

Condensed Proanthocyanidins from Cranberries and Cola Nuts

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CONDENSED proanthocyanidins are members of a widespread group of natural products which occur mainly in fruits and which on treatment with acid yield one molecule of an anthocyanidin and a second of another flavonoid; in all the condensed proanthocyanidins examined so far, the second flavonoid has belonged to the catechin group. The bond between the two units may be of the nature of an ether^{1,2} or a ketal¹⁻⁴ or may be a labile C-C bond.^{5,6} Recently, crystalline derivatives of two condensed proanthocyanidins have been obtained, and thus the foundation has been laid for a precise study of this class of compounds.

The crystalline heptamethyl ether of the diacetyl derivative of a condensed proanthocyanidin isolated from cranberries (*Vaccinium vitis-idaea*) had m.p. 189–190° and was found by mass spectroscopy to have a molecular weight of 758.*

The free product contains 7 phenolic and 2 aliphatic hydroxyl groups, 3 ether oxygen atoms, and one olefinic double bond. The corresponding nona-acetate* was also obtained crystalline. If an ether oxygen is allocated to each of two pyran rings, the remaining ether oxygen can be assigned to the bond linking the two flavonoid units. One half of the molecule affords a product which exhibits the chromatographic behaviour of cyanidin. The n.m.r. spectrum of the acetylated heptamethyl ether, like that of 3-O-acetyl-5,7,3',4'-tetra-O-methylcatechin, has a signal at τ 7.3 p.p.m. (relative to tetramethylsilane as internal standard) indicating a single methylene group. This suggests that one half of the molecule consists of a catechin residue. The product may be a diphenyl ether.

Another condensed proanthocyanidin was

* These compounds gave satisfactory analyses.

¹ K. Freudenberg and K. Weinges, *Tetrahedron Letters*, 1961, 267.

² K. Weinges, *Chem. Ber.*, 1961, **94**, 3032.

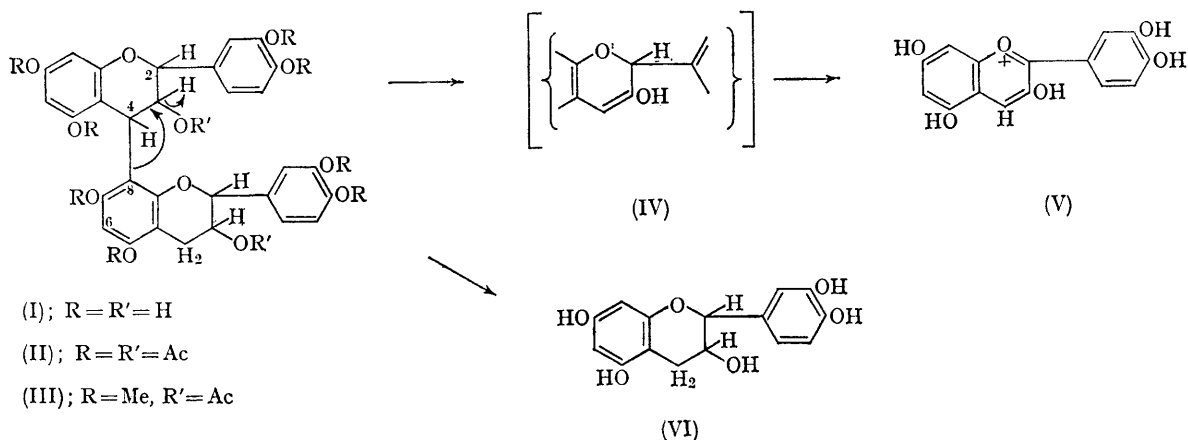
³ K. Freudenberg and K. Weinges, *Angew. Chem.*, 1962, **74**, 182; *Angew. Chem. Internat. Edn.*, 1962, **1**, 158.

⁴ K. Freudenberg and K. Weinges, "The Chemistry of Flavonoid Compounds," ed. T. A. Geissman, Pergamon Press, 1962, p. 197.

⁵ K. Freudenberg, "Summary of Lectures, 6th Congr. Internationale Union der Gerbereichemiker-Verbände," Munich, 1959.

