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A STUDY OF NUCLEAR PRENYLATION AND ALLYLATION OF ISOFLAVONES AND SYNTHESIS OF 4'-METHYL ETHERS OF OSAJIN AND WARANGALONE

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Abstract—Nuclear prenylation of 5,7-dihydroxyisoflavones with prenyl bromide in the presence of methanolic methoxide is found to give a mixture of three compounds viz., 6,8-di-*C*-prenyl (25%), 6-*C*-prenyl (15%) and 7-*O*-prenyl (2%) derivatives. 6,8-Di-*C*-prenyl-4'-methoxy-5,7-dihydroxyisoflavone (IIa) thus obtained gives on oxidative cyclization with DDQ a mixture of two products; the major component agreed with 4'-*O*-methylosajin and the minor component should therefore be 4'-*O*-methylwarangalone.

Nuclear allylation with allyl bromide in the presence of methanolic potash yields a mixture of six products viz, 6-*C*-allyl (17%), 6-*C*-allyl-7-*O*-allyl (5%), 8-*C*-allyl (12%), 8-*C*-allyl-7-*O*-allyl- (3%), 6,8-di-*C*-allyl (2%) and 7-*O*-allyl (3%) derivatives. The difference in the behaviour of prenyl and allyl bromides seems to be due to the greater reactivity of the former.

AS MANY as seventeen naturally occurring isoflavones have been shown to possess an isopentenyl unit either in the open chain form or as a hetero-oxygen ring viz, pyran or dihydropyranol. They are osajin,[1] warangalone[2,3] (iso-osajin or scandenone), chandalone[3], scandinone[2] (osajin-5-methyl ether), pomiferin,[1] derrulone,[4] robustone,[4] toxicarol isoflavone,[5] durmillone,[6] auriculatin,[7] munetone,[8] mundolone,[9] jamaicin,[9] ichthynone,[9] piscerythrone[10] and piscidone.[10] As no one of the compounds has been totally synthesized, a suitable method of introducing an isopentenyl unit in a preformed isoflavone molecule had to be explored.

As a phloroglucinol oxygenation pattern is found in the ring A and the *C*-isopentenyl unit is present either in 6- or 8- or both positions, the introduction of an isopentenyl unit is a normal *C*-alkenylation reaction analogous to *C*-methylation. On this basis, it was considered necessary to examine nuclear prenylation of typical 5,7-dihydroxyisoflavones under the conditions of analogous nuclear methylation.[11] Earlier[12] this prenylation has been brought about under Lewis acid conditions with 5,7-dihydroxy-4'-methoxy- and 5,7-dihydroxy-3',4'-dimethoxyisoflavones by reacting them with prenyl bromide in the presence of zinc chloride in benzene medium, when dihydro-iso-osajin monomethyl ether (Va) and dihydro-isopomiferin dimethyl ether respectively were obtained.

For the present study of nuclear prenylation, 5,7-dihydroxy-4'-methoxyisoflavone (Ia) was chosen as a model having substituents in both benzene rings. It was carried out by treatment with prenyl bromide in the presence of methanolic sodium methoxide. A mixture of three products, separable by column chromatography, was obtained. The first component obtained in maximum yield (ca. 25%) appeared to be a di-prenylated compound on the basis of its elemental analysis, which showed the

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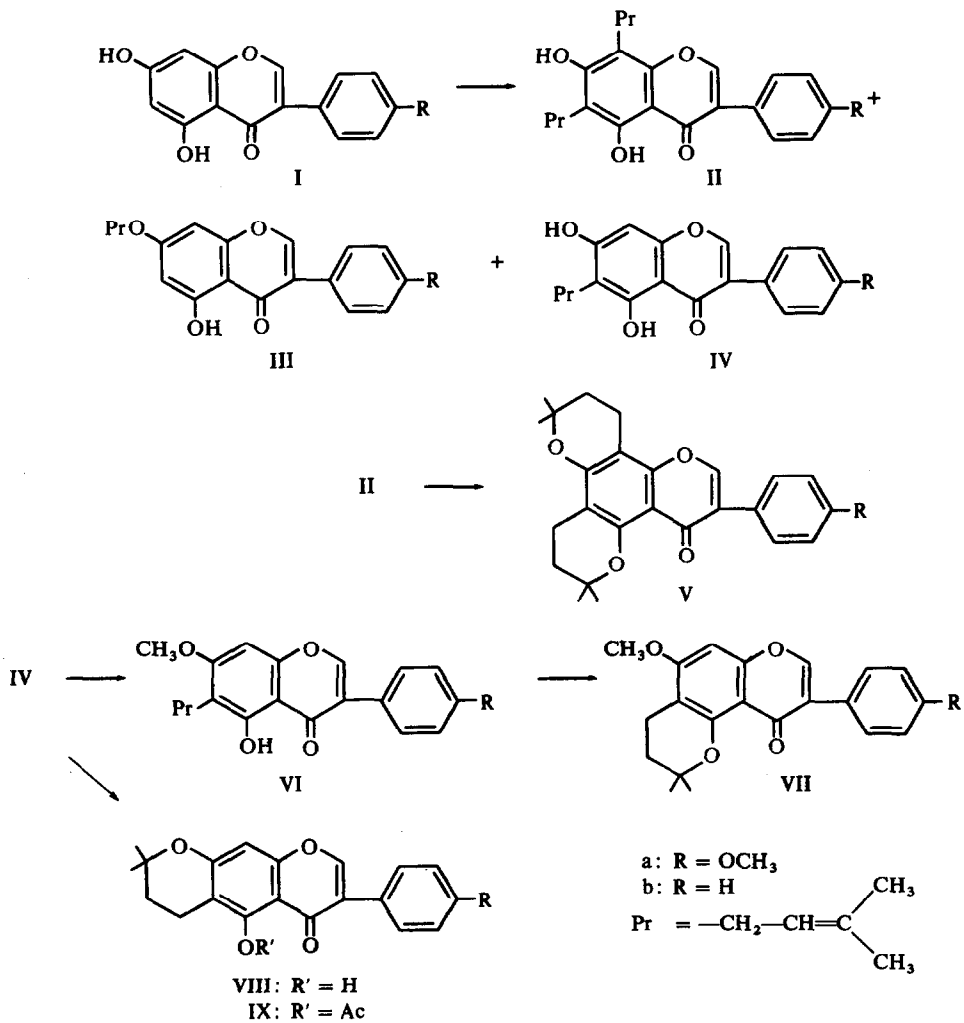
presence of two prenyl units. Its ferric reaction and solubility in sodium carbonate indicated that both the hydroxyls were free and that it had two *C*-prenyl units. That the two prenyl units had entered the two available nuclear positions in the ring A was shown by its NMR spectrum which has the expected resonance signals of two *C*-prenyl units but no signal for an aromatic proton of the ring A. This was further confirmed by treatment of the compound with formic acid which cyclized the prenyl units with adjacent OH groups giving rise to di-(dihydropyrano-) derivative (Va), found to be identical with dihydro-iso-osajin monomethyl ether obtained earlier.[12] Its NMR spectrum (Table 1) agrees with this assigned structure.



