224. *The Constitution of Tannins. Part II. Structure and the Synthesis of Bis-(5 : 7 : 3' : 4'-tetrahydroxy)flavpinacol.*

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It has been shown (this vol., p. 218) that reduction of 2 : 4 : 3' : 4'-tetrahydroxychalkone with zinc dust and dilute alcoholic acetic acid produces an amorphous substance quali- tatively indistinguishable by its reactions from typical phlobatannins. The reduction

product must be either $4 : 7 : 3' : 4'$-tetrahydroxyflavan or the corresponding bis-$4 : 4''$-compound, and phlobatannins must be constituted in the same way.

Since catechin ($3 : 5 : 7 : 3' : 4'$-pentahydroxyflavan) and all similarly constituted compounds are crystalline, it is likely that the above amorphous reduction product (and similar reduction products of other 2-hydroxychalkones already described) is most correctly represented by the bis-$4 : 4''$-formula. It is known, moreover, that reduction of ketones with zinc dust and acetic acid commonly produces compounds of the bis-type; *e.g.*, benzophenone gives benzpinacol and xanthone gives dioxyxanthylene (Gurgenganz and von Kostanecki, *Ber.*, 1895, **28**, 2310).

Furthermore, benzylideneacetophenone (chalkone) by reduction in like manner produces a colourless crystalline compound, m. p. 197° (corr.), having the empirical formula $C_{15}H_{13}O$. The simple (unimolecular) reduction products of chalkone are diphenylallyl alcohol, m. p. 56—57° (Hiroschi Nomura, *Bull. Soc. chim.*, 1925, **37**, 1245), hydrochalkone, m. p. 72°, and hydrochalkol, b. p. 330° (Hübner and Herries, *Annalen*, 1897, **296**, 326; Pfeiffer, Kalckbrenner, Kunze, and Levin, *J. pr. Chem.*, 1928, **119**, 109). Molecular-weight determinations for the reduction product of chalkone give the values 446, 448, and 452 ($C_{30}H_{26}O_2$ requires M, 418); it is therefore also a polymeride of the bis-type. A number of reactions of this bis-reduction product of chalkone have been examined briefly (see Experimental). Similar high-melting reduction products of $2 : 3 : 4 : 4'$-tetramethoxychalkone and of $4'$-hydroxychalkone (this vol., p. 218) must similarly be of the bis-type.

It is likely, then, that reduction of 2-hydroxychalkones by the same method also causes polymerisation. Direct measurements of the hydrogen absorbed during reduction of 2-hydroxychalkones with zinc dust and dilute alcoholic acetic acid are in complete accord with this view; it is clear that one molecule of chalkone absorbs two equivalents of hydrogen on reduction to flavan, whilst for the pinacol structure only one equivalent of hydrogen is needed.

To measure the hydrogen absorbed during the reduction of chalkones, a procedure similar to that employed in the valuation of zinc dust was adopted. In every case the amount of hydrogen absorbed corresponded to the amount required for the production of the bis-type of compound. It may now be concluded that the reduction products of 2-hydroxychalkones are the bis-$4 : 4''$-compounds derived from the flavan corresponding to the chalkone; there is no immediate reason for supposing polymerisation by other than a $4 : 4''$-bond. Since the reduction products of $2 : 4 : 3' : 4'$-tetrahydroxychalkone (this vol., p. 218) and of $2 : 4 : 6 : 3' : 4'$-*pentahydroxychalkone* (presently described) are qualitatively indistinguishable by their reactions from typical phlobatannins, these must be constituted in the same way.

Phlobatannins are, then, polyhydroxy phenolic derivatives of a parent substance, flavpinacol (V; R, R' = H). The system of numbering used to designate the positions of the hydroxyl groups in the flavan is retained. Thus, the reduction product of $2 : 4 : 3' : 4'$-tetrahydroxychalkone (formerly $4 : 7 : 3' : 4'$-tetrahydroxyflavan) becomes bis-($7 : 3' : 4'$-trihydroxy)flavpinacol (V; R = OH, R' = H) and the phlobatannin presently described is *bis-($5 : 7 : 3' : 4'$-tetrahydroxy)flavpinacol* (V; R, R' = OH).

