inhibit the transfer reaction of peptides to puromycin in competition with the peptidyl acceptor, puromycin; this, however, is not the case[22]. Finally, functional antagonism between amino acyl-tRNAs and CM should logically result in inhibition of all peptide bond syntheses in which amino acyl-tRNA is a reactant rather than in the preferential inhibition of the elongation reaction that CM does produce[18,23].

Concerning the central problem, viz. the mechanism of CM's inhibition of protein biosynthesis in susceptible cells, DAS et al.[24] have reported that CM also inhibits the elongation reaction in *Escherichia coli*; the authors have also focused upon the structural relationship between CM and the C-terminal peptide grouping of nascent protein chains as a potential structural basis of CM's action. Moderately high ($1.6 \times 10^{-4} M$) concentrations of CM cause the accumulation of acid-soluble peptides in protoplasts of *Bacillus megaterium*, while CM at $1.25 \times 10^{-3} M$ completely inhibits incorporation of amino acids[25]; these observations are remindful of the differential effects of CM on initiation and elongation of peptides in vitro[18].

Zusammenfassung. Zusammenhänge zwischen Struktur und Wirkung bei Chloramphenicol führen zu der Hypothese, dass das Antibiotikum die Peptidsynthetase der Ribosome dadurch hemmt, dass es den Peptidylpartner der Reaktion antagonisiert. Im Einklang damit steht, dass Chloramphenicol sich spezifisch an Ribosome bindet und selektiv die Elongationsphase der Proteinsynthese hemmt.

F. E. HAHN

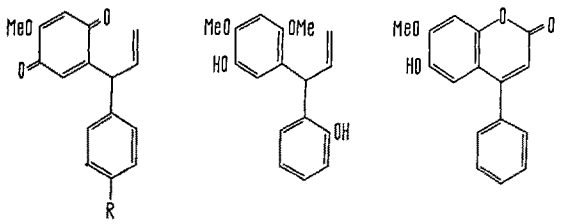
Department of Molecular Biology, Walter Reed Army Institute of Research, Washington (D.C. 20012, USA), 5 April 1968.

[22] I. H. GOLDBERG and K. MITSUGI, Biochemistry *6*, 383 (1967).
[23] M. YUKIOKA and I. H. GOLDBERG, as cited in J. JAYRAMAN and I. H. GOLDBERG, Biochemistry *7*, 418 (1968).
[24] H. K. DAS, A. GOLDSTEIN and L. C. KANNER, Molec. Pharmac. *2*, 158 (1966).
[25] A. I. ARONSON and S. SPIEGELMAN, Biochim. biophys. Acta *53*, 70 (1961).
[26] J. D. DUNITZ, J. Am. chem. Soc. *74*, 995 (1952).

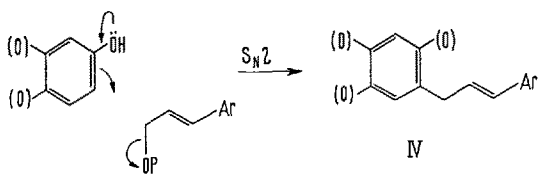
STUDIORUM PROGRESSUS

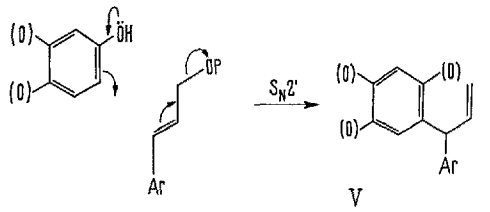
Biogenetic-Like Syntheses of Benzylstyrenes and Neoflavanoids

It is generally considered that flavanoid and isoflavanoid biosynthesis involves initial C-cinnamoylation of a phenolic C_6 unit (or its polyketide equivalent), the chalcone thus formed being cyclized, epoxidized[1] or reduced[2] to furnish the progenitors of the different types of natural flavanoids and isoflavanoids. The biosynthetic origin of neoflavanoids, viz. dalbergiones[3,4] I and related quinol derivatives, e.g. latifolin[5] II, and 4-aryl-coumarins, e.g. dalbergin[6] III, is obscure, although it has been suggested that these also might be derived from the chalcone intermediates by a double 1,2-shift of the B aryl ring[7] or a single 1,3-shift of the A aryl ring[8].

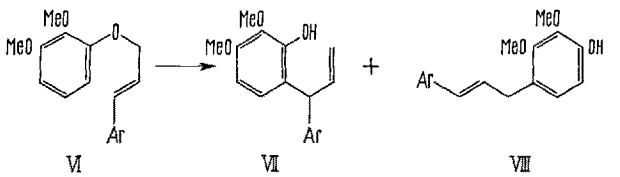


OLLIS and his associates recently reported[9] that benzylstyrenes IV co-occur with neoflavanoids V and they proposed that, in contrast to flavanoid biosynthesis, the formation of IV and V may involve S_N2 type alkylations of polyphenols by cinnamyl pyrophosphate:





As laboratory equivalents of these reactions they synthesized[10] both benzylstyrenes and neoflavanoids by Claisen rearrangement of resorcinol and pyrogallol cinnamyl ethers in boiling dimethylaniline, e.g. VI → VII + VIII.

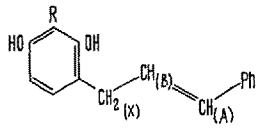


KUMARI, MUKERJEE and SESHADRI[11], however, have questioned the validity of this analogy, since, in attempting to synthesize latifolin dimethyl ether by the Claisen rearrangement, they found that an ortho-methoxycinnamyl group does not apparently migrate. They proposed an alternative biogenetic scheme in which neoflavanoids and benzylstyrenes are formed by 2 *different* processes, the former by initial O-cinnamoylation of a phenol, rearrangement of the ester to a 4-aryl coumarin, and reduction of this to a dalbergione. In accord with OLLIS they considered benzylstyrenes are formed by C-cinnamylation of a phenolic unit and in support of this hypothesis they showed that 1,2,4-trimethoxybenzene condensed with ortho-methoxycinnamyl chloride in ether solution in the

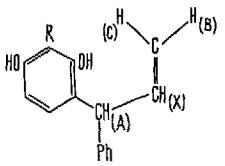
presence of a Lewis acid (fused zinc chloride) to yield a benzylstyrene and dimethyllatifolin.

The rearrangement and condensation reactions described above provide formal mechanistic support for biogenetic C-cinnamylation. However, these reactions utilize extreme conditions (high temperatures, anhydrous media, strong acids) and it seemed appropriate, therefore, to determine whether C-alkylation of polyphenols occurs with cinnamyl alcohol itself in aqueous solutions under only mildly acidic conditions[12]. Like cinnamyl pyrophosphate, protonated cinnamyl alcohol would be expected to give rise readily to a stabilized carbonium ion or incipient carbonium ion in S_N1 or S_N2 reactions. As a result it has now been found that cinnamyl alcohol reacts easily with a variety of phenols in aqueous acetic acid solutions to yield benzylstyrenes and ortho-1-phenyl-allyl-phenols, the former in major amounts.

Thus, warmed with excess of pyrogallol in aqueous acetic acid solution for 2–4 h, cinnamyl alcohol gave the crystalline benzylstyrene IXa, m.p. 106–107°, in 40% yields. (Found: C, 74.5; H, 5.75. Calc. for $C_{15}H_{14}O_3$: C, 74.4; H, 5.83). The structure of this product was



