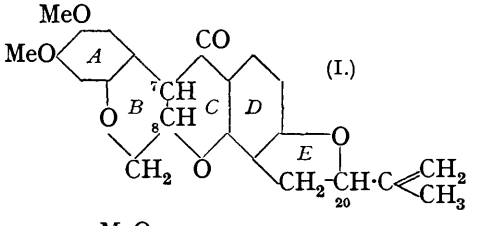
137. *The Methylation and Ease of Ring-fission of Rotenone and Related Substances.*

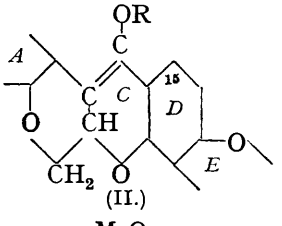
By R. S. Cahn, R. F. Phipers, and J. J. Boam.

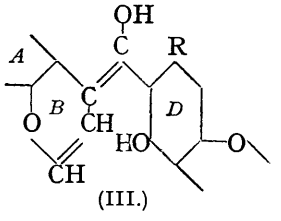
Rotenone, deguelin, and similar substances give methyl ethers derived from the enolic form (II). In similar circumstances toxicarol and dihydrotoxicarol, which contain a phenolic hydroxyl group, give ethers derived from the " open " form (III). This difference shows the greater ease of fission of ring *C* induced by the phenolic hydroxyl group in ring *D* and confirms the views expressed previously.

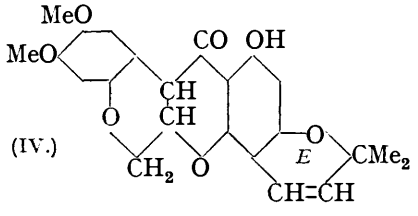
The two types of ether differ markedly in stability to acids, alkalis, and oxidising agents, and in absorption spectra.

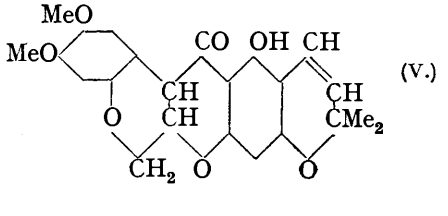
We showed recently (this vol., p. 513) that very mild alkaline reagents racemise C7 and C8 of rotenone (I) and related substances. We concluded that this occurs by enolisation to (II; R = H), followed by fission of ring *C* to give the " open " form (III; R = H). In the case of toxicarol (IV), racemisation is accompanied by formation of its isomeride, β-toxicarol (V); this structural change, which is reversible, was shown to demand formation of (III; R = OH) as an intermediate, and, since the conditions for the









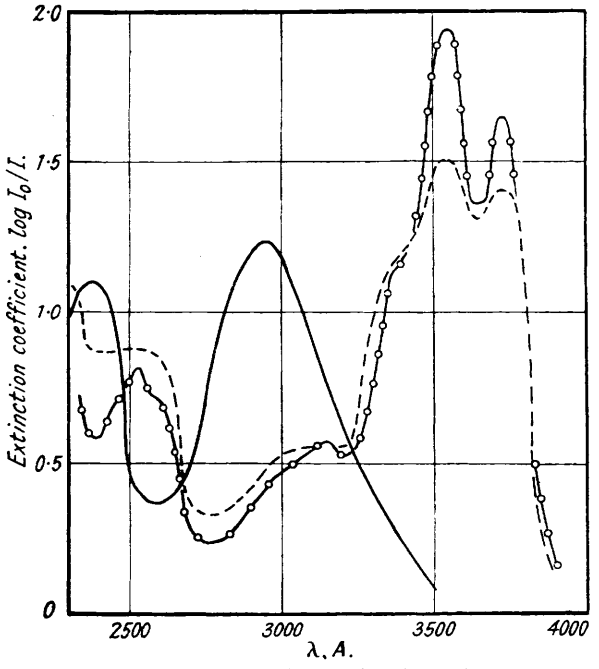


structural change and for racemisation are identical, affords strong evidence for the, at least transitory, existence of (III; R = H) during racemisation also of rotenone and its non-phenolic derivatives. We produced evidence that enolisation of toxicarol by alkali is more facile than that of rotenone, and, since we postulated that enolisation is a necessary preliminary to and a causative agent of fission of ring *C*, it followed that this fission to (III) should occur more readily with substances containing a hydroxyl group in ring *D* than

with substances not containing such a substituent. We now present experimental evidence that this is the case. A somewhat similar conclusion had been drawn by Butenandt and Hilgetag (*Annalen*, 1933, **506**, 158), but their evidence was open to the objection raised by us previously (*loc. cit.*) to their other arguments, and their ideas had not in fact found acceptance by other workers.

