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SYNTHESES IN THE SERIES OF LYCOPODIUM ALKALOIDS VI. PHOTOCHEMICAL ADDITIONS OF VINYLOGOUS IMIDES AND METHYL METHACRYLATE

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We wish to report the photochemical addition of methyl methacrylate to the compound II. We have chosen this system because it is very readily obtainable and can serve both as a model and actual starting material for approaches to a variety of Lycopodium alkaloids.

Compound II was obtained* from the previously described (1) compound I. Compound I was benzylated in dry benzene-dimethylformamide with sodium hydride and benzyl chloride at 115°C. The yield was 90% of compound II [($C_{16}H_{17}NO_2$, m.p. 64-66°C.; m.w. (mass-spectrum) = 255; I.R.: 1700, 1650 1625 cm^{-1}; U.V.: $\lambda_{max.}$ = 296 mμ (ε = 16,000)] .**

Compound II was irradiated with 4 - 5 moles of methyl methacrylate in tetrahydrofuran at -70°C. in a Pyrex container as described previously (1). Chromatography on silica gel gave a 58% yield of the two epimers III and IV in a ratio 1:1. The anti-epimer III crystallized out from acetone [($C_{21}H_{25}NO_4$), m.p. 158°C. (acetone); m.w. (mass-spectrum) = 355; I.R.: 1645 (lactam), 1730, 1705 cm^{-1} (ester, ketone); N.M.R.: singlet (3 H)

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* This experiment was performed by Dr. J. G. McCluskey in connection with other work. The compound II actually used in this work was prepared by Lizzie Poon.

** The mass, I.R. and N.M.R. spectra of all compounds have been recorded. Only the more relevant of these data are given to achieve brevity.

τ = 6.21 p.p.m. (methoxyl), singlet (3 H) τ = 8.65 p.p.m. (C-methyl)] .

Sodium borohydride reduction of III yielded the alcohol V [($C_{21}H_{27}NO_4$), m.p. 147°C. (acetone); m.w. (mass-spectrum) = 357; N.M.R.: singlet (3 H) τ = 6.25 p.p.m. (methoxyl), singlet (3 H) τ = 8.22 p.p.m. (C-methyl)].

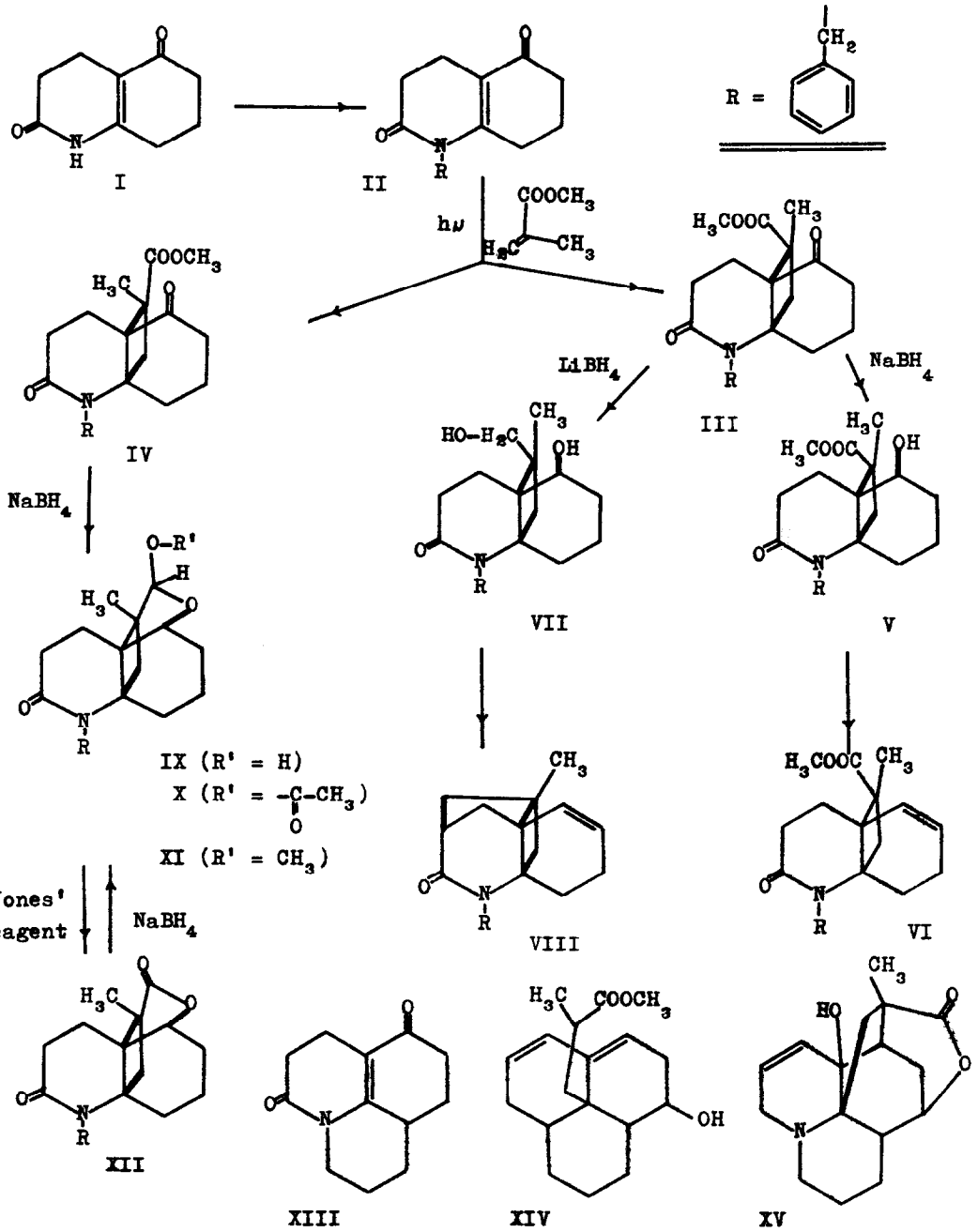
Compound V gave a tosylate which melted at 174°C. (acetone) and on treatment with two moles of sodium hydride in dimethylformamide at 100°C. yielded the oily unsaturated ester VI. This compound was chromatographed until homogeneous in thin-layer chromatography [($C_{21}H_{25}NO_3$), m.w. (mass-spectrum) = 339; I.R.: 1735 (ester), 1645 cm^{-1} (lactam); N.M.R.: singlet (3 H) τ = 6.25 p.p.m. (methoxyl), singlet (3 H) τ = 8.62 p.p.m. (C-methyl), doublet (1 H) τ = 4.42, 4.62 p.p.m., multiplet (1 H) τ = 3.65, 3.85 p.p.m. (vinylic hydrogens)].

