CHEMICAL STUDIES IN RELATION TO THE BIOSYNTHESIS OF SOME NATURAL BENZOFURANS AND RELATED COMPOUNDS. PART I*

B. I. NURUNNABI

Agricultural Experiment Station, Dacca

(Received December 2, 1959)

6-Methoxycoumaranone (I) on reduction with sodium borohydride gives 6-methoxybenzofuran (IV). Condensation of acetone with (I) gives (III), also obtained from (II) by the action of alkali. On the basis of these reactions and of structural relations in natural furanocoumarins and furanoquinolines and related compounds, the hypothesis is put forward that the furan ring is biogenetically related to an *iso*prenoid side-chain.

Cyclisation of the epoxide of suberosin results in the formation of (XV). Methyl ester of coumarilic acid on reduction with lithium aluminium hydride gives (XX). Further reduction of (XX) with sodium in alcohol results in the formation of (XXI). The epoxides (X) and (XVII) on treatment with alcoholic alkali give (XVI) and (XVIII), respectively. On the basis of these reactions and of structural relationship the hypothesis is put forward that epoxidation of *iso*pentenyl and probably allyl side-chains is an essential phase in the process of development of furan ring fused to benzene nucleus and that coumarilic acid is involved in a different route in the biogenesis of these compounds.

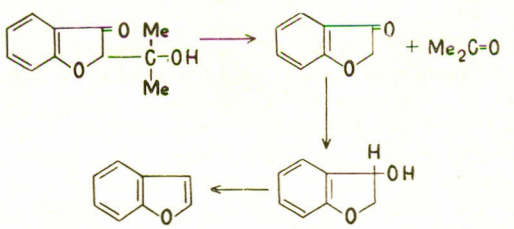
Introduction

The view has been advanced by Birch, Elliott and Penfold[1] that in the biosynthesis of certain resorcinol and phloroglucinol derivatives the *iso*pentenyl side-chain could be introduced *en bloc* in a stage independent of the synthesis of the nucleus. An examination of the structures of a number of natural coumarin derivatives and related compounds, based chiefly on the review by Geissman and Hinreiner[2] supports this idea. The *iso*pentenyl side-chain in some cases contains oxygen; in others it is cyclised to give an *iso*propylfuran derivative or a dimethyl chroman ring system and also there are a number of these compounds in which the side-chain is linked with oxygen rather than with carbon.

The present investigation was undertaken with a view to providing some chemical basis for a hypothesis to explain the formation of an unsubstituted furan ring fused to a benzene nucleus. Several suggestions can be made to explain the biosynthesis of the unsubstituted furan ring: (i) it may be derived from a C_2 side-chain such as acetyl; (ii) it may result by loss of an *iso*propyl group from an *iso*propylfuran derivative formed by cyclisation of an *iso*pentenyl side-chain; or (iii) it may be produced by cyclisation of an *o*-hydroxyphenylacetaldehyde formed by oxidation of an *iso*pentenyl or allyl side-chain.

There is no evidence for or against (i), although plausible routes could be suggested. Route (ii) or (iii) is favoured by considerable structural evidence although against (iii) is the fact that not a single corresponding lactone is known. Oxidation of an intermediate cyclic half-acetal might be expected to occur in a few cases at least. The unsubstituted furan derivatives and *iso*propylfuran derivatives occur commonly in the same plant genera, and *iso*prenoid side-chains are found attached to oxygen in both types of compounds. In the genus *Peucedanum* are found: peucedanin (2′-*iso*propyl-3′-methoxy-1); *iso*imperatorin (5 *iso*pentenyloxy-1); ostruthol (5-$OCH_2CH(OCOO-(CH_3) = CH.CH_3)$ $CH(CH_3)_2OH$-1); oxypeucedanin (5-epoxy-*iso*pentenyloxy-1); nodakenin (2′,3′-dihydro-2′-glucosoxy*iso*propyl-1); athamantin (2′, 3′-dihydro-2′ - hydroxy*iso*propyl-3′-hydroxydi-*iso*valerylester-11), together with the bicyclic coumarins umbelliferone (7-hydroxy-), ostruthin (7-hydroxy-6-geranyl-), and osthol (7-methoxy-8-*iso*pentenyl-).

