811. *The Chemistry of the "Insoluble Red Woods." Part IX.*[1] *Homopterocarpin and Pterocarpin.*

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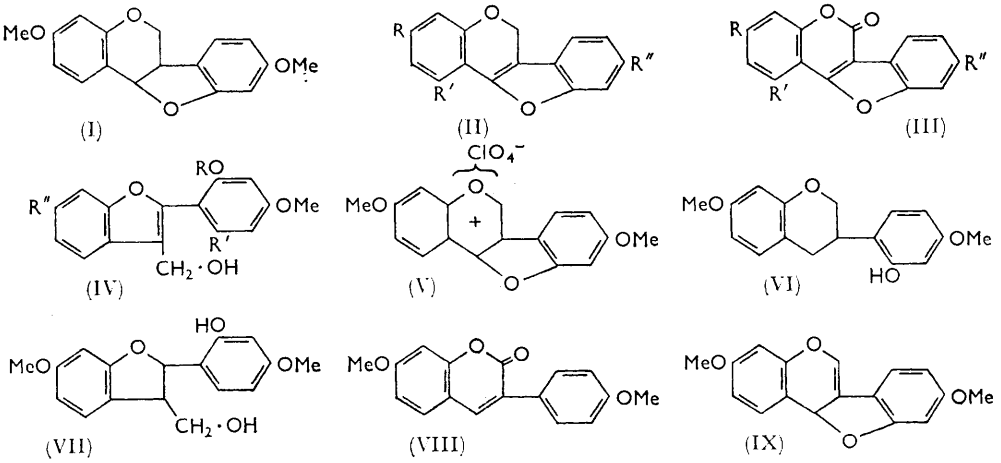
The synthesis of 6,7′-dimethoxychromeno(3′,4′-3,2)coumarone (3,4-dehydrohomopterocarpin) (II; R′ = H, R = R″ = OMe) and of (±)-dihydrohomopterocarpin (VI) are recorded. Dehydrogenation of homopterocarpin yields either 2,3-dehydrohomopterocarpin (IX) or 3-*p*-anisoyl-7-methoxycoumarin (VIII), according to conditions. Pterocarpin similarly gives 7-methoxy-3-(3,4-methylenedioxyphenyl)coumarin.

During investigations directed towards a synthesis of homopterocarpin (I) the chromeno-(3′,4′-3,2)coumarone system (II) has been synthesised.

Reduction of di-*O*-methylcoumestrol (III; R′ = H, R = R″ = OMe) [2,3] with lithium aluminium hydride gave 2-(2-hydroxy-4-methoxyphenyl)-3-hydroxymethyl-6-methoxycoumarone (IV; R = R′ = H, R″ = OMe) which furnished 6,7′-dimethoxychromeno-(3′,4′-3,2)coumarone (3,4-dehydrohomopterocarpin) (II; R′ = H, R = R″ = OMe) when heated. This structure is in agreement with the light absorption (see Experimental section) and the nuclear magnetic resonance spectrum, which shows six aromatic protons, two methoxyl groups (singlets at τ 6·33 and 6·34) and a doublet at τ 5·02 (*J* 1 c./sec.) (O·CH_2·C:C;

[1] Mee, Robertson, and Whalley, Part VIII, *J.*, 1957, 3093.
[2] Bowyer, Robertson, and Whalley, *J.*, 1957, 542.
[3] Emerson and Bickoff, *J. Amer. Chem. Soc.*, 1958, **80**, 4381.

2 protons). Chromeno(3′,4′-3,2)coumarone (II; R = R′ = R″ = H) and 5′,7′-dimethoxychromeno(3′,4′-3,2)coumarone (II; R″ = H, R = R′ = OMe) were similarly prepared from coumarino(3′,4′-3,2)coumarone (III; R = R′ = R″ = H) and 5′,7′-dimethoxycoumarino(3′,4′-3,2)coumarone (III; R″ = H, R = R′ = OMe), respectively. Oxidation of (II; R′ = H, R = R″ = OMe) with triphenylmethyl perchlorate furnished



the pyrylium salt (V) whilst the action of chromic oxide regenerated di-*O*-methylcoumestrol (III; R′ = H, R = R″ = OMe). Attempts to convert (II; R′ = H, R = R″ = OMe) into *cis*-(±)-6,7′-dimethoxychromano(3′,4′-3,2)coumaranone by catalytic hydrogenation ruptured the benzyl ether linkage with the formation of (±)-dihydrohomopterocarpin (VI): experiments on the reduction of (II; R′ = H, R = R″ = OMe) by hydroboronation gave starting material.

