

*Some Derivatives of 2-Phenylindane.*

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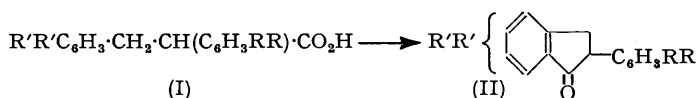
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Some new methoxyphenyl-phenylpropionic acids have been prepared and attempts made to cyclise them to methoxy-2-phenylindanones. The latter, where obtained, have been converted into the corresponding 1-amino- $\alpha$ -methoxy-2-phenylindanes.

THE effect of cyclising reagents on a number of methoxyphenyl-phenylpropionic acids has been investigated as a route to the corresponding methoxy-2-phenylindan-1-ones.

$\beta$ -Methoxyphenyl- $\alpha$ -phenylpropionic acids (I; R = H, R', R' = OMe, H or diOMe) were first synthesised in 60% yield by reduction with sodium amalgam of the corresponding cinnamic acids. Rather higher yields were however obtained by the sequence: (a) condensation of the requisite methoxybenzaldehydes with benzyl cyanide (cf. Frost, *Annalen*, 1888, 250, 159), (b) smooth reduction of the resultant methoxyphenylcinnamonnitriles (resistant to hydrolysis) to the propionitriles, and (c) ready hydrolysis of the propionitriles to the desired acids.

$\alpha$ -Methoxyphenyl- $\beta$ -phenylpropionic acids (I; R, R = OMe, H or diOMe, R' = H) were similarly produced from methoxybenzyl cyanides and benzaldehyde.



$\alpha\beta$ -Diphenylpropionic acid was not cyclised to 2-phenylindan-1-one by concentrated sulphuric acid (contrary to the report by von Miller and Rohde, *Ber.*, 1892, 25, 2095) or by phosphoric oxide in benzene, but cyclisation was easily effected by phosphoric oxide-phosphoric acid (Koebner and Robinson, *J.*, 1938, 1994).

The action of this reagent on acids (I) is summarised in the Table.

Substituents in (I)		Optimum temp.	Max. yield, %	Product (II),	
R,R	R',R'			R	R'
2H	<i>o</i> -OMe,H	—	none	—	—
2H	<i>m</i> -OMe,H	160°	40	2H	5-OMe,H
2H	<i>p</i> -OMe,H	187	20	2H	6-OMe,H
2H	3 : 4-di-OMe <sup>1</sup>	160	30	2H	5 : 6-diOMe
3 : 4-diOMe	3 : 4-di-OMe <sup>2</sup>	—	none	—	—
3 : 4-diOMe	2H	—	—	—	—
<i>p</i> -OMe,H	2H	—	—	—	—
<i>m</i> -OMe,H	2H	—	—	—	—

<sup>1</sup> In contrast to the other acids, this was easily cyclised by phosphoric oxide in benzene. <sup>2</sup> Solmssen (*J. Amer. Chem. Soc.*, 1943, **65**, 2370) has reported the cyclisation of (I; R,R = *p*-OMe,H, R',R = *m*-OMe,H) with phosphoric oxide in benzene.

The methoxy-2-phenyl-1-indanones (II) thus obtained were converted *via* the oximes to the corresponding 1-amino-*x*-methoxy-2-phenylindanes.

During this work, 2-phenylindene was converted into 1-bromo-2-phenylindene with *N*-bromosuccinimide. Attempts to reduce this bromide to the dihydro-derivative led to the prior loss of bromine.

#### EXPERIMENTAL

*m*-Methoxy- $\alpha$ -phenylcinnamionitrile.—*m*-Methoxybenzaldehyde (55 g.), benzyl cyanide (50 g.), ethanol (150 c.c.) and 6*N*-sodium hydroxide solution (5 c.c.) were set aside for 12 hr. The precipitate was filtered off and dissolved in boiling ethanol, from which *m*-methoxy- $\alpha$ -phenylcinnamionitrile (90 g., 90%), m. p. 57°, crystallised on cooling (Found: C, 81.5; H, 5.5. C<sub>16</sub>H<sub>13</sub>ON requires C, 81.7; H, 5.5%).

The following were prepared similarly: *o*-Methoxy- $\alpha$ -phenylcinnamionitrile, m. p. 94° (Found: C, 81.4; H, 5.5%), and  $\alpha$ -*m*-methoxyphenylcinnamionitrile, m. p. 72° (Found: C, 82.1; H, 5.6%).

