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SHORT COMMUNICATION

CONSTITUENTS OF LOCAL PLANTS—X.

THE STEROIDAL ALKALOIDS OF *SOLANUM WRIGHTII* BENTH.

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Abstract—The unripe fruits of *Solanum wrightii* Benth. were found to contain solasonine, solamargine, free solasodine and a saponin which afforded chlorogenin by acid hydrolysis.

Interest in *Solanum* steroidal alkaloids has grown enormously over the past 10 yr on account of their utility as starting materials for the preparation of pregnane derivatives. Compounds with 5:6-unsaturation, such as solasodine and tomatidenol, are most desirable for this purpose. In this laboratory a study of the steroidal alkaloids in some local *Solanum* species has been started and we wish now to report our findings on *S. wrightii* Benth. The literature contains reference[1] to a previous investigation with *S. wrightii* (?) in which solanidine and glucose, rhamnose and arabinose were identified, but the plant investigated may be different from ours in view of the completely different nature of the constituents found.

The green unripe fruits of *S. wrightii* Benth. (syn. *S. macranthum* Carr.) were extracted with methanol containing 5% acetic acid, and the concentrated solution containing the alkaloidal glycosides freed from fatty matter by extraction with benzene–ether. After treatment with ammonia solution, the crude glycoside mixture (about 1·9 per cent of the weight of fresh fruits) was partially purified by repeated precipitation from acid solution with ammonia. Examination of the mixture on silica gel chromatoplates revealed the presence of two spots identical with solamargine and solasonine, and, in addition, a third due to a non-alkaloidal saponin. The total glycoside mixture was hydrolysed with mineral acid and examination of the aglycone fraction by TLC indicated the presence of solasodine as a principal product, along with two minor components. The latter were shown by isolation to be artefacts of hydrolysis, solaso-3,5-diene and a steroid sapogenin.

Although solasonine could be isolated from the mixture in an impure state by the tedious process of fractional crystallization, isolation of both major glycosides was best effected by column chromatography on alumina. This process led to the detection of free solasodine, and the isolation of solamargine, m.p. 303–305°, $[\alpha]_D - 96{\cdot}5°$ (methanol) and solasonine, m.p. 286–289°, $[\alpha]_D - 73{\cdot}2°$ (pyridine), in 0·1% and 0·74% yield respectively (on a fresh weight basis).

The identity of these two alkaloidal glycosides was established, by direct comparison, preparation of the usual derivatives, and by acid hydrolysis to afford solasodine, (25R)-22αN-spirosol-5-en-3β-ol,[2] m.p. 203–205°, $[\alpha]_D - 90°$ (methanol). Besides this aglycone,

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[1] C. Alves, L. N. Prista and M. A. Ferreira, *Garcia Orta* **2**, 713 (1961); C. Alves, L. N. Prista and M. A. Ferreira, *Chem. Abstr.* **61**, No. 12326 (1964).

[2] For nomenclature, cf. K. Schreiber, *Z. Chem.* **2**, 346 (1963).

solaso-3,5-diene, (25R)-22αN-spirosola-3,5-diene, was shown to be present in the hydrolysates from both glycosides by TLC. This compound results by acid-induced dehydration of solasodine, and is commonly formed with aglycones containing a 5:6-unsaturation.[3] The sugars resulting from the hydrolysis of solamargine (glucose and rhamnose) and solasonine (glucose, rhamnose and galactose) were also identified by TLC.

The presence of steroid sapogenins in steroid alkaloid-bearing plants is now recognized as to be expected from the common biogenetic pathway.[4] We have examined the ammoniacal filtrates, after precipitation of the alkaloidal glycosides, by the procedure of Wall *et al.*[5] Beside small amounts of solasodine and solaso-3,5-diene, a sapogenin, m.p. 267–269°, $[\alpha]_D -65°$, was isolated and identified as chlorogenin, by direct comparison and through the preparation of the diacetyl derivative. The biogenetic relation between the commoner solanum alkaloids and mono-hydroxylic steroid sapogenins is both evident and understandable from a consideration of their hydroxyl content and their stereochemistry at C-5, C-22 and C-25. The existence of chlorogenin, (25R)-5α, 22αO-spirostane-3β, 6α-diol, in *S. wrightii*, however, indicates that the relation may be further complicated by an additional hydroxylation or dehydroxylation mechanism induced by enzymes. As far as we are aware, this is the first reported occurrence of chlorogenin in a *Solanum* species. Inspection of the acid hydrolysate by thin-layer chromatography[6] revealed the absence of any other steroid sapogenins. We wish to mention in this connexion that the use of the *p*-anisaldehyde–acetic acid–sulphuric acid reagent (modified Kögi–Mischer reaction for steroids[7]) was a practical means for distinction between steroid sapogenins and steroid alkaloids (as aglycones or glycosides) on the chromatoplates. It gives a non-discriminatory non-fluorescent yellow colour with the first group and a range of colours (fluorescent in u.v.) changing upon heating from pink to dark blue with the second.

