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The Neoflavanoids, a New Class of Natural Products[1]

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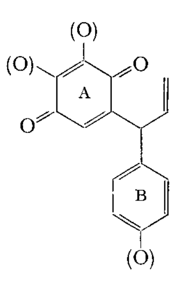
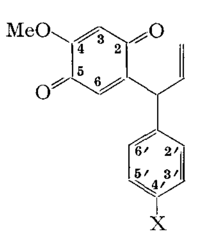
The *Leguminosae* is a large botanical family and its members have provided many examples of natural products of the isoflavonoid[2] and rotenoid[3] types. Recently, in a survey of natural products characteristic of South American *Leguminosae* which we are carrying out in collaboration with Professor O. R. Gottlieb[4], we have isolated representatives of a new class of natural phenolic compounds for which the name neoflavanoids has been suggested[5].

Our initial studies have been concerned with the examination of extractives isolated from the heartwood and sapwood of the botanically related Brazilian genera, *Dalbergia* and *Machaerium*, and this has led to the discovery of a new class of quinones which we call the dalbergiones[5,6]. The dalbergiones may be represented by the types formula (I), and their isolation from both *Dalbergia* and *Machaerium* species supports the view that these genera are taxonomically related.

Dalbergia nigra yielded 3 optically active dalbergiones (II, III, and IV) and their absolute stereochemistry was established in the following way. Catalytic hydrogenation gave tetrahydro-derivatives which were oxidized in alkaline solution to the dihydrodalbergiones (V and VI). Ozonolysis of the dihydrodalbergione (V) gave (−)-α-ethylphenylacetic acid (VII), whereas the dihydro-dalbergione (VI) gave (+)-α-ethyl-*p*-methoxyphenylacetic acid (VIII). It followed that 2 of the dalbergiones isolated from *D. nigra* were R-4-methoxydalbergione (IX) and S-4,4′-dimethoxydalbergione (XII). This antipodal relationship was fully supported by the ORD and CD curves of (IX) and (XII) which were opposite in type, and since the 4′-hydroxy-4-methoxydalbergione (III) showed an ORD curve which corresponded to that of (XII), it followed that 4′-hydroxy-4-methoxydalbergione had the S-configuration (XI).



(I)



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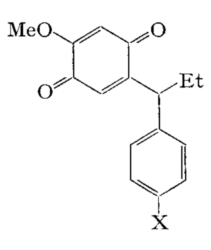
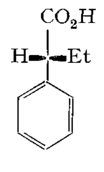
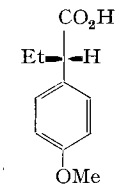
(III) X = OH
(IV) X = OMe



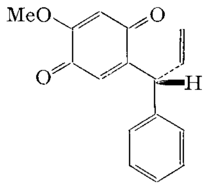
(V) X = H
(VI) X = OMe



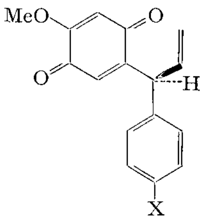
(VII)



(VIII)



(IX)



(X) X = H
(XI) X = OH
(XII) X = OMe

The antipodal relation between R-4 methoxydalbergione (IX) and S-4,4′-dimethoxydalbergione (XII), which were both isolated from the same plant *D. nigra*, provided us with an unusual encounter in natural product chemistry. In the first study of *D. nigra*, the

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[1] This account is based on The Robert Gnehm Lecture given at the Laboratorium für Organische Chemie, Eidgenössische Technische Hochschule, Zürich, on May 14, 1965, and lectures given to the Chemical Societies in Basel and Lausanne on May 19 and 20, 1965.

[2] W. D. Ollis, in *The Chemistry of Flavonoid Compounds* (Ed. T. A. Geissman; Pergamon Press, 1961), p. 353.

[3] W. D. Ollis, in *Symposium on Phytochemistry* (Ed. H. R. Arthur; Hong Kong University Press, 1964), p. 128; L. Crombie, Fortschr. Chem. org. NatStoffe (Ed. L. Zechmeister) *21*, 275 (1963).

[4] Departamento de Química Orgânica, Universidade de Brasília, Brasil.

[5] W. B. Eyton, W. D. Ollis, I. O. Sutherland, O. R. Gottlieb, M. Taveira Magalhães, and L. M. Jackman, Tetrahedron *21*, 2683 (1965).

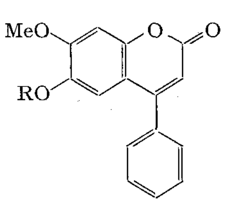
[6] W. B. Eyton, W. D. Ollis, I. O. Sutherland, L. M. Jackman, O. R. Gottlieb, and M. Taveira Magalhães, Proc. chem. Soc. 301 (1962).

dalbergiones (IX and XII) were not initially isolated as such, but the isolation of a substance J-2 was reported[7]. J-2 was unchanged on recrystallization, and at first it was believed to be a pure compound. However, later studies established that J-2 was a quasiracemate derived from R-4-methoxydalbergione (IX) and S-4,4'-dimethoxydalbergione (XII). So far as we are aware, this is the first example[6] of the isolation of a natural product as a quasiracemate, but recently a very interesting case of the isolation of a quasiracemic alkaloid, narcissamine, has been reported by Laiho and Fales[8]. The isolation of natural products as quasiracemates is novel and may well involve the stereospecific synthesis of antipodally related natural products of corresponding structural type. This differs from the much more frequently encountered circumstance in which a stereochemical conformity, that is corresponding chirality, is exhibited among natural products of corresponding structural type.

