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A NEW ONE-STEP SYNTHESIS OF β-CARBOLINES.

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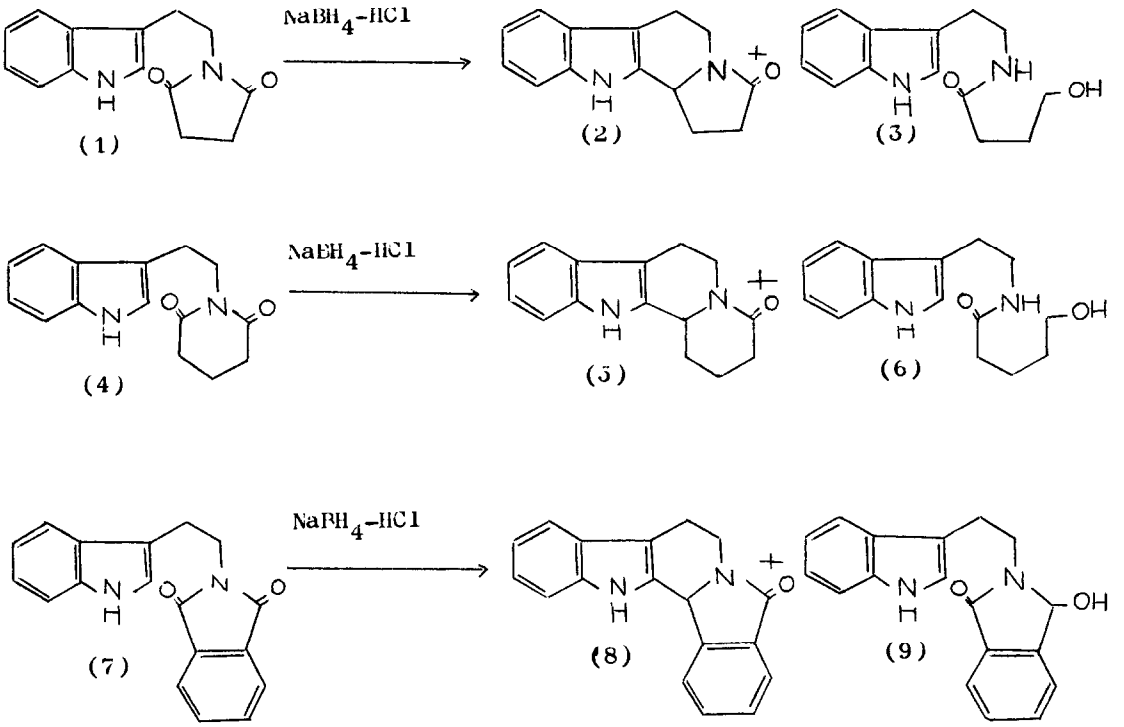
We have previously reported new methods for the reduction of amides to amines[1,2], α-functionalization of amides and imides[3], conversion of tertiary amides to aldehydes via Vilsmeier complexes[4], reduction of imides to seco-amide alcohols with $NaBH_4$[5] and a novel synthesis of β-carbolines[6]. Since the earlier synthesis of β-carbolines[6] proceeded in moderate yield, particularly with 5-membered imides, this has led us to investigate the possibility of developing alternative new methods for the cyclization of N-imidotryptamines to the corresponding β-carbolines. We report here a novel one-step synthesis of β-carbolines by the reductive cyclization of indolic imides with $NaBH_4$ -HCl in excellent yields.

N-Succinimidotryptamine(1)on treatment with excess of $NaBH_4$ and 2N HCl in ethanol at 0°C, afforded the cyclized β-carboline lactam (2)in 98% yield after five hours. When the same reaction was repeated at 24°C, the amide alcohol(3)was obtained in 75% yield and the cyclized β-carboline lactam(2)was formed as a minor product in 15% yields.

N-Glutarimidotryptamine(4)on identical treatment with $NaBH_4$ and 2N HCl in ethanol at 0-6°C afforded the cyclized β-carboline lactam (5) in 97% yield after one hour. At higher temperatures, (24°C), the amide alcohol(6)was obtained in 78% yield and the cyclized lactam(5) in 18% yield.

N-Phthalimidotryptamine(7)when similarly treated with $NaBH_4$ and 2N HCl in ethanol at 24°C and 0°C afforded the β-carboline lactam(8) as the faster moving compound in 90% and 75% yields respectively. The hydroxy lactam(9), m.p. 166°-168°C, was obtained in yields of 5% and 25% at 24°C and 0°C respectively in the reaction, and it cyclized quantitatively to the β-carboline(8) on treatment with conc. HCl at 34°C.

Wenkert[7] and others[8,9] have previously reported difficulties in synthesising β-carboline lactams from N-imidotryptamines under Bischler-Napieralski conditions. The above procedure represents a new high yield method for the synthesis of β-carbolines from N-imidotryptamines.



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