326. *Constitution of the Glucoside Butrin isolated from* Butea Frondosa *Flowers. Part I.*

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BUTRIN, the flavanone glucoside $C_{27}H_{32}O_{15},2H_2O$ isolated from the flowers of *Butea Frondosa* (Lal and Dutt, *J. Indian Chem. Soc.*, 1935, **12**, 4, 262), on hydrolysis with dilute mineral acids gives two molecules of glucose and one of butin, $C_{15}H_{12}O_5$, and is readily hydrolysed by emulsin, showing that it is a β-glucoside.

Butrin contains nine hydroxy-groups, but by the action of acetic anhydride and anhydrous sodium acetate at 130—135° it yields a *deca-acetyl* derivative, $C_{27}H_{22}O_5(O{\cdot}CO{\cdot}CH_3)_{10}$, owing to the rupture of the pyrone ring with simultaneous acetylation of the newly formed phenolic hydroxy-group of the chalkone. This behaviour is common among flavanone derivatives, *e.g.*, naringenin (Asahina and Inubuse, *Ber.*, 1928, **61**, 1514) and carthamidin (Kuroda, J., 1930, 753; *Proc. Imp. Acad. Tokyo*, 1929, **5**, 82). Butrin forms a *nonabenzoyl* derivative but a *tetra*-p-*nitrobenzoyl* derivative by usual procedures.

Methylation of glucosides of polyhydric phenols by methyl iodide and potassium carbonate in dry acetone has been shown to attack only the phenolic and not the hydroxy-groups (J., 1930, 2434), and King and Robertson (J., 1931, 1704) have shown that methylation of the flavanone glucoside hesperidin produces a syrup which yields on hydrolysis 4-hydroxy-2 : 6-dimethoxyphenyl 3 : 4-dimethoxystyryl ketone. Ethylation of butrin with excess of ethyl iodide and potassium carbonate in ethyl-alcoholic solution yields a white O-*diethylbutrin*, m. p. 238°, and an isomeric bright yellow product, m. p. 183·5°. The former is a flavanone derivative and contains no free phenolic group; since this is a diethoxy-compound, butrin must be regarded as a bioside of 7 : 3′ : 4′-trihydroxyflavanone, the position of the biose residue being still undetermined. The bright yellow compound is evidently a *chalkone*. Similarly, on methylation with methyl iodide and potassium carbonate, butrin yields a white O-*dimethylbutrin*, $C_{27}H_{30}O_{13}(OCH_3)_2,7\frac{1}{2}H_2O$, m. p. 224°. Hence, this method of ethylation or methylation, which opens up the pyrone ring completely in the case of hesperidin, does so only partly in the case of butrin, and consequently in butrin the flavanone configuration seems to be more stable than in hesperidin.

Butrin in alcoholic solution gives a pale yellow lead salt (Lal and Dutt, *loc. cit.*), but in hot aqueous solution it forms a bright yellow *lead* salt, $C_{27}H_{30}O_{13}(O{\cdot}Pb{\cdot}OAc)_2,2H_2O$, which must be derived from the chalkone corresponding to butrin, the transformation from flavanone to chalkone having been brought about during the course of its preparation.

EXPERIMENTAL.

4 G. of butrin, recrystallised from 200 c.c. of boiling water by slow cooling, formed a mass of white glistening needles; after standing overnight, these were collected, washed with water, and dried in air (38°) for several days (Found: C, 46·9, 47·1; H, 6·3, 6·3; loss at 120°, 13·6. $C_{27}H_{32}O_{15},5H_2O$ requires C, 47·3; H, 6·1; $5H_2O$, 13·1; $3H_2O$, 7·87%. Loss on keeping over H_2SO_4 or $CaCl_2$ for 10 days, 7·79, 7·64. Found, in dried sample: C, 51·2, 51·2; H, 5·7, 5·6. Calc. for $C_{27}H_{32}O_{15},2H_2O$: C, 51·3; H, 5·7%. Found, for anhydrous substance: *M*, cryoscopic in phenol, 560, 530. Calc. for $C_{27}H_{32}O_{15}$: *M*, 596).

