570. *Compounds of Potential Pharmacological Interest. Part IV.* Aryl and Alkyl Derivatives of 1-Aminoindane.*

By J. A. Barltrop, R. M. Acheson, P. G. Philpott, K. E. MacPhee, and J. S. Hunt.

A number of aryl and alkyl derivatives of 1-aminoindane have been synthesised by the routes shown in the flow-sheet; pharmacological tests are briefly recorded. The cyclisation of β-*p*-methoxyphenyl-β-phenylpropionic acid has been shown to lead to 3-*p*-methoxyphenylindan-1-one (XVII), and not 6-methoxy-3-phenylindan-1-one (XVIII) as suggested by Pfeiffer and Roos.[1]

The reasoning which led us to synthesise phenylindanylamines for pharmacological testing was developed from the following considerations: (i) aminoindanes had been shown [2] to be pharmacologically active; (ii) the diphenylmethyl grouping is an essential feature of a number of pharmacologically active compounds, *e.g.*, amidone (IX), trasentin, benadryl, and Hoechst 10166 (see Adamson [3]); (iii) the amino-3-phenylindanes (III; $R^1 = R^3 = H$, $R^2 = Ph$), while combining the structural features mentioned in (i) and (ii), are ring-closed modifications of the amidone (IX) molecule.

1-Dimethylamino-3-phenylindane was found to be a potent analgesic when tested in rats. In subsequent clinical trials, it was no better than codeine, and sometimes induced untoward gastrointestinal effects. It therefore became important to synthesise modifications in the hope that the analgesic activity could be increased relatively to the tendency to produce side-effects. Some of these modifications have already been described in

* Part III, *J.*, 1956, 706.

[1] Pfeiffer and Roos, *J. prakt. Chem.*, 1941, **159**, 13.

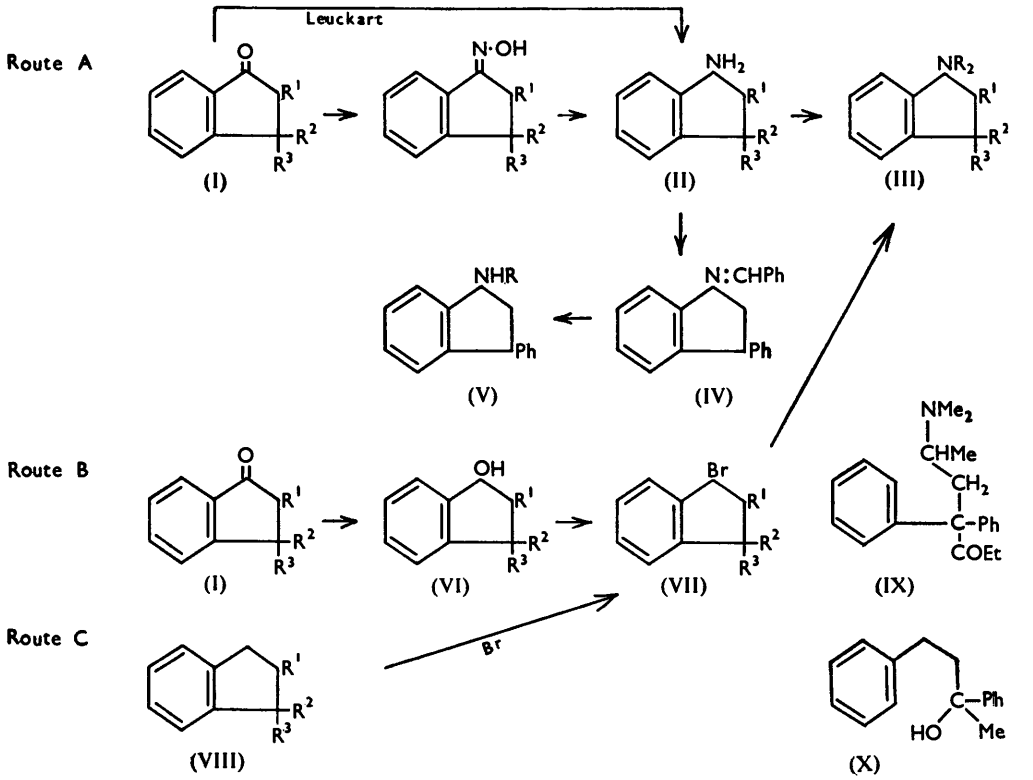
[2] Bry, *Z. exp. Path.*, 1914, **16**, 186; von Braun *et al.*, *Ber.*, 1916, **49**, 2642; 1917, **50**, 56; Levin, Graham, and Kolloff, *J. Org. Chem.*, 1944, **9**, 380; Hofmann and Schellenberg, *Helv. Chim. Acta*, 1944, **27**, 1782.

[3] Adamson, *J.*, 1949, S 144.

Parts I and II of this series. This paper is primarily concerned with the parent 1-dimethylamino-3-phenylindane and related alkyl- and aryl-indanes.

3-Phenylindan-1-one (I; $R^1 = R^3 = H$, $R^2 = Ph$), conveniently prepared [4] by condensing benzene and cinnamic acid, was subjected to the Ingersoll [5] modification of the Leuckart [6] reaction. It was found that at the minimum temperature necessary for reaction, extensive charring of the ketone occurred and the yield of the amine (II; $R^1 = R^3 = H$, $R^2 = Ph$) was only 22%. Hydrogenation of the oxime, under precisely defined conditions, afforded this amine in 85% yield and thus the substance became readily available in quantity.

Methylation of the primary amine with formic acid and formaldehyde gave 1-dimethylamino-3-phenylindane (III; $R = Me$, $R^1 = R^3 = H$, $R^2 = Ph$), but the 1-methylamino-derivative (V; $R = Me$) could only be prepared through the benzylidene derivative (IV), by treatment with methyl sulphate and then hydrolysis. Reduction of the imine (IV) gave 1-benzylamino-3-phenylindane (V; $R = Ph{\cdot}CH_2$). 1-Diethylamino-3-phenylindane (III; $R = Et$, $R^1 = R^3 = H$, $R^2 = Ph$) which was also required for pharmacological testing, was obtained in only 27% yield by alkylating the primary amine with ethyl iodide, and this result emphasised the fact that the primary amine was not a very suitable intermediate for the preparation of the substituted bases. At this point, the second route to compounds of this series was devised.



3-Phenylindan-1-ol (VI; $R^1 = R^3 = H$, $R^2 = Ph$), obtained in 95% yield by reducing the ketone (I; $R^1 = R^3 = H$, $R^2 = Ph$) with lithium aluminium hydride, was converted quantitatively into the bromide (VII; $R^1 = R^3 = H$, $R^2 = Ph$) by hydrogen bromide in

[4] (*a*) Pfeiffer and de Waal, *Annalen*, 1935, **520**, 185; (*b*) Koelsch, Hochmann, and Le Claire, *J. Amer. Chem. Soc.*, 1943, **65**, 59.
[5] Ingersoll, *J. Amer. Chem. Soc.*, 1936, **58**, 1808.
[6] Leuckart and Janssen, *Ber.*, 1889, **22**, 1409.

benzene. Condensation with the appropriate amines now gave 1-diethylamino-3-phenylindane in 45% yield, and 1-dimethylamino-3-phenylindane, identical with specimens obtained by Route A.

Since many of the most potent analgesics have, gamma to the nitrogen atom, a quaternary carbon atom which is lacking in the above compounds, it was felt to be worthwhile linking alkyl groups to $C_{(3)}$ of the phenylindanylamine system.

The first compounds selected for investigation were of the type (III; $R^1 = H$, $R^2 = Ph$, $R^3 = Me$). The 3-methyl-3-phenylindan-1-one (I; $R^1 = H$, $R^2 = Ph$, $R^3 = Me$) required as a starting material was prepared [4b] by condensing a mixture of β-chlorocrotonic and β-chloro*iso*crotonic acid (modified preparation) with benzene to give ββ-diphenylbutyric acid, which was then cyclised. Very variable yields were encountered in the preparation of the ββ-diphenylbutyric acid and on occasion as much as 50% of β-phenylbutyric acid was obtained as by product, showing that, during the reaction, a proton rather than a phenyl group is attached to the β-position. Hydrogen transfers of this type appear to be a general feature of such reactions.[7]

An alternative route to the diphenylbutyric acid was sought in the reaction sequence:

(XI) $CPh_2Me\cdot COMe \longrightarrow CPh_2Me\cdot CO\cdot CH_2X \longrightarrow CPh_2Me\cdot CH_2\cdot CO_2Me$ (XII)

The readily available 3 : 3-diphenylbutan-2-one [8] (XI) was both chlorinated and brominated, and then treated with sodium methoxide in order to effect rearrangement to the ester [9] (XII), but no product was isolated.