The most probable mechanism for the formation of coumarones would consist in the removal of an *iso*propyl side-chain by means of a reverse-aldol reaction as shown below followed by reduction.



It is notable that in all but one of the cases containing an *iso*propylfuran ring, the group is either hyrdoxy*iso*propyl or *iso*propenyl, and in all the dimethylchroman derivatives and in many of those naturally occurring compounds which con tain *iso*pentenyl side-chains attached to oxygen the carbon bearing the gem-dimethyl group has an oxygen attached. Furthermore two out of three furanocoumarins retaining the *iso*propyl group have no oxygen in the 3′-position suggesting that

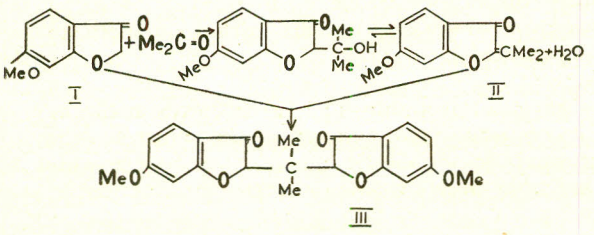
*This work was carried out in the Department of Organic Chemistry, University of Sydney, Sydney, Australia

these substances (peucedanin, athamantin, all in *peucedanum*) all represent arrested stages to unsubstituted furan derivatives.

Only biological work can ultimately prove or disprove such a hypothesis, but the reactions of some coumaranones have been investigated in relation to the above ideas.

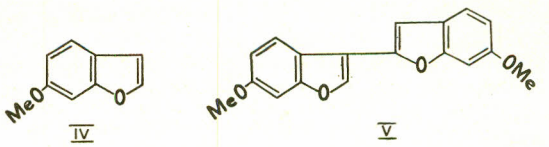
I. Reactions of 6-Methoxy Coumaranone.—In order to provide some basis for a hypothesis such as above the reactions of 6-methoxycoumaran-3-one (I)[3] were first examined.

The *iso*propylidene derivative (II)[4] has been obtained by the condensation of coumaranone (I) and acetone in presence of zinc chloride, and a reversal of such a condensation would provide the most likely route for the loss of an *iso*propyl side-chain. Compound (II) on heating with alkali, for preference in the presence of sodium hydrosulphite to reduce oxidative side-reactions, gave evidence of such reversal by the formation of (III) and acetone. The compound (III) is formed with great ease by reaction between (I) and (II) and is the only product isolated after treating the coumaranone (I) with alkali and a large excess of acetone. These results indicate the ready occurrence of the postulated reversed aldol formation, the process being that below:—

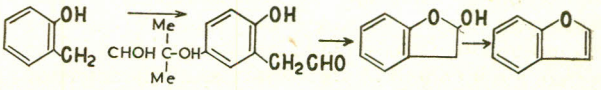


If this view of the biosynthetic process is correct, coumaranones such as (I) should be readily convertible to the furans by reduction. This was demonstrated by reducing (I) with sodium borohydride to obtain preponderantly (IV) with a small amount of a substance which appears to be a reduction product of an analogue of oxindirubin formed. Structure (V) is assigned to this compound on the basis of the known oxygen analogues of indirubin.[5,6] The formation of the compound (V) under these conditions shows how readily (I) undergoes self-condensation followed by reduction and dehydration. The 6-methoxy-coumarone, n_D^{18} 1.156647 gave the picrate,[7] m.p. 64°C. Reduction of (II) with a limited amount of sodium borohydride gave an oily monomeric product which appeared to consist mainly of (IV) together with (III).[4] Thus it appears that the borohydride reacts as a base as well as a reducing agent and the *iso*propylidenecoumaranone is sluggishly reduced.

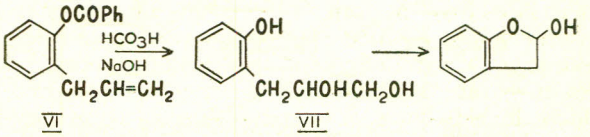
These experiments show that at least a feasible series of chemical mechanisms exists whereby the biosynthetic hypothesis (ii) outlined above could be effective.