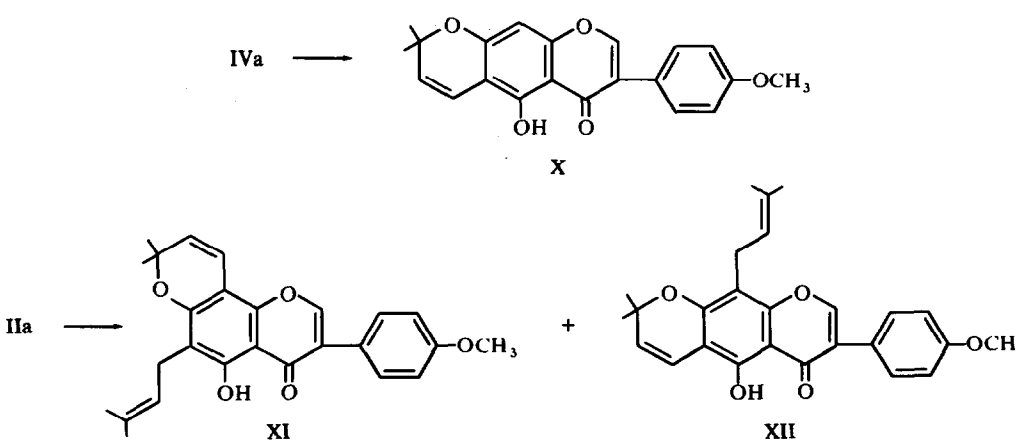
The second product was obtained in very small yield (ca. 2%) and was identified as 7-prenyloxy-4′-methoxy-5-hydroxy-isoflavone (IIIa) on the basis of its elemental analysis and NMR spectrum (Table 1) which shows resonance signals of one prenyl ether proton. The structure (IIIa) was finally confirmed by direct comparison with an

authentic sample synthesized by partial *O*-prenylation of 5,7-dihydroxy-4′-methoxy-isoflavone (Ia); m.m.p. being undepressed and the IR spectra superimposable.

The third component was isolated in about 15% yield. It was soluble in aqueous sodium carbonate and gave a ferric reaction and the elemental analysis showed the presence of one prenyl unit. That this prenyl unit is in the nuclear position of ring A was shown: (1) by its partial methylation and the study of the NMR spectrum of the resulting methyl ether, which indicates the presence of two OMe groups and one *C*-prenyl unit (Table 1); and (2) by cyclization to a dihydro-pyrano derivative (VIIIa) which showed a positive ferric reaction and, therefore, had the 5-OH free and the 7-OH involved in cyclization. The NMR spectrum of acetate IXa shows the presence of one 2,2-dimethyl-dihydro-pyrano unit and the presence of one aromatic proton in the ring A. These data led to the conclusion that the third prenylated product is either the 6-*C*-prenyl or 8-*C*-prenyl derivative of 5,7-dihydroxy-4′-methoxyisoflavone. In order to make a choice between these two structures, the cyclization of the partial methyl ether with formic acid was studied. The resulting dihydro-pyrano derivative was devoid of ferric reaction and therefore had structure VIIa. Based on these data, the 6-*C*-prenyl structure (IVa) was established for the third product and VIa for its methyl ether.

In order to obtain some of the derivatives of naturally occurring pyranoisoflavones, the reaction of the above mentioned *C*-prenylated isoflavones with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) was examined. 6-*C*-Prenyl-4′-methoxy-5,7-dihydroxy-isoflavone (IVa) underwent smooth oxidative cyclization with DDQ. The only product formed was identified as a linear pyrano derivative (X) since it gave a positive ferric reaction and shows the expected NMR spectrum (Table 1).

Next 6,8-di-*C*-prenyl-4′-methoxy-5,7-dihydroxyisoflavone (IIa) was subjected to oxidative cyclization with 1 mole of DDQ. The product was a mixture of two compounds. The major one was identical with 4′-*O*-methylosajin (XI), prepared from natural osajin by partial methylation. The minor compound should, therefore, be 4′-*O*-methylwarangalone which is supported by NMR spectrum.



A parallel series of experiments was carried out on the simpler model 5,7-dihydroxy-isoflavone (Ib). Here also a mixture of three products was obtained and the major

TABLE 1. NMR SPECTRA OF PRENYLATED ISOFLAVONES IN $CDCl_3$ WITH TMS AS INTERNAL REFERENCE STANDARD USING VARIAN A-60 NMR SPECTROMETER (VALUES REPRESENT δ IN PPM)

