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THE STRUCTURE OF ANNULOLINE, A NATURALLY OCCURRING OXAZOLE ALKALOID[1]

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ANNULOLINE ($C_{17}H_{10}ON(OCH_3)_3$),[2] a weakly basic, fluorescent pigment isolated from the roots of seedlings of annual rye grass (Lolium multiflorum) is shown to be 2-(3,4-dimethoxystyryl)-5-(4-methoxyphenyl) oxazole (I) by a study of its spectral and chemical properties and by synthesis. This is the first demonstration of the oxazole ring in Nature.

The presence of three methoxyl groups in annuloline was indicated by analysis and confirmed by its NMR spectrum (determined at 60 mc in carbon tetrachloride and related to tetramethylsilane as a standard) which displayed a sharp signal at -226 c.p.s. (9 hydrogens) and a series of 9 signals from -389 to -453 c.p.s. (10 aromatic and/or olefinic hydrogens). Potassium permanganate oxidation of annuloline yielded anisic and veratric acids. The infrared spectrum implied absence of NH, OH and C=O groups. The presence of a trans disubstituted double bond was indicated by a strong band at 10.35μ and confirmed by catalytic hydrogenation which gave a white solid, m.p. 95-96°, whose infrared spectrum lacked the 10.35μ peak and whose NMR spectrum exhibited a new signal at -183 c.p.s. attributed to methylene

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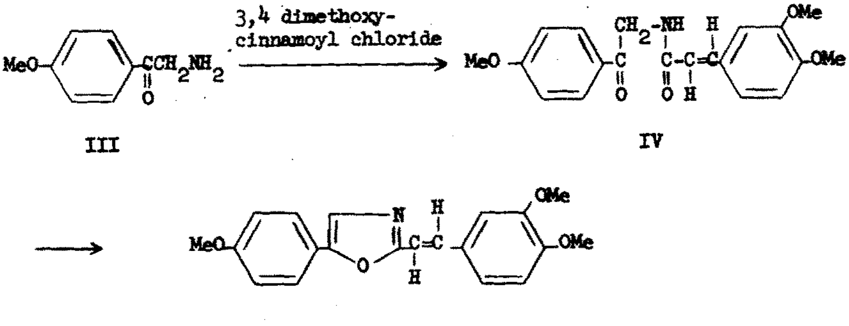
[1] A portion of this work is taken from the Ph.D. thesis of R.S.K., Purdue University, 1962.

[2] B. Axelrod and J.R. Belzile, J. Org. Chem. 23, 919 (1958).

hydrogens ($-CH_2-C=$).

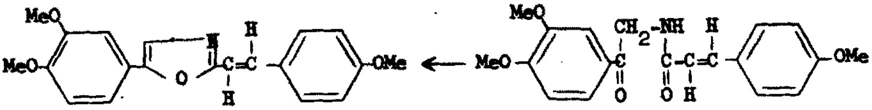
The information above forced the conclusion that the remaining unaccounted atoms (two carbons, a nitrogen and an oxygen) must be in an oxazole or isooxazole ring. A comparison of the properties of annuloline with those of 2,5-diaryl oxazoles[3] and a consideration of "most reasonable" biogenetic pathways suggested it could be represented by I or 5-(3,4-dimethoxyphenyl)-2-(4-methoxystyryl) oxazole (II). Synthesis of these compounds established the identity of annuloline with compound I. The aminoketone (III)[4] was transformed into the amide (IV) which on dehydration with phosphorus oxychloride[5] gave the oxazole I[6], m.p. 114°. The melting



III

IV

I



II

V

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[3] D.G. Ott, F.N. Hayes, E. Hansbury and V.N. Kerr, J. Amer. Chem. Soc. **79**, 5448 (1957).

[4] H.D. Moed, M. Asscher, P.J.A. Van Draanen and H. Niewing, Rec. Trav. Chim. **71**, 933 (1952).

[5] F.N. Hayes, B.S. Rogers and D.G. Ott, J. Amer. Chem. Soc. **77**, 1850 (1955).

[6] Satisfactory analyses were obtained on the hitherto unreported compounds, I, II, IV and V.

point of I was not depressed when mixed with natural annuloline and in addition, the fluorescence, ultraviolet and infrared (solution and KBr discs) spectra were superimposable.

The isomeric amide (V) and oxazole II were prepared by similar procedures. The infrared spectrum and m.p. of oxazole II was clearly different from natural annuloline.

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