We have found that substances of the rotenone and toxicarol series are methylated by methyl sulphate in boiling acetone in the presence of aqueous potassium hydroxide or anhydrous potassium carbonate. For the latter method, the acetone must contain about 1% of water, the reaction failing in presence of only 0·5% or of 2% or more of water. The only reference we have found to methylation of these substances (apart from that of their 7-hydroxy-derivatives) is a statement by Clark (*J. Amer. Chem. Soc.*, 1932, **54**, 2537) that toxicarol cannot be methylated by any method. The conditions used by us are such as

FIG. 1.



Absorption spectra (alcoholic solutions) :
——— *Rotenone*, 0·00302%, 1 cm.
- - - - - - - *Acetylrotenone*, 0·00222%, 1 cm.
o———o *Mutarotenone methyl ether*, 0·00217%, 1 cm.

cause racemisation in the absence of methyl sulphate, and the ethers are thus racemic compounds. iso*Rotenone methyl ether*, for instance, is obtained equally well from *l*- and *dl-iso*rotenone and gives *dl-iso*rotenone on acid hydrolysis; acid hydrolysis has been shown (*loc. cit.*) not to cause racemisation. Treatment of rotenone with alkali does not affect the third asymmetric atom, C20, but racemises C7 and C8, thus affording mutarotenone, a semi-racemic, 1 : 1 molecular compound of ordinary *l*-rotenone and *d-epi*rotenone; C20 is lævorotatory in rotenone and *d-epi*rotenone, but C7—C8, considered together, are dextrorotatory in *d-epi*rotenone and lævorotatory in rotenone. The *methyl* ether obtained from rotenone is a similar molecular compound, for it is formed in equal yield from rotenone or mutarotenone and gives mutarotenone on acid hydrolysis.

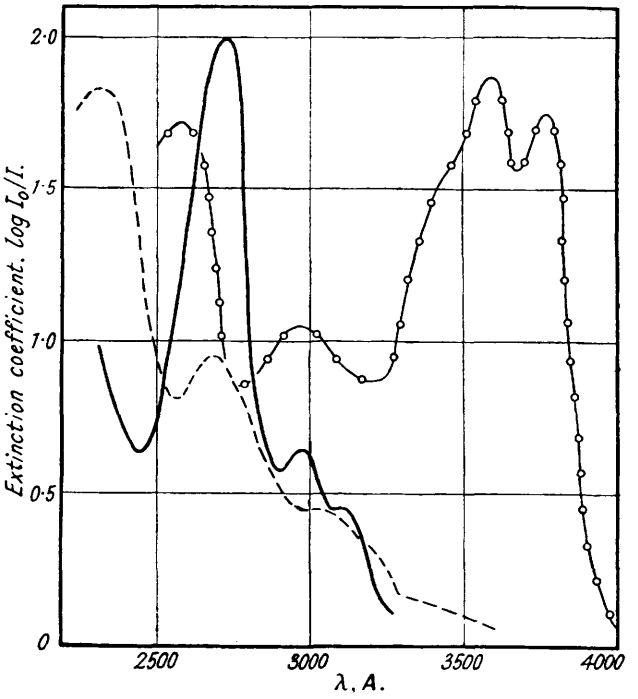
The ethers from rotenone and *iso*rotenone are derivatives (II; R = Me) of the enolic form, analogous to the known acetates (II; R = Ac). The possibility that they are derived by methylation of the phenolic hydroxyl group in ring *D* of the " open " form (III) is excluded by their very ready hydrolysis by dilute acid. Further, as shown in Fig. 1,

the absorption spectrum of rotenone methyl ether has the characteristic maximum of acetylrotenone (with its two well-defined bands and a third less definite band constituting a triplet) and differs radically from that of rotenone. These ethers are unaffected by iodine or by air in alkaline solution, reagents which rapidly attack the CH·CO of rotenone derivatives. They are also remarkably stable to alkali* and are indeed best purified by destroying unmethylated material and accompanying by-products by hot alcoholic alkali hydroxide.

