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SYNTHESIS IN THE SERIES OF DITERPENE ALKALOIDS. IX.

A NEW SIMPLE SYNTHESIS OF VEATCHINE

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Some time ago we have described a simple synthesis of atisine in which the ketalized photo adduct I was an intermediate (1). We now wish to report a simple development of I to the ketones X (2) and XI (3). Both of these compounds have been previously converted to the diterpene alkaloid veatchine XII.

Reduction of I with $LiAlH_4$ in dioxane and mesylation of the product with methane sulfonyl chloride in pyridine gave the compound II* [m.p. 194-196°C.; N.M.R.: singlet (3 H) $\tau = 7.25$ p.p.m. (mesyl), singlet (3 H) $\tau = 9.10$ p.p.m. (C-methyl)]. Oxidation of II with osmium tetroxide and sodium metaperiodate in aqueous tetrahydrofuran containing pyridine at room temperature yielded the cyclobutanone III [m.p. 219-221°C.; I.R. ($CHCl_3$): 1785 cm^{-1} (cyclobutanone)]. Treatment of III with tetrahydrofuran-10% aqueous hydrochloric acid (1:1) at room temperature gave a 48% yield of the crystalline keto acid IV [m.p. 208-210°C.], which was converted by diazomethane into the corresponding methyl ester V [double m.p. 195°, 215°C.; I.R. (KBr): 1735 (ester), 1720 cm^{-1} (ketone); N.M.R.: singlets (3 H) each $\tau = 6.13, 7.22, 9.11$ p.p.m. (ester $-OCH_3$, mesyl, $C-CH_3$). Compound V yielded the ketal VI by treatment with ethylene glycol and p-toluenesulphonic acid in refluxing benzene [m.p. 200-204°C.; N.M.R.: singlet

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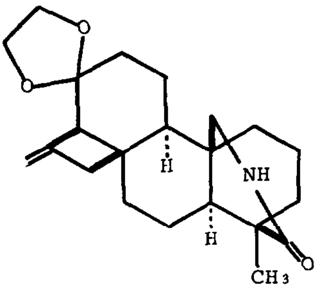
* All crystalline compounds gave checking elemental analyses. All spectra of all the intermediates were recorded and were in agreement with the structures assigned to them. Only selected spectral data are given for the sake of brevity.

(3 H) τ = 6.14 p.p.m. (ester $-OCH_3$), singlet (4 H) τ = 6.32 p.p.m. (dioxolane)]. Reduction of VI with $LiAlH_4$ in THF yielded the alcohol VII [m.p. 184-187°C.]. The compound VII was previously synthesized by Nagata (4) using an entirely different route and the m.p. of 190-193°C. was reported for it. The two materials were, however, not directly compared. Mesylation of the alcohol VII and treatment of the product with sodium azide in DMSO gave the azide VIII in 80% yield [m.p. 213-214°C.; I.R. (KBr): 2080 cm^{-1} (azide)]. Compound VIII was now reduced with $LiAlH_4$ in THF at 0°C. and the primary amine obtained in this manner was immediately converted by treatment with ethyl chloroformate and triethylamine in THF to the oily urethane IX [homogeneous in T.L.C.; N.M.R.: singlet (4 H) τ = 6.12 p.p.m. (dioxolane), singlet (3 H) τ = 7.30 p.p.m. (mesyl), triplet (3 H) τ = 8.75 p.p.m. ($-CH_2-CH_3$), singlet (3 H) τ = 9.15 p.p.m. ($C-CH_3$)]. The urethane IX was now deketalized at room temperature in 10% aqueous HCl-THF (1:1) and the resulting oily ketone was nitrosated in dry dichloromethane at -5°C. with N_2O_4 and sodium acetate. The nitroso urethane was homogeneous in T.L.C. and it was decomposed by sodium ethoxide in refluxing ethanol. The product of this reaction, the crystalline ketone X, was obtained in a yield of 65% [m.p. 216-218°C.]. This compound has been previously described by Nagata *et al*. (2) and a sample kindly sent to us by Professor Nagata was found to be identical with our product by melting point, mixed melting point, T.L.C. and infrared spectrum (KBr). A synthesis of 1,2,3-bicyclooctanone by a method analogous to the transformation IX → X has been recorded previously in the literature (5). The compound X was converted to XI by ketalization, reduction with lithium in ammonia, acetylation and deketalization (6). The synthetic compound XI [m.p. 187°C.; M.W. (mass spec.) = 329] was found to be identical by T.L.C., infrared spectrum (KBr) and mass spectrum with the optically active material of the same structure prepared from veatchine (7). We have already described (3) the conversion of the norketone XI to veatchine XII. The compound XI synthesized by us previously by a different less efficient route (3) was oily, but spectroscopically identical with



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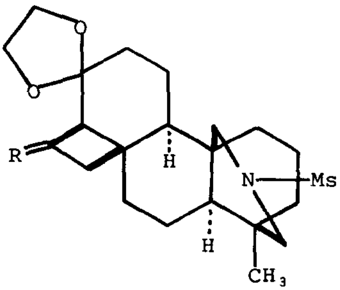
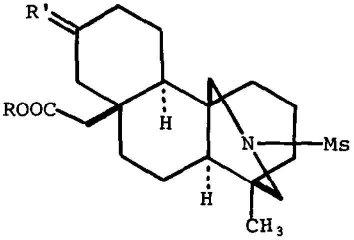


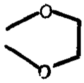
II (R = CH_2)

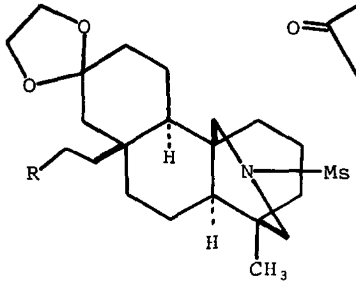
III (R = O)



IV (R = H, R' = O)

V (R = CH_3, R' = O)

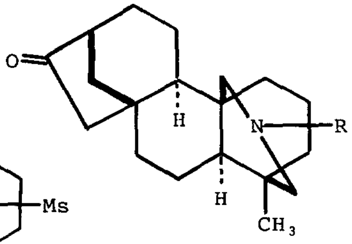
VI (R = CH_3, R' = )



VII (R = OH)

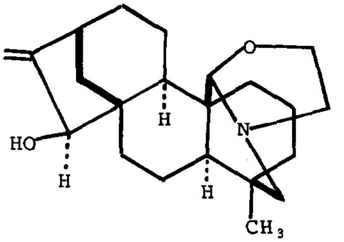
VIII (R = N_3)

IX (R = $-NH-\underset{\underset{O}{\|}}{C}-O-C_2H_5$)



X (R = Ms)

XI (R = $-\underset{\underset{O}{\|}}{C}-CH_3$)



XII

the present crystalline sample.

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