160. *Some Unsymmetrically Substituted αβ-Diethylstilbenes.*

By F. P. Jenkins and J. H. Wilkinson.

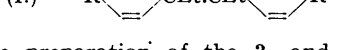
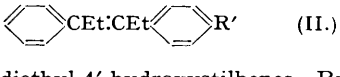
A number of unsymmetrical αβ-diethylstilbenes have been prepared for examination as potential inhibitors of œstrogenic activity. 3- and 4-Amino-α-ethyl-4′-methoxydeoxybenzoin were converted into 3- and 4-amino-αβ-diethyl-4′-methoxystilbene, of which the former underwent demethylation to the 4′-hydroxy-derivative much more readily than the latter. 4-Amidino- and 4-propionyl-αβ-diethyl-4′-methoxystilbene were prepared from the appropriate 4-cyano-stilbene and 4-*p*-cyanophenyl-3-*p*-methoxyphenylhexan-3-ol, respectively. 3-*p*-Aminophenyl-3-*p*-hydroxyphenylhexan-3-ol was obtained by treatment of 4-acetamido-4′-acetoxy-α-ethyldeoxybenzoin with excess of ethylmagnesium iodide.

None of these compounds exhibited anti-œstrogenic activity in mice. The aminohydroxystilbenes and 4-*p*-aminophenyl-3-*p*-hydroxyphenylhexan-3-ol were œstrogenic.

The marked success which attended the introduction of the synthetic œstrogen, diethylstilbœstrol, by Dodds *et al.* (see, *e.g.*, *Proc. Roy. Soc.*, 1939, *B*, **127**, 140; 1940, **128**, 253; 1944, **132**, 83) led us to prepare a number of unsymmetrically substituted analogues in the hope that the change of substituent might produce anti-œstrogenic activity. Apart from a considerable number of mono-ethers and mono-esters and some ether-esters, relatively few analogues having different groups in the 4- and 4′-positions have been described (cf. Solmssen, *Chem. Reviews*, 1945, **37**, 481; Masson, *Rev. Canad. Biol.*, 1944, **3**, 491). Jaeger and Robinson (*J.*, 1941, 744) prepared 4-acetyl-αβ-diethyl-4′-hydroxystilbene (I; R = Ac, R′ = OH) which was examined for progestational activity; Dodds, Golberg, Lawson, and Robinson (*Proc. Roy. Soc.*, 1939, *B*, **127**, 140) tested the 4-hydroxy-derivative (I; R = OH, R′ = H) for œstrogenic activity; Neher and Miescher (*Helv. Chim. Acta*, 1946, **29**, 449) prepared the carboxylic acids (I; R = OH, R′ = CO_2H) and (I; R = OMe, R′ = CO_2H), and Linnell and Sharma (*Quart. J. Pharm.*, 1941, **14**, 259) reported that αβ-diethyl-3 : 4′-dihydroxystilbene (II; R = R′ = OH) was œstrogenic.

Very few basic unsymmetrical diethylstilbenes have been described. Rubin and Wishinsky (*J. Amer. Chem. Soc.*, 1944, **66**, 1948) prepared 4-amino-αβ-diethyl-4′-hydroxystilbene (I; R = NH_2, R′ = OH); Haddow, Harris, Kon, and Roe (*Trans. Roy. Soc.*, 1948, **241**, *A*, 147, 187) examined the effect, on the growth of mouse tumours, of 4-dimethylamino-αβ-diethylstilbene (I; R = NMe_2, R′ = H), and the antibacterial properties of 4-amino-αβ-diethylstilbene (I; R = NH_2, R′ = H) were studied by Brownlee, Copp, Duffin, and Tonkin (*Biochem. J.*, 1943, **37**, 572).

In view of the ease with which the amino-group can be replaced by other substituents, we decided to prepare the 3- and the 4-amino-compound. In addition, since 4-acetyl-αβ-diethyl-4′-hydroxystilbene (Jaeger and Robinson, *loc. cit.*) was reported to have œstrogenic activity of a very low order, the corresponding 4-propionyl derivative appeared worth examining for anti-œstrogenic activity.

