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OXIDATION EXPERIMENTS WITH FLAVONOIDS

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Abstract—It is proposed that phenolic oxidation of a 4(2)-hydroxychalcone(4′[2′]-hydroxyflavanone) serves to initiate transformations to aurone, flavone, dihydroflavonol and isoflavone. Flavonols could be produced by phenolic oxidation of either a 4′-hydroxydihydroflavonol or a 4′-hydroxyflavone. The production of 4-hydroxyphenylcoumarins and derived products could follow a similar pathway from isoflavones. Simple model flavanones and chalcones have been synthesized and their oxidation by potassium ferricyanide studied. The 4′-hydroxy and 2′-hydroxy compounds rapidly give flavone or aurone in high yield, in sharp distinction to the 3′-hydroxy derivatives. The fully methylated flavanones or corresponding chalcones are not oxidized after long periods. The results provide excellent analogies for the proposed biosynthetic pathway. The hydroxyaurone is produced as a metal complex, in which form it is protected from further oxidation, a situation that may have biochemical analogies.

ALTHOUGH the origins of the carbon atoms of flavonoids in plants are known,[1,2] the actual compounds that condense to yield the C_6—C_3—C_6 skeleton and the details of the interconversions between flavonoids are less well understood.

The primary product may well be a glycosylated or free hydroxy chalcone, the conversion of which to a flavanone has been demonstrated *in vivo*[3] and is well known also *in vitro*.[4] The flavanone–chalcone pair play a central role in the further transformations to other flavonoids. The reductions to dihydrochalcones[5,6] and flavans[7] are unexceptional. More interesting is the recently discovered reduction of chalcones to the benzylic alcohols (I) followed by facile cyclization to flav-3-enes.[8,9] It has been pointed out[9] that this sequence provides an alternative pathway, as yet little explored, to flavan-3,4-diols (II), flavylium salts (III) and catechins (IV). (See Fig 1.)

The more important naturally occurring flavonoids are at the same or a higher oxidation level than flavanones, and many special hypotheses have been proposed to explain the genesis of each series. In general such postulates, based on good chemical analogies, particularly with the AFO reaction,[10] have involved the direct manipulation of the C_3 portion of the

[1] J. B. HARBORNE, *Comparative Biochemistry of Flavonoids*, p. 251, Academic Press, London (1967).
[2] H. GRISEBACH and W. BARZ, *Naturwis.* **56**, 538 (1969); H. PACHECO, *Bull. Soc. Franc. Physiol. Vegetale* **15**, 3 (1969).
[3] E. WONG and E. MOUSTAFA, *Tetrahedron Letters* 3021 (1966).
[4] F. M. DEAN, *Naturally Occurring Oxygen Ring Compounds*, p. 335, Butterworth, London (1963).
[5] A. H. WILLIAMS, *Comparative Phytochemistry* (edited by T. SWAIN), p. 297, Academic Press, London (1966).
[6] P. L. SOUTHWICK, N. LATIF, B. M. FITZGERALD and N. M. ZACZECK, *J. Org. Chem.* **31**, 1 (1966).
[7] A. J. BIRCH and M. SALAHUDDIN, *Tetrahedron Letters* 2211 (1964).
[8] A. PELTER and P. STAINTON, *J. Chem. Soc.* (C) 1933, (1967).
[9] J. W. CLARK-LEWIS and D. C. SKINGLE, *Australian J. Chem.* **20**, 2169 (1967); J. W. CLARK-LEWIS and R. W. JEMISON, *Australian J. Chem.* **21**, 2247 (1968); cf. L. JURD, *Chem. & Ind.* 2175 (1967); *Tetrahedron* **23**, 1057 (1967).
[10] F. M. DEAN and V. PODIMUANG, *J. Chem. Soc.* 3978 (1965).

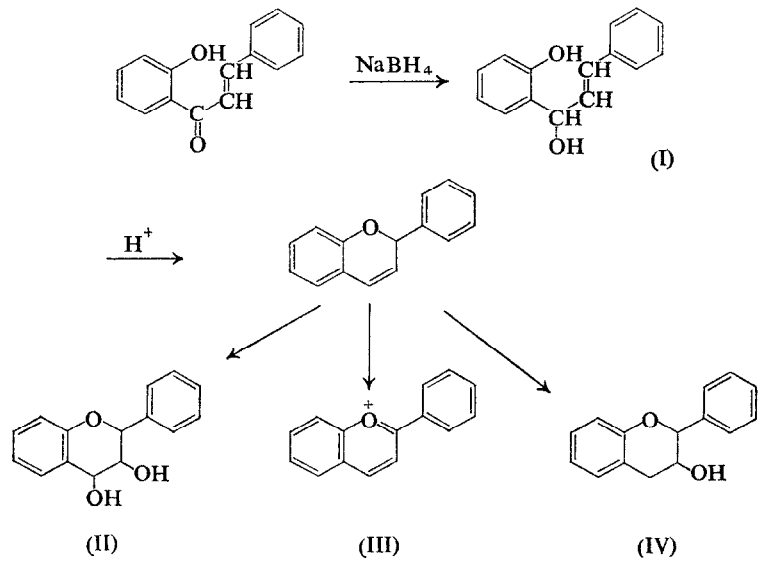


FIG. 1.

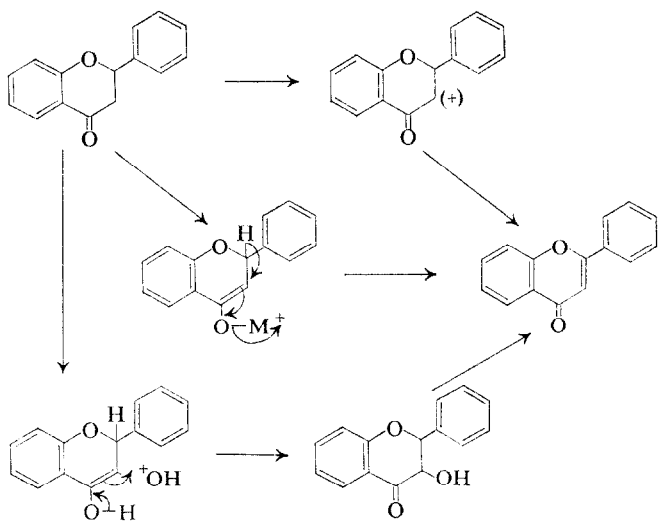


FIG. 2.

molecule. Proposals for the formation of flavones have included (Fig. 2) direct oxidation of a flavanone to give a cation at C-3 which could be transformed to a flavone, flavanonol or isoflavone;[11,12] enolization of the flavanone followed by attack by the equivalent of $OH^{(+)}$ and dehydration[12] or metal assisted enolization followed by an oxidative loss of the metal

[11] A. J. BIRCH, *Chemical Taxonomy* (edited by T. SWAIN), Chapter 6, Butterworth, London (1963).
[12] J. D. BU'LOCK, *Biosynthesis of Natural Products*, p. 90, McGraw-Hill, New York (1965).

would also yield the flavone.[13] Recently evidence has indicated that chalcones rather than flavanones are the more direct precursors of flavones.[14]

