123. *The Bimolecular Condensation of* p-*Propenylanisole (Anethole) under the Influence of Heat.*

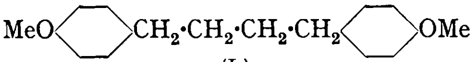
By Norman R. Campbell.

Prolonged heating of anethole in an inert atmosphere yields a crystalline substance which has been identified as 1 : 3-*di*-p-*methoxyphenyl*-2-*methylpropane*. This reaction closely resembles those involving polymerisation of anethole to " *iso*anethole " and " metanethole."

Two well-defined dimerides of anethole have been known for a considerable period. One of these, " *iso*anethole," has been shown by Goodall and Haworth (J., 1930, 2482) to be 1 : 3-di-*p*-methoxyphenyl-2-methyl-*n*-pentene, and the other, " metanethole," is considered by Baker and Enderby (J., 1940, 1094) to be 6-methoxy-1-*p*-methoxyphenyl-2-methyl-3-ethylhydrindene. These are both obtained by direct polymerisation of anethole, linkage taking place between the α-carbon of one molecule and the β-carbon of another.

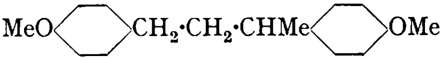
Bimolecular condensation of anethole or of the corresponding phenol, " anol," occurs during the process of demethylation with potassium hydroxide and alcohol under pressure (Campbell, Dodds, and Lawson, *Proc. Roy. Soc.*, 1940, *B*, **128**, 253). " *iso*Anethole " was identified in the remethylated by-products in notable quantity, also dihydro-" *iso*anethole " —arising from hydrogenation of " *iso*anethole " (cf. the production also of *p*-propylanisole). Traces, only, were found of the product of linkage between two α-carbon atoms, 3 : 4-di-*p*-methoxyphenyl-*n*-hexane being obtained in a yield of approximately 0·01—0·02%.

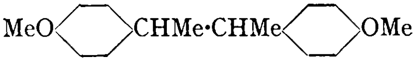
A crystalline substance has now been obtained by heating anethole under reflux in an inert atmosphere for several days. 70—80% of the anethole was recovered unchanged, a yield of about 0·2% of " *iso*anethole " was noted (indicated by isolation of the semicarbazone of methyl α-4-methoxyphenylpropyl ketone), and much of the balance was accounted for by the presence of gum which could not be distilled. The substance is saturated, and analyses of the methyl ether and its parent phenol indicate that it has the structure of a di-*p*-methoxyphenylbutane. The number of possible arrangements for this is strictly limited, since the substance obviously arises from the union of two molecules of anethole, followed by elimination of two carbon atoms and two hydrogen atoms. The possible structures are :


(I.)


(II.)

(III.)



(IV.)

(V.)


Since the yield of crystalline material is notably high for such a reaction, it seems most likely that linking between anethole molecules has occurred from α-carbon to β-carbon. It also appears probable that elimination of two carbon atoms would take place by fission at a double bond—that is, that both eliminated carbons should arise from the same anethole molecule.

The first of these conditions is satisfied by (II), (III), and (IV), and of these, only (II) fulfils the second. Hence structure (II) was considered most promising—a contention supported by the fact that substances of known structures (I), (III), and (V) were physically quite distinct from the material under consideration.

A substance of structure (II) has been synthesised by condensation of 2-*p*-methoxyphenyl-1-methylpropionyl chloride with anisole, and reduction of the resulting ketone by Clemmensen's method. The product showed no depression of melting point on admixture with the unknown substance. Identity of the two substances was inferred. The substance 1 : 3-*di*-p-*methoxyphenyl-2-methylpropane* has been demethylated, and the resulting *phenol* characterised and tested for oestrogenic properties.