The ketone (I; $R^1 = H$, $R^2 = Ph$, $R^3 = Me$) was converted into 3-dimethylamino-1-methyl-1-phenylindane hydrochloride (as III; $R = R^3 = Me$, $R^1 = H$, $R^2 = Ph$) *via* route A and also reduced with lithium aluminium hydride, giving apparently a mixture of *cis*- and *trans*-forms of the alcohol (VI; $R^1 = H$, $R^2 = Ph$, $R^3 = Me$). One of these forms was obtained pure, but reaction with hydrogen bromide and then with dimethylamine gave two isomeric (presumably *cis* and *trans*) modifications of the amine (III; $R = R^3 = Me$, $R^1 = H$, $R^2 = Ph$), one of which was identical with the specimen prepared by route A. In view of what is now known of the stereochemistry of halide ion–alkyl halide exchange reactions and of the stereochemistry of carbonium ions, this result is not unexpected. The diethylamino- and morpholino-derivatives of (III; $R^1 = H$, $R^2 = Ph$, $R^3 = Me$) were also prepared by route B.

As a result of other investigations, yet another route to 3-dimethylamino-1-methyl-1-phenylindane was devised. The alcohol [10] (X), cyclised with 85% sulphuric acid, gave a product shown to be 1-methyl-1-phenylindane (VIII; $R^1 = H$, $R^2 = Ph$, $R^3 = Me$) and not the isomeric 1 : 2 : 3 : 4-tetrahydro-2-phenylnaphthalene, because of the identity of its infrared spectrum with that of an authentic specimen of the indane synthesised by Clemmensen reduction of 3-methyl-3-phenylindan-1-one. Bromination of the hydrocarbon, followed by treatment with dimethylamine, gave 3-dimethylamino-1-methyl-1-phenylindane (III; $R = R^3 = Me$, $R^1 = H$, $R^2 = Ph$) identical with one of the isomers described above. This observation affords further evidence for the formulation of the cyclised hydrocarbon as an indane.

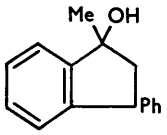
Methylmagnesium iodide and 3-phenylindan-1-one gave the alcohol (XIII) from which was obtained, through the bromide, 1-dimethylamino-1-methyl-3-phenylindane (XIV) accompanied by large amounts of 1-methyl-3-phenylindene.

Cyclisation of α-methyl-ββ-diphenylpropionic acid gave 2-methyl-3-phenylindan-1-one (I; $R^1 = Me$, $R^2 = Ph$, $R^3 = H$), from which 1-dimethylamino-2-methyl-3-phenylindane (III; $R = R^1 = Me$, $R^2 = Ph$, $R^3 = H$) was obtained by route B.

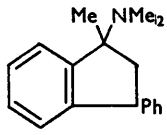
Two phenylindanylamines bearing methoxyl substituents were also synthesised. β-*m*-Methoxyphenyl-β-phenylpropionic acid, prepared from *m*-methoxycinnamic acid and

[7] Blum-Bergmann, *J.*, 1938, 725.
[8] Ramart-Lucas and Salmon-Legagneur, *Bull. Soc. chim. France*, 1929, **45**, 718; Sisido and Nozaki, *J. Amer. Chem. Soc.*, 1948, **70**, 776.
[9] Cf. McPhee and Klingsberg, *J. Amer. Chem. Soc.*, 1944, **66**, 1132.
[10] Stoermer and Kootz, *Ber.*, 1928, **61**, 2330.

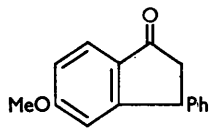
benzene in the presence of aluminium chloride, was cyclised with polyphosphoric acid to 5-methoxy-3-phenylindan-1-one (XV). The formulation of this compound as the 5-methoxy- rather than the 7-methoxy-derivative follows by analogy with many examples



(XIII)

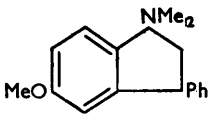


(XIV)

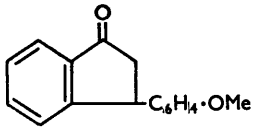


(XV)

in the literature, and in particular from the formation [11] of 5-methoxyindan-1-one from β-*m*-methoxyphenylpropionic acid. The transformation of this ketone into 1-dimethylamino-5-methoxy-3-phenylindane (XVI) was effected through the indanol and the corresponding bromide.



(XVI)



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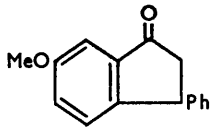
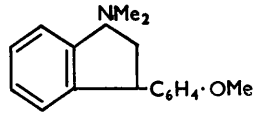


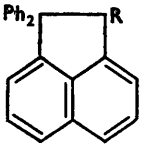
(XVIII)



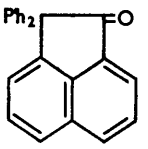
(XIX)

The other isomer (XIX) was prepared from β-*p*-methoxyphenyl-β-phenylpropionic acid. Cyclisation gave a ketone to which Pfeiffer and Roos [1] ascribed the structure (XVIII). This seemed improbable since the inductive effect of the methoxyl group would be expected to deactivate the position *meta* with respect to it, by comparison with an unsubstituted benzene ring. We were therefore of the opinion that the indanone had the structure (XVII) and proved the point by oxidative degradation to 2-*p*-methoxybenzoylbenzoic acid. The indanone was converted into 1-dimethylamino-3-*p*-methoxyphenylindane (XIX), by route B.

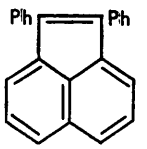
An attempt to prepare the diphenylacenaphthenylamines (XX; R = NR_2) failed (*a*) because it was found to be impossible to prepare the oxime of 2 : 2-diphenylacenaphthenone (XXI) which was required for reduction, and (*b*) because 2 : 2-diphenylacenaphthen-1-ol (XX; R = OH), prepared from the ketone (XXI) by reduction with lithium aluminium hydride, on attempted conversion into the bromide for reaction with dimethylamine, underwent a Wagner–Meerwein rearrangement with the formation of 1 : 2-diphenylacenaphthylene (XXII).



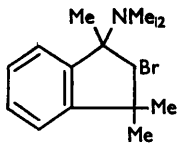
(XX)



(XXI)



(XXII)



(XXIII)

3-Methylindan-1-one [4b] (I; $R^1 = R^3 = H$, $R^2 = Me$) was converted by route B into 1-dimethylamino-3-methylindane (III; R = R^2 = Me, $R^1 = R^3 = H$) and 1-methyl-3-morpholinoindane (III; $R^1 = R^3 = H$, R^2 = Me, NR_2 = morpholino). 3-Ethylindan-1-one (I; $R^1 = R^3 = H$, R^2 = Et) was prepared according to the scheme :

Ph·COEt ⟶ HO·CPhEt·CH_2·CO_2·Et ⟶ CPhEt:CH·CO_2R ⟶ CHPhEt·CH_2·CO_2R

(XXIV) (XXV) (XXVI)

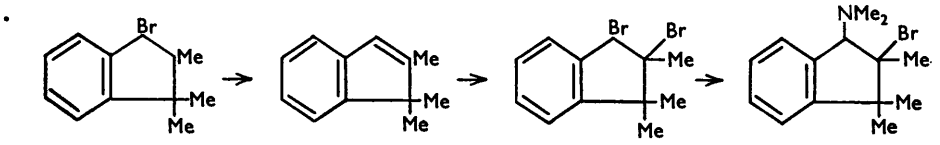
A Reformatsky reaction between ethyl bromoacetate and propiophenone gave ethyl β-hydroxy-β-phenylvalerate (XXIV) which was dehydrated to the pentenoic ester (XXV;

[11] Von Auwers and Hillinger, *Ber.*, 1916, **49**, 2410.

