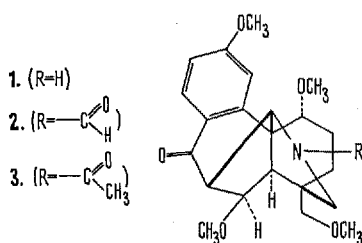


The N-Acyl Group of Oxonitine

Oxonitine is an oxidation product of aconitine in which the aconitine N-alkyl has been converted to an N-acyl group. Oxonitine was first formulated by JACOBS¹ as $C_{33}H_{45}O_{12}N$. Since aconitine, which carries a N-ethyl group, and mesaconitine which is the N-methyl analog of aconitine were reported² to yield the same oxonitine, it would seem logical to conclude that oxonitine is an N-formyl derivative. However, JACOBS³ later presented evidence which, taken at face value, established rigorously the N-acetyl nature of oxonitine. JACOBS changed the molecular formula of oxonitine to $C_{34}H_{45}O_{12}N$ and found that hydrolysis yielded a secondary base. This compound was connected after reacetylation with oxonitine which has never lost the N-acyl group. Just as conclusively as JACOBS has demonstrated the N-acetyl nature of oxonitine, TURNER⁴ has later proved this compound to be a N-formyl derivative.

Now, if all of the rigorous evidence quoted is indeed correct, the conclusion is inescapable, that oxonitine is a mixture of the N-formyl and N-acetyl derivatives. We have recently described the total synthesis of the racemate **1**⁵. The optically active form of this compound may be obtained not only by a simple degradation of delphinine but also of aconitine⁶. The last step of this degradation consists in the hydrolysis of **2** to **1** in the case of delphinine and **3** or **2** to **1** in the case of aconitine. These steps were originally performed in 1958 (before NMR and TLC) and only the crystalline **1** but not the amorphous **2** and **3** were fully characterized. Since we had to prepare **1** for the purpose of comparison with our synthetic racemate we decided to prepare this compound not only from delphinine but also from aconitine and in this latter case to reinvestigate the precursor **2** and/or **3**. This should yield a clean cut decision about the oxonitine N-acyl such as the direct investigation of the highly insoluble nonvolatile and polyfunctional oxonitine cannot provide.



The N-acyl aromatization product from oxonitine corresponding to **2** or **3** or a mixture of these compounds was prepared as described previously⁶. The material remained amorphous and was homogeneous in TLC. Nevertheless, it showed in the mass-spectrum molecular ions corresponding to both **2** and **3** (415, 429) and in the NMR-spectrum a singlet at $\tau = 1.97$ ppm corresponding to the formyl hydrogen of pure **2** (obtained either from delphinine or by total synthesis) and a singlet at $\tau = 7.9$ ppm corresponding to the N-acetyl group of pure **3** (obtained by acetylation of **1**). The material obviously a mixture of **2** and **3** was refluxed with 10% conc. hydrochloric acid in methanol. The basic product of this hydrolysis was fully characterized as **1** and identified with a sample prepared from delphinine and by total synthesis. The neutral product of the hydrolysis was rigorously identified with the acetylation product of **1**. Thus, it has been rigorously proved that the aromatization product of oxonitine is a mixture of **2** and **3** and consequently also 'oxonitine' must be a mixture of the N-acetyl and N-formyl derivatives. Since aconitine is known to contain varying amounts of mesaconitine the explanation of the nature of the oxonitine N-acyl may be at least in part quite trivial and involve the oxidation of the N-methyl and N-ethyl respectively.

Zusammenfassung. Das Oxonitin, welches durch Oxydation von Aconitin mit $KMnO_4$ entsteht, ist ein Gemisch des N-Acetyl- und N-Formyl-Derivats.

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Marmesin or Nodakenetin in *Ficus carica* L.

The Moraceae is listed among those plant families rich in coumarin constituents. In particular, psoralen¹⁻³, bergapten^{2b,3}, coumarin itself³, and umbelliferone⁴ are recorded in *Ficus* spp. Recently, DALL'ACQUA et al.⁵ have reported the occurrence of 4',5'-dihydropsoresalen, umbelliferone and an unidentified compound with the characteristic UV-spectrum of an oxygenated coumarin in leaves of *Ficus carica*. Chromatographic data, the fluorescence under UV-light and the UV-spectrum of their unknown compound matched very well with those given for marmesin in *Ruta pinnata* (Rutaceae)⁶ and in *Lycopersicon esculentum* (Solanaceae)⁷. The fact that marmesin has been suggested as a natural intermediate

in the biosynthesis of linear furocoumarins⁸ prompted us to a full characterization of this compound in *F. carica* leaves.

