

Communications to the Editor

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16-Acetylgitoxin, a New Derivative of Gitoxin

Gitoxin, a new cardiac glycoside, was isolated by Haack, *et al.*¹⁾ from *Digitalis* species and has been established as 16-formylgitoxin. In earlier papers, the writers reported that 16-formyl,^{1*} 16-acetyl,^{2,3)} and 16-propionyl^{2,3)} derivatives of digitalinum verum are obtained from their respective hexaacetyl compounds by partial deacylation.

Deacetylation by snail enzyme³⁾ was carried out on gitoxin pentaacetate⁴⁾ and it was found that there was formation of 16-acetylgitoxin monoacetate by liberation of three acetyl groups in the sugar portion. The reaction product was recrystallized from hydrous methanol and acetone-ether, and afforded 16-acetylgitoxin monoacetate as needles, m.p. 154~158°, *² $[\alpha]_D^{20} + 7.4^\circ$ (pyridine), $[\alpha]_D^{27} + 15.1^\circ$ (MeOH) (*Anal.* Calcd. for $C_{45}H_{68}O_{16}$: C, 62.48; H, 7.92; CH_3CO , 9.95. Found: C, 62.71; H, 7.76; CH_3CO , 9.38. UV: λ_{max}^{EtOH} 217 m μ (log ϵ 4.18)). The presence of one acetyl group in the 16-position was further confirmed by hydrolysis of this substance with 0.05*N* sulfuric acid to give 16-acetylgitoxigenin.

This diacetyl derivative was submitted to deacetylation³⁾ with potassium hydrogencarbonate and was converted to 16-acetylgitoxin, a new derivative of gitoxin. 16-Acetylgitoxin was isolated and purified through column partition chromatography, with formamide-saturated mixture of chloroform and benzene as the developing solvent, and was recrystallized from hydrous methanol to plates, m.p. 227~230°, and from methanol-ether-petroleum ether to plates, m.p. 226~236°, $[\alpha]_D^{20} - 15.7^\circ$ (pyridine), $[\alpha]_D^{27} + 1.1^\circ$ (MeOH) (*Anal.* Calcd. for $C_{43}H_{66}O_{15}$: C, 62.75; H, 8.08; CH_3CO , 5.23. Found: C, 62.64; H, 8.20; CH_3CO , 5.70. UV: λ_{max}^{EtOH} 217 m μ (log ϵ 4.20)). It is easily soluble in methanol, ethanol, acetone, and chloroform, and almost insoluble in water, ether, and benzene. 16-Acetylgitoxin was also hydrolyzed by 0.05*N* sulfuric acid to 16-acetylgitoxigenin.

Gitoxin was partially acetylated by Haack's method,⁵⁾ with acetic anhydride at 0°. Physical and chemical properties of gitoxin diacetate so obtained were examined and it was found that this compound is identical with 16-acetylgitoxin monoacetate prepared from gitoxin pentaacetate.

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*1 This work was reported at the Kantō Local Meeting of the Pharmaceutical Society of Japan, February 20, 1960.

*2 All m.p.s were measured on a Kofler block and are uncorrected.

1) E. Haack, F. Kaiser, H. Spingler: *Naturwiss.*, **42**, 441(1955); *Chem. Ber.*, **89**, 1353(1956).

2) Part XIII: This Bulletin, **7**, 627(1959).

3) Part XIV: *Ibid.*, **7**, 634(1959).

4) Part V: *Ibid.*, **5**, 171(1957).

5) E. Haack, F. Kaiser, H. Günter, H. Spingler: *Ger. Pat.* 1063160.