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REVIEW ARTICLE

POLYPHENOLS OF *PTEROCARPUS* AND *DALBERGIA* WOODS*

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Abstract—The flavanoid and neoflavanoid constituents of the *Pterocarpus* and *Dalbergia* species are reviewed together with related compounds. Several synthetic procedures analogous to biosynthetic pathways are described.

INTRODUCTION

AMONG the trees of the Leguminosae, those of the genera *Pterocarpus* and *Dalbergia* are particularly noted for their durable and valuable timber. *Pterocarpus* species are mainly large trees distributed in tropical regions. *P. santalinus*, commonly known as red sandal, is highly prized in the carving industry, because of the deep red colour of its wood. Another closely related wood, *P. marsupium*, is used as a substitute for teak for various purposes. Furthermore, both woods are employed in folk medicine. A few other species of *Pterocarpus* grow in India, but not all of them are native: Burma padauk (*P. macrocarpus*), Andaman padauk (*P. dalbergioides*), African padauk (*P. sojauxii*), muninga wood of Africa (*P. angolensis*) and narrawood (*P. indicus*) of Malaya and Phillipines. In Africa several other species are available, for example, *P. tinctorius*, *P. osun*, *P. mildbraedii*, *P. erinaceus* and *P. santalinoides*, and many of these are of commercial value.

Polyphenols of Pterocarpus

Chemical investigation of *Pterocarpus* woods started more than 100 years ago, yet new compounds are still being discovered. There are a variety of compounds with different carbon skeletons, some of which have been considered unique to the genus. A broad classification of these components is given below along with the special features of each group.

Isoflavonoids

Isoflavonoids were the earliest compounds to be studied and are major components in the genus. They can be subdivided into three sub-groups; pterocarpans, isoflavones and deoxybenzoins.

Pterocarpans

Pterocarpans are isoflavonoids which have a condensed dihydrofuran system between the heterocyclic and side phenyl rings. Nearly 100 years ago, two pterocarpans (—)-homopterocarpin (I) and (—)-pterocarpin (II)[1] were found to occur very commonly in *Pterocarpus*

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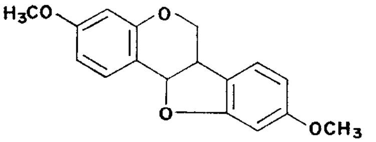
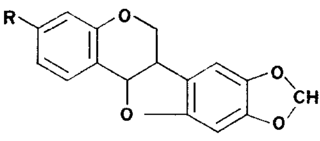
* Based on a paper read at the Wood Extractives Symposium, 161st Meeting of the American Chemical Society in Los Angeles, April 1971.

[1] CAZENEUVE, *Chem. Ber.* 7, 1798 (1874).



(I)



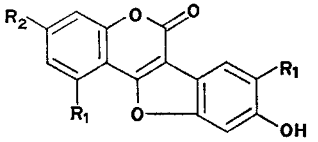
(II) R=OCH$_3$
(III) R=OH

woods. They were first isolated from *P. santalinus*, and then from several other species.[2-8] More recently, (—)-maackiain (III) was recorded as present in *P. dalbergioides*.[9] A number of compounds of this type have also been obtained by Harper *et al.*[10] from the wood of *Swartzia madagascariensis*.

The structures of pterocarpin and homopterocarpin were proposed by groups led by Späth[3] and by Robertson.[11,12] The general methods which they developed have been used in the study of new members of the group, although spectral methods have now become common. A revision of the structure of pterocarpin itself, relating to the position of the methylenedioxy group was made on the basis of NMR spectral data.[13]

Suitable synthetic procedures for the ring system have been developed only recently. In one method[14] used for homopterocarpin synthesis, the important intermediate is the corresponding 2′-hydroxy isoflavone. The partial methyl ether was conveniently made from the trimethyl ether by selective demethylation with aluminium chloride in acetonitrile. Subsequent treatment with sodium borohydride brings about the desired reduction and cyclodehydration. Using this general method, a number of other naturally occurring pterocarpans have also been synthesized.[15,16]

Such structures are not however unique for *Pterocarpus* or related woods. A closely similar compound is the antifungal component, pisatin, isolated from pea pods. 7-Desmethylpterocarpin (inermin) occurs in *Andira inermis*, its *β*-glucoside (trifolirhizin) in *Trifolium pratense*, and a more complex compound, phaseolin in *Phaseolus vulgaris*. The same skeleton is also present in coumestrol (IV) from clover, wedelolactone (V) from *Wedelia calendulacea* and



(IV) R$_1$=H ; R$_2$=OH
(V) R$_1$=OH; R$_2$=OCH$_3$

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[2] B. T. Brooks, *Phillipine, J. Sci.* 5A, 439 (1910).

[3] E. Spath and J. Schlager, *Chem. Ber.* 73, 1 (1940).

[4] F. E. King, C. B. Cotterill, D. H. Godson, L. Jurd and T. J. King, *J. Chem. Soc.* 3693 (1953).

[5] P. L. Sawhney and T. R. Seshadri, *J. Sci. Ind. Res.* 13B, 5 (1954).

[6] A. Akisanya, C. E. L. Bevan and J. Hirst, *J. Chem. Soc*, 2679 (1959).

[7] R. G. Cook and I. D. Rae, *Austral. J. Chem.* 17, 379 (1964).

[8] S. C. Bhrara, A. C. Jain and T. R. Seshadri, *Current Sci.* 33, 303 (1964).

[9] M. R. Parthasarathy, R. N. Puri and T. R. Seshadri, *Indian J. Chem.* 7, 118 (1969).

[10] S. H. Harper, A. D. Kemp and W. G. E. Underwood, *Chem. & Ind.* 562 (1965); *Chem. Commun.* 309 (1965).

[11] A. Robertson, A. McGookin and W. B. Whalley, *J. Chem. Soc.* 787 (1940).

[12] A. Robertson and W. B. Whalley, *J. Chem. Soc.* 1440 (1954).

[13] J. B-son Bredenberg and J. N. Shoolery, *Tetrahedron Letters* 285 (1961).

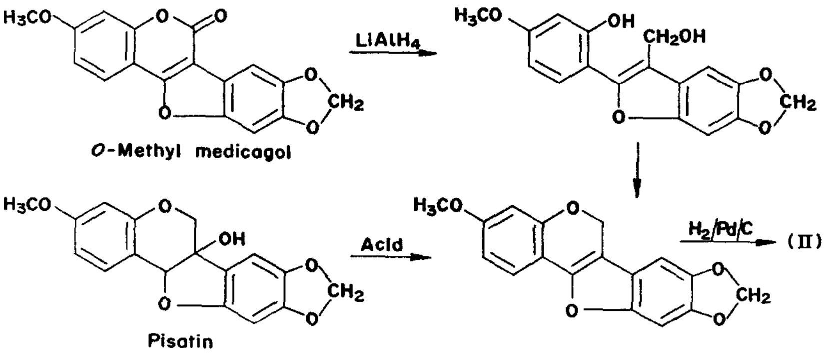
[14] K. Aghoramurthy, A. S. Kukla and T. R. Seshadri, *Current Sci.* 30, 218 (1961).

[15] V. K. Kalra, A. S. Kukla and T. R. Seshadri, *Indian J. Chem.* 4, 201 (1966).

[16] V. K. Kalra, A. S. Kukla and T. R. Seshadri, *Tetrahedron* 23, 3221 (1967).

other related compounds, though these are really coumarin derivatives as they have a lactone ring.

