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THE GLUCOSIDES OF *BUTEA MONOSPERMA*

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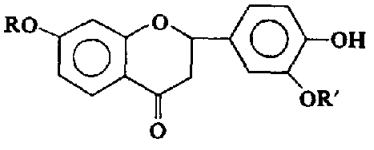
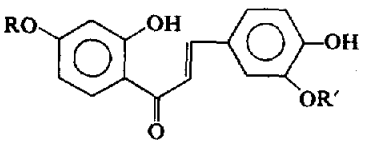
Abstract—A reinvestigation of the flowers of *Butea monosperma* revealed the presence of seven flavonoid glucosides. Two of them are butrin and isobutrin, which have been isolated earlier from the plant. Three glucosides have been identified as coreopsin, isocoreopsin and sulphurein. The remaining two are new and have been assigned the structures IX (monospermoside) and X (isomonospermoside). The glucosides III, IV, IX, and X have been synthesized. The shift in the u.v. spectrum of 3-hydroxy-2′,4,4′-trimethoxy chalcone, on addition of alkali, is similar to what has been earlier noted with 2′-hydroxychalcones.

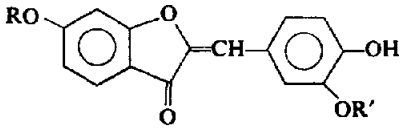
THE PRESENCE, in the flowers of *Butea monosperma*, of the flavonoids, butin (I), butein (II), butrin (III), isobutrin (IV) and palasitrin (V) was reported earlier.[1] A reinvestigation using improved methods has resulted in the isolation of five more glucosides.



(I) R = R′ = H
(III) R = R′ = Glucosyl
(VII) R = Glucosyl, R′ = H
(X) R = H, R′ = Glucosyl



(II) R = R′ = H
(IV) R = R′ = Glucosyl
(VIII) R = Glucosyl, R′ = H
(IX) R = H, R′ = Glucosyl



(V) R = R′ = Glucosyl
(VI) R = Glucosyl, R′ = H

The concentrate of the ethanolic extract of the flowers was successively extracted with light petroleum, ether and ethyl acetate. The light petroleum extract contained waxy material and the ether extract, butin and butein. The ethyl acetate extract gave, on paper chromatography, four yellow bands which were separated into individual bands by preparative paper chromatography.

Band 1 could be separated into two compounds by fractional crystallization from ethanol. These were identified as butrin and isobutrin by comparison with authentic samples. The structures of butrin and isobutrin have now been confirmed by synthesis.

[1] B. PURI and T. R. SESHADRI, *J. Chem. Soc.* 1589 (1955).

Band 2 gave the same colour reactions earlier reported for palasitrin, but careful study disclosed that the compound was sulphurein[2] (VI); identification was made by u.v. spectra and comparison with a synthetic sample, obtained by aerial oxidation of coreopsin in alkaline solution.[2]

Band 3 was separated into two compounds, *A* and *B*, by polyamide column chromatography. Colour reactions, R_f value on paper chromatography and u.v. spectra indicated that *A* was a flavanone monoglycoside. Hydrolysis gave butin, butein and glucose. The green ferric reaction of the glucoside showed that the 3'- and 4'-hydroxyl groups were free. Hence it was butin-7-glucoside (VII), known[3] as isocoreopsin, and this was confirmed by interconversions with coreopsin. *B* was identified as coreopsin (VIII) by R_f values, colour reactions, interconversions with isocoreopsin described above, and by comparison with a sample obtained by condensing resacetophenone-4-glucoside tetraacetate with protocatechuic aldehyde.[5]

Band 4 yielded a yellow crystalline solid, m.p. 194–195°, $C_{21}H_{22}O_{10}$; its colour reactions and u.v. spectra indicated it to be a chalcone glycoside. Hydrolysis with acid gave a mixture of butin, butein and glucose and hence it was a glucoside of butein. Its high R_f value (on paper chromatography) showed it to be a monoglucoside. It was different from coreopsin in R_f values, spectra and colour reactions and therefore did not carry the glucose unit on 4'-hydroxyl. However, its u.v. maximum was shifted with $AlCl_3$ indicating that 2'-position was also free. Lack of any change in the u.v. spectrum with $NaOAc + H_3BO_3$ indicated that the glucose unit may be in the B-ring, linked to 3- or 4-hydroxyl group. As it gave a deep orange-red fluorescence when exposed to ammonia, 4-hydroxyl could be free.[6]

The NMR spectrum of the complete acetate of the glucoside gave signals at δ 2·23, 2·30 and 2·32 (each for three protons of three phenolic acetoxyls) and at δ 2·05 for twelve protons (four acetoxyls of the glucose unit), thus confirming the conclusion that it is a monoglucoside. The first two signals, viz. δ 2·23 and 2·30, are also given by the complete acetate of isobutrin, indicating that the two glycosides have two free phenolic hydroxyls, 2' and 4, in common.

