An Unexpected Rearrangement of 4-Alkylaminoindoles

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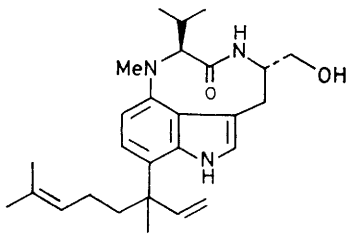
4-Alkylaminoindoles rearrange in good yield to the corresponding 1-alkyl-4-aminoindoles in the presence of 10 mol% hydrated toluene-*p*-sulphonic acid in boiling toluene.

During studies directed towards the total synthesis of teleocidin[1]A (**1**) (lygnbyatoxin[2]) and related potent tumour promotors,[3] we observed a novel and unexpected rearrangement of 4-alkylaminoindoles, the details of which we report here.

The starting 4-alkylaminoindoles (**2**) used in this work were prepared from 4-aminoindole which in turn can be prepared by the excellent Leimgruber and Batcho method.[4] Compound (**2**, R = Me) was obtained in 78 % yield by lithium aluminium hydride reduction of 4-*N*-formylaminoindole while (**2**, R = CH_2Ph) and (**2**, R = CH_2CO_2Et)† were derived by mono-alklyation of 4-aminoindole using potassium carbonate–potassium iodide and the appropriate bromide, in 47 and 84% yields respectively.

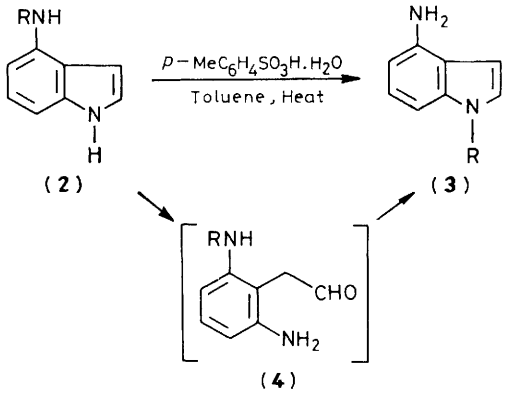


(**1**)

† All new compounds were fully characterised by spectroscopic methods, and accurate mass and/or microanalytical techniques.

Upon heating the indoles (**2**) in toluene containing 10 mol% of monohydrated toluene-*p*-sulphonic acid smooth conversion into the corresponding 1-alkyl-4-aminoindoles (**3**)† was achieved (Table 1). In the absence of water, or using anhydrous camphorsulphonic acid in a similar manner, no rearrangement was observed even after extended periods of time.

We suggest that the mechanism for the rearrangement reaction therefore involves initial ring opening of the 4-alkylaminoindole to produce an intermediate species (**4**) which prefers to undergo ring closure to the more thermodynamically stable 1-alkyl-4-aminoindole system (Scheme 1). This re-



Scheme 1

Table 1

Starting indole (**2**)	Product (**3**) % yield	Reaction time /h
R = Me	75	23
R = CH_2Ph	90	21
R = CH_2CO_2Et	77[a]	44

[a] Plus 13% recovered starting material.

arrangement has potentially useful synthetic applications for the preparation of specifically substituted indoles.

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