Compound No.	H-2	H-6	H-8	H2′,6′	H3′,5′	—OCH₃	—CH=	—CH₂—	=C(CH₃)₂	>C(CH₃)₂	—O—CO—CH₃
IIa	7·90 (s) (1H)	—	—	7·48 (2H) (d, J = 9)	6·96 (2H) (d, J = 9)	3·82 (s) (3H)	5·28 (2H) (m)	3·48 (4H) (d, J = 7)	1·84 (s) 1·75 (s) (12H)	—	—
IIIa	7·86 (s) (1H)	6·37 (2H) (d, J = 2)		7·48 (2H) (d, J = 8·4)	6·96 (2H) (d, J = 9·6)	3·81 (s) (3H)	5·40 (m) (1H)	4·56 (2H[b]) (d, J = 7)	1·76 (s) 1·79 (s) (6H)	—	—
VIa	7·80 (s) (1H)	—	6·36 (s) (1H)	7·45 (2H) (d, J = 8·4)	6·94 (2H) (d, J = 9)	3·81 (s) 3·85 (s) (6H)	5·18 (m) (1H)	3·35 (2H) (d, J = 6)	1·76 (s) 1·67 (s) (6H)	—	—
Va	7·75 (s) (1H)	—	—	7·49 (2H) (d, J = 8·4)	6·91 (2H) (d, J = 8·4)	3·77 (s) (3H)	—	2·69 (m) (4H) 1·84 (m) (4H)	—	1·38 (s) 1·33 (s) (12H)	—
IXa	7·80 (s) (1H)	—	6·76 (s) (1H)	7·45 (2H) (d, J = 8·4)	6·96 (2H) (d, J = 8·4)	3·80 (s) (3H)	—	2·70 (m) (2H) 1·82 (m) (2H)	—	1·36 (s) (6H)	2·43 (s) (3H)
VIIa	7·64 (s) (1H)	—	6·32 (s) (1H)	7·44 (2H) (d, J = 9)	6·88 (2H) (d, J = 9)	3·84 (s) (3·77 (s) (6H)	—	2·61 (m) (2H) 1·75 (m) (2H)	—	1·38 (s) (6H)	—
X	7·77 (s) (1H)	—	6·28 (s) (1H)	7·45 (2H) (d, J = 9)	6·93 (2H) (d, J = 9)	3·82 (s) (3H)	5·58[a] (1H) 6·70[a] (1H)	—	—	1·46 (s) (6H)	—
XI	7·81 (s) (1H)	—	—	7·43 (2H) d, J = 9)	6·94 (2H) (d, J = 9)	3·82 (s) (3H)	5·18 (m) (1H) 5·55 (1H)[a] (d, J = 10) 6·67 (1H)[a] (d, J = 10)	3·34 (2H) (d, J = 8·4)	1·80 (s) 1·68 (s) (6H)	1·47 (s) (6H)	—
XII	7·88 (s) (1H)	—	—	7·49 (2H) (d, J = 8·4)	6·97 (2H) (d, J = 9)	3·85 (s) (3H)	5·22 (m) (1H) 5·63 (1H)[a] 6·75 (1H)[a]	3·41 (2H) (d, J = 7)	1·82 (s) 1·70 (s) (6H)	1·46 (s) (6H)	—

Compound No.	H-2	H-6	H-8	H2′,3′,4′,5′,6′	—CH=	—CH$_2$—	CH_3 \ C= / CH_3	CH_3 \ C / CH_3	—O—CO—CH$_3$
IIb	7·95 (s) (1H)	—	—	7·50 (5H) (broad m)	5·30 (m) (2H)	3·50 (4H) (d, J = 7)	1·77 (s) 1·86 (s) (12H)	—	—
IIIb	7·88 (s) (1H)	6·40 (2H) (d, J = 2)		7·48 (5H) (broad m)	5·48 (m) (1H)	4·59 (2H)[b] (d, J = 8)	1·78 (s) 1·81 (s) (6H)	—	—
Vb	7·79 (s) (1H)	—	—	7·48 (5H) (broad m)	—	2·75 (m) (4H) 1·86 (m) (4H)	—	1·42 (s) 1·39 (s) (12H)	—
IXb	7·80 (s) (1H)	—	6·77 (s) (1H)	7·46 (5H) (broad m)	—	2·72 (m) (2H) 1·82 (m) (2H)	—	1·36 (s) (6H)	2·43 (s) (3H)

s = singlet, d = doublet, m = multiplet

[a] —CH= of chromene ring as a doublet with J = 10 c/s

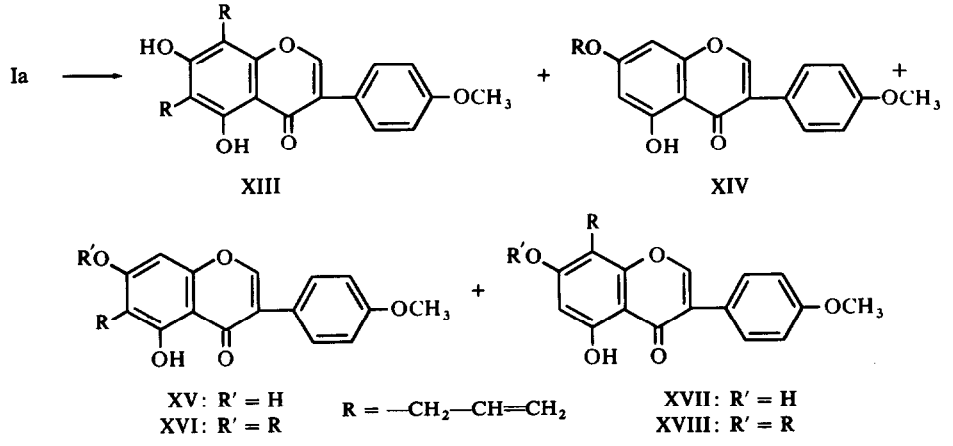
[b] —CH$_2$— of *O*-prenyl unit

compound was the 6,8-di-*C*-prenyl derivative (IIb, 25%). The mono-*C*-prenyl derivative (IVb) was obtained in lesser amount (15%) and the least was that of 7-*O*-prenyl ether (IIIb). The identity of these compounds was established as described above for the 4′-methoxy series.

The above results of nuclear prenylation are analogous to those obtained in the nuclear prenylation of 1,3-dihydroxy-7-methoxyxanthone,[13] 2-methyl-5,7-dihydroxychromone[14] and β-resacetophenone[14] under alkaline conditions and are somewhat different from that of the nuclear prenylation in Lewis acid medium in which case,[12] the product is only the di-(dihydropyrano) derivative.

Earlier in the study of xanthones[13, 15] it was noted that there was considerable difference in the nature of the products obtained by using dimethylallyl bromide and the simpler allyl bromide. In order to determine if this difference is general irrespective of groups of polyphenols used, nuclear allylation of isoflavones was investigated.

5,7-Dihydroxy-4′-methoxyisoflavone (Ia) when refluxed with allyl bromide in the presence of methanolic potash gave a mixture of seven compounds which were first separated into neutral and alkali soluble fractions followed by further separation by column chromatography.



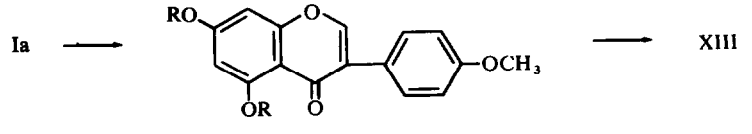
XIII XIV

XV: R′ = H
XVI: R′ = R

R = —CH_2—CH=CH_2

XVII: R′ = H
XVIII: R′ = R

The alkali soluble fraction yielded a mixture of three products contaminated with the starting material (13%). The first product obtained by further column chromatography in 2% yield gave a positive ferric reaction and the elemental analysis showed the presence of two allyl units. That both these allyl units were present in the nucleus was shown by the NMR spectrum (Table 2). Hence it was considered to be 6,8-di-*C*-allyl-4′-methoxy-5,7-dihydroxyisoflavone (XIII). The structure was further supported by its unambiguous synthesis which consists in Claisen rearrangement of 5,7-di-allyloxy-4′-methoxyisoflavone (XIX).



XIX: R = —CH_2—CH=CH_2

TABLE 2. NMR SPECTRAL DATA OF ISOFLAVONES IN $CDCl_3$ USING TMS AS INTERNAL REFERENCE STANDARD TAKEN ON VARIAN A-60 NMR SPECTROMETER (VALUES REPRESENT δ VALUES IN PPM)

Compound No.	H-2	4'-$OC\underline{H}_3$	H2',6'	H3',5'	H-6	H-8	—O—CO—$C\underline{H}_3$	Ar—O—$C\underline{H}_2$	Ar—$C\underline{H}_2$—	$=C\underline{H}_2$	—$C\underline{H}$=
XIII	7·94 (s) (1H)	3·85 (s) (3H)	7·51 (2H) (d, J = 8·4)	7·0 (2H) (d, J = 9·6)	—	—	—	—	3·56 (4H) (d, J = 6)	5·21 (m)[b] (4H)	5·98 (m) (2H)
XV	7·86 (s) (1H)	3·82 (s) (3H)	7·44 (2H) (d, J = 8)	6·97 (2H) (d, J = 9)	—	7·26 (s) (1H)	2·32 (s) (3H) 2·42 (s) (3H)	—	3·36 (2H) (d, J = 6)	5·07 (m)[b] (2H)	5·68 (m) (1H)
XVII	7·97 (s) (1H)	3·83 (s) (3H)	7·48 (2H) (d, J = 8·4)	7·00 (2H) (d, J = 8·4)	6·93 (s)[c] (1H)	—	2·41 (s) (3H) 2·34 (s) (3H)	—	3·56 (2H) (d, J = 6)	5·10 (m)[b] (2H)	5·87 (m) (1H)
XVI	7·83 (s) (1H)	3·80 (s) (3H)	7·46 (2H) (d, J = 8·4)	6·97 (2H) (d, J = 8·4)	—	6·38 (s) (1H)	—	4·59 (2H) (d, J = 4·8)	3·46 (2H) (d, J = 6·5)	5·01 (m)[b] (2H) 5·40 (m)[a] (2H)	5·93 (m) (2H)
XVIII	7·93 (s) (1H)	3·82 (s) (3H)	7·50 (2H) (d, J = 9·0)	6·98 (2H) (d, J = 9·6)	6·41 (s) (1H)	—	—	4·62 (2H) (d, J = 4·8)	3·50 (2H) (d, J = 7·2)	4·99 (m)[b] (2H) 5·39 (m)[a] (2H)	5·90 (m) (2H)

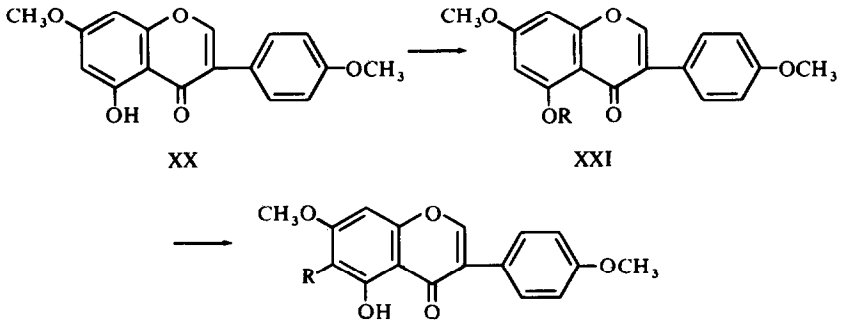
s = singlet, d = doublet, m = multiplet

[a] $C\underline{H}_2$ of Ar—O—CH_2—CH=$C\underline{H}_2$

[b] $C\underline{H}_2$ of Ar—CH_2—CH=$C\underline{H}_2$

[c] This singlet has merged with the resonance signal of 3',5' protons

The second alkali soluble product obtained in the highest yield (ca. 17%) gave a positive ferric reaction and its elemental analysis showed the presence of only one allyl unit. The formation of a diacetate showed the presence of two free hydroxyls and hence the allyl unit could only be in the nucleus. This was also supported by the NMR spectrum of the diacetate (Table 2). Between the two possible structures viz 6-*C*-allyl (XV) and 8-*C*-allyl (XVII) the former was chosen as correct because its 7-*O*-methyl ether was identical with the authentic 6-*C*-allyl derivative (XXII) prepared as follows. 5-Hydroxy-7,4′-dimethoxyisoflavone (XX) was allylated in the 5-position and the resulting compound (XXI) on Claisen migration gave 5-hydroxy-6-*C*-allyl-7,4′-dimethoxyisoflavone (XXII).



The third alkali soluble product formed in 12% yield was found to be isomeric with the above compound and hence it was considered to be the 8-*C*-allyl isomer (XVII). It was confirmed by its unambiguous synthesis which involved Claisen rearrangement of 7-allyloxy-4′-methoxy-5-hydroxyisoflavone.

The neutral fraction of the nuclear allylated product gave three compounds. The first obtained in 5% yield showed a positive ferric reaction and had two allyl units. One allyl unit was located in the nucleus and the other as allyl ether on the basis of its NMR spectral data (Table 2). Further it was found identical with the compound obtained by partial *O*-allylation of 6-*C*-allyl-4′-methoxy-5,7-dihydroxyisoflavone (XV). Thus it is 6-*C*-allyl-7-allyloxy-4′-methoxy-5-hydroxyisoflavone (XVI).

The second component of the neutral fraction formed in 3% yield was found to be isomeric with the first component on the basis of its analytical and spectral data. It was identified as 8-*C*-allyl-7-allyloxy-4′-methoxy-5-hydroxyisoflavone (XVIII) by direct comparison with the compound obtained by partial *O*-allylation of the authentic sample of 8-*C*-allyl-4′-methoxy-5,7-dihydroxyisoflavone (XVII).

The third component also obtained in small yield (3%) was found to be 7-allyloxy-4′-methoxy-5-hydroxyisoflavone (XIV) identical with the authentic sample prepared by partial *O*-allylation of Ia.

The above results on nuclear allylation thus show a substantial difference from those of nuclear prenylation. The first noteworthy difference is that although allyl ethers of *C*-allylated compounds are formed albeit in poor yields, the *O*-prenyl derivative of only the starting material is formed in traces. This may be due to the instability of the prenyl ethers. Another significant difference is that although the di-*C*-prenyl derivative

is formed in larger yields than the di-*C*-allyl derivative, the 8-*C*-prenyl derivative was not isolated, whereas 8-*C*-allyl derivative was obtained in comparable yield.

EXPERIMENTAL

Unless otherwise stated, all m.ps are uncorrected and were taken in a sulphuric acid bath; UV spectra were taken in methanolic soln, the figures given in parenthesis in UV spectra represent log ε values; light petroleum had boiling range 60–80°; silica gel was used for column chromatography and TLC was carried out on silica gel 'G' chromoplates using solvent systems (A) chloroform:benzene (4:1), (B) benzene:light petroleum (3:2) and (C) chloroform:methanol (99:1), R_f values are those taken on TLC.

Nuclear prenylation of 5,7-dihydroxy-4'-methoxyisoflavone (Ia).

To a soln of Ia[16] (4 g) in anhyd MeOH (150 ml) a methanolic soln of NaOMe (7 g Na/100 ml MeOH) was added. The mixture was cooled, treated with prenyl bromide (8·0 ml) in one lot and refluxed for 3 hr. After removal of the solvent, the mixture was treated with ice and acidified in the cold with dil HCl. The solid product was examined on TLC using solvent A which showed the presence of a number of compounds. It was, therefore, subjected to column chromatography and the column eluted successively with (i) benzene: light petroleum (30:70) (ii) benzene:light petroleum (40:60) and (iii) benzene:light petroleum (70:30) thus giving the following three main fractions A to C.

Fraction A crystallized from benzene–light petroleum mixture yielding IIa as pale yellow rhombic plates (1g), m.p. 163–164°; green ferric reaction: R_f 0·86 (solvent A); λ_{max} 270 nm (4·62); ν_{max} 1645 cm^{-1} (isoflavone C=O); (Found: C, 73·8; H, 6·6. $C_{26}H_{28}O_5$ requires: C, 74·3; H, 6·7%).

Fraction B crystallized from benzene–light petroleum mixture and IIIa was obtained as colourless needles (50 mg), m.p. and m.m.p. with an authentic sample (see later) 148–150°; red brown ferric reaction; R_f 0·80 (solvent A); λ_{max} 262 nm (4·63); ν_{max} 1675, 1655 cm^{-1} (isoflavone C=O).

Fraction C crystallized from benzene affording IVa as colourless thick needles (0·6 g), m.p. 215–217°; R_f 0·55 (solvent A); green ferric reaction; λ_{max} 267 nm (4·67); ν_{max} 1640 cm^{-1} (isoflavone >C=O); (Found: C, 71·2; H, 5·5. $C_{21}H_{20}O_5$ requires: C, 71·6; H, 5·7%).

Dihydro-iso-osajin methyl ether (Va). The derivative IIa (200 mg) was heated on a steam bath with formic acid (15 ml) for 1 hr. The resulting yellow soln was poured over ice and the solid collected. It was purified by column chromatography and the fraction which eluted with benzene–EtOAc (98:2) crystallized from MeOH affording the Va as colourless needles (120 mg), m.p. 202–203° (lit.[12] m.p. 198–199°); no ferric reaction; λ_{max} 266 nm (4·62); ν_{max} 1655 cm^{-1} (isoflavone >C=O); (Found: C, 73·8; H, 6·8. $C_{26}H_{28}O_5$ requires: C, 74·3; H, 6·7%).

7-Prenyloxy-4'-methoxy-5-hydroxyisoflavone (IIIa). To an acetone soln of 5,7-dihydroxy-4'-methoxyisoflavone (0·3 g) prenyl bromide (0·17 ml) and ignited K_2CO_3 (0·8 g) was added and the mixture refluxed for 3 hr. Acetone was removed and water added. The solid crystallized from benzene–light petroleum as colourless small needles (0·3 g), m.p. 148–149°; brown ferric reaction, (Found: C, 71·7; H, 5·4. $C_{21}H_{20}O_5$ requires: C, 71·6; H, 5·7%).