R = Et) and then hydrogenated and hydrolysed to β-phenylvaleric acid (XXVI; R = H). Cyclisation of the corresponding acid chloride gave only a 20% yield of 3-ethylindan-1-one, whilst use of polyphosphoric acid [12] gave a 91% yield. The superiority of polyphosphoric acid as a cyclising agent seems to hold generally throughout this series. The 3-ethylindanone was converted by route B into the tertiary amines (III; $R^1 = R^3 = H$, $R^2 = Et$, R = Me and NR_2 = morpholino).

By similar methods, *cyclo*hexyl phenyl ketone was converted into 3-*cyclo*hexylindan-1-one and thence into 1-dimethylamino-3-*cyclo*hexylindane (III; $R^1 = R^3 = H$, R^2 = *cyclo*hexyl, R = Me). Similarly prepared were 2 : 3-dimethyl- and 2 : 3-diethyl-indan-1-one and hence the bases (III; R = $R^1 = R^2$ = Me, R^3 = H, and R = Me, $R^1 = R^2$ = Et, R^3 = H).

3-Dimethylamino-1 : 1-dimethylindane (III; R = $R^2 = R^3$ = Me, R^1 = H was synthesised by route C, by converting 1 : 1-dimethylindane into the 3-bromo-derivative and condensing this with dimethylamine. When 1 : 1 : 2-trimethylindane was subjected to the same procedure, the small quantity of basic material isolated still contained a bromine atom and probably possesses the structure (XXVII). We visualise this substance as arising from the bromotrimethylindane by the annexed reaction sequence. This formulation is



(XXVII)

supported by the isolation from the reaction mixture of a neutral unsaturated fraction, which apparently consisted largely of trimethylindene since on hydrogenation it afforded the initial trimethylindane.

Benzene was added to mesityl oxide by Hoffman's method [13] to give 4-methyl-4-phenylpentan-2-one, which was reduced to the alcohol with lithium aluminium hydride and cyclised to 1 : 1 : 3-trimethylindane. Bromination followed by treatment with dimethylamine gave a small yield of brominated base, which, from the considerations advanced previously, probably possesses the structure (XXIII). A large amount of 1 : 3 : 3-trimethylindene was formed at the same time.

Through the courtesy of Dr. G. E. Ullyot, these compounds were examined pharmacologically by Smith, Kline, and French Laboratories, Philadelphia, U.S.A., with the results shown in Table 1.

TABLE 1.

Substituents in 3-phenylindane	Analgesia in rats (d'Amour–Smith method)	Antihistaminic activity [c]	Anticonvulsant activity (Metrazole treatment in mice)	Hypotensive activity (in anæsthetised cats and dogs)	Antispasmodic activity [d]
1-Amino-	—	—	—		+
1-Dimethylamino-	+ [a]	slight	—	+	
1-Diethylamino-	+ [b]				
1-Dimethylamino-2-methyl- (isomer A)	+ [b]	+		+	
,, ,, (isomer B)	+ [b]	—			
1-Amino-3-methyl	—			+	

3-Dimethylamino-1-methyl- (both isomers), 3-diethylamino-1-methyl-, and 1-methyl-3-morpholino-1-phenylindane showed no analgesic activity.

[a] Doses of 10 mg./kg., orally or intraperitoneally, produced complete analgesia. [b] Activity less than that of codeine. [c] Tested against experimental asthma induced in guinea pigs by aerosolised histamine. [d] Tested against histamine-induced spasm in guinea-pig intestine.

It is interesting that none of the compounds having a quarternary carbon atom was active analgesically. The alkylindanes lacking a phenyl substituent showed no significant pharmacological activity, with the exception of 1-methyl-3-morpholinoindane which possessed some anticonvulsant and muscle-relaxant properties and prolonged the duration of evipal anæsthesia.

[12] Gilmore and Horton, *J. Amer. Chem. Soc.*, 1951, **73**, 1411.
[13] Hoffman, *ibid.*, 1929, **51**, 2542.

Experimental

1-Amino-3-phenylindane.—(*A*) 3-Phenylindan-1-one (4·2 g.) and ammonium formate (3·8 g.) were heated in an oil-bath at 170—180° for 3 hr. When cold, the black solid was washed with water to remove all but unchanged ketone and substituted formamide. The residue was boiled with concentrated hydrochloric acid for 2 hr. and the solution diluted and filtered. On evaporation, colourless needles of 1-amino-3-phenylindane hydrochloride (1 g., 22%) were obtained. Recrystallisation from wet dioxan gave needles, m. p. 225° (decomp.), identical with other specimens described below.

(*B*) A solution of 1-hydroxyimino-3-phenylindane (4·3 g.) in ethanol (100 c.c.), saturated with ammonia, was hydrogenated at 100 atm. and room temperature, in the presence of freshly prepared Raney nickel (0·5 g.). When two mols. of hydrogen had been taken up (4 hr.) the solution was filtered and evaporated *in vacuo*, and the residual oil taken up in ether, dried, and treated with dry hydrogen chloride. *1-Amino-3-phenylindane hydrochloride* (4 g., 84·7%) was precipitated and collected. Two recrystallisations from wet dioxan gave needles, m. p. 225° (decomp.) (Found: C, 72·4; H, 6·6; N, 5·4; Cl, 13·6. $C_{15}H_{15}N$,HCl requires C, 73·3; H, 6·5; N, 5·7; Cl, 14·5%).

When the same catalyst, and the conditions suggested by Paul,[14] *i.e.*, 85°/64 atm., were used with no ammonia present, the yield dropped to 36%, and the solution after reduction smelt strongly of ammonia.

1-Dimethylamino-3-phenylindane.—1-Amino-3-phenylindane hydrochloride (3·3 g.) was converted into the free base and heated on the steam-bath with formic acid (2 g.) and 40% aqueous formaldehyde (3 c.c.). When carbon dioxide evolution had ceased (2½ hr.), the mixture was boiled under reflux for 5 min., cooled, basified with potassium hydroxide solution, and extracted with ether. The residue from the dried extracts was dissolved in dilute hydrochloric acid and treated with nitrous acid to destroy any primary or secondary amines. The solution was washed with ether, basified, and extracted with ether. On passage of dry hydrogen chloride through the cooled dried extracts, an orange gum was precipitated which was dried *in vacuo* over sodium hydroxide. *1-Dimethylamino-3-phenylindane hydrochloride* (3·0 g., 81%), after two recrystallisations from ethanol, yielded rhombs, m. p. 190° (Found: C, 74·2; H, 7·5; N, 4·9. $C_{17}H_{19}N$,HCl requires C, 74·6; H, 7·3; N, 5·1%). The compound is identical with that described in Table 3.

1-Benzylideneamino-3-phenylindane.—1-Amino-3-phenylindane (3 g.) and benzaldehyde (1·53 g.) were heated at 100°/150 mm. A little benzaldehyde distilled over in the steam but this was separated from the water and replaced. The product, a brown gum, was dried *in vacuo* and triturated with ligroin. *1-Benzylideneamino-3-phenylindane* (4 g., 93%), after three recrystallisations from ligroin, was obtained as a cream-coloured solid, m. p. 95·5—96·5° (Found: C, 88·45; H, 6·35; N, 4·5. $C_{22}H_{19}N$ requires C, 88·9; H, 6·4; N, 4·7%).

1-Methylamino-3-phenylindane.—Dimethyl sulphate (2 g.) and 1-benzylideneamino-3-phenylindane (4 g.) were boiled in dry toluene (40 c.c.) for 1½ hr., during which considerable darkening occurred. On cooling, a heavy dark oil separated which was washed with dry toluene and then warmed with water (20 c.c.) to decompose the anil. After being washed with ether, the aqueous solution was basified and extracted with ether, and the extracts were dried. *1-Methylamino-3-phenylindane hydrochloride* (2 g., 58%) was precipitated by dry hydrogen chloride as a red gum. Two recrystallisations from ethyl acetate–ethanol yielded needles, m. p. 230° (Found: C, 73·9; H, 7·1; N, 5·3. $C_{16}H_{17}N$,HCl requires C, 74·0; H, 6·9; N, 5·4%).

