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THIAZOLO [5,4-*a*] ACRIDINES

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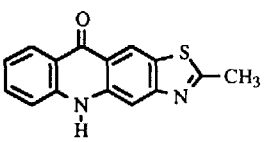
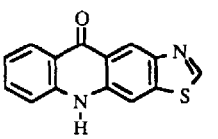
Abstract. The synthesis of thiazolo [5,4-*a*] acridines and acridin-9(10*H*)-ones by cyclisation of anthranilic acids is described. NMR (specially ^{1}H NMR) was used to ascertain their 'bent' structure.

There is a considerable interest in acridines fused with five-membered heterocyclic compounds. In particular when the heterocycle is a thiazole ring, the resulting structures are related to benzothiazoles used as chemotherapeutic agents [1]. Recently, Taraporewala[2] described two such systems, **1** and **2**, obtained by cyclisation of the corresponding anthranilic acids using PPA.

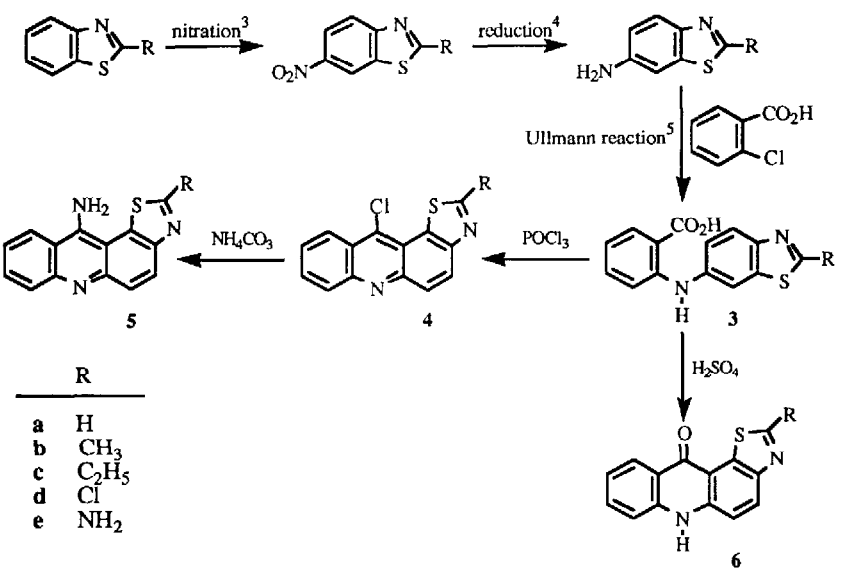


1. [5,4-*b*] series



2. [4,5-*b*] series

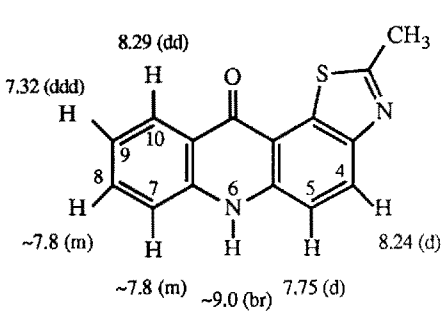
We report here the synthesis of the [5,4-*a*] isomers obtained also from anthranilic acids but with sulfuric acid or phosphorus oxychloride as cyclizing agents :

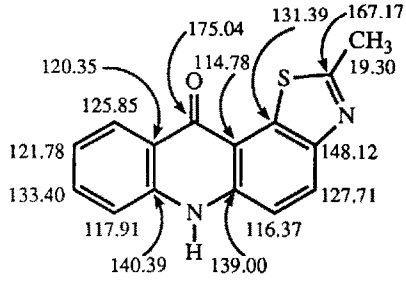


R	
a	H
b	CH_3
c	C_2H_5
d	Cl
e	NH_2

According to this scheme the following compounds were prepared and fully characterized (m.p. in °C; yield) : **3a** (210; 31 %), **3b** (>300; 35 %)[7], **3c** (172; 44 %), **3d** (>300; 33 %), **3e** (>300; 35 %), **4a** (>300; 83 %), **4d** (>300; 88 %), **4e** (>300; 79 %), **5e** (>300; 39 %), **6a** (>300; 94 %), **6b** (>300; 95 %)[7], **6c** (>300; 94 %), **6d** (>300; 81 %), **6e** (>300; 87 %).

That the tetracycles are 'bent', i.e. belong to the [5,4-*a*] series and are not 'linear' ([4,5-*b*] series **2**), was established by NMR, both ^{1}H and ^{13}C [6]. For instance, for compound **6b** (2-methyl-thiazoloacridin-9(10*H*)-one) [8] :





J_{45} = 9.0; J_{89} = 6.0; J_{810} = 1.0

J_{97} = 1.8; J_{910} = 8.0

The assignment was made using bidimensional techniques (^{1}H-^{1}H and ^{1}H-^{13}C). Protons 4 and 5 present an AB system without any other couplings, characteristic of the 'bent' tetracycle. When the central six-membered ring is formed last, 'bent' isomers are usually obtained : pyrazolo [a] acridin-9(10*H*)-ones [9] and 6*H*-imidazo [4,5-*c*] phenothiazines [10]. These results indicate that the 'linear' structures of Taraporewala [2] are exceptional: either PPA plays an unexplained role on the reaction yields mixtures of isomers, the differences arising from purification procedures.

References and notes.

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7. A mixture of 6-amino-2-methylbenzothiazole (1.47 g, 0.009 mol), potassium o-chloro-benzoate (2.1 g, 0.01 mol), pentanol (15 ml) and a catalytic amount of powdered copper is heated at 110°C. Before cooling, the solution is filtered; then the solvent is evapored at low pressure and the oily residue is disolved in ethyl acetate. The organic solution is extracted with NaOH (700ml, 0.1N). By dropwise acidification with concentrated HCl, compound **3b** precipitates (0.83 g).The anthranilic acid **3b** (0.48 g) is heated at 100°C for 2 h. in concentrated H_2SO_4 (5 g, d = 1.84). The acid solution is poured over ice-water. The precipitate is filtered, washed with diluted ammonium hydroxide and dried. 0.38 g of compound **6b** are obtained.
8. Spectra in DMSO-d_6 at 200 MHz (^{1}H) or 50 MHz (^{13}C) (δ in ppm, J in Hz).
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