The anhydrous substance, $[\alpha]_D^{30^\circ} - 81·7^\circ$ in pyridine (*c* 1·681), is very hygroscopic, taking up $2H_2O$ when exposed to air for a few hours. The dihydrate, which is also obtained by crystallisation from boiling rectified spirit (cf. Lal and Dutt, *loc. cit.*), is the most stable hydrate, $[\alpha]_D^{31·5^\circ} - 73·27^\circ$ in water (*c* 0·396).

Lead salt. To butrin (2 g.), dissolved in hot water (150 c.c.), a solution of lead acetate (2 g.) was added; no precipitation took place, although the solution turned yellow and then orange-yellow. On keeping overnight, an orange-yellow *lead* salt separated, which was filtered off and well washed with ice-cold water. Purification, by dissolving this in 50 c.c. of alcohol and adding water to turbidity, afforded ultimately a bright yellow granular precipitate, which was filtered off, washed, and dried in air (2 g.); m. p. 128° (shrinking at 115°). It is readily soluble in cold ethyl or methyl alcohol and in boiling water and is insoluble in other solvents [Found: C, 32·4; H, 3·4; Pb, 36·0. Loss at 80°, 2·7. $C_{27}H_{30}O_{13}(O{\cdot}Pb{\cdot}OAc)_2,2H_2O$ requires C, 33·0; H, 3·2; Pb, 36·9; $2H_2O$, 3·1%].

Nonabenzoyl derivative. To butrin (3 g.), dissolved in pyridine (50 g.), benzoyl chloride (45 g.) was gradually added with vigorous shaking during 5 hours. The product was recrystallised four times from boiling alcohol and obtained as colourless nodules which, after drying over anhydrous calcium chloride for a few days, had m. p. 141°; yield 5·4 g. (calc., 6 g.); $[\alpha]_D^{30^\circ}$ of anhydrous sample + 77·28° in pyridine (*c* 2·525) [Found: C, 69·3, 69·5; H, 4·4, 4·4; loss at 95° for 18 hours, 1·2, 1·3. $C_{27}H_{23}O_6(O{\cdot}CO{\cdot}C_6H_5)_9,H_2O$ requires C, 69·7; H, 4·5; H_2O, 1·2%]. It gives with concentrated sulphuric acid an orange solution, but no coloration with magnesium and methyl-alcoholic hydrochloric acid.

Deca-acetyl derivative. A mixture of butrin (3 g.), anhydrous sodium acetate (3 g.), and acetic anhydride (20 g.) was heated at 130—135° for 5 hours, cooled, and diluted with a large volume of water; the resulting flocculent white precipitate (4·8 g.) crystallised from boiling methyl alcohol as very pale yellow flakes, which were dried over calcium chloride; m. p. 119—120° [Found: C, 54·4; H, 5·0; loss at 95°, 1·7, 1·7. $C_{27}H_{22}O_5(OAc)_{10},H_2O$ requires C, 54·6; H, 5·2; H_2O, 1·7. Found in anhydrous substance: C, 55·4; H, 5·2; $CH_3{\cdot}CO$, 43·4, 42·7. $C_{27}H_{22}O_5(OAc)_{10}$ requires C, 55·5; H, 5·1; $CH_3{\cdot}CO$, 42·3%]; $[\alpha]_D^{30^\circ}$ for anhydrous substance − 79·86° in pyridine (*c* 1·224). It is very soluble in pyridine, glacial acetic acid, chloroform, carbon tetrachloride, ethyl acetate, and fairly so in ethyl and methyl alcohol and in acetone. Its colour reactions resembled those of the benzoyl derivative.

