94. *The Synthesis of Compounds related to the Sterols, Bile Acids, and Œstrus-producing Hormones. Part V. The Synthesis of Conjugated Arylhexadienes, and their Behaviour in the Diels–Alder Reaction.*

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THE " diene-synthesis " introduced by Diels and Alder (*Annalen*, 1928, **460**, 98) has been extended to compounds related to *ζ-phenyl-*$\Delta^{\alpha\gamma}$*-hexadiene* (III; R = X = H) with the object of studying the cyclisation of the adducts such as 3-β-phenylethyl-1 : 2 : 3 : 6-tetrahydrophthalic anhydride (IV; R = X = H), which would be expected to lead to derivatives of *as*-octahydrophenanthrene (V) as in the analogous cyclisation of 1-β-phenylethyl-Δ^{1}-*cyclo*hexene (Cook and Hewett, J., 1933, 1099).

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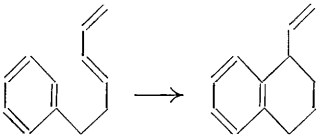
* The initial pure blue colorations produced on the addition of a large volume of 10% aqueous sodium hydroxide to dilute alcoholic solutions of (*a*), (*b*), and (*c*) were identical, but (*b*) underwent oxidation more rapidly than (*a*) and (*c*), which were identical in behaviour. This is shown by a colour change to green and ultimately brownish-yellow. This " oxidation test " is remarkably sensitive towards the presence of catalysts, and the specimen (*b*) doubtless contains a trace of a foreign substance which accelerates the reaction. Delphinidin is one of the compounds which are known to produce such an effect.

By such reactions, and employing the different addenda which are known to undergo the Diels–Alder reaction, it was sought to obtain suitable derivatives of (V) which would serve as intermediates in the synthesis of compounds structurally related to œstrone. For this hormone, the constitution (VI) has now been completely established by synthetical reactions (Cohen, Cook, Hewett, and Girard, J., **1934**, 653; Cohen, Cook, and Hewett, this vol., p. 445). Moreover, compounds of type (V; X = OMe) would probably have marked œstrogenic activity, for this structure is closely related to those almost certainly possessed by certain lactonic and acidic degradation products of œstriol monomethyl ether, obtained by MacCorquodale, Levin, Thayer, and Doisy (*J. Biol. Chem.*, 1933, **101**, 753) by oxidative fission of the five-membered ring, and stated by them to have several times the œstrogenic activity of œstrone.

A number of dienes of type (III) were prepared, but the reactions of these compounds with maleic anhydride did not proceed normally. Only from ζ-phenyl-$\Delta^{\alpha\gamma}$-hexadiene itself was a crystalline *adduct* (IV; R = X = H) obtained in 20% yield.

The arylhexadienes (III; X = H, R = Me; X = OMe, R = Me; X = OMe, R = H), which failed to react normally, yielded resinous products in addition to varying amounts of unchanged maleic anhydride. These products contained amorphous alkali-soluble fractions, the physical properties of which were consistent with polymeric addition products. Such results have already been recorded for certain alkyl butadienes by Farmer and Warren (J., **1931**, 3223), who have drawn attention to the polymerising influence of maleic anhydride on conjugated dienes. Further it is probable that the reagent also induces non-additive polymerisation of the diene through an intermediate derivative of vinyltetralin, for it is known that such cyclisation can be effected by reagents which normally induce polymerisation of olefins.

