1200. *Nuclear Methylated Diethylstilbœstrols as Possible Anti-œstrogens*

By Edward R. Clark and Stella R. O'Donnell

The syntheses of some nuclear methylated analogues of diethylstilbœstrol, using substituted α-ethyldeoxyanisoins as key intermediates, are described. The synthetic procedure which was used yielded, initially, 3,4-diaryl-hex-2-enes, isomeric with the desired stilbenes. Conversion to the stilbene structure has been achieved by iodine equilibration. The structures of the hex-2-enes and stilbenes have been established by n.m.r. spectroscopy. Some of the compounds have been tested for œstrogenic and anti-œstrogenic activity. 3,4-bis-(3,5-dimethyl-4-hydroxyphenyl)hex-2-ene (XI*a*) has been found to antagonise the normal vaginal response to 17β-œstradiol, when tested on mice.

Significant anti-œstrogenic activity has been reported in some members of the stilbœstrol and butœstrol series, the most widely studied compound being dimethylstilbœstrol [1-3] by

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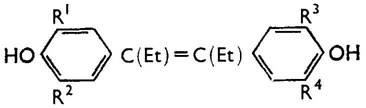
[1] C. W. Emmens and R. I. Cox, *J. Endocrinol.*, 1958, **17**, 265.
[2] C. W. Emmens, R. I. Cox, and L. Martin, *J. Endocrinol.*, 1959, **18**, 372.
[3] C. W. Emmens, R. I. Cox, and L. Martin, *Recent Progr. Hormone Res.*, 1962, **18**, 415.

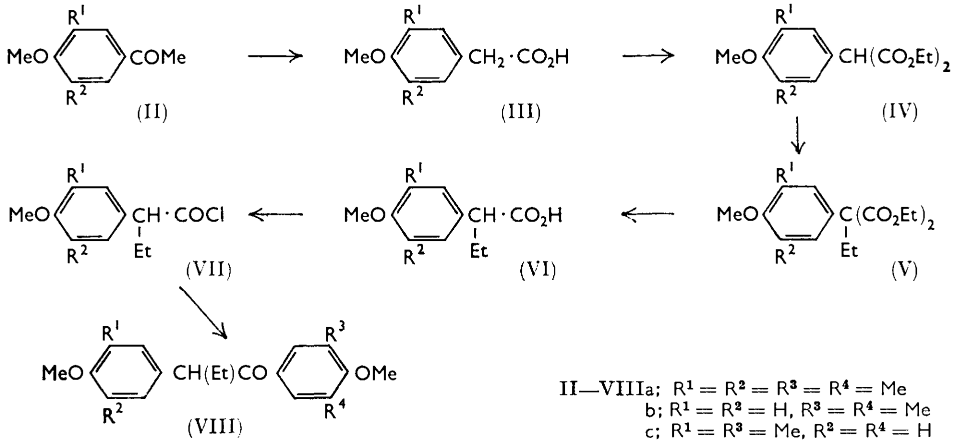
Emmens and his collaborators. These workers suggest that their compounds are competitive inhibitors of œstrogen, and act at a common site in the vagina. However, all the compounds which they investigated also possessed " pro-œstrogenic " activity.[4]

The introduction of methyl groups at positions *ortho* to the phenolic hydroxyl groups in hexœstrol and dienœstrol,[5] and also in the steroidal œstrogens [6,7] has been found to reduce œstrogenic activity. It appeared of interest, therefore, to synthesise analogues of diethylstilbœstrol with methyl substituents adjacent to one or both of the phenolic hydroxyl groups (I *a*, *b*, and *c*). It was hoped that these compounds might possess zero or only very low œstrogenic potencies whilst retaining the ability of the parent diethylstilbœstrol to occupy the " receptor " for œstrogen in the vagina.

(Ia) $R^1 = R^2 = R^3 = R^4 = Me$
(Ib) $R^1 = R^2 = H, R^3 = R^4 = Me$
(Ic) $R^1 = R^3 = Me, R^2 = R^4 = H$



The synthetic route used to obtain the desired compounds required the preparation of the appropriately substituted α-ethyldeoxyanisoins (VIII *a*, *b*, and *c*). Initially, experiments were directed towards the ethylation of 3,3′-dimethyldeoxyanisoin using ethyl iodide and sodium ethoxide, but almost quantitative yields of the starting material were recovered. Recourse was therefore made to the route adopted by Wilds and Biggerstaff,[8] who overcame a similar difficulty in the preparation of α-ethyldeoxyanisoin by using the Friedel–Crafts reaction between α-(4-methoxyphenyl)butyryl chloride (VII; $R^1 = R^2 = H$) and anisole. This necessitated the preparation of α-(4-methoxyphenyl)butyryl chloride and its 3-methyl and 3,5-dimethyl homologues (VII; $R^1 = Me, R^2 = H$ or $R^1 = R^2 = Me$) and their reaction with 2-methylanisole or 2,6-dimethylanisole in the presence of aluminium chloride. The α-arylbutyric acids required were prepared from the appropriately substituted acetophenones (II), which were converted by means of the Kindler modification of the Willgerodt reaction to arylacetic acids (III). Ethylation in the α-position was achieved *via* the related malonates (IV) and (V). The general synthetic route is shown, and is analogous to that previously described by Clark and Linnell [9] for the preparation of α-(4-methoxyphenyl)butyric aid.



II—VIIIa; $R^1 = R^2 = R^3 = R^4 = Me$
b; $R^1 = R^2 = H, R^3 = R^4 = Me$
c; $R^1 = R^3 = Me, R^2 = R^4 = H$

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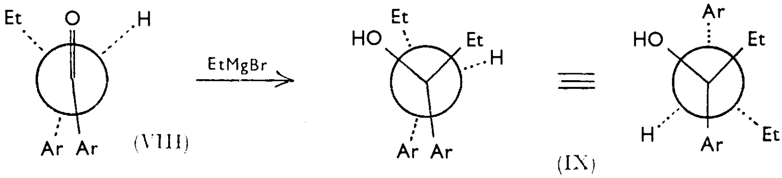
[4] C. W. Emmens, *J. Endocrinol.*, 1941, **2**, 444.
[5] J. A. Hogg and J. Korman, " Medicinal Chemistry," Wiley, New York, vol. II, p. 34.
[6] J. Iriate and H. J. Ringold, *Tetrahedron*, 1958, **3**, 28.
[7] T. L. Patton and L. Dmochowski, *Arch. Biochem. Biophys.*, 1963, **101**, 181.
[8] A. L. Wilds and W. R. Biggerstaff, *J. Amer. Chem. Soc.*, 1945, **67**, 789.
[9] E. R. Clark and W. H. Linnell, *J. Pharm. Pharmacol.*, 1949, **1**, 211.

