163. *Dienoestrol.*

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A second form (m. p. 94—95°) of γδ-bis-4-hydroxyphenylhexane-γδ-diol (I) has been isolated and on dehydration affords *γγ-bis-4-hydroxyphenylhexan-δ-one* (VII), the methyl ether of which is reduced to stilboestrol dimethyl ether (IX). Either *β-chloro-α-*p*-anisyl-Δ^{α}-propene* or *α-chloro-α-*p*-anisyl-Δ^{α}-propene* can be obtained from anethole dichloride, and the corresponding *bromo*-compounds have been prepared. The α-bromo-compound and magnesium afford *dienoestrol dimethyl ether*, and the β-bromo-compound, to which the α-structure was assigned by Balaban *et al.* (*loc. cit.*), similarly yields αδ-di-*p*-anisyl-βγ-dimethyl-$\Delta^{\alpha\gamma}$-butadiene.

The important oestrogen dienoestrol, γδ-bis-4-hydroxyphenyl-$\Delta^{\beta\delta}$-hexadiene, (m. p. 227—228°) was prepared by Dodds, Golberg, Lawson, and Robinson (*Nature*, 1938, **142**, 34; *Proc. Roy. Soc.*, 1939, *B*, **137**, 162) from *p*-hydroxypropiophenone by reduction to γδ-bis-4-hydroxyphenylhexane-γδ-diol (I), m. p. 204—206°, followed by dehydration with acetyl chloride and acetic anhydride to γδ-bis-4-acetoxyphenyl-$\Delta^{\beta\delta}$-hexadiene and hydrolysis. Balaban, Jones, and British Colloids (B.P. 547,027) state that dienoestrol, m. p. 192°, may be obtained from the dimethyl ether, m. p. 161°, resulting from the action of magnesium upon a compound, formulated as α-bromo-α-*p*-anisyl-Δ^{α}-propene (II) and obtained by the action of dilute aqueous sodium hydroxide on αβ-dibromo-β-*p*-anisyl*iso*butyric acid. The lower m. p. attributed to dienoestrol by Balaban *et al.* might be due to the fact that they had isolated a different stereoisomer, but the present authors had good theoretical reasons for thinking that the elimination of hydrogen bromide and carbon dioxide from αβ-dibromo-β-*p*-anisyl*iso*butyric acid would produce β-*bromo*-α-p-*anisyl*-Δ^{α}-*propene* (III), so that the final product of the synthesis would be αδ-bis-4-hydroxyphenyl-βγ-dimethyl-$\Delta^{\alpha\gamma}$-butadiene (IV). In agreement with this conclusion, ozonolysis of the dimethyl ether, m. p. 163°, gave a 73% yield of anisaldehyde together with diacetyl, and catalytic reduction afforded a compound, m. p. 68—69°, which must be *αδ-di-*p*-anisyl-βγ-dimethylbutane* (V), since it is also obtained by the action of magnesium on *β-chloro-α-*p*-anisylpropane.* The bromide (III) is also obtained by the action of alcoholic sodium ethoxide (1·1 mols.) on anethole dibromide and affords β-*p*-anisyl-α-methylacrylic acid, m. p. 158°, by the successive action of magnesium and carbon dioxide. The isomeric bromo-compound (II) has now been prepared by the addition of hydrogen bromide to 1-p-*anisylprop*-1-*yne*, obtained by digesting anethole dichloride successively with pyridine and methyl-alcoholic potash. A small yield of dienoestrol is obtained from this bromide by the successive action of magnesium and anhydrous cupric chloride, followed by demethylation of the product with methylmagnesium iodide.

(I.) $HO{\cdot}C_6H_4{\cdot}CEt(OH){\cdot}CEt(OH){\cdot}C_6H_4{\cdot}OH$

(II.) $MeO{\cdot}C_6H_4{\cdot}CBr{:}CHMe$

(III.) $MeO{\cdot}C_6H_4{\cdot}CH{:}CMeBr$

(IV.) $HO{\cdot}C_6H_4{\cdot}CH{:}CMe{\cdot}CMe{:}CH{\cdot}C_6H_4{\cdot}OH$

(V.) $MeO{\cdot}C_6H_4{\cdot}CH_2{\cdot}CHMe{\cdot}CHMe{\cdot}CH_2{\cdot}C_6H_4{\cdot}OMe$

