Isolation of a 2-Aminoindoline Derivative: a Suggested Intermediate in the Fisher Indole Synthesis

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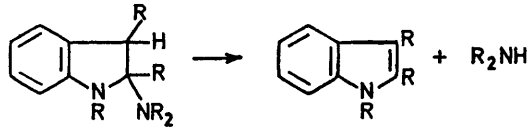
Summary 1-Acetyl-2-*o*-toluidinoindoline undergoes elimination of *o*-toluidine to form 1-acetylindole, a reaction equivalent to the suggested last step of the Fisher indole synthesis.

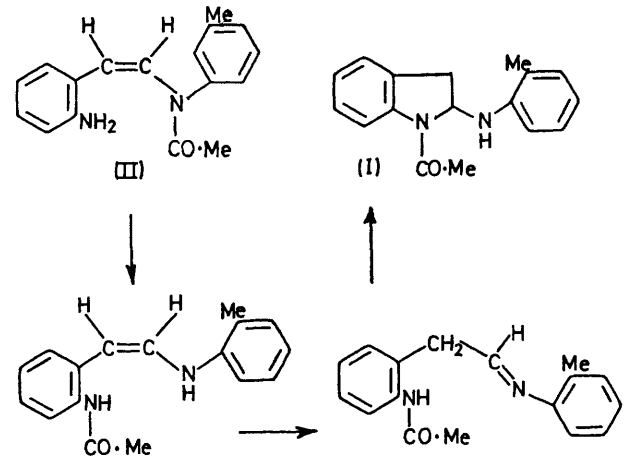
IN the Fisher indole synthesis it is generally assumed[1] that the last intermediate in the mechanistic sequence is a 2-aminoindoline which forms the indole nucleus by elimination of an amine (Scheme 1). The only examples of the isolation of this type of structure are found in cases in which the indole cannot be formed because the last step



SCHEME 1

(the elimination) is blocked by disubstitution at C-3. We have now isolated a 2-aminoindoline which can eliminate the amine and therefore perform the suggested last step of the Fisher indole synthesis. This indoline (I) was formed by intramolecular condensation of (II), catalysed by molecular sieve in refluxing benzene. A mechanism for its formation is suggested in Scheme 2. The compound (I) was isolated as crystals (m.p. 138—140).

The elimination of the 2-amino-function (*o*-toluidine) to form 1-acetylindole was found to proceed with extreme ease.



SCHEME 2

The conversion could be carried out by simply passing the indoline (I) through a silica or alumina column.

The formation of the 1-acetylindoline may be considered further support for Yamamoto's conclusion[2] that an amide nitrogen can add to the imine function and does not require prior conversion into the free amine as had previously been reported.[3]

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[1] B. Robinson, *Chem. Rev.*, 1969, **69**, 227.
[2] H. Yamamoto, *Bull. Chem. Soc. Japan*, 1967, **40**, 425; *J. Org. Chem.*, 1967, **32**, 3693.
[3] N. N. Suvorov and N. P. Sorokina, *Doklady Akad. Nauk S.S.S.R.*, 1961, **136**, 840.