The production of this crystalline compound from anethole by prolonged heating is comparable with the production of " *iso*anethole " from the same material. However, the production of " *iso*anethole " involves saturation of the side chain with retention of a double bond in the aliphatic connecting chain, while the reaction under consideration would appear to yield, as a hypothetical intermediary, an isomer of " *iso*anethole " with a double bond remaining in the side chain. Fission occurs, probably simultaneously with condensation, and two carbon atoms are eliminated from the unsaturated side chain.

EXPERIMENTAL.

Anethole (100 g.) was refluxed in an atmosphere of nitrogen for 7 days and nights, during which time the temperature of the boiling liquid rose from 221° to 260°. Unchanged anethole was removed by distillation at reduced pressure (recovery, 72 g.), and the residue distilled at low pressure. A fraction (b. p. 150—187°/0·2 mm.) was collected and redistilled, the portion, b. p. 150—166°/0·2 mm., being collected. This fraction partly solidified on standing; the crystals were separated by washing with ice-cold light petroleum (b. p. 60—80°) and recrystallised from methyl alcohol and from light petroleum; m. p. 71° (Found : C, 80·0; H, 8·1; OMe, 22·0; *M*, 282. $C_{18}H_{22}O_2$ requires C, 80·0; H, 8·15; OMe, 23%; *M*, 270). Yield, 1·5 g.

The light-petroleum washings were freed from solvent, and the residue dissolved in purified acetone, cooled in ice, and oxidised with powdered potassium permanganate added in small quantities (total, 1 g.), stirring being continued until reaction was complete (20 hrs.). The acetone solution was filtered and evaporated. The residue was distilled at low pressure and a fraction (0·2 g.) obtained boiling below 100°/0·3 mm. This fraction reacted with semicarbazide hydrochloride and sodium acetate in dilute alcohol, giving the semicarbazone of methyl α-4-methoxyphenylpropyl ketone, m. p. 189°, identified by the method of mixed melting points (yield, 0·05 g. of semicarbazone).

1 : 3-*Di*-p-*methoxyphenyl-2-methylpropan-1-one.*—1-*p*-Methoxybenzylpropionic acid (5 g.) was refluxed for 1 hour with thionyl chloride (25 c.c.). The excess of thionyl chloride was distilled off at reduced pressure, the residue dissolved in dry anisole (100 c.c.), and powdered aluminium chloride (4 g.) added, with cooling. The mixture was kept overnight and then poured into dilute hydrochloric acid and ice. After removal of anisole by steam-distillation the residue was extracted with ether, and the ethereal solution washed with water and dilute sodium hydroxide solution, dried, and freed from solvent. The residue was distilled, b. p. 180°/0·3—0·4 mm. (Found : C, 75·9; H, 7·15. $C_{18}H_{20}O_3$ requires C, 76·0; H, 7·1%). Yield, 4·7 g.

1 : 3-*Di*-p-*methoxyphenyl-2-methylpropane.*—The above ketone (3·5 g.) was reduced by boiling with amalgamated zinc wool (15 g.), hydrochloric acid (75 c.c.), water (75 c.c.), and tetrahydronaphthalene (20 c.c.—for dispersal of ketone) for 20 hours. Tetrahydronaphthalene was removed by distillation in steam and on cooling, the residue crystallised. The product, recrystallised from methyl alcohol, had m. p. 71° (Found : C, 80·05; H, 8·35. $C_{18}H_{22}O_2$ requires C, 80·0; H, 8·15%). Yield, 2 g. On admixture with the crystalline product from anethole the m. p. was unchanged.

1 : 3-*Di*-p-*hydroxyphenyl-2-methylpropane.*—1 : 3-Di-*p*-methoxyphenyl-2-methylpropane (1 g.) was heated with potassium hydroxide (2 g.) and absolute alcohol (4 c.c.) in a sealed tube at 200° for 18 hours. The mixture was cooled, diluted with water, filtered, and acidified, and the precipitated *phenol* crystallised from dilute aqueous alcohol and from light petroleum (b. p. 60—80°); m. p. 130° (Found : C, 79·2; H, 7·4. $C_{16}H_{18}O_2$ requires C, 79·3; H, 7·45%). Yield, 0·75 g.

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