(VI.) $MeO{\cdot}C_6H_4{\cdot}CH{:}CMe{\cdot}NMe{\cdot}C_6H_5$

Anethole dibromide and boiling dimethylaniline afford β-(N-*methylanilino*)*anethole* (VI) with elimination of methyl bromide, and the unsaturated amine yields anisaldehyde and acetomethylanilide on oxidation. The elimination of hydrogen chloride from anethole dichloride is controlled by the reagent employed. Thus, pyridine produces *β-chloro-α-*p*-anisyl-Δ^{α}-propene*, b. p. 135—136°/10 mm., which is also obtained by the action of phosphorus pentachloride on anisylacetone. Ozonolysis affords a 60% yield of anisaldehyde and the successive action of magnesium and carbon dioxide yields β-*p*-anisyl-α-methylacrylic acid, and a small amount of αδ-di-*p*-anisyl-βγ-dimethyl-$\Delta^{\alpha\gamma}$-butadiene. The same formula has been ascribed without proof to the products obtained from anethole and phosphorus pentachloride by Ladenburg (*Annalen, Suppl.*, 1877, **8**, 90) and by the distillation of anethole dichloride (Darzens, *Compt. rend.*, 1897, **124**, 564).

*α-Chloro-α-*p*-anisyl-Δ^{α}-propene*, m. p. 43°, is obtained by the action of alcoholic potash on anethole dichloride or from *p*-methoxypropiophenone and phosphorus pentachloride; this isomer resembles α-bromostyrene (Dufraisse, *Compt. rend.*, 1921, **172**, 162) in being readily oxidised in air and we were unable to convert it into dienoestrol dimethyl ether by the action of magnesium.

The pinacol (I) has been obtained from *p*-hydroxypropiophenone and aluminium amalgam in moist ether (Dodds *et al., loc. cit.*) or by electrolytic reduction (Glaxo Laboratories, Robinson, and Resuggan, B.P. 523,515). Its *dimethyl* ether, m. p. 194°, can be obtained from *p*-methoxypropiophenone by reduction electrolytically or with magnesium amalgam and from *p*-anisylmagnesium bromide and dipropionyl, conveniently prepared from propionoin and selenium dioxide. Electrolytic reduction of p-*benzoyloxypropiophenone* results in the simultaneous elimination of the benzoyl group and the main product is an iso*pinacol*, m. p. 94—95°. The *iso*pinacol, which is probably the racemic form of (I), also accompanies the pinacol when the electrolytic reduction of *p*-hydroxypropiophenone is carried out under different conditions and may be separated by taking advantage of its greater solubility in cold acetic acid. The *iso*pinacol is rapidly converted into *γγ-bis-4-hydroxyphenylhexan-δ-one* (VII), m. p. 136°, by hot glacial acetic acid or by mineral acids and, although there are indications that the *iso*pinacol affords a dibenzoate, the pure compound could not be isolated owing to the ease with which it is transformed into *γγ-bis-4-benzoyloxyphenylhexan-δ-one*, m. p. 178°. The keto-phenol (VII) does not react with any of the usual ketonic reagents, but affords a *diacetate*, m. p. 91—92°, and a liquid dimethyl ether (VIII), which yields 4 : 4′-dimethoxybenzophenone on oxidation with chromic anhydride and stilboestrol dimethyl ether (IX), m. p. 124°, on reduction with sodium and amyl alcohol. When the keto-phenol (VII) is fused with potash, it affords αα-bis-4-hydroxyphenylpropane (X), m. p. 134°, which has been synthesised by Wessely, Kerschbaum, Kleedorfer, Prillinger, and Zajic (*Monatsh.*, 1940, **73**, 127). Methylation of the phenol (X) yields αα-di-*p*-anisylpropane, m. p. 44°, which is identical with the product obtained by reducing αα-di-*p*-anisyl-Δ^{α}-propene with sodium and amyl alcohol. The propene was obtained by Gattermann (*Ber.*, 1889, **22**, 1129) as a by-product of a Friedel–Crafts reaction with anisole and propionyl chloride, but the structure assigned to it by him has been disputed by Skraup and Freundlich (*Annalen*, 1923, **431**, 268) on the ground that it depresses the m. p. of an isomeric compound obtained from 4 : 4′-dimethoxybenzophenone and ethylmagnesium bromide, has a yellow colour, and does not exhibit halochromy with concentrated sulphuric acid. We find, however, that Gattermann's compound crystallises from alcohol in colourless plates, m. p. 101°, which give a red coloration with concentrated sulphuric acid.