(I.)  (II.) 

For the preparation of the 3- and 4-amino-αβ-diethyl-4′-hydroxystilbenes, Rubin and Wishinsky's route was employed. The Friedel–Crafts reaction of *m*- and *p*-nitrophenylacetyl chlorides with anisole gave the required 4′-methoxy-3- and -4-nitrodeoxybenzoins which were ethylated by Rubin and Wishinsky's method (*loc. cit.*). Reduction of the nitro-groups with stannous chloride or catalytically gave the corresponding aminodeoxybenzoins, and these, on treatment with ethylmagnesium halides, gave the diethylstilbenes (I and II; R = NH_2, R′ = OMe); the latter was readily demethylated by means of hydriodic acid, but the former gave very poor yields of the aminophenol by this method.

4-*p*-Aminophenyl-3-*p*-hydroxyphenylhexan-3-ol was prepared from 4-amino-α-ethyl-4′-methoxydeoxybenzoin, which readily underwent demethylation with hydrobromic acid. The resulting 4-hydroxy-derivative, however, formed an insoluble complex with ethylmagnesium

iodide from which the starting material was recovered unchanged. The *ON*-dibenzoyl derivative proved insufficiently soluble in ether or anisole, but the more soluble *ON*-diacetyl compound, on treatment with 5 moles of the Grignard reagent, gave the required hexanol or its *N*-acetyl derivative according to the conditions.

αβ-Diethyl-4-methoxy-4′-propionylstilbene (I; R = COEt, R′ = OMe) was prepared from 4-cyano-α-ethyl-4′-methoxydeoxybenzoin by a method similar to that used by Jaeger and Robinson (*loc. cit.*) for the 4-acetyl derivative. The 4-methoxy-4′-propionyl derivative, however, proved much more resistant to hydriodic acid demethylation than Jaeger and Robinson's compound, and we were unable to isolate the corresponding phenol.

4-Cyano-αβ-diethyl-4′-methoxystilbene (Neher and Miescher, *loc. cit.*) reacted with methanolic hydrogen chloride to give the corresponding imino-ether hydrochloride, which on treatment with alcoholic ammonia was converted into 4-amidino-αβ-diethyl-4′-methoxystilbene hydrochloride.

3- and 4-Amino-αβ-diethyl-4′-hydroxystilbene, 3-*p*-aminophenyl-3-*p*-hydroxyphenylhexan-3-ol, 4-amidino-αβ-diethyl-4′-methoxystilbene hydrochloride, and αβ-diethyl-4-methoxy-4′-propionylstilbene were tested for anti-œstrogenic activity in mice by the vaginal smear method, but none was active. With the exception of the amidine, all these compounds were œstrogenic. The œstrogenic activity of the hexanol is a result of some interest since it appears that no other hexanols of this series have been reported active in this respect. The following table, based upon figures kindly determined by Mrs. M. M. Boycott, B.Sc., shows the dose–response relations obtained.

Œstrogenic response in mice.

(The compounds were injected subcutaneously in two equal portions separated by an interval of 24 hours.)

Compound.	Solvent.	Total dose (mg.).	Response, %.
3-Amino-αβ-diethyl-4′-hydroxystilbene	Arachis oil	1	100
4-Amino-αβ-diethyl-4′-hydroxystilbene *	do.	1	100
		0·1	100
		0·01	50
4-*p*-Aminophenyl-3-*p*-hydroxyphenylhexan-3-ol ...	do.	1	100
		0·1	78
		0·01	0
αβ-Diethyl-4-methoxy-4′-propionylstilbene	do.	1	100
4-Amidino-αβ-diethyl-4′-methoxystilbene hydrochloride	Water	1	0

* Rubin and Wishinsky (*loc. cit.*) report that 7·5 γ of this compound were equivalent in œstrogenic potency to one Allen–Doisy rat unit.

Experimental.

(Analyses are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected.)

