

A New Synthesis of β -Carbolines

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A new one step synthesis of β -carbolines is described, which involves the direct conversion of N-imidotryptamines to the corresponding lactams on reaction with P_2S_5 .

The β -carboline system constitutes an integral part of a number of physiologically important indole alkaloids such as ajmalicine, vincamine, and reserpine. The reported difficulties associated with the cyclization of N-imidotryptamines to the corresponding β -carboline lactams [1–3] has led us to develop new improved procedures for the synthesis of β -carbolines [2, 4–8]. We now report another new method which leads directly to the reduced β -carboline lactams instead of the rather unstable enamides obtained previously. This involves refluxing the N-imidotryptamine (obtainable in high yields by condensing tryptamine with the corresponding anhydride) [9] with P_2S_5 in benzene.

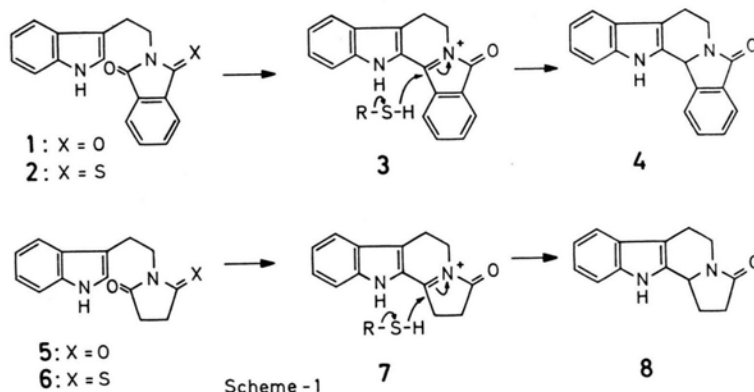
Thus N-phthalimidotryptamine (**1**) was refluxed with P_2S_5 (5 equiv.) in benzene for one hour. T. L. C. showed the formation of two faster moving compounds which were separated by preparative layer chromatography. The major slower moving compound obtained in ~80% yield was identified as the cyclized β -carboline lactam (**4**) (m.p. 203–205 °C). The UV spectrum of the product was typically indolic while its IR spectrum showed the amide carbonyl absorption at 1672 cm^{-1} . The mass spec-

trum afforded the M^+ ion at m/z 274 (100%) while other major peaks were present at 273 (72%), 245 (35%), 217 (24%). The product was found to be spectroscopically and chromatographically identical with an authentic sample of the substance obtained by our previously reported method [6]. The minor faster running compound was identified as the thioimide (**2**). It afforded a typically indolic UV spectrum and the mass spectrum showed the molecular ion at m/z 306 (10%). Other peaks were present at 239 (2%), 211 (5%), 169 (8%), 143 (74%). The addition of $HgCl_2$ during the reaction significantly enhanced the rate of cyclization and resulted in the complete conversion of the starting material to the corresponding β -carboline within 30 mts. without any formation of the thioimide (**2**).

N-Succinoimidotryptamine (**5**) on similar heating with P_2S_5 in benzene for one hour afforded only one product which was identified as the cyclized β -carboline lactam (**8**) (30% yield, m.p. 220–224 °C). The UV spectrum of the compound showed a normal indolic absorption while the mass spectrum showed the parent peak at m/z 226 while other major peaks were present at 225 (12%), 169 (8%), 215 (21%). The structure of the product was confirmed by spectroscopic and chromatographic comparison with an authentic sample prepared by the previously reported procedure. N-Glutarimidotryptamine (**9**) failed to cyclize under the above reaction conditions.

The reaction probably proceeds *via* a monothioimide intermediate (**2**) which undergoes an intramolecular attack by the indole 2-position; subsequent reduction of the intermediate immonium species (**3**) may occur by a hydride transfer reaction from a sulphur-bonded hydrogen (Scheme 1).

The above synthetic procedure offers a direct route for the synthesis of β -carboline lactams and avoids the initial synthesis of the unstable conjugated enamides which was necessary in the earlier methods.



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