Based on the above relationship, a synthesis of (±) pterocarpin has been achieved.[17] The methyl ether of medicagol, a natural coumestan isolated from alfalfa (*Medicago*) and previously synthesized, was reduced with $LiAlH_4$ in tetrahydrofuran to give the intermediate alcohol (60% yield), which was cyclized in boiling diethylene glycol to yield anhydropisatin, earlier obtained from (+) pisatin. Catalytic hydrogenation produced (±) pterocarpin in 60% yield (Scheme 1).

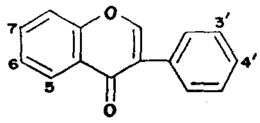


SCHEME 1. SYNTHESIS OF ± PTEROCARPIN.

Isoflavones

A number of isoflavones have been found in *Pterocarpus* species (Table 1). Prunetin and muningin were isolated from *P. angolensis*,[18] and formononetin has been recently reported to occur in *P. indicus*[7,8] wood. Santal was discovered in *P. santalinus*[19] and occurs in only one other source, viz. *P. osun*.[6] An isomer of muningin, 7-methyl tectorigenin, was isolated from muninga wood.[20] More recently, 3′-hydroxy formononetin was obtained from *P. dalbergioides*[9] and the related compound, pseudobaptigenin, from *P. erinaceous*.[21]

TABLE 1. ISOFLAVONES FROM *Pterocarpus*



Compound	Substitution pattern 7	6	5	4′	3′
Prunetin	OCH_3	H	OH	OH	H
Muningin	OCH_3	OH	OCH_3	OH	H
Formononetin	OH	H	H	OCH_3	H
Santal	OCH_3	H	OH	OH	OH
7-*O*-Methyltectorigenin	OCH_3	OCH_3	OH	OH	H
3′-Hydroxyformononetin	OH	H	H	OCH_3	OH
Pseudobaptigenin	OH	H	H	—O—CH_2—O—	

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[17] K. FUKUI and M. NAKAYAMA, *Tetrahedron Letters* 1805 (1966).

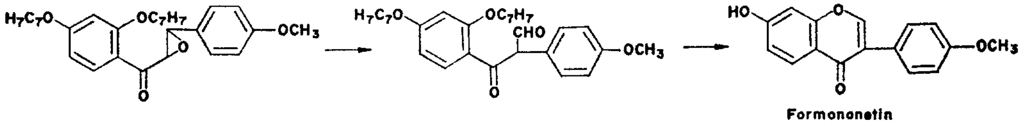
[18] F. E. KING, T. J. KING and A. J. WARWICK, *J. Chem. Soc.* 96 (1952).

[19] A. ROBERTSON, C. W. SUCKLING and W. B. WHALLEY, *J. Chem. Soc.* 1571 (1949).

[20] MORGAN and OSLER, *Chem. & Ind.* 1173 (1966).

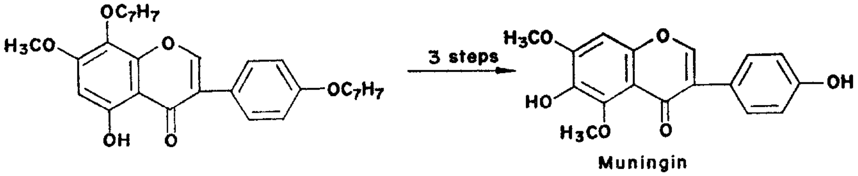
[21] C. E. L. BEVAN, D. E. U. EKONG, M. E. OBASI and J. W. POWELL, *J. Chem. Soc.* 509 (1966).

Prunetin and santal are 7-*O*-methyl ethers of genistein and orobol, respectively; they can be obtained either by partial methylation of these hydroxyisoflavones or by partial demethylation of the complete methyl ethers. Formononetin is 4′-*O*-methyl diadzein and has recently been synthesized using the corresponding dibenzyloxy chalcone epoxide as an intermediate.[22] The epoxide is isomerized with boron trifluoride; subsequent debenzylation produces formononetin in good yield (Scheme 2).



SCHEME 2. SYNTHESIS OF FORMONONETIN.

Muningin (Scheme 3) has the rare feature of possessing a methoxyl group in the 5-position. Since the 5-hydroxy group is less reactive because of chelation with the carbonyl group, it is normally difficult to methylate, especially when other hydroxyls have to be left free. The structure of muningin was established by alkali fusion of its methyl and ethyl ethers.[18] Its synthesis has been effected in two ways: the first starts with the 7-methyl ether of the required tetrahydroxy isoflavone, and the methylation of the 5-hydroxyl is carried out after suitable protection of the 6- and 4′-hydroxyl groups. The protecting groups used are benzoyl and acetyl and these are removed easily after methylation. The difference in reactivity of the various hydroxyl groups makes this method useful.[23,24] The second synthesis makes use of the ring isomeric change of hydroxyisoflavones in alkaline medium; the pyrone ring is easily opened under alkaline conditions.[25] When 5-hydroxy-7,8-dimethoxyisoflavone was boiled with 2% alcoholic potash for 15 min, it was converted smoothly into 5-hydroxy-6,7-dimethoxy isoflavone. Under these conditions 5-hydroxy-7-methoxy-8,4′-dibenzyloxyisoflavone yielded 5-hydroxy-7-methoxy-6,4′-dibenzyloxyisoflavone, which was methylated and debenzylated to yield muningin (Scheme 3).



SCHEME 3. SYNTHESIS OF MUNINGIN.

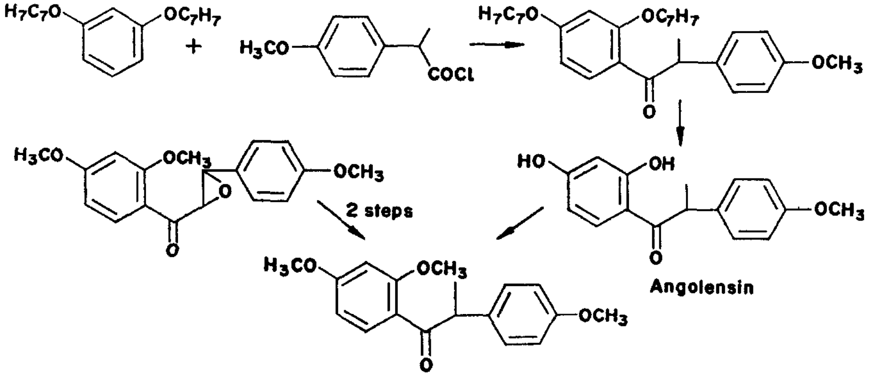
More recently Farkes *et al.*[26] have modified the reaction by using potassium ethoxide in the place of potassium hydroxide. This modification reduces the possibility of decomposition during alkali treatment. Thus, a useful method of synthesis of certain isoflavone methyl ethers is now available.

[22] S. K. GROVER, A. C. JAIN and T. R. SESHADRI, *Indian J. Chem.* **1**, 517 (1963).
[23] S. S. KARMARKAR, K. H. SHAH and K. VENKATARAMAN, *Proc. Ind. Acad. Sci.* **41A**, 192 (1956).
[24] M. L. DHAR and T. R. SESHADRI, *Proc. Indian Acad. Sci.* **43A**, 79 (1956).
[25] M. L. DHAR and T. R. SESHADRI, *Tetrahedron* **7**, 77 (1959).
[26] L. FARKAS and J. VARADY, *Chem. Ber.* **93**, 2685 (1960).

