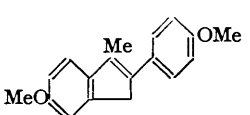
390. *Experiments Relating to Œstrogenic Indenes.*

By D. S. Morris.

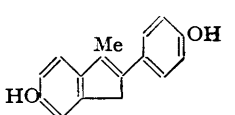
A new synthesis of β-*m*-methoxyphenyl-α-*p*-methoxyphenylpropionic acid is described. Some new indenes have been prepared and shown to possess slight œstrogenic activity.

β-*m*-Methoxyphenyl-α-*p*-methoxyphenylpropionic acid has previously been prepared by Solmmsen (*J. Amer. Chem. Soc.*, 1943, **65**, 2370) and by Silverman and Bogert (*J. Org. Chem.*, 1946, **11**, 34; cf. Davies and Morris, *J.*, 1947, 1697) as an intermediate in the synthesis of œstrogenic indenes. It is now shown that *m*-nitro-α-*p*-nitrophenylcinnamic acid is readily prepared by the Perkin reaction and reduced to the diamino-acid catalytically or by ammoniacal hydrogen sulphide. When diazotised, etc., this is converted into the hydroxy-acid, which on further reduction and methylation yields β-*m*-methoxyphenyl-α-*p*-methoxyphenylpropionic acid.

Silverman and Bogert, and Solmmsen (*locc. cit.*) experienced difficulty in the demethylation of (I) to (II). They observed that (II) was unstable in the free state (probably giving a quinone)



(I.)



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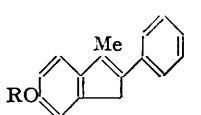


(III.)

but that its diacetate was stable. After failure by many other methods Silverman and Bogert obtained (II), but only in 2—3% yield, by essentially the same technique as that use by Solmmsen, *i.e.*, by heating the dimethoxy-compound with hydrobromic acid in an atmosphere of carbon dioxide. Solmmsen's preparation was, however, shown by Silverman and Bogert to be impure. It was considered that dealkylation might be achieved in better yields if the process could be accomplished with simultaneous acetylation since the diacetate of (II) is reported to be stable, and that dealkylation of such indenes possessing alkoxy-groups other than methoxy might be

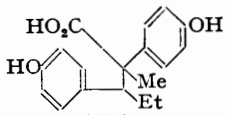
carried out more readily (cf. Trownow and Ladinga, *Ber.*, 1929, **62**, 2844). However, neither hydrogen iodide in presence of acetyl iodide nor hydrogen bromide in presence of acetic anhydride successfully dealkylates the analogous indenes (III) and it would appear that the presence of water is necessary for this operation. Nevertheless it has been demonstrated that the 6-*iso*propoxyindene is more readily dealkylated than the 6-methoxyindene and it is reasonable to suggest that the use of the *iso*proxy-ethers may result in better yields of dihydroxy-indenes.

Dealkylation of 6-*iso*propoxy-2-phenyl-3-*p*-methoxyphenylindene gave an incompletely demethylated substance, probably 6-hydroxy-2-phenyl-3-*p*-hydroxyphenylindene contaminated with the corresponding 3-*p*-methoxy-analogue.