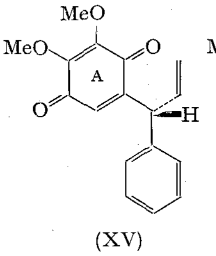
Two dalbergiones have also been isolated from *D. violacea*[6,9] but, in contrast with the compounds isolated from *D. nigra*, they both have the S-configuration. This was unexpected since one was identified as S-4-methoxydalbergione (X), so it was the antipode of the compound (IX) isolated from *D. nigra*. The other compound was S-4'-hydroxy-4-methoxydalbergione (XI).

This study of the absolute stereochemistry of the dalbergiones has revealed 2 biosynthetic situations of some novelty. 4-Methoxydalbergione (II) of either the R-type (IX) or the S-type (X) is produced by 2 plants within the same genus, but whereas *D. violacea* produces 2 dalbergiones (X and XI), both of the S-configuration, *D. nigra* produces 3 dalbergiones, of which 1 (IX) has the R-configuration and 2 (XI and XII) have the S-configuration.

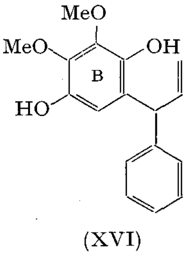
These circumstances encouraged our speculation about possible biosynthetic pathways which could lead to the dalbergiones. In this connection it was noted[6] that the dalbergiones (IX, X, XI, and XII) had a striking structural correspondence to dalbergin (XIII), and *O*-methyldalbergin (XIV), already isolated from *Dalbergia sissoo*[10]. In comparison with the large number of known flavonoids and isoflavonoids, the number of known 4-arylcoumarins was very small. However, with the recognition of a possible biogenetic relation between the dalbergiones and the 4-arylcoumarins[6,11], the need for a name to describe this class collectively arose. For this and other reasons given later the term *neoflavanoid* was suggested[5].



(XIII) R = H
(XIV) R = Me



(XV)



(XVI)

The view[6,11] that compounds of the dalbergione and the dalbergin types are biogenetically related is supported by our observation that both types of natural product have now been isolated from a single plant. *Machaerium scleroxylon*[12,13] has yielded the new dalbergione (XV), its corresponding quinol (XVI), dalbergin (XIII), and *O*-methyldalbergin (XIV). It should be mentioned at this point that although the dalbergiones are not heterocyclic, just as it is customary to regard the natural chalcones as flavonoids and angolensin as an isoflavonoid[2], so we have suggested[5] that dalbergiones should be included in the neoflavanoid class.

Two biosynthetic pathways for the formation of neoflavanoids seem to us to require consideration.

Scheme A is a hypothetical extension of the established routes[14] to flavonoids and isoflavonoids and, just as it has been established that the biosynthesis of isoflavonoids involves a 1,2-aryl migration, so it is proposed for consideration that a further 1,2-aryl migration is possible, thus giving the neoflavanoid skeleton.

The biosynthesis of neoflavanoids according to the hypothetical scheme B involves a process which is formally different from that involved in scheme A. In scheme A *acylation* by cinnamoyl coenzyme A or its equivalent is involved[14], whereas scheme B requires processes equivalent to *alkylation* by a cinnamyl derivative. In many respects scheme B is similar to processes which have already been considered[15] for the introduction of C_5 units ($Me_2C{=}CH{-}CH_2{-}$ and $H_2C{=}CH{-}CMe_2{-}$) onto the skeletons of phenolic compounds. This almost certainly involves alkylation of a phenol or polyketide by dimethylallyl pyrophosphate and the course of the reactions may be represented as

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[7] O. R. Gottlieb and M. Taveira Magalhães, J. org. Chem. *26*, 2449 (1961).

[8] S. M. Laiho and H. M. Fales, J. Am. chem. Soc. *86*, 4434 (1964).

[9] W. D. Ollis, H. J. P. E. M. Landgraf, O. R. Gottlieb, and M. Taveira Magalhães, Anais Acad. bras. Ciênc. *36*, 31 (1963).

[10] V. K. Ahluwalia and T. R. Seshadri, J. chem. Soc. 970 (1957).

[11] T. R. Seshadri, J. Indian chem. Soc. *40*, 497 (1963).