Deoxybenzoin

Angolensin possesses a 3-phenylchroman skeleton without the heterocyclic ring. The biosynthesis of the compound is probably similar to that of isoflavones. The carbon in the 2-position is completely reduced to a methyl group and angolensin is a C-methylated deoxybenzoin. It was first obtained from *P. angolensis*[18] and then from *P. indicus*[7,27]and *P. erinaceus.*[6] Outside *Pterocarpus* it occurs in some *Afrormosia* species.

By avoiding the use of base in extraction, angolensin can be obtained in an optically active form. Its structure was based on the results of alkali fusion of its methyl and the ethyl ethers; it was confirmed by the synthesis[28,29] of (±)-angolensin involving the condensation of resorcinol and *p*-methoxyhydratropic acid following a possible method of biogenesis (Scheme 4); the related *p*-methoxyhydratropic acid occurs with angolensin in *P. indicus.* A more convenient method of synthesis is direct methylation of the reactive —CH_2— of the deoxybenzoin after necessary protection of the hydroxy groups (Scheme 4). Di-*O*-methylangolensin and di-*O*-benzylangolensin have been obtained from 2,4,4′-trimethoxydeoxybenzoin and 2,4-dibenzyloxy-4′-methoxydeoxybenzoin by prolonged methylation with methyl iodide in acetone solution in the presence of anhydrous potassium carbonate.[30] The latter, on catalytic debenzylation, affords (±)-angolensin. A convenient synthesis of the methyl ether of angolensin has been carried out in a different way, starting from the corresponding chalcone via the epoxide[22] (Scheme 4).



Scheme 4. Synthesis of angolensin.

2-Phenylchromans

No 2-phenylchroman was known to occur in *Pterocarpus* woods until 1956, when an examination of the alcohol extracts of many *Pterocarpus* species led to the isolation of liquiritigenin and isoliquiritigenin:[7,31] the former is 7,4′-dihydroxyflavone and the latter, the corresponding chalcone. Co-occurrence of chalcone-flavanone pairs is fairly frequent. (—)-Epicatechin also occurs in *P. marsupium* kino and bark.

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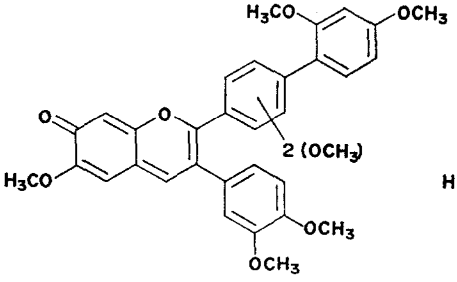
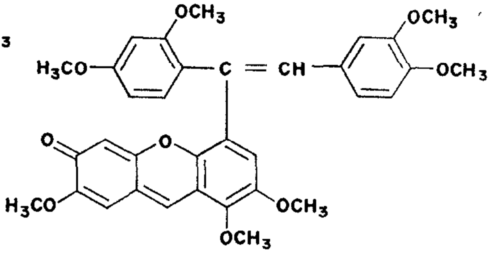
[27] V. N. Gupta and T. R. Seshadri, *J. Sci. Ind. Res.* **15B**, 146 (1956).
[28] V. N. Gupta and T. R. Seshadri, *Proc. Indian Acad. Sci.* **44A**, 223 (1956).
[29] S. K. Aggarwal, S. K. Grover and T. R. Seshadri, *Indian J. Chem.* **9**, 299 (1971).
[30] S. K. Aggarwal, S. K. Grover and T. R. Seshadri, *Indian J. Chem.* **8**, 478 (1970).
[31] P. L. Sawhney and T. R. Seshadri, *J. Sci. Ind. Res.* **15C**, 154 (1956).

An important pigment of this type is the anhydrobenzopyranol, santalin; in 1832 Pelletier obtained a crude preparation. It was not until 1954 that Robertson and Whalley[32] assigned a tentative structure (VI) for santalin methyl ether. Later, Dean[33] suggested that the compound may be related to the xanthones and, based mainly on biogenetic grounds, incorporated a stilbene unit (VII); this latter structure, however, needs definite chemical proof. Neither VI nor VII adequately explains all the chemical reactions of the compound, and further study is therefore required.



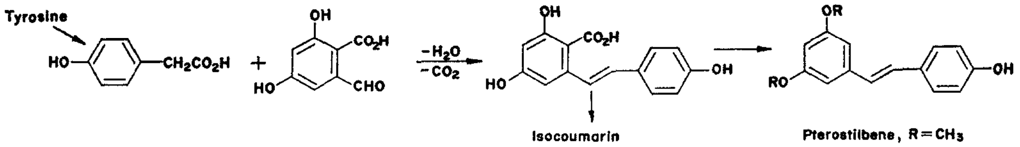
(VI)



(VII)

Stilbenes

The only stilbene that occurs in this genus is pterostilbene. It was isolated first by Späth[34] from red sandalwood (*P. santalinus*). He assigned the correct structure (Scheme 5) and effected its synthesis. It is best isolated as its acetate. Pterostilbene is a potent insecticide and antidiabetic. It appears to be the active principle of *P. marsupium*, used as drug for diabetes. Pterostilbene has been considered a common component of all the *Pterocarpus* woods, just as pinosylvin and its methyl ether are in the pine woods. However, it is absent in a few of the African padauks,[6] e.g. *P. mildbreaedii* and *P. santalinoides*. These woods do not contain any phenolic compounds, but have only terpenoids like acetyloleanolic acid; they are not fungus-resistant. In *P. indicus* and *P. angolensis* also there is no pterostilbene, but the presence of angolensin is considered to provide resistance. Pterostilbene is an example of the combination of the C_8 and C_9 units, which leads by a few steps to the final stilbene (Scheme 5). The justification for this scheme has been discussed in detail elsewhere,[35] especially the substitution pattern and the natural occurrence of the related phenyl isocoumarins.



SCHEME 5. BIOSYNTHESIS OF PTEROSTILBENE.

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[32] A. ROBERTSON and W. B. WHALLEY, *J. Chem. Soc.* 2794 (1954).

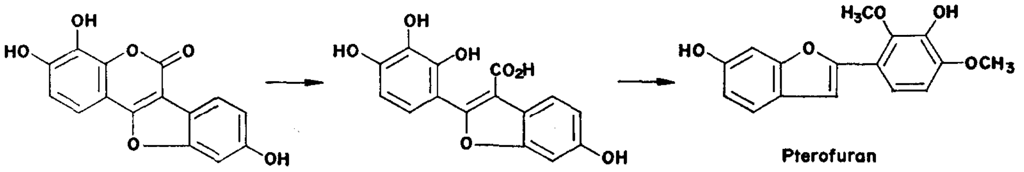
[33] F. M. DEAN, *Naturally Occurring Oxygen Ring Compounds*, p. 414 (1963).

[34] E. SPATH and T. SCHLAGER, *Chem. Ber.* **73**, 881 (1940).

[35] T. R. SESHADRI, *Current Sci.* **26**, 310 (1957).

