

## The Structure of Phloraspin

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Phloraspin (I) has been shown to be a phloroglucinol methylene compound combined of methylphlorobutyrophenone and phlorobutyrophenone-4-methyl ether.

In addition to the known phloroglucinol derivatives from *Dryopteris* fern species, listed in our earlier report<sup>1</sup>, we have now investigated the substance called phloraspin. It was first isolated by Kraft<sup>2</sup>, who called the compound flavaspidinin, m.p. 199°. In a later paper Kraft<sup>3</sup> supposed flavaspidinin to be identical with phloraspin, which had been isolated and described by Boehm<sup>4</sup> in 1903.

According to Boehm<sup>4</sup> phloraspin is a light yellow or nearly colourless substance, m.p. 211°, which is very slightly soluble in most organic solvents except in acetone and chloroform. Ferric chloride causes a red brown colour in ethanol solution. Treated with diazoaminobenzene phloraspin yields benzeneazomethylphlorobutyrophenone, m.p. 182°, which reaction Boehm offered in support of phloraspin being a methylene compound with methylphlorobutyrophenone as one member. The molecular data, C<sub>23</sub>H<sub>28</sub>O<sub>8</sub>, and the methoxyl content of phloraspin lead Boehm to assume that the other half of the phloraspin molecule is a monomethyl ether of phlorobutyrophenone. This assumption has now been confirmed by identifying the decomposition products of phloraspin whereby it was found that the phlorobutyrophenone monomethyl ether was the 4-methyl ether isomer. The structure of phloraspin is furthermore proved by synthesis. Thus, phloraspin is an exception to the other known *Dryopteris* phloroglucinols since butyrylfilicinic acid is not a part of its molecule.

Occasionally phloraspin has been isolated from *Dryopteris austriaca* (Jacq.) Woynar in amounts of about 0.002 % calculated on air dried rhizomes; phloraspin could not be found in every specimen of the same, in agreement with earlier reports<sup>4-6</sup>. In a pure state phloraspin has a melting point of 211–212°. It could be recrystallised from benzene and methanol as yellowish crystals.

The chromatographic behaviour of the phloroglucinol derivatives isolated from *Dryopteris* ferns has been studied by the authors<sup>7</sup>. This earlier study did not include phloraspin which can also be separated by the same method. On papers, buffered to pH 9.1–8.0 and impregnated with formamide, phloraspin

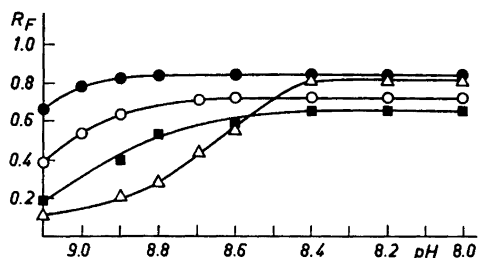


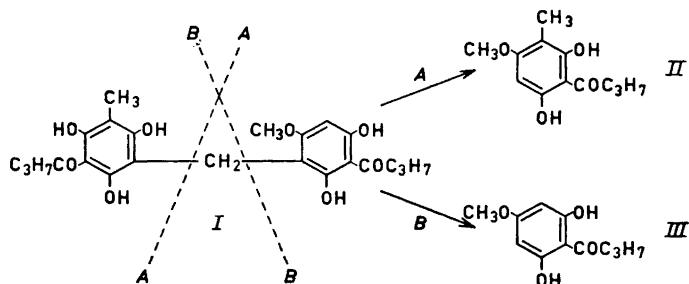
Fig. 1. Variation of the  $R_F$ -values with the pH of the papers. ● aspidinol, ○ florobutyrophenone-4-methyl ether, ■ florobutyrophenone-2-methyl ether, △ phloraspin.

has the  $R_F$ -values shown in Fig. 1. The chromatographing is performed with chloroform-benzene (1:1) solvent; the buffering of the papers is depending on the mixture to be separated <sup>7</sup>.