$\beta$ -*m*-Methoxyphenyl- $\alpha$ -phenylpropiononitrile.—*m*-Methoxy- $\alpha$ -phenylcinnamionitrile (10 g.) was refluxed in ethanol (100 c.c.) with sodium amalgam (2½%; 100 g.) for 1 hr., the ethanol evaporated from the filtered solution, and the residue distilled,  $\beta$ -*m*-methoxyphenyl- $\alpha$ -phenylpropiononitrile (9.6 g., 95%) being collected at 140°/0.02 mm. (Found: C, 81.0; H, 6.4. C<sub>16</sub>H<sub>15</sub>ON requires C, 81.0; H, 6.3%). The following were prepared similarly from the corresponding cinnamionitriles (Freund and Remse, *Ber.*, 1890, **23**, 2859; Frost, *Annalen*, *loc. cit.*):  $\alpha$ -*β*-diphenylpropiononitrile, m. p. 46° (Found: C, 87.1; H, 6.1. Calc. for C<sub>15</sub>H<sub>13</sub>N: C, 87.0; H, 6.3%);  $\beta$ -*o*-methoxyphenyl- $\alpha$ -phenylpropiononitrile, b. p. 140°/0.05 mm. (Found: C, 81.3; H, 6.5%);  $\beta$ -*p*-methoxyphenyl- $\alpha$ -phenylpropiononitrile, m. p. 89° (Found: C, 81.1; H, 6.1; N, 5.8. C<sub>16</sub>H<sub>15</sub>ON requires C, 81.0; H, 6.3; N, 5.9%);  $\beta$ -3 : 4-dimethoxyphenyl- $\alpha$ -phenylpropiononitrile, m. p. 98° (Found: C, 76.5; H, 6.2; N, 5.5. C<sub>17</sub>H<sub>17</sub>O<sub>2</sub>N requires C, 76.4; H, 6.4; N, 5.2%).

$\beta$ -*o*-Methoxyphenyl- $\alpha$ -phenylpropionic Acid.—(i) Sodium amalgam (2½%, 500 g.) was added with stirring during 3 hr. to a solution of *o*-methoxy- $\alpha$ -phenylcinnamic acid (30 g.), sodium hydroxide (20 g.), and water (500 c.c.). The solid, obtained by acidification of the filtered liquid at 0°, was dissolved in hot 60% ethanol, whereupon  $\beta$ -*o*-methoxyphenyl- $\alpha$ -phenylpropionic acid (18 g., 60%), m. p. 135°, crystallised (Found: C, 74.8; H, 6.35. C<sub>16</sub>H<sub>15</sub>O<sub>3</sub> requires C, 75.0; H, 6.25%). (ii) A mixture of  $\beta$ -*o*-methoxyphenyl- $\alpha$ -phenylpropiononitrile (10 g.), sodium hydroxide (10 g.), and ethanol (100 c.c.) was refluxed for 20 hr. and the precipitate (9.7 g., 90%) obtained on acidification was crystallised from aqueous ethanol (Found: C, 75.0; H, 6.0%). In later runs,  $\beta$ -*o*-methoxyphenyl- $\alpha$ -phenylpropionic acid was obtained directly by addition of sodium hydroxide to the solution from sodium-amalgam reduction of *o*-methoxy- $\alpha$ -phenylcinnamionitrile.

The following acids were similarly prepared by methods (i) and (ii) from the corresponding cinnamic acids (Funk and Kostanecki, *Ber.*, 1905, **38**, 940) or cinnamionitriles (Niederl and Ziering, *J. Amer. Chem. Soc.*, 1942, **64**, 885):  $\alpha$ -*β*-Diphenylpropionic acid, m. p. 81° (Found: C, 79.7; H, 6.3. Calc. for C<sub>15</sub>H<sub>14</sub>O<sub>2</sub>: C, 79.7; H, 6.2%);  $\beta$ -*m*-methoxyphenyl- $\alpha$ -phenylpropionic acid, m. p. 47° (Found: C, 75.3; H, 6.4. Calc. for C<sub>16</sub>H<sub>16</sub>O<sub>3</sub>: C, 75.0; H, 6.25%);  $\beta$ -*p*-methoxyphenyl- $\alpha$ -phenylpropionic acid, m. p. 119° (Found: C, 75.4; H, 6.25%);  $\beta$ -3 : 4-dimethoxyphenyl- $\alpha$ -phenylpropionic acid, m. p. 98° (Found: C, 71.2; H, 6.3. Calc. for C<sub>17</sub>H<sub>18</sub>O<sub>4</sub>: C, 71.3; H, 6.3%).