Benzofuran

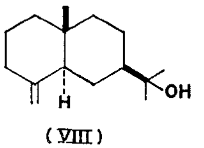
Pterofuran isolated from *P. indicus*[7] belongs to a novel group of benzofurans with a phenyl substituent in the 2-position. Its structure was assigned on the basis of NMR spectra. It does not have the conventional C_{15}-skeleton, but a C_{14}. It may appear to be closely related to stilbenes, but stilbenes with 2-hydroxy group on both benzene rings, do not occur in nature. An alternative origin may be from a C_{15} isoflavan derivative. The furan could be derived from the corresponding coumestan by loss of one carbon, involving two steps; (i) opening of the coumarin ring, and (ii) elimination of carbon dioxide (Scheme 6).



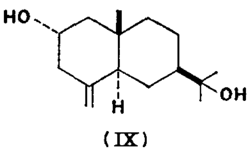
SCHEME 6. BIOSYNTHESIS OF PTEROFURAN.

Terpenoid Compounds from Pterocarpus *Woods*

Till very recently the only compound of this class known to occur in *Pterocarpus* woods was the triterpene acid, acetyloleanolic acid. However, the pleasant aroma of the heartwoods of this genus indicated the possibility of the occurrence of volatile terpenes. A recent investigation has shown the presence of β-eudesmol (VIII) in *P. indicus* heartwood and a closely related sesquiterpenediol, pterocarpol, in *P. macrocarpus* wood.[36] Pterocarpol (IX), $C_{15}H_{26}O_2$ contains an exomethylene double bond and two alcoholic hydroxyl groups, of which one is secondary and the other tertiary. Its structure is based on eudalene, which is formed by selenium dehydrogenation. Detailed chemical and spectral studies indicated that pterocarpol is hydroxy-β-eudesmol with extra hydroxyl in the 2-position. The above mentioned wood is a poor and unsatsifactory source; recently we have obtained pterocarpol more conveniently and in much better yield from *P. santalinus*.[37]



(VIII)



(IX)

Polyphenols of Dalbergia

There are many species in the world belonging to the genus *Dalbergia*. Of India's 35 spp., only 4 are important for good timber; *D. sissoo*, *D. latifolia*, *D. lanceolaria* and D. *paniculata*. Among them, *D. sissoo* is most valued not only for the durability of its timber but also for

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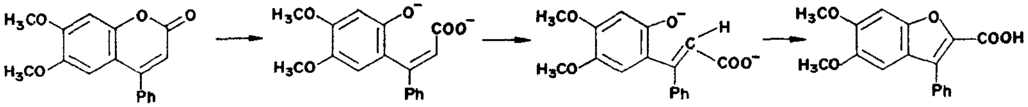
[36] M. R. PARTHASARATHY and T. R. SESHADRI, *Current Sci.* **34**, 115 (1965).

[37] C. P. BAHL, M. R. PARTHASARATHY and T. R. SESHADRI, *Tetrahedron* **24**, 6231 (1968).

its resistance to attack by insects and micro-organisms. *Dalbergia latifolia* is commonly known as 'Black wood' or 'Indian Rose wood', and its timber has almost the same properties and uses as those of *D. sissoo*; because of its colour, it is more commonly used for art work and for drawing-room furniture. The woods of *D. lanceolaria* and *D. paniculata* are not as durable as the above two, but they are also widely used. Other important non-Indian species of *Dalbergia* that have been studied chemically are *D. nigra*, *D. violacea*, *D. baroni*, *D. cochinchinensis*, *D. melanoxylon* and *D. obtusa*. They have provided a large number of neoflavonoid and isoflavonoid derivatives. Considerable data are available on the components of many tree parts, but here attention is restricted to woods and barks.

The study of *Dalbergia* woods began comparatively recently, and *D. sissoo* was the earliest studied;[38] its chief component, dalbergin, was probably the first simple 4-phenylcoumarin isolated as natural product.[41] More recently a number of related compounds have been obtained from this wood and from other sources. The name dalberginoids was first used for them, but there was later a change to the more appropriate name neoflavonoids, embracing related groups of compounds.

Two interesting properties are associated with 4-phenylcoumarins. One is the colour reaction they give with magnesium and hydrochloric acid: initially an emerald green colour is produced which changes to a permanent red similar to that given by normal flavonoids; the formation of 4-phenylbenzopyrilium salts seems to be responsible for this colour. Also, the methyl ethers are readily oxidized with mercuric oxide in alkaline solution to the corresponding coumarilic acids. This conversion involves the formation of the β-phenyl coumaric acid as an intermediate stage under the catalytic influence of mercuric oxide; subsequent ring closure accompanied by dehydrogenation by HgO gives the coumarilic acid[39] (Scheme 7).



SCHEME 7. CONVERSION OF 4-PHENYLCOUMARINS INTO CORRESPONDING COUMARILIC ACID.

The neoflavonoids can be placed under 5 major groups as follows: 4-phenylcoumarins, dalbergiquinols, dalbergiquinones and brazilins.

Dalbergin Group (4-Phenylcoumarins)

This is the largest group among neoflavonoids and contains a number of complex derivatives. There are only a few compounds with substituents in the 4-phenyl ring. The presence of isoprene units and their incorporation into new rings leads to the complexity of products; such compounds are present in oil seeds. Those that occur in *Dalbergia* woods are comparatively simple and are given in Table 2.

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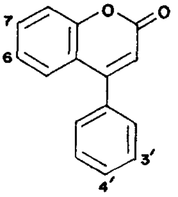
[38] Y. P. KATHPALIA and S. DUTT, *Indian Soap J.* **18**, 213 (1953).

[39] V. K. AHLUWALIA, A. C. MEHTA and T. R. SESHADRI, *Tetrahedron* **4**, 271 (1958).

TABLE 2. 4-PHENYLCOUMARINS IN *Dalbergia* SPECIES



Compound	Substitution	Source	Ref.
Dalbergin	6-Hydroxy-7-methoxy	*Dalbergia sissoo*	40, 41
		D. latifolia	42
		D. baroni	43
		M. scleroxylon	44
Methyl dalbergin	6,7-Dimethoxy	*D. sissoo*	41
		M. scleroxylon	44
Nordalbergin	6,7-Dihydroxy	*D. sissoo*	45
Isodalbergin	6-Methoxy-7-hydroxy	*D. sissoo*	45
Melannein	3′,6-Dihydroxy-4′,7 dimethoxy	*D. melanoxylon*	43
		D. baroni	43
Exostemin	8-Hydroxy-4′,5,7-trimethoxy	*Exostemma caribaeum*	46

Latifolin group (Dalbergiquinols)

Latifolin (X) was isolated as a major component from *Dalbergia latifolia.*[47–49] A second type, methoxyobtusaquinol (XI), is a minor constituent of *Machaerium scleroxylon.* It was isolated by Eyton *et al.*,[44] but its chemistry has not been worked out in detail. The isolation of obtusaquinol (XII) from *D. obtusa* and of kuhlmanniquinol (XIII) from *Machaerium kuhlmanni* and from *M. nictitans* has been briefly reported by Ollis *et al.*[50] These compounds have the carbon skeleton of the 4-phenylcoumarins intact, but the heterocyclic ring is opened.