Reactions of the derived butyryl chlorides with either 2-methylanisole or 2,6-dimethylanisole in the presence of aluminium chloride proceeded satisfactorily to yield the required deoxyanisoins provided that sufficiently long reaction periods were used. Shorter reaction times led to contamination of the product with an impurity, presumably acid chloride (weak absorption peaks in the infrared spectrum at 1770 and 1745 cm.$^{-1}$), which prevented crystallisation of the deoxyanisoin. Removal of all traces of contaminant by hydrolysis and alkaline extraction was found to be essential if satisfactory products were to be isolated at the next stage in the synthesis.

The deoxyanisoins were readily converted to the hexan-3-ols (IX*a*, *b*, and *c*) using ethyl magnesium bromide. Fractional recrystallisation resulted in the isolation of the two diastereoisomeric forms of each of the hexan-3-ols, all of which are crystalline except for one of the isomers of the hexanol (IX*c*).



(VIII)

(IX)

Cram's rule [10] predicts that the major isomer in each case should have the *erythro* structure, as shown. This is consistent with the assignment of the *erythro* structure to the higher melting isomers in the case of hexanols (IX*a*) and (IX*b*) but not in the case of hexanol (IX*c*) where, however, the non-crystalline nature of one isomer leads to doubt regarding its stereochemical purity, and to the relative amounts of each isomer produced.

Initially, the two diastereoisomers of each hexan-3-ol (IX) were dehydrated separately. Phosphorus oxychloride in pyridine failed to remove the elements of water, but phosphorus trichloride in pyridine yielded unsaturated products. Infrared (i.r.) analysis demonstrated that both diastereoisomeric forms of each alcohol produced identical products in similar yields. There seemed to be no advantage, therefore, in separating the diastereoisomeric forms prior to dehydration and in later runs the mixture of isomers was dehydrated. The formation of the same product with equal ease from each isomeric pair of racemates became understandable when it was subsequently demonstrated by nuclear magnetic resonance (n.m.r.) spectroscopy that dehydration of both *erythro* and *threo* forms of the hexan-3-ols with phosphorus trichloride and pyridine yielded the hex-2-ene structures (X) and not the expected stilbenes (XII).

The position of the double bond in the unsaturated products was established by the presence of a doublet at 8·56, 8·56 and 8·52 τ, respectively, for the tetramethylated (X*a*), asymmetrically dimethylated (X*b*), and symmetrically dimethylated (X*c*) diarylhex-2-enes (this order of presenting the results for the three compounds will be adopted in the remainder of this discussion) corresponding to the protons of a CH_3 adjacent to –CH=. A quartet, with subsidiary splitting possibly due to the presence of *cis–trans* isomers, was present at 4·59, 4·54 and 4·5 τ, for the respective compounds, characteristic of the ethylenic proton of CH_3–CH=. The integrated areas under the curves were equivalent to approximately three and one protons respectively, as required for the CH_3–CH= structure. Triplets at 9·2, 9·19 and 9·14 τ, for the respective compounds, correspond to the methyl protons adjacent to methylene, and the integrated areas were again equivalent to the three protons required by the hex-2-ene structures. Further confirmation of the dissymmetry of the products of dehydration of the hexanols (IX*a* and *c*) was the splitting of the absorption due to aromatic methyl into two components at 7·83 and 7·86 τ for (X*a*) and 7·83 and 7·87 τ for compound (X*c*) and the presence of 2 singlets (each of intensity 2) at 3·38 and 3·62 τ due

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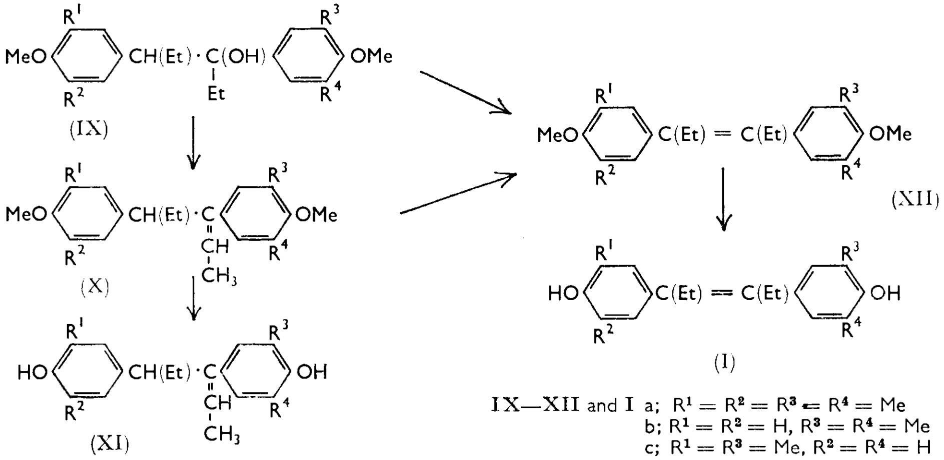
[10] D. J. Cram and F. A. Abd Elhafez, *J. Amer. Chem. Soc.*, 1952, **74**, 5828.

to the aromatic protons of compound (X*a*). As expected, the aromatic methyls of compound (X*b*) yielded a singlet at 7·85 τ. No splitting of the methoxyl proton absorption occurred with compounds (X*a*) and (X*c*), which showed singlets at 6·37 and 6·24 τ respectively, but the methoxyl protons of compound (X*b*) yielded the expected 2 singlets at 6·3 and 6·36 τ. Rather broad triplets at 6·86, 6·77 and 6·77 τ, for the respective compounds, are assigned to the methine group adjacent to methylene. The signal due to the methylenic protons of $CH_3CH_2\overset{|}{C}H-$ has not been firmly identified in the spectra of any of the three compounds. It was expected to show, to a first approximation, as a quintet, since the coupling constants of both the methyl and methine protons with the methylenic protons are about the same (*ca.* 7 c./sec.). No such quintet is observable in the spectrum of any of the three compounds but, in each case, between the aromatic methyl signal at *ca.* 7·8 τ and the doublet at *ca.* 8·5 τ (CH_3 adjacent to CH) there are four peaks (J = *ca.* 7 c./sec.), which could well be the only visible part of the expected quintet. In support of this tentative assignment, the integrated areas between *ca.* 7·7 and *ca.* 8·7 τ equates to the required 17 potons for compound (X*a*) and 11 protons for compounds (X*b*) and (X*c*).

Dehydration of the alcohol (IX*a*) by heating with iodine yielded the stilbene (XII*a*) mixed with the isomeric hex-2-ene (X*a*). After several weeks, the stilbene crystallised from the viscous oil, and was readily isolated by crystallisation from light petroleum. Equilibration of the hex-2-enes (X*a*, *b* and *c*) by heating with iodine similarly yielded a mixture of stilbene and hex-2-ene, but in the case of the asymmetrically dimethylated compound (X*b*) no crystallisation of the stilbene (XII*b*) occurred. That the product was a mixture of the two isomers was demonstrated by the appearance of four distinct peaks of absorption at 6·21, 6·26, 6·28 and 6·33 τ (total intensity equivalent to 6 protons), all due to the protons of methoxyl, and the appearance of a singlet at 7·72 τ due to the aryl methyls of stilbene, in addition to the band at 7·85 τ previously found in the n.m.r. spectrum of the hex-2-ene (X*b*). The intensity of the doublet at 8·52 τ (CH_3 protons of CH_3–CH=) corresponded to only *ca.* 1·2 protons, whereas the two overlapping triplets centred at *ca.* 9·16 and *ca.* 9·24 τ (CH_3 protons of CH_3–CH_2–) corresponded to *ca.* 4·7 protons. The mobile liquid appeared, therefore, to be a mixture of stilbene (XII*b*) and hex-2-ene (X*b*) in the ratio *ca.* 2 : 1.

