BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 39 1541—1543 (1966)

The Co-occurrence of Isoflavonoids at Different Oxidation Levels[1]

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(Received October 20, 1965)

Some biogenetic aspects of the co-occurrence of pseudobaptigenin, maackiain and sophorol are discussed.

In previous papers[2] the isolation from the same plant of two new oxygen heterocycles, which are designated sophorol (V) and maackiain (VI), has been described, and their structures have been elucidated.

Biogenetical interests led the author to examine the other components in this plant. Ethanol extracts contained considerable amounts of a product which was relatively insoluble to polar solvents and exhibited strong infrared absorption bands at 935 cm^{-1} and 1630 cm^{-1}, attributable to aromatic methylenedioxyl and γ-pyrone carbonyl groups respectively. The purification of this fraction afforded the colorless component, $C_{16}H_{10}O_5$.

Ultraviolet, infrared, NMR spectra and some chemical evidences proved that this compound is identical with ψ-baptigenin (III). This was confirmed by a direct comparison of it with synthetic ψ-baptigenin *O*-acetate.

Although ψ-baptigenin is known to occur at the 7-*O*-rhamnoglucoside,[3,4] pseudobaptisin, in *Baptisia tinctoria,* and as 7-*O*-3-methylbut-2-enylyl ether, Maxima substance B, in *Tephrosia maxima,*[5] the present finding is the first example of the occurrence of its aglycone in nature.

In view of the wide problem of aromatic biogenesis, the co-occurrence of ψ-baptigenin, sophorol and maackiain is of interest; it may have some implication regarding the biogenesis of this class of natural products.

It was in 1921 that Robinson first put forward his ideas on the phytosynthetic process of flavonoids[6] (the condensation of the C_6–C_3 unit with the C_6 of ring A).

The biogenesis of isoflavones has recently been investigated with the aid of ^{14}C tracer techniques, by Grisebach,[7] and it has been the subject of an

1) Oxygen Heterocycles. IX. Part of this paper was read before the 14th Annual Meeting of the Chemical Society of Japan, April, 1961. The work has been interrupted since September, 1961 but is published now.

2) Preceding papers.

3) K. Gorter, *Arch. Pharm.,* **235**, 494 (1897).

4) E. Späth and O. Schmidt, *Monatsh,* **53**, 454 (1929); E. Späth and E. Lederer, *Ber.,* **63**, 743 (1930).

4) See for further syntheses.
a) H. S. Mahal, H. S. Rai and K. Venkataraman, *J. Chem. Soc.,* **1934**, 1120, 1769. b) W. Baker, J. Chadderton, J. B. Harborne and W. D. Ollis, ibid., **1953**, 1852. c) L. Farkas, A. Major, L. Pallos and J. Varady, *Ber.,* **91**, 2858 (1958). d) W. B aker, R. Robinson, and N. M. Simpson, *J. Chem. Soc.,* **1937**, 805. e) L. Farkas and V. Szántho, *Acta. Chim. Acad. Sci.* (Hugnary), **19**, 217 (1959).

5) S. Rangaswami and B. U. R. Sastry, *Current Sci.* (India), **24**, 13, 337 (1955).

6) R. Robinson, *Nature,* **137**, 172 (1936).

extensive review article.[8] It has been shown that ring B of formononetin in *Triforlium pratense* can be derived from phenylalanine,[8a] while ring A is derived from acetate.[9] This pathway of the formation of isoflavones seems to be generally acceptable. Although the formation of an intermediary chalcone also seems generally accepted, however, the mechanism of the formation of the isoflavones from intermediary chalcones (accompanied by aryl rearrangement) is still ambiguous.[10]

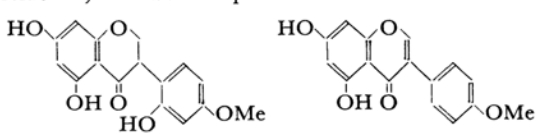
In the present investigation, the common oxygenation pattern in ring A of the three compounds involves the reductive loss of the 5-oxygen function (perhaps in an open-chain forerunner[9]).