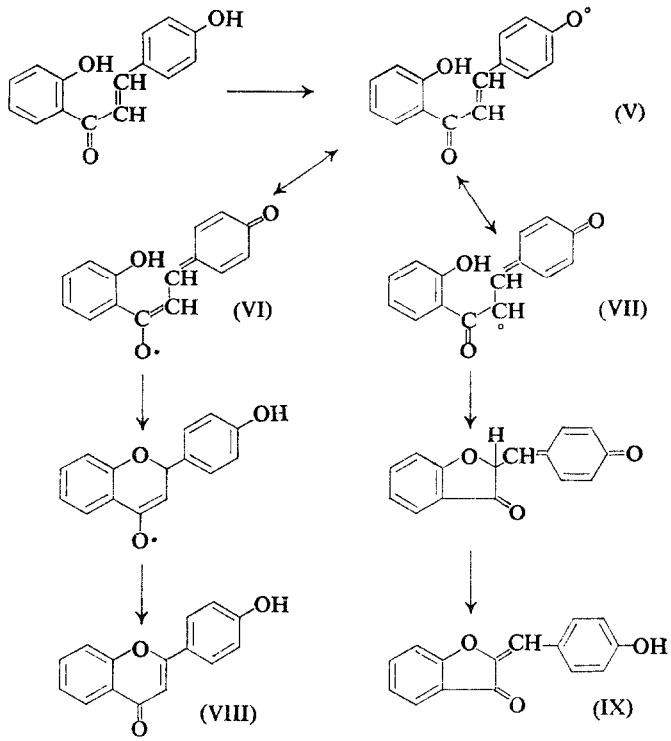
Isoflavones have been thought to arise from chalcones through chalcone epoxides[15,16] or, by analogy with the facile rearrangement of tetra-*O*-methyl-catechin by phosphorus pentachloride,[17] isoflavones could be formed by rearrangement of derivatives of flavanonols.[16]

We have adopted a different approach and have looked at the probable results of oxidative manipulation of the ubiquitous 4′-(or 2′)-hydroxyl groups of ring B of various flavonoids of different oxidation levels. In particular although the results of oxidation are evidenced in the C_3 unit (i.e. chalcone → flavone) the actual site of oxidation would be at a hydroxyl group remote from this. Such considerations lead to chemically plausible schemes for the origins of flavonoids at a higher oxidation level than the chalcone–flavanone pair. In particular, it was a consideration of possible biogeneses of isoflavones[18] which gave rise to the postulate that a 2′- or 4′-hydroxyl group had to be present in the chalcone or flavanone precursor as a prerequisite for migration, and indeed this would seem to be the case.[19]

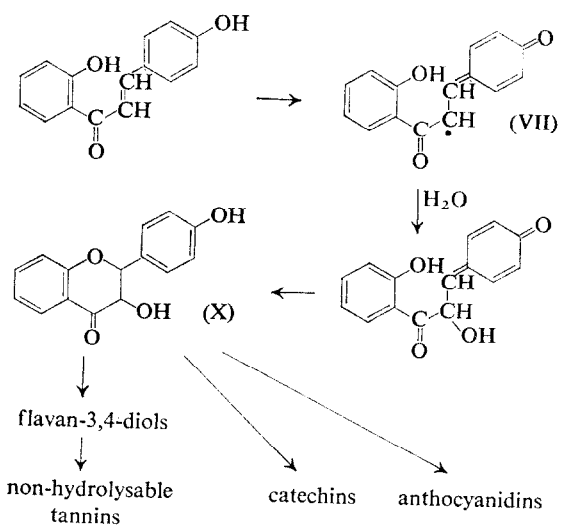
This approach is based on analogies to the production of lignans and lignin[20] and treats the chalcone simply as a modified C_6—C_3 (lignin) unit. The isolation of such products as theaflavin,[21] amentoflavone,[22] silybin[23] etc. attests the ability of plants to oxidatively manipulate ring B of flavonoids. A rather different mode of oxidation is the conversion of dihydrokaempferol to dihydroquercetin and kaempferol to quercetin,[2,24] the latter reaction possibly being of fundamental importance.[24,25] Experiments on the enzymic oxidation of myrcytrin show that oxidative dimerizations involving ring B can occur at the flavonol stage also.[26]

The production of aurones in the laboratory by the potassium ferricyanide oxidation of chalcones was first accomplished by Dean,[10,27] who showed that a 4-hydroxyl group on the chalcone was necessary for the reaction to succeed (Scheme 1). The high yields of aurone were remarkable inasmuch as the product, itself a phenol and capable of further oxidation, is produced in the presence of excess ferricyanide. The oxidation of the 2′-hydroxyl group was implicated in the reaction, as could be the case for those of our mechanisms involving

[13] A. J. BIRCH, *Forschr. Chem. Org. Naturstoffe* **XIV**, 186 (1957).
[14] E. WONG, *Phytochem.* **7**, 1751 (1968); E. WONG and H. GRISEBACH, *Phytochem.* **8**, 1419 (1969).
[15] J. ALGAR and T. MCKENNA, *Proc. R. Irish Acad.* **49**, 225 (1944).
[16] H. GRISEBACH, *Chemistry and Biochemistry of Plant Pigments* (edited by T. W. GOODWIN), p. 279, Academic Press, London (1965); *Chemistry of Natural and Synthetic Colouring Matters*, p. 301, Academic Press, London (1962).
[17] K. FREUDENBERG, G. CARRARA and E. COHN, *Liebig's Ann.* **446**, 87 (1926).
[18] A. PELTER, *Tetrahedron Letters* 897 (1968); A. W. JOHNSON, Ph.D. Thesis, Manchester (1965); J. BRADSHAW, M.Sc. Thesis, Manchester (1969).
[19] W. BARZ and H. GRISEBACH, *Z. Naturforsch* **22**, 627 (1967).
[20] J. M. HARKIN, *Oxidative Coupling of Phenols* (edited by W. I. TAYLOR and A. R. BATTERSBY), p. 243, E. Arnold, London (1967).
[21] A. G. BROWN, C. P. FALSHAW, E. HASLAM, A. HOHNES and W. D. OLLIS, *Tetrahedron Letters* 1193 (1966).
[22] J. B. HARBORNE, *Comparative Biochemistry of Flavonoids*, p. 118, Academic Press, London (1967).
[23] A. PELTER and R. HÄNSEL, *Tetrahedron Letters* 2911 (1968).
[24] H. SMITH and D. B. HARPER, *Phytochem.* **9**, 477 (1970).
[25] M. FURUYA, A. W. GALSTON and B. B. STOWE, *Nature* **193**, 456 (1962); A. W. GALSTON, *Perspectives in Phytochemistry* (edited by J. B. HARBORNE and T. SWAIN), p. 193, Academic Press, London (1969).
[26] H. LÖTH, private communication to authors; H. IMAGAWA and Y. TAKINO, *Agri. Biol. Chem.* **26**, 541 (1962).
[27] F. M. DEAN, *Naturally Occuring Oxygen Ring Compounds*, p. 314, Butterworth, London (1963).



SCHEME 1.



SCHEME 2.

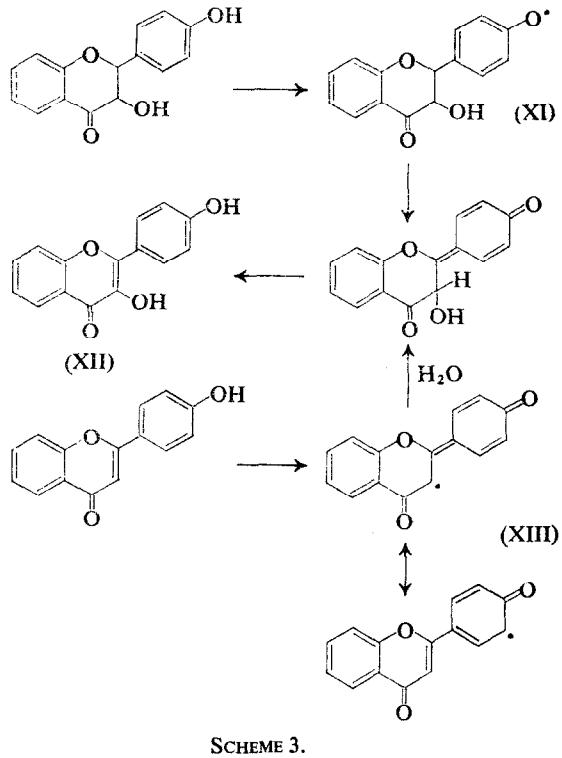
the chalcone. We shall discuss this point later. Using this reaction Wong[28] was able to synthesize hispidol and its 6-glucoside from the corresponding chalcones. He was also able to demonstrate the conversion to the aurone glucoside using cell free extracts. Interestingly, genetic studies have indicated that whilst aurones derive from the same pool as other flavonoids, their synthesis from chalcones is under separate control.[29] There have been no indications that flavones may result from such oxidations, as suggested in Scheme 1.

