[Chem. Pharm. Bull. 12 (3) 386 ~ 388]

UDC 581.19 : 582.471

Structure of Anhydrotaxininol[*1]

Anhydrotaxininol,[1,2] $C_{20}H_{28}O_4$, a product of the ethanolic potassium hydroxide treatment of taxinine (a constituent of *Taxus cuspidata* L.) has been shown to contain an aldehyde, two hydroxyl groups, and an exocyclic methylene.[3,4] As to the nature of the remaining oxygen atom in the molecule, however, no definite conclusion has been drawn so far.

An inference[3] that the oxygen might belong to an unreactive α,β-unsaturated ketone was not accepted by Nakanishi, *et al.*[4,5] who proposed an enol-ether grouping in the molecule.

We have found that while the infrared spectra of anhydrotaxininol (I) and its monoacetate (II)[4] exhibited a band at 1643 and 1648 cm^{-1} (KBr), respectively (besides an absorption due to the aldehyde function at 1720 and 1725 cm^{-1}, respectively), that of anhydrotaxininol bis-3,5-dinitrobenzoate (III)[3] showed the corresponding absorption at a higher frequency, *viz.* 1680 cm^{-1} (KBr).[6] If the band at 1643 cm^{-1} in anhydrotaxininol had been due to an enol-ether bonding, the above shift (barring a rearrangement) would not have been expected upon its conversion into the benzoate. It was most probable, therefore, that the band at 1643 cm^{-1} was due to a hydrogen-bonded conjugated carbonyl which shifted to a higher frequency on cleavage of the hydrogen-bond upon benzoylation of the hydroxyl group. The nuclear magnetic resonance spectrum of anhydrotaxininol exhibited only two olefinic protons due to the exocyclic methylene. Accordingly if there was another double bond in the molecule, it would have to have been fully substituted, in which case the ultraviolet spectrum would have shown an absorption at a longer wave length and higher intensity than the observed absorption at 215 mμ (ε 5300) (EtOH). The above results can be easily rationalized by the assumption that the ketone is hyperconjugated with a cyclopropane moiety.

Treatment of anhydrotaxininol oxime (IV),[3] $C_{20}H_{29}O_4N$, with acetic anhydride gave diacetylanhydrotaxinonitrile (V) which on mild alkaline hydrolysis gave anhydrotaxinonitrile (VI), $C_{20}H_{27}O_3N$, m.p. 275~276°. On further alkaline treatment, this was converted, as a result of β-elimination of elements of hydrogen cyanide, into an α,β-unsaturated ketone, deformyldehydroanhydrotaxininol (VII), $C_{19}H_{26}O_3$, m.p. 212~213°, UV: $\lambda_{\max}^{\mathrm{EtOH}}$ 228 mμ (ε 9300), IR: $\nu_{\max}^{\mathrm{KBr}}$ 1610 (conjugated ketone) and 1645 cm^{-1} (conjugated double bond). As expected the nuclear magnetic resonance spectrum ($CDCl_3$) exhibited, along with two olefinic protons centered at 4.94 τ (multiplet) and 5.22 τ (multiplet) for exocyclic methylene, a new proton centered at 3.98 τ (multiplet) consistent with the presence of a trisubstituted double bond.

Catalytic hydrogenation of deformyldehydroanhydrotaxininol gave a tetrahydro derivative, deformyldihydroanhydrotaxininol (VIII), $C_{19}H_{30}O_3$, m.p. 205~207° and an oily deoxytetrahydro derivative, deformyldeoxydihydroanhydrotaxininol (IX), which was characteri-

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[*1] Presented at the 7th Symposium on the Chemistry of Natural Products, Fukuoka, October, 1963. See reference 11.

1) T. Takahashi: Yakugaku Zasshi, **51**, 401 (1931); *Ibid.*, **52**, 61 (1932); *Idem*: *Ibid.*, **54**, 664 (1934).

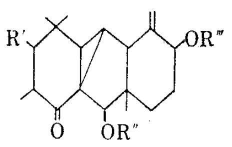
2) H. Kondo, J. Taga, M. Takahashi: Ann. Rept. ITSUU Lab., **10**, 9 (1959).