4′-Methoxy-3-nitrodeoxybenzoin.—*m*-Nitrophenylacetic acid (13 g.) was converted into the chloride by treatment with thionyl chloride as described by Linnell and Roushdi (*Quart. J. Pharm.*, 1941, **14**, 270). The acid chloride in anisole (20 c.c.) was treated with powdered aluminium chloride (15 g.) at +20°. The mixture was set aside for 24 hours with occasional shaking, then heated at 60° for 2 hours. After decomposition with 2N-hydrochloric acid and ice, the mixture was steam-distilled to remove the excess of anisole. The aqueous layer was decanted, and the residue washed successively with 2N-hydrochloric acid and water. On treatment with ether, the oil solidified to a crystalline solid, m. p. 83—84°. Recrystallisation from alcohol gave the required 4′-methoxy-3-nitrodeoxybenzoin (10·1 g., 52%) in pale yellow needles, m. p. 84—85°, unaffected by further crystallisation. Linnell and Roushdi (*loc. cit.*) report m. p. 85—86°.

α-Ethyl-4′-methoxy-3-nitrodeoxybenzoin.—4′-Methoxy-3-nitrodeoxybenzoin (13·1 g.) in absolute ethanol (100 c.c.) was treated with a solution of sodium ethoxide, prepared from sodium (1·2 g.) and ethanol (30 c.c.). Ethyl bromide (7·3 g.) was added, and the mixture heated under reflux for 2 hours. The alcohol was removed by steam-distillation, and the oily residue extracted with ether. Distillation gave the required *product* (12·5 g., 87%) as a pale yellow viscous oil, b. p. 180—181·5°/0·1 mm. (Found: C, 68·4; H, 5·7; N, 4·95. $C_{17}H_{17}O_4N$ requires C, 68·3; H, 5·7; N, 4·7%).

3-Amino-α-ethyl-4′-methoxydeoxybenzoin.—A solution of the foregoing compound (6·4 g.) in alcohol (25 c.c.) was treated with stannous chloride (15·2 g.) and 7N-hydrochloric acid (45 c.c.) and heated under reflux for 1½ hours. The cooled mixture was poured into excess of 10N-sodium hydroxide, and the oil extracted with ether. The ethereal solution was extracted with 4N-hydrochloric acid, and the acid layer made alkaline with sodium hydroxide. The oil was extracted with ether, dried (Na_2SO_4), and distilled. *3-Amino-α-ethyl-4′-methoxydeoxybenzoin* (4·57 g., 80%) was obtained as a pale yellow glass, b. p. 179·5—181°/0·1 mm., which gave pale yellow crystals, m. p. 122—124°, on treatment with ether (Found: C, 75·4; H, 6·8; N, 5·35. $C_{17}H_{19}O_2N$ requires C, 75·8; H, 7·1; N, 5·2%). The *benzoyl* derivative crystallised from alcohol in fine colourless needles, m. p. 174° (Found: C, 77·4; H, 6·1; N, 3·8. $C_{25}H_{23}O_3N$ requires C, 78·0; H, 6·0; N, 3·6%

3-*Amino-α-ethyl-4'-hydroxydeoxybenzoin.*—3-Amino-α-ethyl-4'-methoxydeoxybenzoin (0·7 g.) was heated in acetic acid (3 c.c.) under reflux with 48% hydrobromic acid (2 c.c.) for 1½ hours. After removal of the acids by distillation, the residue was neutralised with sodium carbonate and extracted with ether. The ethereal layer was extracted with 2N-sodium hydroxide, and the aqueous layer heated to expel ether. Acidification with acetic acid gave 3-*amino-α-ethyl-4'-hydroxydeoxybenzoin* (0·53 g., 79%), which crystallised from 60% alcohol in brown plates, m. p. 150—151° (Found : C, 75·4; H, 6·7; N, 5·75. $C_{16}H_{17}O_2N$ requires C, 75·3; H, 6·7; N, 5·5%).