In Scheme 2, a mechanism is suggested for the introduction of a 3-hydroxyl group into the C_{15}-flavonoid skeleton by attack by water or hydroxyl radical on the radical (VII) or its cyclized form. (Nucleophilic attack by water on the equivalent cation would be the two electron equivalent.) This reaction is very important in flavonoid chemistry as it may lead to the production of flavonols, flavan-3,4-diols, catechins, anthocyanidins and products derived from these. Numerous studies have shown that production of 3-hydroxylated flavonoids is subject to specific gene control.[30] If attack on radical (VII) were by ring A of another flavonoid unit, then the 3,8(6)-linked dimers would result, this being the mode of biogenesis put forward by Jackson and his colleages.[31]

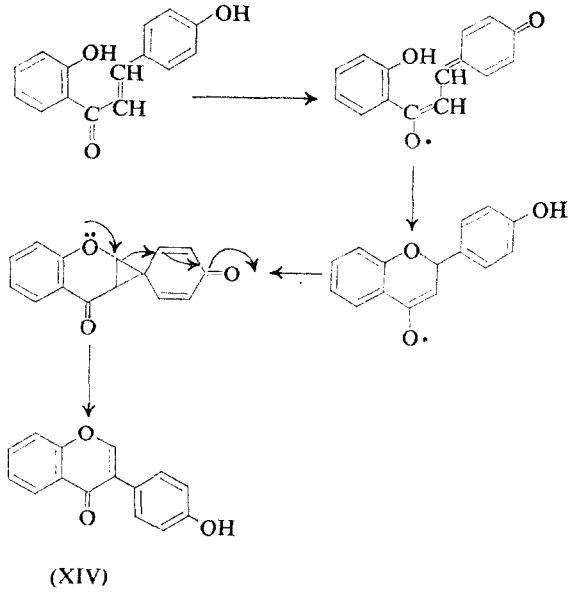
Genetic studies[29] have been taken to indicate the introduction of a 3-hydroxyl group of a flavonol at a relatively early stage of the biosynthesis. However the original papers make it clear that the scheme put forward was a matter of personal preference based on the then current ideas of enzyme specificity, and in fact several other schemes that fit the facts may be devised. The production of flavonols has been taken as a 'primitive' characteristic,[32] more 'advanced' plants synthesizing flavones instead. However the biflavonyls are also characterized as primitive and these may be made *via* the radical (XIII), also involved in the *o*-hydroxylation reaction. As this same radical may give rise to flavonols we prefer to include the possibility of the direct oxidation of 4′-hydroxyflavones to 4′-hydroxyflavonols in Scheme 3, as well as the demonstrated dehydrogenation of dihydroflavonols,[33] which can also go *via* phenolic oxidation. The data on the lack of correlation between the glycosylation pattern of dihydrokaempferol and kaempferol and quercetin in *P. sinensis*[34] is of interest when considering the possibilities inherent in Scheme 3.

We have previously discussed isoflavone formation[18] and Scheme 4 simply elaborates the same idea, but with chalcone as precursor.[14] It suffices to note that all the current biochemical data is in accord with Scheme 4.[35] Presumably the 2′-hydroxyl group frequently found in isoflavonoids serves to stabilize the intermediate radical or cation which produces the spiro-dienone although other possibilities involving the introduction of a 2′-hydroxy group as part of the mechanism of migration have been discussed.[18] Isoflavone synthesis as in Scheme 4 has little in common with the oxidative rearrangements of either Cavill[36] or Ollis.[37] The former probably relies on enolization of the flavanone, whilst the latter is an

[28] E. Wong, *Phytochem.* **5**, 463 (1966); cf. M. Shimokoriyama and S. Hattori, *J. Am. Chem. Soc.* **75**, 2277 (1953).
[29] T. A. Geissman, E. C. Jorgensen and B. Lennart Johnson, *Arch. Biochem. Biophys.* **49**, 368 (1954); T. A. Geissman and E. C. Jorgensen, *Arch. Biochem. Biophys.* **54**, 72 (1955); **55**, 389 (1955).
[30] J. B. Harborne, *Comparative Biochemistry of Flavonoids*, pp. 252–253, Academic Press, London (1967).
[31] B. Jackson, H. D. Locksley and F. Scheinmann, *Chem. Commun.* 1125 (1968).
[32] J. B. Harborne, *Comparative Biochemistry of Flavonoids*, p. 313, Academic Press, London (1967).
[33] L. Patschke and H. Grisebach, *Phytochem.* **7**, 235 (1968).
[34] J. B. Harborne and H. S. A. Sherratt, *Biochem. J.* **78**, 298 (1961).
[35] H. Grisebach and W. Barz, *Naturwiss.* **56**, 538 (1969).
[36] G. W. K. Cavill, F. M. Dean, A. McGookin, B. M. Marshall and A. Robertson, *J. Chem. Soc.* 4573 (1954).
[37] W. D. Ollis, K. L. Ormand and I. O. Sutherland, *J. Chem. Soc.* (c), 119 (1970); W. D. Ollis, K. L. Ormand, B. T. Redman, R. J. Roberts and I. O. Sutherland, *J. Chem. Soc.* (c), 125 (1970).



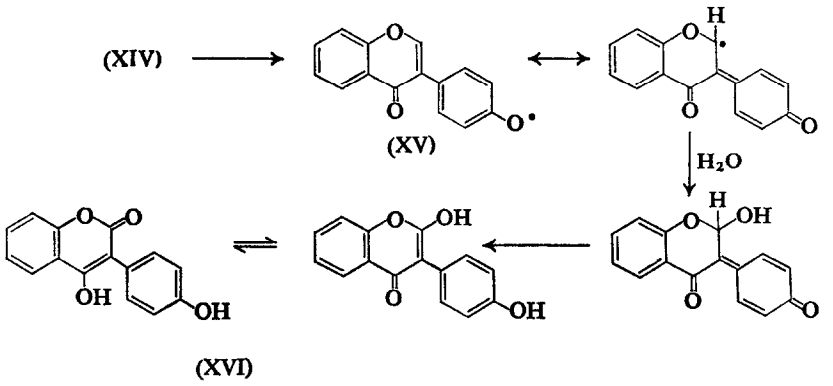
SCHEME 3.



SCHEME 4.

example of the oxidative rearrangement of styrenes using thallic acetate,[38] although as pointed out other mechanisms involving the carbonyl group are possible.

The production of 4-hydroxy-3-phenylcoumarins from isoflavones as in Scheme 5 has been postulated by both Ollis[39] (one- and two-electron processes) and ourselves[40] (one electron process). Further, it has been shown that oxidation of a 2′-hydroxyisoflavone can lead to ring closure.[41]

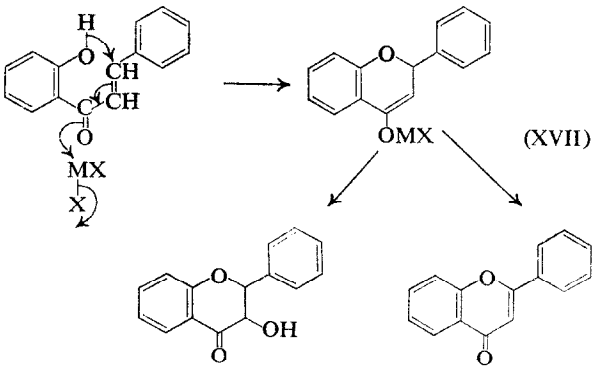


SCHEME 5.

Isoflavonoid derivatives of the pterocarpan series may be formed either by reduction of a 2′-hydroxyisoflavone followed by ring closure or by reduction of a coumestrol type, itself formed by oxidation of a 2′-hydroxyisoflavone.