$$\begin{tikzcd}
(I) \arrow[r] & (HO{\cdot}C_6H_4)_2CEt{\cdot}COEt\ (VII.) \arrow[r] \arrow[d] & (MeO{\cdot}C_6H_4)_2CEt{\cdot}COEt\ (VIII.) \arrow[d] \\
 & (HO{\cdot}C_6H_4)_2CHEt\ (X.) & MeO{\cdot}C_6H_4{\cdot}CEt{:}CEt{\cdot}C_6H_4{\cdot}OMe\ (IX.)
\end{tikzcd}$$

Dienoestrol is somewhat resistant to methylation, but affords a *mono-* and a *di-methyl* ether, m. p. 142° and 130—131° respectively. These are demethylated to dienoestrol by methylmagnesium iodide, but afford an isomeric *compound*, m. p. 189°, with alcoholic potash at 220°.

(*Note added September* 28th, 1943.) Reduction of the compound, m. p. 189°, obtained by the demethylation of dienoestrol dimethyl ether with alcoholic potash, in presence of palladised charcoal affords a mixture of hexoestrol and *iso*hexoestrol in the ratio 2 : 1. The compound cannot therefore be γδ-bis-4-hydroxyphenyl-$\Delta^{\alpha\epsilon}$-hexadiene. Oxidation of the corresponding dimethyl ether with potassium permanganate in aqueous acetone gives a small yield of anisil, and ozonolysis affords a trace of anisil and some acetaldehyde (2 : 4-dinitrophenylhydrazone, m. p. 167—168°). The compound is therefore probably a stereoisomeride of dienoestrol and may be called iso*dienoestrol*. The liquid dimethyl ether of *iso*dienoestrol affords hexoestrol dimethyl ether, m. p. and mixed m. p. 145°, as main product by reduction in presence of palladised charcoal.

EXPERIMENTAL.

1-p-*Anisylprop*-1-*yne*.—Crude β-chloro-α-*p*-anisyl-Δ^{α}-propene, b. p. 135—136°/10 mm. (150 g.), potassium hydroxide (135 g.; 2·9 mols.), and methanol (225 c.c.), refluxed for 8 hours, afforded 1-p-*anisylprop*-1-*yne* (90 g. or 75%) as a colourless liquid, b. p. 115—117°/9 mm. (Found : C, 82·3; H, 7·3. $C_{10}H_{10}O$ requires C, 82·2; H, 6·8%).

α-*Chloro*-α-p-*anisyl*-Δ^{α}-*propene*.—(1) Anethole dichloride (257 g.), when refluxed for 4 hours with a solution of sodium (55 g.; 2·8 atoms) in absolute alcohol (1 l.) gave the crude chloride, b. p. 108—110°/6 mm. (115 g. or 53·6%). α-*Chloro*-α-p-*anisyl* Δ^{α}-*propene*, m. p. 43°, was isolated by freezing (Found : Cl, 19·0. $C_{10}H_{11}OCl$ requires Cl, 19·5%).

(2) Phosphorus pentachloride (55 g.; 1·06 mols.) was added in portions with shaking to *p*-methoxypropiophenone (41 g.) at −5°; after 12 hours, the product was isolated with ether and hydrolysed for 12 hours at room temperature with a solution of potassium hydroxide (14 g.; 1 mol.) in water (14 c.c.) and alcohol (126 c.c.). *p*-Methoxypropiophenone was removed by adding a concentrated aqueous solution of hydroxylamine hydrochloride (7 g.) and potassium hydroxide (11 g.), removing the solvent under diminished pressure, and washing an ethereal solution of the residue with water. The yield of α-chloro-α-*p*-anisyl-Δ^{α}-propene, m. p. 43°, was 20 g. or 44%.

β-*Chloro*-α-p-*anisyl*-Δ^{α}-*propene*.—(1) This *compound*, b. p. 135—136°/10 mm., was obtained in 57% yield by heating anethole dichloride and pyridine (2·3 mols.) on the steam-bath for 2 hours, the operation being repeated with the same amount of pyridine (Found : Cl, 19·4, 19·3. $C_{10}H_{11}OCl$ requires Cl, 19·5%).