It was not possible to investigate the ring closure of, *e.g.*, 2-(2-hydroxy-4-methoxy)-3-hydroxymethyl-6-methoxycoumaran (VII), since in model experiments 3-hydroxymethyl-2-(2,4,6-trimethoxyphenyl)coumarone (IV; R = Me, R′ = OMe, R″ = H) and 2-(2,4-dimethoxyphenyl)-3-hydroxymethyl-6-methoxycoumarone (IV; R = Me, R′ = H, R″ = OMe), which were available from the lithium aluminium hydride reduction of the corresponding 3-carboxylic esters, could not be hydrogenated to the coumarans.

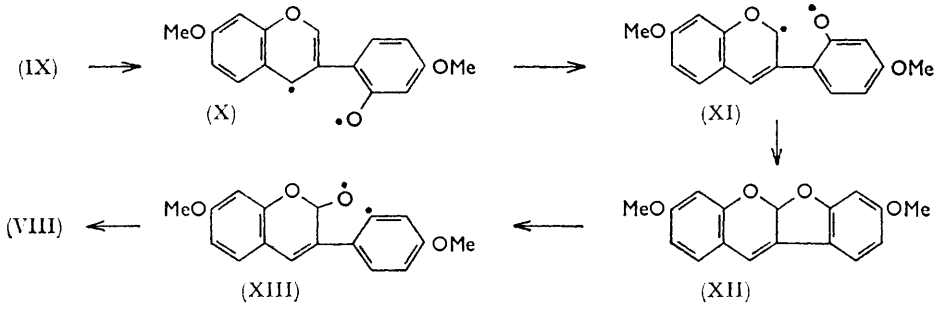
It is of interest that the lithium aluminium hydride reduction of methyl 2-(2,4-dimethoxyphenyl)-6-methylcoumarone-3-carboxylate furnished considerable quantities of a phenolic by-product, presumably by rupture of the furan ring.

Attempts to obtain 6,7′-dimethoxychromeno(3′,4′-3,2)coumarone (II; R′ = H, R = R″ = OMe) from homopterocarpin, showed that the dehydrogenation is critically dependent upon reaction conditions. Thus, whilst the use of mesitylene as the solvent for the dehydrogenation gave 2,3-dehydrohomopterocarpin (IX), dehydrogenation of homopterocarpin at *ca.* 300° with palladium charcoal produced 3-*p*-anisoyl-7-methoxycoumarin (VIII), ($\nu_{max.}$ 1701 cm.$^{-1}$). The formation of the coumarin (VIII) most probably proceeds by a free-radical sequence of the type (I) ⟶ (IX) ⟶ (X) ⟶ (XI) ⟶ (XII) ⟶ (XIII) ⟶ (VIII).

The structure of 2,3-dehydrohomopterocarpin (IX) follows from the fact that it is isomeric with 3,4-dehydrohomopterocarpin (II; R′ = H, R = R″ = OMe), and on oxidation yields di-*O*-methylcoumestrol [cf. the similar oxidation of 5,7,3′,4′-tetramethoxyisoflav-2-ene to 5,7-dimethoxy-3-(3,4-dimethoxyphenyl)coumarin [4]]. In agreement with our failure to isomerise 5,7,3′,4′-tetramethoxyisoflav-2-ene into the corresponding isoflav-3,4-ene and conversely [5] by acid catalysis, 3,4- and 2,3-dehydrohomopterocarpin were not

[4] Baker, *J.*, 1929, 1593.
[5] Anirudhan and Whalley, unpublished observations.

