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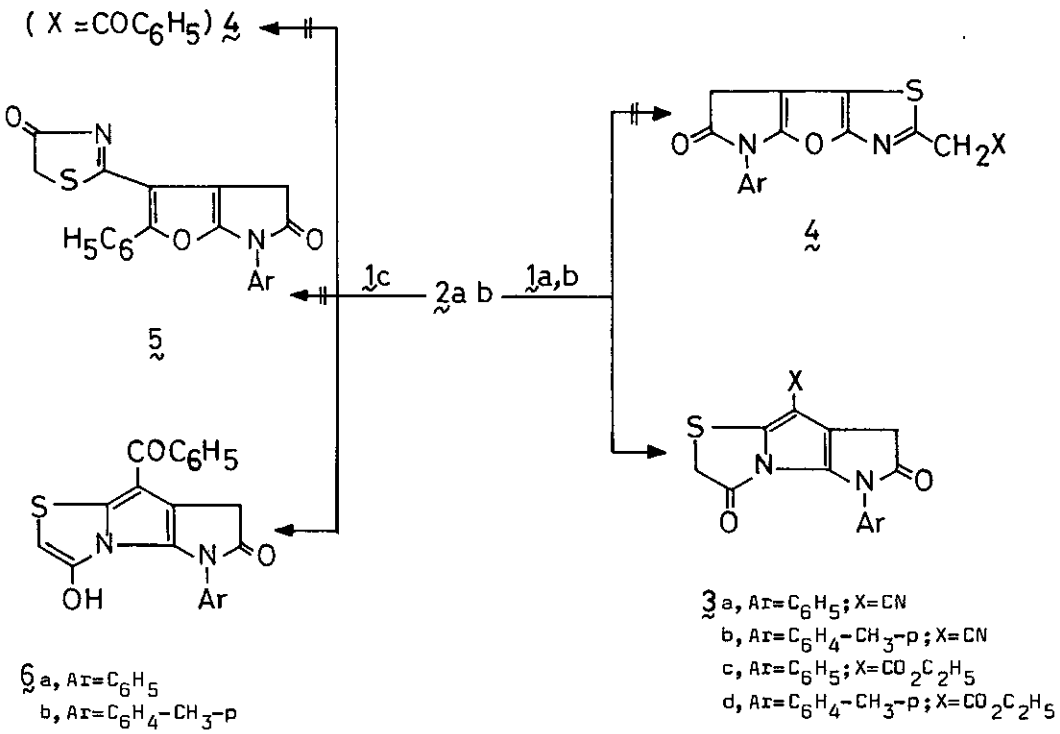
Abstract - The reactions of the 2-functionally substituted methylthiazol-4-one derivatives (1a-c) with N-arylmaleimides (2a,b) and ethyl acrylate have resulted in the synthesis of several new pyrrolo[2,3:4',5']pyrrolo[2,1-b]thiazoles and thiazolo-[2,3-a]pyridine derivatives. The structures of the synthesised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

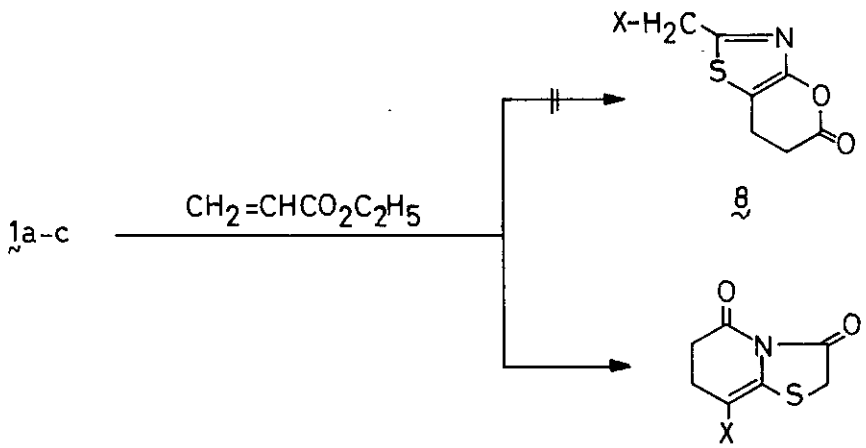
As a part of the program aiming to develop new efficient procedures for the synthesis of azoles[1], azines[2] and azoloazines[3,4] we have recently reported a novel synthesis of thiazolo[2,3-a]pyridine derivatives via the addition of 2-functionally substituted methylthiazoles to cinnamonitrile derivatives[5]. 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 ^{1}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-