Carbethoxybutrin was prepared from butrin (3 g.), dissolved in pyridine (25 c.c.), and ethyl chloroformate (9 g.) in the usual manner, and was obtained on complete evaporation of solvent from methyl-alcoholic solution as a white amorphous mass, m. p. 83—84° after shrinking at 82° (4·3 g.). It is extremely soluble in all organic solvents.

Butrin oxime. This was prepared by refluxing a mixture of butrin (3 g.), hydroxylamine hydrochloride (3 g.), sodium acetate (4 g.), and ethyl alcohol (22 c.c.) for 8 hours. On concentration and subsequent addition of water, a white flocculent precipitate was formed, which, after five crystallisations from alcohol, was obtained as flakes (2·8 g.), m. p. 180° after shrinking at 165° (air-dried). It dissolves in sodium hydroxide to a colourless solution, which turns yellow on heating. With concentrated hydrochloric acid on heating it gives a deep yellow coloration, which with excess of alkali becomes orange (Found: C, 49·8; H, 5·55; N, 2·3; loss at 115°, 5·5; $C_{27}H_{33}O_{15}N,2H_2O$ requires C, 50·1; H, 5·7; N, 2·2; H_2O, 5·6%).

p-*Nitrobenzoyl derivative.* To butrin (2 g.), dissolved in pyridine (40 g.), powdered *p*-nitrobenzoyl chloride (22 g.) was added with vigorous shaking during 3 hours; the product was isolated, and crystallised from dilute pyridine in nodules, m. p. 154° (5·4 g.). It is extremely soluble in pyridine, readily soluble in acetone and ethyl acetate, fairly soluble in hot amyl alcohol, and insoluble in other solvents. It is insoluble in alkali hydroxide solutions [Found in air-dried substance: C, 54·0; H, 4·0; loss at 120°, 1·9. $C_{27}H_{28}O_{11}(C_7H_4O_4N)_4,H_2O$ requires C, 54·5; H, 3·8, loss H_2O, 1·5. Found in anhydrous substance: C, 55·3; H, 3·7; N, 4·8. $C_{27}H_{28}O_{11}(C_7H_4O_4N)_4$ requires C, 55·3; H, 3·7; N, 4·7%]; $[\alpha]_D^{30^\circ}$ of anhydrous substance, − 44·30° in pyridine (*c* 2·891).

O-*Methylbutrin.* This was prepared from butrin (6 g.), dissolved in 5% potassium hydroxide (40 c.c.), by gradually adding methyl sulphate (80 g.) and potassium hydroxide (30%) below 40°; it was obtained as a deep yellow, brittle mass (6·4 g.), m. p. 82—84°, on complete evaporation of the usual organic solvents, but could not be obtained crystalline.

Ethylation of Butrin with Ethyl Iodide.—A suspension of butrin (4 g.) and finely powdered anhydrous sodium carbonate (10 g.) in a mixture of ethyl alcohol (200 c.c.) and ethyl iodide (9 g.) was heated under reflux on the water-bath for 13 hours; more ethyl iodide (13 g.) and sodium carbonate (8 g.) were added, and the mixture refluxed for another 13 hours. The boiling mixture was filtered, and the dry residue twice extracted with alcohol; it was then quite white, and on treatment with cold water left a white crystalline residue which was filtered off and washed free from sodium salts. O-*Diethylbutrin* was obtained as tiny white needles (1·9 g.), m. p. 238°, on recrystallisation from boiling water [Found in sample dried at 120°: C, 56·0, 56·1; H, 6·1, 6·1; OEt, 13·8, 14·1, 14·0. $C_{27}H_{30}O_{13}(OEt)_2,\frac{1}{2}H_2O$ requires C, 56·3; H, 6·2. $C_{27}H_{30}O_{13}(OEt)_2$ requires C, 57·05; H, 6·1; OEt, 13·8. Found, in air-dried sample: loss at 120°, 16·4. $C_{27}H_{30}O_{13}(OEt)_2,7\frac{1}{2}H_2O$ requires $7H_2O$, 16·0%]. On boiling with alcohol it becomes light yellow (m. p. 236°). It is insoluble in benzene, chloroform, ethyl acetate, acetone, ethyl and methyl alcohol. *O*-Diethylbutrin very slowly dissolves in alkali hydroxide but is insoluble in alkali carbonate solutions. On reduction with magnesium and methyl-alcoholic hydrochloric acid it gives a reddish-violet coloration.

