

We have thus obtained the four possible dextro forms. So far, attempts to invert C₈ and C₉ by acidic reagents have either yielded unchanged compounds or intractable mixtures; but further work on this point is in progress.

The work described forms part of a much wider investigation on the structure of ψ -santonin, the results of which will shortly be submitted for publication elsewhere.

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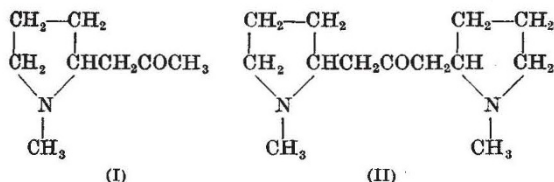
¹ Cleo and Cocker, *J. Chem. Soc.*, 30 (1946).

² Cocker and Lipman, *J. Chem. Soc.*, 533 (1947).

³ Huang Minlon, Lo and Chu, *J. Amer. Chem. Soc.*, **65**, 1780 (1943).
Huang Minlon, *J. Amer. Chem. Soc.*, **70**, 611 (1948).

Syntheses of Hygrine and Cuscohygrine

In his theory of the phytochemical synthesis of alkaloids published in 1917, Robinson¹ suggested that hygrine (I) and cuscohygrine (II) were formed by the condensation of acetone dicarboxylic acid with one and with two molecular proportions respectively of γ -methylaminobutyraldehyde.



Robinson's theory became widely known and is frequently stated in text-books; but no attempt to carry out these reactions seems to have been made for nearly twenty years. Then in 1936 he² announced that "a synthesis of *dl*-hygrine on these lines has proved feasible", but so far as we are aware no account of this synthesis has appeared. Later, Schöpf³ reported that he was unable to obtain *nor*hygrine from γ -aminobutyraldehyde and acetoacetic acid, although the phenyl analogue of this base was formed from the same aldehyde and benzoylacetic acid.

We have now found that acetone dicarboxylic acid condenses smoothly with two molecular proportions of γ -methylaminobutyraldehyde at pH 7 to produce cuscohygrine in excellent yield. The identification of the product was made by direct comparison of several of its derivatives with authentic specimens and by the agreement of the analytical figures with the calculated values. Similarly, we have obtained from the reaction between excess acetoacetic acid and γ -methylaminobutyraldehyde a base

which we believe to be *dl*-hygrine. The physical constants of the base and its derivatives agree with the values recorded in the literature, and the analytical figures also accord with the calculated values. Although we have not yet had the opportunity of making direct comparisons with authentic specimens, there can be little doubt that the synthetic product is *dl*-hygrine.

Full details of this work, including a discussion of the stereochemistry of cuscohygrine, will be published shortly.

We are greatly indebted to Prof. R. L. Shriner of the State University of Iowa for the provision of a sample of authentic cuscohygrine.

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¹ Robinson, R., *J. Chem. Soc.*, 876 (1917).

² Robinson, R., *J. Chem. Soc.*, 1079 (1936).

³ Schöpf, C., *Z. Angew. Chem.*, **50**, 797 (1937).

I WOULD like to congratulate the authors on these syntheses, which are fundamental for the theory. My own synthesis, mentioned in 1936, employed acetonedicarboxylic acid in excess, but was otherwise identical. Though the product was undoubtedly *dl*-hygrine, the opportunity to add the final touches necessary for publication did not occur.

It is very satisfactory that this synthesis will now be placed on record and will become available for reference.

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Mechanism of the Fischer Indole Synthesis

THE mechanism previously proposed^{1,2} for the Fischer indole reaction has assumed that the intermediate stages involve an *o*-benzidine-type re-arrangement. This may be illustrated as follows, considering, as an example, the phenyl hydrazone of cyclohexanone:

