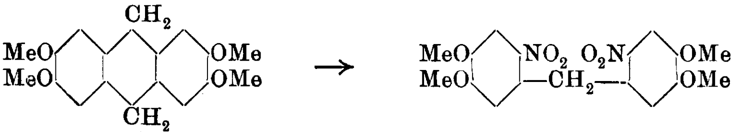
XXX.—*A Reaction of Homopiperonyl and of Homoveratryl Alcohols.*

By (Mrs.) Gertrude Maud Robinson.

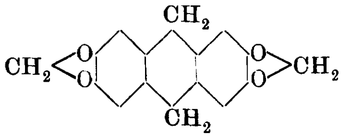
During the course of an examination of the action of phosphorus pentachloride on methylenedioxy-compounds, Ewins (T., 1909, **95**, 1486) treated homopiperonyl alcohol with this reagent, and obtained a compound of high melting point and sparing solubility, which was regarded as dimethylenetetraoxydihydroanthracene (II), but direct proof was not available. Having had occasion to employ homopiperonyl alcohol in connexion with synthetical researches, it was impossible to overlook the readiness with which this alcohol yields the substance obtained by Ewins, under the influence of mineral acids. Further, it was found that homoveratryl alcohol was readily condensed to an analogous substance by treatment, for example, with sulphuric acid in glacial acetic acid solution, and, on attempting to improve the method of preparation of homoveratryl alcohol by the employment of a process of condensation of veratrole and formaldehyde in the presence of 60 per cent. sulphuric acid, the condensation product of the alcohol was obtained in almost theoretical yield. A convenient process for the preparation of large quantities of this substance having been devised, it appeared desirable, in view of the intrinsic interest of the reaction, to make an investigation with the object of proving the constitution of the compound. The following observations show that the condensed homoveratryl alcohol is 2 : 3 : 6 : 7-*tetramethoxy*-9:10-*dihydroanthracene* (I). On distillation of the demethylated substance over zinc dust in a stream of hydrogen, 9:10-dihydroanthracene was obtained, whilst, on simultaneous oxidation and nitration by means of boiling 40 per cent. nitric acid, the condensation product yields 6-nitroveratric acid and 4:5-dinitroveratrole.

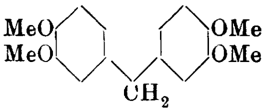
The latter result proves the orientation assumed in the formula to be correct, since no substances with substituents on the positions 3- or 6- of the veratrole ring can yield either of these products on treatment with nitric acid. Other reactions of the substance are described in the experimental portion of the paper, but the product of nitration deserves mention in this place. On treatment with nitric acid in acetic acid solution, the dihydroanthracene suffers fission in accordance with the scheme:



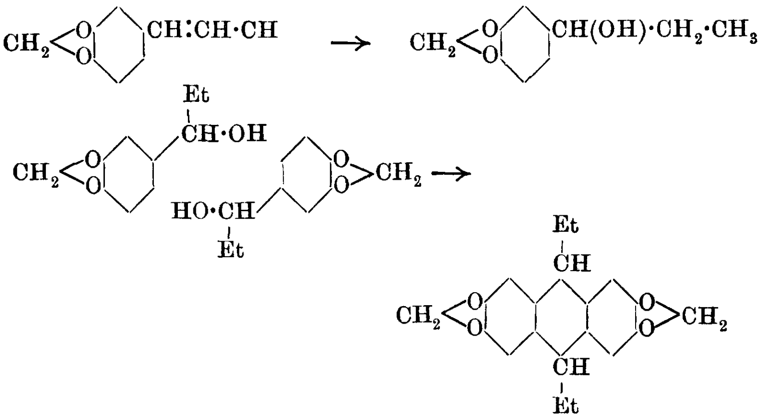
(I.)

