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REDUCTIVE CYCLIZATION OF INDOLIC IMIDES - A NEW β-CARBOLINE SYNTHESIS

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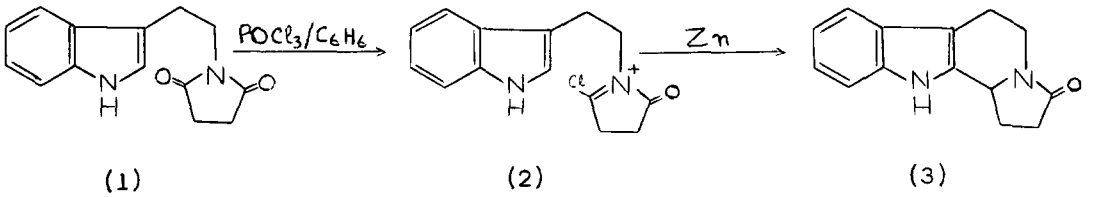
We have recently described new methods using Vilsmeier complexes as intermediates for the reduction of amides to amines with sodium borohydride[1] or zinc-ethanol[2]. These complexes have also been used by us for developing new procedures for α-functionalization of amides[3] and for converting tertiary amides to aldehydes[4] in high yields.

Our finding that cyclic imides can be reductively cleaved to the secoamide alcohol in good yields[5] has led us to examine the possibility of developing a new β-carboline synthesis by the reductive cyclization of indolic imides. We report here a novel procedure for the synthesis of β-carbolines involving the generation of Vilsmeier complexes of imides on treatment with phosphorus oxychloride. These complexes afford the corresponding β-carboline lactams on treatment with zinc dust under mild conditions.

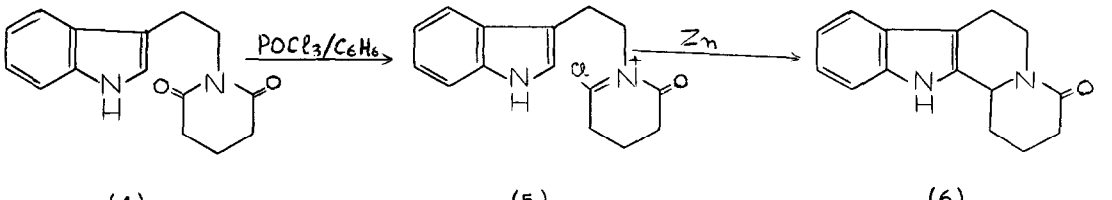
N-Succinimidotryptamine (1) afforded the corresponding complex (2) on refluxing with $POCl_3/C_6H_6$ for 1 hour. The reaction mixture was cooled to 0°C, excess zinc dust added and the solution warmed to 60°C for 1-2 minutes. Aqueous work-up and extraction into ethyl acetate afforded the B-carboline lactam (3) in 50% yields. N-Glutarimidotryptamine (4) on similar heating with $POCl_3$ in C_6H_6 followed by treatment with zinc dust afforded the corresponding cyclized lactam (6) in 60% yields. N-Pthalimidotryptamine (7) on identical treatment with $POCl_3/C_6H_6$ followed by zinc dust afforded the cyclized lactam (9) in 90% yields. The reaction proceeds via uncyclized chloroimmonium intermediates (2), (5) & (8) rather than cyclized enamides. This was demonstrated by aqueous treatment of aliquots prior to zinc dust treatment when the starting imides were recovered quantitatively and no cyclized enamides were detectable.

The above procedure offers an attractive new method for preparing β-carbolines from N-imidotryptamines. Wenkert[6] and others[7,8] have previously reported difficulties in synthesising β-carboline lactams from N-imidotryptamines due to the instability of the intermediate cyclized enamides. The method reported here avoids the intermediacy of these unstable conjugated enamides and offers a direct route to β-carbolines from the readily preparable N-imidotryptamines.

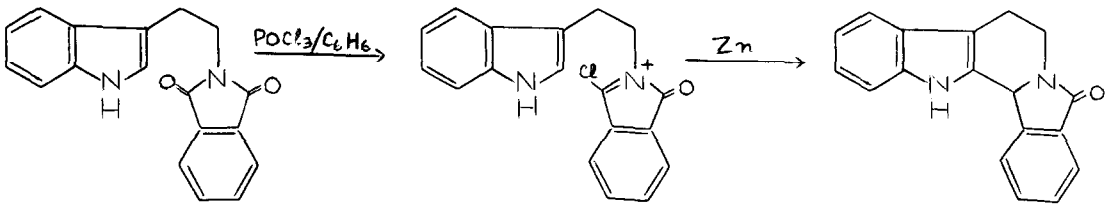
All products gave analytical and spectroscopic data consistent with the assigned structures and the cyclized lactams were identical with genuine samples.



(1) (2) (3)



(4) (5) (6)



(7) (8) (9)

References

1. Atta-ur-Rahman, A. Basha, N. Waheed and S. Ahmad, Tetrahedron Letters, 3, 219, (1976).
2. A. Basha and Atta-ur-Rahman, Experientia, 33, 101 (1977).
3. Atta-ur-Rahman, A. Basha and V.U. Ahmad, Experientia, 32, 1491 (1976).
4. Atta-ur-Rahman and A. Basha, J.Chem.Soc.Chemical Communications, 594, (1976).
5. Atta-ur-Rahman and N. Waheed, Z.Naturforsch, 31b, 287 (1976).
6. E.Wenkert, S.Garrat and K.G.Dave, Canad.J.Chem., 42, 489 (1964).
7. Atta-ur-Rahman, J.Chem.Soc., 736 (1972).
8. J.P.Kutney, N. Abdurahman, C.Gletsos, P.LeQuesne, E.Piers and I.Vlattas, J. Amer.Chem.Soc., 92, 1727 (1970).