EXPERIMENTAL

Thin-Layer Chromatography

A slurry of silica gel G (Merk, 1 g) in water (3 ml) was applied onto glass plates (13 × 7 cm) followed by drying at 120° for 30 min. Chloroform–ethanol–ammonia solution (1%) (2:2:1) was used for the development of glycosides and methanol–chloroform (1:19) for aglycones. The use of several spray reagents, which produce different colours for any given product, was used to confirm the identity.

Isolation of the Steroidal Alkaloid Glycosides

The fresh green fruits of *Solanum wrightii* Benth. (8 kg) were minced with 8 l. of 80% methanol containing 5% acetic acid. The mixture was left at room temperature for 48 hr, filtered, and the residue re-extracted with half the amount of the same solvent. The combined extracts were evaporated under reduced pressure, and the concentrate (1 l.) treated with an equal volume of 10% acetic acid and, after standing, freed from the resinous matter which deposited. Defatting was effected by repeated extraction of the solution with a benzene–ether (1:1) mixture. The aqueous layer was heated to *ca.* 70°, brought to pH 10 with ammonia,

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[3] A. S. Labenskii and N. I. Koretskaya, *Med. Prom. SSSR* **15**, No. 3, 41 (1961).

[4] For example, see H. Sander, *Naturwissenschaften* **48**, 303 (1961); *Planta Med.* **11**, 303 (1963); *Bot. Jahrbücher* **82**, 404 (1963); K. Schreiber and H. Rönsch, *Arch. Pharm.* **298**, 285 (1965); *Ann. Chem.* **681**, 187 (1965).

[5] M. E. Wall, C. R. Eddy, M. L. McClennan and M. E. Klumpp, *Analyt. Chem.* **24**, 1337 (1952).

[6] D. T. El Munajjed, M.B.E. Fayez and A. S. Radwan, *Phytochem.* **4**, 587 (1965).

[7] *Chromatography*, p. 147. Merck, Darmstadt.

and left overnight at room temperature. The precipitate of organic bases was separated by centrifugation, re-dissolved in 5% acetic acid, and re-precipitated with ammonia. This process was repeated twice to give finally a mixture of the crude alkaloidal glycosides (dry 150 g). The original ammoniacal filtrate was kept for investigation of the steroid sapogenin content.

Inspection of alkaloid mixture by TLC revealed the presence of three spots (R_f 0·33, 0·48, and 1·00) due to solasonine, solamargine and an unidentified non-alkaloidal product, respectively, as revealed by direct comparison with authentic materials and spraying with the Dragendorff's, Clark's,[8] chlorosulphonic–acetic acid (1:3), *p*-anisaldhyde[7] and antimony trichloride (20% in chloroform) reagents followed by viewing under u.v. light. A small amount of the crude total glycoside mixture was refluxed in 4% ethanolic HCl for 3 hr and, after the usual working-up, the hydrolysate examined by TLC. The presence of solasodine, solaso-3,5-diene and chlorogenin was revealed by comparison with authentic products.

Resolution of the components of the crude glycoside mixture (12 g) was effected by column chromatography on alumina (1·5 kg) packed in water-saturated *n*-butanol.[9] The early fractions, eluted with the same solvent, removed a small amount of a mixture in which the presence of free solasodine (R_f 0·45) was indicated on the chromatoplates. Later fractions afforded two crystalline products *A* R_f 0·48 (0·99 g) and *B* R_f 0·33 (4·67 g). The first was repeatedly crystallized from aqueous methanol to give colourless prisms, m.p. 303–305° (decomp.), undepressed by an authentic sample of solamargine, $[\alpha]_D - 96·5°$ (methanol). Reported[10] m.p. 301° (decomp.), $[\alpha]_D - 105 \pm 4°$ (methanol).

