## 376. *Constituents of* Filix Mas. *Part III.* Albaspidin.*

By A. McGookin, Alexander Robertson, and T. H. Simpson.

The structure (II) for flavaspidic acid is substantiated by disproportionation to give albaspidin (III) and by synthesis.

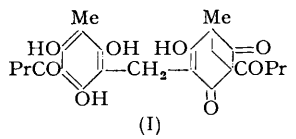
For flavaspidic acid, a constituent of male-fern extract, Boehm (*Annalen*, 1901, **318**, 230) preferred the structure (I) based on the empirical formula $C_{24}H_{28}O_8$ rather than (II) $C_{24}H_{30}O_8$ because on hydrolytic fission with alkalis and zinc dust the compound gave rise to *C*-trimethylphloroglucinol in addition to the fission products expected on the basis of structure (II), *viz.*, *C*-methyl- and *CC*-dimethyl-phloroglucinol, filicinic acid (V; R = H), and *n*-butyric acid. In a re-examination of flavaspidic acid the analytical results obtained, as well as those of Boehm (*loc. cit.*), were found to be in closer agreement with the empirical formula $C_{24}H_{30}O_8$ than with $C_{24}H_{28}O_8$ and, further, with hot aqueous sodium carbonate in the absence of a reducing agent (*e.g.*, zinc) flavaspidic acid readily disproportionated to give albaspidin (III), identical with synthetical material; thus, as in formula (II), the compound contains the normal filicinic acid residue (V; R = H). The second expected symmetrical disproportionation product, 5 : 5′-di-*n*-butyryl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (*J.*, 1951, 3028) was not isolated, probably because the 2 : 4 : 6-trihydroxy-3-methyl-*n*-butyrophenone residue is, as Boehm (*loc. cit.*) observed, much less resistant to fission in alkaline media than butanofilicinic acid. From our studies on the nature of the polyhydroxydiphenylmethane disproportionation reaction (*J.*, 1951, 2021) it appeared clear to us that the production of *CCC*-trimethylphloroglucinol from a compound having structure (II) depended on the mechanism already proposed by Birch (*J.*, 1951, 3028) † and hence that in all probability flavaspidic acid was represented by (II).

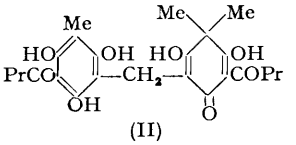
The synthesis of flavaspidic acid from butanofilicinic acid (V; R = Pr·CO) and 2 : 4 : 6-trihydroxy-3-methyl-*n*-butyrophenone (IV) by the method employed for 5 : 5′-di-*n*-

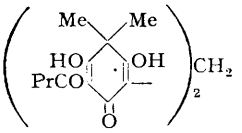
* Part II, *J.*, 1933, 1617.

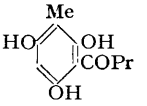
† The work summarised in this paper and in the earlier memoir (*J.*, 1951, 2021), together with the derivation of structure (II) for flavaspidic acid, were described in a thesis presented in July, 1950, by Dr. T. H. Simpson for the degree of Ph.D. of this University. A.R.

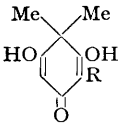
butyryl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (*loc. cit.*) now confirms the structure (II). Although the intermediate butanofilicinic acid has not yet


(I)


(II)


(III)


(IV)


(V)

been synthesised the structure of this compound has been substantiated by its hydrolysis (Boehm, *loc. cit.*) to *n*-butyric acid and filicinic acid (V; R = H), the synthesis of which was described in Part II (*J.*, 1933, 1617).

## Experimental

*Flavaspidic Acid.*—(*a*) The tedious method for the isolation of flavaspidic acid described by Boehm (*Arch. exp. Path. Pharm.*, 1897, **38**, 33) was found unsuitable for large-scale work and the following was adopted. A solution of male-fern extract (1250 g.) in acetone (750 ml). was added dropwise in 3 hr. to well-stirred water (10 l.) containing magnesium oxide (3 kg.), and the mixture agitated for 10 hr. Acidification of the filtered aqueous liquor and the washings from the magnesium salts (10 l. × 3) with dilute hydrochloric acid gave a yellow granular precipitate which was powdered and dried in a vacuum ($P_2O_5$) (yield, 88 g.). On slow evaporation (14 days) a solution of this solid (20 g.) in ether deposited flavaspidic acid which, on recrystallisation from methanol, formed bright yellow prisms, m. p. 157—158°, with a deep red ferric reaction in alcohol; occasionally the form of m. p. 92° was obtained (Found : C, 64·5, 64·5; H, 7·0, 6·8. Calc. for $C_{24}H_{30}O_8$ : C, 64·5; H, 7·0%. Calc. for $C_{24}H_{28}O_8$ : C, 64·8; H, 6·4%). Butanofilicinic acid was prepared from flavaspidic acid by Boehm's method (*loc. cit.*) and had m. p. 95° and a red-brown ferric reaction in alcohol (Found : C, 64·1; H, 7·4. Calc. for $C_{12}H_{16}O_4$ : C, 64·3; H, 7·2%). With diazoaminobenzene it gave the monoazo-derivative, forming orange yellow prisms, m. p. 137°, from methanol (Boehm, *loc. cit.*).

With warm alcoholic diazoaminobenzene flavaspidic acid gave the azo-derivative of 2 : 4 : 6-trihydroxy-3-methyl-*n*-butyrophenone, m. p. 181—182°, identical with a specimen from the synthetic ketone (Part I, *J.*, 1933, 819) (cf. Boehm, *loc. cit.*) (Found : C, 65·2; H, 5·8; N, 8·8. Calc. for $C_{17}H_{18}O_4N_2$ : C, 65·0; H, 5·8; N, 8·9%). Attempts to isolate the azo-derivative of butanofilicinic acid from the reaction mixture were unsuccessful.

A solution of flavaspidic acid (2 g.) in 2N-sodium carbonate (30 ml.) was heated on the steam-bath for ½ hour, cooled, and acidified with dilute hydrochloric acid. Trituration of the flocculent product with methanol (10 ml. × 2) left a colourless residue (0·12 g.), m. p. 138—140°, of albaspidin which on crystallisation from methanol had m. p. 148°, identical with a specimen prepared by the interaction of butanofilicinic acid (0·43 g.), 40% aqueous formaldehyde, and sulphuric acid (1 ml.) in alcohol (10 ml.) at room temperature.

(*b*) A mixture of 2 : 4 : 6-trihydroxy-3-methyl-*n*-butyrophenone (0·5 g.), butanofilicinic acid (2 g.), paraformaldehyde (2 g.), methanol (15 ml.), and sulphuric acid (1 ml.) was agitated at room temperature for 3 days. After the addition of water, the solid was collected, washed, and extracted with hot methanol, leaving slightly impure albaspidin. On being diluted with water (2 ml.) the methanolic extract slowly deposited flavaspidic acid (0·2 g.), m. p. 157—158°, after purification from a little methanol, the properties and reactions of which were identical with those of the natural compound (Found : C, 64·7; H, 6·8%).

University of Liverpool. [*Received, March 5th*, 1953.]