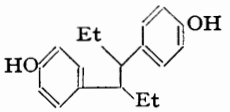
By the use of appropriate reactants with sodium phenylacetate in acetic anhydride, *m*-methoxy-, *m*-*iso*propoxy-, *m*-benzyloxy-, and *m*-hydroxy-α-phenylcinnamic acid were prepared. These cinnamic acids, except the *m*-benzyloxy-acid, were hydrogenated to the corresponding propionic acids when the sodium salts were used in aqueous solution with Raney nickel as catalyst; the free acids resisted hydrogenation in alcohol. Hydrogenolysis of *m*-benzyloxy-α-phenylcinnamic acid accompanied hydrogenation of the double bend and the product isolated was 1-phenyl-2-*m*-hydroxyphenylpropionic acid. 1-Phenyl-2-*m*-methoxy- and -2-*m*-*iso*-propoxy-phenylpropionic acid were readily cyclised to 5-methoxy-* and 5-*iso*propoxy-2-phenyl-indanone respectively, and these in turn were converted into 6-methoxy- and 6-*iso*propoxy-2-phenyl-3-methylindene. 1-Phenyl-2-*m*-benzyloxyphenylpropionic acid was prepared by benzylation of the hydroxy-acid, but attempts at cyclisation by stannic chloride resulted in debenzylation; a trace of a ketonic phenolic substance was found in the alkali-soluble fraction, but the 2 : 4-dinitrophenylhydrazone isolated was impure. Phosphoric oxide and a solution of the acid in benzene was likewise unsatisfactory and ice-cold concentrated sulphuric acid caused debenzylation. Two alternative approaches were made to 5-benzyloxy-2-phenylindanone. The first consisted of an attempt to protect the phenolic group of 1-phenyl-2-*m*-hydroxyphenyl-propionic acid by benzoylation; however, the phenolic group in this acid was highly unreactive towards benzoyl chloride in pyridine and the sole acidic reaction product was benzoic acid. The second consisted of the acetylation of α-phenyl-*m*-hydroxy- to α-phenyl-*m*-acetoxy-cinnamic acid which was hydrogenated in acetic acid in presence of platinum oxide catalyst, presumably to the corresponding propionic acid. The last, an oil, was treated with stannic chloride but failed to yield a ketonic product.

It is worth noting that many of the cyclisations carried out in this field might have been more effectually performed if liquid hydrogen fluoride had been available (Johnson, "Organic Reactions," Vol. II, p. 157; Solmmsen and Wenis, *J. Amer. Chem. Soc.*, 1948, **70**, 4197).

Substituted α-phenylcinnamic acids have not previously been examined for activity, despite their stilbenoid structure. Hunter and Kormann (*J. Amer. Chem. Soc.*, 1948, **70**, 3424) have recently reported that αβ-di-(*p*-hydroxyphenyl)-α-methylvaleric acid (IV) is active; it combines structural characteristics common to hexœstrol (V) and doisynolic acid (VI), and may also be regarded as a substituted β-phenylpropionic acid.



(IV.)



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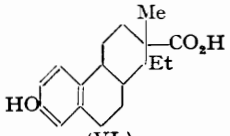

(VI.)

The biological assays, which were carried out by Dr. J. M. Robson, will be reported in detail elsewhere. However it may be stated that in initial assays (5 mg. per mouse) *m*-hydroxy-α-phenyl- and -α-*p*-hydroxyphenyl-cinnamic acid, and α-phenyl-β-*m*-hydroxyphenyl- and α-*p*-methoxyphenyl-β-*m*-methoxyphenyl-propionic acid were inactive. Activity at the 5-mg. level were observed with 6-methoxy- and 6-hydroxy-2-phenyl-3-methylindene and with 6-hydroxy-2-phenyl-3-*p*-hydroxyphenylindene. 6-*iso*Propoxy-2-phenyl-3-*p*-methoxy-phenylindene exhibited no activity. None was active at the 1-mg. level.

Experimental.

m-*Nitro*-α-p-*nitrophenylcinnamic Acid.*—Potassium *p*-nitrophenylacetate was prepared by addition of an alcoholic solution of *p*-nitrophenylacetic acid (18·1 g.) to an aqueous solution of potassium carbonate (6·9 g.), followed by evaporation to dryness under reduced pressure. The residue of crude potassium

* For assignment of structure see Silverman and Bogert (*loc. cit.*).

salt thus obtained was refluxed for 8 hours with acetic anhydride (260 c.c.), *m*-nitrobenzaldehyde (15·1 g.), and pyridine (1 c.c.), in an oil-bath at 150—160°. The product was cooled somewhat, diluted with water, digested on the water-bath for 30 minutes, and cooled to room temperature. The residue obtained by filtration was extracted with hot aqueous sodium carbonate, and the mixture filtered and acidified with dilute hydrochloric acid to yield a crude acidic product which was filtered off and washed with a little cold alcohol. When crystallised from methyl alcohol the crude *acid* gave pale yellow prisms (19 g.), m. p. 222° (Found: C, 57·3; H, 3·3; N, 8·5. $C_{15}H_{10}O_6N_2$ requires C, 57·3; H, 3·2; N, 8·9%).