6-C-Prenyl-7,4'-dimethoxy-5-hydroxyisoflavone (VIa). Compound IVa (100 mg) was partially methylated with one mole Me_2SO_4 (0·03 ml), K_2CO_3 and acetone, and VIa was crystallized from benzene–light petroleum as colourless plates (100 mg), m.p. 122–123°; green ferric reaction; λ_{max} 268 nm (4·66); ν_{max} 1650 cm^{-1} (isoflavone >C=O), (Found: C, 72·6; H, 6·4. $C_{22}H_{22}O_5$ requires: C, 72·1; H, 6·1%).

7,4'-Dimethoxy-2'',2''-dimethyl-3'',4''-dihydropyrano(5'',6'':5,6)-isoflavone (VIIa). The above VIa (150 mg) was heated on a steam bath with formic acid (10 ml) for 1 hr. The resulting yellow soln was poured over ice and the solid subjected to column chromatography and elution with benzene which gave VIIa. This crystallized from benzene–light petroleum as colourless plates (100 mg), m.p. 159–160°; no ferric reaction; λ_{max} 262 nm (4·54); ν_{max} 1645 cm^{-1} (>C=O), (Found: C, 71·7; H, 6·4. $C_{22}H_{22}O_5$ requires: C, 72·1; H, 6·1%).

4'-Methoxy-5-hydroxy-2'',2''-dimethyl-3'',4''-dihydro-pyrano(5'',6'':6,7)-isoflavone (VIIIa). Compound IVa (200 mg) was heated on a steam bath with formic acid (10 ml) for 1 hr as described. The product was subjected to column chromatography and elution with benzene which gave VIIIa. This crystallized from benzene–light petroleum as colourless long plates (140 mg), m.p. 184–185°; green ferric reaction; λ_{max} 265 nm (4·58); ν_{max} 1655 cm^{-1}. (Found: C, 71·6; H, 6·0. $C_{21}H_{20}O_5$ requires: C, 71·6; H, 5·7%).

Its acetate IXa prepared by Ac_2O-pyridine method crystallized from MeOH as colourless needles, m.p. 222–223°; no ferric reaction, (Found: C, 70·0; H, 5·4. $C_{23}H_{22}O_6$ requires: C, 70·0; H, 5·6%).

4'-Methoxy-5-hydroxy-2'',2''-dimethyl-pyrano(5'',6'':6,7)isoflavone (X). To a soln of IVa (250 mg) in dry benzene (10 ml) DDQ (180 mg) was added and the resulting red soln refluxed for 20 min on a boiling water bath, resulting in the separation of colourless hydroquinone. The soln was filtered while hot and the residue washed with benzene. Removal of the solvent gave a residue which was purified by column chromatography. Elution with benzene–light petroleum (1:1) gave the required X which crystallized from light petroleum as colourless plates (180 mg), m.p. 136–137°; λ_{max} 226, 283 nm (4·32, 4·63); ν_{max} 1655 cm^{-1}, (Found: C, 72·0; H, 5·5. $C_{21}H_{18}O_5$ requires: C, 72·0; H, 5·2%).

Reaction of compound IIa *with DDQ (Formation of osajin-4'-methyl ether* (XI) *and warangalone-4'-methyl ether* (XII)

To a soln of IIa (0·5 g) in dry benzene (15 ml) DDQ (200 mg) was added and the soln refluxed for 20 min on a water bath and worked up as described. The residue was chromatographed and the column developed with light petroleum. Elution with benzene–light petroleum (5:95) gave the first few fractions as a single entity. It crystallized from light petroleum as pale yellow needles (90 mg), m.p. 136–137°; green ferric reaction; λ_{max} 273 nm (4·45); ν_{max} 1640 cm^{-1}; (Found: C, 74·2; H, 6·5. $C_{26}H_{26}O_5$ requires: C, 74·6; H, 6·3%). Its mixed m.p. with an authentic sample of osajin-4'-methyl ether, prepared by the partial methylation of natural osajin using 1 mole of Me_2SO_4, K_2CO_3 and acetone, was undepressed and IR spectrum superimposable.

The later fractions were found by TLC (solvent B) to be a mixture of two products. They were separated by preparative TLC using silica gel 'G' plates and the solvent system benzene:light petroleum (3:2). The plates were run 3 times in the same solvent. The first component (R_f 0·32) was identical with osajin-4'-methyl ether while the second compound (R_f 0·25) on recovery from silica gel gave warangalone-4'-methyl ether which crystallized from light petroleum as long thick needles, m.p. 109–110°; green ferric reaction; λ_{max} 285 nm (4·79); ν_{max} 1655 cm^{-1} (>C=O), (Found: C, 74·2; H, 6·8. $C_{26}H_{26}O_5$ requires: C, 74·6; H, 6·3%).

Nuclear prenylation of 5,7-dihydroxyisoflavone (1b)

To a soln of 5,7-dihydroxyisoflavone[16] (3·6 g) in anhyd MeOH (125 ml) a methanolic soln of NaOMe (5·5 g Na/70ml MeOH) was added. The mixture was cooled and treated with prenyl bromide (7·5 ml) in one lot and refluxed for 3 hr. Working up of the mixture as described gave a solid which was subjected to column chromatography and the column eluted successively with (i) benzene:light petroleum (20:80), (ii) benzene:light petroleum (30:70) and (iii) benzene:light petroleum (50:50), thus giving three main fractions A, B and C.

Fraction A crystallized from light petroleum yielding IIb as pale yellow thick needles (0·9 g), m.p. 101–102°; green ferric reaction; R_f 0·91 (solvent A); λ_{max} 268 (4·20); ν_{max} 1650 cm^{-1} (isoflavone >C=O), (Found: C, 76·6; H, 7·0. $C_{25}H_{26}O_4$ requires: C, 76·9; H, 6·7%).

Fraction B crystallized from benzene–light petroleum yielding IIIb as colourless needles (50 mg), m.p. and m.m.p. with an authentic sample (see later) 133–134°; brown ferric reaction; R_f 0·87 (solvent A); λ_{max} 260 nm (4·38); ν_{max} 1655, 1680 cm^{-1} (isoflavone >C=O).