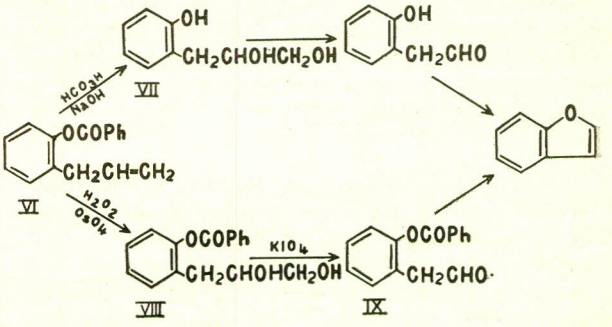
II. Cyclisation of 2-hydroxyphenylacetaldehydes.—The common presence of *iso*prenoid side-chains with the group oxidised to the glycol or the epoxide suggests that such groups might represent arrested stages to the phenylacetaldehyde which could cyclise with an *o*-hydroxyl group to the 2-hydroxydihydrofuran. Dehydration could then give the benzofuran:



To examine the chemical feasibility of this series of reaction the following series of reactions was examined:



The glycol (VII) was readily obtained, but oxidation with either lead tetraacetate or periodic acid produced only polymeric material, although formaldehyde could be detected. If this route were invovled in biosynthesis, the lactones corresponding to the intermediate acetal would be expected as natural products; in fact no such compound is known.

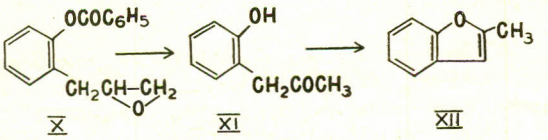


It, therefore, appeared necessary that the benzoyl group of (VI) should be retained for the subsequent steps of oxidation. The first step of oxidation which was accomplished by the action of hydrogen peroxide on *o*-benzoyloxy-allyl-

benzene in the presence of osmium tetroxide[8] resulted in the formation of 1-(*o*-benzoyloxyphenyl)-propan-2 : 3-diol (VIII). The next step was carried out by oxidising (VIII) with periodic acid. The product obtained was *o*-benzoyl-oxyphenylacetaldehyde (IX), characterised by the preparation of a semicarbazone. Attempts to hydrolyse the benzoyl group of the aldehyde with dilute hydrochloric acid or sulphuric acid under various conditions resulted in the formation of resinous products.

These results coupled with structural evidence lend support to the view that furan rings are not likely to arise in nature by the oxidation of glycollic C_5 or C_3 side-chains. The other possibility that furan rings might be formed in nature by the cyclisation of *iso*pentenyl or allyl side-chains containing an epoxide ring was then examined by a study of the reactions of the epoxides of suberosin and *o*-benzoyloxy-allylbenzene.

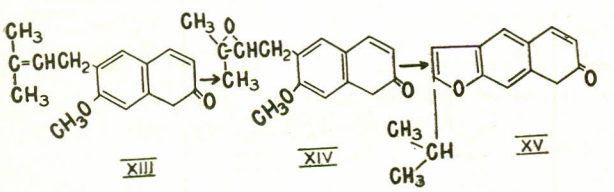
Treatment of such an epoxide with acid was expected to result in hydrolysis and rearrangement to a ketone followed by cyclisation to 2-methyl-coumarone.



X XI XII

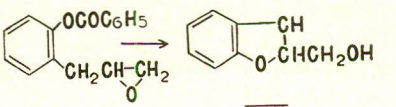
Accordingly *o*-benzoyloxyallylbenzene was converted to the epoxide (X) by treatment with perbenzoic acid, but there was no indication of the formation of postulated cyclisation product (XII) nor could the isomeric ketone (XI) be isolated after treatment of the epoxide with dilute sulphuric or phosphoric acid.