The following acids were prepared by method (ii) only:  $\alpha$ -*p*-Methoxyphenyl- $\beta$ -phenylpropionic acid, m. p. 108° (Found: C, 75.3; H, 6.3. Calc. for  $C_{18}H_{16}O_3$ : C, 75.0; H, 6.25%);  $\alpha$ -*m*-methoxyphenyl- $\beta$ -phenylpropionic acid, m. p. 48° (Found: C, 75.1; H, 6.3%);  $\alpha$ -3:4-dimethoxyphenyl- $\beta$ -phenylpropionic acid, m. p. 137° (Found: C, 71.3; H, 6.4.  $C_{17}H_{16}O_4$  requires C, 71.3; H, 6.3%),  $\alpha\beta$ -bis-3:4-dimethoxyphenylpropionic acid, m. p. 136° (Found: C, 65.8; H, 6.4.  $C_{18}H_{18}O_5$  requires C, 65.7; H, 6.6%).

2-Phenylindan-1-one.— $\alpha\beta$ -Diphenylpropionic acid (15 g.) was quickly added with vigorous shaking to a mixture of phosphoric acid ( $d$  1.75; 120 g.) and phosphoric oxide (120 g.) at 170°. When the mixture had cooled it was poured into water, and the crude product (9 g.; 60%) was isolated by extraction with ether. It was characterised as the oxime, m. p. 159° (Found: C, 80.5; H, 6.1. Calc. for  $C_{18}H_{13}ON$ : C, 80.7; H, 5.8%). Similarly the following indan-1-ones were prepared from the corresponding propionic acids (the temperature of the mixture during addition, and the yield obtained are given in parenthesis): 5-Methoxy-2-phenyl- (160°; 40%), m. p. 110°, from ethanol (Morris, J., 1950, 1913, gives m. p. 115°) (Found: C, 80.5; H, 6.1. Calc. for  $C_{18}H_{14}O_2$ : C, 80.7; H, 5.9%); oxime, m. p. 190° (Found: C, 76.0; H, 6.1; N, 5.6.  $C_{18}H_{15}O_2N$  requires C, 75.9; H, 5.9; N, 5.5%). 6-Methoxy-2-phenyl- (187°; 20%), m. p. 153° (Found: C, 80.8; H, 6.0%); oxime, m. p. 154° (decomp.) (Found: C, 76.3; H, 6.1%). 5:6-Dimethoxy-2-phenyl- (160°; 30%), m. p. 156° (Found: C, 76.0; H, 5.7.  $C_{17}H_{16}O_3$  requires C, 76.1; H, 6.0%); oxime, m. p. 202° (decomp.) (Found: C, 72.2; H, 6.4.  $C_{17}H_{17}O_3N$  requires C, 72.1; H, 6.0%). 5:6-Dimethoxy-2-phenylindan-1-one was also obtained by refluxing  $\beta$ -3:4-dimethoxyphenyl- $\alpha$ -phenylpropionic acid (8 g.), phosphoric oxide (80 g.), and benzene (300 c.c.) for 1 hr., pouring the mixture on ice, and isolating the product (6 g.) from the dried benzene extract.

1-Amino-5-methoxy-2-phenylindane (cf. Braun and Manz, *Ber.*, 1929, 62, 1059). Sodium-amalgam (2½%; 100 g.) was added during 1 hr. to a stirred solution of 1-hydroxyimino-5-methoxy-2-phenylindane (5 g.) in ethanol (60 c.c.) and acetic acid (10 c.c.), the liquid was poured into water, and the mixture acidified with hydrochloric acid. The crude product was isolated with ether and distilled, the fraction (1.7 g.), collecting at 160°/0.15 mm., was dissolved in ether, and hydrogen chloride passed through the solution to precipitate 1-amino-5-methoxy-2-phenylindane hydrochloride (1.9 g.), m. p. 126° (Found: N, 4.9; Cl, 12.5.  $C_{18}H_{18}ONCl$  requires N, 5.1; Cl, 12.9%).

The following were prepared similarly: 1-Amino-6-methoxy-2-phenylindane hydrochloride, m. p. 210° (decomp.) (Found: C, 69.2; H, 6.3.  $C_{18}H_{18}ONCl$  requires C, 69.7; H, 6.3%); 1-amino-5:6-dimethoxy-2-phenylindane hydrochloride, m. p. 210° (Found: C, 66.3; H, 6.5; N, 4.6.  $C_{17}H_{20}O_2$  requires C, 66.7; H, 6.5; N, 4.6%).

1-Bromo-2-phenylindene.—A solution of 2-phenylindene (5 g.) and *N*-bromosuccinimide (4.6 g.) in carbon tetrachloride (50 c.c.) was refluxed for 30 min., the solvent evaporated after filtration, and the residue dissolved in hot aqueous ethanol (80%). When the solution cooled 1-bromo-2-phenylindene (4.8 g., 67%), m. p. 124°, crystallised (Found: Br, 29.2.  $C_{15}H_{11}Br$  requires Br, 29.6%).

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