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SYNTHESES IN THE SERIES OF LYCOPODIUM ALKALOIDS III.
A NOVEL SYSTEM ACTIVE IN PHOTOCHEMICAL ADDITIONS

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In continuation of our efforts to develop methods of potential usefulness in the synthesis of Lycopodium alkaloids, we have turned our attention to annotinine I (1). A priori, the best entry into the system of this compound seemed a Beckmann rearrangement of an oxime of the type II obtainable from the corresponding ketone which in turn is a photoadduct of propene and the cyclopentenone III. The model compound (II, R_1, R_2 = H) was easily obtained (2) but the Beckmann rearrangement, while yielding some of the lactam IV, was unpromising.

Consequently, we have decided to synthesize the system V and to investigate its behaviour in photoadditions. It turned out that compound V is obtainable in quantitative yield when the readily available (3) cyanoethyl derivative VI is allowed to stand in 20% aqueous hydrochloric acid for four days; V, $C_9H_{11}O_2N$; m.p. 300-301°; I.R. ($CHCl_3$) 1700, 1640 cm^{-1}; U.V. λ = 288 mμ (ε = 10,300). Compound V was dissolved in ethyl acrylate and irradiated in a Pyrex container for two days at 0° with a Quartz-Mercury Vapor ultraviolet lamp (Hanovia, 100 watts). The product VII, $C_{14}H_{19}O_4N$; m.p. 143°; I.R. ($CHCl_3$) 1720, 1730, 1665 cm^{-1} was obtained in a yield of 50%. After one crystallization, compound VII was homogeneous in T.L.C. and had a constant melting point; thus, the photo-addition seemed to be stereospecific. Reduction of VII with sodium borohydride yielded a mixture of the two epimeric alcohols VIII, I.R. ($CHCl_3$) 1707 (hydrogen-bonded ester), 1745 (non-bonded ester), 1665 cm^{-1}. Mild alkaline hydrolysis of this mixture, followed by acidification, yielded 50% of the oily compound IX, I.R. ($CHCl_3$) 1760 (lactone), 1665 cm^{-1} (lactam).

Next, we wished to investigate photochemical reactions of the N-substituted system. Compound V was dissolved in acetone and refluxed with an excess of powdered potassium hydroxide and methyl iodide for six hours. Compound X, $C_{10}H_{13}O_2N$; m.p. 69°; I.R. ($CHCl_3$) 1700, 1650, 1630 cm^{-1}; U.V. $\lambda_{max.}$ = 297 mμ (ε = 17,000) was obtained in 80% yield. This material was dissolved in tetrahydrofuran and irradiated at -80° with an excess of allene. The yield, after several crystallizations, was 50% of white crystals which according to melting point and V.P.C. were a mixture of two compounds, XI and XII, in about equal amounts. They were separated by preparative V.P.C.: XI, $C_{13}H_{17}O_2N$; m.p. 85°; I.R. ($CHCl_3$) 1705, 1645, 908 cm^{-1}; U.V. $\lambda_{max.}$ = 293 mμ (ε = 150); N.M.R.

N-CH_3 6.91 τ; XII, $C_{13}H_{17}O_2N$; m.p. 118°; I.R. as X; U.V. $\lambda_{max.}$ = 293 mμ (ϵ = 550); N.M.R. N-CH_3 7.11 τ. When compound XII was hydrogenated with Pd/$BaCO_3$ in ethanol, a mixture of the products XIII and XIV resulted. A stereospecific transformation of XII to XIII was accomplished by the conversion of the keto group of XII to a ketal with ethylene glycol, hydrogenation with platinum oxide in ethanol and deketalization with p-toluenesulphonic acid in acetone; XIII, $C_{13}H_{19}O_2N$; m.p. 112°; I.R. ($CHCl_3$) 1705, 1645 cm^{-1}; N.M.R. $>CH-CH_3$ 8.89, 9.02 τ. The corresponding doublet of the C-methyl in XIV is at 8.73, 8.88 τ.

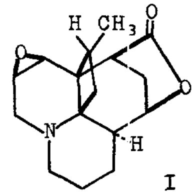
Work proceeding at present in this laboratory shows that when the methyl group in X is replaced by a larger group, the allene addition becomes completely specific and yields exclusively compounds of the type XII. The exploitation of the new photochemical reaction for the synthesis of annotinine starting with the system XV is an obvious possibility. However, an intramolecular photoreaction of a system of the type XVI is also of interest since it provides an exceedingly simple route to lycopodine. Both these applications are under active study.

REFERENCES

(1) K. Wiesner, Z. Valenta, W. A. Ayer, L. R. Fowler and J. E. Francis, Tetrahedron 4, 87 (1958).

(2) M. Fishman, unpublished experiments, U.N.B.

(3) I. N. Nazarov and S. I. Zav'yalov, Zhur. Obshchei Khim. 24, 469 (1954).



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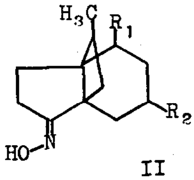

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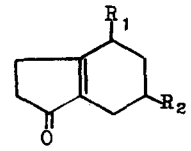

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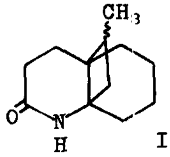

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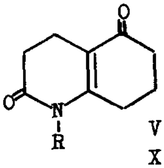
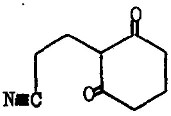


V (R = H)
X (R = CH$_3$)



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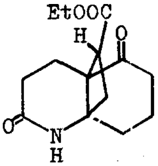

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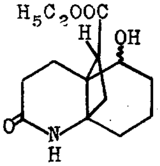

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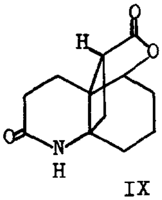

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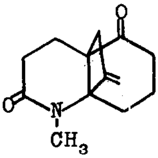

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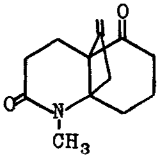

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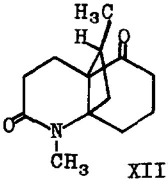

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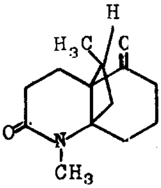

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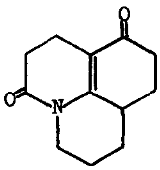

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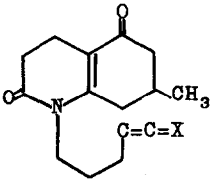

XVI