BIOGENESIS OF NATURALLY OCCURRING 3- AND 4-PHENYLCHROMAN DERIVATIVES AND BENZOPHENONES

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3-Phenylchroman Derivatives

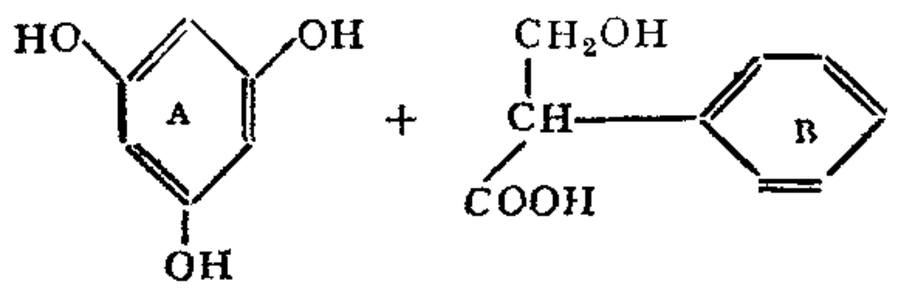
In a recent publication[1] it was pointed out that C_9 units with the forked arrangement occur in nature fairly widely. Besides tropic acid (I *b*), polyporic and pulvinic acid derivatives form substantially numerous groups. Isoflavones, which too have this C_9 unit, have also become a large and important group of plant products. To this should be added the isoflavan derivatives, pterocarpin (II) and homopterocarpin occurring in a number of woods and barks.[2,3] Angolensin (III) which also occurs in certain woods of the *Pterocarpus* species[4,5] is closely related. A more recent discovery is wedelolactone[6] (IV) which is a 3-phenyl coumarin derivative analogous to pterocarpin and homopterocarpin. On account of the large number of types in which the forked C_9 unit occurs, it should be recognised as an independent structural unit just as the linear C_9 unit and as being directly involved in the biogenesis of 3-phenyl-chroman derivatives.

An alternative possibility is to regard the isoflavan structure to be the result of migration of the aryl group from the 2- to the 3-position of the normal flavan (see Robinson[7]). Such migration is known in the degradative study of catechin[8] and in the action of lead tetra-acetate on flavanones.[9] But this idea of the migration of the aryl group is not applicable to all the cases containing the forked C_9 unit. Hence it could be reasonably concluded that isoflavone, isoflavan and 3-phenylcoumarin derivatives are built from phloroglucinol (I *a*) and tropic acid (I *b*) units.

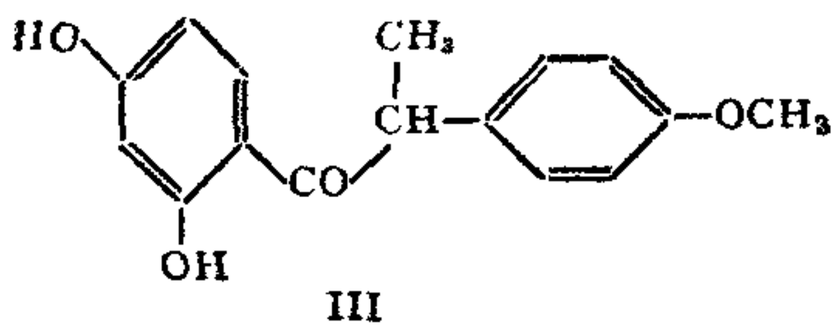
Geissman and Hinreiner,[10] who discussed the various possibilities of the biogenesis of the isoflavan skeleton, have stated that 'the condensation of C_6(B)-iso-C_3 with C_6(A) is mechanistically and biochemically plausible but lacks the support which would be furnished by the existence of C_6(B)iso-C_3 compounds in nature'. This objection may no longer exist because of the study of pulvinic acid and polyporic acid derivatives.