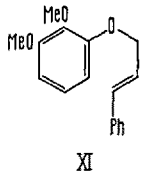
IXa, R=OH
IXb, R=H



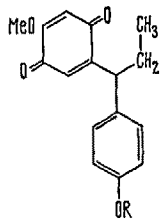
Xa, R=OH
Xb, R=H

established from the NMR-spectrum (100 Mc in CCl_4) of its crystalline triacetate (m.p. 111–112°), which showed the presence of 3 acetyl groups (singlet at δ 2.18), 2 benzylic protons H_X (doublet at δ 3.40), a vinylic proton H_B (sextet at δ 6.09), a vinylic proton H_A (doublet at δ 6.40) and 7 aromatic protons at δ 7.0–7.3, apparent coupling constants $J_{AB} = 16.0$ c/s, $J_{BX} = 6.0$ c/s. After crystallization of the bulk of IXa, the aqueous sodium borate soluble fraction of the reaction residue was a viscous oil containing residual IXa and a second major component which, because of very similar solubilities and chromatographic behavior, has not yet been separated. The NMR-spectrum of the mixture and of its acetate, however, shows that this second component is almost certainly the neoflavanoid Xa. The acetate of the mixture has a series of well-defined signals in the region δ 4.7–5.3 in which IXa triacetate does *not* absorb. On the basis of published[10] first order analyses of similar compounds these signals have been assigned to the aliphatic protons of Xa triacetate as follows: H_A (sextet at δ 4.82), H_C (sextet at δ 4.90), H_B (sextet at δ 5.21), apparent coupling constants $J_{AX} = 6.2$ c/s, $J_{AB} = 1.6$ c/s, $J_{AC} = 1.6$ c/s, $J_{CX} = 17.0$ c/s, $J_{BC} = 1.6$ c/s, $J_{BX} = 10.0$ c/s. The vinylic proton H_X appears as an octet at δ 6.20 (100 Mc in $CDCl_3$). Resorcinol and cinnamyl alcohol condense similarly in aqueous acetic acid to yield the crystalline benzylstyrene IXb, m.p. 91°, and an oily mixture of IXb and, on the basis of the NMR-spectrum, the neoflavanoid Xb.

The ease with which these and other phenols react with cinnamyl alcohol in aqueous solutions provides a plausible chemical basis for enzyme-mediated C-alkylation as proposed by OLLIS. The laboratory condensations probably involve direct C-alkylation by S_N1 and/or S_N2 mechanisms, but it is noteworthy that cinnamyl ethers are cleaved even under these mild conditions and C-alkylation then ensues. Intermolecular transfer of the cinnamyl group from O- to C- was demonstrated by warming 3-cinnamyloxy-veratrole XI with pyrogallol or resorcinol in aqueous acetic acid. Mixtures of C-alkylated pyrogallols and resorcinols, similar to those obtained by the direct reaction of cinnamyl alcohol with pyrogallol or resorcinol, resulted. From these mixtures the crystalline benzylstyrenes IXa and IXb were isolated.