1-Benzylamino-3-phenylindane.—A solution of 1-benzylideneamino-3-phenylindane (7·2 g.) in ethanol (100 c.c.) was hydrogenated, at 1 atm. and room temperature, over Adams catalyst (0·32 g.). The reaction was complete in 1 hr. The solution was filtered and evaporated *in vacuo*, and the residual gum dissolved in dry ether. *1-Benzylamino-3-phenylindane hydrochloride* (7·0 g. 86%) was precipitated by dry hydrogen chloride as a sticky white solid, which was collected and dried *in vacuo* over sodium hydroxide. Crystallisation from ethyl acetate–ethanol yielded needles, m. p. 206·5—207·5° (Found: C, 78·1; H, 6·6; N, 4·2. $C_{22}H_{21}N$,HCl requires C, 78·7; H, 6·6; N, 4·2%).

1-Diethylamino-3-phenylindane.—1-Amino-3-phenylindane hydrochloride (3·3 g.) was converted into the free base (2·8 g.), dissolved in dry acetone (40 c.c.), and refluxed with stirring for 5 hr. with ethyl iodide (8 g.) and anhydrous potassium carbonate (4 g.). The cooled solution was filtered and washed with a little dry acetone, and the combined filtrates were evaporated. The

[14] Paul, *Bull. Soc. chim. France*, 1937, **4**, 1125.

residual oil was taken up in dry ether, filtered, and treated with ethereal hydrogen chloride. The precipitated hydrochloride was dissolved in dilute hydrochloric acid, filtered, cooled to 0°, and treated with a cold solution of sodium nitrite. The solution was washed with ether and basified. The liberated tertiary amine was isolated with ether and converted into the hydrochloride. Crystallisation from ethyl acetate–ethanol gave 1-*diethylamino*-3-*phenylindane hydrochloride* (1·1 g., 27%) as rhombs, m. p. 181—183° (Found: C, 75·1; H, 8·0; N, 4·5; Cl, 11·7. $C_{19}H_{23}N$,HCl requires C, 75·6; H, 8·0; N, 4·6; Cl, 11·8%). The compound is identical with that described in Table 3.

β-*Chlorocrotonic and* β-*Chloro*iso*crotonic Acid.*—Acetoacetic ester (270 g.) was added dropwise to phosphorus pentachloride (830 g.) in a water-cooled flask during 3—4 hr. The mixture was set aside at room temperature for 1 hr. with occasional shaking. The flask was gently warmed to 50—54° until gas evolution ceased (1—2 hr.), cooled, and the red liquid was stirred dropwise into ice and water (6 l.). The red aqueous solution was extracted with benzene. The benzene extracts were filtered and extracted with concentrated sodium carbonate solution. The aqueous extract was filtered and acidified with concentrated hydrochloric acid, and the crystals which separated were collected and repeatedly extracted with hot water to separate the product from tar. The combined filtrates were extracted with ether and dried ($MgSO_4$). Evaporation of the ether gave a mixture of β-chlorocrotonic and β-chloro*iso*crotonic acid (120 g., 48%), as pale yellow needles. The product was considered sufficiently pure for the next preparation.

ββ-*Diphenylbutyric Acid.*—The above β-chloro-acids (50 g.) were condensed with benzene (550 c.c.) in the presence of aluminium chloride (180 g.), essentially as described by Koelsch, Hochmann, and Le Claire.[4b] Distillation gave ββ-diphenylbutyric acid (46 g., 46%) as a honey-coloured oil, b. p. 160—190°/0·26 mm., which solidified. A specimen recrystallised from aqueous ethanol formed needles, m. p. 101° (lit., 102—103°). β-Phenylbutyric acid (18 g., 26%) was recovered in the fore-run as a pale, yellow oil, b. p. 118—128°/0·22 mm. A specimen crystallised from ligroin in rhombs, m. p. 46—47° (lit., 47°) [amide, m. p. 105—107° (lit., m. p. 106—107°)].

3-*Amino*-1-*methyl*-1-*phenylindane.*—To a stirred solution of 3-hydroxyimino-1-methyl-1-phenylindane [4b] (5 g.) in a mixture of methanol (150 c.c.) and ethanol (135 c.c.) was added 3% sodium amalgam (150 g.) in small lumps during 1½ hr. The liquid was kept acid by addition of 30% acetic acid (70 c.c.). The solution was decanted from the mercury, the alcohol distilled under reduced pressure, and the residue boiled with water and filtered while hot. The cooled filtrate was basified, and the liberated amine was isolated with ether and converted into the hydrochloride. 3-*Amino*-1-*methyl*-1-*phenylindane hydrochloride* (3·55 g., 64·7%) crystallised from wet dioxan in irregular plates, m. p. 260° (Found: C, 73·6; H, 6·9; N, 5·3; Cl, 14·1. $C_{16}H_{17}N$,HCl requires C, 74·0; H, 6·9; N, 5·4; Cl, 13·7%).

1-*Methyl*-1-*phenylindane.*—(*A*) 2 : 4-Diphenylbutan-2-ol [10] (12 g.) was added during 30 min. to stirred 85% sulphuric acid (25 c.c.), the temperature being kept at 8—10°. Stirring was continued for a further hour at room temperature. The sticky mixture was extracted with olefin-free ligroin (3 × 50 c.c.), and the combined ligroin extracts were washed with concentrated sulphuric acid until the washings were colourless, and then with water, 5% sodium hydrogen carbonate solution, and water, and dried ($MgSO_4$). Distillation gave 1-*methyl*-1-*phenylindane* (3 g., 27%), b. p. 145—150°/12 mm., n_D^{20} 1·5848 (Found: C, 92·5; H, 7·7. $C_{16}H_{16}$ requires C, 92·3; H, 7·7%).

(*B*) Zinc turnings (50 g.) were amalgamated with a 5% solution of mercuric chloride (100 c.c.), treated with 3-methyl-3-phenylindan-1-one (5 g.) in glacial acetic acid (125 c.c.), and boiled under reflux. Concentrated hydrochloric acid (150 c.c.) was added dropwise during 2 hr. The cooled mixture was extracted with ligroin (3 × 30 c.c.) and the combined ligroin extracts were washed with water, 5% sodium hydrogen carbonate solution, and water and dried ($MgSO_4$). Distillation gave 1-methyl-1-phenylindane (3·8 g.), b. p. 145°/12 mm., n_D^{20} 1·5850. Kuhn–Roth determination under standard conditions gave no evidence of *C*-methyl. The infrared absorption suggested the presence of a *C*-methyl group and was identical with that of the hydrocarbon obtained from the cyclisation of 2 : 4-diphenylbutan-2-ol.

3-*Dimethylamino*-1-*methyl*-1-*phenylindane.*—(*A*) 3-Amino-1-methyl-1-phenylindane hydrochloride (3·5 g.) in aqueous solution was converted into the free base and heated on the steam-bath with formic acid (99—100%; 2 g.) and 40% aqueous formaldehyde (3 c.c.). When evolution of carbon dioxide had ceased (3 hr.), the solution was finally refluxed for 5 min., cooled, and basified. The white precipitate was isolated with ether and dissolved in dilute hydrochloric acid. The ice-cooled acid solution was treated with a solution of sodium nitrite. After being

washed with ether, the aqueous solution was basified and the liberated tertiary amine was isolated with ether and converted into a gummy hydrochloride. Two recrystallisations from ethanol gave *3-dimethylamino-1-methyl-1-phenylindane hydrochloride* (2·5 g., 64·5%) in rhombs, m. p. 229—230° (Found: C, 74·8; H, 7·6; N, 4·6; Cl, 12·1. $C_{18}H_{21}N$,HCl requires C, 75·1; H, 7·7; N, 4·9; Cl, 12·3%).