The constitution of the product is proved by its production in the direct nitration of 3:4:3′:4′-*tetramethoxydiphenylmethane* (III), which was, in its turn, produced by the reduction of the corresponding tetramethoxybenzophenone by sodium and ethyl alcohol. This dinitro-derivative is either completely oxidised on boiling with nitric acid or is converted into a tetranitro-derivative of the diphenylmethane. It is really remarkable that oxidation of the methylene group to carbonyl does not occur simultaneously, but perhaps this is due to the influence of the nitro-groups on the distribution of affinity in the molecule (compare Foulds and Robinson, T., 1914, **105**, 1964). This influence should strengthen the affinity between the carbon and hydrogen atoms of the methylene group, and so enable it to resist oxidation:


(II.)


(III.)

The extraordinary reactivity of homopiperonyl alcohol suggested that the polymerisation of *iso*safrole and similar processes may be due to a series of reactions which find expression in the following scheme:



If this theory were true there should be a *cis*- and a *trans*-form of such polymerides, and, indeed, in the case of di*iso*safrole, Angeli and Mola (*Gazzetta*, 1894, **24**, ii, 127) obtained a polymeride melting at 145°, whilst Puxeddu (*Gazzetta*, 1913, **43**, i, 128) produced a second dimeride of *iso*safrole melting at 95°. Mario Mayer (*Atti R. Accad. Lincei*, 1914, [v], **23**, i, 358) has cleared up much of the confusion existing in regard to these substances, and proves that the di*iso*safrole melting at 95° is converted by distillation into that melting at 145°. Both polymerides boil at 380°, and have identical absorption spectra in acetone solution. There is clearly already strong evidence that these substances are *cis-trans*-isomerides, and, in further support of the view enunciated in the above formulæ, it may be mentioned that di*iso*safrole may be produced from safrole by the use of a solution of sulphuric acid in acetic acid as the polymeriser. Judging from analogy it would seem that the isomeride melting at 145° is the *trans*-compound.

EXPERIMENTAL.

2:3:6:7-*Dimethylenetetraoxy*-9:10-*dihydroanthracene* (II).

This substance was obtained by Ewins (*loc. cit.*) by the action of phosphorus pentachloride on homopiperonyl alcohol, but the condensation occurs with very great facility, and can readily be accomplished by the use of the following conditions:

A solution of concentrated sulphuric acid (2 grams) in glacial acetic acid (20 c.c.) was gradually added to homopiperonyl alcohol (20 grams) dissolved in hot acetic acid (60 c.c.). The white solid which separated out almost at once was crystallised from nitrobenzene, and found to be identical with the compound prepared by Ewins' method. The very sparingly soluble anthracene derivative is sufficiently characteristic, but, to remove all doubt, the crystalline nitro-derivative was prepared by treatment with nitric acid in acetic acid solution, and found to melt at 217° in agreement with the experience of Ewins. In view of the experiments described in the ensuing sections there can be no doubt that the constitution of this compound is that of a dinitrodimethylenetetraoxydiphenylmethane, and the analyses that have been made confirm this conclusion (Found, C=51·9; H=2·9; N=8·2 [Ewins, *loc. cit.*]. $C_{15}H_{10}O_8N_2$ requires C=52·0; H=2·9; N=8·1 per cent.).

2:3:6:7-*Tetramethoxy*-9:10-*dihydroanthracene* (I).

This compound is readily produced by the action of acid condensing agents on homoveratryl alcohol, and was obtained by warming the alcohol (from the reduction of veratraldehyde by sodium amalgam in aqueous alcoholic solution) in glacial acetic acid containing a few drops of concentrated sulphuric acid, and the product was proved by the method of mixed melting points to be identical with that derived by application of the following very much more convenient process:

Veratrole (10 grams) was mixed with sulphuric acid (34 grams of 70 per cent.) and drop by drop with formaldehyde (14 grams of 35 per cent. aqueous solution), the whole being vigorously stirred and then allowed to remain during two hours at the room temperature.

A colourless solid separated from the rose-coloured mixture, and the substance could be obtained in a satisfactory condition by boiling the liquid after adding about 75 c.c. of alcohol and collecting the sparingly soluble, crystalline precipitate. The yield of the crude compound was almost equal to that demanded by theory.