Reduction of III with lithium borohydride gave the diol VII [($C_{20}H_{27}NO_3$), m.p. 176°C. (acetone), m.w. (mass-spectrum) = 329]. This compound gave a ditosylate, m.p. 202°C. Treatment of the ditosylate with two moles of sodium hydride in dimethylformamide at 100°C. yielded compound VIII [($C_{20}H_{23}NO$), m.p. 111°C. (cyclohexane-petroleum ether); m.w. (mass-spectrum) = 293; I.R.: 1645 cm^{-1} (lactam); N.M.R.: singlet (3 H) τ = 9.05 p.p.m. (C-methyl), multiplet (2 H) τ = 4.52, 4.33, 4.08, 3.89 p.p.m. (vinylic hydrogen)].

After crystallization of the anti-keto ester III, the oily syn-keto ester IV remained in the mother liquors. It was not possible to free it of a small amount of III. However, the mass-spectrum of this impure material was identical with the mass-spectrum of pure III. This showed conclusively that we are dealing with a diastereoisomer of III.

Reduction of impure IV with sodium borohydride in methanol at room temperature yielded the hemiacetal IX [($C_{20}H_{25}NO_3$), m.p. 190°C. (acetone); m.w. (mass-spectrum) = 327; I.R.: 3400 (hydroxyl), 1645 cm^{-1} (lactam)].

Acetylation of IX with acetic anhydride in pyridine yielded the


R =
I
II
III
IV
V
VI
VII
VIII
IX (R' = H)
X (R' = -C-CH3)
XI (R' = CH3)
XII
XIII
XIV
XV
hν
LiBH4
NaBH4
NaBH4
Jones' Reagent
NaBH4

acetate X [($C_{22}H_{27}NO_4$), m.p. 153°C. (acetone):, m.w. (mass-spectrum) = 369; I.R.: 1730 (ester), 1645 cm^{-1} (lactam); N.M.R.: singlet (3 H each) τ = 7.88, 8.92 p.p.m. (acetate methyl and C-methyl), singlet (1 H) τ = 4.08 p.p.m. (hydrogen unshielded by acetoxyl and ether oxygen)] .

Treatment of IX with methanolic hydrochloric acid yielded the methyl ether XI [($C_{21}H_{27}NO_3$), m.p. 125°C., m.w. (mass-spectrum) = 341; N.M.R.: singlet (3 H) τ = 6.62 p.p.m. (methoxyl)] .

The oxidation of IX by Jones' reagent gave the lactone XII. This compound was oily but homogeneous in thin-layer chromatography [($C_{20}H_{23}NO_3$), m.w. (mass-spectrum) = 325; I.R.: 1760 (lactone), 1645 cm^{-1} (lactam)].

The lactone XII reformed the hemiacetal IX by treatment with methanolic sodium borohydride at room temperature. It is thus probable that the lactone XII is an intermediate in the anomalous reduction of the syn-adduct IV by sodium borohydride.

A similar study with compound XIII (2) is under way and it is hoped that simple approaches to several types of Lycopodium alkaloids will be feasible from the adducts and their transformation products in this series. Among the more obvious possibilities we might mention lyconnotine XIV (3) and annotine XV (4).

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