(*B*) Bromine (3·22 g.) in carbon tetrachloride (15 c.c.) was added to 1-methyl-1-phenylindane (4·2 g.) in ice-cold carbon tetrachloride (30 c.c.). When the colour was discharged (in a few minutes), the solvent was removed under reduced pressure and the residual oil dissolved in dry dioxan (20 c.c.) and allowed to react with anhydrous dimethylamine (5 g.) in a pressure-bottle. Reaction was allowed to proceed for 24 hr. at room temperature and then at 50° for a further 2 hr. After working up as described above, 3-dimethylamino-1-methyl-1-phenylindane hydrochloride (2 g.) was obtained from ethyl acetate–ethanol in colourless needles, m. p. 230° alone and when mixed with hydrochlorides of the same m. p. described above and in Table 3 (Found: C, 75·4; H, 7·9; N, 4·7%). Bromination of the indane was repeated in the presence of a trace of benzoyl peroxide, and the bromide condensed with dimethylamine in the above manner. Only the amine hydrochloride, m. p. 230°, was isolated.

1-Methyl-3-phenylindan-1-ol.—The Grignard reagent prepared from magnesium (1·3 g.) and methyl iodide (7·5 g.) was treated with a solution of 3-phenylindan-1-one (10·8 g.) in ether (50 c.c.) and heated under reflux for 1 hr. The solution was cooled and treated with saturated ammonium chloride solution. The ether layer was separated and the aqueous layer extracted with ether (3 × 30 c.c.). The combined ether extracts were washed with water, sodium hydrogen carbonate solution, and water and dried ($MgSO_4$). The solvent was removed and the residual oil triturated with ligroin till it was solid. *1-Methyl-3-phenylindan-1-ol* (6·5 g.) crystallised from ligroin in rhombs, m. p. 84—85° (Found: C, 85·4; H, 6·9. $C_{16}H_{16}O$ requires C, 85·7; H, 7·1%).

2-Methyl-3-phenylindan-1-one.—α-Methyl-ββ-diphenylpropionic acid (9 g.) and thionyl chloride (9 c.c.) were heated together under reflux for 1 hr. The excess of thionyl chloride was removed under reduced pressure and the residual oil was dissolved in dry benzene (100 c.c.) and chilled in an ice-bath. Powdered anhydrous aluminium chloride (6 g.) was added during 30 min. and the mixture was left for 12 hr. at room temperature. The complex was decomposed with ice and concentrated hydrochloric acid, and the benzene layer separated, washed with water, sodium hydrogen carbonate solution (no acid was recovered), and water, and then concentrated. The residual oil was distilled, to give *2-methyl-3-phenylindan-1-one* (7·1 g.), a pale yellow viscous oil, b. p. 140—145°/1 mm. (Found: C, 86·4; H, 6·1. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). The 2:4-dinitrophenylhydrazone crystallised from ethanol in brick-red plates, m. p. 183°. Burton and Shoppee [15] give m. p. 179°.

β-m-*Methoxyphenyl-β-phenylpropionic Acid.*—*m*-Methoxycinnamic acid (10 g.) was heated under reflux for 3½ hr. in dry benzene (100 c.c.) in the presence of powdered anhydrous aluminium chloride (20 g.). The cooled mixture was poured on ice and concentrated hydrochloric acid (40 c.c.), the layers were separated, and the aqueous layer was extracted with benzene. The combined benzene solutions were extracted with sodium carbonate solution, and β-m-*methoxyphenyl-β-phenylpropionic acid* was precipitated from the alkaline solution by acidification to Congo-red. The acid separated from aqueous acetic acid in crystals, m. p. 98—99° (10·25 g., 71%) (Found: C, 75·0; H, 6·3. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·2%). Attempts to prepare this acid under milder conditions using the same quantities at 15° or 25° for 4 days gave starting material only.

5-Methoxy-3-phenylindan-1-one.—A slurry of orthophosphoric acid (120 c.c.) and phosphoric oxide (180 g.) was heated at 100° for 2 hr., to give an almost clear solution, to which was added the above diarylpropionic acid (7·5 g.). After being heated at 100° for 2 hr., with occasional swirling, the solution was diluted with ice-water, and the products were isolated with benzene. Acid (1·0 g.) was recovered; *5-methoxy-3-phenylindan-1-one* (4·0 g., 66%) crystallised from ethanol in rods, m. p. 130° (Found: C, 80·4; H, 6·2. $C_{16}H_{14}O_2$ requires C, 80·7; H, 5·9%). The dinitrophenylhydrazone crystallised from ethanol in scarlet needles, m. p. 199—200°.

3-p-*Methoxyphenylindan-1-one.*—β-*p*-Methoxyphenyl-β-phenylpropionic acid (24·4 g.) was cyclised by using orthophosphoric acid (120 c.c.) and phosphoric oxide (180 g.) as for analogous reactions above. The product was worked up as before and distilled, to give 3-p-*methoxyphenylindan-1-one* (4·55 g., 20%), b. p. 150—155°/0·1 mm., which slowly crystallised. Recrystallisation from aqueous methanol gave material, m. p. 73° (Pfeiffer and Roos [1] give m. p. 59°)

[15] Burton and Shoppee, *J.*, 1935, 1160.

(Found: C, 80·4; H, 6·0. $C_{16}H_{14}O_2$ requires C, 80·7; H, 5·9%). The oxime was obtained as fine needles, m. p. 166—167° (Pfeiffer and Roos [1] gave α-form, large needles, m. p. 166·5°). The dinitrophenylhydrazone crystallised from ethanol in red needles, m. p. 182°.

Oxidative Degradation of 3-p-*Methoxyphenylindan*-1-*one*.—3-*p*-Methoxyphenylindan-1-one (0·3 g.), suspended in a solution of potassium permanganate (0·67 g.) and potassium hydroxide (0·3 g.) in water (50 c.c.), was heated under reflux for 2½ hr. by which time the colour was almost discharged. After cooling slightly, the solution was saturated with sulphur dioxide until clear. On chilling, a semicrystalline precipitate was obtained, which was extracted with ether. The ether solution was extracted with sodium carbonate solution, and acidification of the alkaline extracts gave *o*-(*p*-methoxybenzoyl)benzoic acid (0·1 g.). Recrystallisation from water gave colourless plates, m. p. 143° alone or mixed with a sample prepared by acylation of anisole with phthalic anhydride in the presence of aluminium chloride.

1 : 2-*Diphenylacenaphthylene*.—A solution of 2 : 2-diphenylacenaphthen-1-ol (9 g.) in benzene (200 c.c.) was saturated at 0° with hydrogen bromide. The solution rapidly became orange in colour and water separated. The benzene solution was washed with water, until the washings were neutral to litmus, dried, and distilled under reduced pressure. 1 : 2-Diphenylacenaphthylene (7·9 g., 92·3%) was obtained as a red crystalline residue. It recrystallised from acetone in red needles, m. p. 162—163° (lit., 161—163°).

Reduction of Indanones by Lithium Aluminium Hydride (see Table 2).—The ketones in 10—20 vols. of ether were boiled for 2 hr. with ethereal lithium aluminium hydride (30—50% excess). After treatment with dilute acid, the ether layers were washed with water or sodium hydrogen carbonate solution until neutral, dried, and evaporated. The residual alcohols were triturated with ligroin, if necessary, to effect crystallisation. The *indanols*, so prepared, all of which are new, are listed in Table 2.

TABLE 2. *Indan*-1-*ols*.

Alcohol	Yield (%)	Crystal form	Solvent	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
3-Phenyl [a]	95	Needles	Aq. EtOH	94·5—95°	$C_{15}H_{14}O$	86·2	6·9	85·7	6·6
3-Methyl-3-phenyl [a]	45	Needles [b]	EtOH	125	$C_{16}H_{16}O$	86·0	7·1	85·7	7·1
2-Methyl-3-phenyl	86	Rods	Ligroin	123	$C_{16}H_{16}O$	85·4	7·1	85·7	7·1
5-Methoxy-3-phenyl	85	—	Aq. MeOH	112	$C_{16}H_{16}O_2$	80·0	6·8	80·0	6·7
3-*p*-Methoxyphenyl	100	Needles	Ligroin [c]	114	$C_{16}H_{16}O_2$	80·1	6·9	80·0	6·7
3-Methyl	100	—	Aq. MeOH	71—72	$C_{10}H_{12}O$	80·8	8·1	81·0	8·1
3-Ethyl	100	Needles	Ligroin [f]	77—78	$C_{11}H_{14}O$	81·4	8·8	81·5	8·6
2 : 3-Dimethyl	82	Needles	Ligroin	84—85	$C_{11}H_{14}O$	81·7	8·8	81·5	8·6
2 : 3-Diethyl	82	Needles	Ligroin	117 [d]	$C_{13}H_{18}O$	82·2	9·3	82·1	9·5
2 : 2-Diphenylacenaphthen-1-ol [e]	88	Rhombs	EtOH or C_6H_6	136—138	$C_{24}H_{18}O$	89·7	5·4	89·4	5·6

[a] The reaction mixture was not boiled but kept overnight. [b] Evaporation of the mother-liquor gave an almost colourless oil (49·5%) (Found: C, 84·7; H, 7·2. $C_{16}H_{16}O$ requires C, 85·7; H, 7·1%). It was not distilled in order to avoid decomposition and appears to contain the other geometrical *isomer*. [c] The reaction was performed in benzene–ether, and the mixture was kept overnight at room temperature. [d] Sublimes at *ca.* 100°. [e] B. p. 60—80°. [f] B. p. 40—60°.

