The Chemistry of the ' Insoluble Red ' Woods. Part XII.[1] Some Reactions of Isoflavylium Salts

By **Mohga M. E. Badran** and **W. Basil Whalley,*** The School of Pharmacy, The University of London, London WC1N 1AX

Various methoxyisoflavylium perchlorates have been condensed with *NN*-dimethylaniline to yield 2-substituted flav-3-enes, which were oxidised to the corresponding, highly coloured, 2-(*p*-dimethylaminophenyl)isoflavylium salts.

FLAVYLIUM salts (functioning as electrophiles)[2] rapidly condense with *NN*-dimethylaniline to furnish[2,3] 4-substituted flavylium derivatives, of type (1). We now report the results of an analogous investigation with isoflavylium salts which are readily available from our earlier research.[4]

The present work was prompted by our continuing interest in the ' insoluble red ' woods, which furnish, *inter alia*, the complex anhydrobenzopyranol bases santalin[1] and santarubin,[1] to which we have assigned the structural type (2). More recently, unequivocal evidence for these structures has been provided by Merlini *et al.*[5] These pigments exhibit a novel and unique combination of two C_{15} flavanoid equivalents, and one possible biogenetic mode for achieving the first phase of biosynthesis would be as illustrated in (3), a process which would also simply and elegantly explain the co-occurrence of the isomeric santalin and santarubin.

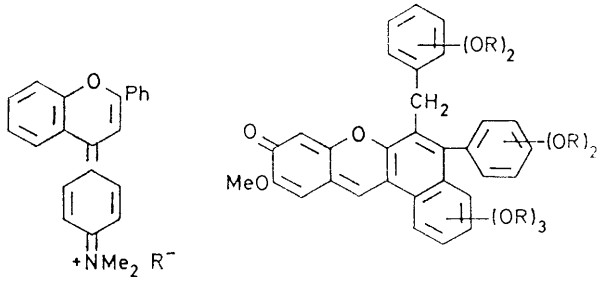
To test the general validity of this hypothesis we have investigated the behaviour of isoflavylium salts as potential electrophiles. Thus, when a solution of 7-methoxyisoflavylium perchlorate[4] (4) and *NN*-dimethylaniline in methanol was warmed on a steam-bath a mixture of the benzopyranol methyl ether (5; R = OMe) and a product formulated as 2-(*p*-dimethylaminophenyl)-7-methoxyisoflav-3-ene (6) was rapidly formed. The condensation proceeded even more readily, and in almost quantitative yield, in the absence of a solvent. The n.m.r. spectrum of (6) has signals at τ 7.15 (6 H, s, NMe_2), 6.36 (3 H, s, OMe), and 2.60—3.80 (14 H, m, aromatic), and was not very informative concerning the structure. The u.v. spectrum [$\lambda_{max.}$ 209, 257, and 335 nm (log ε 4.54, 4.67, and 4.27)] was similar to that of 7-methoxy-2-methylisoflav-3-ene[3] (5; R = Me) [$\lambda_{max.}$ 210, 245, and 323 nm (log ε 4.32, 4.24, and 4.43)] and to that of the methyl ether of 7-methoxy-3-phenylbenzopyranol[4] (5; R = OMe) [$\lambda_{max.}$ 210, 247, and 323 nm (log ε 4.39, 4.20, and 4.45)]; this correspondence clearly supported structure (6) as opposed to the alternative (7). This conclusion is in accord with general theoretical principles.

[1] Part XI, D. W. Mathieson, B. J. Millard, J. W. Powell, and W. B. Whalley, *J.C.S. Perkin I*, 1973, 184.
[2] R. Wizinger and H. Luthiger, *Helv. Chim. Acta*, 1953, **36**, 526.
[3] M. Blackburn, G. B. Sankey, A. Robertson, and W. B. Whalley, *J. Chem. Soc.*, 1957, 1573.
[4] C. A. Anirudhan, W. B. Whalley, and M. M. E. Badran, *J. Chem. Soc.*, 1966, 629.
[5] A. Arnone, L. Camarda, L. Merlini, and G. Nasini, *J.C.S. Perkin I*, 1975, 186.