interconvertible under similar conditions. However, when heated at 190—200° with palladium charcoal 3,4-dehydrohomopterocarpin gave a small quantity of a compound which was most probably 2,3-dehydrohomopterocarpin although lack of material prevented



an unequivocal identification. Although (IX) contains an asymmetric centre the optical rotatory dispersion curve showed it to be optically inactive. This result, together with the probable conversion of (II; R = R″ = OMe, R′ = H) into (IX) under dehydrogenation conditions, indicates that the dehydrogenation of homopterocarpin proceeds by way of stages (I) ⟶ (II; R′ = H, R = R″ = OMe) ⟶ (IX).

The conversion of homopterocarpin into di-*O*-methylcoumestrol is the first unequivocal proof of the tetracyclic nature of homopterocarpin.

Dehydrogenation of pterocarpin under narrowly defined conditions gives 7-methoxy-3-(3,4-methylenedioxyphenyl)coumarin, thereby providing the first degradation product in which the presence of the methylenedioxy-residue has been unequivocally demonstrated.

Experimental

6,7′-*Dimethoxychromeno*(3′,4′-3,2)*coumarone* (II; R = R″ = OMe, R′ = H).—(*a*) A suspension of di-*O*-methylcoumestrol (2 g.) in ether (100 ml.) containing lithium aluminium hydride (0·6 g.) was heated under reflux for 2 hr. After isolation 2-(2-*hydroxy*-4-*methoxyphenyl*)-3-*hydroxymethyl*-6-*methoxy-coumarone* formed prisms (1·5 g.), m. p. 117—118°, from benzene (Found: C, 67·8; H, 5·9. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%). The sodium salt of this coumarone formed silky needles, sparingly soluble in 2N-sodium hydroxide. Cyclisation of this coumarone (0·5 g.) in boiling diethylene glycol during 10 min., gave 6,7′-*dimethoxychromeno*(3′,4′-3,2)-*coumarone* which was purified by chromatography from benzene on alumina followed by crystallisation from alcohol to yield prisms (0·35 g.), m. p. 116°; $\lambda_{max.}$ 230, 242, 335, and 352 mμ (log ε 4·19, 4·16, 4·45, and 4·39, respectively) (Found: C, 72·3; H, 5·4. $C_{17}H_{14}O_4$ requires C, 72·3; H, 5·0%). When a solution of this compound (0·05 g.) in acetic acid (1·5 ml.) containing triphenylmethyl perchlorate (0·1 g.) was refluxed for 1 min., the *pyrylium salt* (0·02 g.) separated in yellowish-brown plates, m. p. 228° (violent decomp.) (Found: Cl, 8·9. $C_{17}H_{13}ClO_8$ requires Cl, 9·3%).

Oxidation of 6,7′-dimethoxychromeno(3′,4′-3,2)coumarone (0·2 g.) in acetic acid (25 ml.) containing chromic anhydride (0·1 g.) occurred during 12 hr. Isolation in the usual manner gave 6,7′-dimethoxycoumarino(3′,4′-3,2)coumarone, identical with an authentic specimen. (*b*) Reduction of 6,7′-dimethoxycoumarino(3′,4′-3,2)coumarone (1 g.) in refluxing tetrahydrofuran (150 ml.) containing lithium aluminium hydride (1·5 g.) gave 3-hydroxymethyl-2-(2-hydroxy-4-methoxyphenyl)-6-methoxy-coumarone as an oil. Distillation of this oil at 14 mm. gave 6,7-dimethoxychromeno(3′,4′-3,2)coumarone which separated from methanol in plates (0·3 g.), m. p. 115°, identical with the product from method (*a*) [Found: C, 72·2; H, 5·2; OMe, 22·0. Calc. for $C_{15}H_8O_2(OMe)_2$: C, 72·3; H, 5·0; OMe, 21·9%)].

