Synthesis of 2-*O*-α-L-Rhamnopyranosyl-D-galactose, a Reported Partial Hydrolysis Product of α-Solanine, and Some Taste-Eliciting Flavonoid 2-*O*-α-L-Rhamnopyranosyl-β-D-galactopyranosides

Solatriose, the carbohydrate moiety of α-solanine, is considered by KUHN et al.[1] to be *O*-β-D-glucopyranosyl-(1 → 3)-*O*-[α-L-rhamnopyranosyl-(1 → 2)]-D-galactose (I). Evidence has been presented that this branched trisaccharide also constitutes the sugar portion of other steroidal alkaloids such as α-solasonine[2] and α-solamarine[3], and biogenetic considerations have led SCHREIBER[4] to suggest that leptine II and the corresponding acetyl-free leptinine II[5,6] are also solatriosides. Partial acid hydrolysis of α-solanine resulted in the liberation of solatriose and two disaccharides identified as 3-*O*-β-D-glucopyranosyl-D-galactose (solabiose) and 2-*O*-α-L-rhamnopyranosyl-D-galactose[1]. We wish to report the synthesis of the latter disaccharide.

Hepta-*O*-acetyl-2-*O*-α-L-rhamnopyranosyl-α-D-galactopyranose (IIa) was prepared in 82% yield by condensation of 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl bromide (III) and 1,3,4,6-tetra-*O*-acetyl-α-D-galactopyranose (IV)[7] in acetonitrile containing $Hg(CN)_2$ and $HgBr_2$. IIa crystallized from ethanol in colourless prisms m.p. 196–198°; $[\alpha]_D^{25}$ +49,40° (*c* 1,74 in methanol). The existence of an α-L biose linkage in the product was confirmed by comparison of the observed optical rotation with values calculated according to KLYNE[8], and by synthesis of IIa (although only in 2,5% yield) by condensation of 3,4-di-*O*-acetyl-1,2-*O*-(1-methoxyethylidene)-L-rhamnose (V)[9] with IV in boiling nitromethane containing $HgBr_2$ as catalyst, a procedure considered to lead stereospecifically to 1,2-*trans*-glycosides[10]. The condensation of III and IV under the conditions of HELFERICH and ZIRNER[7] therefore proceeds, as in the synthesis of neohesperidose (2-*O*-α-L-rhamnopyranosyl-D-glucose)[11], without inversion of configuration at C-1 of the acetylated glycosyl bromide (III). Deacetylation of IIa in 0.4% sodium methoxide

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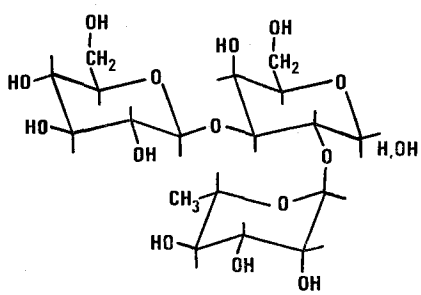

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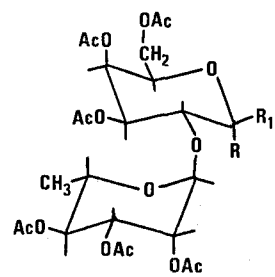
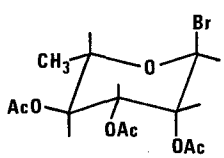


II

a: R = OAc, R_1 = H
b: R = H, R_1 = OAc
c: R = Br, R_1 = H



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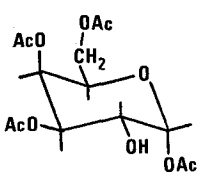

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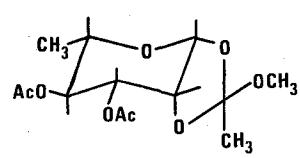

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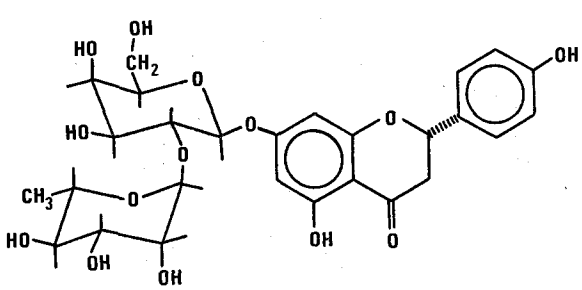

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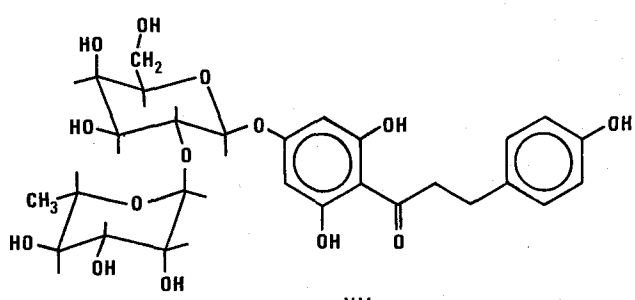

VII

afforded the free sugar which crystallized in 66% yield from methanol-ether as prisms, m.p. 125–126° (dec.); $[\alpha]_D^{22}$ +10,19° (10 min, equil; *c* 2,03 in water).

Hepta-*O*-acetyl-2-*O*-α-L-rhamnopyranosyl-β-D-galactopyranose (IIb) was prepared in 58% yield from IIa by conversion of the latter to the acetylated glycosyl bromide (IIc), and treatment of the product with mercuric acetate in glacial acetic acid (cf. [11,12]). Pure IIb crystallized from ethanol as colourless needles, m.p. 183–184°; $[\alpha]_D^{25}$ +2,53° (*c* 1,74 in methanol).