Hydrogenation of the isoflavene (6) readily gave the isoflavan (8), the n.m.r. spectrum of which exhibited signals at τ 7.12 (6 H, s, NMe_2), 6.92 (2 H, m, CH_2), 6.55 (1 H, m, benzylic proton at C-3), 6.12 (3 H, s, OMe), 4.62 (1 H, d, O·CH), and 2.75—3.38 (12 H, m, aromatic). Comparison of these data with those for the corresponding 7-methoxyisoflavan [4] (9) confirms the structure (6). The isoflav-3-ene (6) formed a monopicrate, a methiodide, and a methosulphate.

Oxidation of the isoflav-3-ene (6) occurred most readily in ethereal solution with hydrogen chloride to form the colourless 3-phenylbenzopyran-2-ol as a gum, characterised as the intensely coloured picrate (10; R = $C_6H_2N_3O_7$), the perchlorate (10; R = ClO_4) and tetrachloroferrate (10; R = $FeCl_4$). [The cation may also be written as (11).]

The isoflav-3-ene (6) is very resistant to the action of alkali. Oxidation with potassium permanganate furnished (i) 4-dimethylaminobenzil (12; R = Me), (ii) 4-methylaminobenzil (12; R = H), (iii) 4-(*N*-methylformamido)benzil (12; R = CHO), and (iv) 2-hydroxy-4-methoxybenzoic acid.



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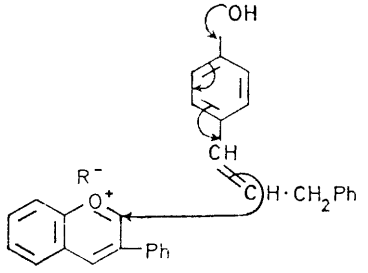

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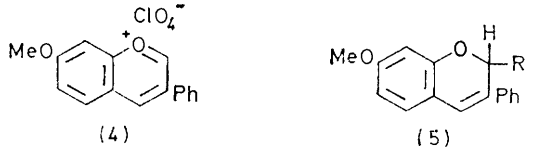

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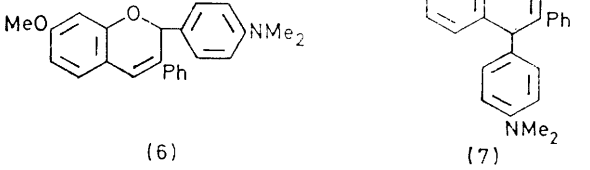

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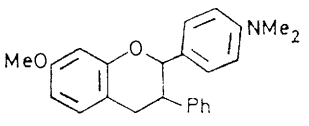

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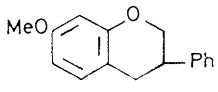

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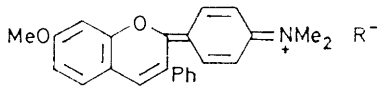

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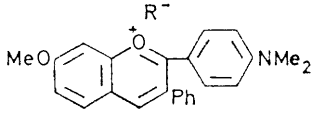

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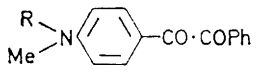

(12)

Similar series of derivatives were prepared by the action of *NN*-dimethylaniline upon 2′,7-dimethoxy-, 3′,4′,7-trimethoxy-, and 4′,5,7-trimethoxy-isoflavylium perchlorates.

The ease of condensation of *NN*-dimethylaniline with 4′,5,7-trimethoxyisoflavylium perchlorate is convincing collateral evidence for the occurrence of substitution at C-2; we have established previously [3] that a C-5 substituent in the flavylium system essentially inhibits substitution at C-4.

These results provide *a priori* evidence for the general validity of the concept that the illustrated mechanism (3) is a feasible step in the biosynthetic derivation of santalin and its congeners from an isoflavanoid residue and an equivalent open chain C_{15} unit.

EXPERIMENTAL

Light petroleum refers to the fraction of b.p. 60—80°.