(±)-*Dihydrohomopterocarpin*.—A solution of 6,7′-dimethoxychromeno(3′,4′-3,2)coumarin (0·12 g.) in acetic acid (5 ml.) containing 10% palladium charcoal (0·1 g.) was shaken for 15 hr. in an atmosphere of hydrogen. After isolation, the alkali soluble portion of the product separated from acid acetic to give (±)-*dihydrohomopterocarpin* (0·06 g.) in prisms, m. p. 132°, having a negative ferric reaction (Found: C, 71·4; H, 6·4. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%).

The ultraviolet and infrared spectra were identical with the corresponding spectra from (−)-dihydrohomopterocarpin. Methylation of (±)-dihydrohomopterocarpin gave the (±)-methyl ether (quantitatively), m. p. 88—89°. Späth and Schlager [6] report m. p. 88—89° for a specimen prepared by an alternative method.

Coumarino(3′,4′-3,2)*coumarone*.—A mixture of α-2-methoxybenzoyl-2-methoxyphenylacetonitrile (0·5 g.) and pyridine hydrochloride (2 g.) was kept at 220—230° for ½ hr. in a stream of carbon dioxide. The mixture was heated (water-bath) with 2N-hydrochloric acid (12 ml.); the solid residue was collected, triturated with cold 2N-sodium hydroxide and purified from alcohol to furnish coumarino(3′,4′-3,2)coumarone (0·25 g.) in plates, m. p. 180° (lit.,[7] 180°) (Found: C, 76·4; H, 3·3. Calc. for $C_{15}H_8O_3$: C, 76·3; H, 3·4%). Acidification of the alkaline filtrate gave 4-hydroxy-3-2′-hydroxyphenylcoumarin in plates, m. p. 266°, from alcohol (Found: C, 70·7; H, 4·1. Calc. for $C_{15}H_{10}O_4$: C, 70·9; H, 4·0%). Govindachari *et al.*[8] report m. p. 253°. The *diacetate* formed needles, m. p. 136°, from alcohol (Found: C, 67·8; H, 4·4. $C_{19}H_{14}O_6$ requires C, 67·5; H, 4·2%).

Formed similarly from α-2,4-dimethoxybenzoyl-2,4-dimethoxyphenylacetonitrile in 20—30% yield, coumestrol di-*O*-methyl ether was identical with a natural specimen.* The use of pyridine hydrochloride rather than hydrobromic acid in the cyclisation of α-benzoylphenylacetonitriles gives an improved yield of coumarino(3′,4′-3,2)coumarones (cf. Chatterjea [9] and Kawase [10]).

Chromeno(3′,4′-3,2)*coumarone*.—Reduction of coumarino(3′,4′-3,2)coumarone (5 g.) with lithium aluminium hydride (1·7 g.) in boiling ether (80 ml.) during 2 hr. furnished 3-*hydroxymethyl*-2-2′-*hydroxyphenylcoumarone* (4·9 g.) in needles, m. p. 128°, from benzene (Found: C, 74·7; H, 5·5. $C_{15}H_{12}O_3$ requires C, 75·9; H, 5·0%). A solution of this alcohol (5 g.) in benzene (30 ml.) was treated with phosphorus tribromide (2 ml.). 12 Hours later 30% sodium hydroxide (40 ml.) was added and the mixture was refluxed for ½ hr. After isolation *chromeno*(3′,4′-3,2)-*coumarone* (1·3 g.) separated from alcohol in prisms, m. p. 89° (Found: C, 80·8; H, 4·2. $C_{15}H_{10}O_2$ requires C, 81·1; H, 4·5%); $\lambda_{max.}$ 240, 295, 300, and 333 mμ (log ε, 4·28, 3·97, 4·09, and 4·28, respectively).

Oxidation of this chromene (0·05 g.) with triphenylmethyl perchlorate (0·05 g.) in warm acetic acid (4 ml.) furnished the *pyrylium perchlorate* in yellow plates, m. p. 245° (violent decomp.), from acetic acid (Found: Cl, 10·8. $C_{15}H_9ClO_6$ requires Cl, 11·1%).