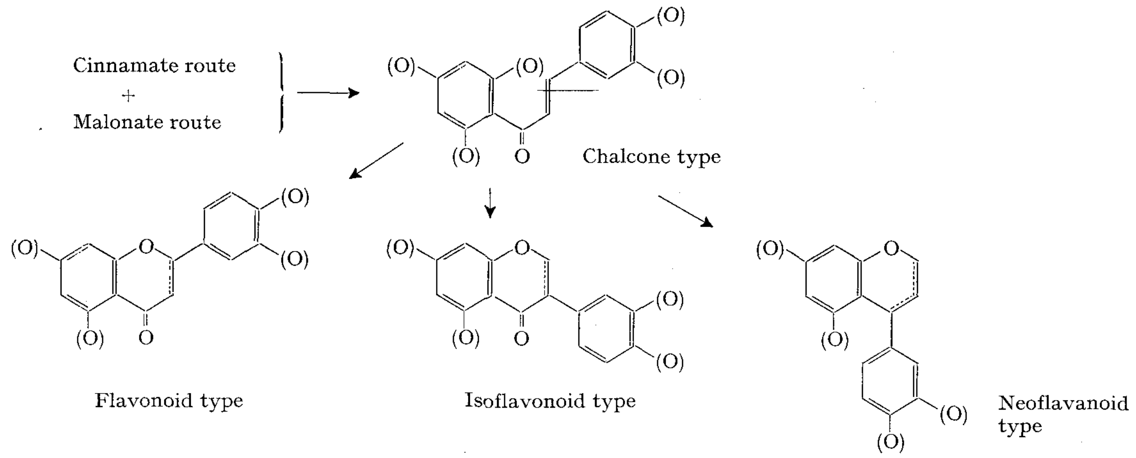
[12] O. R. Gottlieb, M. Fineberg, I. Salignac de Souza Guimarães, M. Taveira Magalhães, W. D. Ollis, and W. B. Eyton, Anais Acad. bras. Ciênc. *36*, 33 (1964).

[13] W. B. Eyton, W. D. Ollis, M. Fineberg, O. R. Gottlieb, I. Salignac de Souza Guimarães, and M. Taveira Magalhães, Tetrahedron *21*, 2967 (1965).

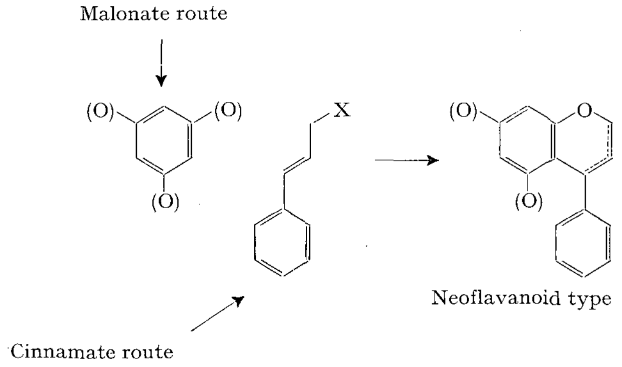
[14] H. Grisebach and W. D. Ollis, Experientia *17*, 4 (1960), and references there cited. – A. C. Neish, *Cinnamic Acid Derivatives as Intermediates in the Biosynthesis of Lignin and Related Compounds*, in *Formation of Wood in Forest Trees* (Academic Press, 1964), p. 219. – A. C. Neish, in *Biochemistry of Phenolic Compounds* (Ed. J. B. Harborne, Academic Press, 1964), p. 295. – H. Grisebach, *Biosynthesis of Flavonoids*, in *Chemistry and Biochemistry of Plant Pigments* (Ed. T. W. Goodwin; Academic Press, 1965), p. 279.

[15] W. D. Ollis and I. O. Sutherland, in *Recent Developments in the Chemistry of Natural Phenolic Compounds* (Ed. W. D. Ollis; Pergamon Press, 1961), p. 74.

Scheme A



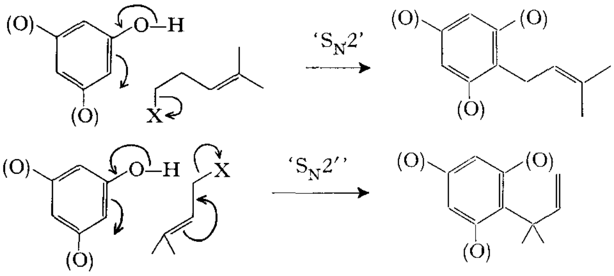
Scheme B



Hypothetical biosynthetic pathways leading to the neoflavanoid type
(the indicated positions of unsaturation and oxygenation are only illustrative)

in scheme C. In this scheme the terms 'SN2' and 'SN2'' are used to direct attention to the site of substitution; they are not used to express an opinion about the detailed mechanism of these biochemical reactions.

Scheme C.

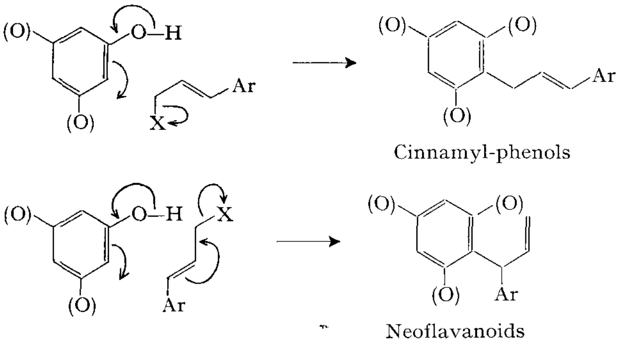


An interpretation of the association of two types of isoprenoid residues with the structures of some natural phenols[15].

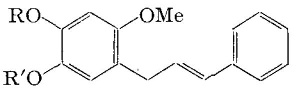
The principles of scheme C may now be applied to the hypothesis represented by scheme B and this leads to the recognition, summarized in scheme D, that alkylation by cinnamyl pyrophosphate (or its equivalent) could lead either to the neoflavanoid type or to the cinnamyl-phenol type.