The hot, yellow, alcoholic extracts on cooling after concentration deposited deep yellow crystalline nodules which melted completely at 166° although droplets appeared at 142° (yield 2·2 g.). These were boiled with alcohol and the small quantity of white substance, m. p. 232°, remaining undissolved was identified as *O*-diethylbutrin. The alcoholic filtrate on concentration deposited bright yellow crystals, m. p. 154—160°, raised by two crystallisations from slightly diluted alcohol to 183°. It is soluble in alkali hydroxides to a yellow solution, and slightly soluble in alkali carbonate. It is the *chalkone* derivative isomeric with white *O*-diethylbutrin [Found, in sample dried at 140°: C, 55·2, 55·4; H, 6·0, 6·1. $C_{27}H_{30}O_{13}(OEt)_2,H_2O$ requires C, 55·4; H, 6·3. Found, in air-dried sample: loss at 125°, 8·3. $C_{31}H_{40}O_{15},4\frac{1}{2}H_2O$ requires $3\frac{1}{2}H_2O$, 8·6%].

Methylation of Butrin with Methyl Iodide.—A suspension of butrin (4 g.) and anhydrous potassium carbonate (4 g.) in methyl alcohol (200 c.c.) and methyl iodide (13 g.) was heated under reflux on the steam-bath for 13 hours; more methyl iodide (5 g.) and potassium carbonate (4 g.) were then added and the mixture was refluxed for another 10 hours. The hot mixture was filtered, and the residue washed with methyl alcohol. The dry residue was freed from potassium salts by treatment with 70 c.c. of distilled water, and recrystallised from boiling water in tiny white needles, m. p. 224° (3·4 g.) (Found: C, 45·8, 45·9; H, 6·8, 6·8; loss at 140°, 17·9. $C_{29}H_{36}O_{15},7\frac{1}{2}H_2O$ requires C, 45·9; H, 6·7; loss, 17·8%. Found, in a sample dried at 140°: C, 54·9, 54·8; H, 5·9, 5·8; CH_3O, 9·9, 10·2. $C_{29}H_{36}O_{15},\frac{1}{2}H_2O$ requires C, 55·0; H, 5·8; CH_3O, 9·8%).

O-*Dimethylbutrin* is insoluble in benzene, chloroform, carbon tetrachloride, acetone, ether, and light petroleum, slightly soluble in boiling ethyl and methyl alcohol and in cold water but readily in boiling water, and extremely soluble in pyridine. It gradually dissolves in alkali hydroxides to bright yellow solutions, but is insoluble in alkali carbonate solutions. It gives a reddish-violet coloration with magnesium and methyl-alcoholic hydrochloric acid and is a flavanone derivative.

Action of Hydrogen Peroxide on Butrin.—To an ice-cooled mixture of butrin (2·2 g.) in methyl alcohol (100 c.c.), 4% hydrogen peroxide (80 c.c.) and 16% potassium hydroxide (20 c.c.) were added under ice cooling. When kept at 0—5° for 24 hours, the orange-red solution turned bright yellow, and bright yellow nodules separated. The solution on treatment with excess of carbon dioxide, concentration at ordinary temperature to 20 c.c., and extraction with acetone and methyl alcohol in succession gave no crystalline substance, but on hydrolysis with dilute mineral acid and concentration it deposited tiny pale yellow needles, giving a green coloration with neutral ferric chloride. On recrystallisation, these had m. p. 360° and were identified as fisetin (Found, in sample dried at 130°: C, 62·8; H, 3·8. Calc. for $C_{15}H_{10}O_6$: C, 62·9; H, 3·5%).

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