4-Phenylchroman Derivatives

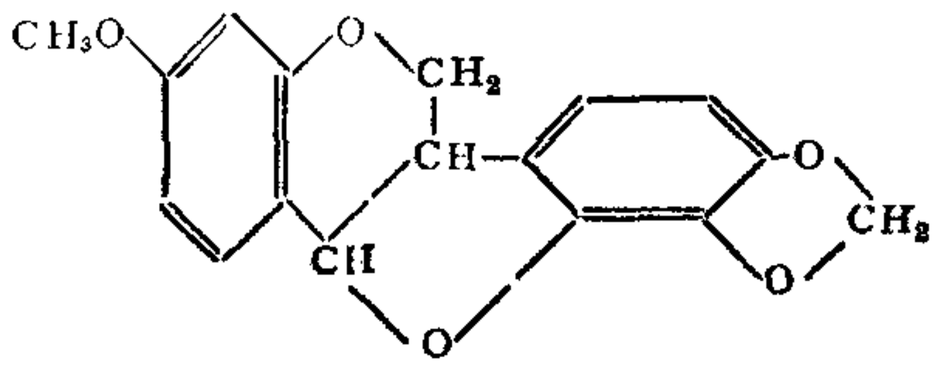
4-Phenylchroman derivatives have been rather rare. Brazilin (V *a*) and hæmatoxylin



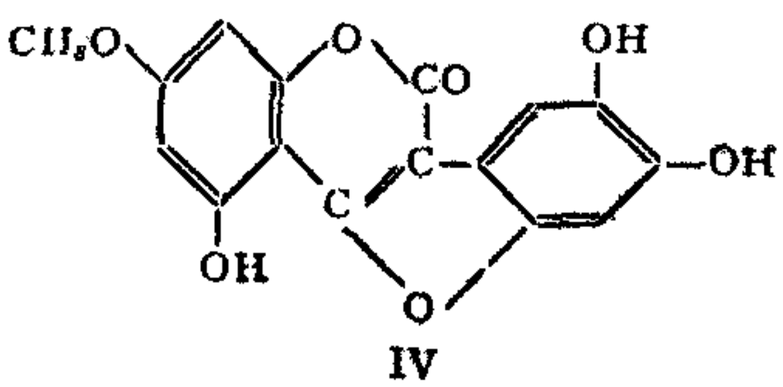
I (*a*) I (*b*)



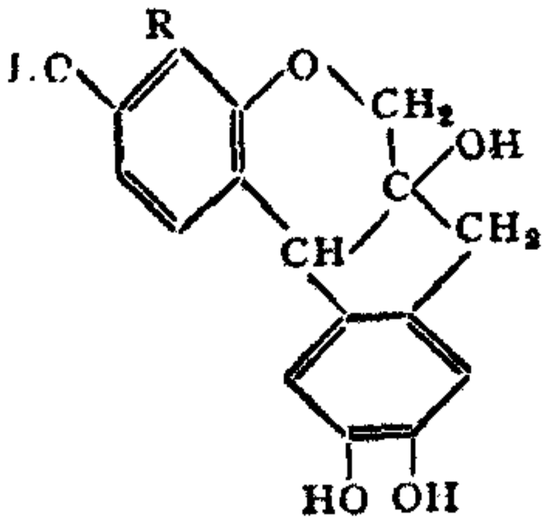
III



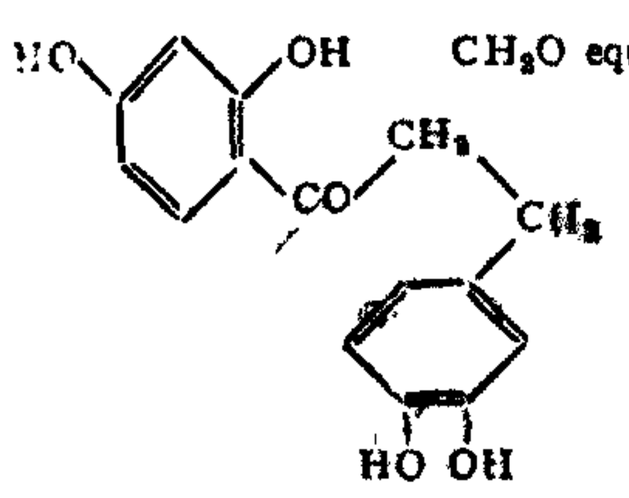
II



IV



V *a*, R=H
b, R=OH



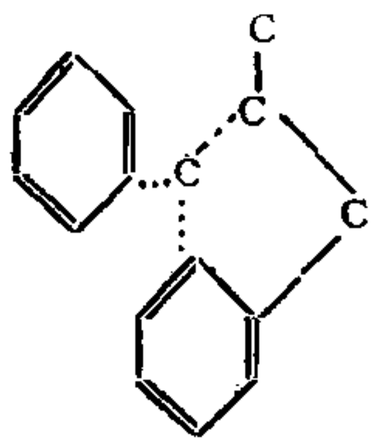
VI

(V b) were the only examples for a considerably long time and Robinson[11] indicated a possible relation with dihydro-butein (VI) which is undoubtedly a 2-phenylchromanone derivative. But he also noted the difficulty of explaining the location of the aliphatic hydroxyl group.