(2) A 24% yield of this chloro-compound was also obtained from anisylacetone and phosphorus pentachloride, the same technique being used as that employed in preparing the α-isomer. The structure of the material obtained from anethole dichloride and pyridine was verified (*a*) by the production of anisaldehyde (isolated as 2 : 4-dinitrophenylhydrazone, m. p. 254°) in 60% yield on ozonolysis in chloroform solution with 3% ozonised oxygen and (*b*) by the isolation of β-*p*-anisyl-α-methylacrylic acid, m. p. 158°, and of αδ-di-*p*-anisyl-βγ-dimethyl-$\Delta^{\alpha\gamma}$-butadiene, m. p. 162° (see below), from the products obtained by the successive action of magnesium (5 g.) and of carbon dioxide on a solution of the chloro-compound (25 g.) in anhydrous ether (125 c.c.).

β-(N-*Methylanilino*)*anethole*.—An exothermic reaction occurred when anethole dibromide (308 g.) was mixed with dimethylaniline (250 c.c.; 2 mols.) and, after 24 hours, the mixture was washed with dilute acid and water, to remove dimethylaniline, dried, and distilled. Fraction (1), b. p. 112—113°/7 mm., probably consisted of 1-*p*-anisylprop-1-yne, and fraction (2), b. p. 200—205°/1 mm., solidified on cooling and crystallised from alcohol in colourless leaflets, m. p. 116° (Found : C, 80·8; H, 7·8; N, 5·4. $C_{17}H_{19}ON$ requires C, 80·6; H, 7·5; N, 5·5%). The yield was 100 g. or 39·5% and oxidation with potassium permanganate in acetone solution afforded anisaldehyde (2 : 4-dinitrophenylhydrazone, m. p. 254°) and acetomethylanilide, m. p. 103°.

β-*Bromo*-α-p-*anisyl*-Δ^{α}-*propene* (III).—(1) αβ-Dibromo-β-*p*-anisyl*iso*butyric acid and dilute aqueous sodium hydroxide under the conditions described by Balaban *et al.* (*loc. cit.*) afforded β-*bromo*-α-p-*anisyl*-Δ^{α}-*propene*, b. p. 130—132°/6 mm., in 73% yield (Found : Br, 35·1. $C_{10}H_{11}OBr$ requires Br, 35·25%).

(2) Anethole dibromide and 1·7N-alcoholic potash (1·1 mols.) gave a 40% yield of the same compound when boiled for 3 hours. When the product obtained by either method was converted into a Grignard reagent and carbonated at −10°, it afforded β-*p*-anisyl-α-methylacrylic acid, m. p. 158°, in 25% yield and the structure was further confirmed by conversion of the bromide into αδ-di-*p*-anisyl-βγ-dimethyl-$\Delta^{\alpha\gamma}$-butadiene (see below).

αδ-*Di*-p-*anisyl*-βγ-*dimethyl*-$\Delta^{\alpha\gamma}$-*butadiene* (as IV).—The preceding bromo-compound was brought into reaction with magnesium as described by Balaban *et al.* (*loc. cit.*); the product crystallised from light petroleum–benzene in colourless laminæ, m. p. 163°. Ozonisation of the unsaturated compound (0·1 g.) in chloroform (25 c.c.) with 0·5% ozone for 3 hours at 0°, decomposition of the ozonide with water, and distillation of the liquid furnished a distillate with a strong odour of diacetyl and which afforded nickel dimethylglyoxime after reaction with hydroxylamine. Anisaldehyde (0·06 g. or 73%) was obtained by extracting the residue with ether and was identified by the preparation of its semicarbazone, m. p. 209°, and 2 : 4-dinitrophenylhydrazone, m. p. 254°. [Stilboestrol dimethyl ether, m. p. 124°, afforded *p*-methoxypropiophenone (2 : 4-dinitrophenylhydrazone, m. p. 190—191°) when ozonised under the same conditions.]