III. Cyclisation of the Epoxides of Isopentenyl and Allyl Side-chains.—Suberosin (XIII)[9] extracted from *Zanthoxylum suberosum* readily gave the epoxide (XIV) when treated with perbenzoic acid. The epoxide on refluxing with hydrobromic acid and red phosphorus demethylated and cyclised to anhydro-nodakenetin (XV).[10]



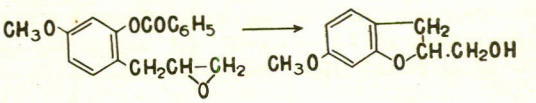
XIII XIV XV

Treatment of the epoxide of *o*-benzoyloxy-allylbenzene with alcoholic sodium hydroxide solution resulted in the formation of a substance $C_9H_{10}O_2$, which was insoluble in alkali and gave no colour with ferric chloride and no derivative with 2:4-dinitrophenyl-hydrazine hydrochloride. However, a derivative was obtained with 3:5-dinitrobenzoyl chloride, and a Kuhn-Roth determination of this derivative showed that there was no C-CH_3 group present. The properties of this cyclisation product suggest that it may be identical with 2-hydroxymethylcoumaran (XVI).[11]



X XVI

A similar cyclisation product was obtained from the alkaline treatment of the epoxide of 2-benzoyloxy-4-methoxy-allylbenzene (XVII).



XVII XVIII

The allyl ether of monomethyl-resorcinol was prepared by the method described by Claisen[12] and rearranged to 2-hydroxy-4-methoxy-allyl-benzene.[13] This compound gave a benzoate which readily gave the epoxide with perbenzoic acid. In alcoholic sodium hydroxide solution cyclisation occurred to give a compound which was insoluble in alkali, gave no colour with ferric chloride and no derivative with 2:4-dinitrophenyl-hydrazine hydrochloride. A derivative was obtained with 3:5-dinitrobenzoylchloride and a Kuhn-Roth determination showed that there was no C-CH_3 group present. The cyclisation product in this case is probably 2-hydroxymethyl-6-methoxy-coumaran (XVIII).

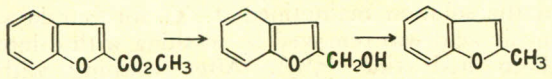
It seems clear, therefore, that the epoxides of isopentenyl side-chains can be converted to coumarones under acid conditions. Further work on the behaviour of the epoxides of *o*-hydroxy-allylbenzenes under mild alkaline conditions is necessary. It is obvious that cyclisation does occur in the latter cases and the products isolated suggest that this route may be involved in the biosynthesis.

IV. Decarboxylation and Reduction of Coumarilic Acid.—Apparently decarboxylation of coumarilic acid derived from coumarins constitutes another biologically possible mechanism but since decarboxylation does not occur readily[14] this route is less likely to be involved in the biosynthesis of unsubstituted furan rings.

2-Methylbenzofuran (XXI) was, however, obtained by reducing the methyl ester of coumarilic

acid in two stages. Reduction of (XIX) with lithium aluminium hydride gave the alcohol (XX), confirmed by the preparation of a derivative, m.p. 133°C., with 3:5-dinitrobenzoyl chloride.

Further reduction of the alcohol (XX) with sodium in alcohol resulted in the formation of (XXI).



XIX XX XXI

Experimental

Melting points are uncorrected. Microanalyses were carried out partly by the C.S.I.R.O. Microanalytical Laboratory and partly by the Microanalytical Laboratory, University of Sydney.

(*a*) *6-Methoxycoumaranone.*—This compound was obtained from α-bromo-resacetophenone-dimethyl-ether and potassium acetate by the method described by Blom and Tambor.[3]

(*b*) *Reduction of 6-Methoxy-coumaran-3-one with Sodium Borohydride.*—6-Methoxy-coumaran-3-one (0.5 g.) was dissolved in absolute ethanol (20 ml.). An excess (20%) of sodium borohydride dissolved in absolute ethanol was added to the warmed solution, and the mixture refluxed for one hour. After cooling, it was acidified with hydrochloric acid (5N), allowed to stand for two hours, diluted and extracted with ether and the solvent evaporated to small bulk, then passed through a column of alumina. The washings, on evaporation, gave a mixture of solid and oil which were separated by filtration.

The solid was recrystallised from ethanol, m.p. 144-5°C. (Found: C, 738.4; H, 4.9. Calc. for $C_{18}H_{14}O_4$: C, 73.3; H, 4.8).