Although the proposal in scheme D has not yet been examined by the appropriate plant feeding experiments, it is nevertheless gratifying to note that we have now recognized a number of cinnamyl-phenols as natural products and that these occur in association with neoflavanoids. Thus *D. violacea* has yielded not only the neoflavanoids S-4-methoxydalbergione (X)

Scheme D



and S-4'-hydroxy-4-methoxydalbergione (XI), but also the cinnamyl-phenols violastyrene (XVIIa) and isoviolastyrene (XVIIb).



(XVIIa) R = H, R' = Me
(XVIIb) R = Me, R' = H

The neoflavanoid (II) and violastyrene (XVIIa) have been synthesized by processes which may be regarded as being somewhat analogous mechanistically to those associated with scheme D. The Claisen rearrangement of the cinnamyl ether (XVIII) gave the phenol (XIX), which by oxidation with Fremy's salt gave racemic 4-methoxydalbergione (II)[16]. Similarly, violastyrene (XVIIa) was obtained as the sole product

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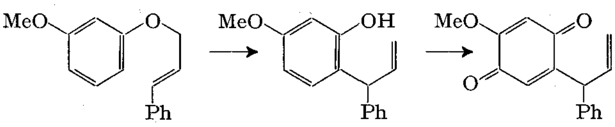
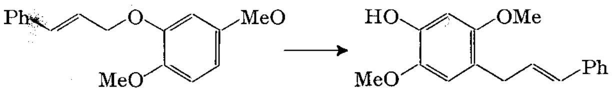
[16] M. F. Barnes, W. D. Ollis, I. O. Sutherland, O. R. Gottlieb, and M. Taveira Magalhães, Tetrahedron *21*, 2707 (1965).

from the Claisen rearrangement of the cinnamyl ether (XX)[17].



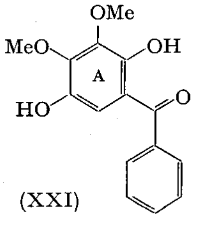
(XVIII) (XIX) (II)



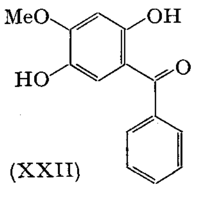
(XX) (XVIIa)

A non-enzymic analogy to scheme D is provided by the observation that alkylation of 2,5-dimethoxyphenol with diphenyl cinnamyl phosphate yields violastyrene (XVIIa) directly[17]. Although it is appreciated that natural cinnamyl-phenols could arise as reduction products of chalcones (scheme A), we nevertheless feel that the natural association of cinnamyl-phenols and neoflavanoids makes scheme D an attractive alternative for consideration.

Another possible role of neoflavanoids in biosynthetic programmes is indicated by the co-occurrence of the new natural benzophenone, scleroin (XXI), with the neoflavanoids (XIII, XIV, XV, and XVI) in the plant *Machaerium scleroxylon*[12,13].



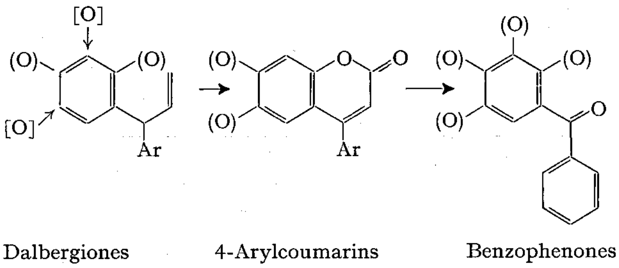
(XXI)



(XXII)

The similarity between the oxygenation patterns on ring A of scleroin (XXI), the dalbergione (XV), and the dalbergiquinol (XVI) suggests that dalbergiones, 4-arylcoumarins, and some benzophenones may be interrelated biogenetically by the following biodegradative sequence (scheme E).

Scheme E



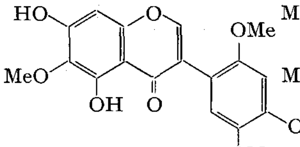
Dalbergiones 4-Arylcoumarins Benzophenones

The isolation of representatives of the 3 structural types indicated in scheme E from a single plant source lends strong support to earlier proposals[11,18,19] concerning the biosynthesis of certain oxygenated benzophenones. Thus, although some natural benzophenones are certainly formed by polyketide routes involving either aliphatic or aromatic acids plus chain-extension by malonate[20], the alternative suggested by scheme E may well account for the observed co-occurrence of some benzophenones with neoflavanoids.

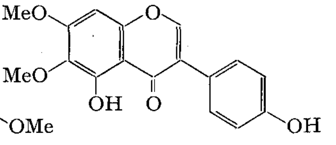
Examination of *D. violacea*[17] has provided a group of structurally related natural products which also fits in well with schemes D and E. The compounds which have been isolated include violastyrene (XVIIa) and isoviolastyrene (XVIIb) (the cinnamyl-phenol type), S-4-methoxydalbergione (X), S-4′-hydroxy-4-methoxydalbergione (XI), and dalbergin (XIII) (the neoflavanoid type), and cearoin (XXII) (the benzophenone type). All these compounds show a striking structural correspondence.