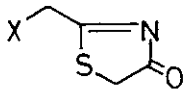


6 a, Ar=C_6H_5
b, Ar=C_6H_4-CH_3-p

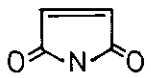
3 a, Ar=C_6H_5; X=CN
b, Ar=C_6H_4-CH_3-p; X=CN
c, Ar=C_6H_5; X=$CO_2C_2H_5$
d, Ar=C_6H_4-CH_3-p; X=$CO_2C_2H_5$



7 a, X=CN
b, X=$CO_2C_2H_5$
c, X=COC_6H_5



1a, X=CN
b, X=$CO_2C_2H_5$
c, X=COC_6H_5



2a, Ar=C_6H_5
b, Ar=C_6H_4-CH_3-p

ination of water. Here in addition to structures 6 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 7a-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
3a	DMF/H_2O	pale yellow	250-252	70	$C_{15}H_9N_3O_2S$
3b	methanol	yellow	280-281	62	$C_{16}H_{11}N_3O_2S$
3c	DMF/H_2O	pale yellow	264-266	68	$C_{17}H_{14}N_2O_4S$
3d	acetic acid	yellow	190	71	$C_{18}H_{16}N_2O_4S$
6a	acetic acid	yellow	240-241	65	$C_{21}H_{14}N_2O_3S$
6b	DMF/H_2O	yellow	225	55	$C_{22}H_{16}N_2O_3S$
7a	methanol	colourless	195	65	$C_8H_6N_2O_2S$
7b	methanol	colourless	143	70	$C_{10}H_{11}NO_4S$
7c	methanol	colourless	172	66	$C_{14}H_{11}NO_3S$

*Satisfactory elemental analyses for all the compounds were obtained.

Table 2: IR and ^1H NMR data of compounds 3, 6 and 7

Comp.	IR(KBr), cm^{-1}	^1H NMR(DMSO), δ ppm.
3a	3010, 2990(saturated CH_2); 2220 (CN); 1700, 1680(two ring C=O) and 1650(C=C).	2.2(m, 2H, CH_2); 4.66(m, 2H, thiazole CH_2) and 7.25(m, 5H, aromatic protons).
3b	3000, 2980(saturated CH_2); 2230 (CN); 1710, 1690(two ring C=O) and 1650(C=C).	2.2(m, 4H, two CH_2); 4.0(m, 3H, CH_3) and 7.2(m, 4H, aromatic protons).
3c	3020, 2990(saturated CH_2); 1730 (ester C=O); 1690, 1670(two ring C=O) and 1650(C=C).	
3d	3020, 2980(saturated CH_2); 1740 (ester C=O); 1700, 1680(two ring C=O) and 1630(C=C).	1.3(t, 3H, CH_3); 2.0(s, 3H, CH_3); 2.2 (m, 2H, CH_2); 4.16(q, 2H, CH_2); 4.66 (m, 2H, ring CH_2) and 7.3(m. 4H, aromatic protons).
6a	3500(OH); 2990(saturated CH_2); 1740(exocyclic C=O); 1680(ring C=O) and 1640(C=C).	
6b	3450(OH); 2980(saturated CH_2); 1730(exocyclic C=O); 1690(ring C=O) and 1650(C=C).	3.9(m, 2H, CH_2); 6.85(s, 1H, thiazole-CH); 7.3~8.0(m, 10H, aromatic protons) and 12.1(s, br, 1H, OH).
7a	3100, 3000(saturated CH_2); 2220 (CN); 1690, 1670(two ring C=O) and 1640(C=C).	
7b	3000, 2985(saturated CH_2); 1740 (ester C=O); 1685, 1670(two ring C=O) and 1650(C=C).	
7c	2990, 2980(saturated CH_2); 1730 (exocyclic C=O); 1690, 1670(two ring C=O) and 1640(C=C).	

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