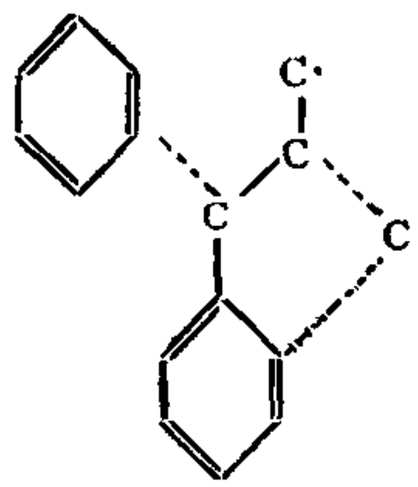
Geissman and Hinreiner[12] considered two possibilities (VII *a* and b) in which the C_6 and C_9 units of flavans could incorporate a single carbon to yield the brazilin type. They have preferred the latter (VII *b*) as more probable. This may mean the assumption of a 4-phenylchroman derivative as intermediate.

More recently Whalley[13] also adopted the 4-phenylchroman as the basic skeleton, but for its formation suggested an extension of the idea of migration originally applied for the formation of an isoflavan from a normal flavan. He proposed a further shift from the 3-phenyl (VIII) to the 4-phenylchroman (VIII *a*) and pointed out that this solved the abovementioned difficulty about the location of the aliphatic hydroxyl group.

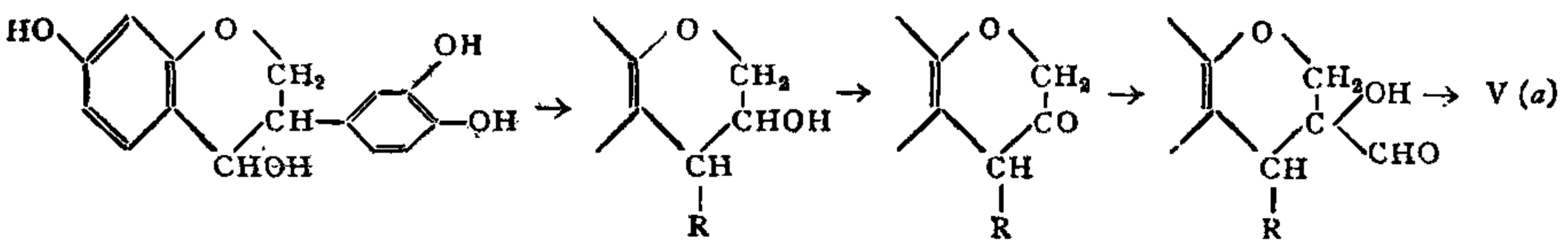
The main point that Whalley made out for suggesting the double migration was that there were few 4-phenylchroman derivatives occurring in nature. Recently more members of the 4-phenylchroman group have been discovered in plant products. Calophyllolide[14] (IX) obtained from the fruits of *Calophyllum inophyllum* has been shown to be a 4-phenylcoumarin derivative. Dalbergin (X *a*) and methyldalbergin (X *b*) are examples of simpler 4-phenylcoumarins and they are found in the wood of *Dalbergia sissoo*.[15,16] Consequently this type should also be considered to be the result of a more direct path of biosynthesis. The units involved would appear to be the same as in normal flavans, *i.e.*, phloroglucinol unit and C_9 linear unit. But the *α*-carbon atom of the latter is used for linking with the former. In this connection may be mentioned the condensation of phenols with cinnamic acid to yield 4-phenyldihydrocoumarin.[17] The evolution of brazilin with the *β*-hydroxyl group seems to offer no difficulty in this scheme. The possible stages