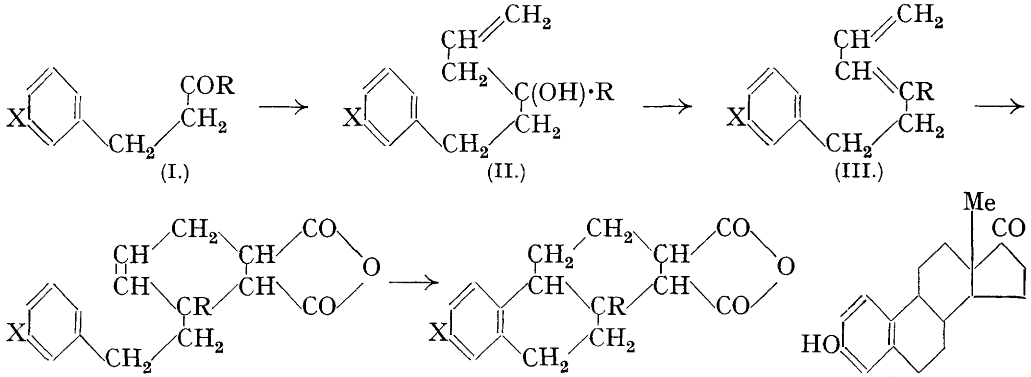


The phenylethyltetrahydrophthalic anhydride (IV; R = X = H) was unexpectedly resistant to the action of cyclising reagents, and under none of the conditions described in the experimental section was there any evidence of the formation of the octahydrophenanthrene derivative (V; R = X = H). In an experiment in which the anhydride was not directly recovered unchanged, it was heated with sulphuric acid in acetic acid at 100° and was converted into a resinous substance. The latter yielded, however, on dehydrogenation with selenium, 3-β-*phenylethylphthalic anhydride* as the only crystalline product, and not the desired anhydride of phenanthrene-1 : 2-dicarboxylic acid. Cyclisation was in no way facilitated by opening the anhydride ring. The *methyl hydrogen* ester corresponding to the anhydride (IV; R = X = H) was submitted to the action of sulphuric acid, to which reference was recently made by Darzens (*Compt. rend.*, 1934, **199**, 1426) for the cyclisation of somewhat analogous arylated unsaturated acids to hydronaphthalene derivatives. The product, in the present instance, again gave 3-β-phenylethylphthalic anhydride on hydrolysis of surviving ester groups, followed by dehydrogenation. Finally the *dimethyl* ester was shown to be unchanged after prolonged treatment with aluminium chloride, by its conversion at the end of the experiment into the original anhydride.

No explanation can be offered for the persistent failure of these cyclisation attempts, although it may be noted here that 1-phenylacetyl-Δ^1-*cyclo*hexene shows a similar resistance to cyclisation (Cook and Hewett, *loc. cit.*).

The hypothesis that a *p*-methoxyl group would facilitate cyclisation and overcome this resistance could not be tested, as the desired 3-β-3′-methoxyphenylethyl-1 : 2 : 3 : 6-tetrahydrophthalic anhydride (IV; R = H, X = OMe) could not be prepared. The failure to obtain this adduct from maleic anhydride and ζ-m-*methoxyphenyl*-$\Delta^{\alpha\gamma}$-*hexadiene* (III; R = H, X = OMe) is consistent with the view enunciated above regarding the polymerising influence of maleic anhydride on the diene, for the cyclisation to a tetralin derivative would be enhanced by the powerful para-activating effect of the methoxyl group.

The first method used for the synthesis of phenylhexadienes (III) consisted in dehydration of the *carbinols* (II; R = H or Me, X = H or OMe) resulting from the action of allyl bromide and magnesium on β-phenylpropaldehyde (I; R = X = H), benzylacetone (I; R = Me, X = H), and m-*methoxybenzylacetone* (I; R = Me, X = OMe). The latter ketone was readily obtained by reduction of *m*-methoxybenzylideneacetone.

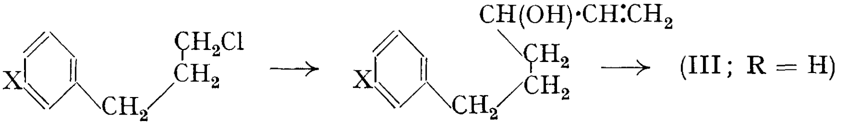

(I.) (II.) (III.) (IV.) (V.) (VI.)

Although carbinols of type (II) could conceivably be dehydrated either to a conjugated, $\Delta^{\alpha\gamma}$-, or to a non-conjugated hexadiene, it was anticipated, in view of the well-known tendency of ethylenic linkings to become conjugated (see, for example, Prévost, Donzelot, and Balla, *Compt. rend.*, 1934, **198**, 1041), that the main product would be the desired conjugated diene.