Latifolin is an optically active compound with an asymmetric centre in the benzylic position. The ORD curve is not helpful in establishing the absolute configuration. A study has therefore been made of the oxidation products obtained by CrO_3 oxidation of dihydrolatifolin dimethyl ether. The *para* quinone is yellow and the *ortho*, red. Both the quinones show a marked negative Cotton effect. Since the negative Cotton effect with similar curve shape has been correlated with *R* configuration in the related 4-methoxydalbergenone, the latifolin quinones and consequently latifolin should also have the *R*-configuration.[51]

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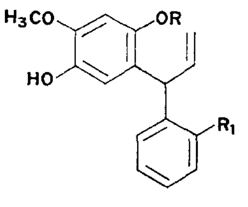
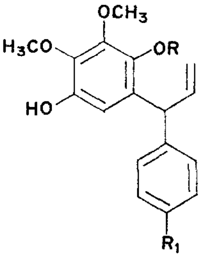
[40] V. K. AHLUWALIA, P. L. SAWHNEY and T. R. SESHADRI, *J. Sci. Ind. Res.* **15B**, 66 (1956).
[41] V. K. AHLUWALIA and T. R. SESHADRI, *J. Chem. Soc.* 970 (1957).
[42] M. M. RAO and T. R. SESHADRI, *Tetrahedron Letters* 211 (1963).
[43] B. J. DONNELLY, D. M. X. DONNELLY and A. M. O'SULLIVAN, *Tetrahedron* **24**, 2617 (1968).
[44] W. B. EYTON, W. D. OLLIS, M. FINEBERG, O. R. GOTTLIEB, I. SALIGNAC DE SOUZA GUIMARAES and M.T. MAGALHAES, *Tetrahedron* **21**, 2697 (1965).
[45] S. K. MUKHERJEE, T. SAROJA and T. R. SESHADRI, *Tetrahedron* **27**, 799 (1971).
[46] F. SANCHEZ-VIESCA, *Phytochem.* **8**, 1821 (1969).
[47] S. BALAKRISHNA, M. M. RAO and T. R. SESHADRI, *Tetrahedron* **18**, 1503 (1962).
[48] D. KUMARI, S. K. MUKERJEE and T. R. SESHADRI, *Tetrahedron* **21**, 1495 (1965).
[49] D. M. X. DONNELLY, M. R. GEOGHEGAN, B. J. NANGLE and R. A. LAIDLAW, *Tetrahedron Letters* 4451 (1965).
[50] W. D. OLLIS, B. T. REDMAN, R. J. ROBERTS, I. O. SUTHERLAND and O. R. GOTTLIEB, *Chem. Commun.* 1392 (1968).
[51] D. KUMARI, S. K. MUKERJEE and T. R. SESHADRI, *Tetrahedron Letters* 3767 (1966).



(X) R = CH$_3$, R$_1$ = OH
(XII) R = R$_1$ = H

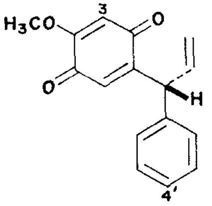


(XI) R = R$_1$ = H
(XIII) R = CH$_3$, R$_1$ = OH

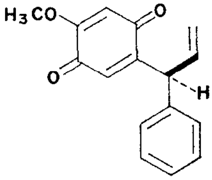
Dalbergenone group (*Dalbergiquinones*)

Dalbergiquinones are also found in *Dalbergia* species and are closely related to the latifolin group. Their occurrence is restricted to *Dalbergia* and *Machaerium* woods. The known compounds are given in Table 3. The explanation for the name has been given earlier.

TABLE 3. NATURAL DALBERGENONES



R



S

Compound	Stereo chemistry	Source	Ref.
Dalbergenone	R	*D. nigra*	52
		D. latifolia	42, 53
		D. obtusa	50
Dalbergenone	S	*D. sissoo*	54
		D. violacea	55
		D. baroni	56
		D. spruceana	57
4′-Hydroxydalbergenone	S	*D. nigra*	57
		D. violacea (syn. *D. miscolobium*)	
4′-Methoxydalbergenone	S	*D. nigra*	57
		D. violacea	57
3-Methoxydalbergenone	R	*M. scleroxylon*	44
		M. nictitans	50
		M. kuhlmanni	50
3-Methoxy-4′-hydroxy-dalbergenone	R	*M. nictitans*	50

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[52] W. B. EYTON, W. D. OLLIS, I. O. SUTHERLAND, L. M. JACKMAN, O. R. GOTTLIEB and M. T. MAGALHAES, *Proc. Chem. Soc.* 301 (1962).

[53] C. B. DEMPSEY, D. M. X. DONNELLY and R. A. LAIDLAW, *Chem. & Ind.* 491 (1963).

[54] V. K. AHLUWALIA and T. R. SESHADRI, *Current Sci.* **32,** 455 (1963).

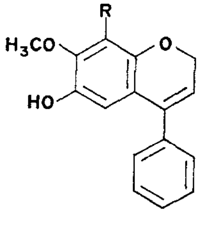
[55] W. B. EYTON, W. D. OLLIS, I. O. SUTHERLAND, O. R. GOTTLIEB, M. TAVEIRA MAGALHAES and L. M. JACKMAN, *Tetrahedron* **21,** 2683 (1965).

[56] B. J. DONNELLY, D. M. X. DONNELLY and C. B. SHARKEY, *Phytochem.* **4,** 337 (1965).

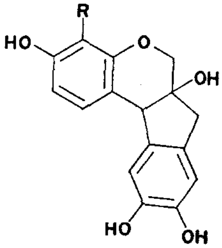
[57] W. D. OLLIS, *Recent Advances in Phytochemistry* (edited by T. J. MABRY), Vol. I, pp. 329–74, North Holland Publication, Amsterdam (1968).

Dalbergichromene Group (Neoflavenes)

These are more closely related to the coumarins and only two are known. Dalbergichromene[45] was obtained as a pale yellow crystalline compound, m.p. 99–100°. It has the molecular formula $C_{16}H_{14}O_3$ and is thus isomeric with dalbergenone. From the NMR spectrum of the compound and by its synthesis from dalbergenone, its structure (XIV) was determined. Dalbergichromene is the first neoflavene isolated from the genus *Dalbergia* and the second natural neoflavene, the earlier being kuhlmannene (XV)[50] occurring in *Machaerium kuhlmanni* and *M. nictitans.*



(XIV) R=H
(XV) R=OCH_3



(XVI) R=H
(XVII) R=OH

Brazilin Group

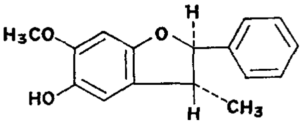
Brazilin (XVI) and haematoxylin (XVII) have been known for a long time. The former was obtained from Brazil wood and sappan wood, and the latter, from logwood. It is obvious that they are derivatives of 4-phenylchromans with the addition of a —CH_2— forming a new condensed ring. These compounds are not found in *Dalbergia* species.

Other Compounds

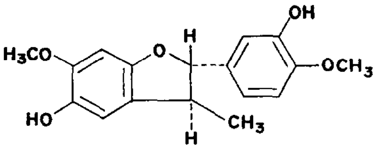
The following groups of compounds also occur in *Dalbergia* species but they are not neoflavonoids in structure: furans, benzyl styrenes, benzophenones, flavonoids and isoflavonoids.

The Furan Group

Obtusafuran (XVIII)[58] and melanoxin (XIX)[59] are the only *furans* in *Dalbergia.* From the nature of the skeleton they are related to normal flavonoids and not to the neoflavonoids. Those directly related to neoflavonoids have not yet been discovered, but they are conveniently synthesized from 4-phenylcoumarins through the intermediate coumarilic acids.



(XVIII)



(XIX)

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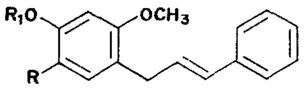
[58] M. Gregson, W. D. Ollis, B. T. Redman, I. O. Sutherland and H. H. Dietrichs, *Chem. Commun.* 1394 (1968).