As has previously been emphasized,[11] 2'-oxygenation in ring B of sophorol raises an interesting problem. Regarding the introduction of the 2'-oxygen function for isoflavonoids, a process involving the participation of an intermediary coumarin has been suggested by Ollis and Grisebach.[8] However, a recent investigation has shown that the ortho-hydroxylation of *trans-p*-methoxy cinnamic acid could occur; this may be generally true for the *ortho*-oxidation of cinnamic acids.[12]

Considering these speculations and experimental facts, the following tentative scheme of biogenesis to account for the co-occurrence of ψ-baptigenin, sophorol and maackiain can be drawn.

In the chart, the formation of an ether ring by an attack of the benzylic hydroxyl group on the 2' position (e. g., IV)[12a] would be improbable, because of the possibility of the easy formation of the benzylic cation.

2-Oxygenated isoflavanone and simple isoflavone may be derived from the common intermediate, either cinnamic acid (I) or chalcone (II). In this connection, it is noteworthy that in *Ferreirea spectabilis* a relationship parallel to the present example, i. e., the co-occurrence of isoflavone, biochanin-A and a 2'-oxygenated isoflavanone, ferreirin, has been reported.[13]



A possible interrelationship between 2'-oxygenated isoflavanones and coumaranochromans was originally suggested by King.[14] Although the possibility of maackiain being a forerunner of sophorol

7) H. Grisebach and N. Doerr, *Naturwissenschaften*, **17**, 514 (1959); H. Grisebach, *Z. Natur.*, **14b**, 802 (1959); H. Grisebach and N. Doerr, *Z. Natur.*, **15b**, 284 (1960).

8) H. Grisebach and W. D. Ollis, *Experientia*, **17**, 4 (1961).

8a) Regarding shikimic acid→aromatic amino acids pathways see D. B. Sprinson, *Adv. Carbohyd. Chem.*, **15**, 235, (1960). B. D. Davis, in "Biochemist's Handbook," Ed. by C. Long, E & F. N. John S. Pon Ltd., London (1961), p. 595. J. M. Edwards and L. M. Jackman, *Aust. J. Chem.*, **18**, 1227 (1965).

9) A. J. Birch, *Fortschr. Chem. Org. Naturst.*, **14**, 186 (1957); A. J. Birch "Perspectives in Organic Chemistry," Ed. by A. R. Todd, Interscience Publishers Inc., New York (1956), p. 134; A. J. Birch and H. Smith "Chemical Society Symposia, Bristol 1958," Chemical Society Special Publication, No. 13, The Chemical Society, London (1958), p. 1.

10) H. O. House, D. J. Reif and R. L. Wasson, *J. Am. Chem. Soc.*, **79**, 2490 (1957); H. Grisebach and W. Barz, "Biogenesi Delle Sostanze Naturali," Milano, (1964), p. 102.

11) H. Suginome, *Tetrahedron Letters*, **1960**, 16.

12) S. A. Brown, *Phytochem.*, **2**, 137 (1963); D. J. Austin and M. B. Meyers, *Tetrahedron Letters*, **1964**, 765.

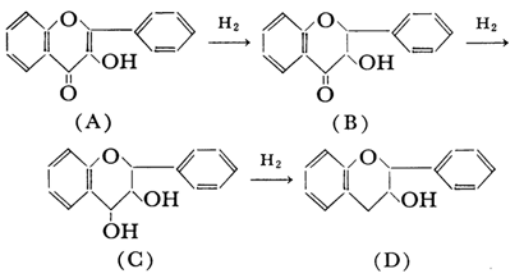
12a) S. Shibata and M. Yamazaki, "Shokubutsu-seibun no Seigosei," Tokyo Kagaku dojin, Tokyo (1965), p. 182.