αδ-*Di*-p-*anisyl*-βγ-*dimethylbutane* (V).—(i) A solution of the aforesaid unsaturated compound (0·55 g.) in warm acetone (100 c.c.) was shaken with hydrogen in the presence of 6% palladium–charcoal (1 g.), 2·1 mols. of hydrogen being absorbed in 2 hours. The resulting mixture of tetrahydro-compounds (0·49 g.), m. p. 68—75°, on crystallation from alcohol afforded a portion (0·45 g.), m. p. 73—75°, and the mother-liquor deposited crystals, m. p. 67—73°, which on sublimation at 170°/1 mm. and recrystallisation from alcohol furnished αδ-*di*-p-*anisyl*-βγ-*dimethylbutane*, m. p. 68—69° (Found : C, 80·6; H, 8·6. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·7%). There was a depression in m. p. when this preparation was mixed with αω-di-*p*-anisylhexane, m. p. 70—71°, prepared by the method of Richardson and Reid (*J. Amer. Chem. Soc.*, 1940, **62**, 413). (ii) Reduction of anisylacetone (50 g.) with sodium (50 g.; 7·1 atoms) and absolute alcohol (600 c.c.) gave the secondary alcohol (11 g. or 22%), b. p. 108—109°/2 mm., which afforded β-chloro-α-*p*-anisylpropane, b. p. 89—90°/1 mm., with hydrogen chloride in benzene solution. The yield was 43%, and the chloro-compound gave the butane, m. p. and mixed m. p. 68°, when a dry ethereal solution was boiled with a large excess of magnesium for 4 hours.

γδ-*Bis*-4-*hydroxyphenylhexane*-γδ-*diol* (*Pinacol, m. p.* 204—206°).—This compound, prepared from *p*-hydroxypropiophenone by reduction with aluminium amalgam (Dodds *et al.*, *loc. cit.*) or by electrolytic reduction (Glaxo Laboratories, Robinson, and Resuggan, B.P. 523,515), has been further characterised by the preparation of a *dibenzoate*, m. p. 235—236° (Found : C, 75·1; H, 5·9; Bz, 41·3. $C_{32}H_{30}O_6$ requires C, 75·4; H, 5·9; Bz, 41·2%), and a *ditoluene*-p-*sulphonate*, prisms from benzene, m. p. 205° (Found : C, 62·2; H, 5·5. $C_{32}H_{34}O_8S_2$ requires C, 62·8; H, 5·6%).

γδ-*Di*-p-*anisylhexane*-γδ-*diol*.—The *dimethyl* ether of the preceding pinacol crystallised from ethyl acetate in prisms, m. p. 194° (Found : C, 73·0; H, 7·9. $C_{20}H_{26}O_4$ requires C, 72·7; H, 7·9%), and afforded γγ-di-*p*-anisylhexan-δ-one (see below) as main product when dehydrated by boiling with acetic anhydride–acetyl chloride. It was prepared by three methods : (1) A solution of *p*-methoxypropiophenone (32 g.) and mercuric chloride (11·5 g.) in dry ether (150 c.c.) was added to fine magnesium turnings (10 g.) and dry benzene (100 c.c.), and the mixture boiled for 48 hours. After addition of water (25 c.c.) and 1 hour's boiling, the product was acidified with hydrochloric acid, and the benzene layer washed, dried, and evaporated. Distillation afforded 28 g. of recovered ketone, and crystallisation of the solid residue from benzene–alcohol gave 1 g. of the pure methyl ether. (2) Electrolysis of a solution of *p*-methoxypropiophenone (22 g.) and sodium hydroxide (20 g.) in alcohol (200 c.c.) and water (50 c.c.), the method described in B.P. 523,515 for the reduction of *p*-hydroxypropiophenone being used, afforded 4·9 g. (22%) of γδ-di-*p*-anisylhexane-γδ-diol. (3) A mixture of selenium dioxide (12 g.) and propionoin (20 g.), prepared from ethyl propionate in 52—55% yield by the method of Snell and McElvain (*J. Amer. Chem. Soc.*, 1931, **53**, 750), was slowly distilled; the aqueous distillate, b. p.

90—130°, afforded dipropionyl, b. p. 129—130°, after drying and fractionation. The yield, 7 g. (35·5%), was decreased when the propionoin was diluted with alcohol. A solution of dipropionyl (15 g.) in dry ether (100 c.c.) was slowly added to a Grignard reagent prepared from *p*-bromoanisole (118 g.; 4·7 mols.), magnesium (15·3 g.), and dry ether (500 c.c.); after 3 days, the mixture was refluxed for 2 hours and decomposed with ice-cold hydrochloric acid. After removal of ether and anisole (37 g.) the solid was crystallised from benzene, and 5·75 g. (13%) of γδ-di-*p*-anisylhexane-γδ-diol, m. p. 192—194°, were obtained.