Dehydration of the carbinols (II) was not readily accomplished. Much of *ζ-phenyl-Δ^{α}-hexen-δ-ol* (II; R = X = H) was recovered unchanged after heating with potassium hydrogen sulphate, the remainder being converted into polymeric material. With the tertiary carbinols (II; R = Me, X = H or OMe) dehydration occurred more readily, but the yields of diene were unsatisfactory on account of its extensive polymerisation to non-volatile substances. The dienes obtained were treated with maleic anhydride (see p. 433), but no crystalline additive compounds resulted.

On account of the poor yields of diene and the uncertainty as to their homogeneity, another route to these compounds was investigated. γ-Phenylpropyl alcohol, readily obtained from benzylmagnesium chloride and ethylene oxide, was converted into its chloride (VII; X = H) by the action of thionyl chloride in the presence of pyridine or dimethylaniline.

γ-Phenylpropylmagnesium chloride was condensed with acraldehyde to give *ζ-phenyl-Δ^{α}-hexen-γ-ol* (VIII; X = H), which was dehydrated by dropping it on potassium hydrogen sulphate at 150—160° at such a reduced pressure that the diene was removed from the reaction flask as it was formed.


(VII.) (VIII.)

Apart from the very unlikely alternative production of an allene derivative (compare Klages and Klenk, *Ber.*, 1906, **39**, 2552; Reif, *ibid.*, 1908, **41**, 2740), such a reaction could yield only the desired conjugated diene. The product consisted essentially of (III; R = X = H), but contained a small proportion of unchanged carbinol which could not be removed by fractional distillation.

ζ-m-*Methoxyphenyl-$\Delta^{\alpha\gamma}$-hexadiene* (III; R = H, X = OMe) was likewise obtained by dehydration of the *carbinol* (VIII; R = H, X = OMe) resulting from the condensation of the magnesium derivative of γ-m-*methoxyphenylpropyl chloride* (VII; X = OMe) with acraldehyde. The required γ-m-*methoxyphenylpropyl alcohol* was readily obtained by Bouveault reduction of methyl *m*-methoxycinnamate or, more satisfactorily, *methyl* or *ethyl* β-m-*methoxyphenylpropionate*. Analysis showed that the diene (III; R = H, X = OMe) was contaminated with an appreciable amount of unchanged carbinol, which was ultimately removed by treatment with phenyl *iso*cyanate, followed by fractional distillation in a vacuum. The purified diene not only failed to give a crystalline adduct with maleic anhydride, but was recovered, apparently unchanged, after heating at 100° for 6 hours with acraldehyde, another reactant which is known normally to undergo the Diels–Alder reaction.

Crystalline 3 : 5-dinitrobenzoates were prepared to characterise the new carbinols described in this paper.

EXPERIMENTAL.

β-*Phenylpropaldehyde*.—Under the following conditions the aldehyde was obtained in 67% yield as its bisulphite compound. On a larger scale the yield was not so satisfactory. Ethyl orthoformate (21 g.) was gradually added to a well-cooled Grignard solution prepared from β-phenylethyl chloride (24·1 g.), anhydrous ether (100 c.c.), and magnesium turnings (4·17 g.) activated with iodine. After refluxing for several hours the reaction mixture was decomposed with ice and ammonium chloride, and the ethereal solution separated. The acetal remaining after evaporation of the ether, a yellow oil (31 g.), was hydrolysed by boiling for 1 hour with 5*N*-hydrochloric acid (100 c.c.). The resulting oil was extracted with ether and shaken with an excess of cold saturated sodium hydrogen sulphite solution. The bisulphite compound, colourless leaflets, was collected (17·2 g.), and the ethereal mother-liquor evaporated and again boiled with acid (40 c.c.). The product gave a further quantity (5·4 g.) of bisulphite compound. This was distilled in steam with an excess of sodium carbonate, giving the free aldehyde, b. p. 98—100°/13 mm. The semicarbazone had m. p. 127° as given by Michael and Garner (*Amer. Chem. J.*, 1906, **35**, 266). By the dry distillation of a mixture of calcium β-phenylpropionate (60 g.) and formate (120 g.), only 9 g. of pure aldehyde were obtained.