The crystalline stilbenes (XII*a* and *c*) produced much simpler spectra, showing no absorption in the 4·6, 6·8, and 8·5 τ regions (absence of CH_3–CH= and $CH_3-CH_2-\overset{|}{C}H-$ structures). The tetramethylated diethylstilbœstrol dimethylether (XII*a*) exhibited the expected singlets at 3·21 τ (aromatic protons, intensity 4), 6·26 τ (methoxyl protons, intensity 6) and 7·71 (aryl methyl protons), as well as a triplet at 9·23 τ (intensity 6) corresponding to the methyl protons of CH_3–CH_2–. The expected quartet due to methylene adjacent to methyl was partly obscured by the intense peak produced by aryl methyl. Only three of the expected four peaks (J = 7·5 c./sec.) were visible, but the integrated area under the curve between 7·58 and 8·13 τ accounted for the sixteen protons required by the stilbene structure. This masking of the methylene group absorption was also seen in the spectrum of the symmetrically dimethylated stilbene (XII*c*), where two of the peaks of the quartet appear as shoulders on either side of the aryl methyl absorption (singlet at 7·81 τ). Here again the integrated area under the curve between 7·67 and 8·17 τ accounted for the 4 methylenic and 6 aryl methyl protons required by the stilbene structure. The aliphatic methyls produced a triplet at 9·27 τ (intensity 6), and the methoxyl groups the expected singlet at 6·2 τ (intensity 6). Similar overlapping of the aryl methyl and methylenic signals was seen in the spectra of the tetramethylated and dimethylated stilbœstrols (I*a* and *c*).

Initial attempts to split the methoxyl groups to yield the related phenols were made on the hex-2-ene structures, using pyridine hydrochloride at 230° and HBr in acetic acid. Demethylation was achieved, in both instances, as indicated by a hydroxyl peak in the region of OH-stretching in the i.r. spectra, but unfortunately all attempts at purification of the products failed. The use of methyl magnesium iodide at 170° was more satisfactory, and yielded the required phenolic compounds from the hex-2-ene dimethyl ethers (X*a*, *b* and *c*) and the stilbene dimethyl ethers (XII*a* and *c*). Potassium hydroxide in triethylene glycol was also used successfully to obtain the tetramethylated diethylstilbœstrol (I*a*), but the yield and quality of the product was inferior to that obtained using methyl magnesium iodide.



IX—XII and I a; $R^1 = R^2 = R^3 = R^4 = Me$
b; $R^1 = R^2 = H, R^3 = R^4 = Me$
c; $R^1 = R^3 = Me, R^2 = R^4 = H$

Isolation of a pure sample of the phenolic unsymmetrically dimethylated hex-2-ene (XI*b*) was difficult. The material was not crystalline, and it was very sensitive to air oxidation. It was finally purified by chromatography on silica gel in the absence of oxygen. The symmetrically dimethylated (XI*c*) and the tetramethylated (XI*a*) phenolic hex-2-enes, on the other hand, are crystalline, and could be isolated by repeated crystallisation, though the tetramethylated compound (XI*a*) tended to separate as an oil, and recoveries were small. Better results were obtained by chromatography. Chromatography was essential for the preliminary purification of the tetramethylated diethylstilbœstrol (I*a*) following demethylation by means of potassium hydroxide in triethylene glycol, and was advantageous in the purification of the product of Grignard demethylation.

The electronic absorption spectra (see Table) are consistent with the structures assigned by n.m.r. (cf. absorption of diethylstilbœstrol and ψ-diethylstilbœstrol[11]). It will be seen that in each case conversion of the hex-2-ene to the corresponding stilbene produces a shift of the maximum to longer wavelength. Demethylation to produce the free phenols also produces a bathochromic shift except in the case of the asymmetrically dimethylated hex-2-enes (X*b*) and (XI*b*).

Series	*a*		*b*		*c*	
Compound No.	$\lambda_{max.}$ mμ	ε	$\lambda_{max.}$ mμ	ε	$\lambda_{max.}$ mμ	ε
(X)	No peak 220—250	—	230s	17,550	232	16,900
(XI)	235s	12,180	226s	16,575	235·5	13,200
(XII)	236s	13,330	—	—	239	16,950
(I)	242	14,420	—	—	242	14,080

The hex-2-ene compounds were assayed for œstrogenic activity using the Allen–Doisy vaginal smear test in ovariectomised mice. The test compound and standard (diethylstilbœstrol) were administered subcutaneously in arachis oil. The tetramethylated compound (XI*a*) was inactive at 1 mg. The asymmetrically dimethylated compound

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[11] J. Derkosch and G. Friedrich, *Sitzungsber. Akad. Wiss. Wien*, 1953, **162** (IIB), 1146.

(XI*b*) possessed 0·015 times, and the symmetrically dimethylated compound (XI*c*) 0·2 times, the activity of diethylstilbœstrol. Preliminary investigations of these compounds in tests for anti-œstrogenic activity in mice have indicated that the tetramethylated compound (XI*a*), at an intravaginal dose level of 25 μg, produces a highly significant inhibition of the vaginal response to simultaneously administered 17β-œstradiol. These biological tests, together with those on the stilbenes (I*a* and *c*), will be reported in detail elsewhere.

EXPERIMENTAL

Ultraviolet spectra were determined on a Hilger Uvispek spectrophotometer, model H700 and i.r. spectra on a Perkin-Elmer Infracord spectrophotometer, model 137.

4-*Methoxy*-3-*methylphenylacetic Acid.*—4-Methoxy-3-methylacetophenone (112 g.), sulphur (33 g.) and morpholine (89·6 g.) were stirred together and gently boiled under reflux for 16 hr., allowed to cool to *ca.* 70°, and poured into hot absolute ethanol (110 ml.) containing benzene (2 ml.). The isolated and dried morpholide (146 g.) was heated under reflux with 10% aqueous potassium hydroxide for 18 hr., the cooled solution acidified with hydrochloric acid, and the precipitated acid recrystallised from dilute ethanol, yielding 4-methoxy-3-methylphenylacetic acid (92 g.), m. p. 93·5—94·5° (Found: C, 66·7; H, 6·6. Calc. for $C_{10}H_{12}O_3$: C, 66·7, H, 6·7%).

4-*Methoxy*-3-*methylphenylacetyl chloride* was prepared from the acid (78 g.) using thionyl chloride (80 g.) in the usual way. Yield 72·3 g., b. p. 133—134°/4 mm.

Ethyl 4-*Methoxy*-3-*methylphenylacetate.*—The acid (131 g.) was esterified in the usual way using absolute ethanol (200 ml.) and concentrated sulphuric acid (15 ml.). Yield 121 g., b. p. 143—145°/9 mm. (Found: C, 68·75; H, 7·45. $C_{12}H_{16}O_3$ requires C, 69·25; H, 7·7%).

Diethyl 3,5-*Dimethyl*-4-*methoxyphenylmalonate.*—Sodium (11·7 g.) was added to dry ethanol (200 ml.). When the solution had cooled to about 60°, a mixture of ethyl 3,5-dimethyl-4-methoxyphenylacetate [12] (108 g.) and redistilled ethyl oxalate (74 g.) was added rapidly with stirring. The flask was maintained at 60° for 1 hr. The cooled mixture was acidified with dilute sulphuric acid, the oily layer separated, and the aqueous layer extracted with benzene. The oily layer and benzene extracts were combined and dried ($MgSO_4$). The benzene was distilled off, and the residual red oil decomposed by raising the temperature to 190° during 30 min. and holding that temperature for 1½ hr. Distillation of the residual red-brown oil yielded *diethyl* 3,5-*dimethyl*-4-*methoxyphenylmalonate* as a greenish-yellow, mobile liquid (100 g.), b. p. 144—150°/0·8 mm. (Found: C, 65·8; H, 7·6. $C_{16}H_{22}O_5$ requires C, 65·3; H, 7·5%).

Diethyl 4-*methoxy*-3-*methylphenylmalonate* was similarly synthesised from ethyl 4-methoxy-3-methylphenylacetate (121·6 g.), diethyl oxalate (85·4 g.), and sodium (13·5 g.). Yield 105·7 g., b. p. 147—148°/0·8 mm. (Found: C, 64·1; H, 7·3. $C_{15}H_{20}O_5$ requires C, 64·3; H, 7·15%).

Diethyl Ethyl(3,5-*dimethyl*-4-*methoxyphenyl*)*malonate.*—A solution of sodium ethoxide was formed from sodium (8·1 g.) and dry ethanol (97 ml.). Diethyl 3,5-dimethyl-4-methoxyphenylmalonate (100 g.) was added to this solution at 50—60°. When the solution had cooled to 35°, ethyl iodide (57·6 g.) was added as rapidly as possible with stirring, and the reaction mixture maintained at 35° for 6 hr. The ethanol was then removed by distillation, the residue diluted with water (110 ml.), and acidified with dilute acetic acid. The ester was taken into ether, and the ethereal solution was washed with 10% sodium thiosulphate and water, and dried ($MgSO_4$). Distillation yielded *diethyl ethyl*(3,5-*dimethyl*-4-*methoxyphenyl*)*malonate* as a light green, fluorescent, mobile liquid (94 g.), b. p. 144—147°/0·9 mm. (Found: C, 67·3; H, 8·0. $C_{18}H_{26}O_5$ requires C, 67·05; H, 8·15%).

Diethyl ethyl(4-*methoxy*-3-*methylphenyl*)*malonate* was similarly prepared from diethyl 4-methoxy-3-methylphenylmalonate (113 g.), ethyl iodide (98 g.) and sodium (14·4 g.). Yield 100 g., b. p. 147—148°/0·8 mm. (Found: C, 66·15; H, 7·95. $C_{17}H_{24}O_5$ requires C, 66·3; H, 7·8%).

α-(3,5-*Dimethyl*-4-*methoxyphenyl*)*butyric Acid.*—Diethyl ethyl(3,5-dimethyl-4-methoxyphenyl)malonate (94 g.) was hydrolysed by heating (4 hr.) with 10% ethanolic potassium hydroxide (750 ml.); the ethanol was distilled off, the residue poured into water (2 l.), and the solution acidified with hydrochloric acid. The precipitated acid was dried, dissolved in hot, dry acetone and the insoluble potassium chloride filtered off. The acetone was distilled off, and the residue heated under reduced pressure (100—120°/20 mm.) until effervescence was

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[12] F. Bennington, R. D. Morin, L. C. Clark, and R. P. Fox, *J. Org. Chem.*, 1958, **23**, 1979.

complete. The product (m. p. 91—93°) was recrystallised from light petroleum (b. p. 40—60°), yielding white needle-crystals of α-(3,5-*dimethyl*-4-*methoxyphenyl*)*butyric acid* (45 g.), m. p. 95—96° (Found: C, 70·2; H, 8·1. $C_{13}H_{18}O_3$ requires C, 70·2; H, 8·15%).

α-(4-*Methoxy*-3-*methylphenyl*)*butyric acid* was similarly obtained from diethyl ethyl-(4-methoxy-3-methylphenyl)malonate (120 g.). Yield 51·1 g., m. p. 82·5—83·5° (Found: C, 68·95; H, 7·55. $C_{12}H_{16}O_3$ requires C, 69·25; H, 7·7%).

α-(3,5-*Dimethyl*-4-*methoxyphenyl*)*butyryl Chloride*.—α-(3,5-Dimethyl-4-methoxyphenyl)-butyric acid (45 g.) and excess of thionyl chloride (70 g.) were heated under reflux for 3 hr. The excess of thionyl chloride was removed, and distillation of the residue yielded a greenish, mobile, faintly pungent liquid (40 g.), b. p. 150—156°/18 mm.

α-(4-*Methoxy*-3-*methylphenyl*)*butyryl chloride* was similarly prepared from α-(4-methoxy-3-methylphenyl)butyric acid (49·8 g.). Yield 48·8 g., b. p. 143—146°/8 mm.

3,5-*Dimethyl*-α-*ethyldeoxyanisoin*.—A mixture of 2,6-dimethylanisole (72 g.) and dry carbon disulphide (175 ml.) was cooled to below 5° in an ice–salt bath, and dry, powdered aluminium chloride (50 g.) was added slowly, with stirring, keeping the temperature below 5°. When all the aluminium chloride had been added, α-(4-methoxyphenyl)butyryl chloride (70 g.) was added slowly, with stirring, maintaining the temperature below 5°. When addition was complete the flask was allowed to warm to room temperature, and then heated on a water-bath for 2½ hr. The mixture was then poured into crushed ice containing a little concentrated hydrochloric acid. The upper yellow oil was separated, the aqueous layer extracted with ether, and the ethereal extracts combined with the oil. The combined organic layers were washed with 2N-sodium hydroxide and water, and dried ($MgSO_4$). Removal of the ether and excess 2,6-dimethylanisole left a viscous, red liquid, distillation of which yielded 3,5-*dimethyl*-α-*ethyldeoxyanisoin* (76 g.), as a viscous, orange liquid, b. p. 172—182°/0·04 mm. (Found: C, 76·7; H, 7·55. $C_{20}H_{24}O_3$ requires C, 76·9; H, 7·75%). Left for 10 days, the orange liquid solidified. Recrystallisation from 95% ethanol yielded white needles of 3,5-dimethyl-α-ethyldeoxyanisoin, m. p. 60—61° (Found: C, 76·9; H, 7·6%), $\nu_{max.}$ (Nujol) 1686vs cm.$^{-1}$ (aryl ketone).