Thus, the representatives of the *Dalbergia* and *Machaerium* genera which have been examined have provided a number of natural product types, which fits in with biogenetic proposals summarized by schemes D and E. However, as members of the *Leguminosae* family, one might also expect isoflavonoids[2] to be present in these plants. This is indeed the case. Thus, *D. nigra* has also yielded the isoflavone caviunin (XXIII)[21], and 7-*O*-methyltectorigenin (XXIV) has been isolated from the green pods of *D. sissoo*[22]. *D. violacea* has yielded[17] di-*O*-methyldaidzein (XXVb), a known isoflavone derivative not previously detected as a natural product, and the new isoflavanone violanone (XXVI).

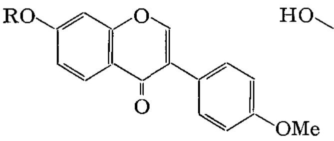
The co-occurrence of neoflavanoids and isoflavonoids is also exemplified by a study of *D. Spruceana*



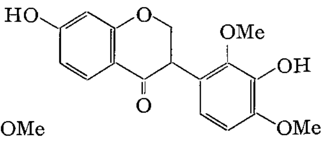
(XXIII)



(XXIV)



(XXVa) R = H
(XXVb) R = Me



(XXVI)

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[17] M. GREGSON, Ph.D. Thesis, University of Sheffield (1965).

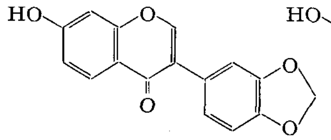
[18] T. A. GEISSMAN and E. H. HINREINER, Bot. Rev. *18*, 208 (1952).

[19] T. R. SESHADRI, Current Sci. *26*, 239 (1957).

[20] A. J. BIRCH, Proc. chem. Soc. 3 (1962). – J. H. RICHARDS and J. B. HENDRICKSON, in *The Biosynthesis of Steroids, Terpenes, and Acetogenins* (Benjamin, New York 1964), p. 47.

[21] O. R. GOTTLIEB and M. TAVEIRA MAGALHÃES, J. org. Chem. *26*, 2449 (1961). – S. F. DYKE, W. D. OLLIS, and M. SAINSBURY, J. Org. Chem. *26*, 2453 (1961).

[22] V. K. AHLUWALIA, G. P. SACHDEV, and T. R. SESHADRI, Indian J. Chem. *3*, 474 (1965).



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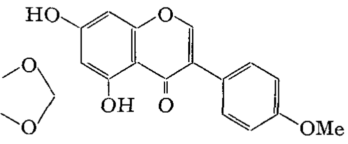
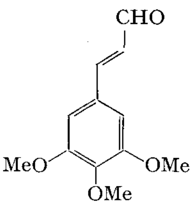
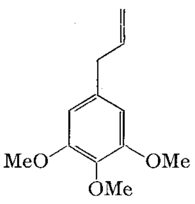


(XXVIII)



(XXIX)

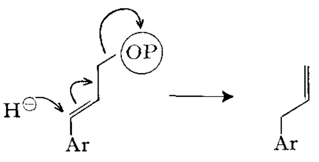


(XXX)

which is in progress[23]. Of the 19 natural products isolated from this source, 16 have been identified. This number includes 4 isoflavones, caviunin (XXIII), formononetin (XXVa), ψ-baptigenin (XXVII), and biochanin-A (XXVIII); 2 neoflavanoids, S-4-methoxydalbergione (X) and dalbergin (XIII); 2 C_9-compounds, 3,4,5-trimethoxycinnamic aldehyde (XXIX) and elemicin (XXX); a group of 5 structurally related pterocarpans; benzoic acid, β-sitosterol, and *O*-acetyloleanolic acid. These results direct particular attention to the natural co-occurrence of isoflavonoids and neoflavanoids, but some other points of interest may also be mentioned.

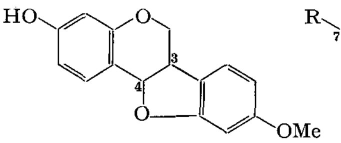
The co-occurrence of the neoflavanoids (X and XIII) with the C_9-compounds (XXIX and XXX) is compatible with scheme B. The biogenetic formation of the natural allyl phenols[24] may well involve a process equivalent to the hydride reduction of cinnamyl phosphates (scheme F). This reaction sequence is mechanistically similar to scheme D, which is under consideration[13] for the biosynthesis of neoflavanoids and cinnamyl-phenols.

Scheme F

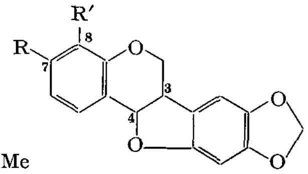


It may be noted that the isolation of benzoic acid with the neoflavanoids (X and XIII) could be regarded as fitting in with scheme E if benzoic acid can be accepted as the ultimate product of such a biodegradative process.

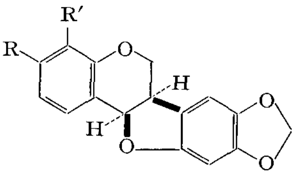
The natural products isolated from *D. Spruceana* were available in quite small amounts and considerable assistance in their structural examination was provided by mass spectrometry. This is illustrated by our investigation of the 5 pterocarpans which we have isolated from this source. The structures (XXXI–XXXV) were initially proposed on the basis of their mass and NMR spectra from which their structural correspondence was immediately indicated. The formation of significant ions with their indicated structures and *m/e* values is summarized in Table I.