ζ-*Phenyl*-Δ^{α}-*hexen*-δ-*ol* (II; X = R = H).—A solution of allyl bromide (17·6 g.) and β-phenylpropaldehyde (15 g.) in anhydrous ether (40 c.c.) was added with shaking during 50 minutes to magnesium turnings (3·54 g.) covered with ether. A fairly vigorous reaction was promoted by addition of a trace of iodine and a drop of methyl iodide. The mixture was gently refluxed for 2 hours and kept for a further 2 hours. The product was shaken with ice and dilute hydrochloric acid and the ethereal extract was washed with sodium carbonate and dried. After removal of the ether the residue was distilled, giving a product (14·1 g.), b. p. 135—140°/13 mm. This carbinol was converted into its 3 : 5-*dinitrobenzoate*, which crystallised from ethyl alcohol in colourless prismatic needles, m. p. 82—83°, by heating with a slight excess of 3 : 5-dinitrobenzoyl chloride in pyridine solution at 100° for 15 minutes (Found : C, 61·8; H, 5·4. $C_{19}H_{18}O_6N_2$ requires C, 61·6; H, 5·1%). Pure ζ-*phenyl*-Δ^{α}-*hexen*-δ-*ol*, a colourless viscous oil, b. p. 130°/11 mm., was obtained by hydrolysis of the dinitrobenzoate with sodium hydroxide in aqueous alcohol (Found : C, 81·6; H, 9·25. $C_{12}H_{16}O$ requires C, 81·8; H, 9·1%). Bromine absorption (pyridine sulphate dibromide reagent; Rosenmund and Kuhnhenn, *Z. Unters. Nahr. Genussm.*, 1923, **46**, 154) corresponded to one double bond.

Dehydration. After the carbinol (8 g.) had been heated with potassium hydrogen sulphate (12 g.) for 1 hour at 160—170°, the product was extracted and distilled, giving only unchanged carbinol (5·2 g.), as indicated by boiling point and bromine absorption, and leaving a viscous resinous residue of polymeric material.

ζ-*Phenyl*-δ-*methyl*-Δ^{α}-*hexen*-δ-*ol* (II; X = H, R = Me).—A solution of allyl bromide (16·2 g.) and benzylacetone (15 g.), prepared by reduction of benzylideneacetone with sodium amalgam (Harries and Eschenbach, *Ber.*, 1896, **29**, 383), was added during 3/4 hour to magnesium turnings (3·3 g.). The Grignard reaction was carried out as described for the previous carbinol and yielded 15·2 g. of product, b. p. 133·5—135°/10 mm. The 3 : 5-*dinitrobenzoate* crystallised from methyl alcohol in rhombic tablets, m. p. 80—81° (Found : C, 62·3; H, 5·85. $C_{20}H_{20}O_6N_2$ requires C, 62·5; H, 5·3%). The ester was hydrolysed to regenerate the pure *carbinol*, a colourless viscous oil, b. p. 135°/13 mm. (Found : C, 82·2; H, 9·7. $C_{13}H_{18}O$ requires C, 82·0; H, 9·54%). Bromine absorption indicated one double bond in the molecule.

Dehydration. The best yield of diene was obtained by heating the carbinol (9 g.) with freshly fused and finely powdered potassium hydrogen sulphate for 45 minutes at 140—150°. In this way were obtained a diene fraction (4·5 g.), b. p. 115—119°/12 mm., and unchanged carbinol

(2·8 g.), leaving a resinous residue. The first fraction was fractionated over sodium, giving almost pure *ζ-phenyl-δ-methyl-$\Delta^{\alpha\gamma}$-hexadiene* (III; X = H, R = Me), a colourless mobile liquid (3·45 g.), b. p. 116°/12 mm., $n_D^{13\cdot3°}$ 1·5321, $d_{4°}^{13\cdot3°}$ 0·9152, whence $[R_L]_D$ = 58·28 (calc., 57·86) (Found : C, 90·0; H, 9·6. $C_{13}H_{16}$ requires C, 90·7; H, 9·3%).