XI

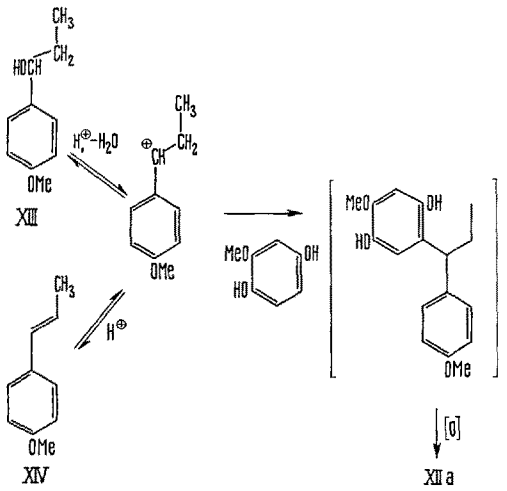


XIIa, R=Me
XIIb, R=H

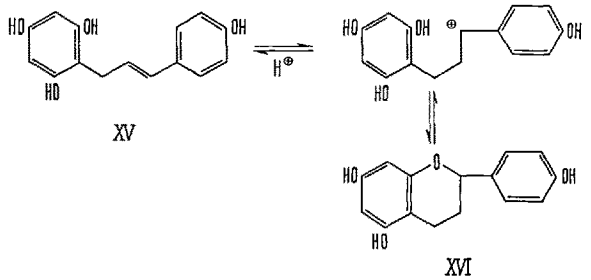
Reduction and subsequent oxidation of natural dalbergiones yields optically active dihydrodalbergiones[3] of types XIIa and b. The racemic modifications of XIIa and b are easily synthesized by simple condensation reactions. Thus, 1-(4-methoxyphenyl)-propan-1-ol XIII condenses readily with methoxyquinol in aqueous acetic acid and, on allowing the solution to stand exposed to air, a yellow quinone, $C_{17}H_{18}O_4$, m.p. 138–139°, crystallizes in yields of about 50%. On reductive acetylation it gives a quinol diacetate, $C_{21}H_{24}O_6$, m.p. 92–93°. The UV-spectrum of the quinone, λ_{max}^{EtOH} 264, ~ 350 nm (ε_{max} 17100, 1106), and its NMR-spectrum, which shows the presence of the >CH-CH_2-CH_3 group, the A_2B_2 system of 4 aromatic protons, and 2 quinonoidal protons (singlet at δ 5.82 and doublet, $J = 1.0$ c/s, at δ 6.52), closely agrees with those reported[3] for optically active XIIa. The quinone, therefore, is a lower melting, racemic modification of dihydro-S-4,4'-dimethoxydalbergione (m.p. 159–162°). Racemic XIIa is also formed by reaction of anethole XIV, a natural propenylbenzene, with methoxyquinol in aqueous acetic acid. The yield of XIIa in this case is low probably

[1] H. GRISEBACH and W. D. OLLIS, Experientia *17*, 4 (1960) and references cited therein.
[2] J. W. CLARK-LEWIS, R. W. JEMISON, D. C. SKINGLE and L. R. WILLIAMS, Chemy Ind. 1455 (1967).
[3] W. B. EYTON, W. D. OLLIS, I. O. SUTHERLAND, O. R. GOTTLIEB, M. T. MAGALHAES and L. M. JACKMAN, Tetrahedron *21*, 2683 (1966).
[4] B. J. DONNELLY, D. M. X. DONNELLY and C. B. SHARKEY, Phytochem. *4*, 337 (1965).
[5] S. BALAKRISHNA, M. M. RAO and T. R. SESHADRI, Tetrahedron *18*, 1503 (1962).
[6] V. K. AHLUWALIA and T. R. SESHADRI, J. chem. Soc. 970 (1957).
[7] W. B. WHALLEY, Chemy Ind. 1049 (1956).
[8] M. H. BENN, Experientia *24*, 9 (1968).
[9] W. B. EYTON, W. D. OLLIS, M. FINEBERG, O. R. GOTTLIEB, I. S. DE S. GRUIMARAES and M. T. MAGALHAES, Tetrahedron *21*, 2697 (1965).
[10] M. F. BARNES, W. D. OLLIS, I. D. SUTHERLAND, O. R. GOTTLIEB and M. T. MAGALHAES, Tetrahedron *21*, 2707 (1965).
[11] D. KUMARI, S. K. MUKERJEE and T. R. SESHADRI, Tetrahedron *22*, 3491 (1966).
[12] Phenols have been C- and O-cinnamylated previously by reaction with cinnamyl bromide in strongly alkaline media, viz. sodium in dry benzene or potassium carbonate in anhydrous acetone[10].