Fraction C crystallized from benzene affording IVb as colourless silky needles (0·55 g), m.p. 210–211°; R_f 0·64 (solvent A); green ferric reaction; λ_{max} 266, 302 nm (4·51, 3·92 resp); ν_{max} 1640 cm^{-1} (isoflavone >C=O), (Found: C, 74·0; H, 5·7. $C_{20}H_{18}O_4$ requires: C, 74·5; H, 5·6%).

2'',2''-Dimethyl-3'',4''-dihydropyrano(5'',6'':5,6)-2''',2'''-dimethyl-3''',4'''-dihydropyrano(5''',6''': 7,8)isoflavone (Vb). The derivative IIb (200 mg) was heated on a steam bath with formic acid (15 ml) for 1 hr and the product worked up as described. The solid was chromatographed and elution with benzene–EtOAc (99:1) gave the required derivative Vb which crystallized from benzene–light petroleum as colourless needles (100 mg), m.p. 233–234°; no ferric reaction; λ_{max} 265 nm (4·62); ν_{max} 1655 cm^{-1} (isoflavone >C=O), (Found: C, 76·6; H, 6·4. $C_{25}H_{26}O_4$ requires: C, 76·9; H, 6·7%).

7-Prenyloxy-5-hydroxyisoflavone (IIIb). To an acetone soln of Ib (0·2 g) prenyl bromide (0·12 ml) and K_2CO_3 (0·5 g) was added and the soln refluxed for 3 hr and worked up as described for *O*-prenylation. The solid crystallized from benzene–light petroleum as colourless needles (0·2 g), m.p. 132–133°; green ferric reaction, (Found: C, 74·2; H, 5·6. $C_{20}H_{18}O_4$ requires: C, 74·5; H, 5·6%).

5-Hydroxy-2'',2''-dimethyl-3'',4''-dihydropyrano(5'',6'':6,7)isoflavone (VIIIb). The derivative IVb (200 mg) was heated on a steam bath with formic acid (12 ml) for one hr and the product worked up as before. The solid was chromatographed and the fraction which was eluted with benzene crystallized from benzene yielding VIIIb as colourless crystals (120 mg), m.p. 204–205°; green ferric reaction; λ_{max} 262, 304 nm (4·44, 3·78 resp); ν_{max} 1650 cm^{-1} (isoflavone >C=O); (Found: C, 74·3; H, 5·7. $C_{20}H_{18}O_4$ requires: C, 74·5; H, 5·6%). Its acetate (IXb) prepared by Ac_2O-pyridine method crystallized from MeOH as colourless needles, m.p. 175–176°; no ferric reaction, (Found: C, 72·1; H, 5·8. $C_{22}H_{20}O_5$ requires: C, 72·5; H, 5·5%).

Nuclear allylation of 5,7-dihydroxy-4'-methoxyisoflavone

To a soln of 5,7-dihydroxy-4'-methoxyisoflavone (3 g) in anhyd MeOH (150 ml) allyl bromide (4 ml) and KOH (3·5 g) was added and the soln refluxed for 20 hr. During this period more of allyl bromide (1·5 ml) and KOH (2 g) were added simultaneously after 8 and 12 hr. The solvents were distilled under reduced pressure and water (250 ml) added. The resulting mixture was extracted with chloroform and the aqueous soln acidified and extracted with ether. The chloroform layer (neutral-fraction) was examined on TLC (solvent A) which showed the presence of three compounds A, B and C. The alkali soluble fraction on TLC examination (solvent C) indicated the presence of four compounds D, E, F and G. These two fractions were separately subjected to column chromatography and the compounds separated as follows:

The components of the neutral fraction were gradually eluted with (i) light petroleum (ii) benzene–light petroleum (5:95) and (iii) benzene–light petroleum (10:90) when the following three compounds were obtained:

Compound A crystallized from light petroleum as colourless needles (150 mg), m.p. 113–114°; green ferric reaction; R_f 0·50 (solvent A); λ_{max} 267 nm (4·55); ν_{max} 1650 cm^{-1} (>C=O), (Found: C, 72·0; H, 5·8. $C_{22}H_{20}O_5$ requires: C, 72·5; H, 5·5%). These data along with NMR data establish it as 6-*C*-allyl-7-allyloxy-4'-methoxy-5-hydroxyisoflavone (XVI).

Compound B crystallized from light petroleum as XVIII in almost colourless plates (100 mg), m.p. and m.m.p. with an authentic sample (see later) 76–77°; λ_{max} 264 nm (4·82); ν_{max} 1660 cm^{-1} (>C=O).

Compound C crystallized from benzene–light petroleum giving XIV as colourless needles (100 mg), m.p. and m.m.p. with an authentic sample (see later) 172–173°; green ferric reaction; λ_{max} 261 nm (4·53); ν_{max} 1660 cm^{-1} (>C=O).

The components D–G of the alkali soluble fraction were eluted successively from the column with (i) benzene:light petroleum (1:1), (ii) benzene alone, (iii) benzene:EtOAc (99:1) and (iv) benzene:EtOAc (98:2).

Compound D crystallized from benzene–light petroleum yielding XIII as colourless long needles (50 mg), m.p. and m.m.p. with an authentic sample (see later) 139–140°; green ferric reaction; λ_{max} 269 nm (4·62).

Compound E crystallized from benzene as colourless plates (500 mg), m.p. 184–185°; green ferric reaction; λ_{max} 266 nm (4·34); ν_{max} 1640 cm^{-1} (>C=O); (Found: C, 70·1; H, 5·4. $C_{19}H_{16}O_5$ requires: C, 70·4; H, 5·0%).

These data along with the NMR data established it as XV. Its partial methyl ether prepared by acetone–K_2CO_3 method crystallized from benzene–light petroleum as colourless plates, m.p. and m.m.p. with an authentic sample (see later) 148–149°; ν_{max} 1650 cm^{-1}.

Compound F crystallized from benzene yielding XVII as colourless needles (350 mg), m.p. and m.m.p. with an authentic sample (see later) 199–201°; green ferric reaction; R_f 0·29 (solvent C); λ_{max} 266 nm (4·55); ν_{max} 1650 cm^{-1} (—C=O).

Compound G crystallized from benzene yielding the unchanged Ia (400 mg).

