Tetrahedron Letters No.33, pp. 2847-2848, 1969. Pergamon Press. Printed in Great Britain.

SYNTHESIS OF (±) FICINE*

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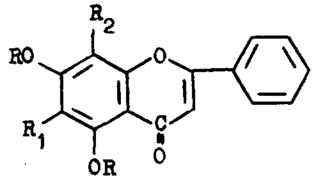
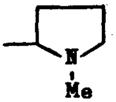
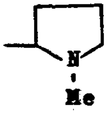
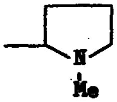
(Received in UK 3 June 1969; accepted for publication 16 June 1969)

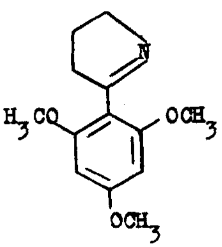
The alkaloids ficine (Ia) and isoficine (Ib) isolated[1] from Ficus pantoniana King are unique in being the only alkaloids incorporating a flavone moiety. A synthesis of (±) ficine has been achieved through the following sequence of reactions.



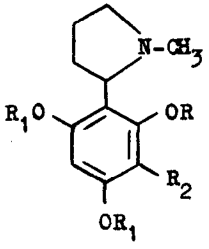
Ia : R, R_1 = H; R_2 = 

Ib : R, R_2 = H; R_1 = 

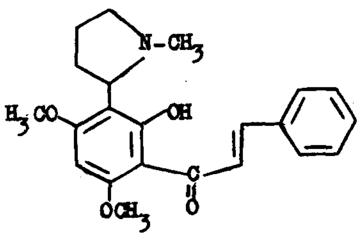
Ic : R = CH_3; R_1 = H; R_2 = 



II



III : R, R_1 = CH_3; R_2 = H
IV : R, R_1 = CH_3; R_2 = $COCH_3$
V : R = H; R_1 = CH_3; R_2 = $COCH_3$



VI

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[*] Contribution No.163 from CIBA Research Centre

Reaction of 1,3,5-trimethoxybenzene with γ-amino butyric acid and PPA followed by basification gave 2-(2',4',6'-trimethoxyphenyl)-Δ^1-pyrroline[2] (II) m.p. 116° whose methiodide, m.p. 186° was reduced with sodium borohydride to give 1-methyl-2-(2',4',6'-trimethoxyphenyl)pyrrolidine (III), m.p. 57°. Friedel-Crafts acylation of (III) with glacial acetic acid and PPA yielded the trimethoxyacetophenone (IV), m.p. 95° which on treatment with an equimolar quantity of boron trichloride[3] in methylene chloride solution was smoothly demethylated selectively to (V), m.p. 80°. This compound gave a positive Gibbs' test, characteristic for phenols having the para position unsubstituted. This o-hydroxyacetophenone (V) on condensation with benzaldehyde in the presence 0.1 N alkali gave the chalcone (VI), m.p. 148° which on refluxing with methanolic hydrochloric acid gave a mixture of diastereoisomeric flavanones, dehydrogenated without separation by treatment with trityl perchlorate[4] to the dimethoxyflavone Ic, m.p. 142°. Facile demethylation of Ic occurred with aluminium bromide in carbon disulphide solution at room temperature to yield (±) ficine, (Ia), m.p. 233°, identical with a natural sample[5] (m.p., m.m.p., UV, IR and TLC). Since ficine has been converted to isoficine by treatment with hydrochloric acid, our method constitutes also a formal synthesis of isoficine.

Acknowledgement : We thank Dr. S.R. Johns, CSIRO, Melbourne, for a sample of natural ficine and Dr. S. Selvavinayakam and his staff for the analytical and spectral data.

REFERENCES

1. S.R. Johns, J.H. Russel and M.L. Heffernan, Tetrahedron Letters, 1987 (1965).
2. Satisfactory elemental analyses have been obtained for all new compounds.
3. F.M. Dean, J. Goodchild, L.E. Houghton, J.A. Martin, R.B. Morton, B. Parton, A.W. Price and Nongyow Somvichien, Tetrahedron Letters, 4153 (1966).
4. A. Schönberg and G. Schütz, Ber., 93, 1466 (1960).
5. The optical activity of natural ficine has not been recorded.