

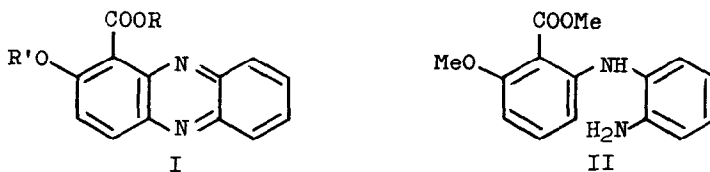
SYNTHESIS OF METHYL 2-METHOXYPHENAZINE-1-CARBOXYLATE

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(Received in UK 8 January 1968)

In a recent publication¹, Olsen and Richards have confirmed that 2-hydroxyphenazine-1-carboxylic acid (I, R = R' = H) is the structure of



a metabolite of Pseudomonas aureofaciens² by spectroscopic methods and the synthesis of a degradation product, 2-methoxy-1-methylphenazine; an X-ray structure determination was in agreement with this finding.

We had already come to a similar conclusion on the basis of spectral and chemical evidence and sought the synthesis of the pigment itself. This has been achieved by an application of the nitrobenzene cyclisation of 2-aminodiphenylamines³ to give methyl 2-methoxyphenazine-1-carboxylate (I, R = R' = Me); since Olsen and Richards¹ have shown that the dimethyl compound, obtained from the metabolite by the action of diazomethane, can be converted back to the natural product by successive hydrolyses with concentrated hydrochloric acid and alkali, this synthesis constitutes a synthesis of the natural product itself.

2-Methoxy-6-nitrobenzoic acid⁴ was converted to its methyl ester with diazomethane; hydrogenation then gave methyl 2-amino-6-methoxybenzoate. Condensation of this ester with 2-iodonitrobenzene gave a nitrodiphenylamine which was hydrogenated to give methyl 2'-amino-3-methoxydiphenylamine-2-carboxylate (II). The cyclisation in refluxing nitrobenzene was slow, requiring 114 hrs. and gave methyl 2-methoxyphenazine-1-carboxylate (I, R = R' = Me) identical with the dimethyl derivative of the natural product⁵ on the basis of mixed melting point and electronic, infrared and p.m.r. spectra.

References

1. E. S. Olsen and J. H. Richards, J. Org. Chem., 32, 2887 (1967).
2. A. J. Kluyver, J. Bacteriol., 72, 406 (1956); J. I. Toohy, C. D. Nelson and G. Krotkov, Canad. J. Bot., 43, 1055 (1965).
3. R. B. Herbert and F. G. Holliman, Tetrahedron, 21, 663 (1965), and previous papers by F. G. Holliman and co-workers.
4. T. Takahashi and Y. Hamada, J. Pharm. Soc. (Japan), 75, 1434 (1955).
5. Isolated from the crude pigments (mainly phenazine-1-carboxylic acid) of Ps. aureofaciens kindly supplied by W. C. Heynes, Northern Regional Laboratory, Peoria, Illinois.