The production of flavonoids not bearing a hydroxyl group on the B ring and above the flavanone oxidation level is not explained by Schemes 1–5. It has been suggested that such compounds are made in a totally different fashion from other flavonoids,[42] but if it be assumed that the general mode of biosynthesis is the same, either a 4′-hydroxyl group is lost after flavone formation or the oxidation proceeds by a different pathway. The removal of hydroxyl groups *para* to a carbonyl group has been demonstrated in the microbial degradation of flavonoids[43] but it is by no means clear that this can occur in plants. It may be that these compounds arise directly from chalcones by a modification of the Birch proposal, as in Scheme 6. Cyclization of the 2′-hydroxychalcone is initiated by a metal ion to yield the metal enolate (XVII) *directly*. The proposal differs from previous suggestions in that (XVII) does not arise from the ketone by initial enolization of the flavanone. This difference is very real as regards rates of reaction, as was strikingly shown by Ellis[44] in his study of the lead tetra-acetate oxidation of 3,3,5,5-tetramethylcyclohexanone as compared with its magnesio-enolate, the latter oxidizing very much faster than the former. Indeed the extremely rapid oxidation of phenols, with lead tetra-acetate, as compared with ketones,[45]

[38] R. J. OJELLETTE, G. KORDOSKY, C. LEVIN and S. WILLIAMS, *J. Org. Chem.* **34**, 4104 (1969).
[39] C. P. FALSHAW, R. A. HARMER, W. D. OLLIS, R. E. WHEELER, V. R. LALITHA and N. V. SUBBA RAO, *J. Chem. Soc.* (C) 374 (1969).
[40] A. PELTER and P. STAINTON, *J. Chem. Soc.* (C), 701 (1966).
[41] C. P. FALSHAW, W. D. OLLIS, J. A. MOORE, K. MAGNUS, *Tetrahedron Suppl. No.* 7, 333 (1966).
[42] F. M. DEAN, *Naturally Occurring Oxygen Ring Compounds*, p. 606, Butterworth, London (1966).
[43] J. B. HARBORNE, *Comparative Biochemistry of Flavonoids*, p. 293, Academic Press, London (1967).
[44] J. W. ELLIS, *Chem. Commun.* 406 (1970).
[45] R. CRIEGEE, *Oxidation in Organic Chemistry* (edited by K. WIBERG), p. 277, Academic Press, New York (1965).



SCHEME 6.

is an example of the same principle. The ketone must enolize prior to oxidation, the enolization being the rate limiting step.[46–48] Such a scheme may have actually been realised by Ollis and his colleagues in the oxidation of 2′-hydroxy-4,4′-dimethoxychalcone to 4′7-dimethoxyflavone[37] by thallic acetate. However the long period of heating plus the isolation of flavanone and the low yield of product do not allow any meaningful speculation regarding the mechanism of that reaction. We are actively working to provide examples of oxidation *via* Scheme 6 as well as the other Schemes shown.

This paper reports attempts to provide *in vitro* analogies to Scheme 1. Compounds (XVIII)–(XXVI) were produced as substrates for oxidation, and the oxidizing agent of choice was potassium ferricyanide with a redox potential of 360 mV as compared with 451 mV for laccase. Furthermore, similarities between laccase oxidation and ferricyanide oxidation have been demonstrated in xanthone formation.[48] Oxidations were carried out in alkaline solution in identical conditions of ionic strength and proportions of reactants unless otherwise stated. This means that frequently di-anions and certainly mono-anions are always present, but for simplicity this is not considered when discussing possible mechanisms. The compounds were chosen as simple flavonoids with a commonly occurring oxygenation pattern in ring A, but complications associated with a 5-hydroxyl group of a flavanone (6′- of a chalcone) were avoided in the first instance. In general the substances were produced by condensing the appropriate hydroxy-aldehyde with peonol followed by equilibration with sodium acetate.[49] The flavanone–chalcone mixture was resolved on polyamide columns.[50]

When 2′,4-dihydroxy-4′-methoxychalcone (XVIII) was reacted with the oxidizing mixture for 10 min the product was a mixture of one part of chalcone and four parts of either flavone or aurone. Acetylation followed by preparative TLC gave the chalcone diacetate and flavone acetate m.p. 150–151°, identical in all respects with an authentic sample. Hydrolysis gave 4′-hydroxy-7-methoxyflavone, also identical with an authentic sample. The chalcone was 80% converted to flavone, and the yield was almost quantitative. To our

[46] K. ICHIKAWA and Y. YAMAGUCHI, *Nippon Kagaku Zasshi* **73**, 415 (1952); *Chem. Zentral* 4095 (1956).
[47] H. B. HENBEST, D. N. JONES and J. P. SLATER, *J. Chem. Soc.* 4472 (1961); C. W. K. CAVILL and D. H. SOLOMON, *J. Chem. Soc.* 4426 (1955).
[48] J. E. ATKINSON and J. R. LEWIS, *Chem. Commun.* 803 (1967).
[49] G. ZEMPLEN, R. BOGNAR and L. MESTER, *Chem. Ber.* **75**, 1432 (1942); C. DAHL, Ph.D. Thesis, Australian National University (1968).
[50] R. NEU, *Nature* **182**, 660 (1958); *Arch. Pharm.* **293**, 169 (1960).

knowledge this is the first report of a flavone being produced by this method and in view of the aurone production by Wong[28] from 2',4,4'-trihydroxychalcone and the 4'-glycosyl derivative it was unexpected. In our hands oxidation of the former chalcone yielded only trimer (not fully characterized) even under very mild conditions. When the corresponding flavanone (XIX) was oxidized the same mixture of chalcone and flavone was obtained. However when 2'-hydroxy-4',4-dimethoxychalcone (XX) was exposed to the same conditions even for as long as 24 hr no oxidation at all could be traced. The starting material was recovered as a mixture of chalcone and flavanone identical to that produced on acidification of a basic solution of the chalcone of the same ionic strength. Further when 4'-hydroxy-7-methoxyflavone was treated with the oxidizing mixture for 10 min it was recoverered, although 4'-hydroxy-6-methoxyaurone was completely destroyed.

When 2',3-dihydroxy-4'-methoxychalcone (XXI) was treated with alkaline potassium ferricyanide for 10 min no oxidation occurred, but after 18 hr only dark intractable gums were isolated. So far no discrete products of this oxidation have been isolated. When the corresponding flavanone (XXII) was exposed to oxidation for 10 min only a mixture of (XXI) and (XXII) was recovered. The fully methylated flavanone (XXIII) dissolved in the reaction mixture (presumably as the chalcone anion) but was not oxidized at all, even when left for 18 hr.

When the oxidizing mixture was added to 2,2'-dihydroxy-4'-methoxychalcone (XXIV) a red-brown precipitate was formed immediately. The precipitate was spun down as rapidly as possible and examined separately from the supernatant liquid. The latter on work-up and acetylation gave mainly mono- and di-acetylated chalcone, together with a small quantity of aurone acetate and some intractable, unidentifiable material.

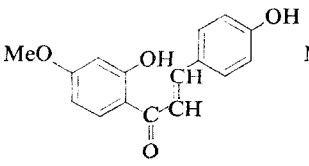
The large bulk of the material was in the complex and from this 2'-hydroxy-6-methoxyaurone and its acetate were isolated. Comparisons with authentic materials confirmed the identities of the substances. No flavone could be detected.

TABLE 1. PRODUCTS FROM OXIDATION OF 2,2'-DIHYDROXY-4-METHOXYCHALCONE

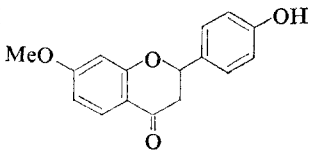
	% Total organic	% Chalcone	% Aurone
Supernatant liquid	23	18	1
Complex	77	2	75

The breakdown of material recovered is shown in the table, from which it is clear that oxidation to the aurone is rapid and occurs completely in the complex (the small amount of aurone from the supernatant liquid was almost certainly due to finely divided complex which was left due to the need for a speedy work-up procedure).