3) J. Taga: Ann. Rept. ITSUU Lab., **11**, 1 (1960); *Idem*: This Bulletin, **8**, 934 (1960).

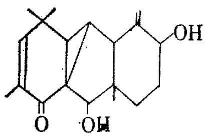
4) M. Kurono, Y. Nakadaira, S. Onuma, K. Sasaki, K. Nakanishi: Abstracts, 5th Symposium on the Chemistry of Natural Products, Sendai, Japan. p. 21-1 (1961).

5) M. Kurono, S. Onuma, K. Sasaki, K. Nakanishi: A paper orally presented at the 16th Annual Meeting of the Chemical Society of Japan, Tokyo, 1963.

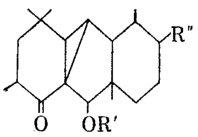
6) W.A. Ayer, W.I. Taylor: J. Chem. Soc., **1955**, 2227.



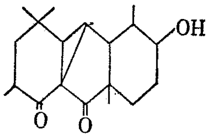
I : R'=CHO, R'', R'''=H
II : R'=CHO, R''=H, R'''=Ac
III : R'=CHO, R'', R'''=3, 5-dinitrobenzoyl
IV : R'=CH=NOH, R'', R'''=H
V : R'=CN, R'', R'''=Ac
VI : R'=CN, R'', R'''=H



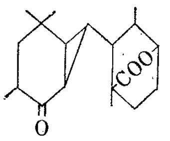
VII



VIII : R'=H, R''=OH
IX : R', R''=H
X : R'=H, R''=OAc



XI



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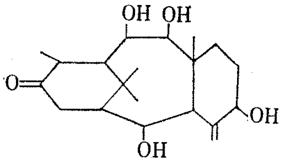

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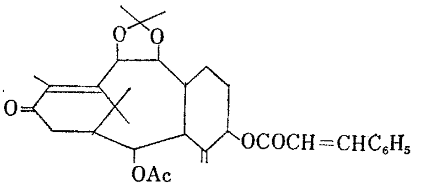
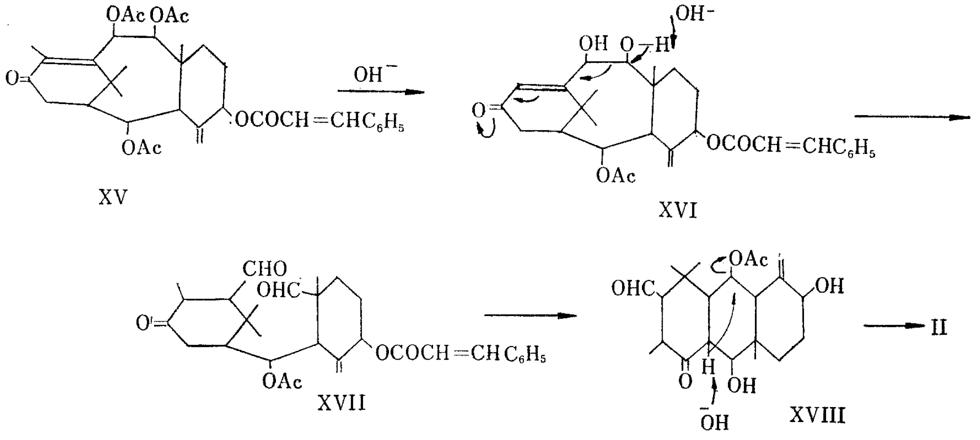


XIV



zed as its 3,5-dinitrobenzoate, $C_{26}H_{32}O_7N_2$, m.p. 191~192°. Formation of IX indicated that one of the hydroxyl groups in the compound is allylic to a double bond, as in taxinine itself.[7~10)]

The Raman spectrum of this deoxytetrahydro derivative (IX) confirmed the absence of double bonds and the optical rotatory dispersion of the tetrahydro derivative (VIII) exhibited a negative Cotton effect with the first extrimum at 310 mμ which did not shift remarkably on changing the solvent from methanol to dioxane, excluding again a possibility of an α,β-unsaturated ketonic moiety in the molecule.