The alkaline cleavage <sup>8</sup> of phloraspin yielded aspidinol (II) and desaspidinol (= phlorobutyrophenone 4-methyl ether) (III), both identified by paper chromatographic separation <sup>7</sup>. The  $R_F$ -curves on papers buffered to pH 9.1–8.0 were identical with the  $R_F$ -curves obtained for authentic specimens of aspidinol, m.p. 142–143°, and desaspidinol, m.p. 127–128°\* (Fig. 1). The  $R_F$ -curve of phlorobutyrophenone 2-methyl ether distinctly differs from the  $R_F$ -curves obtained for the products which were formed by the alkaline cleavage of phloraspin.

These decomposition products can be explained by the phloraspin structure I: aspidinol and desaspidinol are obtained when the methylene bridge is broken along A—A and along B—B, respectively.

Phloraspin was synthesised by dissolving methylphlorobutyrophenone, m.p. 162–163°, and desaspidinol, m.p. 127–128° in dilute alkali and treating the solution with formaldehyde. The reaction product consisted of phloraspin together with the two symmetrical compounds, *i.e.*, methylene-bis-methylphlorobutyrophenone and methylene-bis-desaspidinol. Phloraspin was isolated from the mixture by recrystallisation from benzene and methanol. The melting



\* Desaspidinol (= phlorobutyrophenone-4-methyl ether) is earlier reported to have a m.p. of 113°<sup>10</sup> and 121–123°<sup>11</sup> while the corresponding 2-methyl ether has a m.p. of 130°<sup>10</sup>. Proof was needed to give conclusive evidence of our desaspidinol with the m.p. of 127–128° being the true 4-methyl isomer. This proof is published elsewhere <sup>12</sup>.

point of the synthetic phloraspin was 212–213° showing with natural phloraspin a mixed melting point of 211–212°.

In a recent report by Klevstrand<sup>9</sup> a melting point of 216–218° is given for phloraspin. According to our observations, as well as to an earlier report by Widén<sup>6</sup>, phloraspin undergoes decomposition when heated to the temperature of fusion visible by a dark red colour of the fused material. When heating is carried out rapidly somewhat higher melting points may be obtained, in our case 215–216° was observed, but the lower melting point mentioned is considered to be the more correct.

### EXPERIMENTAL

*Isolation of phloraspin.* The "raw aspidin" from *Dryopteris austriaca* rhizomes was obtained as previously described<sup>1</sup>. Flavaspidic acid, aspidin and albaspidin were isolated according to Aho<sup>5</sup>. The mother liquid was dried in vacuum and phloraspin obtained by crystallisation from benzene. Repeated recrystallisations from benzene and methanol yielded phloraspin in a pure state with a m.p. of 211–212°. (Found: C 63.90, 63.72; H 6.70, 6.65; OCH<sub>3</sub> 7.02. Calc. for C<sub>23</sub>H<sub>28</sub>O<sub>8</sub>: C 63.88; H 6.48; OCH<sub>3</sub> 7.17.)

*Alkaline cleavage of phloraspin.* Phloraspin (300 mg) was dissolved in aqueous sodium hydroxide (2 M, 50 ml), zinc dust (600 mg) was added and the mixture heated on a steam bath for 5 min. After addition of water (50 ml) the solution was filtered, acidified with sulphuric acid (10 %) and extracted with ether. The ethereal solution was evaporated to dryness and the residue dissolved in acetone. The acetone solution was paper chromatographed<sup>7</sup>; aspidinol and desaspidinol were identified as the main components among the decomposition products formed.

*Synthesis of phloraspin.* Phloraspin was synthesised from methylphlorobutyrophenone and desaspidinol as follows: methylphlorobutyrophenone (2.1 g) and desaspidinol (2.1 g) were dissolved in potassium hydroxide (200 ml, 1 %) and formaldehyde (0.6 ml, 40 %) was added. The mixture was kept at room temperature for 15 min and made acidic with hydrochloric acid (10 %). The precipitate was filtered off, washed with water and dried. After several recrystallisations from benzene and methanol phloraspin was freed from the symmetrical compounds formed and obtained in a pure state with a m.p. of 212–213°, mixed m.p. with natural phloraspin, of 212–213°. (Found: C 63.79, 63.67; H 6.70, 6.67; OCH<sub>3</sub> 7.06. Calc. for C<sub>23</sub>H<sub>28</sub>O<sub>8</sub>: C 63.88; H 6.48; OCH<sub>3</sub> 7.17.)

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Received May 10, 1961.