3-*Amino-αβ-diethyl-4'-methoxystilbene.*—3-Amino-α-ethyl-4'-methoxydeoxybenzoin (4·05 g.) in anhydrous ether (30 c.c.) was added during 1 hour to a solution of the Grignard reagent, prepared from magnesium (1·08 g.), ethyl iodide (7 g.), and anhydrous ether (20 c.c.), mechanical stirring being employed. Stirring was continued for a further 3 hours, and next morning the mixture was decomposed with ammonium chloride solution. The ethereal layer was washed with water and dried (Na_2SO_4). The solvent was removed but, when distillation of the residue was attempted, partial dehydration of the 4-*m*-aminophenyl-3-*p*-methoxyphenylhexan-3-ol occurred, so the residue was heated at 200°/20 mm. for 1 hour to complete the conversion into the required *stilbene*, which distilled at 149—151°/0·1 mm. and was obtained as a pale yellow oil (3·03 g., 72%), which darkened on storage (Found : C, 80·9; H, 8·1; N, 5·0. $C_{19}H_{23}ON$ requires C, 81·2; H, 8·2; N, 5·0%).

3-*Amino-αβ-diethyl-4'-hydroxystilbene.*—A mixture of the foregoing stilbene (2 g.), acetic acid (6 c.c.), and 48% hydrobromic acid (6 c.c.) was heated under reflux for 2 hours, and the acids were then removed. The gummy residue was neutralised with sodium carbonate and washed with water. It was dissolved in ether and extracted with 2N-sodium hydroxide, and the alkaline solution acidified with acetic acid. The *product* (1·07 g., 56%) was extracted with ether and distilled, b. p. 220—230° (air-bath)/0·1 mm., to give a pale yellow glass which became brown on storage. On treatment with ether it slowly crystallised. Recrystallisation from methanol gave colourless crystals, m. p. 163—164° (Found : C, 80·2; H, 7·85; N, 5·25. $C_{18}H_{21}ON$ requires C, 80·9; H, 7·9; N, 5·25%).

4'-Methoxy-4-nitrodeoxybenzoin was prepared from *p*-nitrophenylacetyl chloride [from the acid (181 g.)], anisole (260 c.c.), and aluminium chloride (200 g.) by a method similar to that used for the 3-nitro-isomer. This procedure was more convenient and gave higher yields than that of Rubin and Wishinsky (*loc. cit.*). After storage at room temperature overnight, the mixture was heated to 60° for 4 hours with frequent shaking. The cooled solution was poured into a mixture of ice (800 g.) and hydrochloric acid (*d* 1·16; 200 c.c.). The oily solid which separated was drained and triturated several times with water, then with alcohol (200 c.c.). The solid obtained was heated under reflux with alcohol (1 l.); the mixture was cooled, and the crystalline solid separated by decantation. Recrystallisation from alcohol gave the required product, m. p. 110—111°, raised to 114° by a second recrystallisation from alcohol (Found : C, 66·4; H, 4·85; N, 5·4. Calc. for $C_{15}H_{13}O_4N$: C, 66·4; H, 4·8; N, 5·2%); the yield was 204 g. (83%). Rubin and Wishinsky (*loc. cit.*) report m. p. 117—118°. The 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid in orange needles, m. p. 212° (Found : N, 15·1. $C_{21}H_{17}O_7N_5$ requires N, 15·5%).

4-*Amino*-4'-*methoxydeoxybenzoin.*—4'-Methoxy-4-nitrodeoxybenzoin (2·71 g.) was hydrogenated in benzene (30 c.c.) at 20° under atmospheric pressure in the presence of Adams's platinum oxide (0·3 g.); the uptake after 20 minutes was 750 c.c. (Calc. : 720 c.c.). The catalyst was removed, and the filtrate shaken with 2N-hydrochloric acid to precipitate the hydrochloride of the product. The solid was dissolved in hot water and converted into the required *base* by treatment with alkali. Recrystallisation from alcohol gave buff-coloured needles, m. p. 136—137° (Found : C, 74·5; H, 6·2; N, 5·8. $C_{15}H_{15}O_2N$ requires C, 74·7; H, 6·2; N, 5·8%). The *acetyl* derivative crystallised from alcohol in colourless needles, m. p. 175° (Found : C, 71·9; H, 6·0; N, 5·1. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·0; N, 4·95%).

