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ADINA ALKALOIDS: 10-β-D-GLUCOSYLOXYVINCOSIDE LACTAM .

R. T. Brown and W. P. Blackstock

Department of Chemistry, The University, Manchester M13 9PL.

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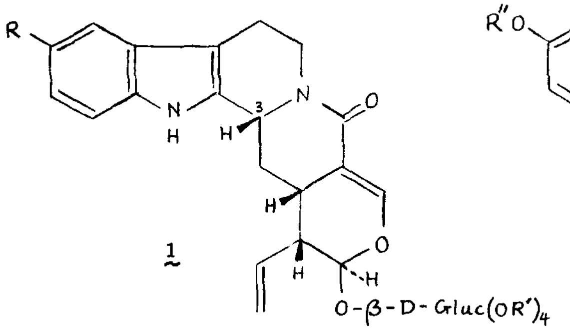
From fresh shoots of Adina rubescens[1] we have obtained a new glycosidic alkaloid (1a), characterised as the acetate (1b) $C_{48}H_{56}N_2O_{12}$ $[\alpha]_D^{25}$ -86° ($CHCl_3$). On the basis of colour reactions and spectral data it was thought to be related to vincoside lactam (1c) which also occurs in the same plant. Although the UV spectrum [$\lambda_{max.}$ 231, 273 (inf.) 294 (inf.) 310 (inf.)] was not immediately informative, IR bands at 1655 and 1600 cm.$^{-1}$ suggested a β-alkoxyacrylamide chromophore[2], and subtraction of its expected contribution [$\lambda_{max.}$ 240 nm] from the UV absorption left a spectrum [$\lambda_{max.}$ 287 nm] very similar to that of 2,3-dimethyl-5-methoxyindole [$\lambda_{max.}$ 284 nm].[3] The identity of the UV spectra of the acetate and the free glycoside, and the absence of any shift on addition of alkali indicated a phenolic ether. These conclusions were supported by the NMR spectrum with aromatic hydrogen signals at τ 2.55 (1H, d, J=2Hz), 2.81 (1H, d, J=9Hz) and 3.14 (1H, dd, J=1,9Hz) attributable to H-9, 12 and 11 respectively; the acrylamide proton H-17 appeared at τ 2.90 as a doublet (J=2Hz) due to allylic coupling with H-15. Furthermore, the presence of two hexose functions was indicated by eight acetate peaks between τ 7.92 and 8.03, two protons at 6.24 (H-5$'$, H-5$''$), four at 5.80 (H_2-6$'$ and H_2-6$''$), and eight (H-1$'$ - 4$'$, H-1$''$ - 4$''$) between τ 4.5 and 5.4 in addition to H-21 and three olefinic hydrogens. This was confirmed by the mass spectrum where successive losses of two hexose tetraacetate fragments (330) from the molecular ion at m/e 1012 gave peaks at m/e 682 and 352 - transitions which were supported by mass measurement and the appropriate metastable peaks at 459.6 and 181.5.

The suspected presence of a vinyl group was substantiated by catalytic hydrogenation of the octaacetate to a dihydroderivative which was then deacetylated under Zemplen conditions to the free diglycoside (2a). Subsequent hydrolysis with β-glucosidase removed both sugar units, thereby establishing their identity, and gave a dihydroaglucone (2b), $C_{20}H_{22}N_2O_4$. In neutral solution this had a similar UV spectrum to the starting material, but on addition of alkali there was now a shift to $\lambda_{max.}$ 326 nm.

At this point the evidence was consistent with the gross structure 1a but with undefined stereochemistry. Recently we reported[4] that the C-3 configuration in lactams of this type could be established as in simpler cases[5] from the sign of the Cotton effect between 250 and 300 nm in ORD and CD spectra. Since that of our compound was negative $[[\Theta]_{273}$ $-25,000]$ the configuration of H-3 was β, as in vincoside lactam. In order to complete the structure determination a correlation was necessary with material synthesised from known compounds.

Condensation of secologanin acetate and 5-hydroxytryptamine (serotonin) in glacial acetic acid at 100° afforded the desired 3β isomer, 10-hydroxyvincoside lactam (1d), directly; subsequent acetylation gave the 10-acetoxy derivative (1e) M^+724, $\lambda_{max.}$ 232, 273, 286, 294 nm. This variation of the usual procedure[6] was convenient since the 3α condensation product did not lactamise under these conditions and was readily separated. Catalytic hydrogenation followed by Zemplen deacetylation afforded a dihydroglucoside (2a) which was hydrolysed by β-glucosidase to the dihydroaglucone (2b). This compound was indistinguishable from that obtained from the natural diglucoside; furthermore both samples were converted to identical mixtures of epimeric acetates (TLC, NMR, UV, CD and mass spectra). Since the stereochemistry of secologanin is known[7] the complete structure of the diglucoside is consequently 1a.



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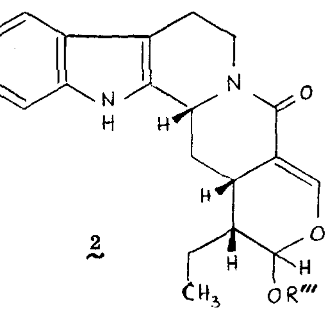

2

	R	R'	R''	R'''
a.	O-β-D-Gluc(OH)$_4$	H	β-D-Gluc(OH)$_4$	β-D-Gluc(OH)$_4$
b.	O-β-D-Gluc(OAc)$_4$	Ac	H	H
c.	H	H	Ac	Ac
d.	OH	Ac	H	β-D-Gluc(OAc)$_4$
e.	OAc	Ac	Ac	β-D-Gluc(OAc)$_4$

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