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A NEW SYNTHESIS OF PYRROLES[1]

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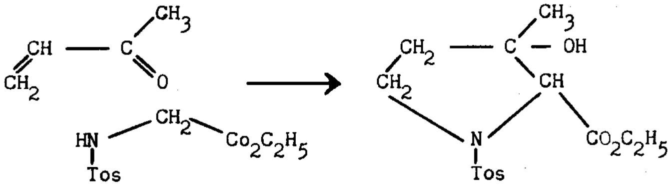
IN the course of porphyrin syntheses we required 2-alkoxycarbonylpyrroles, unsubstituted in the 5-position, e.g. (III). Such compounds are not directly accessible by the usual routes, and we wish to report an apparently general synthesis of them.

For example, condensation of N-tosylglycine ethyl ester with methyl vinyl ketone in dry t-butyl alcohol/ether containing potassium t-butoxide (2 days at room temperature) gave 78 per cent of the 3-hydroxy-N-tosylpyrrolidine (I), (Found: C, 54.9; H, 6.4; N, 3.87; S, 10.0. $C_{15}H_{21}O_5NS$ requires C, 55.0; H, 6.5; N, 4.3; S, 9.8%), m.p. in the range 88-100°, presumably a mixture of stereoisomers. Alternatively the methiodide of the Mannich base from acetone, formaldehyde and piperidine could be substituted for methyl vinyl ketone (yield 48 per cent).



I

Dehydration of the pyrrolidine (I) with phosphorus pentoxide in boiling benzene afforded the Δ^3-pyrroline (II), (Found: C, 58.2; H, 6.2;

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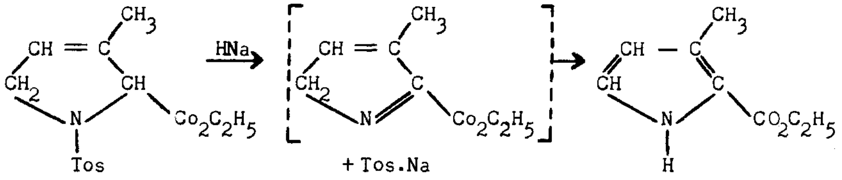
[1] The gist of this communication was presented in lectures at the Universities of Bristol and Hull on 2 and 16 November, 1961.

N, 4.4. $C_{15}H_{19}O_4NS$ requires C, 58.2; H, 6.2; N, 4.5%), (83%), m.p. 132°. The location of the double bond in the pyrroline ring was deduced from the proton magnetic resonance spectrum (multiplet at τ 4.54, area 1, corresponding to the vinyl proton at position 4; doublet (J ~ 1 c/s) at 8.32, area 3, corresponding to the 3-methyl group), and molecular models show that formation of the Δ^2-pyrroline would be sterically hindered.



II III

As we expected from consideration of other eliminations of sodium toluene-p-sulphinate from N-tosyl compounds,[2] treatment of the pyrroline (II) with sodium hydride in boiling tetrahydrofuran produced 2-ethoxycarbonyl-3-methylpyrrole (III), (Found: C, 63.2; H, 7.4; N, 9.2. Calc. for $C_8H_{11}NO_2$: C, 62.8; H, 7.4; N, 9.1%), m.p. 58° (lit.[3] m.p. 56°). A very similar elimination has been observed recently during an investigation of dehydroproline derivatives.[4]

Variants of this synthesis, particularly those involving other Mannich bases, are being explored and full details will be reported elsewhere.

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[2] W.R. Bamford and T.S. Stevens, J. Chem. Soc. 4735 (1952); G.R. Proctor, Chem. & Ind. 408 (1960).

[3] H. Fischer and O. Wiedermann, Z. Physiol. Chem. 155, 69 (1926).

[4] A.V. Robertson, J.E. Francis and B. Witkop, J. Amer. Chem. Soc. 84, 1709 (1962).