(XXXI)

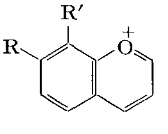
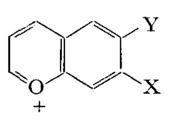
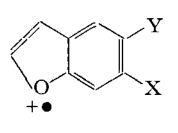


(XXXII) R = OH, R′ = H
(XXXIII) R = R′ = OH
(XXXIV) R = OMe, R′ = OH
(XXXV) R = OH, R′ = OMe
(XXXVI) R = R′ = OMe



(XXXVIIa) R = R′ = OH
(XXXVIIb) R = OMe, R′ = OH
(XXXVIIc) R = OH, R′ = OMe

Table I. Significant ions observed in the mass spectra of the pterocarpans (XXXI–XXXV)

(XXXI; *m/e* 270) → *m/e* 147	*m/e* 161	*m/e* 148
(XXXII; *m/e* 284) → *m/e* 147	*m/e* 175	*m/e* 162
(XXXIII; *m/e* 300) → *m/e* 163	*m/e* 175	*m/e* 162
(XXXIV; *m/e* 314) → *m/e* 177	*m/e* 175	*m/e* 162
(XXV; *m/e* 314) → *m/e* 177	*m/e* 175	*m/e* 162
		
R = OH, R′ = H; *m/e* 147 R = R′ = OH; *m/e* 163 R = OMe, R′ = H; *m/e* 177 R = H, R′ = OMe; *m/e* 177	X = OMe, Y = H; *m/e* 161 X–Y = O·CH_2·O; *m/e* 175	X = OMe, Y = H; *m/e* 148 X–Y = O·CH_2·O; *m/e* 162

The details of the fragmentation patterns of pterocarpans are still under investigation[23], but the information given in Table I in association with NMR

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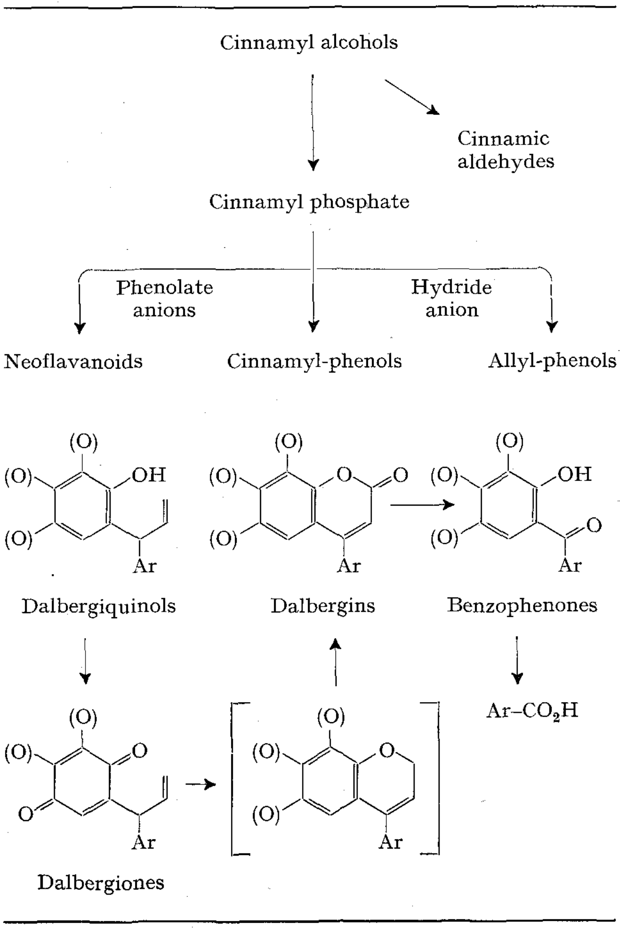
[23] Mrs. J. T. Cook, unpublished results.

[24] A. J. Birch, in *Chemical Plant Taxonomy* (Ed. T. Swain; Academic Press, 1963), p. 141.

evidence[25] established the main features of the structures (XXXI–XXXV). The constitutions (XXXI and XXXIV) were finally settled by synthesis[23] and, since methylation of the compounds (XXXIII, XXXIV, and XXXV) gave the same compound (XXXVI), this also established the constitutions (XXXIII and XXXV). Methylation of (XXXII) gave (±)-pterocarpin.

An interesting situation has emerged regarding the absolute stereochemistry of the pterocarpans isolated from *D. Spruceana*. The compounds (XXXI and XXXII) were isolated as racemates, whereas the 7,8-dioxygenated pterocarpans (XXXIII, XXXIV, and XXXV) all show optical rotatory dispersion characteristics demonstrating that they have the corresponding absolute configuration at C_3 and C_4; this has subsequently[26] been established as that shown in formulae (XXXVIIa, b, and c). Previously the absolute configuration of (−)-pterocarpin has been discussed[27] in relation to the absolute configuration of the natural rotenoids[28], but clearly this relation is unlikely to be significant biogenetically, now that it is established that pterocarpans do not conform to one stereochemical pattern even in the single plant *D. Spruceana*.