3,3′-*Dimethyldeoxyanisoin* was prepared in a similar manner from 4-methoxy-3-methylphenylacetyl chloride (39·7 g.), 2-methylanisole (36·6 g.), and aluminium chloride (26·7 g.). In this case, however, the required ketone crystallised on evaporation of the ether, and was recrystallised from methanol as white needles (40 g.), m. p. 78—79·5° (Found: C, 75·8; H, 7·0. $C_{18}H_{20}O_3$ requires C, 76·05; H, 7·05%), $\nu_{max.}$ (Nujol) 1684vs cm.$^{-1}$ (aryl ketone).

3,3′,5,5′-*Tetramethyl*-α-*ethyldeoxyanisoin* was similarly prepared from 2,6-dimethylanisole (34 g.), dry aluminium chloride (23 g.) and α-(3,5-dimethyl-4-methoxyphenyl)butyryl chloride (40 g.). Distillation of the ethereal extract yielded 3,3′,5,5′-tetramethyl-α-ethyldeoxyanisoin (13 g.), b. p. 187—188°/0·001 mm., as a viscous yellow liquid, which solidified on leaving for 10 days (Found: C, 77·65; H, 8·5. $C_{22}H_{28}O_3$ requires C, 77·5; H, 8·3%). The i.r. spectrum of a fraction (b. p. 178—183°/0·001 mm.) showed a strong absorption band at 1770 cm.$^{-1}$ (possibly due to unreacted acid halide). The material was heated under reflux with 10 per cent. ethanolic potassium hydroxide, the mixture cooled, diluted with water, and the oil taken into ether. Evaporation of the ether left a viscous liquid, which solidified to a yellowish-white solid, m. p. 64—66°. Recrystallisation of the solidified ketone from 95% ethanol yielded white crystals of 3,3′,5,5′-*tetramethyl*-α-*ethyldeoxyanisoin* (41 g.), m. p. 69—70° (Found: C, 77·75; H, 8·0%), $\nu_{max.}$ (Nujol) 1686vs cm.$^{-1}$ (aryl ketone).

Increasing the period of heating on the water-bath to *ca.* 3 hr. reduced the contamination with acid chloride so that no hydrolytic process for its removal was required.

3,3′-*Dimethyl*-α-*ethyldeoxyanisoin* was prepared, as for 3,5-dimethyl-α-ethyldeoxyanisoin, from α-(4-methoxy-3-methylphenyl)butyryl chloride (34 g.), 2-methylanisole (28 g.) and aluminium chloride (20 g.). The *required ketone* was obtained as a viscous, golden-yellow oil (43 g.), b. p. 200—208°/0·005 mm. (Found: C, 76·95; H, 7·8. $C_{20}H_{24}O_3$ requires C, 76·9; H, 7·7%), $\nu_{max.}$ (liquid film) 1669vs cm.$^{-1}$ (aryl ketone).

3-(3,5-*Dimethyl*-4-*methoxyphenyl*)-4-(4-*methoxyphenyl*)*hexan*-3-*ol*.—3,5-Dimethyl-α-ethyldeoxyanisoin (9·4 g., m. p. 60—61°) was dissolved in dry ether (40 ml.) and the solution added dropwise to a Grignard reagent prepared from magnesium turnings (2·9 g.), ethyl iodide (18·7 g.) and dry ether (100 ml.). When addition was complete, the mixture was heated under reflux on a water-bath for 1 hr., and then left overnight. The mixture was decomposed by pouring into ice and dilute sulphuric acid, and the ethereal layer separated. The aqueous layer was extracted with ether, and the combined ethereal solutions washed with 10% sodium thiosulphate solution and water, and dried ($MgSO_4$). Removal of the ether yielded a yellow, slightly viscous liquid which solidified to an orange solid (11·1 g., m. p. 79—82°). Fractional crystallisation of 7 g. from 95% ethanol yielded the two racemates of 3-(3,5-*dimethyl*-4-*methoxyphenyl*)-4-(4-*methoxyphenyl*)*hexan*-3-*ol*: (*a*) the *erythro racemate* as clusters of white rhombic crystals, m. p. 134·5—136° (3·8 g.) (Found: C, 77·1; H, 8·7. $C_{22}H_{30}O_3$ requires C, 77·2; H, 8·8%), $\lambda_{max.}$ (ethanol) 225 (ε 24,300), 276 (ε 2,980), 285 mμ (ε 2,075), $\nu_{max.}$ (Nujol) 3571 cm.$^{-1}$ (OH); (*b*) the *threo racemate*, obtained by evaporation of the mother-liquors of crystallisation of the *erythro* isomer and recrystallisation of the resulting solid from 95% ethanol : water (3 : 1), as white tetragonal crystals, m. p. 83—84° (1·5 g.) (Found: C, 77·3; H, 8·8%), $\nu_{max.}$ (Nujol) 3509 cm.$^{-1}$(OH).

3,4-*Bis*-(3,5-*dimethyl*-4-*methoxyphenyl*)*hexan*-3-*ol*.—A Grignard reagent was prepared from magnesium turnings (2·9 g.) dry ether (100 ml.), and ethyl iodide (18·7 g.); 3,3′,5,5′-tetramethyl-α-ethyldeoxyanisoin (10 g.) dissolved in dry ether (50 ml.) was then added slowly. The mixture was worked up as described above. Fractional crystallisation, from 95% ethanol, of a small portion (1 g.) of the product yielded the two racemates of 3,5-*bis*-(3,5-*dimethyl*-4-*methoxyphenyl*)*hexan*-3-*ol*: (*a*) the *erythro racemate* (0·6 g.), as white cubic crystals, m. p. 149—150° (Found: C, 77·75; H, 9·20. $C_{24}H_{34}O_3$ requires C, 77·8; H, 9·25%) $\nu_{max.}$ (Nujol) 3546 cm.$^{-1}$ (OH); (*b*) the *threo racemate*, as white needle crystals, m. p. 95—96° (Found: C, 77·75; H, 9·1%), $\nu_{max.}$ (Nujol) 3521 cm.$^{-1}$ (OH).

3,4-*Bis*-(4-*methoxy*-3-*methylphenyl*)*hexan*-3-*ol* was similarly prepared from α-ethyl-3,3′-dimethyldeoxyanisoin (43 g.), magnesium turnings (13·4 g.), ethyl iodide (86 g.) and dry ether (500 ml.). Recrystallisation of the semi-solid product from 95% ethanol yielded crystalline 3,4-*bis*-(4-*Methoxy*-3-*methylphenyl*)*hexan*-3-*ol* (7·6 g.), m. p. 141—142·5° (Found: C, 77·7; H, 8·85. $C_{22}H_{30}O_3$ requires C, 77·2; H, 8·75%), $\lambda_{max.}$ (ethanol) 209 (ε 22,800), 230 (ε 23,400), 276—277 mμ (ε 4,140), $\nu_{max.}$ (Nujol) 3546 cm.$^{-1}$ (OH).