Complete methylation, followed by hydrolysis with acid and also with emulsin, gave a compound which had the u.v. spectrum shown in Fig. 1. When sodium ethoxide was added to the ethanolic solution, band II (255 nm) shifted to 282 nm with increase in intensity while band 1 (357 nm) moved to 335 nm with decrease in intensity and there appeared a very low intensity band at 405 nm. These features have been earlier recorded[7] for chalcone with only 2'-hydroxylation. A hydroxyl group at any other position has been said to give a bathochromic shift of the *band* 1. But, in the present case, the lack of $AlCl_3$ shift in the u.v. spectrum of the chalcone partial methyl ether and its negative ferric reaction ruled out 2'-hydroxylation. Also, the properties of the glucoside indicated 3-glucosidation. Since no u.v. spectrum of a chalcone with only 3-OH free seems to have been reported in ethanolic sodium ethoxide solution, 3-hydroxy-2',4,4'-trimethoxy chalcone has now been synthesized; the synthetic compound agreed with the trimethyl ether obtained from the glucoside in TLC and colour reactions; the u.v. spectra in ethanol and with NaOEt were also identical. These studies show that the above-mentioned idea that only chalcones with only 2'-hydroxyl free give these u.v. characteristics is wrong and requires modification. The compound from *band* 4 is

[2] M. SHIMOKORIYAMA and S. HATTORI, *J. Am. Chem. Soc.* **75**, 1900 (1953).
[3] B. PURI and T. R. SESHADRI, *J. Sci. Ind. Res. India* **13B**, 321 (1954).
[4] T. A. GEISSMAN, *J. Am. Chem. Soc.* **63**, 2689 (1941).
[5] L. FARKAS and L. PALLOS, *Chem. Ber.* **92**, 1263 (1959).
[6] J. B. HARBORNE, *Phytochem.* **1**, 203 (1962).
[7] L. JURD and R. M. HOROWITZ, *J. Org. Chem.* **26**, 2561 (1961).

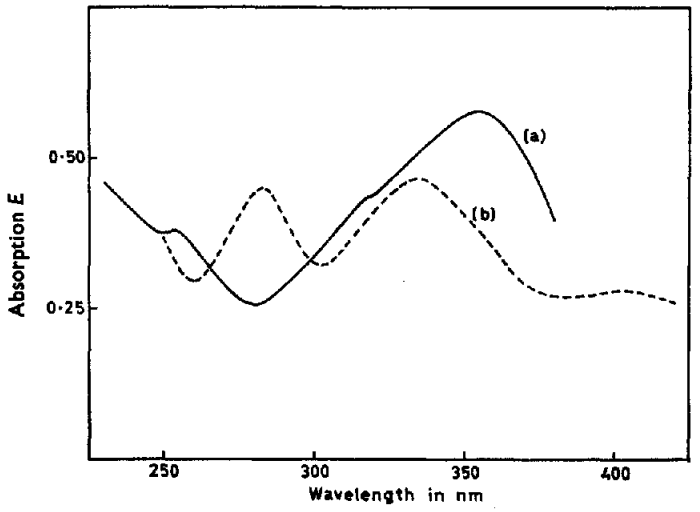


FIG. 1. U.V. SPECTRUM OF 3-HYDROXY-2′,4,4′-TRIMETHOXY CHALCONE; (*a*) IN ETHANOL, (*b*) IN ETHANOLIC NaOEt.

therefore butein-3-β-D-glucoside (IX), now reported for the first time and is named "monospermoside".