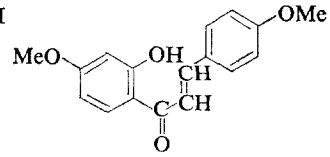
Interestingly acetylation of the material from the complex gave only a small percentage of the aurone acetate, the large bulk of material was present as substance running quite differently from the aurone acetate on both columns and by TLC and with different spectral properties but having the same analysis. It seems probable that the material is a mixture of (XXVII) and (XXVIII). On treatment with either strong aqueous acid or base, hydroxyaurone is produced quantitatively. Acetylation of the aurone itself did not yield this material which therefore comes directly from a complex. The reaction mixture may be left for many hours and aurone is still produced in good yield. In addition the reaction was carried out



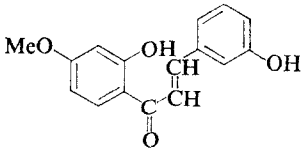
(XVIII)



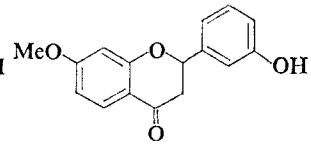
(XIX)



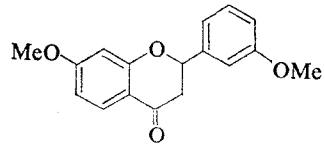
(XX)



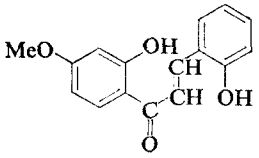
(XXI)



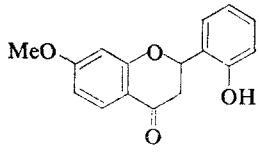
(XXII)



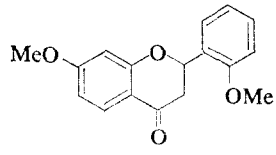
(XXIII)



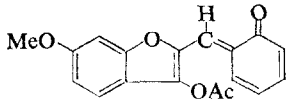
(XXIV)



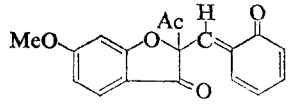
(XXV)



(XXVI)



(XXVII)



(XXVIII)

with a large excess of potassium ferricyanide, and on work-up a 91 per cent yield of recrystallized hydroxy-aurone was isolated. However if 2′-hydroxy-6-methoxyaurone itself is added to the original reaction mixture it is totally destroyed within 5 min.

When 2′-hydroxy-7-methoxyflavanone (XXV) was added to the oxidizing mixture complex formation was not immediate but took place over *ca.* 5 min. If however the flavanone was allowed to stand in the alkaline solution before potassium ferricyanide was added then complex formation was instantaneous. The oxidation products were the same as for the chalcone, and these results would imply that it was the chalcone that was the more immediate precursor of the aurone, as in biological systems.

When 2′,7-dimethoxyflavanone (XXVI) was added to the oxidizing mixture, no reaction could be detected after 18 hr.

DISCUSSION

The first noteworthy point was the lack of oxidation of any compound in which the hydroxyl group on the B ring was methylated, although in every case a free phenolic group (hydrogen-bonded) was available on ring A (the methylated flavanones would have to dissolve as the chalcone anions). In no case could oxidation on ring A be observed, although

the recovery of material was excellent. This is in line with observations on natural systems by Brown who states[51]

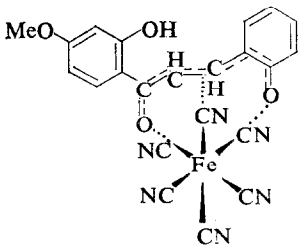
> "... it has been found that certain hydroxylated anthraquinones and anthrones e.g. alizarin-2-glucoside, are not oxidized in the presence of laccase, probably as the result of strong hydrogen bonding between the 1-hydroxyl group and the carbonyl group that makes such molecules resistant to the formation of aryloxy radicals".

Chelation may deactivate ligands to ferricyanide oxidation in *in vitro* systems[52] also. If a radical were produced on ring A from the methylated flavanones, there seems no reason why dimerizations or quinone formation should not proceed. For these reasons we tend to discount oxidation of the 2′-hydroxyl group of the chalcones in the mechanisms given in the various schemes.

Secondly there is, as predicted, a great difference between the compounds bearing a 3′-hydroxyl group on ring B, and those with a 2′- or 4′-hydroxyl group. The former oxidizes slowly and gives no discrete products, the latter oxidize rapidly to single products in high yield (see Fig. 3).

Thirdly although the result of oxidation is a modification of the C_3 unit of the C_6-C_3-C_6 starting material, a free 2′- or 4′-hydroxy group is an absolute requirement for the oxidation, which is clearly a phenolic oxidation. Alkylation of these phenolic groups completely inhibits reaction.

The details of the oxidations are not clear. As the precipitated complex yields only aurone, it seems safe to assume that in it the 2′-hydroxyl group is brought close to the α-carbon atom of the chalcone. A Catalin model of an outer sphere complex of form (XXIX) shows that the oxygen interactions are very favourable and that the hydroxyl group in question is almost on top of the required carbon atom. The acetylation results also favour this type of



(XXIX)

complex. The 4-hydroxychalcone gives a flavone, but this is not general as previously recorded results showed that aurones may result from such systems. It may be that the electron releasing methoxyl group prevents complex formation, but a systematic study would be required before any hypotheses could be presented.

One further point of interest is that the complex acts as a protecting device for the hydroxyaurone which is very rapidly destroyed by an oxidizing environment in which the

[51] B. R. Brown, *Oxidative Coupling of Phenols* (edited by W. I. Taylor and A. R. Battersby), p. 197, E. Arnold (1967).
[52] D. G. Lambert and M. M. Jones, *J. Am. Chem. Soc.* **82**, 4615 (1966).

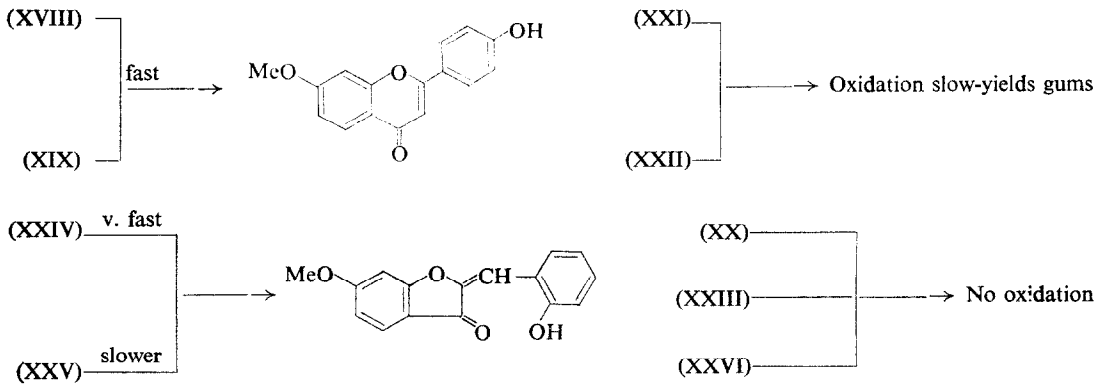


FIG. 3.

complex survives for long periods. This may well have biochemical analogies. 4′-Hydroxy-7-methoxyflavone however survives possibly because the redox potential of the oxidizing agent is not sufficiently high to initiate reaction.

The experiments outlined provide experimental analogies for Scheme 1 and experiments designed to test the other schemes are in hand.