Table II. A biogenetic proposal to interrelate the neoflavanoids with their natural congeners



The natural co-occurrence of the racemic forms (XXXI and XXXII) and the optically active forms (XXXIII, XXXIV, and XXXV) as members of a single group of structurally related natural products is unusual, and recalls the isolation discussed earlier of antipodally related dalbergiones (IX, XI, and XII) from *D. nigra*. The occurrence in different species of derivatives of (+)-, (−)-, and (±)-maackiain (XXXII) is relevant[29].

In our investigation of *Dalbergia* and *Machaerium* species, the association of isoflavonoids with neoflavanoids does raise the following interesting question. Are the isoflavonoids and neoflavanoids both produced according to scheme A, or are the isoflavonoids produced by the normal route of scheme A and the neoflavanoids as indicated in scheme B? The direct answer to this question cannot be given until appropriate feeding experiments can be carried out. This is under investigation. However, the study of the biosynthesis of heartwood constituents does present considerable technical difficulties, and until these are resolved it is still necessary to rely upon structure comparison in order to make biogenetic analyses. Until more direct evidence is available, the results which have been described suggest that the biogenetic proposals outlined in Table II are justified[30].

Zusammenfassung. Der Name Neoflavanoid wurde für eine neuerdings erkannte Gruppe von phenolischen Naturstoffen vorgeschlagen, die durch ein Gerüst von 15 Kohlenstoffatomen vom 4-Aryl-chroman-Typ charakterisiert sind. In dieser Hinsicht ergänzen die Neoflavanoide die wohlbekannten Flavanoide und Isoflavanoide. Es wird jedoch in Betracht gezogen, dass die Neoflavanoide biosynthetisch sehr wohl auf einem ganz anderen Wege gebildet werden könnten als die Flavanoide und die Isoflavanoide. Die beiden letzteren Verbindungsgruppen entstehen über Polyketide unter Beteiligung von Cinnamat, während die strukturellen Muster, die für Neoflavanoide typisch sind, darauf hin-

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[25] J. B.-SON BREDENBERG and J. N. SHOOLERY, Tetrahedron Letters 285 (1961).

[26] Since this lecture was given the absolute configuration of pterocarpans has been established (S. ITÔ, Y. FUJISE, and A. MORI, Chem. Comm. 595 (1965)).

[27] J. W. CLARK-LEWIS, Rev. Pure Appl. Chem. *12*, 96 (1962).

[28] C. DJERASSI, W. D. OLLIS, and R. C. RUSSELL, J. chem. Soc. 1448 (1961). – G. BÜCHI, L. CROMBIE, P. J. GODIN, J. S. KALTENBRONN, K. S. SIDDALINGAIAH, and D. A. WHITING, J. chem. Soc. 2843 (1961).

[29] W. COCKER, T. DAHL, C. DEMPSEY, and T. B. H. MCMURRY, J. chem. Soc. 4906 (1962). – H. SUGINOME, Experientia *18*, 161 (1962). – S. SHIBATA and Y. NISHIKAWA, Chem. pharm. Bull., Tokio *11*, 167 (1963), and references there cited.

[30] Finally I should like to express my thanks to our Brazilian collaborators and I refer to our special debt to Professor O. R. GOTTLIEB (University of Brasilia) and Professor H. M. ALVES (University of Minas Gerais). I must also thank most warmly Mrs. JUDITH COOK, Dr. W. B. EYTON, Dr. C. P. FALSHAW, Dr. M. GREGSON, and Dr. I. O. SUTHERLAND, for it is their experimental work that I have described in this paper.

weisen, dass ihre Biosynthese formell durch Cinnamylierung von Phenolen oder den entsprechenden Polyketiden vor sich geht. Diese Annahme hat dazu geführt, dass man nach Fällen gesucht hat, in denen Neoflavanoide und C-Cinnamylphenole gleichzeitig auftreten; Beispiele dafür können jetzt angegeben werden.

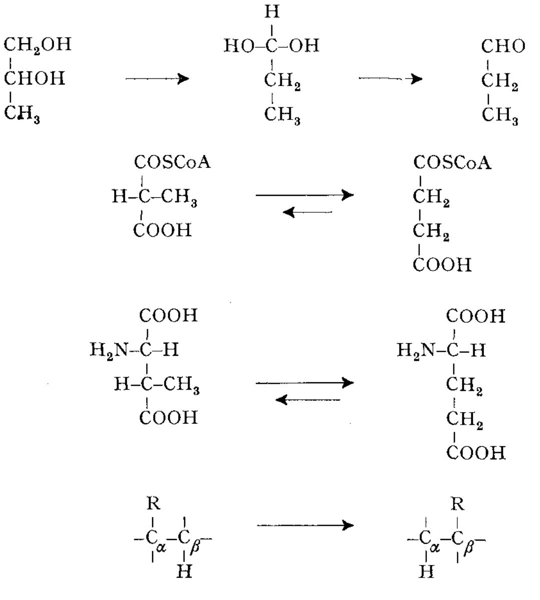
Die Neoflavanoide wurden bisher aus *Dalbergia* und *Machaerium*-Arten isoliert und umfassen Dalbergichinole, Dalbergione und Dalbergine. Es ist wahrscheinlich, dass diese Verbindungen in der Natur durch Biooxydation ineinander übergehen und dies erklärt ihr gemeinsames Vorkommen mit strukturell verwandten Benzophenonen. Man kann erwarten, dass auch Neoflavene als Naturstoffe gefunden werden.