Derivatives of 7-Methoxyisoflavylium Perchlorate.—A mixture of 7-methoxyisoflavylium perchlorate (0.3 g) and *NN*-dimethylaniline (0.3 ml) was warmed on a steam-bath for 1—2 min; methanol (5 ml) was then added. Purification of the crystalline precipitate from methanol gave 2-(p-*dimethylaminophenyl*)-7-*methoxyisoflav*-3-*ene* (6) (0.28 g) in needles, m.p. 151° [Found: C, 80.5; H, 6.5; N, 4.0; OMe, 9.2. $C_{23}H_{20}NO(OMe)$ requires C, 80.6; H, 6.5; N, 3.9; OMe, 8.7%]. Prepared quantitatively in alcoholic solution, the *picrate* formed golden-yellow plates, m.p. 184° (decomp.) [Found: C, 61.8; H, 4.5; N, 9.2; OMe, 5.5. $C_{29}H_{23}N_4O_8$(OMe) requires C, 61.4; H, 4.5; N, 9.5; OMe, 5.3%].

Hydrogenation of this isoflav-3-ene (60 mg) dissolved in ethanol (60 ml) containing 5% palladium–carbon (25 mg) proceeded rapidly to yield 2-(p-*dimethylaminophenyl*)-7-*methoxyisoflavan* (8) (40 mg), which separated from ethanol in needles, m.p. 125° (Found: C, 79.9; H, 7.0; N, 3.9; OMe, 7.1. $C_{24}H_{25}NO_2$ requires C, 80.2; H, 7.0; N, 3.9; OMe, 8.6%). The *picrate* formed yellow needles, m.p. 167° (decomp.) (from ethanol) (Found: C, 61.2; H, 4.9; N, 9.1. $C_{30}H_{28}N_4O_9$ requires C, 61.2; H, 4.8; N, 9.5%). Methyl-

ation of the isoflavene (6) (25 mg) in boiling acetone (10 ml) containing an excess of methyl iodide during 4 h, gave the *quaternary methiodide* (25 mg), which formed plates, m.p. 130° (decomp.) (from light petroleum–acetone–ethyl acetate) (Found: C, 59.6; H, 5.6; I, 24.2; N, 2.1. $C_{25}H_{26}INO_2$ requires C, 60.1; H, 5.2; I. 25.3; N, 2.8%). Prepared similarly, the *methosulphate* formed needles, m.p. 163° (decomp.) (from light petroleum) (Found: C, 63.9; H, 6.0; N, 2.6; S, 6.1. $C_{26}H_{29}NO_6S$ requires C, 64.6; H, 6.0; N, 3.0; S, 6.7%).

2-(p-*Dimethylaminophenyl*)-7-*methoxy*-3-*phenyl*-1-*benzopyran*-2-*ol*.—A solution of the isoflavene (6) (0.2 g) in ethyl acetate (20 ml) was saturated at 0 °C with hydrogen chloride. The solution became intense blue-brown in colour; 24 h later the mixture was diluted with methanol (20 ml) and the solvent removed *in vacuo*. The residue was dissolved in methanol (20 ml) containing sodium acetate and the colourless solution was diluted with water (50 ml). The product was extracted with chloroform to yield 2-(*p*-dimethylaminophenyl)-7-methoxy-3-phenyl-1-benzopyran-2-ol as a gum. Prepared from a solution of this pyranol in methanol by addition of 60% perchloric acid, 2-(p-*dimethylaminophenyl*)-7-*methoxyisoflavylium perchlorate* formed intensely blue needles, m.p. 262° (decomp.) (Found: C, 62.6; H, 4.8; Cl, 7.9; N, 2.8. $C_{24}H_{22}ClNO_6$ requires C, 63.3; H, 4.9; Cl, 7.8; N, 3.1%). The *picrate* separated from ethanol in olive-green plates, m.p. 221° (decomp.) (Found: C, 61.2; H, 4.1; N, 9.3. $C_{40}H_{24}N_4O_9$ requires C, 61.6; H, 4.1; N, 9.6%). The *tetrachloroferrate* separated from methanol in dark blue rosettes, m.p. 177° (decomp.) (Found: C, 51.5; H, 3.9; Fe, 9.5; N, 2.0. $C_{24}H_{22}Cl_4FeNO_2$ requires C, 52.0; H, 4.0; Fe, 10.1; N, 2.5%).