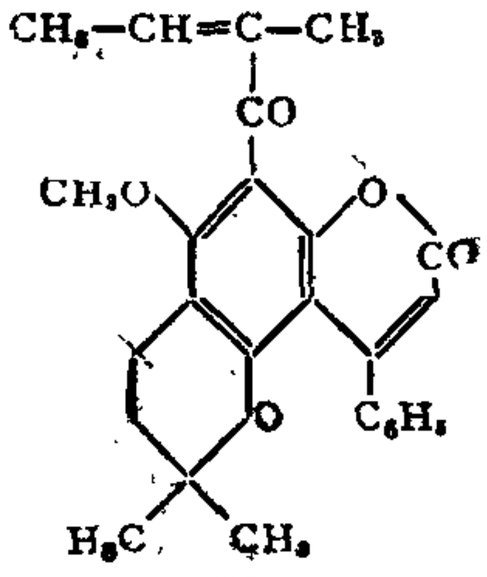
VII (*a*)



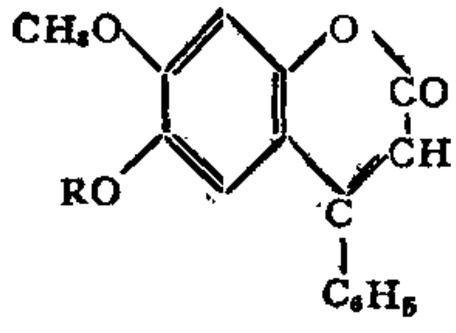
VII (*b*)



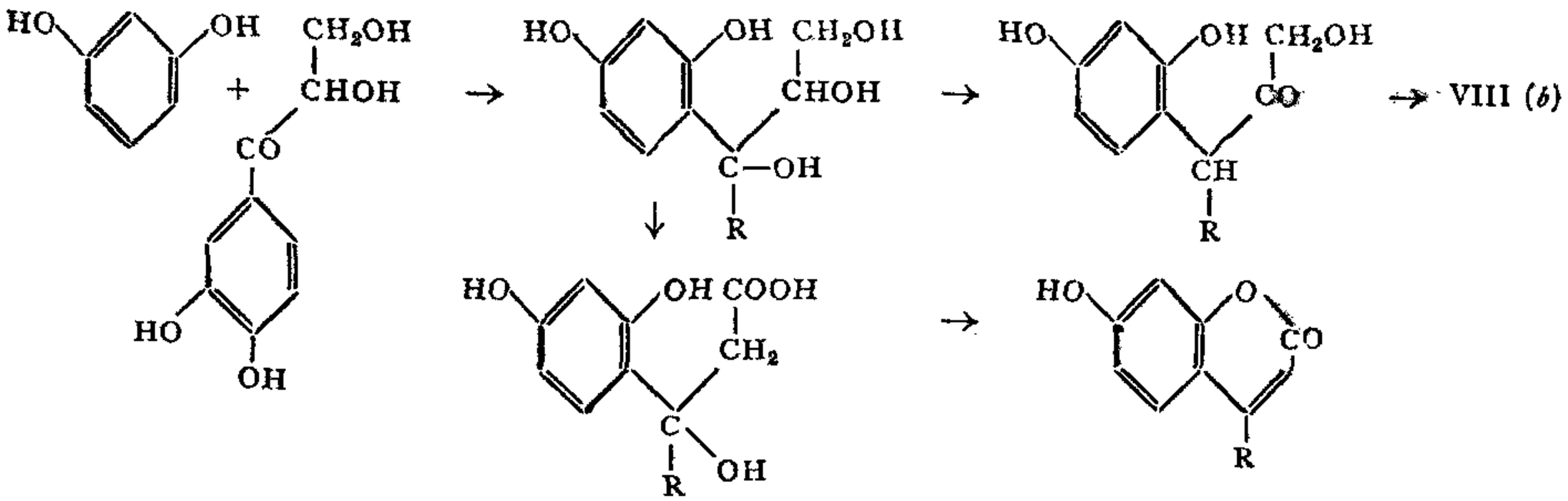
VIII VIII *a* VIII *b*



IX



X *a*, R=H
b, R=CH_3



Benzophenones

Table I

Name	Formula: Position of hydroxyl groups	Formula: Position of methoxyl groups
Maclurin (*a*) ..	2, 4, 6, 3′, 4′	
Cotoin (*b*) ..	2, 6	4
Hydrocotoin (*b*) ..	2	4, 6
Methyl hydrocotoin (*b*) ..	..	2, 4, 6
Protocotoin (*b*) ..	2	4, 6 (3′ : 4′-, *methylene dioxy*)
Methyl protocotoin (*b*) ..	..	2, 4, 6 (3′ : 4′-methylene dioxy)
Para-Hydroxy benzophenone (*c*)	4	..