Preparation of 1-*Dialkylaminoindanes from Indan*-1-*ols* (see Table 3).—The indanol in benzene was saturated with hydrogen bromide at 0°, decanted from the water which separated, and washed with water until neutral, then dried and evaporated *in vacuo*. The residual bromoindane was a pale yellow oil, which, without further purification, was immediately treated with excess of secondary amine in dioxan in a pressure-bottle. After the reaction (conditions in Table 3), the precipitate of dialkylamine hydrobromide was washed with ether, and the solvent was removed from the combined filtrates. The residual oil, in ether, was treated with ethereal hydrogen chloride. The aminoindane hydrochloride was precipitated, and was washed with ether and dried *in vacuo* over sodium hydroxide. In the case of the morpholino-derivative, morpholine was boiled under reflux with the bromoindane in benzene and the product isolated as above.

Ethyl β-*Hydroxy*-β-*phenylvalerate*.—Propiophenone (31·5 g., 1 mol.), ethyl bromoacetate (46·7 g., 1 mol.), zinc wool (19·8 g., 1 g.-atom), and dry benzene (200 c.c.) were heated under reflux in the presence of a trace of iodine. After 2 hr. a vigorous reaction set in which was complete in 6 hr. The complex was decomposed with 10% sulphuric acid and washed with water and sodium hydrogen carbonate solution. The dried benzene solution on distillation gave *ethyl* β-*hydroxy*-β-*phenylvalerate* (38 g., 73%), b. p. 104°/0·5 mm., m. p. 34—35° [from light

TABLE 3. *1-Dialkylaminoindane salts prepared from the indanols.*

Ring subst.	Amino-group	Condensn. temp.	Condensn. hr.	Yield (%)	Crystal form	M. p.	Formula	Found (%) C	Found (%) H	Found (%) N	Found (%) Cl	Required (%) C	Required (%) H	Required (%) N	Required (%) Cl
3-Ph	NMe_2	70°	3	82	Rhombs [a]	191—192° [d]	$C_{17}H_{19}N$,HCl	74·0	7·2	5·1	13·1	74·6	7·3	5·1	13·0
3-Ph	NEt_2	80	2	42	Rhombs [b]	180—181 [e]	$C_{19}H_{23}N$,HCl	75·1	8·1	4·9	11·8	75·6	8·0	4·6	11·8
3-Me-3-Ph (isomer A) [f]	NMe_2	65	3		Rhombs [a]	229—230 [d]	$C_{18}H_{21}N$,HCl	74·5	8·0	4·9	12·7	75·1	7·7	4·9	12·3
				86	Needles [a]	155—156	$C_{18}H_{21}N,C_6H_3O_7N_3$	60·1	5·1	11·5	—	60·0	5·0	11·7	—
3-Me-3-Ph (isomer B) [g]	NMe_2	65	3		Rhombs [a]	197—200	$C_{18}H_{21}N$,HCl	74·5	7·9	5·0	12·7	75·1	7·7	4·9	12·3
3-Me-3-Ph	NEt_2	80	4	80	Rhombs [b]	150—180 [h]	$C_{20}H_{25}N$,HCl	76·3	8·0	4·6	11·3	76·1	8·2	4·4	11·3
3-Me-3-Ph	$N<[CH_2]_4>O$	80	3½	74	Rods [a]	238—239	$C_{20}H_{23}ON$,HCl	72·7	7·6	4·0	—	72·8	7·3	4·3	—
1-Me-3-Ph [i]	NMe_2	15	12	7	Rhombs [b]	220	$C_{18}H_{21}N$,HCl	74·8	7·5	5·2	—	75·1	7·7	4·9	—
2-Me-3-Ph (isomer A) [j]	NMe_2	15	12	32	Rhombs [b]	236—237	$C_{18}H_{21}N$,HCl	74·7	7·8	4·8	—	75·1	7·7	4·9	—
2-Me-3-Ph (isomer B) [j]	NMe_2	15	12	28	Rods [b]	210	$C_{18}H_{21}N$,HCl	74·8	7·9	4·6	—	75·1	7·7	4·9	—
					Needles [a]	179—180	$C_{18}H_{21}N,C_6H_3O_7N_3$	60·2	5·0	11·6	—	60·0	5·0	11·7	—
5-MeO-3-Ph [k]	NMe_2	40	12	—	Crystals [c]	219 (decomp.)	$C_{18}H_{21}ON$,HCl,½H_2O	68·9	7·3	4·2	10·4	69·2	7·4	4·5	11·4
					Needles [a]	167	$C_{18}H_{21}ON,C_6H_3O_7N_3$	57·8	5·3	10·9	—	58·1	4·9	11·3	—
3-*p*-MeO·C_6H_4	NMe_2	15	12	—	Needles [b]	211—212	$C_{18}H_{21}ON$,HCl	71·1	7·4	4·5	11·6	71·2	7·3	4·6	11·7
					Needles [a]	135	$C_{18}H_{21}ON,C_6H_3O_7N_3$	57·9	4·9	11·3	—	58·1	4·9	11·3	—
3-Me	NMe_2	40	12	—	Rhombs [b]	202	$C_{12}H_{17}N$,HCl	68·2	8·4	6·5	—	68·1	8·5	6·6	—
					Needles [a]	167—168	$C_{12}H_{17}N,C_6H_3O_7N_3$	53·1	5·2	13·6	—	53·5	4·9	13·9	—
3-Me [l]	$N<[CH_2]_4>O$	—	3	—	Rods [b]	195—196 (decomp.)	$C_{14}H_{19}ON$,HCl	65·9	7·8	5·7	14·4	66·3	7·9	5·5	14·0
					Plates [a]	162—163	$C_{14}H_{19}ON,C_6H_3O_7N_3$	53·8	4·9	12·8	—	53·8	4·9	12·6	—
3-Et	NMe_2	40	12	—	Plates [c]	165—166	$C_{13}H_{19}N$,HCl	69·5	8·9	5·6	—	69·2	8·9	6·2	—
					Needles [a]	165	$C_{13}H_{19}N,C_6H_3O_7N_3$	54·4	5·6	13·4	—	54·5	5·3	13·4	—
3-Et	$N<[CH_2]_4>O$	—	3	—	Needles or plates [c]	199—201	$C_{15}H_{21}ON$,HCl	66·8	8·1	5·5	14·0	67·3	8·2	5·2	13·3
					Plates [a]	168	$C_{15}H_{21}ON,C_6H_3O_7N_3$	55·0	5·4	11·8	—	54·8	5·2	12·2	—
3-*cyclo*Hexyl	NMe_2	40	12	—	Needles [b]	181—183	$C_{17}H_{25}N$,HCl,H_2O	69·0	9·3	4·5	—	68·6	9·4	4·7	—
					Needles [a]	171—172	$C_{17}H_{25}N,C_6H_3O_7N_3$	58·9	6·0	11·3	—	58·5	5·9	11·9	—
2 : 3-Me_2 [m]	NMe_2	15	12	52	Glass	—	—	—	—	—	—	—	—	—	—
					Rhombs [a]	158—159	$C_{13}H_{19}N,C_6H_3O_7N_3$	54·6	5·4	13·1	—	54·5	5·3	13·4	—
2 : 3-Et_2 [n]	NMe_2	15	24	45	Glass	—	—	—	—	—	—	—	—	—	—