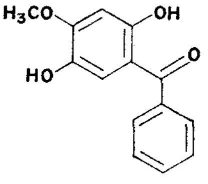
[59] B. J. Donnelly, D. M. X. Donnelly, A. M. O'Sullivan and J. P. Prendergast, *Tetrahedron* **25**, 4409 (1969).

Benzyl Styrenes (Cinnamyl Phenols)

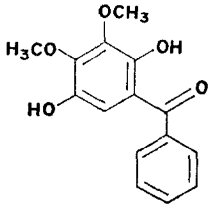
Obtusastyrene (XX), violastyrene (XXI) and isoviolastyrene (XXII) are the important members in *Dalbergia*; others occur in *Machaerium* species.[57] They accompany the latifolin group and are isomers; however, their molecular skeletons are those of 2-phenylchromans that constitute normal flavonoids. They are chalcones with $C{=}O$ group reduced to $—CH_2—$.



(XX) $R{=}R_1{=}H$
(XXI) $R{=}OCH_3; R_1{=}H$
(XXII) $R{=}OH; R_1{=}CH_3$



(XXIII)



(XXIV)

Laboratory experiments indicate that they are readily formed by the isomerization of latifolin derivatives in the presence of BF_3 as catalyst. The presence of substituent groups has an important effect on the ease of this isomerization.[60]

Benzophenones

Benzophenone derivatives are frequently found in *Dalbergia* and related woods and seem to represent oxidation products of the dalbergin and latifolin groups; e.g. cearoin (XXIII), from *D. cearensis* and *D. miscolobium*.[57] A related compound, scleroin (XXIV), occurs in *Machaerium scleroxylon*.[44]

2-*Phenylchroman Group (Flavonoids)*

Among the compounds isolated from heartwood of *D. latifolia*, liquiritigenin[61] is a normal flavonoid. Its presence along with the neoflavonoids (dalbergin and dalbergenone) supports the existence of common origin for the two groups and their formation from the same component C_6 and C_9 units.

3-*Phenylchroman Group (Isoflavonoids)*

Although several isoflavones could be isolated from the flowers, leaves and root bark of *D. sissoo*[62,63] and *D. lanceolaria*,[64,65] they are not found in heartwoods; but the heartwood of *D. paniculata* is rich in isoflavonoids.[66] It gave a good amount of sissotrin, biochanin-A 7-glucoside (XXV), and a lesser amount of paniculatin, a new genistein-6,8-di-*C*-glucoside. Paniculatin was present in larger amounts in the bark,[67] which also contained two free isoflavones (biochanin-A and formononetin). *C*-Glycosides of isoflavones are a new group, whose study has grown during the past 10 years. Paniculatin (XXVI) is the only representa-

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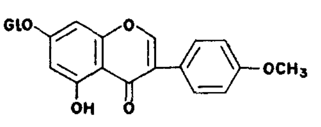
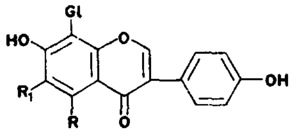
[60] D. KUMARI, S. K. MUKERJEE and T. R. SESHADRI, *Tetrahedron Letters* 1153 (1967).
[61] G. D. BHATIA, S. K. MUKERJEE and T. R. SESHADRI, *Indian J. Chem.* 3, 422 (1965).
[62] A. BANERJI, V. V. S. MURTI, T. R. SESHADRI and R. S. THAKUR, *Indian J. Chem.* 1, 25 (1963).
[63] A. BANERJI, V. V. S. MURTI and T. R. SESHADRI, *Indian J. Chem.* 4, 70 (1966).
[64] A. MALHOTRA, V. V. S. MURTI and T. R. SESHADRI, *Current Sci.* 36, 484 (1967).
[65] A. MALHOTRA, V. V. S. MURTI and T. R. SESHADRI, *Tetrahedron* 23, 405 (1967).
[66] V. NARAYANAN and T. R. SESHADRI, *Indian Acad. Wood Sci.* 1, 1 (1970).
[67] V. NARAYANAN and T. R. SESHADRI, *Indian J. Chem.* 9, 14 (1971).

tive of isoflavone di-*C*-glucosides; mono-*C*-glucosides were known earlier, e.g. puerarin (XXVII).[68]

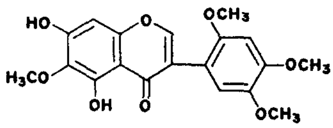
Formononetin (Scheme 2) and caviunin (XXVIII) are the two heartwood isoflavones obtained from *D. baroni*[43] and *D. nigra*,[69] respectively. Some pterocarpans are stated to occur in *Dalbergia* species[57] but details have not been published.



(XXV)



(XXVI) R=OH; R₁=glucosyl
(XXVII) R=R₁=H



(XXVIII)

Biogenesis and Synthesis of Neoflavonoids

The natural origin of dalbergiquinols (latifolin group) and of the whole group of neoflavonoids has been the subject of recent intensive study. As already mentioned, the 4-phenylcoumarins form the largest group among neoflavonoids and at present number over 20. The others are comparatively less in number and are less widely distributed.

Shortly after the discovery of 4-phenylcoumarins, the suggestion was made that they are formed by the linkage of the same C_6 and C_9 units which give rise to the larger group of flavonoids.[70] With the isolation of latifolin, its close structural relationship with dalbergins was emphasized.[47] A fuller discussion of biogenesis including dalbergenones was made in 1963.[71] Subsequently it was proposed that 4-phenylcoumarins are the likely precursors of the whole group of neoflavonoids.[72,73] They themselves are formed by *O*-acylation of a reactive phenol with cinnamoyl coenzyme A, followed by cyclization of the cinnamic ester. The work of Kunesch and Polonsky showing that the C_9 unit of 4-phenylcoumarin arises from phenylalanine without aryl migration supports this proposal.[74] Our recent work,[75,76] following up this line of thought in effecting laboratory synthesis is briefly recounted below (Scheme 8):

$$\begin{tikzcd}
 & \text{Isoflavonoids} & \text{Chalcones} \arrow[l] \arrow[r] & \text{Flavonoids} & \\
 & & C_6 + C_9 \arrow[u, "C\text{-Acylation}"'] \arrow[d, "O\text{-Acylation and ring closure}"'] & & \\
\text{4-Phenylchromenes} & & \text{4-Phenylcoumarins} \arrow[ll] \arrow[r] & \text{Dalbergiquinols} \arrow[r] & \text{Dalbergiquinones}
\end{tikzcd}$$

SCHEME 8. BIOGENETIC RELATIONSHIPS OF FLAVONOIDS AND NEOFLAVONOIDS.

Synthesis of 4-Phenylcoumarins

The earliest known and the best method of obtaining simple 4-phenylcoumarins is the Pechmann condensation of phenols (C_6 unit) with benzoylacetic ester (C_9 unit). We have,

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[68] S. SHIBATA, T. MURAKAMI, Y. NISHIKAWA and W. BUDIDARMO, *Congr. Sci. Pharm.* 214 (1959); *Chem. Abs.* **56**, 3564 (1962).

[69] O. R. GOTTLIEB, and M. T. MAGALHAES, *J. Org. Chem.* **26**, 2449 (1961).

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

[71] T. R. SESHADRI, *J. Indian Chem. Soc.* **40**, 497 (1963).