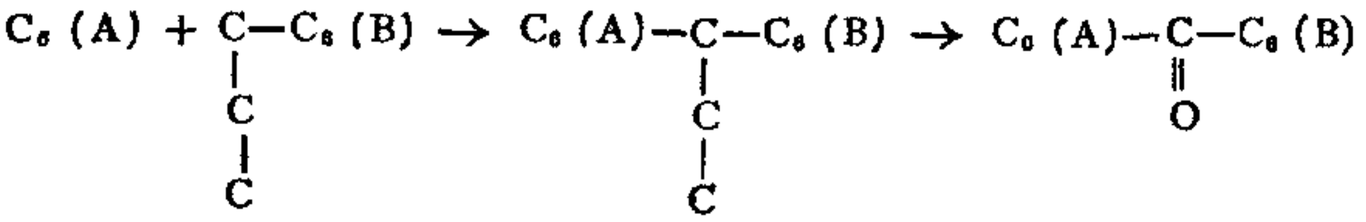
(*a*) From wood of *Morus tinctoria*, (*b*) From *Cotto* Bark
(*c*) From leaves of *Talauma mexicana*.

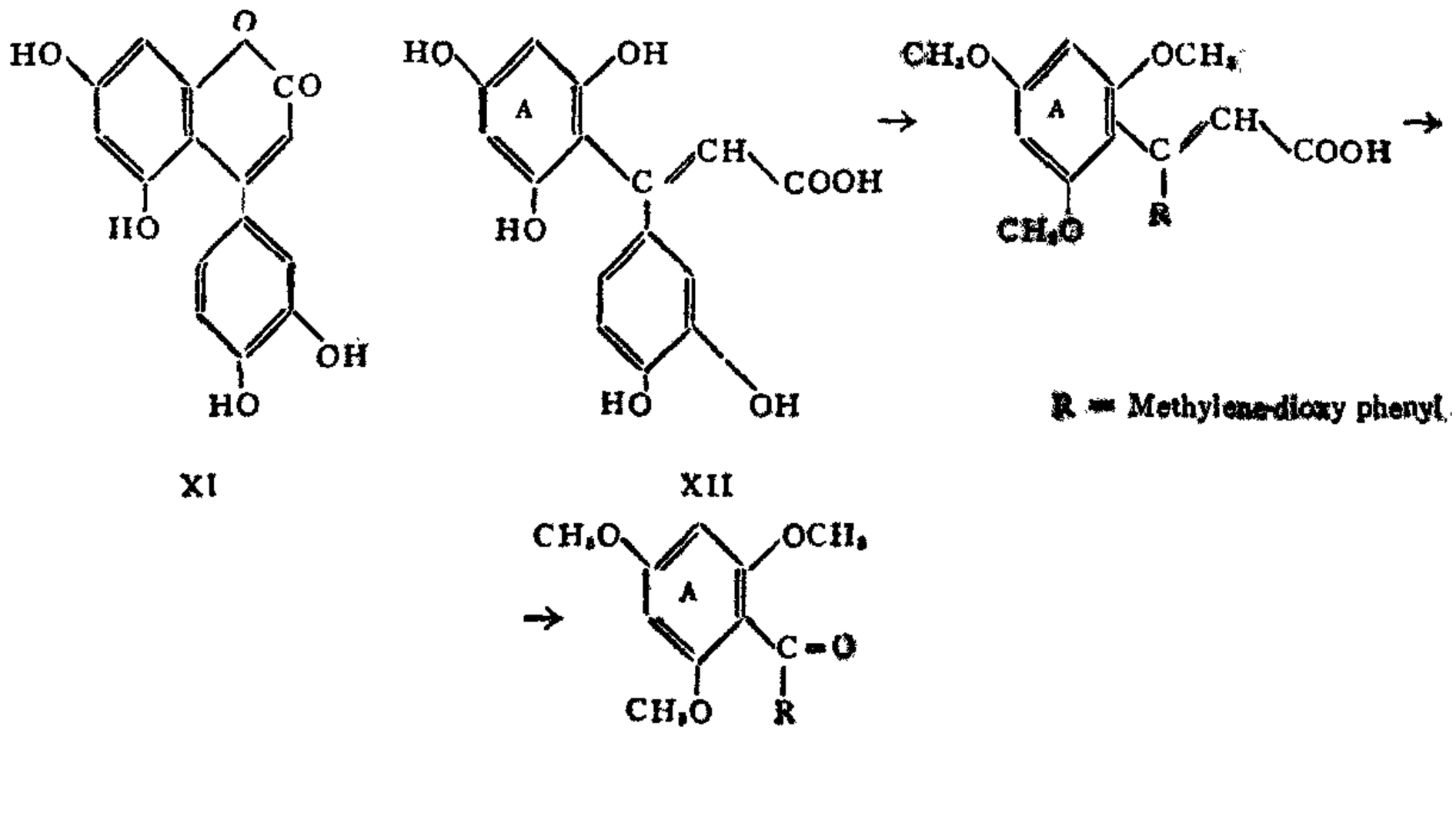
indicated above are analogous to what has been suggested in the case of normal flavonoids.[18,19] The α-ketonic C_3 unit employed is similar to related ketones occurring as lignin units.