In view of the fact that the flavanone–chalcone isomers I and II, III and IV and VII and VIII were isolated from the same plant, it could be expected that the flavanone glucoside corresponding to monospermoside may also be present. Therefore, the mother liquor (aq. methanol) left after crystallization of monospermoside was subjected to column chromatography over polyamide and eluted with 10% ethanol; it gave a product which could be crystallized from methanol–ethyl acetate to yield a colourless solid, m.p. 163°. Its colour reactions, u.v. spectrum and shift with sodium acetate are consistent with its formulation as butin-3′-glucoside (X). Final confirmation was obtained by its conversion into monospermoside with alkali. The natural monospermoside, in turn, gave the flavanone glucoside when heated in aqueous sodium acetate solution. This new 3′,4′,7-trihydroxyflavanone-3′-glucoside is, therefore, named isomonospermoside.

For the synthesis of monospermoside, isobutrin and their flavanone-isomers, protocatechuic aldehyde-3-glucoside was required; it was earlier[8] synthesized by steps of partial acetylation of protocatechuic aldehyde (to the 3-acetate), mesylation, deacetylation and condensation with acetobromoglucose, followed by saponification. In the present work, protocatechuic aldehyde-4-benzyl ether was condensed with acetobromoglucose and the product on catalytic (Pd-C) hydrogenolysis gave the desired compound as the tetraacetate. It was condensed with resacetophenone to yield a yellow chalcone glucoside, identical with monospermoside in all respects; its conversion to isomonospermoside has been described earlier in this paper.

Though the constitutions of butrin and isobutrin were established earlier, their synthesis was not carried out and this has now been done. Condensation of protocatechuic aldehyde-3-(tetra-*O*-acetyl) glucoside with resacetophenone-4-(tetra-*O*-acetyl) glucoside, in alkali, gave a product identical with isobutrin, which has been conveniently converted into butrin by the use of aq. sodium acetate.

[8] B. HELFRICH and P. PAPALAMBROU, *Liebigs Ann. Chem.* **551**, 242 (1942).

EXPERIMENTAL

The m.ps are uncorrected. U.v. spectra were recorded in ethanol, on a Perkin–Elmer spectrophotometer; additional reagents used are indicated at appropriate places; log ϵ values are given in brackets. NMR spectra were recorded on a Varian A-60 spectrometer, using $CDCl_3$ as the solvent; only significant signals are cited; chemical shifts are given in ppm relative to internal standard TMS.

Isolation of the Glycosides

Dried flowers (500 g) of *Butea monosperma* (syn. *B. frondosa*) were extracted with EtOH (cold and hot) and the solvent distilled off. The residue, after extraction with light petroleum and Et_2O, was dissolved in minimum amount of H_2O and extracted with ethyl acetate continuously for 2 weeks. The ethyl acetate extract, after concentration, was chromatographed on 3 MM paper with BAW (6:1:2) as the solvent, (R_f 0·48, 0·68, 0·73 and 0·79). The yellow bands were cut and extracted with hot EtOH.

Band 1 (*butrin and isobutrin*). Fractional crystallization of band 1 (R_f 0·48) yielded two compounds. The first was a colourless solid, m.p. 190–191°d; λ_{max} 314 (3·76), 270 (4·17) and 230 (sh) nm; identified as butrin by comparison, with an authentic sample. The second compound formed yellow crystals from EtOH, m.p. 192–193° (acetate, m.p. 108–110°); λ_{max} 377 (4·19), 300 (3·83) and 255 (sh) nm; +$AlCl_3$, 430 nm; +NaOEt, 427 nm ν_{max}^{KBr} 3520, 1640, 1575, 1515, 1070 cm^{-1}. The m.p. and colour reactions agreed with properties of isobutrin; direct comparison confirmed the identity. The spectra were not recorded earlier.

Band 2 (*sulphurein*). *Band* 2 gave a deep yellow solid, m.p. 185–190°d (loss of H_2O at 90° and sintering at 165°). $FeCl_3$—brown, aq. NaOH—purple, H_2SO_4—violet; λ_{max} 405 nm; +NaOEt, 512 nm; +NaOAc + H_3BO_3, 445 nm. The properties indicated that it was sulphurein and this was confirmed by comparison with a synthetic sample.

Band 3 (*coreopsin and isocoreopsin*). This was chromatographed on a column of polyamide; elution with 10% and 30% aq. EtOH gave two fractions, *A* and *B*. Fraction *A* yielded a pale-coloured solid; λ_{max} 312, 269, 230 nm; +NaOAc, no shift; giving green $FeCl_3$ reaction and red colour with aq. NaOH. It was identified as isocoreopsin by interconversions with coreopsin. Fraction *B* yielded a yellow compound, identified as coreopsin by comparison with a synthetic sample.