[72] D. KUMARI, S. K. MUKERJEE, T. SAROJA and T. R. SESHADRI, *Current Sci.* **35**, 477 (1966).

[73] D. KUMARI, S. K. MUKERJEE and T. R. SESHARDI, *Tetrahedron* **22**, 3491 (1966).

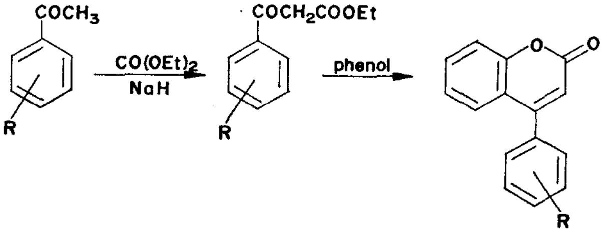
[74] G. KUNESCH and J. POLONSKY, *Chem. Commun.* 317 (1967).

[75] S. K. MUKERJEE, T. SAROJA and T. R. SESHARDI, *Indian J. Chem.* **7**, 671 (1969).

[76] S. K. MUKERJEE, T. SAROJA and T. R. SESHADRI, *Indian J. Chem.* **8**, 21 (1970).

therefore, utilized this method and, as the necessary preliminary step, improved the method of preparation of the esters.[75]

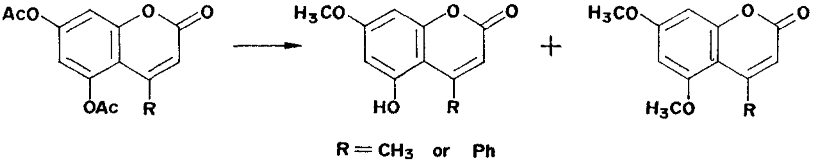
Benzoylacetic esters were earlier prepared from ethyl acetoacetate. Although this gives the simple benzoylacetic ester in high yields, for substituted ones it is not good. We have, therefore, used a modification of the method of Wallingford *et al.*,[77] who condensed substituted acetophenones with excess of diethyl carbonate in the presence of sodium ethoxide. The modification consists in using sodium hydride as the base and carrying out the reaction in a mixture of ether and tetrahydrofuran, using lower temperatures and avoiding excess of ketone (Scheme 9).



SCHEME 9. SYNTHESIS OF 4-PHENYLCOUMARINS.

Partial Methylation of 4-Phenylcoumarins

Partial methylation seems to be a natural process involved in the formation of various substituted 4-phenylcoumarins. Laboratory studies have shown that a number of factors are involved in the process. The most important is the acidity of the concerned hydroxyl groups arising out of the conjugation with the lactone carbonyl. In 5,7-dihydroxycoumarin the one in the 5-position is more reactive. This is modified by a steric factor when the 4-position is substituted by a methyl or phenyl group (Scheme 10). In this case, the 5-hydroxyl becomes less reactive as compared to 7-hydroxyl.[78] In 6,7- and 7,8-dihydroxy compounds the difference between the 7- and the other hydroxyl groups is more marked. Even then direct partial methylation of polyhydroxycoumarins does not give good yields. It is far better to use the acetates for methylation in a suitable solvent.



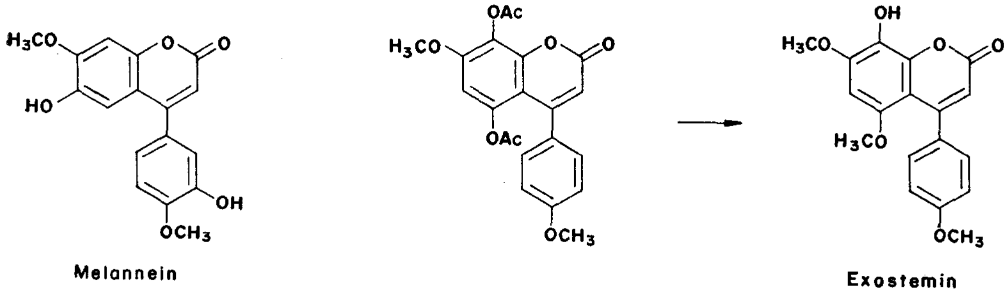
SCHEME 10. SYNTHESIS OF *O*-METHYL ETHERS OF 4-PHENYLCOUMARINS

Melannein (Scheme 11), as a partial methyl ether, is significant in that the pattern in both the rings A and B is similar and the more acidic 7- and 4′-hydroxy groups are methylated. The best approach to the synthesis of this molecule is by the partial methylation of the acetate of 6,7-dihydroxy-4-(3,4-dihydroxyphenyl) coumarin. The nature of the solvent has

[77] V. H. WALLINGFORD, A. H. HOMEYER and D. M. JONES, *J. Am. Chem. Soc.* **63**, 2252 (1941).

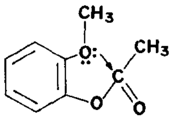
[78] S. K. MUKERJEE, T. SAROJA and T. R. SESHADRI, *Indian J. Chem.* **7**, 844 (1969).

also a marked effect: besides the boiling point, the dielectric constant is very important. Partial methylation was fastest and most selective in DMF at 90°. The reaction was complete in 30 min; melannein[78] was produced in about 70 % yield after deacetylation of the product. The efficacy of this new reaction condition has been studied with a number of select polyhydroxy 4-phenylcoumarins, and the synthesis of exostemin also accomplished[79] (Scheme 11).



SCHEME 11. MELANNEIN AND EXOSTEMIN.

The methylation of a phenol acetate seems to take place in two steps. The first is the production of phenoxide ion on the surface of K_2CO_3 by loss of acetyl group; the 7-acetoxyl undergoes preferential deacetylation. This step is found to be facile and takes place even in contact with silica gel. The second step involves the methylation of the phenoxide ion by methyl iodide whose ionization is favoured by solvent efficiency. DMF seems to play a major role in this second step.[78] Methylation of the phenoxide is very fast in this medium. After the 7-methoxyl is formed, the neighbouring acetoxyl group becomes resistant because of the stabilizing effect of coordination, as shown in (XXX). A good yield of partial methyl ether results.

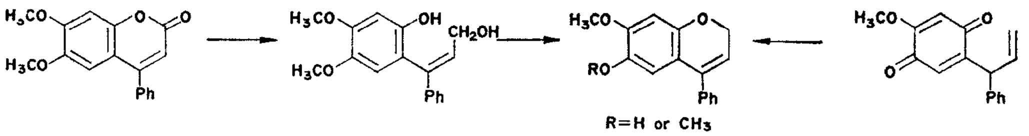


(XXX)

4-*Phenylchromenes*[45]

Similar to the 4-phenylcoumarins are the 4-phenylchromenes; both have the same carbon skeleton. It is obvious that the chromenes are related to the coumarins and are the products of a reduction process. As a result of our idea that they are formed in nature from 4-phenylcoumarins (through the stages of reduction to cinnamyl alcohols followed by cyclization), the cyclization of several diphenyl allyl alcohols with different reagents has been investigated (Scheme 12). The best reagent is a strong cation exchange resin (IR 120, H^+ form) in refluxing benzene medium. 6,7-Dimethoxy-4-phenylchrom-3-ene, obtained in this way from methyl dalbergin, was identical with methyl dalbergichromene in all respects. In a similar way 7-methoxy-4-phenylchrom-3-ene and 6,7-dimethoxy-4-(2-methoxyphenyl) chrom-3-ene were prepared from the corresponding 4-phenylcoumarins. The first stage reduction of the concerned coumarins to the cinnamyl alcohols is discussed in the next section.