Oxidative Degradation of the Isoflav-3-*ene* (6).—Potassium permanganate (1 g) in water (27 ml) was added during 5 h to a solution of the isoflav-3-ene (0.2 g) in acetone (25 ml) (with stirring). The products from three oxidations were isolated in the normal manner and combined to yield (i) 4-dimethylaminobenzil [6] (30 mg), m.p. 114° (Found: C, 75.4; H, 6.1; N, 5.8. Calc. for $C_{16}H_{15}NO_2$: C, 75.8; H, 6.0; N, 5.5%), identical with an authentic specimen; (ii) 4-*methylaminobenzil* (25 mg) in yellow prisms, m.p. 85° (from light petroleum) (Found: C, 75.1; H, 5.5; N, 6.0. $C_{15}H_{13}NO_2$ requires C, 75.3; H, 5.4; N, 5.9%), $\nu_{max.}$ 1 630 (C=O), 1 670 (C=O), and 3 370 cm^{-1} (NH), τ 1.93—3.53 (9 H, m, ArH), 5.33br (1 H, s, NH), and 7.10 (3 H, s, NMe); (iii) 4-(*N-methylformamido*)*benzil* (10 mg), which separated from light petroleum in yellow needles, m.p. 118° (Found: C, 71.5; H, 4.8; N, 5.6. $C_{16}H_{13}NO_3$ requires C, 71.9; H, 4.9; N, 5.2%), τ 0.28 (1 H, s, CHO), 1.80—2.73 (9 H, m, ArH), and 6.63 (3 H, s, NMe); (iv) 2-hydroxy-4-methoxybenzoic acid (20 mg), identical with an authentic specimen.

Derivatives of 4′,7-*Dimethoxyisoflavylium Perchlorate*.—Prepared from this perchlorate (0.1 g) and dimethylaniline (0.1 ml), 2-(p-*dimethylaminophenyl*)-4′,7-*dimethoxyisoflav*-3-*ene* formed needles (80 mg), m.p. 128° (from methanol) [Found: C, 77.2; H, 6.3; N, 3.4; OMe, 16.5. $C_{23}H_{19}NO(OMe)_2$ requires C, 77.5; H, 6.5; N, 3.6; OMe, 16.0%]. The *picrate* separated from ethanol in golden-brown needles, m.p. 161° (decomp.) (Found: C, 60.9; H, 4.6; N, 8.6. $C_{31}H_{28}N_4O_{10}$ requires C, 60.4; H, 4.6; N, 9.1%).

2-(*p*-Dimethylaminophenyl)-7-methoxy-3-(4-methoxyphenyl)-1-benzopyran-2-ol formed a colourless gum, the *perchlorate* of which separated from methanol in intensely green plates, m.p. 233° (decomp.) (Found: C, 61.8; H, 5.0; Cl, 7.4; N, 2.5. $C_{25}H_{24}ClNO_7$ requires C, 61.8; H, 5.0; Cl, 7.3; N, 2.9%). The *picrate* formed olive-green plates, m.p. 205° (decomp.) (from ethanol) (Found: C, 60.5; H, 4.3; N, 8.7. $C_{31}H_{26}N_4O_{10}$ requires C, 60.6; H, 4.3; N, 9.1%).

Hydrogenation of 2-(*p*-dimethylaminophenyl)-4′,7-dimethoxyisoflav-3-ene gave the *isoflavan* in needles, m.p. 177° (from ethanol) [Found: C, 76.7; H, 7.1; N, 3.5; OMe, 16.8. $C_{23}H_{21}NO(OMe)_2$ requires C, 77.1; H, 7.0; N, 3.6; OMe, 15.9%]. The *picrate* formed yellow needles, m.p. 155° (decomp.) (from aqueous ethanol) (Found: C, 60.9; H, 5.1; N, 8.2. $C_{31}H_{30}N_4O_{10}$ requires C, 60.2; H, 4.9; N, 9.1%).

Derivatives of 2′,7-*Dimethoxyisoflavylium Perchlorate*.—Prepared in the usual manner, 2-(p-*dimethylaminophenyl*)-2′,7-*dimethoxyisoflav*-3-*ene* formed needles, m.p. 131° (from methanol) [Found: C, 77.7; H, 6.6; N, 3.6; OMe, 16.1. $C_{23}H_{19}NO(OMe)_2$ requires C, 77.5; H, 6.5; N, 3.6; OMe, 16.0%]. The *picrate* separated from aqueous ethanol in golden-yellow needles, m.p. 147° (decomp.) (Found: C, 60.5; H, 4.6; N, 8.9. $C_{31}H_{28}N_4O_{10}$ requires C, 60.4; H, 4.6; N, 9.1%).