The oil, b.p. 67°C./1.5-2.0 mm., n_D^{18} 1.5664, (Found: C, 72.9; H, 5.5. $C_9H_8O_2$ requires: C, 73.0; H, 5.4), gave a picrate,m.p. 64°C., and a trinitrobenzene derivative, m.p. 56°C.

(*c*) *Reduction of 6-Methoxy-2-isopropylidene-coumaran-3-one with Sodium Borohydride.*—6-Methoxy-2-*iso*propylidene-coumaran-3-one (1.5 g.) was treated with sodium borohydride as above. The solid obtained from the reaction mixture was removed by filtration and recrystallised from absolute ethanol, m.p. 203-4°C., not depressed in mixed melting-point with an authentic specimen of 2,2-bis-(6′-methoxy-coumaran-3′-one)-propane. (Found: C, 68.7, H, 5.5, $C_{21}H_{20}O_6$ requires: C, 68.5; H, 5.5).

After removal of the solid, the mother liquors were extracted with ether, which was dried over sodium sulphate and then removed by distillation under reduced pressure. The residual oil distilled at 80°C./0.8 mm. (Found: C, 73.3; H, 6.2. $C_9H_8O_2$ requires: C, 73.0; H, 5.4).

(*d*) *Self-condensation of 6-Methoxy-2-isopropylidene-coumaran-3-one.*—6-Methoxy-2-isopropylidene-coumaran-3-one (100 mg.) was dissolved in absolute ethanol (10 ml.) and a solution of sodium hydrosulphite (50 mg.) in sodium hydroxide solution (0.5 ml., 10%) added. The mixture was refluxed on a water bath under nitrogen for forty minutes and distilled into 2:4-dinitrophenylhydrazine hydrochloride solution. The yellow precipitate was identified as acetone 2:4-dinitrophenylhydrazone. After cooling, a solid separated from the residue and was recrystallised from absolute ethanol, m.p. 203-204°C., not depressed in mixed melting point with an authentic specimen of 2,2-bis-(6′-methoxy-coumaran-3′-one)-propane.[4]

(*e*) *Condensation of 6-Methoxy-2-isopropylidene-coumaran-3-one with 6-Methoxy-coumaran-3-one.*—6-Methoxy-2-isopropylidene-coumaran-3-one (50 mg.) and 6-methoxy-coumaran-3-one (50 mg.) were dissolved in absolute ethanol. The system was filled with nitrogen and sodium hydroxide solution (2 drops, 10%) added. On standing, a solid separated and was recrystallised from absolute ethanol, m.p. 203-204°C., not depressed in mixed melting-point with an authentic specimen of 2,2-bis-(6′-methoxy-coumaran-3′-one)-propane.[4]

No acetone 2:4-dinitrophenylhydrazone could be obtained from the mother liquors.

(*f*) *Benzoylation of o-Allylphenol.*—*o*-Allylphenol[12] (67 g.) in pyridine (79 g.) was treated with excess freshly-distilled benzoyl chloride and the mixture was left overnight. After dilution with water it was extracted with ether and the extract washed with hydrochloric acid (5N; 4 × 25 ml.), saturated sodium bicarbonate solution, sodium hydroxide solution (5%) and water. After drying over anhydrous sodium sulphate the solvent was evaporated and the residue distilled, b.p. 162°C./1.5 mm. Approximately, the theoretical yield of benzoate was obtained. (Found: C, 80.5; H, 6.1. $C_{16}H_{14}O_2$ requires: C, 80.1; H, 5.9).

(*g*) *1-(o-Hydroxyphenyl)-propan-2:3-diol.* — The benzoate of *o*-allylphenol (11.9 g., 0.05 M) was dissolved in formic acid (42.3. ml.) at 25°C. Hydro-

gen peroxide (5.9 g., 30%, 0.0513 M, 2.5% in excess) was added gradually, the temperature being maintained at 40°C. After standing two hours at this temperature, the bulk of formic acid was removed by distillation under reduced pressure in an atmosphere of nitrogen. The mixture was diluted with water and extracted with ether and then ethyl acetate. The combined extracts were washed with saturated sodium bicarbonate solution and after drying the solvents were evaporated. The oily residue could not be induced to crystallise and was hydrolysed by refluxing with excess aqueous methanolic sodium hydroxide for two hours.