Similar acid-labile enolic *ethers* are obtained from deguelin (VI) and dihydrodeguelin.

Methylation of toxicarol gives, as anticipated, a *dimethyl* ether by both methods. However, in contrast to the ethers discussed above, this substance is stable even to 10% mineral acid, whereas 2% acid suffices to hydrolyse the enolic ethers. In further contrast,

FIG. 2.



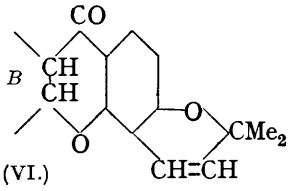
Absorption spectra (alcoholic solutions):

——— *Toxicarol*, 0·00234%, 1 cm.
- - - - - - - *Toxicarol dimethyl ether*, 0·00206%, 1 cm.
o———o *Diacetyltoxicarol*, 0·00335%, 1 cm.

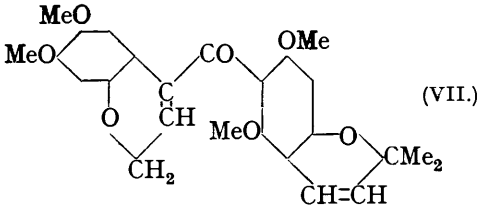
it is very readily resinified by alkali and absorbs oxygen rapidly in the presence of dilute alkali. These properties find a natural explanation if the ether is the αβ-unsaturated ketone (VII), derived from the "open" form (III; R = OH), and this structure is in agreement with the absorption spectrum. As shown in Fig. 2, the absorption of diacetyltoxicarol, which has the structure (II; R = Ac) but with the second acetoxy-group attached to C15, closely resembles that of acetylrotenone and rotenone methyl ether, but the absorption of toxicarol dimethyl ether differs from that of toxicarol and the diacetate. The structure (VII) is further in line with formation of the ether in equal yield from α- and from β-toxicarol, as also with the results of hydrogenation.

* On account of the stability to air and alkali it was possible that the ethers might have advantages as insecticides, but experiments by Mr. Craufurd-Benson of this Organisation showed that they have relatively little toxicity compared with their unmethylated prototypes.

Hydrogenation of the dimethyl ether gives smoothly a *tetrahydro*-ether, in which all the methoxyl groups are retained and which we believe to be (VIII). Dihydro-α-toxicarol



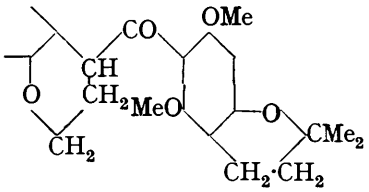
(VI.)

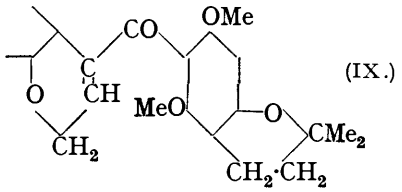


(VII.)

[as (IV), but with the ethylenic linking in ring *E* reduced] gives a *dimethyl* ether, which is stable to acid and is thus believed to be (IX); on hydrogenation this yields the same tetrahydro-ether (VIII) as is obtained from toxicarol dimethyl ether.

(VIII.)





(IX.)

We did not investigate reduction of mutarotenone methyl ether owing to the possibilities for isomerism, but used instead deguelin methyl ether. The product appeared to have lost a methyl group, which was not unexpected behaviour for an enolic ether, but the analytical figures for carbon and hydrogen were unintelligible, and, with only a small amount of material available, we were unable to establish the course of this reaction.

It is noteworthy that the yield of toxicarol dimethyl ether is 50%, whereas that of the enolic ethers is at most 30%. With the latter is obtained much gum, which is not unreacted starting material, and we think it at least possible that these gums contain the " open " phenolic ethers derived from (III; R = H).

