Tetrahedron Letters No.19, pp. 1767-1771, 1967. Pergamon Press Ltd. Printed in Great Britain.

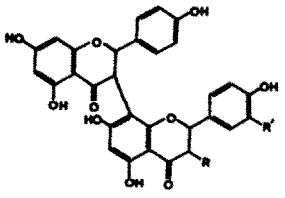
ON THE QUESTION OF THE STRUCTURES OF GB1, GB1a and GB2, A NEW GROUP OF BISFLAVONOIDS.

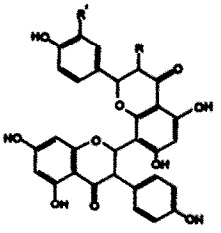
Andrew Pelter,

Department of Chemistry, University of Manchester, Manchester 13.

(Received 2 March 1967)

The compounds GB1, GB1a and GB2, phenolic extractives from the heartwood of Garcinia buchananii, have been represented by the structures Ia, Ib and Ic respectively.[1] These formulae are of particular interest inasmuch as the two flavonoid units are linked from C_3 of one unit to a position on the phloroglucinol ring of another such unit. This represents a new mode of linkage for a condensed, reduced flavonoid, the previous proven modes involving C_4 of the flavonoid.[2,3,4]





I(a), R = OH, R' = H

(b), R = H, R' = H

(c), R = H, R' = OH

II(a), R = OH, R' = H

(b), R = H, R' = H

(c), R = H, R' = OH

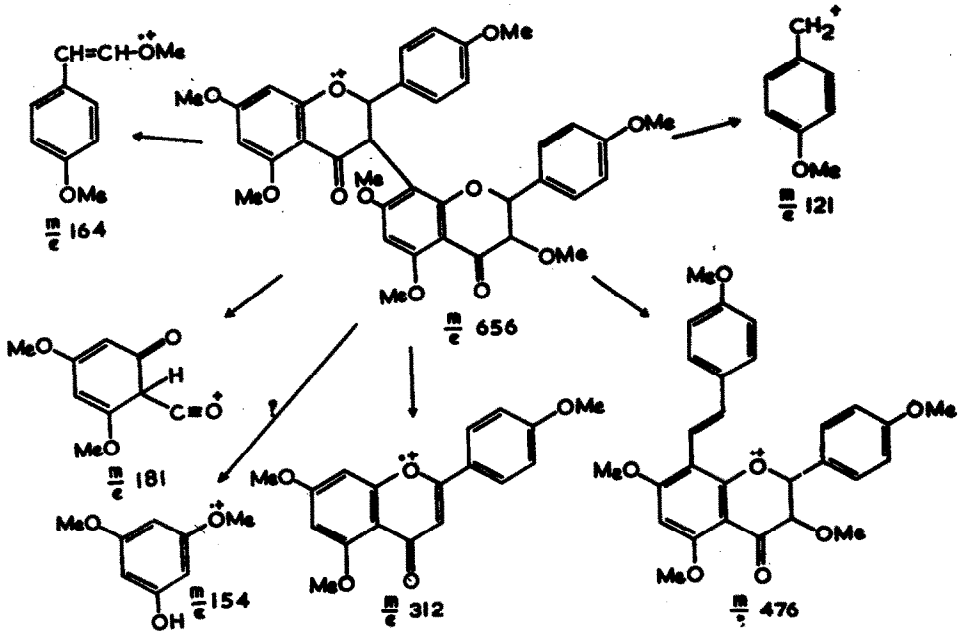
The evidence in favour of I(a) for GB1, from which the formulae of the other two compounds follow, may be summarised as follows:-

(i) GB1 (and GB1a) are degraded by base to yield phloroglucinol and p-hydroxybenzoic acid.

(ii) The wave lengths of the peaks in the U.V.spectrum are consistent with a naringenin chromophore.

(iii) The mass spectrum of GB1 heptamethyl ether may be interpreted as in the Figure.