After cooling, the solution was saturated with carbon dioxide and the methanol removed by distillation. The slightly alkaline solution was extracted with ether. Evaporation of the solvent gave 1-(*o*-hydroxyphenyl)-propan-2:3-diol, b.p. 175°C./1.2 mm. (Found: C, 64.0; H, 7.3. $C_9H_{12}O_3$ requires: C, 64.3; H, 7.2).

(*h*) *Oxidation of the Benzoate of o-Allylphenol with Hydrogen Peroxide in the Presence of Osmium Tetroxide.*—A three-necked flask was fitted with a mechanical stirrer, two dropping funnels and a reflux condenser. To a mixture of anhydrous sodium sulphate (10 g.), absolute ether (20 ml.) and ethereal osmium tetroxide (2 ml., 1%), were added dropwise, ethereal solutions of hydrogen peroxide (7.3 N) and the benzoate of *o*-allylphenol (2.5M, 11.9 g.). The addition of the benzoate (1 ml.) resulted in the formation of a brown complex with osmium tetroxide. Hydrogen peroxide was then added alternately with the benzoate and the mixture was stirred until it became light yellow. Next day carbon dioxide was passed through the flask with stirring to remove any formaldehyde. The mixture was diluted, the ether layer separated and washed several times with water, sodium hydroxide (1%), sodium bisulphite and water. After drying over sodium sulphate the solvent was evaporated when the residue crystallised. 1-(*o*-Benzoyloxy-phenyl)-propan-2:3-diol, m.p. 82°C., was recrystallised from benzene as white plates. (Found: C, 70.6, H, 5.8. Calc. for $C_{16}H_{16}O_4$: C, 70.6; H, 5.9).

(*i*) *Oxidation of 1-(o-Benzoyloxyphenyl)-propan-2:3 diol with Periodic Acid.*—1-(*o*-Benzoyloxyphenyl)-propan-2:3-diol (2 g.) was dissolved in ethanol (100 ml., 70%). Potassium (meta) periodate (200 ml., 5.7 g. in N H_2SO_4) was rapidly added. After two and a half hours the solution was extracted with ether, the extract washed with saturated sodium bicarbonate solution, and evaporated.

Treatment of a small portion of the residue with semicarbazide hydrochloride gave *o*-benzoyloxyphenyl-acetaldehyde semicarbazone, m.p. 184°C., which crystallised from absolute ethanol (Found: C, 64.4; H, 5.1. Calc. for $C_{16}H_{15}O_3N_3$: C, 64.6; H, 5.1).

(*j*) *Epoxidation of o-Benzoyloxy-allylbenzene.*—*o*-Benzoyloxy-allylbenzene (11.9 g., 0.05 M) was added to a solution of perbenzoic acid in chloroform (140 ml., 7.6 g., 10% in excess of 0.05 M) and the solution maintained at 0°C. for four days. Benzoic acid was removed by washing with dilute sodium hydroxide (5%). After washing with water the solution was dried over sodium sulphate and the solvent evaporated. The residual oil was distilled, the fraction boiling at 173°C./1.5 mm. being collected. This fraction consisted of the epoxide of *o*-benzoyloxy-allylbenzene. (Found: C, 75.9; H, 5.7. Calc. for $C_{16}H_{14}O_3$: C, 75.6; H, 5.6).

(*k*) *Alkaline Hydrolysis of the Epoxide of o-Benzoyloxy-allylbenzene.*—The epoxide of *o*-benzoyloxy-allylbenzene (20 g.) was dissolved in absolute ethanol (50 ml.) and sodium hydroxide (50 ml.; 20%) added. The mixture was allowed to stand in a stoppered flask at room temperature for five days. The alkaline solution was diluted with water and the separated oil extracted with ether. The solvent was washed several times with water and dried over sodium sulphate. After evaporation of the solvent 2-hydroxymethyl-coumaran was distilled, b.p. 108°C./1.0 mm. (Found: C, 71.7; H, 6.3. $C_9H_{10}O_2$ requires: C, 72.0; H, 6.7). The yield was 60% of the theoretical amount.