Evaporation of the mother liquors yielded the other isomer as a very viscous oil (34·5 g.) which could not be induced to crystallise (Found: C, 77·75; H, 8·7%) $\lambda_{max.}$ (ethanol) 209 (ε 25,200), 227 (ε 17,500), 276 mμ (ε 4,050), $\nu_{max.}$ (liquid film) broad peak 3509 cm.$^{-1}$ (OH).

3-(3,5-*Dimethyl*-4-*methoxyphenyl*)-4-(4-*methoxyphenyl*)*hex*-2-*ene*.—3-(3,5-Dimethyl-4-methoxyphenyl)hexan-3-ol (10 g. recrystallised, mixture of racemates) was dissolved in dry pyridine (120 ml.) and phosphorus trichloride (25·5 ml.) added at 0° with stirring. The mixture was stirred overnight at 20° and then added dropwise to ice and water (*ca.* 3 litres), when a yellow solid precipitated. After extracting with ether, the gelatinous, yellow solid and emulsion, which remained in the ethereal layer, was filtered off and washed with ether. The combined ethereal solutions were washed with dilute hydrochloric acid, water, sodium hydrogen carbonate solution, and water, and finally dried ($MgSO_4$). Removal of the ether and traces of pyridine yielded a mobile, yellow liquid (6·1 g.). Distillation yielded 3-(3,5-*dimethyl*-4-*methoxyphenyl*)-4-(4-*methoxyphenyl*)*hex*-2-*ene* (5·8 g.), as a greenish-yellow, slightly viscous liquid, b. p. 124—140°/0·0004 mm. (Found: C, 81·05; H, 8·90. $C_{22}H_{28}O_2$ requires C, 81·45; H, 8·70%), $\lambda_{max.}$ (ethanol) *ca.* 230 shoulder (ε 17,550), 277 (ε 2,475), 285 mμ (ε 1,800), $\nu_{max.}$ (liquid film) 1379w (symmetrical CH deformation of $C-CH_3$), 1370w (in plane deformation of hydrogen of $R^1R^2C = CHR^3$), 1252s (aralkyl ether), 885m (1,2,3,5-tetrasubstituted benzene), 833s cm.$^{-1}$ (1,4-substituted benzene).

Left for many weeks, the liquid slowly crystallised, but all attempts to recrystallise the sticky solid were unsuccessful.

3,4-*Bis*-(3,5-*dimethyl*-4-*methoxyphenyl*)*hex*-2-*ene*.—3,4-Bis-(3,5-dimethyl-4-methoxyphenyl)-hexan-3-ol (10 g., recrystallised, mixture of racemates) in dry pyridine (75 ml.) was treated with phosphorus trichloride (23·5 ml.) as described above. Distillation of the product yielded 3,4-*bis*(3,5-*dimethyl*-4-*methoxyphenyl*)*hex*-2-*ene* (6·05 g.) as a yellowish-green, slightly viscous liquid, b. p. 126—140°/0·001 mm. (Found: C, 81·5; H, 8·95. $C_{24}H_{32}O_2$ requires C, 81·8; H, 9·15%), $\lambda_{max.}$ (ethanol) *ca.* 278 mμ shoulder (ε 1,400). After leaving for some weeks, the liquid partially solidified, but could not be recrystallised from light petroleum (b. p. 60—80° or 40—60°), benzene–light petroleum, or ethanol–water. $\nu_{max.}$ (CCl_4 solution) 1398w (symmetrical CH deformation of $C-CH_3$), 1382w (in plane deformation of ethylenic hydrogen of $R^1R^2C=CHR^3$), 1230s (aralkyl ether) and 877m cm.$^{-1}$ (1,2,3,5-tetrasubstituted benzene).

3,4-*Bis*-(4-*methoxy*-3-*methylphenyl*)*hex*-2-*ene*.—3,4-Bis-(4-methoxy-3-methylphenyl)hexan-3-ol (7·8 g., non-crystalline) was treated with phosphorus trichloride (21 ml.) as described above. Distillation of the product yielded 3,4-*bis*-(4-*methoxy*-3-*methylphenyl*)*hex*-2-*ene* (4·2 g.), b. p. 147—154°/0·02 mm. (Found: C, 81·7; H, 8·95. $C_{22}H_{28}O_2$ requires C, 81·4; H, 8·7%),

$\lambda_{max.}$ (ethanol) 232 (ε 16,900), 276—278 (ε 4,630), *ca.* 284 mμ shoulder (ε 4,250), $\nu_{max.}$ (liquid film) 1376w (symmetrical CH deformation of $C{-}CH_3$) 1359w (in plane vibration of ethylenic hydrogen in $R^1R^2C{=}CHR^3$, 1248s (aralkyl ether) 890m, 813s cm.$^{-1}$ (1,2,4-trisubstituted benzene).

3-(3,5-*Dimethyl*-4-*hydroxyphenyl*)-4-(4-*hydroxyphenyl*)*hex*-2-*ene*.—3-(3,5-Dimethyl-4-methoxyphenyl)-4-(4-methoxyphenyl)-hex-2-ene (3·0 g.) dissolved in dry ether was added to a Grignard reagent prepared from methyl iodide (16·5 g.), magnesium (2·81 g.) and dry ether (80 ml.). The ether was removed by distillation and the residue heated at 160—170° for 4 hr., with the apparatus assembled for distillation to ensure complete removal of combined ether. After cooling, the glass-like solid was decomposed with wet ether, with cooling, and the mixture acidified with dilute hydrochloric acid. The ethereal layer was separated, and the aqueous layer further extracted with ether. The combined ethereal layers were washed with water, sodium hydrogen carbonate solution, water, 10% sodium thiosulphate solution, and water. Extraction of the ethereal solution with 2N-sodium hydroxide and acidification of the cooled alkaline layer precipitated an oil, which was taken into ether and washed with water, and dried ($MgSO_4$). Removal of the ether left a clear, orange, liquid which formed a glass (2·7 g.). Purification of the glass-like product by adsorption chromatography on silica gel using sodium-dried, redistilled benzene, with exclusion of oxygen, yielded 3-(3,5-*dimethyl*-4-*hydroxyphenyl*)-4-(4-*hydroxyphenyl*)*hex*-2-*ene* as a pale yellow glass (Found: C, 81·05; H, 8·2. $C_{20}H_{24}O_2$ requires C, 81·0; H, 8·2%), $\lambda_{max.}$ (ethanol) *ca.* 226 shoulder (ε 16·575), 275 (ε 3,510), 280 mμ (ε 3,235), $\nu_{max.}$ (CCl_4 solution) 3571m (OH stretching), 1380w (symmetrical CH deformation of $C{-}CH_3$), 1365w (in plane deformation of ethylenic hydrogen of $R^1R^2C{=}CHR^3$), 1195vs and 1170vs (phenolic OH deformations), 872m (1,2,3,5-tetrasubstituted benzene), 835s cm.$^{-1}$ (1,4-disubstituted benzene). N.m.r. spectrum: (i), a broad hump (intensity 2) stretching from 4·29 to 4·79 τ with 2 peaks superimposed at 4·46 and 4·58 τ (ethylenic proton of $CH_3CH{=}$ and phenolic proton of non-methylated ring); (ii), a broad singlet (intensity 1) at 5·42 τ (phenolic proton of methylated ring); (iii), a broad, partially resolved, triplet (intensity 1) at 6·76 τ (CH proton of $-CH_2\overset{|}{C}H{-}\overset{|}{C}{=}$); (iv), a series of peaks (total intensity 11) extending from 7·73 to 8·65 τ with one sharp singlet at 7·89 τ (6 aryl methyl protons) and a doublet at 8·54 τ (methyl protons of $CH_3CH{=}$), the remainder being probably a partially obscured quintet due to the methylenic protons of $CH_3CH_2\overset{|}{C}H-$; (v), a triplet (intensity 3) at 9·17 τ (methyl protons of CH_3CH_2-).