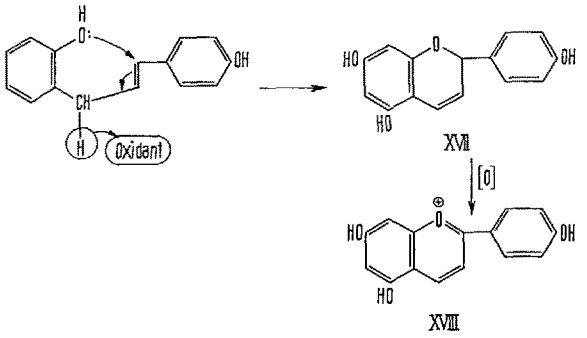
due to competitive self-condensation of XIV and to its limited protonation under the mildly acidic conditions:



The condensation reactions described in this communication demonstrate that at least in terms of chemical reactivity cinnamylation of polyphenols is a much more facile process than their cinnamoylation. Furthermore, benzylstyrenes with hydroxyl or methoxyl substituents in the para positions of *both* aryl rings should be formed even more readily and be highly susceptible to modification by cyclization and oxidation reactions. Benzylstyrenes, rather than chalcones, could be the precursors, therefore of at least some natural flavanoids, e.g. in *Xanthorrhea* species 4′,5,7-trihydroxyflavan XVI co-occurs[13] with a red pigment which appears to be a flavylium-flavan condensation product of the dracorubin-type[14]. The flavan and the flavylium salt could be derived from the benzylstyrene XV. This should protonate readily and cyclize to XVI.



Oxidation of the allylic methylene group could lead to the flav-3-ene XVII, which may be oxidized directly to the flavylium salt XVIII or disproportionate to a mixture of XVI and XVIII. In this connection it is noteworthy that CLARK-LEWIS[15] recently suggested that flav-3-enes may be the immediate precursors in plants of flavylium salts and flavans[16].



Zusammenfassung. Im Zusammenhang mit dem Problem der Biosynthese der Flavone, Isoflavone und Neoflavone wurden die entsprechenden Benzylstyrole und Neoflavone synthetisiert.

L. JURD

Western Regional Research Laboratory, Agricultural Research Service, U.S. Department of Agriculture, Albany (California 94710, USA),
2 May 1968.

[13] A. J. BIRCH and M. SALAHUDDIN, Tetrahedron Lett. *32*, 2211 (1964).

[14] A. ROBERTSON, W. B. WHALLEY and J. YATES, J. chem. Soc. 3117 (1950). – M. BLACKBURN, G. B. SANKEY, A. ROBERTSON and W. B. WHALLEY, J. chem. Soc. 1573 (1957).

[15] J. W. CLARK-LEWIS and D. C. SKINGLE, Aust. J. Chem. *20*, 2169 (1967).

[16] Acknowledgments. The author is indebted to L. M. WHITE, Miss G. SECOR and Mrs. N. BENNETT for elemental analyses and measurement of NMR-spectra.

PRO EXPERIMENTIS

Méthode de marquage des Crustacés Décapodes

L'existence d'un comportement distinct, si on compare les animaux isolés aux animaux groupés, a été mise en évidence en particulier chez les Insectes[1] et les Crustacés[2] où les exemples d'effet de groupe, nombreux dans le premier cas, sont rares dans le second.

Des études récentes[2] concernant ce problème, ont montré que les phénomènes d'adaptation chromatique du Natantia *Crangon crangon* (Linné) soumis à un effet de groupe, sont exactement inverses selon que l'animal est seul ou qu'il se trouve en présence de congénères. La nécessité de comparer les réactions individuelles, à court et long termes, de chaque Crevette maintenue au sein du groupe, avec les réactions présentées par la même Crevette isolée, nous a conduit à mettre au point, pour nos élevages expérimentaux, un procédé de marquage simple et durable.

Les signes colorés pratiqués sur la carapace ne sont pas souhaitables car ils restent sur l'exuvie lors de la mue. La

[1] P. P. GRASSÉ, Experientia *2*, 77 (1946).

[2] C. CHASSARD, C. r. hebd. Séanc. Acad. Sci., Paris *257*, 2169 (1963).