Materials and methods. Fresh leaves (700 g) of *F. carica* L., collected in September, were homogenized with methanol (3 l) at room temperature. After 3 h extraction with continuous stirring, the suspension was filtered. The filtrate was concentrated in vacuo to remove the solvent, and the residue was taken up in 60% methanol. Chlorophylls and other fat-soluble material were removed by extraction into hexane, according to STECK and BAILEY⁹. The residual aqueous methanol solution was concentrated in vacuo, and the aqueous residue was sub-

Rf values ($\times 100$) and UV data of marmesin from *F. carica*

Compound	Solvents					λ_{max} nm	
	BuOH/H ₂ O	IAW	2% HOAc	BAW	5% MC	MeOH	KOH
Unknown	92	87	59	96	59	245, 330	245, 331
Marmesin	93	87	60	95	59	248, 335	248, 334
Unknown + marmesin	92	87	59	96	54	—	—

BuOH/H₂O, butanol saturated with water; IAW, *iso*-propanol-ammonia-water (10:1:1); BAW, butanol-acetic acid-water (4:1:5); 5% MC, methanol-chloroform (5:95) TLC plates.

jected to liquid-liquid extraction with ether overnight to remove 'free' compounds.

The extracted aqueous residue was hydrolyzed at 100°C for 2 h after being made 2*N* in HCl. The hydrolysate was extracted with ether as described above to remove 'bound' compounds. The components of the 2 ether extracts (before and after hydrolysis) were separately fractionated into 'neutral' and 'phenolic' fractions by extraction with 5% NaOH. The alkaline aqueous phases were acidified and back-extracted with ether. The 4 ether extracts thus obtained were concentrated and chromatographed on Whatman 3 mm paper with 2% acetic acid (2% HOAc) as descending solvent. Additional data for identification were obtained by UV-spectroscopy and rechromatography of the eluates on Whatman No. 1 paper. Authentic (\pm) marmesin was applied to each chromatogram as a standard.

Results and discussion. The chromatograms were observed under UV-light (360 nm). In the hydrolysate 'neutral' fraction only a band with purple fluorescence at Rf 0.56–0.73 was observed. This was eluted with methanol and the UV-spectra of the eluate showed the characteristic maxima of marmesin not only in methanol but also in the presence of diagnostic reagents (Table). Characterization of the compound was carried out by chromatography in several solvents (Table). The amounts available (0.6 mg) were insufficient to permit an estimation of its optical activity and thus its complete identification with either (+) marmesin or (–) nodakenetin.

The co-occurrence of psoralen, bergapten and an α -hydroxy-isopropylidihydrofurocoumarin in *F. carica* lends further support to the hypothesis of the latter system as a natural precursor in the biosynthesis of

linear furocoumarins⁸. The presence of marmesin or nodakenetin in the acid hydrolysate indicates its occurrence in *F. carica* possibly as a glycoside, perhaps as the β -D-glucoside, marmesinin¹⁰.

Resumen. Marmesina, o su isómero óptico nodakenetina, fue identificada en hojas de higuera (*F. carica*) y su presencia en una planta rica en psoraleno y bergapteno favorece la hipótesis de que tal dihidrofurocoumarina actúa como precursor natural en la biosíntesis de furocoumarinas lineales.

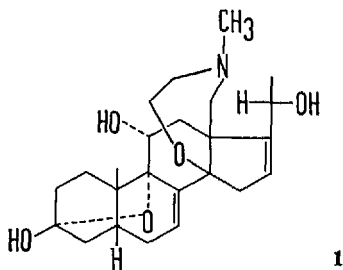
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- 10 We thank Dr. D. J. AUSTIN, Swedish Tobacco Company, Stockholm, for his criticism and revision of the manuscript.

Zur Synthese des Batrachotoxinins: Synthese von 3 β -Acetoxy-16 β , 20 β -dihydroxy-4'-methyl-18-nor-5 β , 14 β -pregnano [13, 14-f]hexahydro-1', 4'-oxazepin-3'-on(20a)

Die Wirkstoffe des kolumbianischen Pfeilgiftes, die Batrachotoxine und das Hydrolyseprodukt Batrachotoxinin A (1) wurden von WITKOP et al. aus der Haut des Frosches *Phylllobates aurotaenia* isoliert¹ und deren Konstitution durch Röntgenstrukturanalyse² und Partialsynthese³ aufgeklärt.



Über die Synthese einer Verbindung mit wesentlichen Strukturmerkmalen von 1, jedoch mit fehlenden Δ^7 - und Δ^{16} -Doppelbindungen und mit der 17-Isseitenkette wurde kürzlich von WEHRLI et al.⁴ berichtet.

In dieser Publikation soll eine Synthese beschrieben werden, bei der die Bildung des Homomorpholinringes in

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