Rotenone, *iso*rotenone, deguelin, and dihydrodeguelin differ only in the nature of ring *E* and give enolic ethers of type (II). Toxicarol and dihydrotoxicarol have in ring *E* the structure of deguelin and dihydrodeguelin, respectively, but give " open " ethers. It is thus clearly the original phenolic hydroxyl group in ring *D* which causes the relatively easier fission of its neighbouring ring *C* in the toxicarol series. We regard this proof and the incidental isolation of actual derivatives of the " open " form as the final steps in the series of arguments developed in our earlier publication.

In the preparation of dihydrotoxicarol dimethyl ether we isolated also a small amount of a *monomethyl* ether. Toxicarol gives a similar by-product, but the properties of this *substance* (cf. p. 740) leave us in doubt whether it is really the monomethyl ether.

Experimental

Methoxyl determinations were carried out as described previously. The [α] values are only approximate, as no accurate polarimeter was available; temperatures and concentrations are therefore omitted, but the latter were usually 5—6% in this and our previous work.

Mutarotenone Methyl Ether.—(*a*) Rotenone (2 g.), methyl sulphate (2 c.c.), and potassium carbonate (5 g.) in acetone (20 c.c.) were heated under reflux for 1—2 hours, the mixture then poured into water, and the gummy product crystallised from alcohol (the use of too little alcohol led to separation of oils). The m. p. of the product thus obtained varied, but a rather large number of crystallisations was always needed for purification. However, if the crude crystalline product was heated in 20 parts of 2% alcoholic potassium hydroxide for 15 minutes under reflux and the mixture was then cooled, acidified with acetic acid, and, if necessary, concentrated until crystallisation occurred, one to three further crystallisations usually sufficed. The crude, oily product gave discoloured gums when heated with alkali, as would be expected if " open " ethers were present. Varying the time of heating the original mixture beyond the limits stated gave reduced yields. The yield of pure product from the above batch was usually

about 30%, but it was often less from larger batches. In experiments starting with dried acetone, we recovered unchanged rotenone when the acetone contained 0, 0·25, or 0·5% of water, and got mutarotenone when the acetone contained 2% of water.

Pure *mutarotenone methyl ether* forms needles, m. p. 141°, $[\alpha]_D$ −130° in benzene [Found: C, 70·5, 70·8; H, 6·2, 6·1; OMe, 23·0. $C_{21}H_{15}O_3(OMe)_3$ requires C, 70·55; H, 5·9; OMe, 22·8%]. The m. p. is unreliable as a criterion of purity (cf. the analogous molecular compound, mutarotenone), being little influenced by the presence of impurities, but depressions of 5° or more are obtained after about equal amounts of the ether and mutarotenone have been mixed on a porous tile. One specimen having approximately the correct m. p. was shown by its absorption spectrum to contain 30% of rotenone. The ether is insoluble in alkali, gives no colour with ferric chloride and none in the Goodhue test; it gives a blue colour in the Durham test. It is more soluble in the usual organic solvents than is rotenone or mutarotenone, and this is responsible for the difficulty in purifying it by crystallisation. It gives no oxime under the conditions used for rotenone. It absorbs no oxygen when stirred in 1% alcoholic sodium hydroxide solution under air and is unaffected by iodine and sodium acetate in hot alcohol or by heating under reflux for 1 hour in 5% alcoholic potassium hydroxide solution with or without the addition of 20% of water.

(*b*) The same ether was obtained in the same yield from mutarotenone by the above method.

(*c*) Potassium hydroxide (2 g.) in water (30 c.c.) was added to a hot solution of rotenone (4 g.) and methyl sulphate (4 c.c.) in acetone (100 c.c.), and heating was continued for 10 minutes. The resultant red solution was poured into water, made feebly acid, and kept overnight. The supernatant liquid was then decanted from the gummy product, which by several crystallisations from alcohol gave the ether (0·2 g.), m. p. 141—142°.

(*d*) Attempted methylation by method (*a*), but using methyl *p*-toluenesulphonate in place of methyl sulphate (cf. p. 740), gave mutarotenone.