EXPERIMENTAL

All m.ps were measured on a Koffler block and are uncorrected. I.r. spectra were obtained on Perkin-Elmer 237 and 257 spectrometers. U.v. spectra were obtained on a Unicam SP800 spectrometer. PMR spectra were obtained on a Varian 100 Mc machine. Chemical shifts are expressed in τ values relative to trimethylsilane (TMS) as internal standard. Deuterochloroform ($CDCl_3$), hexadeuteroacetone [$(CD_3)_2CO$] or hexadeuterodimethylsulphoxide (DMSO-d_6) solutions were used where appropriate. Mass spectra were obtained variously on the AEI MS.9 and MS.12 spectrometers at 70 eV unless otherwise stated. Silica gel plates supplied by Merk were used for TLC. For column chromatography, silicic acid was supplied by Koch-Light and polyamide by Woelm.

Preparation of Chalcones

All condensations of substituted acetophenones with substituted benzaldehydes to yield hydroxychalcones were carried out by the method detailed below.

2′,4-*Dihydroxy*-4′-*methoxychalcone* (*XVIII*). Peonol (1·6 g; 0·01 mole) and *p*-hydroxybenzaldehyde (1·2 g; 0·01 mole) were together dissolved in the minimum quantity of 95% EtOH. KOH soln. (19 g; 60%, w/w) was added and the mixture diluted with H_2O until the solid mass just dissolved. The solution was kept at 25° for 48 hr, during which time a yellow solid had precipitated. The mixture was diluted with H_2O until all the solid had redissolved and acidified with a stream of CO_2 to give a yellow solid which yielded the title chalcone (2·3 g; 82%) on recrystallization from MeOH m.p. 176–7° (Lit[53] m.p. 176–7°) λ_{max} (EtOH) 370, 306, 240 nm.

4,4′-*Dimethoxy*-2′-*hydroxychalcone* (*XX*). Peonol (1·6 g; 0·01 mole) and anisaldehyde (1·4 g; 0·01 mole) were condensed by the above method to yield the chalcone (XX) m.p. 90–91° (Lit[54] m.p. 92°) (2·4 g; 87%). PMR ($CDCl_3$) τ 6·18 [(s), 6H, (4,4′ OMe's)]; 3·58 [(m) 2H (H3′,H5′)]; 3·11 [(d) J = 9 c/s. 2H (H3, H5)]; 2·14 [(d) J = 9 c/s 2H (H2, H4)]; 2·33 [(d) J = 9 c/s. 1H (H6′)]; 2·53 [(d) J = 15 c/s. 1H (Hα)]; 2·17 [(d) J = 15 c/s. 1H (Hβ)]; −3·50 [(s) 1H (2′OH)]. λ_{max}. (EtOH) 365, 310 nm.

2′,3-*Dihydroxy*-4′-*methoxychalcone* (*XXI*). Peonol (16·4 g; 0·1 mole) and *m*-hydroxybenzaldehyde (12·1 g; 0·1 mole) were similarly condensed to yield the *chalcone* (XXI) m.p. 182–3° (EtOH–water) (19 g; 67%) m^+ = 270·088106. $C_{16}H_{14}O_4$ requires 270·089202. λ_{max} (EtOH) 354, 315 nm.

2,2′-*Dihydroxy*-4′-*methoxychalcone* (*XXIV*). Peonol (16·4 g; 0·1 mole) and salicylaldehyde (12·1 g; 0·1 mole) were condensed together to give the *chalcone* (XXIV) m.p. 178–9° (EtOH) (22 g; 80%) m^+ = 270·088106. $C_{16}H_{14}O_4$ requires 270·089202. PMR [$(CD_3)_2CO$] τ 6·12 [(s) 3H (4′MeO)]; 1·5–3·5 [(m) 9H (Hα, Hβ, A and B ring protons); 0·88 [(s) 1H (2-OH)]; −3·58 [(s) 1H (2′OH)]. λ_{max}. (EtOH) 372, 310 nm.

[53] T. A. GEISSMAN and R. W. CLINTON, *J. Am. Chem. Soc.* **68**, 697 (1946).
[54] S. VON KOSTANECKI and K. J. UPPER, *Chem. Ber.* **37**, 4161 (1904).

Preparation of Flavanones

(a) *Isomerization of the hydroxychalcones.*[49] The hydroxychalcone (10 g) was dissolved in MeOH (1 l.) and sat. aq. Na acetate added (*ca.* 500 ml) until the solution was saturated with respect to both chalcone and sodium acetate. The mixture was refluxed for 30 hr and then extracted with benzene. The benzene soluble fraction was chromatographed[50] on polyamide (500 g) from which elution with MeOH–H_2O (1:1) yielded flavanone and with absolute MeOH yielded chalcone. The following flavanones were prepared in this manner:

4′-Hydroxy-7-methoxyflavanone (*XIX*). m.p. 162–3° (Lit.[55] m.p. 160° (9 g; 90%). λ_{max}. (EtOH) 272, 312 nm).

3′-Hydroxy-7-methoxyflavanone (*XXII*). m.p. 137–8° (9·0 g; 90%) m^+ = 270·088369. $C_{16}H_{14}O_4$ requires 270·089202. λ_{max} (EtOH) 273, 314 nm.

2′-Hydroxy-7-methoxyflavanone (*XXV*). m.p. 192–3° (lit.[56] m.p. 193–4°) (9·6 g; 96%). PMR [$(CD_3)_2CO$] τ 6·11 [(s) 3H (7-MeO)]; 7·12 [(quartet of doublets) 2H (3-H's)]; 4·18 [(dd) 1H (H2)] 2·2–3·5 [(m) 8H (A and B ring protons; 2′OH)]. λ_{max}. (EtOH) 273, 312 nm.

(b) *Direct preparation of flavanones:*

3′,7-Dimethoxyflavanone (*XXIII*). Peonol (1·6 gm; 0·01 mole) and *m*-methoxybenzaldehyde (1·3 g; 0·01 mole) were condensed in the manner outlined above for chalcone preparation to yield the flavanone as a pale yellow precipitate from the diluted alkaline solution before acidification. Any chalcone present was removed by rapidly washing the filtered precipitate with ice cold 5% KOH. Recrystallization from MeOH gave 3′,7-dimethoxyflavanone (XXIII) as yellow needles (2·3 g; 84%) m.p. 103–4° (Lit.[54] m.p. 104°) λ_{max}. (EtOH) 272, 312 nm.

The corresponding chalcone was prepared by dissolving the flavanone in 50% NaOH followed by rapid acidification (Congo red) with conc. HCl. Crystallization from MeOH yielded 2,3′-dimethoxy-2′-hydroxychalcone m.p. 78–9° (Lit.[54] m.p. 80–81°) λ_{max}. (EtOH) 351, 315 nm.

2,7-Dimethoxyflavanone (*XXVI*). Peonol (1·6 g;, 0·01 mole) and *o*-methoxybenzaldehyde (1·3 g; 0·01 mole) yielded under the above conditions the title flavanone (XXVI) m.p. 102–3° (lit[54] m.p. 103°) (2·2 g; 80%) PMR ($CDCl_3$) τ 6·17 [(s) 6H (2′,7 MeO's)] 7·14 [(quartet of doublets) 2H (H3's)]; 4·18 [(d.d) 1H (H2)]. 2·1–3·5 [m(7H)]. λ_{max}. (EtOH) 273, 310 nm.

The corresponding chalcone recrystallized from MeOH in yellow needles m.p. 93–4[8] (lit.[54] m.p. 94°). λ_{max}. (EtOH) 368, 310 nm.

Preparation of Aurones[57]

2′-Hydroxy-6-methoxyaurone. 6-methoxycoumaranone[58] (1 g; 0·066 mole) and salicylaldehyde (0·8 g; 0·066 mole) were dissolved in hot EtOH (10 ml) and piperidine (1 ml) added. The resulting deep red sol. was allowed to stand at 25° for 18 hr. The crystalline material that had separated out was collected and recrystallized from HOAc to give 2-hydroxy-6-methoxyaurone m.p. 258–9° (decomp.). (Lit.[57] m.p. 259° [decomp.]) (1·6 g; 95%). λ_{max}. (EtOH) 392, 332, 262, 250 nm.

