally substituted 2-thiazolin-4-one derivatives (1a,b; 0.01 mol) reacted with N-arylmaleimides (2a,b; 0.01 mol; heating under reflux in dioxane for 5 h) to yield products resulting from addition of 1a,b to the maleimide and elimination of water. Two theoretically possible structures were considered (cf. structures 3 and 4). Structure 4 was readily ruled out based on IR spectra of these products which revealed strong absorption for the ring C=O group as well as <sup>1</sup>H NMR spectra which showed resonance for thiazole H-5 protons. Compound 1c reacted also with 2a,b to yield also products from addition and elim-





- 1a, X=CN  
 b, X=CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>  
 c, X=COC<sub>6</sub>H<sub>5</sub>



- 2a, Ar=C<sub>6</sub>H<sub>5</sub>  
 b, Ar=C<sub>6</sub>H<sub>4</sub>-CH<sub>3</sub>-p

ination of water. Here in addition to structures 5 or 4 (X=COPh) the furo [2,3-b]-pyrrole structure 5 seemed possible. However, structure 6 was readily established for the reaction products based on IR spectra which revealed three different C=O groups. Moreover, the reaction products proved very stable to acid and alkaline treatment, and conditions that are expected to effect cleavage of the furan or pyrone derivatives.

Compounds 1a-c reacted with ethyl acrylate to yield the thiazolo [2,3-a]pyridine derivatives 3a-c formed via addition of the acrylate to the exocyclic active methylene group and cyclisation by elimination of ethanol. The other possible structure 8 was ruled out based on IR spectra which revealed absorption pattern different from that expected for such compounds.

It is clear from the above results that the reaction of 1a-c with activated double bonds opens a new general approach for synthesis of differently substituted fused thiazole derivatives.

Table 1: List of the pyrrolo [2,3: 4',5'] pyrrolo [2,1-b]thiazoles (3 and 6) and thiazolo [2,3-a]pyridines (7)

Product*	Solvent of cryst.	Colour	M.p. (°C)	Yield (%)	Mol. formula
<u>3a</u>	DMF/H <sub>2</sub> O	pale yellow	250-252	70	C <sub>15</sub> H <sub>9</sub> N <sub>3</sub> O <sub>2</sub> S
<u>3b</u>	methanol	yellow	280-281	62	C <sub>16</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub> S
<u>3c</u>	DMF/H <sub>2</sub> O	pale yellow	264-266	68	C <sub>17</sub> H <sub>14</sub> N <sub>2</sub> O <sub>4</sub> S
<u>3d</u>	acetic acid	yellow	190	71	C <sub>18</sub> H <sub>16</sub> N <sub>2</sub> O <sub>4</sub> S
<u>6a</u>	acetic acid	yellow	240-241	65	C <sub>21</sub> H <sub>14</sub> N <sub>2</sub> O <sub>3</sub> S
<u>6b</u>	DMF/H <sub>2</sub> O	yellow	225	55	C <sub>22</sub> H <sub>16</sub> N <sub>2</sub> O <sub>3</sub> S
<u>7a</u>	methanol	colourless	195	65	C <sub>9</sub> H <sub>6</sub> N <sub>2</sub> O <sub>2</sub> S
<u>7b</u>	methanol	colourless	143	70	C <sub>10</sub> H <sub>11</sub> N <sub>2</sub> O <sub>4</sub> S
<u>7c</u>	methanol	colourless	172	66	C <sub>14</sub> H <sub>11</sub> N <sub>2</sub> O <sub>3</sub> S

\*Satisfactory elemental analyses for all the compounds were obtained.

Table 2: IR and  $^1\text{H}$  NMR data of compounds 3, 5 and 7

Comp.	IR(KBr), $\text{cm}^{-1}$	$^1\text{H}$ NMR(DMSO), $\delta$ ppm.
<u>3a</u>	3010, 2990(saturated $\text{CH}_2$ ); 2220 (CN); 1700, 1680(two ring $\text{C=O}$ ) and 1650( $\text{C=C}$ ).	2.2(m, 2H, $\text{CH}_2$ ); 4.66(m, 2H, thiazole $\text{CH}_2$ ) and 7.25(m, 5H, aromatic protons).
<u>3b</u>	3000, 2980(saturated $\text{CH}_2$ ); 2230 (CN); 1710, 1690(two ring $\text{C=O}$ ) and 1650( $\text{C=C}$ ).	2.2(m, 4H, two $\text{CH}_2$ ); 4.0(m, 3H, $\text{CH}_3$ ) and 7.2(m, 4H, aromatic protons).
<u>3c</u>	3020, 2990(saturated $\text{CH}_2$ ); 1730 (ester $\text{C=O}$ ); 1690, 1670(two ring $\text{C=O}$ ) and 1650( $\text{C=C}$ ).	
<u>3d</u>	3020, 2980(saturated $\text{CH}_2$ ); 1740 (ester $\text{C=O}$ ); 1700, 1680(two ring $\text{C=O}$ ) and 1630( $\text{C=C}$ ).	1.3(t, 3H, $\text{CH}_3$ ); 2.0(s, 3H, $\text{CH}_3$ ); 2.2(m, 2H, $\text{CH}_2$ ); 4.16(q, 2H, $\text{CH}_2$ ); 4.66(m, 2H, ring $\text{CH}_2$ ) and 7.3(m, 4H, aromatic protons).
<u>5a</u>	3500(OH); 2990(saturated $\text{CH}_2$ ); 1740(exocyclic $\text{C=O}$ ); 1680(ring $\text{C=O}$ ) and 1640( $\text{C=C}$ ).	
<u>5b</u>	3450(OH); 2980(saturated $\text{CH}_2$ ); 1730(exocyclic $\text{C=O}$ ); 1690(ring $\text{C=O}$ ) and 1650( $\text{C=C}$ ).	3.9(m, 2H, $\text{CH}_2$ ); 6.85(s, 1H, thiazole-CH); 7.3~8.0(m, 10H, aromatic protons) and 12.1(s, br, 1H, OH).
<u>7a</u>	3100, 3000(saturated $\text{CH}_2$ ); 2220 (CN); 1690, 1670(two ring $\text{C=O}$ ) and 1640( $\text{C=C}$ ).	
<u>7b</u>	3000, 2985(saturated $\text{CH}_2$ ); 1740 (ester $\text{C=O}$ ); 1685, 1670(two ring $\text{C=O}$ ) and 1650( $\text{C=C}$ ).	
<u>7c</u>	2990, 2980(saturated $\text{CH}_2$ ); 1730 (exocyclic $\text{C=O}$ ); 1690, 1670(two ring $\text{C=O}$ ) and 1640( $\text{C=C}$ ).	

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