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SECOLOGANIN AGLYCONE

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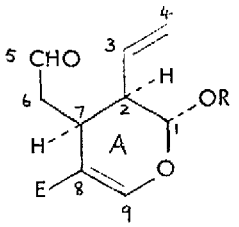
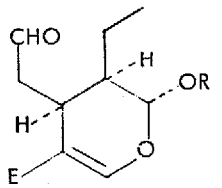
In connection with our interest in the biomimetic syntheses of monoterpenoid alkaloids[1-5] we have investigated the removal of the sugar from secologanin[6] (1) and some of its derivatives. Cleavage of dihydrosecologanin (3) with β-glucosidase at 37° in pH 5.0 buffer for 1 - 3 hours yielded a single product $C_{11}H_{16}O_5$, $[\alpha]_D^{25}$ + 47° ($CHCl_3$). As anticipated for an aglycone, the UV spectrum had λ_{max} 237 nm with a reversible shift to 275 nm on addition of alkali attributable to ionisation of a β-hydroxyacrylate chromophore (cf. [4]). Acetylation afforded a monoacetate $[\alpha]_D^{25}$ + 62° (MeOH), and brief treatment with trifluoracetic acid followed by methanol gave a methyl acetal $[\alpha]_D^{25}$ + 17° which no longer exhibited a UV base shift. However, the absence of an aldehydic proton in the NMR spectrum was incompatible with a simple aglycone (4), and eventually spectral data established the novel bicyclic hemiacetal structure 5. In particular, a broadened singlet at τ 4.68 and a pair of doublets (J = 8, 5 Hz) at τ 4.88 were attributed to H-1 and H-5 respectively, and since only the latter moved to τ 4.00 on acetylation the alternative structure 9 could be excluded. Furthermore, decoupling experiments revealed a substantial long range interaction between H-1 and H-7, in accordance with their ideal W-configuration in 5.

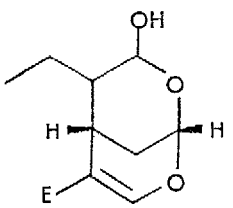
Formation of the bicyclic hemiacetal from the initial aglycone 4 cannot occur in a simple manner since an inversion of configuration at C-1 from S to R is required. Two plausible mechanisms are summarised in the Scheme, differing in the origin of the ring B ethereal oxygen, derived from aldehyde functions at C-5 in I and at C-1 in II. Since route II would involve a ring opening to a dialdehyde which could cyclise to both 4 and 9, the absence of the latter compound tended to preclude this mechanism



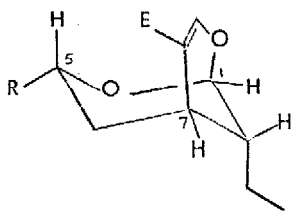
	R
1	β-D-Gluc
2	H



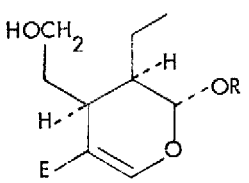
	R
3	β-D-Gluc
4	H



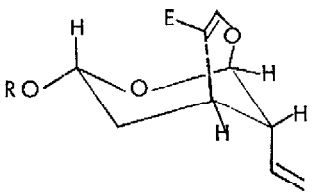
9



	R
5	OH
6	OAc
7	OMe
8	H

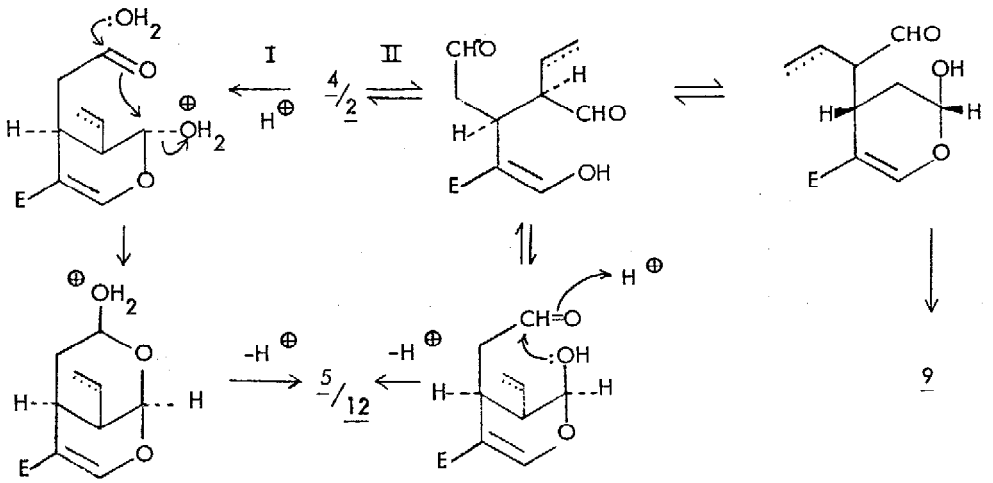


	R
10	β-D-Gluc
11	H



	R
12	H
13	Ac

Scheme.



E = CO_2Me

but was not conclusive. To test the feasibility of route I a model system was required which could cyclise in only one way. Reduction of 3 with sodium borohydride afforded tetrahydrosecologanin (10) [penta-acetate $[\alpha]_D^{25}$ -99^o (MeOH)] which was cleaved with β-glucosidase in pH5 buffer to a simple aglycone (11), as shown by formation of a diacetate derivative. On standing overnight in the same buffer or on treatment with trifluoroacetic acid the initial product was converted to a second compound, $C_{11}H_{16}O_4$, $[\alpha]_D^{25}$ + 120^o ($CHCl_3$) formulated as 8 since it could not be acetylated and the UV spectrum was unaffected by alkali. Confirmation of the bicyclic structure was obtained from the absence of hydroxyl or aldehyde absorptions in IR and NMR spectra, and the assignment of H-1 to a broadened singlet at τ 4.79 and the C-5 methylene group to a multiplet at τ 6.39. The most likely mode of cyclisation is analogous to route I and hence provides support for its operation in the case of dihydrosecologanin.

In an identical manner the sugar could be removed from secologanin (1) itself to give an analogous aglycone (12). Although considerably less stable it could be characterised as the monoacetate (13) $[\alpha]_D^{25}$ + 32^o ($CHCl_3$) whose NMR spectrum confirmed the presence of a vinyl group. On catalytic hydrogenation it gave a dihydro derivative identical to 6 in all respects. The vinyl group in ring-opened analogues of secologanin aglycone is known to rearrange spontaneously to an ethylidene conjugated with the C-1 aldehyde[3,7]. Hence its retention in 12 strongly suggests that ring A in 2 remains intact and cyclisation occurs *via* backside displacement of water from C-1 by a C-5 oxygen as in route I. These results support the suggestion that a similar mechanism operates in the formation of mancunine derivatives[1,2].

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