3′-Hydroxy-6-methoxyaurone. 6-methoxycoumaranone (1 g; 0·066 mole) and *m*-hydroxybenzaldehyde ((0·8 g; 0·066 mole) yielded under the above conditions, the desired *aurone* m.p. 234–6° (decomp.) (1·3 gm; 69%) m^+ = 268·072835. $C_{16}H_{12}O_4$ requires 268·073552. λ_{max}. (EtOH) 329, 260 nm.

4′-Hydroxy-6-methoxyaurone. 6-Methoxycoumaranone (1 g; 0·066 mole) and *p*-hydroxybenzaldehyde yielded under the above conditions, the desired aurone m.p. 270–2° (decomp.) (1·5 g; 85%) m^+ = 268·073092. $C_{16}H_{12}O_4$ requires 268·073552. λ_{max}. (EtOH) 394, 338 (sh) 259 nm.

Preparation of Flavones[59]

2′-Hydroxy-7-methoxyflavone. Iodine (30 mg) in ethanol (3 ml) was added to a refluxing solution of 2,2′-dihydroxy-4′-methoxychalcone (32 mg) and sodium acetate (0·2 g) in EtOH (3 ml) over a period of 90 min The mixture was refluxed for a further 4 hr. Dilution with H_2O followed by extraction with ether, drying (Na_2SO_4) and removal of solvents gave a pale oil which slowly solidified. Recrystallization from EtOH gave the required flavone m.p. 253–4° (28 mg; 82%). λ_{max}. (EtOH) 326, 252 nm.

4′-Hydroxy-7-methoxyflavone. 4′-Hydroxy-7-methoxyflavanone (XIX) (32 mg) under the same condition yielded the flavone m.p. 260–1° (Lit.[60] m.p. 260°) (26 mg; 75%) PMR [$(CD_3)_2CO$] τ 6·02 [(s) 3H (7 MeO)]; 3·30 [(s) 1H (H3)]; 2·1–2·5 [(m) 3H (aromatic H's)]; 3·0–3·2 [(m) 4H (aromatic H's)]. λ_{max}. (EtOH) 328, 254 nm.

[55] G. D. Bahatia, S. K. Mukerjee and T. R. Seshadri, *Tetrahedron Suppl. No.* 7, 139 (1966).
[56] H. S. Mahal, H. S. Rai and K. Venkataraman, *J. Chem. Soc.* 866 (1935).
[57] R. B. Desai and J. N. Ray, *J. Indian Chem. Soc.* **35**, 83 (1958).
[58] K. von Auwers, *Chem. Ber.* **47**, 3307 (1914); *Liebig's Ann.* **405**, 243 (1914).
[59] N. Narasimhachari and T. R. Seshadri, *Proc. Indian Acad. Sci.* **30A**, 151 (1949).
[60] N. Arnard and K. Venkataraman, *Proc. Indian Acad. Sci.* **26A**, 279 (1947).

Oxidation Experiments

*Oxidation of 2',4-dihydroxy-4'-methoxychalcone. (XVIII)** The chalcone (XVIII) (900 mg; 0·0033 mole) was dissolved in aq. 2N NaOH (6 ml; 0·12 mole) to give a deep orange solution. $K_3Fe(CN)_6$ (2·1 g; 0·006 mole) in H_2O (30 ml) was added immediately, the mixture becoming a dark reddish-brown. After 10 min the mixture was made up to 250 ml (H_2O) and acidified with HOAc to pH 4, when a yellow solid precipitated. This was centrifuged, the supernatant liquid removed, and the solid washed with H_2O until the test for $Fe(CN)_6$ anion was negative. The precipitate was collected and dried *in vacuo* at room temp. to yield a yellow product (890 mg). $\lambda_{max.}$ (EtOH) 253, 315 (s), 328, 370 (s).

In $(CD_3)_2CO$ the solid showed two methoxyl peaks in the PMR spectra at τ 6·02 and τ 6·14 with intensities in the ratio 4:1. Moreover a peak as a singlet at τ 3·3 with one third of the intensity of the peak at τ 6·02, was the singlet proton of either C-3 of a flavone or C-β of the corresponding aurone. A large peak at *m/e* 268 in the mass spectrum confirmed oxidation had taken place.

The mixture (500 mg) was dissolved in pyridine (5 ml) and Ac_2O (2 ml) added. After leaving overnight the mixture was poured into H_2O (100 ml) and extracted with $CHCl_3$. The $CHCl_3$. extract was washed with $NaHCO_3$ to remove any excess HOAc and with saturated $CdCl_2$ solution to remove excess pyridine. The $CHCl_3$ was removed to yield the acetylated mixture (495 mg).

Analytical TLC on silica gel plates using benzene–ethyl acetate (1:1) as solvent showed 2 spots only. Spot A (R_f 0·67) was pale yellow and after exposure to NH_3 became dark yellow in visible light and red under short wave u.v. light. Its R_f and chemical behaviour were in all respects identical with those of an authentic sample of 2',4-diacetoxy-4'-methoxychalcone. Spot, B, R_f 0·51, was darker yellow becoming deep orange-yellow on exposure to NH_3 and bright yellow under u.v. light.[61] Its properties were in all respects identical with authentic 4'-acetoxy-7-methoxyflavone.

The crude acetylated mixture (500 mg) was directly crystallized from EtOH to give the flavone acetate (375 mg) m.p. 150–1° (lit.[60] m.p. 149–50) mmp with authentic 4'-acetoxy-7-methoxyflavone 150–1°. PMR ($CDCl_3$) τ 7·69 [(s) 3H (4'-$OCOCH_3$)]; 6·11 [(s) 3H (7-OMe)]; 3·24 [(s) 1H (H-3)]; 3·26–3·33 [(m) 2H (H-6, H-8)]. 2·83 [(d) J = 9 c/s 2 H (H-3', H-5')]; 2·11 [(d) J = 9 c/s 2H (H-2', H-6')]; 2·32 [(d) J = 9 c/s 1H (H-5)]. $\lambda_{max.}$ (EtOH) 318, 252 nm.

The mother liquors were collected and the solvent removed. The mixture left was resolved by TLC in the same system as for the analysis, to yield 2',4-diacetoxy-4'-methoxychalcone (85 mg) and further 2'-acetoxy-7-methoxyflavone (20 mg).

From 500 mg of acetylated product the total yield of the flavone acetate was 395 mg (79%) and of the chalcone diacetate 85 mg (17%).

Oxidation of 4'-hydroxy-7-methoxyflavanone (XIX). The flavanone (XIX) (300 mg) was oxidized in the same manner as the corresponding chalcone, and work-up after 10 min gave an identical mixture of the flavone acetate (238 mg; 77%) and of chalcone diacetate (47 mg; 16%).

Oxidation of 4,4'-dimethoxy-2'-hydroxychalcone (XX). The chalcone (XX) (300 mg) was treated with the standard oxidizing mixture. Work-up after 24 hr at room temp. gave a mixture of the chalcone (XX) and the corresponding flavanone (6:1, by examination of the u.v. spectrum) (290 mg) identical to that produced on acidification of an alkaline solution of the chalcone which had been made up to the same ionic strength as the oxidizing mixture with K_2SO_4.

Oxidation of 4'-hydroxy-7-methoxyflavone. The title flavone (30 mg) was treated as for the corresponding flavanone. After 10 min the product (22 mg) had identical u.v. ($\lambda_{max.}$ (EtOH) 326, 252 nm) and m.p. 260–1° as the starting materials. The mixed m.p. with starting materials was undepressed.

Oxidation of 4'-hydroxy-6-methoxyaurone. When the title aurone (30 mg) was subjected to normal oxidizing conditions for 10 min no water-insoluble material could be extracted. There was no trace of the starting material.

Oxidation of 2',3-dihydroxy-4'-methoxychalcone (XXI). (*a*) The chalcone (XXI) (300 mg) was exposed to oxidation by $K_3Fe(CN)_6$ for 10 min. Work-up as usual gave starting materials in quantitative yield. (b). The chalcone (XXI) (300 mg) was oxidized for 19 hr at room temp. and worked-up by acidification as usual. This produced a tarry material which was extracted into ethyl acetate. Removal of the solvents yielded a gum which resisted all attempts at separation and analysis.