The following natural phlobatannins all give green colours with ferric salts and, by fission with fused alkali, phloroglucinol and protocatechuic acid (or catechol by decarboxylation of this acid) as decomposition products. The number of individuals may not be so great as the list indicates: Barbitamao, callutannic acid, canaigre, cherry, Kola, filitannic acid, fraxitannic acid, hop, chestnut, larch, mangrove, oak bark, oenotannin, pinicortannic acid, quinotannic acid, rhatany, rhodotannic acid, sorbitannic acid, fragarianin, tannecortepinic acid, tormentilla, willow, and spruce.

Bis-($5 : 7 : 3' : 4'$-tetrahydroxy)flavpinacol must possess the fundamental hydroxylated pattern of all these natural phlobatannins. Substitution of the hydrogen in the hydroxyl groups of the " phloroglucinol residue " might account for individual differences between the natural tannins without altering the fission products. Substitution of the hydrogen in the hydroxyl groups of the " catechol residue " is unlikely, as this would deprive the product of iron-greening properties. Various nuclear substituents such as carboxyl, formyl, methyl, etc., are similarly possible.

For the synthesis of bis-(5 : 7 : 3' : 4'-tetrahydroxy)flavpinacol, phloracetophenone tribenzoate (I) was condensed with protocatechualdehyde dibenzoate (II) to give 2 : 4 : 6 : 3' : 4'-pentabenzoyloxychalkone (III), which was hydrolysed to the corresponding 2 : 4 : 6 : 3' : 4'-pentahydroxychalkone (IV). This, by reduction in the usual way, gave bis-(5 : 7 : 3' : 4'-tetrahydroxy)flavpinacol (V; R, R' = OH).
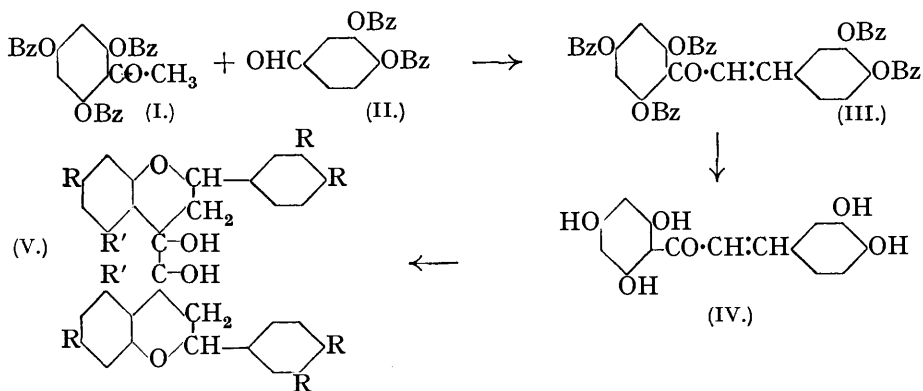
In the following table the qualitative reactions of the synthetic substance are compared with those of natural hemlock tannin; the tests, except the first one, were carried out in 0·5% aqueous solution, which was, in each case, light orange-yellow. For comparison, the tests with gallotannin are given in the fourth column.

Reagent.	Bis-(5 : 7 : 3' : 4'-tetra-hydroxy)flavpinacol.	Hemlock tannin.	Gallotannin.
Alcoholic FeCl₃	Dark blue-green colour	Dark green colour	Dark blue-black ppt.
Aqueous FeCl₃	Dark blue-green colour, changing to dark ppt.	Dark green colour, changing to dark ppt.	Dark blue-black ppt.
Gelatin	Ppt.	Ppt.	Ppt.
Lead acetate	Light-coloured ppt. sol. in acetic acid	Light-coloured ppt. sol. in acetic acid	Light-coloured ppt. sol. in acetic acid
Boiling 5% HCl (phlobaphene reaction)	Red ppt. in 10—15 mins.	Red ppt. in 10—15 mins.	Nil (no red colour; no ppt.)
Bromine water	Heavy orange-yellow ppt.	Heavy yellow ppt.	No ppt.
Calcium hydroxide	Faint pink colour	Faint pink colour	Nil
Sodium sulphite	Pink colour	Pink colour	Nil
Nitrous acid	Immediate red-brown ppt.	Immediate red-brown ppt.	Colour changes to red; no ppt.
Copper sulphate	Faint green colour	Faint green colour	Light-green ppt.
Copper sulphate + NH₃ aq.	Heavy dark ppt.	Heavy dark ppt.	Dark ppt.
Aqueous ammonia	Soln. darkens slowly	Soln. darkens slowly	Soln. darkens slowly
HCHO + HCl	Ppt. on warming	Ppt. on warming	No ppt.
Potass. dichromate	Dark red-brown ppt.	Dark brown ppt.	Brown ppt.
K₃Fe(CN)₆ + NH₃ aq.	Orange-red colour	Orange-red colour	Transient lilac colour, changing to dark ppt.