3,4-*Bis*-(3,5-*dimethyl*-4-*hydroxyphenyl*)*hex*-2-*ene*.—3,5-Bis-(3,5-dimethyl-4-methoxyphenyl)-hex-2-ene (3·0 g.) was demethylated using methyl magnesium iodide as described above. The ethereal extracts of the reaction product were extracted with 2N-sodium hydroxide solution. The ethereal layer was washed with water and dried ($MgSO_4$). Removal of the ether left an orange solid (1·95 g.). Acidification and extraction of the alkaline layer yielded a further 0·5 g. of the same material (identity shown by i.r. analysis). Recrystallisation from ethanol–water (1 : 1) on a small scale yielded crystals of 3,4-*bis*-(3,5-*dimethyl*-4-*hydroxyphenyl*)*hex*-2-*ene*, m. p. 120—121·5° (Found: C, 80·85; H, 8·7. $C_{22}H_{28}O_2$ requires C, 81·4; H, 8·7%), $\lambda_{max.}$ (ethanol) *ca.* 235 shoulder (ε 12,180), 276 mμ (ε 3,515), $\nu_{max.}$ (CCl_4 solution) 3571m (OH stretching), 1315m and 1195vs (OH deformation and C–O stretching of phenol), 1380w (symmetrical CH deformation of $C{-}CH_3$), 1365w (in plane deformation of hydrogen of $R^1R^2C{=}CHR^3$), 880s cm.$^{-1}$ (1,2,3,4-tetrasubstituted benzene). The bulk of the material was purified by adsorption chromatography on silica gel using dry, redistilled benzene. N.m.r. spectrum: (i), a partially resolved quartet (intensity 1) at 4·46 τ (ethylenic proton of $CH_3CH{=}$); (ii), a broad singlet (intensity 2) at 5·46 τ (2 phenolic protons); (iii), a broad multiplet (basically a triplet, intensity 1) at 6·73 τ (CH proton of $-CH_2{-}\overset{|}{C}H{-}\overset{|}{C}{=}$); (iv), a series of peaks (total intensity 14) extending from 7·58 to 8·36 τ, with two sharp singlets at 7·77 and 7·80 τ (aryl methyl protons), the remaining peaks being probably due to the methylenic protons of $CH_3CH_2\overset{|}{C}H-$); (v), a doublet (intensity 3) at 8·47 τ (methyl protons $CH_3CH{=}$); (vi), a triplet (intensity *ca.* 3) at 9·12 τ (methyl protons of CH_3CH_2-).

3,4-*Bis*-(4-*hydroxy*-3-*methylphenyl*)*hex*-2-*ene*.—3,4-Bis-(4-methoxy-3-methylphenyl)hex-2-ene (2·8 g.) was demethylated by heating with methyl magnesium iodide [prepared from magnesium (2·4 g.), and methyl iodide (14·2 g.)] as described above. Evaporation of the ethereal solution of the alkali-soluble product yielded a viscous material (1·59 g.) which crystallised from carbon tetrachloride. Repeated crystallisation from 30% aqueous ethanol, or benzene–light petroleum

(60—80°), yielded 3,4-*bis*(4-*hydroxy*-3-*methylphenyl*)*hex*-2-*ene* (0·8 g.), m. p. 135—137° (Found: C, 80·8; H, 8·05. $C_{20}H_{24}O_2$ requires C, 81·0; H, 8·2%), $\lambda_{max.}$ (ethanol) 212·5 (ε 22,060), 235·5 (ε 13·200), *ca.* 277 mμ shoulder (ε 5,590), $\nu_{max.}$ (CCl_4 solution) 3640s (OH stretching), 1376m (symmetrical CH deformation of $C-CH_3$), 1320s, 1185s cm.$^{-1}$ (OH deformation and C–O stretching of phenol).

α,α′-*Diethyl*-4,4′-*dimethoxy*-3,3′,5,5′-*tetramethylstilbene*.—3,4-Bis(3,5-dimethyl-4-methoxyphenyl)hex-2-ene (1 g.) and iodine 30 mg.) were heated together on a water-bath for 4 hr. The mixture was dissolved in ether, the iodine removed by extraction with sodium thiosulphate solution, and the ethereal solution dried. Evaporation of the ether left a sticky solid which, on recrystallisation from light petroleum (b. p. 60—80°), yielded white crystals of α,α′-*diethyl*-4,4′-*dimethoxy*-3,3′,5,5′-*tetramethylstilbene* (105 mg.), m. p. 105—105·5° (Found: C, 81·65; H, 9·05. $C_{24}H_{32}O_2$ requires C, 81·8; H, 9·15%), $\lambda_{max.}$ (ethanol) 215—216 (ε 25,830), *ca.* 236 mμ shoulder (ε 13,330), $\nu_{max.}$ (CCl_4 solution) 1372m (symmetrical CH deformation of $C-CH_3$), 1230vs (aralkyl ether), 875s cm.$^{-1}$ (1,2,3,5-tetrasubstituted benzene).

Identical material (2·14 g.) was obtained when 3,4-bis-(3,5-dimethyl-4-methoxyphenyl)-hexan-3-ol (10 g.) was heated with iodine (0·1 g.), at 130—150° for 1½ hr. Retreatment of the material obtained from the mother-liquors of recrystallisation, yielded a further 1·3 g. of the required product.