Hydrolysis of Mutarotenone Methyl Ether.—The ether (1 g.) was heated under reflux in alcohol (18 c.c.) containing concentrated sulphuric acid (2 c.c.). The product (0·7 g.), isolated after 60 minutes by pouring into water, crystallised from alcohol in clusters of small needles, $[\alpha]_D$ −80° in benzene, m. p. 146°, raised by further crystallisation to 148° (alone or mixed with an authentic sample). Hydrolysis was actually complete after 15 minutes' heating, as was shown by working up a small portion of the reaction mixture. Identity was confirmed by dissolving the product (0·5 g.) in carbon tetrachloride (5 c.c.), from which rotenone–carbon tetrachloride solvate (0·25 g.; identified in the usual way by conversion into rotenone, etc.) separated; the gum obtained from the carbon tetrachloride mother-liquors deposited 0·1 g. of mutarotenone from ether, but no further crystalline material was obtained. This behaviour is typical of mutarotenone. Taken in conjunction with the mixed m. p. and the rotation, it leaves no doubt as to identity.

Mutarotenone (0·6 g.) was similarly obtained when the ether (1 g.) was heated with alcohol (20 c.c.) containing concentrated sulphuric acid (0·4 c.c.). When, however, only 0·1 c.c. of sulphuric acid was used, the product tended to separate from alcohol as an oil, indicating incomplete hydrolysis; only unchanged ether (0·1 g.), m. p. 137—140° (mixed m. p.), was obtained crystalline. When the ether (0·5 g.) was heated under reflux for ½ hour in alcohol (7·5 c.c.) containing sulphuric acid (2·5 c.c.), isomerisation accompanied hydrolysis, and the product was *dl-iso*rotenone (0·1 g.), m. p. 161—163°, raised to 163—166° by mixing with an authentic specimen and depressed to 150—153° by mixing with rotenone.

dl-iso*Rotenone Methyl Ether.*—*dl-iso*Rotenone (5 g.), potassium carbonate (12·5 g.), and methyl sulphate (5 c.c.) in acetone (50 c.c.) were heated under reflux for 4 hours (better than 2 hours in this case). The oily product, isolated by pouring the mixture into water and decanting the supernatant liquid, was dissolved in hot alcohol. Crystals (1·5 g.), m. p. 165—175°, separated. When these were dissolved in hot alcohol and the crystals which separated within 1—2 hours were collected, pure dl-iso*rotenone methyl ether* (0·6 g.) was obtained as colourless plates, m. p. 189—190° [Found: C, 70·4; H, 5·7; OMe, 21·7 (micro; Weiler), 23·2 (Boam). $C_{21}H_{15}O_3(OMe)_3$ requires C, 70·55; H, 5·9; OMe, 22·8%], the m. p. being unchanged by further crystallisation. Concentration of the mother-liquor and collection of the crystals which separated again within 1—2 hours gave a further 0·5 g. of the ether, m. p. 188—190°. If, however, the alcoholic solutions were kept for longer times before collection of the crystals, the yield was higher but the material usually began to melt at about 165° and probably contained *iso*rotenone, since it gave the Goodhue test, which is not given by the pure ether. The crude crystalline product may also be purified by hot 2% alcoholic potassium hydroxide, as detailed for mutarotenone methyl ether; the technique of crystallisation just described then becomes unnecessary.

Purification of *iso*rotenone methyl ether is in any case not difficult, as the ether is the least soluble component of the reaction product.

*l-iso*Rotenone, when treated similarly, gave a similar yield of the same ether (mixed m. p.; α 0°), which required the same technique for purification. It was entirely racemised during the reaction, for the crude product, m. p. 165—175°, had α 0° in benzene.

Hydrolysis of the ether by dilute acid, as described for mutarotenone methyl ether, gave *dl-iso*rotenone

Methyl Ethers of Deguelin and Dihydrodeguelin.—A mixture of deguelin (1 g.), potassium carbonate (2 g.), methyl sulphate (1 c.c.), and acetone (10 c.c.) was boiled under reflux for 2 hours and then poured into water. Trituration of the gummy product with alcohol gave *deguelin methyl ether* (0·4 g.), m. p. 143—148°. Recrystallisation from alcohol yielded needles, m. p. 149—150° [Found: OMe, 24·4. $C_{21}H_{15}O_3(OMe)_3$ requires OMe, 22·8%].