The substance was recrystallised from benzene, and obtained in long, colourless needles, which melt sharply and without decomposition at 227°:

0·1122 gave 0·2940 CO_2 and 0·0667 H_2O. $C=71·5$; $H=6·6$.
$C_{18}H_{20}O_4$ requires $C=72·0$; $H=6·7$ per cent.

The substance is very sparingly soluble in ether or alcohol, as well as in cold benzene, ethyl acetate, or acetic acid. It is soluble, however, in the last three solvents when hot, and crystallises from the solutions on cooling.

It dissolves in sulphuric acid to a rose solution, which rapidly becomes magenta, and on addition of water the colour disappears. On gently warming its solution in sulphuric acid, the colour changes to violet, and an almost black precipitate is obtained on the addition of water.

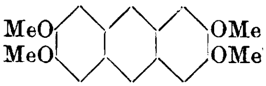
On boiling 10 grams of the tetramethoxydihydroanthracene with hydriodic acid (D 1·7; 35 grams) during half-an-hour, and pouring into water, a dark-coloured precipitate was obtained. This was collected, washed with sodium hydrogen sulphite solution, dried, and distilled in a stream of hydrogen over zinc dust in the usual manner.

In this way a product was obtained which solidified in contact with alcohol, and was crystallised from pyridine. It melted at 106°, and at the same temperature when mixed with a specimen of 9:10-dihydroanthracene prepared from anthraquinone by reduction with hydriodic acid and phosphorus in the way described by Liebermann and Topf (*Annalen*, 1882, **212**, 5).

Oxidation of the Hydroanthracene by Nitric Acid: Formation of 4:5-*Dinitroveratrole and* 6-*Nitroveratric Acid.*

Tetramethoxydihydroanthracene (4 grams) was boiled with nitric acid (50 c.c. of 40 per cent.) until a clear solution resulted, a condition achieved in about three hours. The liquid was rendered alkaline by means of sodium carbonate and extracted with chloroform; the solvent then removed from the extract by distillation, and the residue crystallised from water. The pale yellow needles so obtained were identified by direct comparison with 4:5-dinitroveratrole (m. p. 132°). The aqueous alkaline solution was rendered acid to Congo-red paper by means of hydrochloric acid and evaporated to dryness, the residue extracted with ether in a Soxhlet apparatus, the ether removed by distillation, and the remaining substance several times recrystallised from water. It melted at 187—188°, and was identified as 6-nitroveratric acid.

2:3:6:7-*Tetramethoxyanthracene*,



The removal of the two hydrogen atoms from the dihydro-derivative cannot readily be accomplished by any of the usual methods, and although the compound was ultimately obtained by the method described below, it could not be obtained in sufficient amount for a complete investigation.

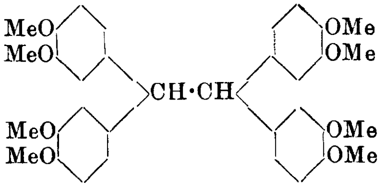
Tetramethoxydihydroanthracene was mixed with a large excess of litharge and distilled from a hard glass flask. The yellow distillate solidified, and was found to be a mixture of unchanged substance and the anthracene derivative. The latter is very much more soluble in cold benzene than the former, and the crude product was accordingly digested with cold benzene, and the filtered yellow solution evaporated. The residue was crystallised from ethyl acetate, and obtained in very pale yellow prisms, which melted at about 141° with loss of solvent of crystallisation, re-solidified, and fused again at about 169°:

0·1165 gave 0·2926 CO_2 and 0·0686 H_2O. C=68·5; H=6·5.

$C_{18}H_{18}O_4,C_4H_8O_2$ requires C=68·4; H=6·7 per cent.

It thus appears that this anthracene derivative crystallises from ethyl acetate with one molecule of solvent of crystallisation. The crystals, on boiling with water, lost ethyl acetate, which was recognised by its odour. On crystallisation from alcohol the compound was obtained free from solvent of crystallisation, and melted at 173°. On account of the wastefulness of the process and the small yield obtained it was not deemed advisable to prepare sufficient of the material for analysis, as it is quite certain that the first specimen, the analysis of which is recorded above, really contained the solvent of crystallisation. The most characteristic property of the tetramethoxyanthracene is the brilliant blue fluorescence which its solutions in most solvents exhibit. In sulphuric acid solution it passes through the same colour changes as its dihydro-derivative.

s-*Tetraveratrylethane*,



It was thought that the foregoing anthracene derivative might be produced (*a*) by condensing hydroveratroin internally, or (*b*) by the condensation of veratrole and glyoxal under suitable conditions.