The diene (3·3 g.) was kept at room temperature for some hours with maleic anhydride (1 mol.) dissolved in it, being occasionally warmed to redissolve the anhydride which crystallised. There was no sign of reaction, and the yellow solution was heated at 100° for 16 hours. At no time was any heat developed, as is normally observed in this reaction according to other workers. The resulting viscous resin was freed from oil with ether, leaving an amorphous white powder (1·9 g.) insoluble in all solvents except pyridine, and slowly dissolving to some extent when heated with aqueous sodium hydroxide. It could not be obtained crystalline by precipitation from pyridine solution, from which it separated as a voluminous flocculent solid which was not further investigated.

m-*Methoxybenzylacetone*.—This ketone was obtained in good yield by the reduction of *m*-methoxybenzylideneacetone (Bauer and Vogel, *J. pr. Chem.*, 1913, **88**, 332) with sodium amalgam in weakly acid solution under the same conditions as those used for the preparation of benzylacetone (Harries and Eschenbach, *loc. cit.*). After purification through its bisulphite compound, it had b. p. 151—152°/10 mm. (Found : C, 73·9; H, 8·0. $C_{11}H_{14}O_2$ requires C, 74·1; H, 7·93%). It gave a *semicarbazone*, crystallising from alcohol in colourless plates, m. p. 127—128° (Found : C, 61·3; H, 8·0. $C_{12}H_{17}O_2N_3$ requires C, 61·2; H, 7·3%).

*ζ-*3*-Methoxyphenyl-δ-methyl-Δ^{α}-hexen-δ-ol* (II; X = OMe, R = Me).—The Grignard reaction was carried out as described above, with allyl bromide (17·6 g.), magnesium (4·0 g.), *m*-methoxybenzylacetone (22·25 g.), and anhydrous ether (50 c.c.). The product (19·0 g.), b. p. 165—170°/12 mm., was converted into its 3 : 5-*dinitrobenzoate*, which crystallised from glacial acetic acid in microscopic needles, m. p. 111—112·5° (Found : C, 60·6; H, 5·9. $C_{21}H_{22}O_7N_2$ requires C, 60·8; H, 5·4%). The latter was hydrolysed to the pure *carbinol*, b. p. 166°/11 mm. (Found : C, 76·1; H, 9·5. $C_{14}H_{20}O_2$ requires C, 76·3; H, 9·16%).

Dehydration. The carbinol (10 g.) was heated for periods varying from 35 to 60 minutes at 150° with potassium hydrogen sulphate (20 g.). The product, worked up in the usual way, gave on distillation about 6 g. of mobile colourless liquid, b. p. 145—150°/12 mm., and some unchanged carbinol. The first fraction was redistilled over sodium, but satisfactory analytical figures were not obtained with any fraction. This product gave, with maleic anhydride, similar results to those described in the case of (III; X = H, R = Me).

*γ-Phenyl-*n*-propyl Alcohol*.—A Grignard solution prepared from benzyl chloride (72·25 g.), magnesium (13·85 g.), and anhydrous ether (320 c.c.) was chilled and slowly treated with an ice-cold solution of ethylene oxide (25 g.) in ether (30 c.c.). After standing over-night, the reaction mixture was freed from ether, heated in a boiling water-bath for 1 hour, and decomposed with ice and ammonium chloride. After extraction with ether the product was isolated in the usual way. Yield 45 g., b. p. 117—118°/12—13 mm. For conversion into γ-phenyl-*n*-propyl chloride, the alcohol (44·8 g.) was dissolved in pyridine (30 c.c.), cooled in ice, and treated slowly with thionyl chloride (39·4 g.). After 30 minutes in ice, the mixture was heated at 100° for 15 minutes, treated with dilute hydrochloric acid, and extracted with ether. The extract was washed with water, sodium carbonate, and finally with water, and dried. After removal of the ether, the residue was distilled under reduced pressure, giving 25 g. of chloride, b. p. 95—97°/12 mm. A higher-boiling fraction (about 150°/12 mm.) was obtained which crystallised. This, m. p. 52°, was identified as dibenzyl, which was probably formed in the above Grignard reaction with benzyl chloride.

The yield of chloride was increased to 33 g. (from 40 g. of the alcohol) when the equivalent amount of dimethylaniline was used instead of pyridine.