FIGURE.



The production of the ion at $\frac{m}{e}$ 312 is in line with the breakdown of xanthorrhone and hydroxyxanthorrhone,[4] whilst most of the other ions are explained by the reverse Diels-Alder reactions characteristic of flavanones.[5,6] The production of dimethylphloroglucinol is odd, as simple analogous flavanones do not show this ion, and although it is produced by xanthorrhone and hydroxyxanthorrhone, the only other bisflavonoids combining a flavanone system, a special explanation had to be put forward[4] which is not applicable here. The ion at $\frac{m}{e}$ 121 is rather large, but there are analogies in the literature.[5]

(iv) The 100 Mc. N.M.R. spectrum shows the expected number of aromatic protons, in particular only three hydrogen atoms between two oxygen atoms on a benzene ring being evidenced. The aliphatic protons show as a diffuse doublet at τ4.38($J \sim$ 10c) (1H) coupled to a doublet at τ5.4(1H), both protons being assigned to ring F. A further doublet at

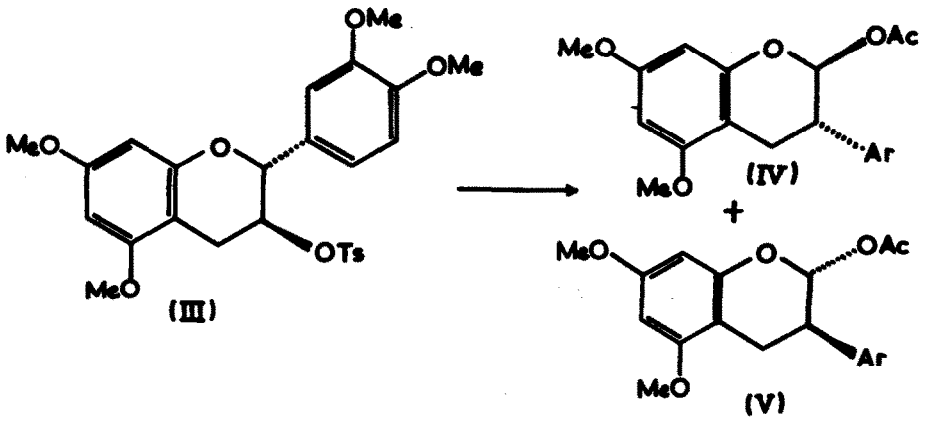
τ5.0(1H) is coupled to a proton, obscured by the methoxyl groups at τ6.2, these being attributed to ring C.

All this evidence is consistent with structure Ia, and from this Ib and Ic follow.

From the general viewpoint of the structure of condensed tannins any new linkage between two reduced flavonoid units is of the utmost importance, as once verified analogies may be built up for more complex products. It is therefore necessary to point out that structures IIa, IIb and IIc are completely consistent with the published evidence for GB1, GB1a and GB2 respectively, and may even be preferred to the structures put forward in the original papers.

Thus the chemical degradations would proceed equally well for compounds of the structures II(a-c), this including the oxidation of GB1a with iodine and sodium acetate[7] to give a bisflavone type compound. Again the N.M.R.spectra would not be able to distinguish the two types of compound, in each case ring C being substituted at C_2 and C_3 by an aromatic ring. In the mass spectrum of GB1 heptamethyl ether, all the ions would be produced by the same processes and would have the same structures with the exception of the ion at $\frac{m}{e}$ 312, which would have an isoflavone type structure, instead of a flavone type, these being indistinguishable in the mass spectrometer.