α-Ethyl-4'-methoxy-4-nitrodeoxybenzoin, prepared in 84% yield substantially as described by Rubin and Wishinsky (*loc. cit.*), had b. p. 198—201°/0·1 mm. (lit., 210—215°/0·8 mm.) (Found : C, 68·6; H, 5·75. Calc. for $C_{17}H_{17}O_4N$: C, 68·3; H, 5·7%). When excess of sodium ethoxide and ethyl iodide were employed, as used by Jaeger and Robinson (*loc. cit.*) for the corresponding 4-cyano-compound, some decomposition occurred, and varying amounts of an unidentified yellow mobile liquid, b. p. 76—81°/0·3 mm., 261°/760 mm., n_D^{25} 1·437, were formed (Found : C, 66·5; H, 7·45; N, 3·5%). Also the main product was contaminated with *p*-anisic acid, m. p. 184° (Found : C, 63·3; H, 5·05. Calc. for $C_8H_8O_3$: C, 63·2; H, 5·25%).

4-*Amino-α-ethyl-4'-methoxydeoxybenzoin.*—α-Ethyl-4'-methoxy-4-nitrodeoxybenzoin (15 g.) was hydrogenated in benzene (50 c.c.) at 20°/1 atm. in the presence of Adams's platinum oxide (0·3 g.) : hydrogen uptake was 3770 c.c. (Calc. : 3640 c.c.). The catalyst was filtered off, and the filtrate shaken with 5N-hydrochloric acid (30 c.c.). The sparingly soluble hydrochloride formed a gummy precipitate which hardened overnight. After being washed with benzene and ether it was triturated with 2N-sodium hydroxide (100 c.c.). The base was extracted with ether and dried (Na_2SO_4), and the solvent removed. The residue (12·9 g., 95%), a pale brown viscous oil, crystallised on storage to a buff-coloured solid, which after crystallisation from ether had m. p. 100—101° (Found : C, 75·7; H, 7·1; N, 5·15. Calc. for $C_{17}H_{19}O_2N$: C, 75·8; H, 7·1; N, 5·2%). Rubin and Wishinsky (*loc. cit.*) report m. p. 97—98·5°. The *benzoyl* derivative crystallised from alcohol in colourless clusters, m. p. 164° (Found : C, 77·0; H, 6·3; N, 3·9. $C_{24}H_{23}O_3N$ requires C, 77·2; H, 6·15; N, 3·75%).

4-*Amino-α-ethyl-4'-hydroxydeoxybenzoin.*—4-Benzamido-α-ethyl-4'-methoxydeoxybenzoin (43·8 g.) was heated in acetic acid (145 c.c.) under reflux with 48% hydrobromic acid (190 c.c.) for 3 hours. The *product*, isolated as described for 3-amino-α-ethyl-4'-hydroxydeoxybenzoin, crystallised from aqueous alcohol in colourless plates, m. p. 113—114° (Found : C, 75·1; H, 6·75; N, 5·3%). The *diacetyl* derivative separated from 60% alcohol in colourless needles, m. p. 113—114° (Found : C, 70·5; H, 6·3; N, 4·25. $C_{20}H_{21}O_4N$ requires C, 70·8; H, 6·2; N, 4·15%). The *dibenzoyl* derivative crystallised

from alcohol in fine colourless needles, m. p. 230—231°, sparingly soluble in most organic solvents (Found C, 77·6; H, 5·4. $C_{30}H_{25}O_4N$ requires C, 77·8; H, 5·4%). An attempt was made to convert the aminophenol into the corresponding cyanophenol, but, after treatment of the diazo-solution with cuprous cyanide, the product did not give satisfactory analytical results.

4-Amino-αβ-diethyl-4′-methoxystilbene was prepared by Rubin and Wishinsky's method (*loc. cit.*), 4-*p*-aminophenyl-3-*p*-methoxyphenylhexan-3-ol (m. p. 112°, lit. 113—114°) being isolated as an intermediate (Found: C, 76·2; H, 8·2; N, 4·9. Calc. for $C_{19}H_{15}O_2N$: C, 76·3; H, 8·35; N, 4·7%). At 200°/20 mm., the hexanol underwent dehydration to the required stilbene, b. p. 176—177°/0·3 mm. (Found: C, 81·2; H, 8·0; N, 4·95. Calc. for $C_{19}H_{23}ON$: C, 81·2; H, 8·2; N, 4·95%). The American workers report b. p. 180—182°/1 mm.