⁶ K. Freudenberg, *J. Indian Leather Technol. Assoc.*, 1960, **8**, 186.

isolated from cola nuts, the fruit of *Cola acuminata*; to it we have ascribed the formula (I). The formula $C_{30}H_{26}O_{12}$ can be calculated for the free proanthocyanidin from the compositions of its crystalline derivatives (II)* and (III)* [*i.e.* $2(C_{15}H_{14}O_6 - 2H)$]. Being a *C*-substituted phloroglucinol, it decomposes on treatment with acid into catechin (VI) and the leuco-form of cyanidin (IV), which then undergoes oxidation in the presence of the acid to yield cyanidin (V).



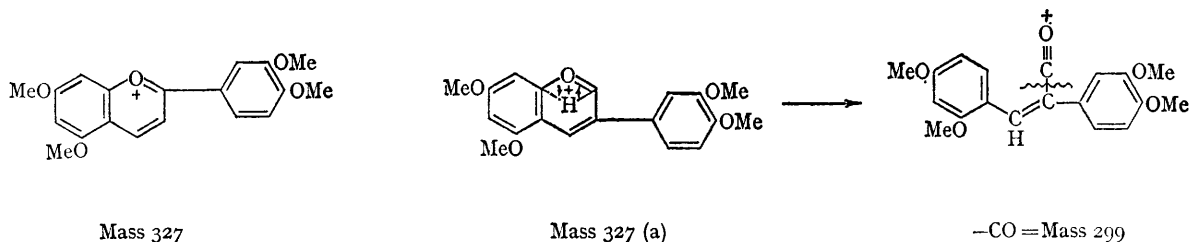
In certain cases, the bond between phloroglucinol (or a phloroglucinol derivative) and its *C*-substituent can be cleaved by acids, *e.g.* in phlobaphenes,^{7,8} in dicatechin,⁹ in catechin,¹⁰ and in R. Boehm's¹¹ 2,4,6,2',4',6'-hexahydroxydiphenylmethane.¹⁰

The infrared spectra of (II) and (III) show practically no absorption due to free hydroxyl groups; the proanthocyanidin contains 8 phenolic and 2 aliphatic hydroxyl groups and 2 ether oxygen atoms. Its cleavage with acid to give cyanidin (V) and catechin (VI), which were detected by chromatography, makes structure (I)

for the proanthocyanidin likely. However, the bond between the two halves of the molecule need not necessarily be between C-8 and C-4; an analogous linkage between C-8 and C-2, C-6 and C-4, or C-6 and C-2 is also possible. This type of bonding is also assumed to occur in the condensates obtained from flavandiols with acids.^{7,8}

The mass spectrum of (III), m.p. 173—174°*, contains a parent peak at mass 774 plus signals at mass numbers 714, 654, 503, 492, 327, 299, 165, and

151, characteristic of fragments of (III). The peaks at mass 714 and 654 indicate that 2 moles of acetic acid are split off readily from (III). This elimination can proceed towards both C-4 and C-2. The polymethoxydiflavene cations of mass 654 so formed can undergo further fragmentation to give a dimethoxybenzyl cation of mass 151 or the corresponding tropylium cation plus a dimethoxyphenylacetylene radical of mass 162; this follows from comparison of the spectrum with those of 3-*O*-acetyl-5,7,3',5'-tetra-*O*-methylcatechin and 5,7,3',4'-tetramethoxy-2-flavene. The fragments with 503 mass units (654—151) and 492 mass units



⁷ K. Freudenberg, *Experientia*, 1960, **16**, 101.

⁸ K. Freudenberg and K. Weinges, *Chem. and Ind.*, 1959, 486.

⁹ K. Freudenberg and K. Weinges, *Annalen*, 1963, **668**, 94.

¹⁰ K. Weinges, unpublished work.

¹¹ R. Boehm, *Annalen*, 1903, **329**, 269.

(654—162) are broken down further with liberation of the fragments of masses 176 and 165 to the fragment with 327 mass units. It is immaterial whether it is the upper or lower half of the molecule (III) which decomposes during fragmentation. The fragment of mass 327 must undergo partial or complete phenyl migration during its decomposition to give the isomeric cation 327 (a), which can then lose the carbonyl group, as indicated, to form

the fragment of mass 299. The mass spectrum is thus consistent with the structure (I) or one of its variants mentioned.

The formation of these condensed proanthocyanidins can be explained by dehydrogenation of catechins or epicatechins, irrespective of whether the subunits are linked through an ether oxygen or by C-C condensations as in (I).

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