m-*Amino*-α-p-*aminophenylcinnamic Acid.*—(a) *By hydrogenation of the dinitro-acid.* The above acid (18·4 g.) in methyl alcohol (500 c.c.) was hydrogenated at room temperature and pressure in presence of Raney nickel (20 g.). Six moles of hydrogen were absorbed. Removal of the catalyst and most of the solvent gave the *amino-acid* as glistening brown plates (10 g.), m. p. 208° (from methyl alcohol). When exposed to air the plates changed to a yellow powder (Found: C, 70·0; H, 5·6; N, 11·9. $C_{15}H_{14}O_2N_2$ requires C, 70·9; H, 5·5; N, 11·0%). The *diacetyl* derivative was prepared as pale buff-coloured needles, m. p. 277° (decomp.) (Found: C, 67·0; H, 5·8; N, 7·5. $C_{19}H_{18}O_4N_2$ requires C, 67·5; H, 5·3; N, 8·3%).

(b) *By reduction of the dinitro-acid with ammoniacal hydrogen sulphide.* A stream of hydrogen sulphide was passed through a suspension of the dinitro-acid (1 g.) in aqueous ammonia (20 c.c.; 6N.) for 1 hour. The mixture was boiled until the hydrogen sulphide and ammonia were completely expelled, cooled, and filtered, and the solid washed with boiling water. The filtrate when acidified with glacial acetic acid gave an acid (0·3 g.), m. p. and mixed m. p. 207—208°, identical with that obtained by hydrogenation as above.

m-*Hydroxy*-α-p-*hydroxyphenylcinnamic Acid.*—The crude amine (2·56 g.) in a suspension of dilute sulphuric acid [concentrated acid (3 c.c.) and water (24 c.c.)] was diazotised at 0° with a solution of sodium nitrite (1·4 g.) in water (5 c.c.). The ice-cold solution was added drop-wise to a boiling solution of sulphuric acid [concentrated acid (3 c.c.) in water (24 c.c.)]. The solution was boiled for 10 minutes with a little charcoal and filtered hot. The filtrate when cooled deposited yellowish-brown needles which were recrystallised from hot water to give an *acid* (1·5 g.), m. p. 230° (decomp.) (Found: C, 67·1; H, 4·8. $C_{15}H_{12}O_4$ requires C, 70·4; H, 4·7%). Two crystallisations from aqueous alcohol gave pale brown needles of a *hydrate*, m. p. 256° (Found: C, 65·6; H, 4·9. $C_{15}H_{12}O_4,H_2O$ requires C, 65·7; H, 5·1%)]. The acid (0·5 g.) was shaken with sodium hydroxide (0·25 g.) in water (5 c.c.) and benzoyl chloride (0·7 g.) for 2 hours. The oil obtained was acidified, washed with water, and taken up in ether and the crude acid extracted with sodium carbonate solution. Addition of dilute hydrochloric acid then precipitated the *dibenzoate* which crystallised from aqueous alcohol in small plates, m. p. 195° (Found: C, 75·1; H, 5·0. $C_{29}H_{20}O_6$ requires C, 75·0; H, 4·3%).