A condensation product of hydroveratroin could be obtained by the use of tin tetrachloride, but it melted at 104°, and in this and other properties it resembled tetramethoxydeoxybenzoin (*Annalen*, 1903, **329**, 48). On the other hand, the condensation of glyoxal and veratrole in the presence of sulphuric acid led to the formation of the normal condensation product, that is to say, tetraveratrylethane. The experiment was carried out as follows: A mixture of veratrole (10 grams), glyoxal sodium hydrogen sulphite (10 grams), and sulphuric acid (34 grams of 70 per cent.) was shaken vigorously, and concentrated sulphuric acid (10 grams) gradually added. After the addition of the acid the mixture was warmed on the water-bath for ten minutes and then diluted with water. The solid which separated was collected and crystallised from benzene and then again from ethyl acetate. It was obtained in colourless needles, which melted at 148°:

0·1344 gave 0·3458 CO_2 and 0·0803 H_2O. C=70·2; H=6·6.

$C_{34}H_{38}O_8$ requires C=71·0; H=6·6 per cent.

The substance dissolves in sulphuric acid to a plum-coloured solution, which on the addition of water becomes first green and then pink.

3:4:3′:4′-*Tetramethoxydiphenylmethane* (III).

The starting point for the preparation of this diphenylmethane is the corresponding benzophenone, which was obtained by Kostanecki and Tambor (*Ber.*, 1906, **39**, 4027). Several points of simplification of procedure are, however, worthy of notice. Veratraldehyde is quantitatively oxidised to veratric acid by warm 2 per cent. aqueous potassium permanganate, and the product is at once obtained in the pure condition.

Then the acid yields the chloride by simply warming with one molecular proportion of phosphorus pentachloride, and after distilling away the phosphoryl chloride on a water-bath in a vacuum, the residue may be directly treated with aluminium chloride and veratrole in carbon disulphide solution. This reaction was carried out with only a gentle application of heat towards the end of the operation. After decomposition with ice-water, the mixture was distilled in a current of steam and the residue washed with ether, in which veratroylveratrole is very sparingly soluble, and crystallised from ethyl acetate. Veratraldehyde could in this series of processes be converted into more than its own weight of the final product.

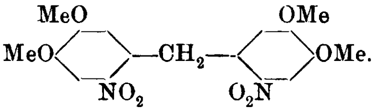
Veratroylveratrole (17 grams) was dissolved as far as possible in 200 c.c. of boiling ethyl alcohol, and the solution treated with 22 grams of sodium cut in rather large pieces. The flask was heated under reflux in an oil-bath and the temperature regulated from time to time, so that the reaction was always as vigorous as was consistent with the prevention of loss by frothing. When the mixture had been heated during two hours, and a certain quantity of sodium remained undissolved, water was added and the cooled solution extracted with ether, the ethereal solution washed with water, dried, and distilled finally in a vacuum. The greater part of the product distilled at 257°/24 mm., and the substance solidified on cooling and keeping. It could be crystallised from aqueous alcohol and again from light petroleum (b. p. 60—70°), and was obtained in colourless, glistening leaflets, melting at 70°:

0·1295 gave 0·3362 CO_2 and 0·0824 H_2O. C = 70·8; H = 7·1.
$C_{17}H_{20}O_4$ requires C = 70·8; H = 6·9 per cent.

The substance gives in sulphuric acid a magenta coloration, which might perhaps suggest contamination with the corresponding benzhydrol, but careful crystallisation does not remove this property to any degree, and it appears to be characteristic of the compound.

On treatment with concentrated sulphuric acid and formaldehyde followed by addition of water and collection of the dark precipitate, a product was obtained which, on crystallisation from benzene, yielded tetramethoxydihydroanthracene identical with the substance described above and melting at 227°.