α,α′-*Diethyl*-4,4′-*dimethoxy*-3,3′-*dimethylstilbene*.—3,4-Bis(4-methoxy-3-methylphenyl)hex-2-ene (5 g.), on heating with iodine (0·1 g.) as described above, yielded the *required stilbene* (1·35 g.), m. p. 112—114° (Found: C, 81·45; H, 8·6. $C_{22}H_{28}O_2$ requires C, 81·4; H, 8·7%), $\lambda_{max.}$ (ethanol): 210 (ε 30,400), 239 (ε 16,950), *ca.* 275 mμ shoulder (ε 6,570), $\nu_{max.}$ (CCl_4 solution) 1373m (symmetrical deformation of $C-CH_3$), 1236 (aralkyl ether), 887m cm.$^{-1}$ (1,2,3,5 aryl substitution).

Iodine Equilibration of 3-(3,5-*Dimethyl*-4-*methoxyphenyl*)-4-(4-*methoxyphenyl*)*hex*-2-*ene*.—3-(3,5-Dimethyl-4-methoxyphenyl)-4-(4-methoxyphenyl)hex-2-ene (1 g.), when heated with iodine (50 mg.) as described above, yielded a mobile liquid (0·7 g.) b. p. 153—180° (bath temperature)/6 × 10^{-4} mm. (Found: C, 80·8; H, 8·45. $C_{22}H_{28}O_2$ requires C, 81·45; H, 8·7%). $\lambda_{max.}$ (ethanol) *ca.* 232 shoulder (ε 14,420), *ca.* 278 mμ shoulder (ε 3,660).

α,α′-*Diethyl*-4,4′-*dihydroxy*-3,3′,5,5′-*tetramethylstilbene*.—(*a*) α,α′-Diethyl-4,4′-dimethoxy-3,3′,5,5′-tetramethylstilbene (1·32 g.) was demethylated using methyl magnesium iodide [prepared from magnesium (1·4 g.) and methyl iodide (8·5 g.)] as described for the hex-2-ene isomer. The reaction mixture was decomposed, and the products extracted into ether, in the usual way. Evaporation of the ether yielded a pink solid (1·18 g.). Chromatography of the residue (0·5 g.) on a silica gel column (165 × 18 mm.) using benzene as solvent yielded, following some yellow viscous oil (0·02 g.), three crystalline fractions: A (0·36 g.), m. p. 163—166°; B (0·05 g.), m. p. 153·5—157°; C (0·01 g.). Recrystallisation of fraction A from light petroleum (b. p. 60—80°) yielded the *required phenolic stilbene* (270 mg.), m. p. 165—166° (Found: C, 81·25; H, 8·55. $C_{22}H_{28}O_2$ requires C, 81·4; H, 8·7%), $\lambda_{max.}$ (ethanol) 215 (ε 29,840), 242 (ε 14,420), *ca.* 280 mμ shoulder (ε 5160), $\nu_{max.}$ (KCl disc) 3480s (OH), 1330s, 1220vs, 1170vs. (OH deformation and C–O stretching of phenol), 875s cm.$^{-1}$ (1,2,3,5-tetrasubstiuted benzene). N.m.r. spectrum: (i), singlet (intensity *ca.* 4) at 3·27 τ (aromatic protons); (ii), singlet (intensity *ca.* 2) at 4·36 τ (phenolic protons); (iii), singlet at 7·77 τ (protons of aryl methyl), peaks at 7·84, 7·93 and 8·1 τ possibly part of a quartet due to the methylenic protons of CH_3CH_2- (total intensity of region 7·6—8·17 τ is *ca.* 16); (iv), triplet (intensity 6) at 9·26 τ (methyl protons of CH_3CH_2-). Recrystallisation of fractions B and C yielded a further 48 mg. of the required phenol, m. p. 163—165·5°, not depressed on admixture with recrystallised fraction A.

(*b*) α,α′-Diethyl-4,4′-dimethoxy-3,3′,5,5′-tetramethylstilbene (1 g.), potassium hydroxide (2 g.) and triethylene glycol (8 ml.) were stirred together and heated at 200—220° for 2½ hr. The cooled mixture was diluted with water, acidified with hydrochloric acid, and extracted with ether. The ethereal solution was washed with water and sodium hydrogen carbonate solution, and dried ($MgSO_4$). Distillation of the ether yielded a viscous residue (0·97 g.). Chromatography of a portion (0·8 g.) on silica gel using benzene as solvent yielded a viscous oil (0·41 g.), followed by crystalline material (0·25 g.) (a further 50 mg. of orange solid was obtained from later fractions). Recrystallisation of the crystalline material from light petroleum (b. p. 60—80°) yielded the required *phenolic stilbene* (127 mg.), m. p. 160—163°, not depressed on admixture with the authenticated material (Found: C, 81·75; H, 8·55%). The i.r. spectrum was identical with that of the product obtained using methyl magnesium iodide.

α,α′-Diethyl-4,4′-dihydroxy-3,3′-dimethylstilbene.—α,α′-Diethyl-4,4′-dimethoxy-3,3′-dimethylstilbene (1·5 g.) was demethylated using methyl magnesium iodide [prepared from magnesium (1·14 g.) and methyl iodide (6·7 g.)] as described above. The alkali-soluble product (1·26 g.) was a viscous oil which partly solidified on standing. Trituration with carbon tetrachloride (25 ml.) yielded needle crystals (1·03 g.). Repeated crystallisation from carbon tetrachloride and finally from benzene yielded the required *stilbene* (0·3 g.), m. p. 142—143° (Found: C, 80·5; H, 7·9. $C_{20}H_{24}O_2$ requires C, 81·0; H, 8·1%), $\lambda_{max.}$ (ethanol) 214 (ε 20,640), 242 (ε 14,080), *ca.* 277 mμ shoulder (ε 5,300). N.m.r. spectrum: (i), singlet (intensity *ca.* 2) at 5·22 τ (phenolic H); (ii), singlet at 7·73 τ (protons or aryl methyl); peaks at 7·81, 7·92 and 8·05 τ possibly part of a quartet due to methylenic protons of CH_3CH_2– (total intensity of region 7·6—8·1 τ is 10); (iii), triplet (intensity 6) at 9·24 τ (methyl protons of CH_3CH_2–).

We thank Parke Davis and Company Ltd. for their generous financial support to S. R. O'D. during the course of this work. N.m.r. spectra were recorded on a Varian A60 spectrometer by kind permission of Professor Lythgoe of the Department of Organic Chemistry. We are grateful to Dr. P. R. Brook for discussions on the interpretation of the n.m.r. spectra. N.m.r. spectra recordings were carried out by Mr. A. R. Bennet and Mrs. M. S. Pearce, and microanalyses by Mr. J. A. Stewart and Mr. F. R. Daubney, of the University Microanalytical Laboratory.

DEPARTMENT OF PHARMACOLOGY, THE SCHOOL OF MEDICINE,
UNIVERSITY OF LEEDS, LEEDS 2.
[Present address: (S. R. O.'D.) DEPARTMENT OF PHYSIOLOGY, UNIVERSITY OF QUEENSLAND,
BRISBANE, AUSTRALIA.]
[*Received, May 25th,* 1965.]