ζ-Phenyl-Δ^{α}-hexen-γ-ol (VIII; X = H).—A Grignard solution prepared from γ-phenyl-*n*-propyl chloride (22 g.), magnesium (3·5 g.), and anhydrous ether (90 c.c.) was treated at 0° with a solution of acraldehyde (8 g.) in ether (15 c.c.), added dropwise. After standing at room temperature for 2 hours, the mixture was gently refluxed for 15 minutes and decomposed with ice and ammonium chloride. The product (15·2 g.), b. p. 133—135°/12 mm., was isolated from the ethereal solution and converted into the 3 : 5-*dinitrobenzoate*, fine needles, from alcohol, m. p. 113—114° (Found : C, 61·4; H, 4·9. $C_{19}H_{18}O_6N_2$ requires C, 61·6; H, 5·1%). The latter was hydrolysed, giving the pure *carbinol*, b. p. 135°/12 mm. (Found : C, 81·5; H, 9·3. $C_{12}H_{16}O$ requires C, 81·8; H, 9·1%).

ζ-Phenyl-$\Delta^{\alpha\gamma}$-hexadiene (III; X = R = H).—If the carbinol is heated with twice its weight of potassium hydrogen sulphate at atmospheric pressure, about 65—70% is converted into high-boiling polymeric material, giving a yield of only 10—15% of diene and some unchanged carbinol, but under the following conditions about 50% of crude diene was obtained. The carbinol (28·5 g.) was slowly run through a tapering tap-funnel on finely powdered, freshly fused potassium hydrogen sulphate (43 g.) in a Claisen flask, fitted with a well-cooled receiver, and maintained at 12 mm. pressure in an oil-bath at 145—150°. Under these conditions the carbinol did not readily distil out of the reaction flask. Addition occupied 6 hours and an aqueous oily distillate collected in the receiver. This was dissolved in ether, dried, and, after removal of ether, distilled, giving the crude diene (12·6 g.), b. p. 100—105°/12 mm., and a fraction, b. p. 105—125°/12 mm., which probably contained some unchanged carbinol and was discarded. The *diene* was redistilled over sodium, and was obtained as a light, colourless, mobile liquid, b. p. 99·5—100·5°/11 mm., the carbon content of which (1% below the theoretical) indicated the persistence of a small quantity of carbinol. Repeated fractionation gave a product with the same boiling point as above, having $n_D^{13°}$ 1·5446, $d_{4°}^{13°}$ 0·9304, whence $[R_L]_D$ 53·7 (calc., 53·08) (Found : C, 90·5; H, 9·1. $C_{12}H_{14}$ requires C, 91·1; H, 8·9%).

3-β-*Phenylethyl*-1 : 2 : 3 : 6-*tetrahydrophthalic anhydride* (IV; R = X = H).—The above diene (III; X = R = H) (1·6 g.) and maleic anhydride (1·0 g.) were dissolved in warm xylene (2 c.c.), and the yellow solution kept at room temperature for 4 days. The crystalline product which separated (0·65 g.) was recrystallised from benzene–light petroleum, forming narrow colourless leaflets, m. p. 123—125° (Found : C, 75·1; H, 6·7. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·3%). In other experiments polymerisation also occurred to an appreciable extent, rendering the isolation of the adduct somewhat troublesome. The latter decomposed alkaline permanganate slowly and its bromine absorption was only 75% of the theoretical value, but Diels and Alder (*Ber.*, 1929, **62**, 557, 2084) have noted the difficulty with which similar adducts are attacked by bromine. The anhydride was also hydrolysed with potassium hydroxide in aqueous alcohol, and the acid isolated in good yield as its *acid potassium salt dihydrate*, which crystallised from water in fine needles (Found : loss at 100°, 10·05. $C_{16}H_{17}O_4K,2H_2O$ requires loss, 10·3%. Found : equiv., for anhydrous material, 315; calc., 312).

Cyclisation experiments. (*a*) The above adduct (1 g.) was treated with aluminium chloride (1·1 g.) in carbon disulphide at 0° and kept thus for 18 hours. After decomposition with ice and dilute hydrochloric acid, the original material was isolated unchanged from the carbon disulphide (m. p. and mixed m. p.).

(*b*) The same mixture was boiled for 6 hours with the same negative result.

(*c*) A mixture of the adduct (1·9 g.) and aluminium chloride (2·1 g.) in pyridine (20 c.c.) was kept at room temperature for 4 days. After decomposition as above, and extraction with chloroform, 1·2 g. of unchanged material, m. p. 124°, were obtained as the only crystalline substance.