Hydrogenation of m-*Hydroxy*-α-p-*hydroxyphenylcinnamic Acid and Methylation of the Product.*—The acid (0·5 g.) in an excess of aqueous sodium hydroxide was hydrogenated in presence of Raney nickel. The catalyst was removed by filtration, the filtrate acidified with hydrochloric acid and extracted with ether, and the ethereal solution extracted with aqueous sodium hydrogen carbonate. By acidification of the alkaline solution and extraction with ether, an oily acid was obtained which did not readily crystallise. It was soluble in hot water and aqueous alcohol and tended to crystallise from ethyl alcohol. However, when methylated in alkaline solution with an excess of methyl sulphate, a crystalline acid (0·3 g.), m. p. 104°, was obtained. A mixed m. p. with *m*-methoxy-α-*p*-methoxyphenyl-β-*m*-methoxyphenylpropionic acid obtained by an alternative procedure showed no depression.

m-iso*Propoxybenzaldehyde.*—To *m*-hydroxybenzaldehyde (61 g.) in a solution of sodium (11·5 g.) in alcohol (200 c.c.), *iso*propyl bromide (61·5 g.) was added and the mixture refluxed for 5 hours. The residue obtained by removal of the solvent was taken up in ether, washed with dilute sodium hydroxide solution, dried, and distilled, to give an oil (43 g.), b. p. 110—113°/2 mm. (Found: C, 73·6; H, 7·45. $C_{10}H_{12}O_2$ requires C, 73·2; H, 7·3%).

m-*Methoxy*-α-*phenylcinnamic Acid.*—(*a*) Sodium phenylacetate (102 g.), *m*-methoxybenzaldehyde (88 g.), and glacial acetic acid (500 c.c.) were heated under reflux at 160° for 6 hours [cf. Solmmsen's procedure (*loc. cit.*) for the analogous preparation using sodium *p*-methoxyphenylacetate]. The product was worked up by pouring it into water and the oil was isolated. The aqueous portion was acidified and gave phenylacetic acid. The oily layer was digested with sodium carbonate solution and extracted with ether. Acidification of the aqueous alkaline portion gave phenylacetic acid as the sole acidic product, and from the ethereal solution *m*-methoxybenzaldehyde was obtained by drying, evaporation, and distillation.

(*b*) Sodium phenylacetate (15·8 g.), *m*-methoxybenzaldehyde (13·6 g.), anhydrous sodium carbonate (5 g.), pyridine (0·5 c.c.), and acetic anhydride (10·6 c.c.) were heated for 2 hours at 180°. The cooled product was diluted with water (300 c.c.), made alkaline with sodium hydroxide (30 c.c.; 6N.), and digested on the water-bath for 30 minutes (cf. the procedure given in "Organic Reactions," Vol. II, p. 262, for the preparation of α-phenylcinnamic acid). The mixture was cooled and extracted with ether and the alkaline layer acidified with dilute hydrochloric acid. The acid product obtained was washed with alcohol and dissolved in sodium carbonate, and the sodium carbonate solution acidified with dilute hydrochloric acid to give a white crystalline product (5 g.), m. p. 191—192° (from ethyl alcohol) (Found: C, 75·0; H, 5·8. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·5%).

(*c*) *m*-Methoxybenzaldehyde (30 g.), sodium phenylacetate (25·2 g.), acetic anhydride (34 g.), and pyridine (1 c.c.) were refluxed for 8 hours at 160—170°. On working up of the product as in (*b*) above, the acid (20 g.), m. p. 191—192°, was obtained [this method involved using an excess of the aldehyde and was based on the procedure of Bacharach and Brogan (*J. Amer. Chem. Soc.*, 1928, **50**, 3533) for the preparation of cinnamic acid].

m-iso*Propoxy*-α-*phenylcinnamic Acid.*—*iso*Propoxybenzaldehyde (41 g.), sodium phenylacetate (40 g.), acetic anhydride (150 c.c.), and pyridine (1 c.c.) were heated under reflux for 5 hours at 150—160°. The product was cooled somewhat, diluted with water (200 c.c.), boiled for 10 minutes, diluted with more water (200 c.c.) and thoroughly cooled. A white crystalline mass was formed which was soluble in hot, but insoluble in cold, alkali; acidification of its aqueous solution gave a crude *acid* which was washed with cold alcohol (100 c.c.) and finally crystallised from hot alcohol (400 c.c.) to give pale yellow needles (38 g.), m. p. 159° (Found: C, 76·5; H, 5·8. $C_{18}H_{18}O_3$ requires C, 76·6; H, 6·4%).