When this ether (0·2 g.) had been boiled for ½ hour in alcohol (10 c.c.) containing sulphuric acid (0·5 c.c.), the solution, after cooling, deposited deguelin (0·1 g.), which after recrystallisation from alcohol had m. p. 170° alone or mixed with an authentic specimen.

Dihydrodeguelin (1 g.), when heated with potassium carbonate (2 g.) and methyl sulphate (2 c.c.) in acetone (40 c.c.) for 5 hours, gave a crude *methyl* ether (0·7 g.), m. p. 147°, which was obtained as stout, colourless needles, m. p. 152—154°, after two crystallisations from alcohol (Found: C, 70·5; H, 6·0. $C_{24}H_{26}O_6$ requires C, 70·3; H, 6·3%).

It is remarkable that dihydrodeguelin, in contrast to deguelin, does not give the Goodhue test.

Hydrogenation of Deguelin Methyl Ether.—The ether (1 g.) in a previously reduced mixture of Adams's platinum catalyst (about 0·05 g.) and acetic acid (50 c.c.) absorbed 154 c.c. (N.T.P.) of hydrogen (1 mol. = 54 c.c.). Dilution of the filtered solution with water and two crystallisations of the precipitate (0·75 g.) from alcohol gave pale yellow leaflets, m. p. 155—157° (Found: C, 69·3; H, 5·55; OMe, 15·9%). A substance with three methoxyl groups requires 22% or more of OMe. The product is probably not dihydrodeguelin (Calc. for $C_{23}H_{24}O_6$: C, 69·7; H, 6·1%), and is definitely not dihydrodeoxydeguelin (Calc. for $C_{23}H_{26}O_5$: C, 72·2; H, 6·8%).

Methylation of Toxicarol.—(*a*) Toxicarol (20 g.), anhydrous potassium carbonate (40 g.), and methyl sulphate (20 c.c.) in acetone (400 c.c.) were heated under reflux for 2 hours. The gummy product, obtained by pouring the mixture into water, crystallised readily when triturated with hot alcohol. The *dimethyl* ether (VII) (10 g.) was collected from the cooled solution as greenish-yellow, red, or even purple needles, m. p. 168—169°. In spite of the colour, it was nearly pure, for the pure ether, which is pale yellow, melts at 169—170° (Found: C, 68·5; H, 6·05. $C_{25}H_{26}O_7$ requires C, 68·4; H, 6·0%). The colour varied greatly in different preparations, but appeared to be definitely less intense or even absent if the aqueous mixture was acidified before the gummy product settled to the bottom of the vessel. The red colour, often very tenaciously retained, has been removed by boiling the product in alcohol with a fairly large amount of charcoal for 2 hours and, in another experiment, by passing the ether in chloroform through a short column of activated alumina; on the other hand, on another occasion the colour was deepened by boiling the ether with charcoal in alcohol. The ether gives no colour with ferric chloride and is unchanged by acetylation. In the Goodhue test it gives a blue colour with a much more pronounced red tinge than is usual. The ether, even when pure, is rapidly resinified by hot alcoholic sodium hydroxide, addition of even one drop of alkali causing appearance of a brown colour within 30 seconds. The red impurity leads to the production of blue or green colours by traces of mineral acid, but the yellow ether has been recovered unchanged after heating on the water-bath for 1 hour with 20% alcoholic sulphuric acid. The ether in 1% alcoholic sodium hydroxide absorbs oxygen very rapidly when stirred under air; it absorbs iodine under the conditions used for dehydrogenation. It gives only a faint brown colour in the Durham reaction.

(*b*) By the above method β-toxicarol (1 g.) gave needles (0·3 g.), m. p. 167—168°, which resembled the above ether in every way and did not depress its m. p.