Reference compounds

7-Allyloxy-4'-methoxy-5-hydroxyisoflavone (X1V). A soln of 5,7-dihydroxy-4'-methoxyisoflavone (1·1 g) in dry acetone (50 ml) was refluxed with allyl bromide (0·35 ml) and anhyd K_2CO_3 (4 g) for 3 hr. The insoluble K-salts were filtered off, washed with hot acetone and the solvent removed to yield a solid which on crystallization from MeOH gave XIV as colourless needles (1·1 g), m.p. 170–171°; R_f 0·38 (solvent A), (Found: C, 70·4; H, 5·1. $C_{19}H_{16}O_5$ requires: C, 70·4; H, 5·0%).

8-C-*Allyl-4'-methoxy-5,7-dihydroxyisoflavone* (XVII). The above XIV (0·9 g) was heated under reduced press at 200–210° for 2·5 hr. It was then cooled and dissolved in ether. The ether extract was extracted with 8% Na_2CO_3 aq and the alkaline extract acidified with dil HCl. The solid thus obtained crystallized from benzene as colourless needles (0·6 g), m.p. 199–200°; R_f 0·29 (solvent C); (Found: C, 70·5; H, 5·1. $C_{19}H_{16}O_5$ requires: C, 70·4; H, 5·0%).

8-C-*Allyl-7-allyloxy-4'-methoxy-5-hydroxyisoflavone* (XVIII). A mixture of XVII (200 mg), dry acetone (15 ml), allyl bromide (1 mole equiv, 0·07 ml) and anhyd K_2CO_3 (0·5 g) was refluxed for 3 hr. The required XVIII crystallized from light petroleum as colourless needles, m.p. 76–77°; R_f 0·42 (solvent A), (Found: C, 72·1; H, 5·6. $C_{22}H_{20}O_5$ requires: C, 72·5; H, 5·5%).

5,7-*Diallyloxy-4'-methoxyisoflavone* (XIX). To an acetone soln, of 5,7-dihydroxy-4'-methoxyisoflavone (1·1 g) allyl bromide (1 ml) and anhyd K_2CO_3 (5 g) was added and the mixture refluxed for 72 hr till no ferric reaction was obtained. The product (XIX) crystallized from benzene–light petroleum as colourless silky needles (1·0 g), m.p. 94–95°; no ferric reaction, (Found: C, 72·0; H, 5·8. $C_{22}H_{20}O_5$ requires: C, 72·5; H, 5·5%).

6,8-*Di-C-allyl-4'-methoxy-5,7-dihydroxyisoflavone* (XIII). The above XIX (0·8 g) was heated at 205–210° under reduced press for 2 hr. The product was dissolved in ether and extracted with 1% KOH aq. The alkaline extract was acidified and the solid so obtained crystallized from benzene–light petroleum as colourless long needles (0·6 g), m.p. 139–140°; R_f 0·83 (solvent C), (Found: C, 72·3; H, 5·2. $C_{22}H_{20}O_5$ requires: C, 72·5; H, 5·5%).

5-*Allyloxy-7,4'-dimethoxyisoflavone* (XXI): To a soln of XX (1 g) in acetone (50 ml) excess allyl bromide and K_2CO_3 was added and the soln refluxed till no ferric reaction. The resulting soln was filtered and acetone removed. The solid crystallized from benzene–light petroleum as colourless needles (1 g), m.p. 106–107°; no ferric reaction, (Found: C, 70·6; H, 5·7. $C_{20}H_{18}O_5$ requires: C, 71·0; H, 5·4%).

6-C-*Allyl-7,4'-dimethoxy-5-hydroxyisoflavone* (XXII). The above XXI (0·6 g) was heated at 200–210° under reduced press for 2 hr. The resulting solid crystallized from benzene–light petroleum as colourless plates (0·5 g), m.p. 148–149°; green ferric reaction, (Found: C, 71·0; H, 5·3. $C_{20}H_{18}O_5$ requires: C, 71·0; H, 5·4%).

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REFERENCES

[1] *Naturally Occurring Oxygen Ring Compounds* (Edited by F. M. Dean), p. 380. Butterworths, London (1963).
[2] A. Pelter and P. Stainton, *J. Chem. Soc.* (C) 701 (1966).
[3] C. P. Falshaw, R. A. Harmer, W. D. Ollis, R. E. Wheeler, V. R. Lalitha and N. V. Subba Rao, *Ibid.* 374 (1969)
[4] A. J. East, W. D. Ollis and R. E. Wheeler, *Ibid.* 365 (1969).
[5] S. H. Harper and W. G. E. Underwood, *Ibid.* 4203 (1965).
[6] W. D. Ollis, C. A. Rhodes and I. O. Sutherland, *Tetrahedron* **23**, 4741 (1967).
[7] L. Crombie, B. Tuck and D. A. Whiting, *J. Chem. Soc.* (C) 1899 (1968).
[8] S. F. Dyke, W. D. Ollis and M. Sainsbury, *Ibid.* 749 (1966).
[9] A. C. Jain, *An Evaluation of the recent methods of isoflavone Synthesis*, Hyderabad Symposium on *Synthesis of physiologically active heterocyclic compounds* Dec (1964).
[10] C. P. Falshaw, W. D. Ollis, J. A. Moore and K. Magnus, *Tetrahedron* Suppl. No. **7**, 333 (1966).
[11] A. C. Jain and T. R. Seshadri, *Quart Rev.* **10**, 169 (1956).
[12] K. S. Raizada, P. S. Sarin and T. R. Seshadri, *J. Sci. Industr. Res. India* **19B**, 499 (1960).
[13] A. C. Jain, V. K. Khanna and T. R. Seshadri, *Tetrahedron* **25**, 2787 (1969).
[14] A. C. Jain, Pyare Lal and T. R. Seshadri, *Ind. J. Chem.* **7**, 1072 (1969)
[15] A. C. Jain, V. K. Khanna and T. R. Seshadri, *Ibid.* **7**, 1182 (1969)
[16] W. Baker, J. Chadderton, J. B. Harborne and W. D. Ollis, *J. Chem. Soc.* 1852 (1953).