Satisfactory analyses were obtained for both anomeric hepta-acetates, and the IR- and NMR-spectra were in conformity with structures IIa and IIb. Neither product possesses physical properties in agreement with those of the compound, m.p. 75–80°; $[\alpha]_D^{19}$ −3,5°, isolated by KUHN et al.[1], and described as a hepta-acetate of 2-*O*-α-L-rhamnopyranosyl-D-galactose. The chromatographic properties reported for the free sugar derived from α-solanine are, however, in close agreement with those of the synthetic product which suggests that the acetate of KUHN et al[1]. might be an impure, amorphous preparation of the β-D anomer (IIb).

Hexa-*O*-acetyl-2-*O*-α-L-rhamnopyranosyl-α-D-galactopyranosyl bromide (IIc), m.p. 98–100°; $[\alpha]_D^{17}$ +121,20° (*c* 3,40 in chloroform) has been employed in the synthesis of naringenin 7-[2-*O*-α-L-rhamnopyranosyl-β-D-galactopyranoside] (VI) by a procedure essentially the same as described by AURNHAMMER[13] for the synthesis of flavanone neohesperidosides and rutinosides. Hydrogenation of VI with an equal mass of 10% Pd/C in 8,5% ethanolic KOH under a pressure of 1 bar, yielded the corresponding dihydrochalcone (VII). Compounds VI and VII failed to crystallize, but were obtained pure by chromatography; $[\alpha]_D^{17}$ −66.74° (*c* 4.78 in ethanol) and $[\alpha]_D^{21}$ −83.58° (*c* 2.48 in methanol), respectively.

Organoleptic studies revealed VI to be as bitter as the isomeric neohesperidoside, naringin, and VII to be as sweet as the corresponding naringin dihydrochalcone. The findings of HOROWITZ and GENTILI[14] indicate that the C-3 and C-4 hydroxyl groups of the D-glucose unit are of fundamental importance in determining the taste properties of flavanone and dihydrochalcone neohesperidosides. Similar conclusions were reached by EVANS[15], and BIRCH et al.[16] for other D-glucose derivatives, and the results are in conformity with the hypothesis of SHALLENBERGER and ACREE[17] that the saporous unit of sugars is the α-glycol group, and that its effect is most pronounced when its conformation is synclinal.

Flavanone VI differs from the isomeric naringin merely in respect of the configuration of C-4 of the D-hexose unit which NMR studies indicate to be stabilized in the *C1* conformation in both cases. Moreover, a synclinal conformation of the C-3 and C-4 hydroxyl groups is retained in both compounds, and this might be of particular significance in accounting for the lack of difference in the taste properties of these flavanone glycosides. Similar considerations apply in respect of VII and naringin dihydrochalcone. D-Galactose is, however, itself only about one-half as sweet as D-glucose. This has been ascribed to intramolecular hydrogen bond formation between the axial C-4 hydroxyl group and the ring oxygen atom in D-galactopyranose (*C1* conformation), resulting in less effective intermolecular hydrogen bonding at the taste bud receptor site[17]. If this explanation is correct, the results of the present study indicate that the mechanism is either inoperative in VI and VII, or its effect is greatly outweighed by the taste-enhancing effects of the substituents at C-1 and C-a of the D-galactose units.

Zusammenfassung. Ein acetyliertes, aus α-Solanin gewonnenes Spaltprodukt, das für Hepta-*O*-acetyl-2-*O*-α-L-rhamnopyranosyl-D-galaktopyranose angesehen wurde, stimmt in physikalischen Eigenschaften mit dem α- oder β-Heptaacetat des synthetisch dargestellten Disaccharids nicht überein. Naringenin-7-[2-*O*-α-L-rhamnopyranosyl-β-D-galaktopyranosid] (VI) und das entsprechende Dihydrochalkon (VII) wurden synthetisiert. Flavanon VI ist ebenso bitter wie Naringin, während VII gleichen Süssungsgrad wie Naringin-Dihydrochalkon zeigt.

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Adrenochrome-Thiol Addition Products

Aminochromes, such as adrenochrome (I) react readily with compounds containing an –SH group to give a variety of products (for a list of references see HEACOCK[1] and POWELL et al.[2]). In general three major types of products are formed: a) 5,6-dihydroxyindoles, b) 5,6-dihydroxyindole-4-thioethers and c) aminochrome-thiol addition products. It was suggested, largely on the basis of paper chromatographic and spectroscopic evidence, that the third group of compounds (i.e. the addition products) were structurally similar to the better known adrenochrome-sodium bisulphite addition compound (II)[3,4] in which the bisulphite residue is attached to the 9-position of the aminochrome ring system[5,6].

At low pH's the 5,6-dihydroxyindoles and 5,6-dihydroxyindole-4-thioethers predominate; however at mildly acidic or neutral pH's the addition compound appears to be the major product formed. All previous attempts to obtain the latter in solid form have been unsuccessful, due to the ease with which it decomposes on attempted isolation, the thiol-addition products being considerably less stable than the corresponding sodium bisulphite addition products. VAN ESPEN[7] has reported that stable semicarbazones and *p*-nitrophenylhydrazones can be prepared form the adrenochrome-sodium bisulphite addition product. A solid *p*-nitrophenylhydrazone derivative of a typical thiol-aminochrome addition product (i.e. that