Band 4 (*monospermoside and isomonospermoside*). Crystallization from aq. MeOH yielded monospermoside as yellow crystalline solid (500 mg), m.p. 194–195°; $FeCl_3$—brown; aq. NaOH—deep yellow; λ_{max} 377 (4·40), 312 (sh), 255 (sh) nm; +$AlCl_3$, 423 nm; +NaOEt, 438 nm; +NaOAc + H_3BO_3, no shift; ν_{max}^{KBr} 3450, 1635, 1505, 1060, 800 cm^{-1}. (Found: C, 57·8; H, 5·1. $C_{21}H_{22}O_{10}$ required: C, 57·1; H, 5·1%.) Acetate: colourless crystals from MeOH, m.p. 160°. NMR spectrum: δ 2·23 (3H), δ 2·30 (3H) and δ 2·32 (3H) (for three phenolic acetoxyls) and δ 2·05 (12H) (for four alcoholic acetoxyls).

Hydrolysis. The gluciside (0·01 g) was refluxed for 2 hr with aq. H_2SO_4 (7%, 5 ml) and cooled. After Et_2O extraction the aqueous solution was neutralized with $BaCO_3$, filtered and evaporated. The residue contained glucose, identified by paper chromatography. The ether extract was found to be a mixture of butin and butein by paper chromatography and u.v. spectra. [Found: glucose, 42·5. $C_{21}H_{22}O_{11}$ required: glucose (1 unit), 41·5%.]

Methylation and hydrolysis. Monospermoside (100 mg) in dry acetone (10 ml) was refluxed with Me_2SO_4 (0·09 ml) and K_2CO_3 (1 g) till it gave no $FeCl_3$ reaction. The product was worked up in the usual manner and hydrolysed with aq. H_2SO_4 (5%) and with emulsin, independently. The hydrolysate was extracted with Et_2O, the Et_2O evaporated and the residue crystallized from aq. MeOH, m.p. 105° (not sharp); λ_{max} 357 (4·27), 255 (4·05); +NaOEt, 405, 335 and 282 nm; identical with a synthetic sample of 3-hydroxy-2′,4,4′-trimethoxy chalcone, obtained by treating resacetophenone dimethyl ether (0·18 g) and isovanillin (0·15 g) in alcohol (3 ml) with aq. KOH (50%; 0·5 ml) and working up, after 24 hr, in the usual manner (m.p. 115°).[9]

Isomonospermoside

The mother liquor, after removal of monospermoside, was chromatographed over polyamide and eluted with 10% EtOH (aq.) yielding a colourless solid (100 mg), m.p. 163°, $FeCl_3$—no colour; Mg/HCl—deep violet; aq. NaOH—deep yellow; λ_{max} 310 (3·78), 278 (4·08) and 230 (sh) nm; +NaOAc, 330, 278 nm. This was identified as isomonospermoside by conversion into monospermoside. The compound (10 mg) was dissolved in aq. NaOH (5%, 2 ml), warmed for a few minutes and cooled. The solution was then acidified, extracted with ethyl acetate, and the ethyl acetate extract was concentrated and crystallized, yielding yellow solid, m.p. 193–194°, mixed m.p. with monospermoside undepressed; i.r. superimposable with that of monospermoside.

Synthesis of the Glucosides

Protocatechuic aldehyde-4-benzyl ether. Protocatechuic aldehyde (2 g) in dimethyl formamide (10 ml) was stirred with benzyl chloride (2 ml) and anhydrous $NaHCO_3$ (5 g) for 4 hr at 90°. The mixture was filtered, the filtrate was diluted with H_2O and extracted with Et_2O. The ether solution was extracted with aq. Na_2CO_3

[9] J. B. LAL, *J. Indian Chem. Soc.* **16**, 296 (1939).