[79] S. K. MUKERJEE, T. SAROJA and T. R. SESHADRI, *Tetrahedron* **24**, 6527 (1968).

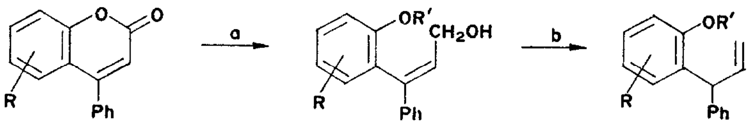


SCHEME 12. SYNTHESIS OF 4-PHENYLCHROMENES.

The facile isomerization of dalbergenones into the dalbergichromenes indicates an alternative path of biogenesis, the original precursors, however, being 4-phenylcoumarins (see later).

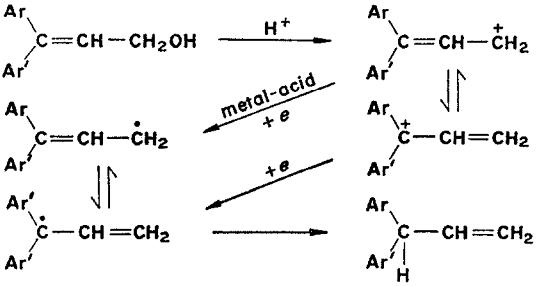
Conversion of 4-Phenylcoumarins into the Latifolin Type

The most important step proposed in the present scheme of biogenesis is the formation of the latifolin type from the corresponding 4-phenylcoumarins. This transformation requires two stages of reduction; (a) reduction of a coumarin to a cinnamyl alcohol, and (b) reductive elimination of the alcoholic hydroxyl group (Scheme 13).



SCHEME 13. SYNTHESIS OF DALBERGIQUINOLS.

LAH is a convenient reagent for step (a)[76]; step (b) is found to proceed smoothly with simple cinnamyl alcohols by means of a mixture of $AlCl_3$ and LAH. However, though 6,7-dimethoxy-4-(2-methoxy phenyl) coumarin gave the allyl alcohol in excellent yields, the stage (b) did not proceed satisfactorily to yield latifolin dimethyl ether by the method described above. This was eventually accomplished by shaking a solution of the above allyl alcohol in DMF containing concentrated hydrochloric acid with amalgamated zinc dust until the alcohol disappeared. The reaction consists of the initial formation of carbonium ion[80] followed by mild reduction with the metal-acid combination (Scheme 14).[76]

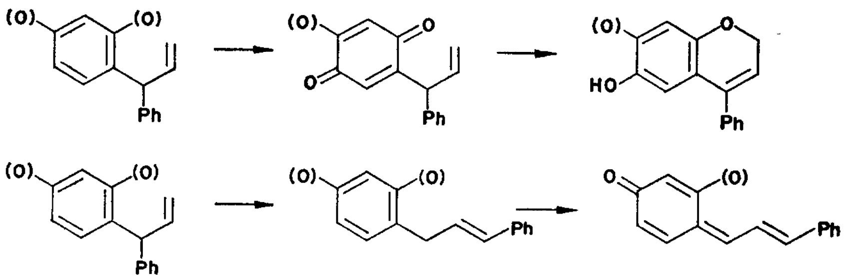


SCHEME 14. INTRACONVERSIONS IN THE DALBERGIQUINOL SERIES.

Conversions into Other Neoflavonoids

The latifolin type thus produced, occupies a key position in the biogenetic scheme. All other sub-groups of neoflavonoids can be derived from it by steps which can be considered to be applicable to biogenesis (Scheme 15). Thus oxidation leads to the dalbergiquinones,

[80] L. JURD, *Tetrahedron* **25**, 1407 (1969).



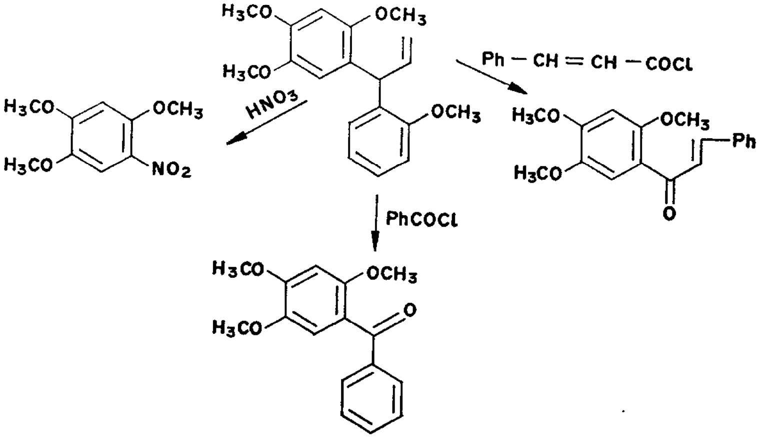
SCHEME 15. BIOGENESIS OF NEOFLAVONOIDS.

which can further isomerize to the neoflavenes. Alternatively, as already indicated, the latter can also arise by direct cyclization of the diphenyl allyl alcohols.[45,76]

Conversion into Other Types

As already mentioned there are a number of types that occur along with neoflavonoids› though they are not neoflavonoids in structure. It has been demonstrated[60] that the latifolin type undergoes easy isomerization into the co-occurring cinnamyl phenols which are not neoflavonoids. This reaction could take place in nature and account for the formation of cinnamyl phenols. Oxidation of the latter to the recently discovered quinone methides[81] has been shown to be feasible in the laboratory. Obtusafuran[58] and melanoxin,[59] the two recently discovered dihydrofurano compounds of *Dalbergia* woods are not related to neoflavonoids in structure and may be produced from normal flavonoids of the flavylium salt type by steps of oxidation and reduction. However, it is possible to consider their origin from the latifolin type through an intermediate cyclopropane derivative whose facile formation from latifolin has recently been reported.[76,82]

A characteristic property of the latifolin system is its readiness to undergo ionic displacements:[83] e.g. when latifolin dimethyl ether was treated with a number of suitable



SCHEME 16. REACTIONS OF LATIFOLIN METHYLETHER.

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[81] M. GREGSON, W. D. OLLIS, B. T. REDMAN, I. O. SUTHERLAND and H. H. DIETRICHS, *Chem. Commun.* 1395 (1968).

[82] D. KUMARI, S. K. MUKERJEE and T. R. SESHADRI, *Tetrahedron Letters* 4169 (1967).

[83] D. KUMARI, S. K. MUKERJEE and T. R. SESHADRI, *Indian J. Chem.* 4, 479 (1966).

cations, the C_9 unit was displaced by a new group. Thus by the action of a mixture of benzoyl chloride and anhydrous $AlCl_3$ (source of benzoylium ion), 2,4,5-trmethoxybenzophenone was obtained in good yields. Similarly when cinnamoyl chloride was used, instead, it yielded the corresponding chalcone. With dil. HNO_3 under mild conditions the nitro-derivative was obtained as the sole product in high yields. Although this reagent is well known for its oxidation of para dimethoxy groups to para quinones, no such quinonoid products could be obtained in this reaction.[83]

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Key Word Index—Pterocarpus; *Dalbergia*; Leguminosae; chemotaxonomy; flavonoids; neoflavonoids; desoxybenzoins; pterocarpans; terpenes.