6:6′-*Dinitro*-3:4:3′:4′-*tetramethoxydiphenylmethane*,



This substance is obtained by the following two methods:

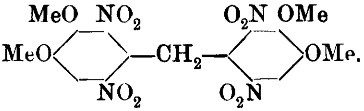
(*a*) Tetramethoxydihydroanthracene (2 grams) was mixed with glacial acetic acid (15 c.c.) and nitric acid (D 1·42; 6 c.c.), and heated until a vigorous reaction occurred, which was then allowed to proceed without further application of heat. On the addition of water, yellow crystals separated, and these were collected and recrystallised several times from ethyl acetate, in which solvent the substance is sparingly soluble in the cold. The pale yellow needles melted at 183°:

0·1162 gave 0·2306 CO_2 and 0·0516 H_2O. C = 54·1; H = 4·9.
$C_{17}H_{18}O_8N_2$ requires C = 54·0; H = 4·8 per cent.

For some at present inexplicable reason this compound does not give satisfactory values on estimating nitrogen by the direct method. The results obtained were always too high. The nature of the substance appears, however, to be established by the above analyses and also by the following method of preparation:

(*b*) Tetramethoxydiphenylmethane (see above) was dissolved in ten times its weight of glacial acetic acid and nitrated in the cold by the addition of twice its weight of ordinary concentrated nitric acid. After allowing to remain five minutes, the nitro-derivative was precipitated by water, collected, crystallised from ethyl acetate, and identified with the substance obtained as in (*a*) by direct comparison and the method of mixed melting points.

2 : 6 : 2′ : 6′-*Tetranitro*-3 : 4 : 3′ : 4′-*tetramethoxydiphenylmethane*,



The dinitro-derivative described in the previous section was dissolved in fifteen times its weight of nitric acid, and the solution boiled during two minutes, when a rather vigorous oxidation occurred and brown fumes were evolved. A solid, crystalline substance separated, however, and after addition of water this was collected and recrystallised from ethyl acetate. The sparingly soluble substance crystallised in almost colourless, rhombic prisms, melting at 210°:

0·1364 gave 0·2188 CO_2 and 0·0462 H_2O. C=43·7; H=3·7.

$C_{17}H_{16}O_{13}N_4$ requires C=43·6; H=3·4 per cent.

It is clear from this analysis that the methylene group of the substance has remained intact and unoxidised, and that the process is merely one of nitration accompanied by complete oxidation of a portion of the substance. In some experiments with fuming nitric acid a considerable amount of oxalic acid was obtained as the product of the reaction.

Di-iso*safrole.*

A mixture of *iso*safrole (10 grams), acetic acid (15 c.c.), and sulphuric acid (0·5 c.c.) was heated on the steam-bath during three hours. The product was diluted with water, and distilled in a current of steam to remove acetic acid and a small quantity of unchanged *iso*safrole. The polymeride remained as a viscid mass, and was separated as far as possible from the aqueous liquid and dissolved in the smallest possible amount of ethyl acetate. On the addition of alcohol just insufficient in amount to precipitate oily matter, and on keeping the liquid, a substance crystallised slowly, and was collected. This proved to be the di-*iso*safrole melting at 145°, and the compound gave that melting point after crystallisation from glacial acetic acid. The larger amount of the polymerides remained in the solution, and may be distilled in a vacuum after removal of the solvent; the viscid oil boiled at 255°/30 mm. Mario Mayer (*Atti R. Accad. Lincei*, 1914, [v], **23**, i, 358) states that di-*iso*safrole melting at 92° yields the isomeride melting at 145° on distillation, but the oil obtained as above did not crystallise.

Unfortunately no crystalline nitro-derivative was obtained from this compound, although the experiments were conducted under the most varied conditions. On the other hand, there was always evidence of the production of a fatty acid higher in the series than acetic acid, and this acid is probably propionic acid, since it yields a sparingly soluble silver salt and a characteristic barium salt. The odour of the acid was also suggestive of propionic acid.

THE UNIVERSITY OF SYDNEY.

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