(1%) to remove the unreacted protocatechuic aldehyde and its 3-benzyl ether, formed in a small quantity. It was then extracted with aq. NaOH (1%), the aqueous solution acidified and re-extracted with Et_2O. The Et_2O extract was evaporated and the residue crystallized from aq. MeOH, yielding colourless needles (1·5 g, m.p. 122°).[10]

4-Benzyl-protocatechuic Aldehyde-3-(tetra-O-acetyl) Glucoside

The above benzyl ether (1 g) in dry pyridine (10 ml) was stirred with anhydrous $CaSO_4$ (1 g) and $AgCO_3$ (2 g) for 0·5 hr, 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosylbromide (3 g) was then added and the stirring was continued for 3 more hours. The mixture was then filtered, the filtrate was diluted with aq. acetic acid (10%; 100 ml) and extracted with large amounts of Et_2O. The Et_2O solution was evaporated and the residue crystallized from Et_2O, when the desired 3-β-(tetra-*O*-acetyl) glucoside of protocatechuic aldehyde-4-benzyl ether was obtained as colourless needles (1 g; m.p. 141–142°). (Found: C, 60·8; H, 5·7. $C_{28}H_{30}O_{12}$ required: C, 61·2; H, 5·4%.)

Protocatechuic Aldehyde-3-β-(tetra-O-acetyl) Glucoside

The above benzyl glucoside (500 mg) in EtOH (100 ml) was hydrogenated over Pd–C (5%; 50 mg), taking care to avoid over-hydrogenation. 1·5 g more of the benzyl ether was hydrogenated in three lots and the combined product, after filteration and evaporation, was chromatographed over SiO_2 and the required protocatechuic aldehyde-3-β-(tetra-*O*-acetyl) glucoside was eluted with benzene; colourless crystals from benzene (600 mg; m.p. 148–149°); ν_{max}^{KBr} 3760, 1765, 1690, 1610, 1515, 1450, 1250, 1040, 770 cm^{-1}. (Found: C, 53·4; H, 5·3. $C_{21}H_{24}O_{12}$ required: C, 53·8; H, 5·1%.)

Monospermoside and Isomonospermoside

Resacetophenone (100 mg) was added to aq. KOH (60%; 1·5 ml) containing a few drops of EtOH. The mixture was cooled in ice and protocatechuic aldehyde-3-glucoside tetraacetate (300 mg) was added. The mixture was allowed to stand at room temp. for 48 hr with occasional shaking. Then it was neutralized with aq. H_2SO_4 (10%) under vigorous cooling and extracted with Et_2O, followed by ethyl acetate. The ethyl acetate extract was dried, concentrated and diluted with Et_2O, yielding a yellow compound, m.p. 188–190°; mixed m.p. with monospermoside 187–190°. λ_{max} 376, 312 (sh) and 256 nm; +NaOEt, 438 nm. Direct comparison of the R_f values and i.r. spectra proved the identity.

Monospermoside (10 mg) in aq. NaOAc (2 ml) was warmed on a water-bath for 0·5 hr, cooled and extracted with ethyl acetate. The ethyl acetate extract, on crystallization from EtOAc, gave isomonospermoside, identical with the natural sample, by colour reactions and cochromatography.

Isobutrin and Butrin

To resacetophenone-4-β-(tetra-*O*-acetyl) glucoside (m.p. 130–131°)[11] (250 mg) in aq. KOH (60%; 5 ml) were added protocatechuic aldehyde-3-(tetra-*O*-acetyl) glucoside (250 mg) and a few drops of EtOH. After 72 hr at room temp., it was neutralized with aq. H_2SO_4 (10%) and extracted with *n*-BuOH. The BuOH solution, on dilution with Et_2O, gave a yellow amorphous solid (50 mg), purified by polyamide column chromatography; m.p. and mixed m.p. with isobutrin, 188–190°; λ_{max} 378, 300 and 255 (sh) nm; +NaOEt 428 nm. (Found: C, 53·9; H, 5·9. $C_{27}H_{32}O_{15}$ required: C, 54·4; H, 5·4%.) 20 mg of the synthetic compound was acetylated with acetic anhydride and pyridine and the acetate (m.p. 120–122°) did not depress the m.p. of the acetate of the natural sample of isobutrin. They had superimposable i.r. spectra.

Isobutrin (50 mg) in aq. NaOAc (200 mg in 2 ml) was left at room temp. for 3 days. The solvent was slowly evaporated at 60° and the residue crystallized from EtOH to remove the sodium acetate. The mother liquor was diluted with acetone and the precipitate purified by preparative TLC on polyamide layers yielding butrin as a colourless solid, λ_{max} 314, 270 and 230 (sh) nm; identified by colour reactions, cochromatography and u.v. spectrum.

[10] *Beilsteins Handbuch der Organischen chemie* (4th edition), Vol. 8, p. 257 (1925).
[11] N. MAUTHNER, *J. Prakt. Chem.* **160**, 33 (1942).