(*l*) *Preparation of 3:5-Dinitrobenzoate of 2-Hydroxymethyl-coumaran.*—3:5-Dinitrobenzoyl chloride (1 g.) was dissolved in benzene (10 ml.) and 2-hydroxymethyl-coumaran (1 g.) dissolved in pyridine (2 ml.) added. The mixture was refluxed for thirty minutes. After cooling it was diluted with ether and washed with hydrochloric acid (2N), sodium hydroxide (5%) and water. After drying over sodium sulphate the solvents were evaporated and the solid derivative, m.p. 114.5°C. recrystallised from light petroleum, b. p. 60-90°C. (Found: C, 55.9; H, 3.6. Calc. for $C_{16}H_{12}O_7N_2$: C, 55.8; H, 3.5). A Kuhn-Roth determination was negative.

(*m*) *Benzoylation of 2-Hydroxy-4-methoxy-allylbenzene.*—2-Hydroxy-4-methoxy-allylbenzene (16.4 g., 0.1 M) was benzoylated as in (f). The reaction mixture, after dilution with water, was extracted with ether and the extract washed with hydrochloric acid (5 N, 4×25 ml.), sodium hydroxide (10%) and water. After drying over sodium sulphate the solvent was evaporated and the residue distilled. The benzoate distilled at 173°C./

1.1 mm. (Found: C, 76.4; H, 5.6. Calc. for $C_{17}H_{16}O_3$: C, 76.1; H, 6.0).

(*n*) *Epoxidation of 2-Benzoyloxy-4-methoxy-allylbenzene.*—2-Benzoyloxy-4-methoxy-allylbenzene (13.4 g., 0.05 M) was added to a solution of perbenzoic acid in chloroform (140 ml., 7.59 g., 10% in excess of 0.05 M) and the solution maintained at 0°C. for forty-eight hours. Benzoic acid was removed by washing with dilute sodium hydroxide (5%). After washing with water the solution was dried over sodium sulphate and the solvent evaporated. The epoxide of 2-benzoyloxy-4-methoxy-allylbenzene distilled at 196°C./0.75 mm. (Found: C, 72.6; H, 5.7. Calc. for $C_{17}H_{16}O_4$: C, 72.8; H, 5.7).

(*o*) *Alkaline hydrolysis of the Epoxide of 2-Benzoyloxy-4-methoxy-allylbenzene.*—The epoxide of 2-benzoyloxy-4-methoxy-allylbenzene (5 g.) was dissolved in absolute ethanol (25 ml.) and sodium hydroxide (25 ml. 20%) added. The mixture was kept at room temperature for five days. The alkaline solution was diluted with water and extracted with ether. The extract was washed several times with water and dried over sodium sulphate. After evaporation of the solvent the residual oil was distilled, b.p. 138°C./1.5 mm. It was insoluble in dilute alkali and gave no colour with ferric chloride. Treatment with 3:5-dinitrobenzoyl chloride gave a derivative, m.p. 140°C. (Found: C, 54.6; H, 3.8. Calc. for $C_{17}H_{14}O_7N_2$: C, 54.6; H, 3.8). A Kuhn-Roth determination was negative.

(*p*) *Epoxidation of Suberosin.*—Suberosin (12.2 g., 0.05 M) was added to perbenzoic acid in chloroform (150 ml., 7.6 .g, 10% in excess of 0.05 M). The mixture was maintained at 0°C. for twenty-four hours. Benzoic acid was removed by washing with sodium hydroxide (10%) and the chloroform washed with water and dried over sodium sulphate. After evaporation of the solvent the epoxide of suberosin was recrystallised from methanol, m.p. 120-1°C. (Found: C, 69.1; H, 6.2. Calc. for $C_{15}H_{16}O_4$: C, 69.2; H, 6.2).

