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A PARTIAL SYNTHESIS OF (±)-PISATIN FROM PTEROCARPIN

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REVISION of the formula of pterocarpin from (I, R = H) to (II, R = H) on the basis of NMR measurements[1] is strongly supported by comparison of synthetic (±)-III with the (-)-compound obtained by hydrogenolysis of maackiain methyl ether followed by methylation[2] since maackiain is identical with inermin[2] and methylation of the latter gives pterocarpin.[3] However, a similar infra-red comparison also appeared to support (I)[4] and a direct comparison with (±)-III from pterocarpin seemed desirable.

The structure of the antifungal substance pisatin[5] formulated[6] as I (R = OH) requires similar revision to II (R = OH).[7]

The key substance for final confirmation of the structure of pterocarpin and the partial synthesis of (±)-pisatin seemed to us to be IV (R = H) conceivably obtainable from pterocarpin by acid fission of the dihydrofuran ring as shown, although previous work had indicated only the

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1 J.B. Bredenberg and J.N. Schoolery, Tetrahedron Letters 9, 285 (1961).

2 H. Suginome, Experientia 15, (IV), 161 (1962).

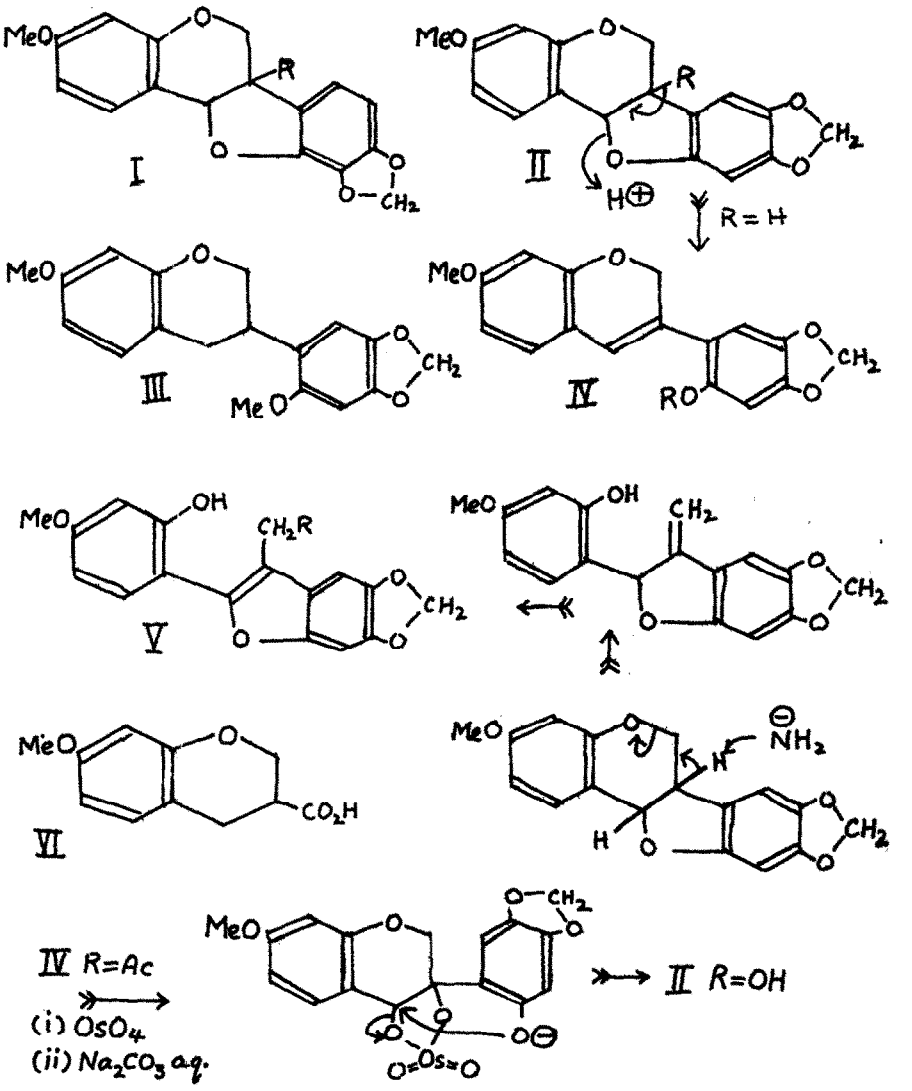
3 W. Cocker, T. Dahl, C. Dempsey and T.B.H. McMurry, Chem. & Ind. 216 (1962).