γδ-Bis-4-hydroxyphenylhexane-γδ-diol(iso*Pinacol, m. p.* 94—95°).—The *iso*pinacol was obtained as by-product when *p*-hydroxypropiophenone was reduced electrolytically as described in B.P. 523,515 and could be separated from the pinacol by taking advantage of its greater solubility in cold acetic acid. On one occasion when a faulty porous pot was used the *iso*pinacol was the main product of the reduction. Benzoylation of *p*-hydroxypropiophenone by the Schotten–Baumann method afforded p-*benzoyloxypropiophenone*, which crystallised from alcohol in needles, m. p. 117° (Found: C, 75·6; H, 5·5. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·5%). Electrolysis of a solution of the benzoyl derivative (20 g.) and sodium hydroxide (10 g.) in dioxan (200 c.c.) and water (50 c.c.), the apparatus and technique described in the patent mentioned above being used, and rebenzoylation of the product by the Schotten–Baumann method resulted in the production of 10 g. of γγ-bis-4-benzoyloxyphenylhexan-δ-one, m. p. 178°, so that the *iso*pinacol must be the main product of the reduction. The low-melting form of γδ-bis-4-hydroxyphenylhexane-γδ-diol separated from cold acetic acid as a white microcrystalline powder, m. p. 94—95° (Found: C, 71·5; H, 7·1; *M*, cryoscopic in camphor, 309. $C_{18}H_{22}O_4$ requires C, 71·5; H, 7·3%; *M*, 302). The *compound* was very labile and readily underwent pinacolin rearrangement when warmed with acids. Benzoylation by the Schotten–Baumann method produced a product, m. p. 175°, which probably contained the dibenzoate (Found: C, 77·2; H, 5·7. $C_{32}H_{30}O_6$ requires C, 75·4; H, 5·9%. $C_{32}H_{28}O_5$ requires C, 78·0; H, 5·7%), but only γγ-bis-4-benzoyloxyphenylhexan-δ-one (see below) could be obtained by fractional crystallisation and this ketone was readily obtained in pure condition when the crude benzoate was digested with acetic acid for a few minutes.

γγ-Bis-4-hydroxyphenylhexan-δ-one.—When the *iso*pinacol was warmed with acid, it afforded *γγ-bis-4-hydroxyphenylhexan-δ-one*, which separated from benzene–light petroleum (b. p. 100°) in prisms, m. p. 136° (Found: C, 76·0; H, 7·1. $C_{18}H_{20}O_3$ requires C, 76·1; H, 7·0%). The *dibenzoate* crystallised from benzene–light petroleum in prismatic needles, m. p. 178° (Found: C, 77·7; H, 5·8. $C_{32}H_{28}O_5$ requires C, 78·0; H, 5·7%), and afforded the phenol when boiled with 10% alcoholic potash. The ketone afforded an acetate, m. p. 91—92°, but did not react with hydroxylamine, semicarbazide or 2 : 4-dinitrophenylhydrazine. Methylation with methyl sulphate and aqueous sodium hydroxide yielded a liquid dimethyl ether, which afforded 4 : 4′-dimethoxybenzophenone, m. p. 143—144° (2 : 4-dinitrophenylhydrazone, m. p. 200—201°), when oxidised with chromic anhydride in acetic acid solution. The dimethyl ether (2 g.) was reduced with sodium (6 g.) in boiling amyl alcohol (40 c.c.) to stilboestrol dimethyl ether (0·05 g.), m. p. and mixed m. p. 124°. When γγ-bis-4-hydroxyphenylhexan-δ-one or its diacetate (1 g.) and potassium hydroxide (2 g.) were maintained at 200° for ½ hour, the neutral product obtained crystallised in prisms, m. p. 134° (Found: C, 78·9; H, 7·0. Calc. for $C_{15}H_{16}O_2$: C, 78·9; H, 7·0%), apparently identical with the αα-bis-4-hydroxyphenylpropane described by Wessely *et al.* (*loc. cit.*). Methylation with methyl sulphate and aqueous sodium hydroxide afforded αα-di-*p*-anisylpropane, m. p. 44°. αα-Di-*p*-anisyl-Δ^{α}-propene, prepared as described by Gattermann (*loc. cit.*), had b. p. 180—185°/1 mm. and crystallised from alcohol in colourless plates, m. p. 101°. Reduction of the propene (2 g.) with sodium (2 g.) in boiling amyl alcohol (30 c.c.) afforded unchanged propene (1·1 g.) and a small amount of αα-di-*p*-anisylpropane, m. p. and mixed m. p. 44°.