Similarly, reduction of 5′,7′-dimethoxycoumarino(3′,4′-3,2)coumarone [2] (1 g.), furnished 2-(2-hydroxy-4,6-dimethoxyphenyl)-3-hydroxymethylcoumarone as an oil which upon distillation at 1 mm. gave 5′,7′-*dimethoxychromeno*(3′,4′-3,2)*coumarone* in plates (0·3 g.), m. p. 114°, from methanol [Found: C, 72·2; H, 5·2; OMe, 22·0. $C_{15}H_8O_2(OMe)_2$ requires: C, 72·3; H, 5·0; OMe, 21·8%].

3-*Hydroxymethyl*-2-(2,4,6-*trimethoxyphenyl*)*coumarone* (With A. B. Nolan).—Prepared quantitatively from 2-(2,4,6-trimethoxyphenyl)coumarone-3-carboxylic acid [2] by the methyl sulphate–potassium carbonate method in boiling acetone, the *ester* formed prisms, m. p. 136°, from methanol [Found: C, 66·7; H, 5·4; OMe, 35·8. $C_{15}H_5O_2(OMe)_4$ requires C, 66·7; H, 5·3; OMe, 36·3%]. Reduction of this ester (1 g.) in boiling ether (150 ml.) containing lithium aluminium hydride (0·4 g.), during 4 hr., gave 3-*hydroxymethyl*-2-(2,4,6-*trimethoxyphenyl*)-*coumarone* (0·7 g.) in prisms, m. p. 147°, from methanol [Found: C, 68·5; H, 5·8; OMe, 28·9. $C_{15}H_9O_2(OMe)_3$ requires C, 68·8; H, 5·8; OMe, 29·5%]. The p-*nitrobenzoate* separated from alcohol in yellow plates, m. p. 151° (Found: C, 64·5; H, 4·7; N, 3·2. $C_{25}H_{21}NO_8$ requires C, 64·8; H, 4·6; N, 3·0%).

2-(2,4-*Dimethoxyphenyl*)-3-*hydroxymethyl*-6-*methoxycoumarone* (With A. B. Nolan).—A solution of 5′,7′-dimethoxycoumarino(3′,4′-3,2)coumarone [2] (1 g.) in methanol (25 ml.) and 50% aqueous potassium hydroxide (25 ml.) was heated on the steam-bath whilst 50% aqueous potassium hydroxide (20 ml.) and methyl sulphate (8 ml.) were added alternatively in portions during 2 hr. The cooled mixture was diluted with water (20 ml.), filtered, and acidified to yield 2-(2,4-*dimethoxyphenyl*)-6-*methoxycoumarone*-3-*carboxylic acid* in prisms (0·8 g.), m. p.

* We thank Dr. O. H. Emerson, U.S. Department of Agriculture, for this comparison.

[6] Späth and Schlager, *Ber.*, 1940, **73**, 1.
[7] Chatterjea and Roy, *J. Ind. Chem. Soc.*, 1957, **34**, 98.
[8] Govindachari, Nagarajan, and Parthasarathy, *J.*, 1957, 548.
[9] Chatterjea, *J. Indian Chem. Soc.*, 1959, **36**, 254.
[10] Kawase, *Bull. Chem. Soc., Japan*, 1959, **32**, 690.

176° (decomp.), from methanol (Found: C, 65·7; H, 5·0. $C_{18}H_{16}O_6$ requires C, 65·9; H, 4·9%). The *methyl ester* separated from methanol in prisms, m. p. 103° [Found: C, 66·4; H, 5·4; OMe, 35·9. $C_{15}H_6O_2(OMe)_4$ requires C, 66·7; H, 5·3; OMe, 36·3%].

Reduction of this ester (1 g.) in boiling ether (250 ml.) containing lithium aluminium hydride (0·4 g.) occurred during 3 hr. to give 2-(2,4-*dimethoxyphenyl*)-3-*hydroxymethyl*-6-*methoxycoumarone* which separated from methanol in prisms (0·3 g.), m. p. 81° [Found: C, 69·2; H, 6·0; OMe, 28·6. $C_{15}H_9O_2(OMe)_3$ requires C, 68·8; H, 5·8; OMe, 29·5%]. The p-*nitrobenzoate* formed yellow needles, m. p. 167°, from alcohol (Found: C, 64·9; H, 4·6. $C_{25}H_{21}NO_8$ requires C, 64·8; H, 4·6%).