4-*Amino-αβ-diethyl-4′-hydroxystilbene.*—The 4-amino-4′-methoxy-compound was demethylated by the method described for the 3-amino-derivative, but the yield was markedly inferior to that obtained by the method of Rubin and Wishinsky, who report b. p. 180—185°/0·1 mm. Our product had b. p. 200—202°/0·7 mm. (Found: C, 80·4; H, 8·0; N, 5·25. Calc. for $C_{18}H_{21}ON$: C, 80·9; H, 7·9; N, 5·25%). After storage for several weeks the viscous oily product deposited crystals which were collected and recrystallised successively from methanol and light petroleum (b. p. 80—100°). Colourless aggregations, m. p. 134—137°, were obtained. Admixture with authentic *trans*-4-amino-αβ-diethyl-4′-hydroxystilbene (Weiss, *J. Amer. Chem. Soc.*, 1949, **71**, 2944), m. p. 180—183°, raised the m. p. to 160—163°, thus suggesting that the crystals consist of a mixture of the *cis*- and the *trans*-form. However, shortage of material precluded any further work on their separation.

Reaction of 4-*Acetamido-4′-acetoxy-α-ethyldeoxybenzoin with Ethylmagnesium Bromide.*—The acetamido-compound (6·6 g.), dissolved in anisole (70 c.c.), was added during ½ hour to a mechanically stirred solution of ethylmagnesium bromide, prepared from magnesium (2·4 g., 5 equivs.), ethyl bromide (12 g.), and anhydrous ether (30 c.c.). The mixture was stirred at 25° for 2 hours and set aside overnight. The complex was decomposed with ammonium chloride solution and the ether–anisole layer was extracted with 2N-sodium hydroxide. Acidification of the alkaline extract with acetic acid yielded a gummy solid, which distilled at 245—250° (bath-temp.)/0·05 mm. The distillate deposited crystals, m. p. 194—197°, on treatment with ether. After recrystallisation from the methanol, these formed colourless needles, m. p. 200—201°, of 4-p-*acetamidophenyl*-3-p-*hydroxyphenylhexan*-3-*ol* (Found: C, 73·4; H, 7·65. $C_{20}H_{25}O_3N$ requires C, 73·4; H, 7·3%). Admixture with *trans*-4-amino-αβ-diethyl-4′-hydroxystilbene, m. p. 180—183°, produced a depression of 17°.

A second experiment, in which the diacetyl compound (12 g.) in anisole (120 c.c.) was treated with ethylmagnesium iodide [from magnesium (4·25 g.), ethyl iodide (27·6 g.), and anhydrous ether (75 c.c.)] at 50°, gave a gum which distilled at 231—237°/0·1 mm. The pale yellow glass obtained (4·7 g.) partly crystallised on treatment with ether, and crystallisation from methanol gave colourless crystals of 4-p-*aminophenyl*-3-p-*hydroxyphenylhexan*-3-*ol* (2·48 g.), m. p. 174—176°, raised to 181—182° by repeated recrystallisation from the same solvent (Found: C, 76·0; H, 7·7; N, 4·8. $C_{18}H_{23}O_2N$ requires C, 75·8; H, 8·1; N, 4·9%). Admixture with either *trans*-4-amino-αβ-diethyl-4′-hydroxystilbene (m. p. 180—183°) or 4-*p*-acetamidophenyl-3-*p*-hydroxyphenylhexan-3-ol produced a depression. 50 Mg. were treated in pyridine (1 c.c.) with *p*-nitrobenzoyl chloride (130 mg., 4 equivs.) at 20° for 1 hour, then 15 minutes at 60—70°. Water was added to precipitate the ON-*di*-p-*nitrobenzoyl* derivative (81 mg.), which was collected, washed with 0·1N-sodium carbonate and water, and dried at 80°. Crystallisation from methanol gave pale yellow prisms, m. p. 101—102° (Found: N, 7·1. $C_{32}H_{29}O_8N_3$ requires N, 7·2%).