(*d*) A solution of the adduct (0·5 g.) in glacial acetic acid (2·5 c.c.) and concentrated sulphuric acid (0·4 c.c.) was heated at 100° for 1¼ hours, cooled, decomposed with ice-water, and extracted with chloroform. The dried extract was evaporated, leaving a viscous oil (200 mg.) which could not be purified. This was heated with selenium (0·3 g.) at 310—320° for 22 hours. The crystalline product, 3-β-phenylethylphthalic anhydride, was sublimed in a vacuum and recrystallised from benzene–light petroleum, forming almost colourless, pointed blades, m. p. 153—154° (15 mg.), identical with the product described below (*e*).

(*e*) The adduct was converted by methyl alcohol into its *methyl hydrogen* ester, which crystallised from aqueous methyl alcohol in colourless, lustrous, flat needles, m. p. 137—138° [Found : C, 70·6; H, 7·0 (microanalysis by Dr. A. Schoeller); equiv., 294·5. $C_{17}H_{20}O_4$ requires C, 70·8; H, 7·15%; equiv., 288]. A solution of this (0·3 g.) in 85% sulphuric acid (1 g.) was kept at 12° for 3 days. The acidic product precipitated by water was extracted with chloroform, from which it was removed with sodium carbonate solution. The latter was acidified and extracted with ether. After removal of ether, the residue was freed from ester groups by hydrolysis with 10% aqueous potassium hydroxide (15 c.c.). The resultant acidic product (0·2 g.) was resinous, and was dehydrogenated by heating with platinum-black (50 mg.) at 300° for 6 hours. The crystalline product was dissolved in benzene, filtered, freed from solvent, sublimed at 170°/0·1 mm., and finally recrystallised from *cyclo*hexane, from which 3-β-*phenylethylphthalic anhydride* separated in cream-coloured pointed leaflets (30 mg.), m. p. 153—154° (soft at 148°) [Found : C, 76·1; H, 4·7 (microanalysis by Dr. A. Schoeller). $C_{16}H_{12}O_3$ requires C, 76·2; H, 4·8%).

(*f*) The anhydride (IV; R = X = H) was converted by methyl-alcoholic hydrogen chloride into the dimethyl ester, a somewhat viscous liquid, b. p. 155—160°/0·1 mm. A solution of the latter (1·5 g.) in carbon disulphide (10 c.c.) was treated with aluminium chloride (1·5 g.)

and kept at 0—4° for 7 days. It was decomposed with ice and a little hydrochloric acid. The carbon disulphide extract was evaporated to dryness, and the residue hydrolysed with 10% potassium hydroxide in aqueous alcohol (25 c.c.). The acidic product was converted into an anhydride by heating with acetyl chloride and finally distilled in an oil-bath at 200°/0·2—0·3 mm. The product separated from benzene–light petroleum in colourless microscopic crystals (0·5 g.), m. p. 123° alone or mixed with the original anhydride (IV; R = X = H).

Methyl m-*Methoxycinnamate*.—This ester, b. p. 162°/13 mm., was obtained in excellent yield by the action of methyl-alcoholic hydrogen chloride on *m*-methoxycinnamic acid, which was obtained, practically in quantitative yield, by the condensation of *m*-methoxybenzaldehyde with malonic acid under the conditions prescribed by Brand and Horn (*J. pr. Chem.*, 1927, **115**, 374). Reduction of the ester (17 g.) by sodium and alcohol by Bouveault's method gave an unsatisfactory yield (3 g.) of the required γ-m-*methoxyphenyl*-n-*propyl alcohol*, b. p. 155—157°/15 mm. (Found: C, 72·0; H, 8·5. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·5%), which was purified through its 3 : 5-*dinitrobenzoate*; this crystallised from methyl alcohol in pale yellow plates, m. p. 69—70° (Found: C, 56·5; H, 5·0. $C_{17}H_{16}O_7N_2$ requires C, 56·6; H, 4·5%). A 60% yield of the same alcohol was obtained by similar reduction of the corresponding saturated methyl or ethyl ester. *m*-Methoxycinnamic acid (55 g.) was dissolved in dilute sodium hydroxide solution (*ca.* 500 c.c.) and kept faintly alkaline to phenolphthalein while 1200 g. of 2·5% sodium amalgam were slowly added. Reaction was completed on a warm water-bath. The aqueous solution was acidified, and β-*m*-methoxyphenylpropionic acid separated as an oil which slowly solidified. After crystallisation from benzene–ligroin, the acid, m. p. *ca.* 40°, was esterified with the appropriate alcoholic hydrogen chloride, affording excellent yields of *methyl*, b. p. 148°/15 mm. (Found: C, 67·7; H, 7·2. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·2%), and *ethyl* β-m-*methoxyphenylpropionate*, b. p. 156—157°/15 mm. (Found: C, 69·0; H, 7·7. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·8%).