Die Dalbergione stellen ein interessantes Beispiel dar für das gleichzeitige natürliche Vorkommen von strukturell verwandten Naturstoffen entgegengesetzter Konfiguration und dies war der Grund dafür, dass man ein Dalbergion-Paar zuerst als Quasirazemat isolierte.

SPECIALIA

Coenzym B_{12} als gemeinsamer Wasserstoffüberträger der Dioldehydrase- und der Methylmalonyl-CoA-Mutase-Reaktion

Vor kurzem konnte nachgewiesen werden, dass bei der durch Propandioldehydrase katalysierten Umwandlung von (*R*)- und (*S*)-Propan-1,2-diol zu Propionaldehyd (Gl. 1) neben der Wanderung eines Wasserstoffatoms von C-1 und C-2 auch eine Wanderung der sekundären OH-Gruppe von C-2 nach C-1 stattfindet, wobei Propan-1,1-diol als Zwischenstufe auftritt[1]. Daraus ergibt sich eine formale Analogie zwischen der Propandioldehydrase-Reaktion und zwei weiteren durch Coenzym B_{12} katalysierten Umlagerungen, der Methylmalonyl-CoA-Mutase- (Gl. 2) und der Methylasparaginsäure-Mutase-Reaktion (Gl. 3)[2,3]. Die drei Reaktionen lassen sich durch das allgemeine Schema (Gl. 4) darstellen.



$$\begin{array}{c}CH_2OH\\|\\CHOH\\|\\CH_3\end{array} \longrightarrow \begin{array}{c}H\\|\\HO{-}C{-}OH\\|\\CH_2\\|\\CH_3\end{array} \longrightarrow \begin{array}{c}CHO\\|\\CH_2\\|\\CH_3\end{array} \quad (1)$$

$$\begin{array}{c}COSCoA\\|\\H{-}C{-}CH_3\\|\\COOH\end{array} \rightleftarrows \begin{array}{c}COSCoA\\|\\CH_2\\|\\CH_2\\|\\COOH\end{array} \quad (2)$$

$$\begin{array}{c}COOH\\|\\H_2N{-}C{-}H\\|\\H{-}C{-}CH_3\\|\\COOH\end{array} \rightleftarrows \begin{array}{c}COOH\\|\\H_2N{-}C{-}H\\|\\CH_2\\|\\CH_2\\|\\COOH\end{array} \quad (3)$$

$$\begin{array}{c}R\quad\\|\quad|\\-C_\alpha-C_\beta-\\|\quad|\\\quad H\end{array} \longrightarrow \begin{array}{c}\quad R\\|\quad|\\-C_\alpha-C_\beta-\\|\quad|\\H\quad\end{array} \quad (4)$$

Nachfolgend wird über Versuche berichtet, welche weitere mechanistische Ähnlichkeiten zwischen zwei dieser Reaktionen aufdecken.

Der hohe Wert ($k_H/k_D \sim 10$) des für die Propandioldehydrase-Reaktion auftretenden Isotopeneffektes[4] liess a priori als wenig wahrscheinlich erscheinen, dass die Wanderung des Wasserstoffatoms intramolekular erfolgt[5]. Tatsächlich konnten vor kurzem ABELES et al.[6] zeigen, dass diese Wanderung einen intermolekularen Prozess darstellt und darüber hinaus, dass die wandernden Wasserstoffatome intermediär an das C-5′ des Coenzyms gebunden werden[7]. Die intermolekulare Natur des Vorganges konnten wir auf folgendem Wege bestätigen.

Umsetzung eines Gemisches von an C-1 dideuteriertem und von isotopenfreiem (*RS*)-Propan-1,2-diol mit der Propandioldehydrase aus *Aerobacter aerogenes* in Gegenwart von Coenzym B_{12}, gefolgt von in situ-Reduktion des entstandenen Propionaldehyds mit Hefe-Alkohol-Dehydrogenase und NADH lieferte Proben von Propan-1-ol, deren Isotopenzusammensetzung in Funktion der Reaktionszeit nach Bildung der Phenylurethane massenspektrometrisch[8] untersucht wurde. Die erhaltenen Resultate (vgl. Tabelle) zeigen, dass das Produkt erhebliche Mengen monodeuterierter Molekeln enthält, obwohl der Gesamt-

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[2] H. EGGERER, P. OVERATH, F. LYNEN und E. R. STADTMAN, J. Am. chem. Soc. *82*, 2643 (1960).

[3] A. MUNCH-PETERSEN und H. A. BARKER, J. biol. Chem. *230*, 649 (1958).

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[5] Für allgemeine Diskussion vgl. F. H. WESTHEIMER, Chem. Rev. *61*, 265 (1961).

[6] R. H. ABELES und B. ZAGALAK, J. biol. Chem. *241*, 1245 (1966).

[7] P. A. FREY und R. H. ABELES, J. biol. Chem. *241*, 2732 (1966).

[8] Die Aufnahme und Auswertung der Massenspektren verdanken wir Herrn Dr. J. SEIBL.