Solvent.	Solubilities.		
Water	Soluble; conc. solns. red; dil. solns. yellow	Soluble; conc. solns. red; dil. solns. yellow	
EtOH, MeOH, EtOAc, Me₂CO	Readily sol. to dark red solution	Readily sol. to dark red solution	
Et₂O, C₆H₆, ligroin, CHCl₃	Insol.	Insol.	
Sodium hydroxide	Readily sol., dark soln., bleached by acid	Readily sol., dark soln., bleached by acid	

In addition to the above tests, hide powder absorbed the product quantitatively from aqueous solution; and a piece of cleaned and scraped sheepskin immersed in a concentrated solution showed no sign of decomposition after 4 months and assumed the characteristics of leather. In control tests decomposition proceeded rapidly after a few days.

EXPERIMENTAL.

Reactions of the Chalkone Reduction Product, $C_{30}H_{26}O_2$.—(1) It decolorises permanganate and bromine water and is therefore unsaturated. Estimation of the unsaturation by the pyridine sulphate–bromine method (Rosenmund and Kuhnhenn, *Z. Unters. Nahr. Genussm.,* 1923, **46**, 154) indicates the formation of a dibromide, $C_{30}H_{26}O_2Br_2$.

(2) With boiling alcoholic potash it loses a molecule of water to give a substance crystallising in fine colourless needles, m. p. 112° (Found : C, 89·5; H, 6·0. $C_{30}H_{24}O$ requires C, 90·0; H, 6·0%).

(3) With boiling alcoholic sulphuric acid, by loss of water, two isomeric products result : (*a*) identical with the above, m. p. 112°; (*b*) m. p. 178°, stout needles (Found : C, 89·4; H, 6·0%). Both (*a*) and (*b*) are unsaturated and give dibromo-derivatives.

(4) With phosphorus and hydrogen iodide in boiling acetic acid, two products are obtained, m. p. 161° (Found : C, 89·1; H, 6·7. $C_{30}H_{26}O$ requires C, 89·5; H, 6·6%), and m. p. 189° (Found : C, 88·8; H, 6·9. $C_{30}H_{28}O$ requires C, 89·2; H, 6·9%).

(5) It gives no keto-derivatives.

Measurement of the Hydrogen absorbed during the Reduction of Chalkones.—A small flask (50 c.c.) was joined through a reflux condenser to the top of a gas burette, a suitable mass of the chalkone with an excess (at least ten times the mass of the chalkone) of zinc dust was weighed into it, and a known volume of alcoholic acetic acid (15%) added. An exactly similar control apparatus (no chalkone) was prepared, the internal volume of each being the same, and the two flasks were heated to boiling in the same bath of hot water. Hydrogen was evolved and heating was continued with occasional shaking until the difference between simultaneous burette readings became constant (1–1½ hours) and the characteristic chalkone colour had disappeared. After cooling, the difference in burette readings (corrected) represented the volume of hydrogen absorbed by the chalkone in reduction. The results are tabulated below : the amounts of zinc dust and acetic acid were varied slightly in different cases, but were always the same for experiment and corresponding control. The conditions were made as nearly as possible comparable with the qualitative experiments, although it was not possible to arrange for the portionwise addition of the zinc dust (this would lengthen the time necessary for the reduction).