The Dehydrogenation of Homopterocarpin.—(*a*) A mixture of homopterocarpin (1 g.) and 30% palladium–charcoal (0·2 g.) was heated at 280—300° during 45 min. The mixture was extracted with benzene and the extract purified by chromatography on alumina. Elution with benzene furnished 3-p-*anisoyl*-7-*methoxycoumarin* (0·1 g.) in pale yellow needles, m. p. 186°, from benzene or alcohol (Found: C, 72·0; H, 5·2. $C_{17}H_{14}O_4$ requires C, 72·3; H, 5·0%), identical (m. p., mixed m. p., and infrared spectrum) with a specimen prepared by the interaction of 2-hydroxy-4-methoxybenzaldehyde (2 g.) and *p*-methoxyphenylacetic acid (2·2 g.) in refluxing acetic anhydride (10 ml.) during 48 hr.; $\lambda_{max.}$ 264 and 298 mμ (log ε 4·25 and 4·06, respectively) (Found: C, 72·2; H, 5·2%). (*b*) A solution of homopterocarpin (1 g.) in mesitylene (20 ml.) containing 30% palladium–charcoal (0·2 g.) was refluxed for 3 hr. in a stream of carbon dioxide. Purification of a benzene extract of the reaction mixture by chromatography on alumina gave 2,3-*dehydrohomopterocarpin* which formed plates (0·1 g.), m. p. 193°, from methanol; $\lambda_{max.}$ 227 and 303 mμ (log ε 4·21 and 4·07, respectively) [Found: C, 72·2; H, 5·2; OMe, 21·8%; *M*, 312. $C_{15}H_8O_2(OMe)_2$ requires C, 72·3; H, 5·0; OMe, 22·0%; *M*, 282).

Oxidation of a solution of this dehydrohomopterocarpin (0·2 g.) in acetic acid (100 ml.) containing chromic anhydride (0·1 g.) occurred during 12 hr. After isolation in the usual manner 6,7′-dimethoxycoumarino(3′,4′-3,2)coumarone (0·05 g.) was purified by chromatography from benzene on alumina followed by crystallisation from methanol to yield needles, m. p. 197°, identical (m. p., mixed m. p., and infrared spectrum) with an authentic specimen [2] (Found: C, 68·8; H, 4·4. Calc. for $C_{17}H_{12}O_5$: C, 68·9; H, 4·1%).

The Dehydrogenation of Pterocarpin.—A solution of pterocarpin (1 g.) in 1-methylnaphthalene (20 ml.) containing 30% palladium charcoal (0·2 g.) was refluxed for 1 hr. Isolated as for the homopterocarpin analogue, 7-*methoxy*-3-(3,4-*methylenedioxyphenyl*)*coumarin* (0·05 g.) formed yellow needles, m. p. 199°, from methanol, identical (m. p., mixed m. p., and infrared spectrum) with an authentic specimen (Found: C, 68·8; H, 4·2. $C_{17}H_{12}O_5$ requires C, 68·9; H, 4·1%).

A solution of 3,4-methylenedioxyphenylacetic acid (3 g.) in acetic anhydride (10 ml.) containing 2-hydroxy-4-methoxybenzaldehyde (1·5 g.) was refluxed for 50 hr., and poured into alcohol (100 ml.). Purification of the precipitate from alcohol gave 7-methoxy-3-(3,4-methylene dioxyphenyl)coumarin in yellow needles (1 g.), m. p. 200° (Found: C, 68·8; H, 4·2%).

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Infrared spectra were determined in a paraffin mull using an Infracord spectrophotometer: ultraviolet spectra were determined in alcohol using a Perkin-Elmer 137 U.V. spectrophotometer. Nuclear magnetic resonance spectra were determined on a Varian A.60 spectrometer in deuteriochloroform solution by Miss J. Lovenack.

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