m-*Benzyloxy-α-phenylcinnamic Acid.*—*m*-Benzyloxybenzaldehyde (Rapson and Robinson, *J.*, 1935, 1533) (21·2 g.), sodium phenylacetate (15·8 g.), acetic anhydride (200 c.c.), and pyridine (1 c.c.), heated at 150—160° for 5 hours, gave an *acid* (19 g.), m.p. 181—182° (Found: C, 80·2; H, 5·5. $C_{22}H_{18}O_3$ requires C, 80·0; H, 5·5%).

m-*Hydroxy-α-phenylcinnamic Acid.*—*m*-Hydroxybenzaldehyde (24·4 g.), sodium phenylacetate (31·6 g.), acetic anhydride (130 c.c.), and pyridine (0·5 c.c.) were refluxed for 8 hours at 150—160°. The mixture was cooled somewhat, diluted with water (200 c.c.), and digested on the water-bath for 10 minutes. When thoroughly cooled, a solid product was filtered off and digested with sodium hydroxide solution for 30 minutes. A crude *acid* was obtained by acidification, dissolved in sodium carbonate solution, treated with charcoal, and acidified to give needles (28 g.), m. p. 187—188° (Found: C, 74·5; H, 5·3. $C_{15}H_{12}O_3$ requires C, 75·0; H, 5·0%).

α-Phenyl-β-m-*methoxyphenylpropionic Acid.*—A solution of *m*-methoxy-α-phenylcinnamic acid (19 g.) in dilute sodium carbonate solution was made just alkaline to phenolphthalein. When this was shaken with hydrogen at room temperature and pressure in presence of Raney nickel (5 g.), the theoretical amount of hydrogen was absorbed. Removal of the catalyst and acidification gave an oil (19 g.), a portion of which was purified for analysis by high-vacuum distillation, having b. p. 190—200°/0·4—0·6 mm. (Found: C, 74·8; H, 6·4. $C_{18}H_{16}O_3$ requires C, 75·0; H, 6·25%).

α-Phenyl-β-m-iso*propoxyphenylpropionic Acid.*—*m-iso*Propoxy-α-phenylcinnamic acid was hydrogenated as in the previous hydrogenation and gave prisms, m. p. 86°, from alcohol (Found: C, 76·0; H, 7·2. $C_{18}H_{20}O_3$ requires C, 76·0; H, 7·1%).

α-Phenyl-β-m-*benzyloxyphenylpropionic Acid.*—α-Phenyl-*β-m*-benzyloxyphenylcinnamic acid, hydrogenated as above, absorbed two moles of hydrogen and the product contained benzyl alcohol and an acidic oil, b. p. 150—153°/0·1 mm. (Found: C, 74·4; H, 5·9. $C_{15}H_{14}O_3$ requires C, 74·4; H, 5·8%). After a long time, the oil solidified to needles m. p. 75°, identical with *α-phenyl-β*-m-*hydroxyphenylpropionic acid* obtained by hydrogenation, in a like manner, of *m*-hydroxy-α-phenylcinnamic acid. The propionic acid (20 g.) in alcohol (50 c.c.) was added to a solution of sodium (3·8 g.) in absolute alcohol (50 c.c.). Benzyl bromide (27·2 g.) was added and the mixture refluxed for 5 hours. The mixture was diluted with water, made alkaline with sodium hydroxide solution (40 c.c.; 10%), and digested on the water-bath for 2 hours. The product was taken up in ether, and the alkaline layer was separated and acidified to give an oil which was crystallised from methyl alcohol to give needles (12 g.), m. p. 111—112° (Found: C, 79·1; H, 5·6. $C_{22}H_{20}O_3$ requires C, 79·5; H, 6·0%).