Dienoestrol.—The reaction between 1-*p*-anisylprop-1-yne and a 32% (w./v.) solution of hydrogen bromide in acetic acid was exothermic; the temperature rose rapidly if the mixture were not cooled and decomposition occurred. Dry hydrogen bromide (16·5 g.; 1 mol.) was passed into an ice-cold solution of the propyne (30 g.) in benzene (100 c.c.) and, after 2 hours at 0°, 20 c.c. of the solvent were removed in a vacuum at 20°; hardly any hydrogen bromide was liberated. Half the residual solution was added to magnesium turnings (2·5 g.; 0·5 atom) and ether (100 c.c.) and, when the brisk reaction had subsided, the mixture was boiled for an hour; after the addition of another 2·5 g. of magnesium and the rest of the benzene solution, the mixture was refluxed for a further 2 hours, and anhydrous cupric chloride (28 g.; 1 mol.) then added. When the vigorous reaction abated, the mixture was boiled for 12 hours, and the product worked up in the usual way. Distillation afforded (i) anethole (9 g.), b. p. 80—85°/1·5 mm., (ii) 3 g., b. p. 104—105°/1·5 mm., probably the propyne, and (iii) a resinous residue (14 g.). The last was dissolved in ether and evaporated with a solution of methylmagnesium iodide (from magnesium, 3·1 g., methyl iodide, 19 g., and ether, 150 c.c.). When the residue was heated to 170°, there was a vigorous reaction with some carbonisation. The product was decomposed with ice-cold dilute hydrochloric acid, and a solution of the alkali-soluble portion of the product precipitated with carbon dioxide. The precipitate, sublimed at 130°/1 mm., afforded dienoestrol (0·05 g.), m. p. and mixed m. p. 230—233°.

When dienoestrol (5 g.) and an ethereal solution of diazomethane (140 c.c.; 2·2 mols.) were kept at room temperature for 4 days, 3·5 g. of dienoestrol were recovered and 0·7 g. of *dienoestrol monomethyl ether* obtained. This was soluble in alcoholic alkali and separated from aqueous alcohol in needles, m. p. 142° (Found: C, 81·0; H, 7·2; OMe 11·1. $C_{19}H_{20}O_2$ requires C, 81·4; H, 7·1; OMe, 11·1%). Methylation of dienoestrol in N-sodium hydroxide (4·3 mols.) with methyl sulphate (4·0 mols.) afforded the monomethyl ether in 73% yield together with the *dimethyl* ether, m. p. 130—131° (Found: C, 81·4; H, 7·5; OMe, 21·4, 21·5. $C_{20}H_{22}O_2$ requires C, 81·6; H, 7·5; OMe, 21·1%). The mono- and the di-methyl ether were obtained in 29 and 30% yield respectively when dienoestrol, methyl iodide (3·6 mols.), and 0·2N-methyl-alcoholic potash (1·2 mols.) were boiled for an hour. Ozonolysis of dienoestrol dimethyl ether in glacial acetic acid solution afforded a 16% yield of anisil, m. p. 133°, characterised by conversion into 2 : 3-*di*-p-*anisylquinoxaline*, m. p. and mixed m. p. 149—150° (Found: C, 77·2; H, 5·4; N, 7·8. $C_{22}H_{18}O_2N_2$ requires C, 77·2; H, 5·3; N, 8·2%). *Dienoestrol dibenzyl ether* separated from benzene in prisms, m. p. 205° (Found: C, 85·4; H, 6·5. $C_{32}H_{30}O_2$ requires C, 85·9; H, 6·8%). *Dienoestrol ditoluene*-p-*sulphonate* had m. p. 168° (Found: C, 66·2; H, 5·1. $C_{32}H_{30}O_6S_2$ requires C, 66·8; H, 5·2%). *Dienoestrol dibenzoate* separated from benzene–light petroleum in needles, m. p. 224° (Found: C, 80·3; H, 5·3. $C_{32}H_{26}O_4$ requires C, 81·0; H, 5·3%).

Demethylation of dienoestrol dimethyl ether with methylmagnesium iodide (2·5 mols.) at 175° regenerated dienoestrol, but demethylation with alcoholic potash at 220° afforded an isomeric *compound*, m. p. 189° (Found: C, 81·1; H, 6·8. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·7%), which afforded a liquid methyl ether.

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