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7) K. Ueda, S. Uyeo, Y. Yamamoto, Y. Maki : Tetrahedron Letters No. 30, 2167 (1963).
8) M. Kurono, Y. Nakadaira, S. Onuma, K. Sasaki, K. Nakanishi : *Ibid.*, No. 30, 2153 (1963).
9) K. Nakanishi, M. Kurono, N. S. Bhacca : *Ibid.*, No. 30, 2161 (1963).
10) D. H. Eyre, J. W. Harrison, R. M. Scrowston, B. Lythgoe : Proc. Chem. Soc., **1963**, 271.

Acetylation of deformyldihydroanhydrotaxininol (VIII) with acetic anhydride in pyridine afforded an oily monoacetate (X), IR $\nu_{\max}^{\mathrm{CHCl_3}}$ $\mathrm{cm^{-1}}$: 1640 (ketone), 1722 (acetyl), characterized as its 3,5-dinitrobenzoate, $C_{28}H_{34}O_9N_2$, m.p. 202∼203°. Chromium trioxide oxidation of the monoacetate (X) in acetic acid followed by alkaline hydrolysis gave a hydroxydiketone (XI), $C_{19}H_{28}O_3$, m.p. 186∼188°, which exhibited two carbonyl bands at 1725 (hyperconjugated five-membered ring ketone) and 1670 $\mathrm{cm^{-1}}$ (hyperconjugated six-membered ring ketone) (KBr), or at 1735 and 1669 $\mathrm{cm^{-1}}$ ($CHCl_3$).

The molecule upon attempted reductive cleavage (zinc-sodium hydroxide-ethanol) of the presumed cyclopropane ring underwent a reversed Claisen condensation, giving the lactone (XII), $C_{19}H_{28}O_3$, m.p. 226∼227°, UV: $\lambda_{\max}^{\mathrm{EtOH}}$ 205 mμ (ε 5900), IR: $\nu_{\max}^{\mathrm{KBr}}$ 1668 $\mathrm{cm^{-1}}$ (hyperconjugated six-membered ring ketone) and 1748 $\mathrm{cm^{-1}}$ (δ-lactone) along with a small amount of a reduction product, identical with deformyldihydroanhydrotaxininol (VIII). In contrast to the compounds mentioned above, this lactone showed in the nuclear magnetic resonance spectrum ($CDCl_3$) a high field multiplet (1H) centered at 9.25 τ, providing definite evidence that the compound contains a cyclopropane ring.

All these findings together with the fact that anhydrotaxininol afforded a homologue[*2] of anthracene on selenium dehydrogenation[3)] are in good agreement with the formula (I) which can be deduced from the structure of taxinine (XV). The reasons for this conclusion are as follows. Since neither taxinol[7)] (XIII) nor isopropylidene bisdeacetyltaxinine[11)] (XIV) undergoes any transformations upon alkaline treatment except for hydrolysis of ester groups in the latter case, it is clear that the double bond in conjugation with the carbonyl group and the readily hydrolizable α-glycol ester grouping in taxinine are essential for the skeletal rearrangement of taxinine to anhydrotaxininol. It is considered, therefore, that the first step of the transformation involves a retro aldol cleavage of the first formed α-glycol to give an intermediate dialdehyde which then undergoes an aldol condensation and simultaneous elimination of elements of acetic acid to furnish the end product anhydrotaxininol (XV→XVI→XVII→XVIII→II).

A full report of this work will be made at a later date and the stereochemistry of anhydrotaxininol and taxinine will be discussed in a separate communication.

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Received January 18, 1964

[*2] Very recently Professor E. Ochiai, Director of the ITSUU Laboratory, Tokyo, has kindly informed us in a private communication that Mr. J. Taga succeeded in proving the structure of this product to be 1,2,3,8-tetramethylanthracene by a synthetic method. See This Bulletin, **12**, 389 (1964).

11) S. Uyeo, K. Ueda, Y. Yamamoto, Y. Maki: Abstracts, 7th Symposium on the Chemistry of Natural Products, Fukuoka, Japan, **1963**, p. 226.