5-*Methoxy-2-phenylindanone.*—α-Phenyl-*β-m*-methoxyphenylpropionic acid (19 g.) in dry ether (100 c.c.) containing pyridine (3 drops), and thionyl chloride (10 g.) were warmed on the water-bath for 30 minutes. The solution was evaporated to dryness under reduced pressure, thrice treated with dry benzene (50 c.c.), and evaporated to dryness after each addition. The residue was dissolved in dry benzene (100 c.c.), and the solution cooled to 5° and treated with a solution of stannic chloride (22 g.) in benzene (25 c.c.). After 90 minutes with intermittent shaking, the product was worked up by pouring it on ice and extraction in ether. The ethereal solution was washed successively with dilute hydrochloric acid, water, and sodium carbonate solution, dried (Na_2CO_3), and evaporated, to give an oil which crystallised from alcohol in small needles (12 g.), m. p. 115° (Found: C, 80·1; H, 5·9. $C_{16}H_{14}O_2$ requires C, 80·6; H, 5·9%). The 2 : 4-*dinitrophenylhydrazone* formed orange-red needles, m. p. 236°, from alcohol (Found: C, 63·1; H, 4·2; N, 14·4. $C_{22}H_{18}O_5N_4$ requires C, 63·0; H, 4·3; N, 13·4%).

5-iso*Propoxy-2-phenylindanone.*—Reaction as in the preceding paragraph gave this *ketone* as prisms (14 g.), m. p. 124—125° (Found: C, 81·0; H, 7·2. $C_{18}H_{18}O_2$ requires C, 81·3; H, 6·8%). The 2 : 4-*dinitrophenylhydrazone* formed orange-red plates, m. p. 227—228°, from aqueous alcohol (Found: N, 12·0. $C_{24}H_{22}O_5N_4$ requires N, 12·6%).

6-*Methoxy-2-phenyl-3-methylindene.*—5-Methoxy-2-phenylindanone (8 g.) in toluene (100 c.c.) was added to methylmagnesium iodide prepared from methyl iodide (9·6 g.), magnesium (1·6 g.), and ether (50 c.c.). The same procedure was used as in the previously described Grignard reactions and the *indene* was obtained as needles (8 g.), m. p. 98—99° (from alcohol) (Found: C, 86·7; H, 6·9. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8%).

6-iso*Propoxy-2-phenyl-3-methylindene.*—5-*iso*Propoxy-2-phenylindanone (2 g.) similarly gave this *indene* as plates (2 g.), m. p. 86° (from alcohol) (Found: C, 85·6; H, 7·2. $C_{19}H_{20}O$ requires C, 86·4; H, 7·6%).

6-iso*Propoxy-2-phenyl*-3-p-*methoxyphenylindene.*—Prepared similarly, this *indene* was obtained as needles (1·4 g.), m. p. 145—146° (from alcohol) (Found: C, 83·7; H, 6·9. $C_{25}H_{24}O_2$ requires C, 84·3; H, 6·7%).

Attempted Cyclisation of α-Phenyl-β-m-*benzyloxyphenylpropionic Acid.*—(*a*) By the technique used in the previous cyclisations, α-phenyl-*β-m*-benzyloxyphenylpropionic acid (4·5 g.) was converted into the acid chloride [by thionyl chloride (2 g.)] and treated in cold benzene with stannic chloride (5 g.). When worked up as before, the non-acidic fraction (4 g.) consisted of a gum containing benzyl chloride and no ketonic derivatives could be prepared. The alkali-soluble fraction (0·2 g.) was divided into two portions, one which was soluble in aqueous sodium carbonate and the other in aqueous sodium hydroxide. The former on long storage in aqueous-alcoholic solution afforded α-phenyl-*β-m*-hydroxyphenylpropionic acid, m. p. and mixed m. p. 75°. The latter gave rise to an unidentified 2 : 4-dinitrophenylhydrazone, m. p. 192° (darkens at 140°) (crystallised from aqueous alcohol) (Found: C, 58·2; H, 4·4; N, 14·2. $C_{21}H_{16}O_5N_4$ requires C, 62·4; H, 4·0; N, 13·9%).

(*b*) α-Phenyl-*β-m*-benzyloxyphenylpropionic acid (1 g.), phosphoric oxide (2 g.), and benzene (50 c.c.), heated on the water-bath for 1 hour, gave a non-acidic gum from which no ketonic derivative could be prepared.