13) F. E. King and K. G. Neill, *J. Chem. Soc.*, **1952**, 4752; F. E. King, M. F. Grundon and K. G. Neill, ibid., **1952**, 4580.

14) F. E. King and W. Bottomley, ibid., **1954**, 1399.

can not be entirely excluded, the co-occurrence of maackiain and sophorol can perhaps be better understood by assuming the presence of a reductive process (isoflavanone → chromanocoumaran) in nature. Furthermore, a close laboratory analogy to this process involving mild experimental procedures has recently been achieved by the authors.[15]

The corresponding reduction sequence was already noted by King[14] in the flavonol→catechin series, as is illustrated by structures A→D, beginning with flavonol and ending with catechins.



It has previously been noted[11] that sophorol has the essential core and the oxygenation pattern of rotenoids. Speculative pathways on the biogenesis of rotenoids have been proposed by Robinson,[16] by Schmid et al.,[17] and by Grisebach and Ollis.[8] The problem has also recently been reviewed.[18]

Experimental[19]

The Isolation and Purification of ϕ-Baptigenin. —A light brown solid obtained from the ethanol extracts of *Maackia amurensis Rupr. et Maxim. var. Buergeri (Maxim). C. K. Schneid* (3 kg.) was digested with boiling dilute methanol. (Methanol/water 1 : 1). An insoluble material (0.9 g.) was thus collected. Four grams of this material were dissolved in aqueous 2 N sodium hydroxide (20 ml.), and the solution was filtered from a small amount of an insoluble material. After acidification, the material was collected by filtration and then recrystallized from a large volume of ethanol, yielding crystals of ϕ-baptigenin. (M. p. 294°C (decomp.)),[20] 200 mg. UV λ_{max} (ε_{max}): 223 (16820), 251 (16350), 294 (11730).

IR: 3150 (w) (phenolic OH); 1630 (s) (γ-pyrone C=O), 1621 (s), 1598 (s), 1574 (s) and 1490 (s) (aromatic C=C); 1032 (s) and 935 (s) (C–O–C–O–C–). *O*-Methyl ether[21] with dimethylsulfate and potassium carbonate in dry acetone (m. p. 182°C, short needles from ethanol.)

UV λ_{max} (ε_{max}): 223 (25040), 249 (20580), 263 (20880) and 293 (16830). IR: 1636 (γ-pyrone carbonyl); 1625, 1607, 1573 and 1487 (aromatic C=C); 1037 and 906 cm^{-1} (C–O–C–O–C). *O*-Acetate[22] (m. p. 178°C, short needles from ethanol), 1641 cm^{-1} (C=O), 1656 cm^{-1} (acetate C=O).

The author is grateful to Professors Tōshi Irie, Takeshi Matsumoto and Tadashi Masamune for their kind interest in this work, and to Professor Naoto Inoue, Tohoku University, for providing the sample of synthetic ϕ-baptigenin acetate.

15) H. Suginome and T. Iwadare, *Experientia*, **18**, 163, (1962).
16) Sir R. Robinson, "The Structural Relations of Natural Products," Oxford University Press, Oxford (1955), p. 43.
17) O. A. Stamm, H. Schmid and J. Büchi, *Helv. Chim. Acta*, **41**, 2006 (1958).
18) L. Crombie, *Fortschr. Chem. Org. Naturstoffe*, **21**, 275 (1963).
19) Melting points are uncorrected. Ultraviolet spectra were taken in ethanol, and infrared spectra were taken in Nujol unless otherwise stated. Elemental analyses by Mr. Kusuo Narita, Department of Pharmacy, Faculty of Medicine, Hokkaido University.
20) Reported m. p. 292°C,[4b] m. p. 292—293°C.[4a]
21) Reported m. p. 179—180°C.[4a]
22) Reported m. p. 173°C,[3] m. p. 176°C,[4a] m. p. 165°C.[4b]