[a] From ethanol. [b] From ethanol–ethyl acetate. [c] From ethanol–ethyl acetate–ether. [d] Unchanged on admixture with a sample prepared by the alternative route. [e] M. p. 181—183° on admixture with a sample prepared by the alternative route. [f] Prepared from the crystalline indanol. [g] This geometric isomer was isolated from the mother-liquors of the previous compound; a mixture had m. p. 180—191°. [h] Mixture of geometric isomers. [i] Evaporation of the ethereal filtrate from this compound gave *1-methyl-3-phenylindene*, b. p. 129°/1 mm., n_D^{18} 1·6145 (Found: C, 93·1; H, 6·9. $C_{16}H_{14}$ requires C, 93·2; H, 6·8%). [j] Isomer B was obtained from the mother-liquors of isomer A; mixed m. p. 203—207°. A saturated solution of isomer B in ethanol–ethyl acetate, when seeded with isomer A, yielded the latter as the main product. The picrates of the isomers were identical (mixed m. p.). Isomers A and B are different crystalline forms of the same substance. [k] Much tar was formed in the amine condensation, and the product was initially purified by acid–base treatment. [l] No solvent was used in the condensation with morpholine. [m] The *methiodide*, needles from ethanol–ethyl acetate, had m. p. 148—149° (Found: C, 51·0; H, 6·9; N, 4·3. $C_{14}H_{22}NI$ requires C, 50·8; H, 6·6; N, 4·2%). [n] The *methiodide*, needles from ethanol–ethyl acetate, had m. p. 166° (Found: C, 53·7; H, 7·3; N, 4·0. $C_{16}H_{26}NI$ requires C, 53·5; H, 7·2; N, 3·9%). The *ethiodide*, needles from ethanol–ethyl acetate, had m. p. 170° (Found: C, 54·7; H, 7·5. $C_{17}H_{28}NI$ requires C, 54·7; H, 7·5%).

petroleum (b. p. 40—60°)] (Found: C, 70·1; H, 7·9. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·1%). A further portion was hydrolysed to the *acid* (m. p. 120—121°) with alcoholic potassium hydroxide (Found: C, 67·7; H, 7·0. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·2%).

Ethyl 3-*Phenylpent*-2-*enoate*.—A solution of ethyl β-hydroxy-β-phenylvalerate (20 g.) in dry benzene, boiling under reflux, was treated with phosphoric oxide (30 g.) in portions. After 3 hr., the benzene layer was decanted and the phosphoric acid washed with benzene. The combined benzene solutions were set aside over anhydrous potassium carbonate overnight before evaporation under reduced pressure. The residue, on distillation, gave the pentenoate (13 g., 71%), b. p. 95—105°/0·1 mm. (lit., b. p. 145°/14 mm.). A portion was hydrolysed to the acid, plates, m. p. 95—96° (Found: C, 75·25; H, 6·9. Calc. for $C_{11}H_{12}O_2$: C, 75·0; H, 6·8%).

β-*Phenylvaleric Acid*.—The preceding ester (2·0 g.) in ethanol (20 c.c.) was hydrogenated at room temperature and pressure in the presence of Adams catalyst (0·15 g.) (1 hr.). The solution was filtered and the ester hydrolysed with alcoholic potassium hydroxide (4·0 g.). The resulting solution was evaporated under reduced pressure, and the residue was dissolved in water and acidified to Congo-red. The precipitated β-phenylvaleric acid (1·7 g., 97·4%) was collected and dried. Recrystallisation from light petroleum (b. p. 60—80°) gave crystals, m. p. 63° (lit., m. p. 66°).

3-*Ethylindan*-1-*one*.—(*A*) A benzene solution of β-phenylvaleric acid (9·0 g., 1 mol.) was heated under reflux with phosphorus pentachloride (12·0 g., 1·1 mol.) until no more hydrogen chloride was evolved. The mixture was cooled, stirred at room temperature, and treated with powdered anhydrous aluminium chloride (8 g., 1·1 mol.) in portions with cooling. The mixture was stirred for 2 hr. and kept overnight before being poured on ice and concentrated hydrochloric acid (16 c.c.). The benzene was separated and the aqueous layer extracted with benzene. The combined benzene solutions were washed with sodium hydrogen carbonate solution, dried, and evaporated. The residue, on distillation, gave 3-*ethylindan*-1-*one* (2·0 g., 25%), b. p. 116°/10 mm. The *semicarbazone* was obtained from ethanol as crystals, m. p. 189° (Found: C, 66·4; H, 6·9; N, 19·1. $C_{12}H_{15}ON_3$ requires C, 66·4; H, 6·9; N, 19·35%); the dinitrophenylhydrazone had m. p. 197°.

(*B*) A slurry of orthophosphoric acid (85%; 240 c.c.) and phosphoric oxide (372 g.) was heated at 100° for 2 hr. to give an almost clear solution to which β-phenylvaleric acid (16 g.) was added. An orange solution was obtained and this was heated for 2 hr. at 100° with occasional swirling. The solution was cooled and poured on ice and water and extracted with benzene. The benzene was washed with sodium carbonate solution, dried, and distilled, giving 3-ethylindan-1-one (13·1 g., 91%).

Ethyl β-cyclo*Hexyl*-β-*phenylacrylate*.—*cyclo*Hexyl phenyl ketone[16] (34·4 g.), ethyl bromoacetate (31 g.), and zinc wool (12·5 g.) were allowed to react in benzene (130 c.c.) for 2 hr. and worked up as described for the preparation of ethyl β-hydroxy-β-phenylvalerate. The benzene solution of ethyl β-*cyclo*hexyl-β-hydroxy-β-phenylpropionate, so obtained, was immediately dehydrated by boiling under reflux with phosphoric oxide (50 g.) added in portions during 1 hr. The solution, after being heated for a further 2 hr., was cooled and filtered. The solid was washed with benzene, and the combined benzene solutions were placed over potassium carbonate and later distilled. *Ethyl* β-cyclo*hexyl*-β-*phenylacrylate* (27·7 g., 59%) was collected as an oil, b. p. 100/0·2 mm. A portion, hydrolysed to the acid, and crystallised from ligroin, had m. p. 141—142° (ref. 16 gives m. p. 144·5°).

β-cyclo*Hexyl*-β-*phenylpropionic Acid*.—An ethanolic solution of ethyl β-*cyclo*hexyl-β-phenylacrylate (23·7 g.) was hydrogenated at atmospheric temperature and pressure in the presence of 2% palladised strontium carbonate (12·0 g.). The solution was filtered and the ester hydrolysed with alcoholic potassium hydroxide. The ethanol was removed under reduced pressure, water added, and the solution acidified to Congo-red, to give the propionic acid (17·6 g., 83%). Recrystallisation from light petroleum (b. p. 60—80°) gave crystals, m. p. 98° (ref. 16 gives m. p. 101°).

3-cyclo*Hexylindan*-1-*one*.—(*A*) A solution of β-*cyclo*hexyl-β-phenylpropionic acid (5·0 g.) in dry benzene (40 c.c.) was heated under reflux with phosphorus trichloride (1·5 c.c., 0·77 mol.) until no more hydrogen chloride was evolved. The cooled solution was filtered and the precipitate washed with dry benzene (10 c.c.). The solution was stirred at 0°, treated with powdered anhydrous aluminium chloride (2·88 g., 1 mol.), stirred for 2 hr., poured on ice and concentrated hydrochloric acid (6 c.c.), and worked up in the usual way, giving 3-cyclo*hexylindan*-1-*one* (0·5 g., 10·8%), b. p. 150°/0·8 mm. Crystallisation from ligroin gave colourless

[16] Nenitzescu and Gavat, *Ber.*, 1937, **70**, 1886.

crystals, m. p. 49° (Found: C, 84·3; H, 8·3. $C_{15}H_{18}O$ requires C, 84·1; H, 8·4%). A scarlet dinitrophenylhydrazone, m. p. 199—200°, was prepared.