For reduction to the alcohol, the ester, preferably the ethyl ester (100 g.), was dissolved in absolute alcohol (400 c.c.) and treated with nut-size sodium (77·5 g.) during 1—1¼ hours. The mixture was heated for 6 hours at 130°. Alcohol was added to remove excess of sodium, and the residual alcohol was distilled off. The pasty mass was treated with a large volume of water, and the product salted out, extracted with ether, and isolated in the usual way. Yield, 48 g. of γ-*m*-methoxyphenyl-*n*-propyl alcohol, which gave the same dinitrobenzoate as that obtained from the reduction product of the corresponding cinnamic ester above.

γ-m-*Methoxyphenyl*-n-*propyl Chloride* (III; X = OMe).—The alcohol (45 g.) was treated with thionyl chloride (21 c.c.) in dimethylaniline solution (31 c.c.) in the same way as γ-phenylpropyl alcohol, giving the *chloride* (46·5 g.), b. p. 137°/15 mm. (Found: Cl, 19·0. $C_{10}H_{13}OCl$ requires Cl, 19·2%).

ζ-m-*Methoxyphenyl*-Δ^{α}-*hexen*-γ-*ol* (VIII; X = OMe).—The preceding chloride (37 g.) was converted into a Grignard reagent (4·9 g. of magnesium and 150 c.c. of ether), which was condensed with acraldehyde (12 g.) as in the preparation of (VIII; X = H). The product (29 g.), b. p. 170—175°/15 mm., was converted into the 3 : 5-*dinitrobenzoate*, colourless needles, m. p. 106—107°, from alcohol (Found: C, 59·9; H, 5·4. $C_{20}H_{20}O_7N_2$ requires C, 60·0; H, 5·0%), and the pure *carbinol*, a colourless viscous oil, b. p. 177°/14 mm., regenerated by hydrolysis (Found: C, 75·3; H, 8·9. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·8%).

Dehydration. The carbinol (24 g.) was added slowly (5 hours) to powdered, freshly fused potassium hydrogen sulphate (38 g.) contained in a vacuum distillation apparatus, maintained at 15—16 mm. pressure, in an oil-bath at 165—170°. The distillate was dried in ethereal solution and redistilled, giving a mobile liquid (11·1 g.), b. p. 140—150°/17 mm. On account of the boiling point range, this was treated again with 24 g. of dehydrating agent in the same way. The final product was fractionated, giving (i) 7·6 g., b. p. 143—145°/17 mm., and (ii) 7·8 g., b. p. 146—150°/17 mm. Fraction (i) was redistilled over sodium, but the product had only 81·3% of carbon (theoretical, 82·9), which could not be increased by redistillation. It was therefore dissolved in benzene (6·1 g. in 7 c.c.), phenyl *iso*cyanate (1 c.c.) added, and the mixture kept at room temperature for 48 hours. The solution was filtered, benzene removed, and the residue distilled (5·2 g.), and redistilled over sodium, giving the pure *diene* (III; X = OMe, R = H) (3 g.), b. p. 149°/18 mm. (Found: C, 82·5; H, 8·7. $C_{13}H_{16}O$ requires C, 82·9; H, 8·6%). When this was treated with maleic anhydride under the various conditions already described, no normal reaction ensued. Varying amounts of maleic anhydride were recovered unchanged, leaving high-boiling resinous residues. The diene was also heated in a sealed tube at 100° for 6 hours with acraldehyde (2 mols.), but 80% of it was recovered as a liquid, b. p. 140°/14 mm.

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