Chalkone.	Wt., g.	H absorbed, c.c.	H required, c.c. Flavan.	Pinacol.
2-Hydroxy-3 : 4-dimethoxy	0·2234	10·35	17·8	8·9
,, ,,	0·2180	11·1	17·2	8·6
,, ,,	0·2009	7·3	16·0	8·0
,, ,,	0·3577	14·2	28·2	14·1
2-Hydroxy-3 : 4 : 4′-trimethoxy	0·2396	9·2	17·2	8·6
,, ,,	0·2012	8·1	14·2	7·1
2-Hydroxy-3 : 4 : 3′ : 4′-tetramethoxy	0·1437	4·8	9·6	4·8
2-Hydroxy-3 : 4-dimethoxy-3′ : 4′-methylenedioxy	0·0914	2·8	6·2	3·1
2 : 4-Dihydroxy-4′-methoxy	0·0530	2·1	4·4	2·2
2 : 4 : 4′-Trihydroxy	0·1046	4·4	9·2	4·6
,, ,,	0·2074	7·8	18·1	9·1
2 : 4 : 3′ : 4′-Tetrahydroxy	0·1548	5·3	12·8	6·4
2-Hydroxy-3 : 4-dimethoxy	0·2054	9·3	16·4	8·2
2 : 4 : 6 : 3′ : 4′-Pentahydroxy	0·3040	9·7	22·4	11·2

Owing to the strongly acidic character of 2 : 4 : 3′ : 4′-tetrahydroxy- and 2 : 4 : 6 : 3′ : 4′-pentahydroxy-chalkone, in order to obtain intelligible results on reduction in a closed system, it was necessary to replace the acetic acid used normally by 0·6% alcoholic hydrogen chloride. That this change produces no change in the reduction product was shown by qualitative experiments and by measurements on 2-hydroxy-3 : 4-dimethoxychalkone with the same acid. The values obtained are the last three in the table.

2 : 4 : 6 : 3′ : 4′-Pentahydroxychalkone.—A solution of phloracetophenone tribenzoate (9·6 g.; 1 mol.) and protocatechualdehyde dibenzoate (8·0 g.; slight excess over 1 mol.) in dry ethyl acetate saturated at 0° with anhydrous hydrogen chloride became yellow, orange and finally clear light red. It was protected from moisture and kept at 0° for 12 hours and the solvent was then evaporated on the water-bath. The residual transparent reddish-brown syrup was boiled with 150 c.c. of alcohol for removal of initial materials, the alcohol decanted when cold, and the residue washed with cold alcohol. *2 : 4 : 6 : 3′ : 4′-Pentabenzoyloxychalkone* separated from much alcohol in pale yellow nodules (Found : C, 72·9; H, 4·3. $C_{50}H_{32}O_{11}$ requires C, 74·2; H, 4·0%. $C_{50}H_{32}O_{11}$,EtOH requires C, 73·0; H, 4·45%).

A boiling solution of 2 : 4 : 6 : 3′ : 4′-pentabenzoyloxychalkone (11·5 g.) in alcohol (350 c.c.) was treated, in a nitrogen atmosphere, with aqueous potassium hydroxide (9 g., 11 mols., in 350 c.c.) dropwise during 4 hours, alcohol distilling at an equal rate. The product was cooled, acidified, and (now removed from the nitrogen atmosphere) treated with sodium chloride and extracted with ethyl acetate. The dark red extract was dried (sodium sulphate) and evaporated; the residue was extracted with benzene (Soxhlet) until all the benzoic acid had been removed and then with acetone. On removal of the acetone 2 : 4 : 6 : 3′ : 4′-*pentahydroxychalkone* was obtained, which crystallised from dilute alcohol in orange-brown microscopic prisms, m. p. 245° after sintering at 215°. For analysis the chalkone was dried over sodium hydroxide for 2 hours at 100°/15 mm. (Found : C, 63·0; H, 4·3. $C_{15}H_{12}O_6$ requires C, 62·5; H, 4·2%).

Bis-(5 : 7 : 3′ : 4′-*tetrahydroxy*)*flavpinacol*.—To a boiling solution of 2 : 4 : 6 : 3′ : 4′-pentahydroxychalkone (1·5 g.) in alcohol (30 c.c.), glacial acetic acid (7 c.c.) and zinc dust (5 g.) were added portionwise during 15 minutes. The solution, which changed from opaque red-brown to transparent pale orange-brown, was filtered, cooled rapidly, diluted with water (300 c.c.), saturated with sodium chloride, treated with bicarbonate, and extracted with ethyl acetate. The dark brown extract was dried (sodium sulphate) and evaporated to dryness in a vacuum The orange-red vitreous residue powdered to a light red, amorphous solid. For analysis, it was dried over sodium hydroxide for $2\frac{1}{2}$ hours at 100°/15 mm. (Found : C, 62·3; H, 4·65. $C_{30}H_{26}O_{12}$ requires C, 62·2; H, 4·5%).