(*B*) Orthophosphoric acid (40 c.c.), phosphoric oxide (62 g.), and β-*cyclo*hexyl-β-phenylpropionic acid (2·5 g.) were allowed to react as in previous cyclisations; 0·35 g. of acid was recovered and 3-*cyclo*hexylindan-1-one (1·6 g., 81% calc. on acid used) was obtained crystalline without distillation.

α-*Methyl*-β-*phenylbutyric Acid.*—Ethyl α-methyl-β-phenylcrotonate (20 g.) (obtained by dehydrating, with phosphoric oxide in boiling benzene, the product from a Reformatsky reaction between acetophenone and ethyl β-bromopropionate) in ethanol (60 c.c.) was converted into *ethyl* α-*methyl*-β-*phenylbutyrate* by hydrogenation for 16 hr. over platinum oxide (1·5 g.) at atmospheric pressure. The saturated ester was a mobile oil (19 g.), b. p. 128—130°/12 mm. (Found: C, 75·5; H, 8·8. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%), and on hydrolysis with aqueous potassium hydroxide afforded the acid, m. p. 152°.

2 : 3-*Dimethylindan*-1-*one.*—α-Methyl-β-phenylbutyric acid (22·3 g.) was cyclised as described for α-methyl-ββ-diphenylpropionic acid with thionyl chloride (22 ml.) in benzene (100 ml.) and subsequently aluminium chloride (18·5 g.) was added. Some acid (1·5 g.) was recovered and 2 : 3-dimethylindan-1-one (16·5 g., 88%), a yellow mobile oil, distilled at 118—120°/10 mm. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol in brick-red needles, m. p. 179—180° (Found: C, 60·5; H, 4·7. $C_{17}H_{16}O_4N_4$ requires C, 60·0; H, 4·7%).

Ethyl α-*Ethyl*-β-*hydroxy*-β-*phenylvalerate.*—A solution of propiophenone (33·5 g.) and ethyl α-bromobutyrate (50 g.) in dry benzene (400 c.c.) was boiled under reflux with zinc turnings (20 g.) for 10 hr. The mixture was cooled and decomposed with 10% sulphuric acid. The benzene layer was separated, washed with water, sodium hydrogen carbonate solution, and water, dried, and distilled, giving *ethyl* α-*ethyl*-β-*hydroxy*-β-*phenylvalerate* (20 g.), b. p. 155—160°/10 mm. It crystallised from ligroin in needles, m. p. 61—62° (Found: C, 71·8; H, 8·7. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·8%). Ivanoff [17] claims to have made this compound, but gives no b. p., m. p., or analytical data.

Ethyl α-*Ethyl*-β-*phenylpent*-2-*enoate.*—Phosphoric oxide was added to a solution of ethyl α-ethyl-β-hydroxy-β-phenylvalerate (20 g.) in boiling benzene (200 c.c.) in successive quantities during 2 hr., until no further reaction was observed. Working up as described for the other acrylates gave *ethyl* α-*ethyl*-β-*phenylpent*-2-*enoate* (18 g.), b. p. 144—150°/12 mm. (Found: C, 77·7; H, 8·6. $C_{15}H_{20}O_2$ requires C, 77·6; H, 8·6%). A sample on hydrolysis afforded the *acid*, b. p. 132°/1 mm. (Found: C, 76·6; H, 7·6. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%).

Ethyl α-*Ethyl*-β-*phenylvalerate.*—Ethyl α-ethyl-β-phenylpent-2-enoate (18 g.) in ethanol (100 c.c.) was hydrogenated for 8 hr. over platinum oxide (0·5 g.) at atmospheric pressure. *Ethyl* α-*ethyl*-β-*phenylvalerate* (17 g.) was a mobile oil, b. p. 130—136°/12 mm. (Found: C, 76·7; H, 9·4. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·4%). Hydrolysis with potassium hydroxide in 50% aqueous ethanol yielded the *acid* (11 g.), b. p. 120—125°/1 mm. (Found: C, 75·6; H, 8·5. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%). The amide was also an oil.

2 : 3-*Diethylindan*-1-*one.*—α-Ethyl-β-phenylvaleric acid (10 g.) was cyclised as described for the corresponding dimethyl compound by thionyl chloride (10 ml.), benzene (100 ml.), and aluminium chloride (7·0 g.), and gave 2 : 3-*diethylindan*-1-*one* (7 g.), b. p. 134—135°/12 mm. (Found: C, 82·8; H, 8·4. $C_{13}H_{16}O$ requires C, 83·0; H, 8·5%). The 2 : 4-*dinitrophenylhydrazone* separated from ethanol in brick-red needles, m. p. 161° (Found: C, 62·0; H, 5·2; N, 15·0. $C_{19}H_{20}O_4N_4$ requires C, 62·0; H, 5·4; N, 15·2%).

3-*Dimethylamino*-1 : 1-*dimethylindane.*—Bromine (22 g.) in carbon tetrachloride (50 c.c.) was added to an ice-cold solution of 1 : 1-dimethylindane (20·1 g.) in carbon tetrachloride (30 c.c.). When the colour had been discharged, the solvent was removed under reduced pressure and the residual oil in dry dioxan (20 c.c.) was treated with anhydrous dimethylamine (15 g.). 3-*Dimethylamino*-1 : 1-*dimethylindane hydrochloride* (15 g.), isolated in the usual way, crystallised from ethyl acetate–ethanol in needles, m. p. 192—193° (Found: C, 68·9; H, 8·8; N, 6·5. $C_{13}H_{19}N,HCl$ requires C, 69·2; H, 8·9; N, 6·2%). The *methiodide* separated from ethyl acetate–ethanol in colourless needles, m. p. 182—183° (Found: C, 51·1; H, 6·7; N, 4·3. $C_{14}H_{22}NI$ requires C, 50·8; H, 6·6; N, 4·2%).

Attempted Preparation of 3-*Dimethylamino*-1 : 1 : 2-*trimethylindane.*—Bromine (18·1 g.) in carbon tetrachloride (50 c.c.) was added to an ice-cold solution of 1 : 1 : 2-trimethylindane (18·1 g.) in carbon tetrachloride (50 c.c.). The discharge of colour took only a few minutes and was accompanied by the evolution of some hydrogen bromide. The solvent having been

[17] Ivanov, *Bull. Soc. chim. France*, 1940, **7**, 569.

evaporated, the residual oil was allowed to react for 12 hr. at room temperature with dimethylamine (12·5 g.) in dioxan. Working up in the usual way gave a salt (0·5 g.), probably *2-bromo-3-dimethylamino-*1 : 1 : 2-*trimethylindane hydrochloride* which crystallised from dioxan in rhombs, m. p. 195—196° (Found: C, 52·9; H, 6·6; N, 4·3; Cl + Br, 36·5. $C_{14}H_{20}NBr,HCl$ requires C, 52·8; H, 6·6; N, 4·4; Cl + Br, 36·2%). The ethereal solution on distillation yielded a colourless oil, b. p. 93°/12 mm. This decolorised potassium permanganate and analysis indicated that it was impure 1 : 1 : 2-trimethylindene (Found: C, 87·9; H, 9·2. Calc. for $C_{12}H_{14}$: C, 91·1; H, 8·9%). A sample was hydrogenated over palladised calcium carbonate (with uptake of 1·1 mols. of hydrogen), and the product identified as 1 : 1 : 2-trimethylindane, b. p. 89°/12 mm., n_D^{18} 1·5158.

Attempted Preparation of 1-*Dimethylamino-*1 : 3 : 3-*trimethylindane.*—Bromine (9·6 g.) in carbon tetrachloride (20 c.c.) was added to an ice-cold solution of 1 : 1 : 3-trimethylindane (9·6 g.) in carbon tetrachloride (50 c.c.). Further reaction as in the previous experiment gave, probably, *2-bromo-*1-*dimethylamino-*1 : 3 : 3-*trimethylindane hydrochloride* (0·5 g.), needles (from ethyl acetate–ethanol), m. p. 198° (Found: C, 53·2; H, 6·5; N, 4·1%). The *picrate* separated from ethanol in rhombs, m. p. 157—158° (Found: C, 47·3; H, 4·1; N, 10·9; Br, 15·5. $C_{14}H_{20}NBr,C_6H_3O_7N_3$ requires C, 47·0; H, 4·5; N, 11·0; Br, 15·7%).

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