αβ-Diethyl-4-methoxystilbene-4′-carbiminomethyl Ether (*Methyl αβ-Diethyl-4-methoxystilbene-4′-carboximidate*) *Hydrochloride.*—A mixture of 4-cyano-4′-methoxy-αβ-diethylstilbene (Neher and Miescher, *loc. cit.*) (1·93 g.) and anhydrous methanol (0·8 c.c.) was saturated at 0° with dry hydrogen chloride. The vessel was stoppered and set aside for 4 days, after which the excess of methanol and hydrogen chloride was removed under reduced pressure. The residue was dissolved in methanol and crystallisation was induced with ether. The *salt* (1·85 g., 77%) was obtained as a white crystalline powder, m. p. 160—162° (Found: N, 4·05; Cl, 10·1. $C_{21}H_{25}O_2N$,HCl requires N, 3·9; Cl, 9·9%).

4-*Amidino-αβ-diethyl-4′-methoxystilbene Hydrochloride.*—Finely powdered imino-ether hydrochloride (0·77 g.) was shaken mechanically with 10% alcoholic ammonia (4 c.c.) for 2 hours. The solid dissolved almost immediately, but the imino-ether base soon separated. This gradually redissolved during 48 hours. The mixture was evaporated under reduced pressure and crystallisation of the residue was induced with methanol and ether. Recrystallisation from water gave the required *amidine hydrochloride* as colourless needles, m. p. 202—203° (Found: C, 69·6; H, 7·25; N, 8·05; Cl, 10·2. $C_{20}H_{24}ON_2$,HCl requires C, 69·7; H, 7·25; N, 8·1; Cl, 10·3%).

3-p-*Methoxyphenyl*-4-p-*propionylphenylhexan*-3-*ol.*—A solution of 4-*p*-cyanophenyl-3-*p*-methoxyphenylhexan-3-ol (Jaeger and Robinson, *loc. cit.*) (5 g.) in anhydrous ether (25 c.c.) was added to a mechanically stirred, cooled solution of ethylmagnesium bromide, prepared from magnesium (2·5 g.), ethyl bromide (10·6 g.), and anhydrous ether (100 c.c.). The mixture was heated under reflux for 8 hours and set aside overnight. Decomposition was effected with acetic acid (30 c.c.) and water (20 c.c.), the ether was removed by distillation, and the mixture heated on a water-bath for 2 hours. The crude product was extracted with ether and freed from solvent. The residue was mixed with Girard's reagent T (4·5 g.), alcohol (45 c.c.), and acetic acid (4·5 c.c.) and heated under reflux for 1 hour. 3-p-*Methoxyphenyl*-4-p-*propionylphenylhexan*-3-*ol* was isolated by the procedure described by Jaeger and Robinson for 4 acetyl-αβ-diethyl-4′-methoxystilbene. It distilled at 220—230° (air-bath)/0·01 mm. as a pale yellow oil (2·46 g., 49%) (Found: C, 77·3; H, 8·15. $C_{22}H_{28}O_3$ requires C, 77·6; H, 8·2%).

αβ-Diethyl-4-methoxy-4′-propionylstilbene.—The above hexanol (3·15 g.) was heated with iodine (0·2 g.) and xylene (20 c.c.). Part of the solvent was slowly distilled to remove the water formed during

dehydration. The cooled solution was shaken with a solution of sodium thiosulphate to remove iodine, and dried (Na_2SO_4). The solvent was removed, and the residue distilled at 176—178°/0·06 mm. The *product* (2·7 g.) was a pale yellow oil (Found: C, 81·9; H, 7·9. $C_{22}H_{26}O_2$ requires C, 82·1; H, 8·1%).

Demethylation by boiling with hydriodic acid failed, only a trace of alkali-soluble material being formed. Most of the methoxy-derivative was recovered unchanged.

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