(*c*) Potassium hydroxide (6 g.) in water (100 c.c.) was added to a boiling solution of toxicarol (20 g.) and methyl sulphate (10 c.c.) in acetone (1200 c.c.); the mixture was then evaporated to about 250 c.c. during 30 minutes and poured into water. The red gum precipitated was repeatedly crystallised from alcohol containing a little benzene and thus gave the dimethyl ether (9 g.) as pink, stout prisms from a dilute, or needles from a concentrated, solution; they had m. p. 168—170° alone or mixed with the ether prepared by method (*a*) [Found: OMe, 28·3, 29·1. $C_{21}H_{14}O_3(OMe)_4$ requires OMe, 28·3%]. Concentration of the mother-liquors and finally evaporation at room temperature gave a *substance*, which after repeated crystallisation

from alcohol–benzene formed pale yellow rhombs, m. p. 190—192°. From analyses (Found: C, 67·8, 67·6; H, 5·7, 5·6; OMe, 22·0, 21·5%), we thought this to be toxicarol monomethyl ether [Calc. for $C_{21}H_{15}O_4(OMe)_3$: C, 67·9; H, 5·7; OMe, 21·4%], but it appears to be identical with the product described in the following paragraph, where its nature is discussed.

(*d*) Toxicarol (10 g.), methyl *p*-toluenesulphonate (6 g.), and potassium carbonate (20 g.) in acetone (200 c.c.) were heated under reflux for 3 hours. The product was isolated in the usual way as pale yellow crystals (3·8 g.), m. p. 171—180°, from alcohol. Two crystallisations from alcohol, during which a small amount of less soluble, high-melting material was allowed to remain undissolved and removed, gave a product, m. p. 181—184°, also giving fairly correct analytical results for toxicarol monomethyl ether (Found: C, 67·45; H, 5·65%). The m. p. was not raised above 182—184° by crystallisation from alcohol or acetic acid, but the substance melted at about 186° when mixed with the product, m. p. 190—192°, described in (*c*). Diagnosis as the monomethyl ether appeared confirmed by further methylation of the substance by method (*a*) to give very pure dimethyl ether in 70% yield. The preparation was repeated several times with modification of the method of isolating the product in attempts to explain the divergence in melting points and the fact that a green colour developed within 15—60 seconds, but not instantaneously, when a drop of ferric chloride solution was added to the substance in alcohol. In one experiment no methylation occurred and we isolated only α- and β-toxicarol (this was, in point of time, the first occasion on which we obtained β-toxicarol); in some experiments we obtained unworkable gums, but in yet others we were able to obtain the substance, m. p. about 182°, without difficulty. From one sample, m. p. 182°, we isolated α-toxicarol by means of alkali but were unable to identify the non-phenolic portion. From another sample we obtained dihydro-β-toxicarol by hydrogenation. In the Durham reaction the substance gives the blue colour given by β-toxicarol and by dihydro-α-toxicarol monomethyl ether. We thus leave the nature and indeed the homogeneity of these substances, m. p. 182—184° and 190—192°, in doubt.

(*e*) Attempts to methylate toxicarol by the Schotten–Baumann method with or without the addition of ether, by pyridine and methyl sulphate in the cold (30 minutes), and by diazomethane failed.

Methylation of Dihydro-α-toxicarol.—Dihydro-α-toxicarol (2 g.), anhydrous potassium carbonate (4 g.), and methyl sulphate (2 c.c.) in acetone (20 c.c.) were heated under reflux for 5 hours. The mixture was diluted with water and shaken with ether. The ethereal layer was washed successively with aqueous potassium hydroxide, dilute hydrochloric acid, and water, dried, and evaporated. Slow crystallisation of the residue from alcohol gave a mixture of feathery needles and large prisms, which were separated by hand-picking. Repeated crystallisation of the needles from alcohol, in which they were sparingly soluble, gave colourless needles, m. p. 202°; these give no colour with ferric chloride and are thus the true *monomethyl* ether of dihydro-α-toxicarol (phenolic group methylated without ring-fission) [Found: C, 67·7; H, 6·2; OMe, 21·7. $C_{21}H_{17}O_4(OMe)_3$ requires C, 67·6; H, 6·1; OMe, 21·8%]. Repeated crystallisation of the prisms from alcohol, in which they were more soluble than were the needles, gave the "*dihydro-dimethyl ether*" (IX) as colourless prisms or plates, m. p. 176° [Found: C, 67·5; H, 6·1; OMe, 28·7. $C_{21}H_{16}O_3(OMe)_4$ requires C, 68·2; H, 6·4; OMe, 28·8%]. In the Durham test the monomethyl ether gives a blue colour, the dimethyl ether only a very pale brown.