Although the corresponding benzopyranol was a gum, 2-(p-*dimethylaminophenyl*)-2,7′-*dimethoxyisoflavylium perchlorate* formed intensely blue needles, m.p. 278° (decomp.) (from methanol) (Found: C, 61.2; H, 5.0; N, 2.2. $C_{25}H_{24}ClNO_7$ requires C, 61.8; H, 5.0; N, 2.9%). The *picrate* formed dark blue prisms, m.p. 244° (decomp.) (from ethanol) (Found: C, 61.5; H, 4.5; N, 9.4. $C_{31}H_{26}N_4O_{10}$ requires C, 60.6; H, 4.3; N, 9.1%).

Derivatives of 3′,4′,7-*Trimethoxyisoflavylium Perchlorate*.—Prepared in the usual manner, 2-(p-*dimethylaminophenyl*)-3′,4′,7-*trimethoxyisoflav*-3-*ene* formed needles, m.p. 80° (from methanol) [Found: C, 64.6; H, 6.25; N, 3.4; OMe, 22.6. $C_{23}H_{18}NO(OMe)_3$ requires C, 74.8; H, 6.5; N, 3.4; OMe, 22.3%]. The *picrate* separated from aqueous ethanol in golden-yellow needles, m.p. 180° (decomp.) (Found: C, 59.6; H, 4.8; N, 8.4. $C_{32}H_{30}N_4O_{11}$ requires C, 59.4; H, 4.7; N, 8.7%).

Oxidation of this isoflav-3-ene with hydrogen chloride during 24 h, in ethyl acetate, gave the unstable 2-(p-*dimethylaminophenyl*)-3′,4′,7-*trimethoxyisoflavylium chloride* in cherry-red needles, m.p. 149° (decomp.) (Found: C, 64.8; H, 5.8. $C_{26}H_{27}ClNO_4$ requires C, 64.1; H, 5.8%). The *perchlorate* formed intensely dark blue plates, m.p. 138° (decomp.) (from methanol) (Found: C, 59.7; H, 5.1; Cl, 6.9; N, 2.3. $C_{26}H_{26}ClNO_8$ requires C, 50.6; H, 5.1; Cl, 6.9; N, 2.7%). The *picrate* separated from alcohol in dark blue prisms, m.p. 190° (decomp.) (Found: C, 59.7; H, 4.3; N, 8.7. $C_{32}H_{28}N_4O_{11}$ requires C, 59.6; H, 4.4; N, 8.7%).

Derivatives of 4′,5,7-*Trimethoxyisoflavylium Perchlorate*.—The condensation product from *NN*-dimethylaniline and this perchlorate was a gum, which was oxidised to 2-(*p*-dimethylaminophenyl)-5,7-dimethoxy-3-(4-methoxyphenyl)-benzo[*b*]pyran-2-ol (non-crystalline). The *perchlorate* separated from methanol as intensely green-blue leaflets, m.p. 144° (decomp.) (Found: C, 59.7; H, 5.1; N, 2.3. $C_{26}H_{26}ClNO_8$ requires C, 60.5; H, 5.1; N, 2.7%). The corresponding *picrate* formed dark violet prisms, m.p. 180° (decomp.) (from ethanol) (Found: C, 59.4; H, 4.6; N, 8.6. $C_{32}H_{28}N_4O_{11}$ requires C, 59.6; H, 4.4; N, 8.7%).

Derivatives of 2′,4′,7-*Trimethoxyisoflavylium Perchlorate*.—2-(p-*Dimethylaminophenyl*)-2′,4′,7-*trimethoxyisoflav*-3-*ene* separated from methanol in needles, m.p. 131° (Found: C, 74.9; H, 6.6; N, 3.1. $C_{26}H_{27}NO_4$ requires C, 74.8; H,

[6] H. Staudinger, *Ber.*, 1913, **46**, 3535.

6.5; N, 3.4%). The *picrate* formed green rosettes, m.p. 168° (decomp.) (from aqueous ethanol) (Found: C, 59.5; H, 4.7; N, 8.5. $C_{32}H_{30}N_4O_{11}$ requires C, 59.4; H, 4.7; N, 8.7%).

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