The production of the structures II(a-c), presumably from naringenin would involve an aryl shift during the dimerisation and it is worthwhile to consider the possibility of such an occurrence. In 1961, Mayer and Merger[8] envisaged the condensation of two catechin units with each other to proceed with a Wagner-Meerwein shift. This result however was disputed by Freudenberg and Weinges[9], who suggested a condensation at C_2 followed by ring closure to a dihydrofuran derivative, and proceeding without rearrangement. The rearrangement, under varying conditions of derivatives of trans-flavan-2-ol has been observed. Whalley and Mehta[10] have remarked that the rearrangement of (+)-catechin tetramethyl ether by the reaction of phosphorus pentachloride may be the first example of a 1,2-shift involving neighbouring group participation and retaining optical activity. Their own studies showed that acetolysis of (III) gave a mixture of (IV) and (V). This would indicate that rearrangement was not synchronous with the attack of acetate anion, the intermediate being stabilised by participation of the lone pair on the heterocyclic oxygen atom.



The biogenesis of GB1, GB1a and GB2 may involve a nucleophilic attack by the phloroglucinol ring of naringenin upon a derivative, such as a pyrophosphate, of a flavanonol. As the aryl and hydroxyl groups of such compounds are trans,[11] it is clear that this reaction could well go with rearrangement, such a course being favoured also by the bulky nature of the incoming group which could attach itself to the less hindered C_2 position. Whalley and Mehta[10] have studied the acetolysis of (±)-taxifolin and have only been able to characterise a small yield of luteolin, most of the reaction going through unknown side reactions. In this case no rearrangement products were characterised.

A further possibility for the biogenesis of GB1, GB1a and GB2 is the oxidative formation of a radical at C_3 of naringenin, followed by radical coupling with another molecule of naringenin. Cavill et al[12] have studied the reaction of flavanones with lead tetraacetate and state that the results are best explained by a rearrangement of the radical produced at C_3 to yield the isoflavones isolated.

Thus with either mode of biosynthesis a rearrangement is possible, and it is proposed that the question of whether GB1, GB1a and GB2 are represented by I(a-c) or II(a-c) be held to be sub judice, until further evidence is presented. In particular the proposed linkage from C_3 of a flavonoid to another such unit may not be taken as proven, a C_2 linkage being at least as possible.

The only spectroscopic evidence that may have any bearing on the matter is the ion at $\frac{m}{e}$ 121 in the mass spectrum of GB1 heptamethyl ether. If this is assumed to arise from C_2 of a flavanone, then its presence or absence in GB2 heptamethyl ether might be indicative of the structure. However in view of the unexplained presence of the ion due to dimethylphloroglucinol, great caution must be exercised in the interpretation of spectra in this unexplored field and a decision must await the classical trial of synthesis.

REFERENCES.

1. B.Jackson, H.D.Locksley and F.Scheinmann, Tetrahedron Letters, 787 (1967)
2. S.E.Drewes, D.G.Roux, J.Feeney and S.H.Eggers, Chem.Comm., 368, (1966).
3. S.E.Drewes, D.G.Roux, H.M.Saayman, J.Feeney and S.H.Eggers, Chem.Comm., 370 (1966).
4. A.J.Birch, C.J.Dahl and A.Pelter, Tetrahedron Letters, 481 (1967).
5. A.Pelter, P.Stainton and M.Barber, J.Heterocyclic Chem., 2, 262 (1965).
6. C.S.Barnes and J.L.Occolowtiz, Australian J.Chem., 17, 975 (1964).
7. R.N.Goel, V.B.Mahesh and T.R.Seshadri, Proc.Ind.Acad.Sci., 47A, 184 (1958).
8. W.Mayer and F.Merger, Ann, 644, 70, 79 (1961).
9. K.Weinges and K.Freudenberg, Ann, 668, 92 (1963).
10. P.P.Mehta and W.B.Whalley, J.Chem.Soc., 5327 (1963).
11. F.M.Dean, "Naturally Occurring Oxygen Ring Compounds", (Butterworths), p.350.
12. G.W.K.Cavill, F.M.Dean, A.McGookin, B.M.Marshall and A.Robertson, J.Chem.Soc., 4573 (1954)