Hydrolysis of *A* (1 g) by refluxing with HCl (2 N, 10 ml) in methanol (10 ml) solution for 3 hr afforded solasodine hydrochloride which was crystallized from aqueous methanol containing a trace of HCl to give needles, m.p. 277–280°, $[\alpha]_D - 77·1°$ (methanol). Reported[11] m.p. 265–270°, $[\alpha]_D - 92 \pm 25°$. The free aglycone was obtained by treating a hot solution of the crude salt in 70% methanol with ammonia solution followed by boiling for 10 min. Upon cooling, the product which deposited was shown by TLC to consist mainly of solasodine (R_f 0·45) beside a trace of solaso-3,5-diene (R_f 0·78) by comparison with authentic materials. Crystallization of the crude product from aqueous methanol gave long plates of solasodine, m.p. 203–205° (undepressed), $[\alpha]_D - 90°$ (methanol). Reported [12] m.p. 201°, $[\alpha]_D - 100°$ (methanol). The following derivatives were also prepared: *O*-benzoate, m.p. 209–216° (reported[13] m.p. 216–217°), *N*-nitroso, m.p. 259–261° (decomp.) (reported[14] m.p. 260·5–262·5°) and picrate, m.p. 146–150° (reported[15] m.p. 144°).

The aqueous acid hydrolysate from solamargine was tested for sugars on silica gel chromatoplates (system: toluene–isopropanol–ethyl acetate–water, 2:10:5:2·5) and shown to contain glucose (R_f 0·44) and rhamnose (R_f 0·78) by spraying with the diphenyl amine–aniline–phosphoric acid.

Product *B* was purified by repeated crystallization from aqueous methanol to give solasonine as needles, m.p. 286–289° (decomp.) (undepressed), $[\alpha]_D - 73·2°$ (pyridine). Reported[15] m.p. 284·5°, $[\alpha]_D - 68·7°$ (ethanol). Hydrolysis of 1 g of this glycoside with acid

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[8] E. G. C. Clarke, *Nature* **181**, 1152 (1958).

[9] R. Kuhn and J. Löw, *Chem. Ber.* **88**, 289 (1955).

[10] L. H. Briggs, E. G. Brooker, W. E. Harvey and A. L. Odell, *J. Chem. Soc.* 3587 (1952).

[11] H. L. De Wall, L. P. Neethling and G. W. Perold, *J. Suid-Afrik. Chem. Inst.* **13**, 45 (1960).

[12] D. A. H. Taylor, *J. Chem. Soc.* 4216 (1958).

[13] L. H. Briggs and T. Oshea, *J. Chem. Soc.* 1654 (1952).

[14] R. C. Bell and L. H. Briggs, *J. Chem. Soc.* 1 (1942).

[15] R. C. Bell, L. H. Briggs and J. J. Carroll, *J. Chem. Soc.* 12 (1942).

as previously described followed by crystallization from 70% ethanol containing a trace of HCl gave solasodine hydrochloride, m.p. 277–280°, $[\alpha]_D - 77{\cdot}1°$ (methanol). The free aglycone (R_f 0·45) was obtained from the crude salt and was shown to be mixed with trace amounts of solaso-3,5-diene (R_f 0·78). It was purified by crystallization from aqueous methanol to give solasodine, m.p. 203–205° (undepressed), $[\alpha]_D - 91°$ (methanol). The sugars present in the acid hydrolysate were shown to be glucose (R_f 0·44), galactose (R_f 0·35) and rhamnose (R_f 0·78).

Isolation of Chlorogenin

The ammoniacal filtrate obtained after isolation of the crude glycosides (see above) was thrice extracted with water-saturated *n*-butanol (total 5 l.) and the extract washed with water, then concentrated *in vacuo* to 250 ml. Ethanol (150 ml) and conc. HCl (100 ml) were added and the mixture was refluxed for 3 hr. After removal of most of solvent a resin was formed which was shown by TLC to contain solasodine and solaso-3,5-diene. The clear solution was neutralized with ammonia to afford more of these two products and the filtrate was diluted with water then extracted with chloroform. The residue (3·2 g) from this extract was refluxed in benzene (150 ml) solution with methanolic NaOH (5%, 100 ml) for 30 min. After working-up, the resulting product was shown on the chromatoplates to consist of solasodine (R_f 0·45), solaso-3,5-diene (R_f 0·78) and another product (R_f 0·34) giving a yellow colour with the *p*-anisaldehyde reagent. Repeated crystallization of this mixture from chloroform–methanol gave the product with R_f 0·34 as needles, m.p. 267–269°, undepressed by authentic chlorogenin, $[\alpha]_D - 65{\cdot}0°$, reported[16] m.p. 276°, $[\alpha]_D - 64°$. The diacetate was obtained as lustrous needles, m.p. 160–164° (undepressed). Reported[16] m.p. 158°. The i.r. spectrum (Nujol) of the diacetate and authentic chlorogenin diacetate were identical in every detail.

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[16] M. E. WALL and H. A. WALENS, *J. Am. Chem. Soc.* 77, 5661 (1955).