Oxidation of 3'-hydroxy-7-methoxyflavanone (XXII). Treatment of the flavanone (XXII) (300 mg) with the oxidizing mixture and work-up as usual after 30 min gave a mixture of the flavanone (XXII) and the chalcone (XXI). (1:3, by consideration of the u.v. spectrum) identical to the mixture recovered on acidification of a basic solution of the flavanone made up to the same ionic strength with K_2SO_4.

Oxidation of 3',7-dimethoxyflavanone (XXIII). The flavanone (XXIII) (300 mg) was dissolved in NaOH to yield a solution of the chalcone anion, which was subjected to the oxidizing mixture for 18 hr. Work-up as usual gave only the flavanone (XXIII) and the corresponding chalcone (1:3, by consideration of the u.v.

* The method used here was used in all other oxidation experiments unless otherwise stated.

[61] M. K. SEIKEL in *Chemistry of Flavanoid Compounds* (edited by T. A. GEISSMAN), p. 51, Pergamon Press, Oxford (1962).

spectrum) (283 mg), identical with the mixture recovered on acidification of basic solution of the flavanone made up to the same ionic strength with K_2SO_4.

Oxidation of 2,2′-*dihydroxy*-4′-*methoxychalcone* (*XXIV*). The chalcone (XXIV) (900 mg) was treated with alkaline $K_3Fe(CN)_6$ as usual. On addition of the ferricyanide a precipitate immediately formed and this was at once spun down at 1500 g for 5 min. The supernatant liquid and complex were worked up separately, then acetylated. From the supernatant liquid 232 mg of solid were obtained and from the complex 779 mg.

Acetylated material from supernatant liquid. The mixture (232 mg) was resolved by preparative TLC (silica plates; ethyl acetate–benzene [3:7]; each plate run twice) into four bands. Band I, Deep yellow, R_f 0·79; band II, pale yellow, R_f 0·69; band III, yellow-red, R_f 0·51; band IV, dark yellow, R_f 0·0.

Band I. m.p. 145–6° (116 mg) λ_{max}. (EtOH) 343 (sh), 317, 268 nm. λ_{max}. (0·002M NaOEt) 396, 301, 279 nm. The PMR was identical with that of 2-acetoxy-2′-hydroxy-4′-methoxychalcone τ ($CDCl_3$) 7·60 [(s) 3H (2-$OCOCH_3$)]; 6·15 [(s) 3H (4′OMe)]; *ca.* 3·5 [(m) 2H (H-3′, H-5′)]; 2·0–2·9 [(m) 7H (Hα, Hβ and aromatic H's)]; −3·28 [(s) 1H (2′OH)]. The mmp. of band I with the authentic chalcone monoacetate was undepressed.

Band II. m.p. 165–6° (45 mg.) λ_{max}. (EtOH) 323, no shift on the addition of base, had a PMR spectrum identical with that of authentic 2′2-diacetoxy-4′-methoxychalcone. τ ($CDCl_3$) 7·66 [(s) 3H (2′-$OCOCH_3$)]; 7·60 [(s) 3H (2-$OCOCH_3$)]; 6·21 [(s) 3H 4′-OMe]; 2·2–3·5 [(m) 9H]. Mixed m.p. with authentic 2,2′-diacetoxy-4′-methoxychalcone. 166–7°.

Band III. (15 mg) contained a mixture of the chalcone diacetate and a small quantity of 2′-acetoxy-6-methoxyaurone as indicated by TLC and PMR comparisons.

Band IV. (~ 40 mg) consisted of an, as yet unidentified, intractable gum.

Acetylated material from complex. The mixture (779 mg) was subjected to column chromatography on silicic acid using increasing concentrations of ethyl acetate in benzene. The following fourteen gross fractions were collected.

TABLE 2. CHROMATOGRAPHY OF ACETYLATED MATERIAL FROM COMPLEX

Fraction	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Weight (mg)	18	24	20	20	50	43	12	29	115	250	230	125	70	90

Fraction 1 was identified as 2,2′-diacetoxy-4′-methoxychalcone. Fractions 2–3 were 3′-*acetoxy*-6-*methoxyaurone*, m.p. 161–2° (Lit.[58] m.p. 160) mmp. with authentic material 161–2°. λ_{max}. 326, 260 nm. ν_{max}. 1760, 1690 cm^{-1}. The PMR spectrum was identical with that of an authentic sample of the aurone acetate. τ ($CDCl_3$) 7·60 [(s) 3H (2′-$OCOCH_3$)]; 6·10 [(s) 3H (6-OMe)]; 3·08 [(s) 1H (Hβ)]; 3·30 [(m) 2H (H-5, H-7)]; 2·5–3·0 [(m) 3H (H4′, H-5′ H-6′)]; 2·28 [(d) J = 10 c/s 1H (H-4)]; 1·7 [(d) 1H (H-3′)].

Although there appeared to be two main compounds (fractions 5–7; 8–14) [Analysis: C = 69·2%, H = 4·4%; $C_{16}H_{12}O_4$ requires C = 69·2%, H = 4·3%] it was found that treatment of each of these fractions with conc. HCl or with 60% NaOH, qusntitatively yielded a red solid m.p. 257–8. λ_{max} (EtOH) 392, 323, 262, 250, mixed m.p. with authentic 2′-hydroxy-6-methoxyaurone 258–9°. A compound sample derived from all these fractions had identical PMR to that of authentic 2′-hydroxy-6-methoxyaurone. τ (DMSO-d_6) 6·07 [(s) 3H (6 MeO)]; 2·6–3·3 [(m) 6H (2′OH, 5 aromatic H's)]; 2·82 [(s) 1H (Hβ)]; 2·31 [(d) J = 9 c/s. 1H (H-4)]; 1·80 [(d,d) 1H (H-3′)]. Acetylation of this material gave rise to an acetate with identical u.v., i.r,. PMR and mass spectra and m.p. to authentic 2′-acetoxy-6-methoxyaurone.

Oxidation of 2′-*hydroxy*-7-*methoxyflavanone* (*XXV*). When the oxidation of the flavanone (XXV) (300 mg) was carried out under identical conditions to those employed for the corresponding chalcone (XXIV) complex formation was slow (*ca.* 5 min) but the products (287 mg) after formation of the complex were identical in all respects to those derived from the chalcone (XXIV).

When the alkaline solution of the flavanone (XXV) was left for 10 min prior to addition of the oxidant then complex formation was immediate, the products being the same as before.

Oxidation of 2,2′-*dihydroxy*-4′-*methoxychalcone* (*XXIV*) *with excess ferricyanide.* The chalcone (XXIV) (300 mg; 0·001 mole) was dissolved in 2N NaOH (2 ml; 0·004 mole) and $K_3Fe(CN)_6$ (1·4 g; 0·004 mole) in water (10 ml) added. A dark brown precipitate formed. Work-up as usual of the total mixture gave an orange-yellow product which on crystallization from HOAc gave 2′-hydroxy-6-methoxyaurone (273 mg; 91%) m.p. 259–60° mmp. with authentic sample 259–60°.

Oxidation of 2′,7-*dimethoxyflavanone* (*XXVI*). The flavanone (XXVI) (300 mg) was subjected to the standard oxidizing conditions for 18 hrs. Work-up produced a mixture of the flavanone (XXVI) and the corresponding chalcone (280 mg) (chalcone–flavanone, 2·6:1, by consideration of the u.v. spectrum) identical to that obtained by acidification of an alkaline solution of the flavanone of the same ionic strength.

Oxidation of 2'-hydroxy-6-methoxyaurone. The title aurone (300 mg) was subjected to the standard oxidiz ing conditons. After 5 min no water insoluble material could be extracted. There was no trace of starting material.

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