(*q*) *Demethylation and Cyclisation of the Epoxide of Suberosin.*—The epoxide of suberosin (2 g.) and red phosphorus (1 g.) were added to hydrobromic acid (150 ml., sp. gr. 1.5). The mixture was refluxed for one hour, diluted with water and extracted with ether (3 × 30 ml.). The extract was washed with sodium hydroxide (0.5%), then with water, and the solvent evaporated. Anhydro-nodakenetin, m.p. 136°-7°C., was recrystallised from methanol. (Found: C, 73.5; H, 5.3. $C_{14}H_{12}O_3$ requires: C, 73.7; H, 5.3).

(*r*) *Methyl Coumarilate.*—A round-bottomed flask (250 ml.) containing absolute methanol (50 ml.) was cooled in an ice bath and dry hydrogen chloride was passed until the increase in weight was two grammes. Coumarilic acid (10 g.) was added and the mixture refluxed for four hours. After cooling it was diluted with water and extracted with ether. The ethereal solution was washed with saturated sodium carbonate solution and then with water, and dried over anhydrous potassium carbonate. After evaporation of the solvent, the ester was recrystallised from ether, m.p. 54-5°C.

(*s*) *2-Hydroxymethyl-coumarone.*—Lithium aluminium hydride (1.08 g., twice the required amount) was rapidly transferred to a three-necked flask (300 ml.) provided with a mechanical stirrer, dropping funnel and a reflux condenser. Dry ether (25 ml.) was added immediately. The mixture was stirred continuously for two hours after the addition had been completed. The flask, was then placed in an ice bath and water added dropwise cautiously to decompose the excess hydride. The ether solution was separated by filtration and dried over anhydrous sodium sulphate. After evaporation of the solvent, the oil distilled, b.p. 108°C./1 mm. Treatment of a small portion of this oil with 3:5-dinitrobenzoyl chloride gave a derivative, m.p. 133°C., from benzene/ether. (Found: C, 56.3; H, 3.1. Calc. for $C_{16}H_{10}O_7N_2$: C, 56.1; H, 3.0).

(*t*) *2-Methyl-coumarone.*—Sodium (2.48 g.) was placed in a two-necked round-bottomed flask (250 ml.) provided with a reflux condenser and dropping funnel. 2-Hydroxymethyl-coumarone (1.0 g.) dissolved in dry ethanol (25 ml.) was added in several portions. A vigorous reaction took place and, after it had subsided, the mixture was refluxed on a water-bath for one hour. After cooling, water was added and the mixture extracted with ether. The ethereal extract was washed with water and dried over sodium sulphate. The solvent was evaporated and the oil distilled, b.p. 52°C./2-0 mm. (Found: C, 81.8; H, 6.0. C_9H_8O requires: C, 81.8, H, 6.1).

Acknowledgements.—The author wishes to express his gratitude to Professor A. J. Birch for his kind help and advice and also to Dr. E. Ritchie and Dr. P. Elliott for many helpful suggestions. Finally he would like to thank the Colombo Plan Authorities for a fellowship.

References

1. A. J. Birch, P. Elliott and A. Penfold, Australian J. Chem., **7**, 169 (1954).
2. T. A. Geissman and E. Hinreiner, Bot. Rev., **18**, 77(1952).

3. A. Blom and J. Tambor, Chem. Ber., **38**, 3590 (1905).
4. R. L. Shriner and J. Anderson, J. Am. Chem. Soc., **60**, 1415 (1938).
5. K. Fries and W. Pfaffendorf, Chem. Ber., **43**, 212 (1910).
6. K. Fries and W. Pfaffendorf, ibid., **44**, 114 (1911).
7. Stoermer, Ann. Chem. Liebigs, **312**, 335 (1900).
8. R. Criegie, ibid., **75**, 522 (1936).
9. J. Ewing, G. K. Hughes and E. Ritchie, Australian J. Sci. Research, **3A**, 342 (1950).
10. E. Spath, K. Eiter and T. Meinhard, Chem. Ber., **75**, 1623 (1942).
11. H. Normant, Compt. rend., **218**, 683 (1944).
12. L. Claisen, Ann. Chem. Liebigs, **418-419**, 69 (1919).
13. F. Mauthner, J. prakt. Chem., **102**(2), 41 (1921).
14. Rud, Fittig and G. Ebert, Ann. Chem. Liebigs, **216**, 163 (1882).