4 A. Robertson and W.B. Whalley, J. Chem. Soc. 1440 (1954).

5 I.A.M. Cruickshank and D.R. Perrin, Nature, Lond. 187, 799 (1960).

6 D.R. Perrin and W. Bottomley, Nature, Lond. 191, 76 (1961).

7 D.R. Perrin, personal communication.



production of red resins. In fact the action of 10 N hydrochloric acid diluted to 0.2 N with ethanol at the b.p. for 10 min gave IV (R = H) $C_{17}H_{18}O_5$, m.p. 124-126°, its ultra-violet absorption (λ_{max} 340 mμ ε 22,280, sgoulder at 295 mμ) differs from that of pterocarpin (λ_{max} 310, 286 mμ with

inflexion at 280 mμ) in the expected way and is similar to that of models.[8]

Methylation gave IV (R = CH_3) which on hydrogenation (Pd-C) produced (±)-III, m.p. 110-111°, λ_{max} 300, 290 mμ, shoulder at 228 mμ; this is the m.p. recorded by Suginome[2] for the synthetic (±) substance and differs considerably from that (86°)[4] of the synthetic compound based on (I). There is no doubt whatever that pterocarpin is correctly represented by II (R = H).

In view of the extreme sensitivity of compounds in this series to acid, particularly in the case of pisatin itself, we believe that the best method of closing an oxide ring is by a base-catalysed displacement reaction. This was accomplished by reaction of IV (R = Ac) m.p. 150-152° with osmium tetroxide followed by gentle hydrolysis with 0.1 N aqueous sodium carbonate. The product (yield about 46 per cent) is a neutral compound $C_{17}H_{14}O_6$, m.p. 188-190° with the presumed structure of (±)-pisatin, II (R = OH). The displacement reaction should, as shown, give rise to a cis ring-junction. The substance has the ultra-violet spectrum reported[5,6] for pisatin, λ_{max} 309, 286 mμ λ_{inflex} 281 mμ, and on treatment with acid it produces a substance (λ_{max} 339, 357 mμ) with similar absorption (λ_{max} 339, 358 mμ) to that reported to arise by the same process from (+)-pisatin.

However, careful infra-red comparison using solutions of different concentrations in CCl_4 showed no appreciable differences. Unfortunately (±)-pisatin is rather insoluble and the solutions were more dilute than desirable, but other solvents cut out most of the section of the spectrum required for comparison. In view of this and of the error already introduced in this series through infra-red comparisons, it is as well to be cautious but if the synthetic material is not identical with (±)-pisatin, the latter can only be the isomer with a trans ring-junction.

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[8] R.B. Bradbury and D.E. White, J. Chem. Soc. 871 (1953).

Pisatin may have the opposite absolute configuration to pterocarpin,[6] and if so, its biogenesis may well involve a compound of type IV rather than a direct oxidation of pterocarpin.

Reaction of pterocarpin with potassamide in liquid ammonia results in fission of the other ether ring and production of a substance $C_{17}H_{14}O_5$, λ_{max} 271, 322 mμ, ε 4.13, 4.39, m.p. 120-122°, with the properties to be expected of V (R = H). This reaction must proceed as shown. The ultraviolet spectrum of substance V (R = OC_2H_5) obtained by the action of heat or light on an ethanolic solution of anhydropisatin,[6] is very similar to that of V (R = H).

A parallel series of reactions can be carried out with homopterocarpin; discussion of these and some other reactions of pterocarpin will be made at a later date.[9]

Oxidations by means of potassium permanganate in acetone solution[10] of either (-) dihydropterocarpin or of (-) dihydrohomopterocarpin, obtained by sodium and liquid ammonia reduction, gave rise to the same acid (VI) m.p. 146-149° $[\alpha]_D^{23}$ +29.8° (ethanol C = 1.4 per cent) and they must have the same absolute configurations (cf.[2]).

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[9] C.W.L. Bevan, A.J. Birch, B. Moore and S.K. Mukerjee, J. Chem. Soc. submitted for publication.

[10] A. McGookin, A. Robertson and W.B. Whalley, J. Chem. Soc. 787 (1940).