(*c*) The acid (1 g.) was slowly added to concentrated sulphuric acid (2 c.c.) at −5° and stirred for 30 minutes, the temperature being kept below 0°. The mixture was poured on ice and the acid extracted with sodium carbonate solution. None of the starting material was recovered and the oily acid obtained slowly crystallised after 2 weeks. The m. p. and mixed m. p. identified the product as *m*-hydroxy-α-phenylcinnamic acid.

Attempts to Dealkylate 6-Alkoxyindenes.—(*a*) 6-Methoxy-2-phenyl-3-methylindene (1 g.), glacial acetic acid (15 c.c.), and acetyl iodide (3 c.c.) containing 12% of hydrogen iodide, heated under reflux for 5 minutes, afforded only gums and none of the original indene was recovered. A similar result was observed when the 6-*iso*propoxyindene was used and when either indene was treated in a similar manner on the water-bath.

(*b*) The 6-methoxyindene (0·5 g.), glacial acetic acid (10 c.c.), acetic anhydride (1 c.c.), and 50% hydrogen bromide in acetic acid (2 c.c.) were refluxed for 10 minutes. The mixture was cooled and poured on ice. A crystalline product was obtained which was washed with water and boiled with aqueous alkali for 30 minutes. The alkali-soluble fraction crystallised as pale greenish-brown needles (5 mg.), m. p. 152—153°. Analysis indicated that this compound was probably the impure 6-indenol (Found: C, 82·7; H, 6·7. Calc. for $C_{16}H_{14}O$: C, 86·5; H, 6·3%). From the neutral fraction the 6-methoxyindene (0·48 g.) was obtained by crystallisation from aqueous alcohol.

(*c*) The 6-*iso*propoxyindene was treated as in (*b*); no phenolic product was isolated though a faint turbidity was observed when the alkaline extract was acidified.

When a longer time of heating was used neither the 6-methoxy- nor the 6-*iso*propoxy-indene was recovered and no phenolic product was obtained.

(*d*) A solution was prepared by mixing hydrogen bromide in acetic acid (15 c.c. of 50%) with acetic acid (70 c.c.) and water (15 c.c.). This solution (20 c.c.) was used in the dealkylation experiments shown in the table below. The indene (1 g.) was heated under reflux in an atmosphere of nitrogen and then separated into phenolic and neutral fractions by dilution with water and extraction with sodium hydroxide.

Indene.	Reflux time, hours.	Phenolic fraction, mg.	Neutral fraction, mg.	M. p. of phenolic fraction.
6-Methoxy-	1	Only turbid (*ca.* 2 mg.)	950	—
6-*iso*Propoxy-	1	20	900	148—149°
6-Methoxy-	4	110	800	148
6-*iso*Propoxy-	4	460	200	147—148

The phenolic fractions were combined and crystallised from aqueous alcohol to give a pale buff-coloured powder, m. p. 154—155° (Found: C, 86·4; H, 6·3. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). The respective neutral fractions from these experiments, with the exception of the last, were shown to be the original 6-alkoxyindenes. In the last experiment only, an oil was obtained from the neutral fraction.

Dealkylation of 6-iso*Propoxy-2-phenyl-3-p-methoxyphenylindene.*—The indene (0·5 g.) was heated under reflux with the hydrogen bromide solution (3 c.c.) for 4 hours and the product isolated as before. The crude phenolic fraction (0·35 g.) was a buff-coloured solid and was purified by percolation in ether–benzene through a column of alumina. Elution with benzene–alcohol was necessary and the product was finally obtained as a buff-orange powder (0·25 g.), m. p. 225—230°, from aqueous alcohol (Found: C, 83·7; H, 5·5. $C_{21}H_{16}O_2$ requires C, 84·0; H, 5·3%). Dealkylation was incomplete (Found: OMe, 1·3. $C_{22}H_{18}O_2$ requires OMe, 9·8%).

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