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THE REACTIVITY OF BIOLOGICALLY INTERESTING INDOLE SYSTEMS WITH 3-PYRROLIN-2-ONE

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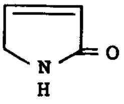
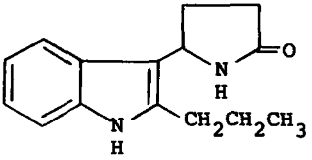
The selective reactions of aminoacids in protic solvents are particularly interesting especially in regard to the possibility of modifying the structure of only a few of the aminoacids present in a polypeptide system.

In previous research we reported the possibility of introducing substituted allyl chains onto tryptophan at biological pH values[1], and the high reactivity of indole with 3-pyrrolin-2-one (I) in acetic medium[2]. Now the reaction of (I) with indole systems has been investigated, with the view of utilizing (I) as a selective reagent for tryptophan.

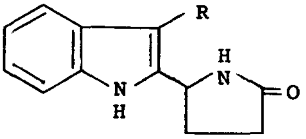
The reaction of (I) with 2-*n*-propyl-indole forms the compound (II), substituted in the 3-position of the indole nucleus (m.p. 263°, 80%), while the reaction of (I) with skatole produces the compound (IIIa), substituted in the 2-position (m.p. 210°, 82%); similarly, with N-acetyl-tryptamine the compound (IIIb) was obtained (m.p. 223°, 75%).

(I)

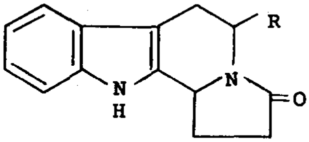




(II)



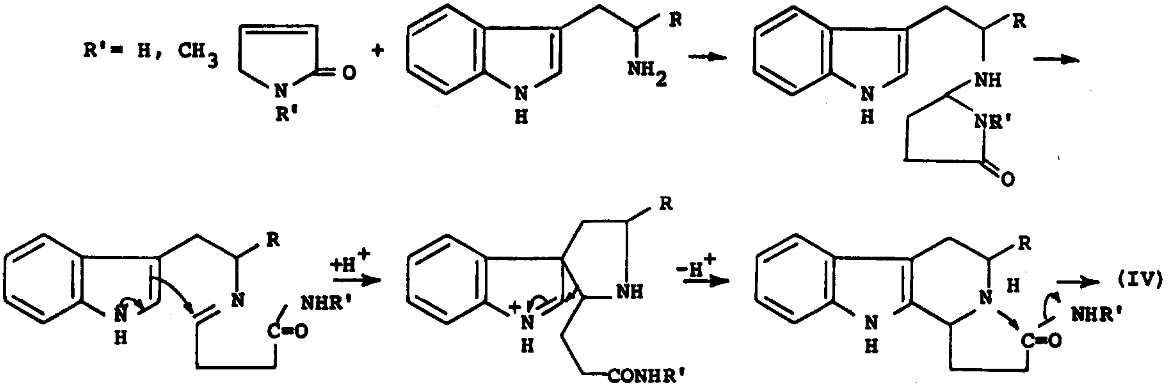
(IIIa) R = CH_3
(IIIb) R = CH_2CH_2NHAc



(IVa) R = H
(IVb) R = CO_2Me

The reaction of (I) with tryptamine has a different course: in this case the product obtained has analytical and spectrographic characteristics corresponding to the structure (IVa) (m.p. 253-54°, 85%). An analogous result was also obtained by the reaction of (I) with the methyl ester of tryptophan, from which the compound (IVb) was isolated (m.p. 202°, 80%).

The mechanism reported below seems to be the most likely one in the formation of (IVa) and (IVb):



The possibility of the formation of (IVa) and (IVb) is in agreement with the results of Jackson[3] and was also supported by the course of the reaction between the methyl ester of succinic monoaldehyde and tryptamine, which gave (IVa) in high yield. Furthermore, in agreement with the elimination of the amidic nitrogen, (IVa) was also obtained from the reaction of 1-methyl-3-pyrrolin-2-one and tryptamine.

Under the same reaction conditions used in the cases presented[4], no reaction was found with other aminoacids; in particular the experiments carried out with tyrosine were negative. These results therefore suggest a new possibility of modifyind peptide structures and simultaneously present a new synthetic route to β-carboline systems.

Satisfactory analysis were obtained for all compounds; the u.v., i.r., n.m.r. and mass spectra agree with the proposed structures.

REFERENCES

[1] G. Casnati, A. Guareschi, M. Francioni and A. Pochini, *Tetrahedron Letters*, 1969, 2485.

[2] V. Bocchi and G. P. Gardini, *Org. Prep. Proced.*, 1, 271 (1969).

[3] A.H. Jackson, B. Naidov and P. Smith, *Tetrahedron*, 24, 6119 (1968).

[4] Equimolecular quantities of (I) and indoles were refluxed in acetic acid for 30-60 minutes.

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