A Novel Heterocyclization Method. Synthesis of some Benzimidazoles and Benzoxazoles

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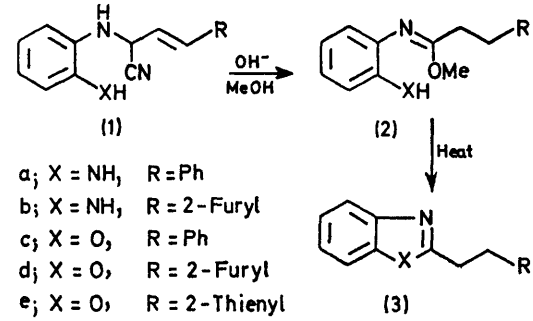
Summary Intramolecular cyclization of 1-methoxy-3-substituted-propylidene-*o*-aminoanilines and -*o*-aminophenols provides a convenient new synthesis of some 2-(β-substituted-ethyl)-benzimidazoles and -benzoxazoles, respectively.

DISPLACEMENT of the alkoxy-group of imino-esters by nucleophiles is fairly well known.[1] It would be expected that a nucleophile appropriately situated within an imino-ester could, by an addition–elimination mechanism, result in cyclization. We report such a ready heterocyclization for the synthesis of benzimidazoles (**3a** and **b**) and benzoxazoles (**3c–e**).

The *ortho*-substituted anilinonitriles (**1**) were readily prepared by reaction[2] of αβ-unsaturated aldehydes with KCN, AcOH and *o*-phenylenediamine or *o*-aminophenol. Treatment of α-aminonitriles (**1**) with methanolic KOH at room temperature[2] apparently gave good yields of imino-esters (**2**). Imino-esters (**2a** and **b**), easily identified by a characteristic i.r. absorption band at *ca.* 1645 cm^{-1}, were



thermally labile and on heating were converted into benzimidazoles (**3a** and **b**), respectively by loss of MeOH.

However, imino-esters (**2c–e**) appeared to be considerably less stable than (**2a**) or (**2b**), since here the only products isolated were benzoxazoles (**3c–e**). These apparently were the result of cyclization of the intermediate imino-esters (**2c–e**) during work-up. Physical and synthetic data are presented in the Table.

TABLE

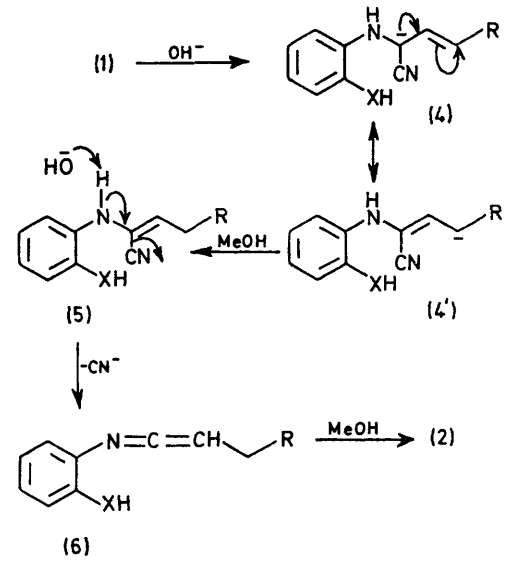
Physical and synthetic data for α-aminonitriles, benzimidazoles, and benzoxazoles

	α-Aminonitrile (**1**)		Benzimidazole or benzoxazole (**3**)	
Compound[a]	Yield (%)	M.p. (°C)	Yield (%)	M.p. (°C) or b.p.
a	73	106—108	95	184—185[b]
b	80	92·5—94	92	167—168
c	97	115—116	62	52—53·5[c]
d	92	85—87	82	104—109 at 0·5 mmHg
e	75	116—118	85	47—48

[a] The new compounds in the Table gave satisfactory analytical data; i.r., u.v., and n.m.r. data are in agreement with the assigned structures. [b] Lit.,[3] m.p. 189—190°. [c] Lit.,[4] m.p. 54·5°.

The mechanism for the formation of imino-esters (**2**) from α-anilinonitriles (**1**) is similar to that proposed[2] for the conversion of αβ-unsaturated aldehydes into saturated imino-esters *via* α-aminonitriles. A possible route is presented in the Scheme.

Since imino-esters (**2c–e**) have not been isolated, it is possible that benzoxazoles (**3c–e**) arise directly from the intramolecular addition of OH to the ketenimine function in intermediate (**6**).



SCHEME

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