Geissman and Hinreiner[20] noticed the close similarity in substitution pattern between naturally occurring benzophenones (see Table I) and flavonoids. As one of two possible methods of their formation they suggested the linking of the C_6(A) and C_9(B) parts through an α-carbon of (B) and subsequent degradation of the C_{15} unit.

But they felt they had no compelling evidence to support it. The frequent methylation of the compounds was also recognised by the above authors who suggested that methylation was a later stage in the synthetic process.

The larger occurrence of 4-phenylchroman derivatives and particularly the recent discovery of 4-phenylcoumarins in Nature seems to provide the evidence for the general scheme and





also further details of the evolution. The biogenesis of these two groups of C_{15} compourds has already been discussed. All the observations are satisfactorily explained if 4-phenylcoumarins (XI) or better the corresponding coumaric acids (XII) are taken as the precursors undergoing oxidation to yield benzophenones. This oxidation has been found to take place readily in the laboratory.[15] Among the methyl ethers there are examples where all the hydroxyl groups are engaged This would indicate that resistance to methylation is not present and finds explanation if the reaction could be considered to take place at the coumaric acid stage (see XII) in these cases. For the formation of the partial methyl ethers the benzophenone stage may be suitable.

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8. Freudenberg *et al.*, *Ann.*, **1925, 441,** 157.
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16 Ahluwalia *et al.*, *Prac. Ind. Acad. Sci.*, **1957, 45A,** 15.
17. Simpson and Stephen, *J.C.S.*, **1956, 1382.**
18. Robinson, *Nature*, **1936, 137,** 172.
19. — *et al.*, *Phil. Trans. Roy. Soc.*, London, **1939, 230 B,** 149.
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PUBLICATION OF SCIENTIFIC LITERATURE IN USSR DURING 1957

THE USSR Academy of Sciences will put out close to 1,500 titles and issue of Journals totalling 32,000 signatures in 1957. The range of subjects will cover all spheres of the humanitarian, natural and technical sciences.

In the scientific and technical part of the programme of publications envisaged by the Academy, mention may be made of books on mathematics, physics and chemistry, including works by the mathematicians A. M. Lyapunov and N. N. Luzin, Geophysicist P. P. Lazarev, Physicist Y. I. Frenkel, Organic Chemist A. N. Butlerov, and Radiochemist V. G. Khlopin.

The computation mathematics series, recently organised by the Computation Centre of the Academy, will contain articles on methods of solving mathematical problems, estimates of errors of different methods and the solution of concrete mathematical problems.

The biography of the great mathematician N. I. Lobachevsky, including 360 documents of archive materials unpublished previously, has been prepared by the Institute of History of Natural and Technical Sciences.

Revised and supplemented editions of Academician A. F. Joffe's *Physics of Semi-Conductors* first issued in 1955, will be put out, as also L. I. Brekhovakikh's monograph on "Waves in Layered Media".

To commemorate the Fiftieth Death Anniversary of I. D. Mendoleyev, the great Russian Chemist. the Academy has collected articles from Soviet scientists for issuing them as "Classics of Science" and also to arrange publication of a book entitled *The Periodic Law*, describing Mendoleyev's classical works on the subject.

A volume of previously unpublished manuscripts of Charles Darwin and a monograph by Academician N. I. Vavilov on "World Resources of Local and Selected Varieties of Cereals, Grains, Legumes and Flax and Their Use in Plant Breeding" will also be published.

In addition, the publication of important books on the different branches of engineering, biochemistry, microbiology, soil sciences, zoology, physiology, botany, genetics and forestry is in the programme.