When the dimethyl ether (IX) (0·2 g.) was boiled under reflux in 5% alcoholic hydrochloric acid (10 c.c.) for ½ hour, the product had a bright, deep green colour. It was, however, completely decolorised by charcoal, and the dimethyl ether (IX) was recovered unchanged.

The "Tetrahydro-dimethyl Ether" (VIII) *of Toxicarol.*—(*a*) The dimethyl ether (VII) (m. p. 169—170°; 2 g.) of toxicarol in glacial acetic acid (50 c.c.) containing a previously reduced Adams's platinum catalyst absorbed 2 mols. of hydrogen. The gummy precipitate obtained by diluting the filtered solution with water, when crystallised from alcohol, gave the "*tetrahydro-dimethyl ether*" (VIII) (1·44 g.) as colourless leaflets, m. p. 175—176° [Found: C, 67·8; H, 6·9; OMe, 29·2. $C_{21}H_{18}O_3(OMe)_4$ requires C, 67·9; H, 6·8; OMe, 28·0%]. These strongly depress the m. p. of the dihydro-ether (IX), which melts at the same temperature.

(*b*) The dihydro-ether (IX) (0·5 g.), hydrogenated in acetic acid (50 c.c.) in the same way, gave the tetrahydro-ether, m. p. 176° alone or mixed with the ether prepared by method (*a*), and depressed by admixture with the starting material.

Methylation of Derris *Extract.*—(*a*) A commercial *Derris* extract (10 g.; rotenone content 27%; Goodhue value 48·5; OMe 13·5%), methyl sulphate (10 c.c.), and potassium carbonate (10 g.) in acetone (100 c.c.) were heated under reflux for 2 hours. An excess of powdered ammonium carbonate was gradually introduced and the mixture was kept for 2—3 hours after

the main exothermic reaction had ceased. The whole was then poured into water and extracted with ether. The ethereal layer was exhaustively washed with water, dried, and evaporated. The product had Goodhue value 35 and OMe 16·2%. Repetition of the process gave a product having $[\alpha]_D$ −43·7° in benzene (mol. wt. assumed as that of rotenone), OMe 16·9%, and Goodhue value 28. This [α] was about a half to one-third of that of the original extract; [α] of the extract could not be determined accurately on account of the colour, and treatment with charcoal removed some optically active material. A third methylation gave material with OMe 18·0% and Goodhue value about 15. The product was a reddish resin, resembling pitch in consistency. Removal of every trace of methyl sulphate is essential for stability, and the ammonium carbonate procedure is convenient for this purpose. Rotenone and deguelin were main ingredients of the original extract; thus, methylation is evidenced by the decrease in Goodhue value (cf. Cahn, Phipers, and Boam, *J. Soc. Chem. Ind.*, 1938, in the press) as well as by the increase in methoxyl content.

(*b*) A Sumatra-type extract (rotenone content 4%; ferric chloride value 60; Goodhue value 14; OMe 12·5%) gave similarly a product having OMe 17·4%, ferric chloride value 19·5, and Goodhue value 22. A second treatment gave a product having OMe 21·9%, ferric chloride value 0 (trace of yellow colour only), and Goodhue value 31 (having the violet-red shade characteristic of toxicarol dimethyl ether). Toxicarol was a main ingredient of the original extract, and methylation is evidenced by the decrease in ferric chloride value (cf. *loc. cit.*) and the increase in Goodhue value (due to formation of toxicarol dimethyl ether) as well as by the change in methoxyl content.

Absorption Spectra.—We are much indebted to Dr. A. E. Gillam, who, by kind permission of Professor I. M. Heilbron, determined the absorption spectra recorded, using the technique detailed in our earlier paper. Data for rotenone, toxicarol, and the acetyl derivatives are taken from that paper. Maxima and molecular extinction coefficients observed for the ethers in freshly prepared solution in purified alcohol were:

	λ of max. in A.	Mol. extinction coeff., ε.
Rotenone methyl ether	3735	31,000
	3540	36,500
	2530	15,200
Toxicarol dimethyl ether	2310	39,000
	2680	20,200

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