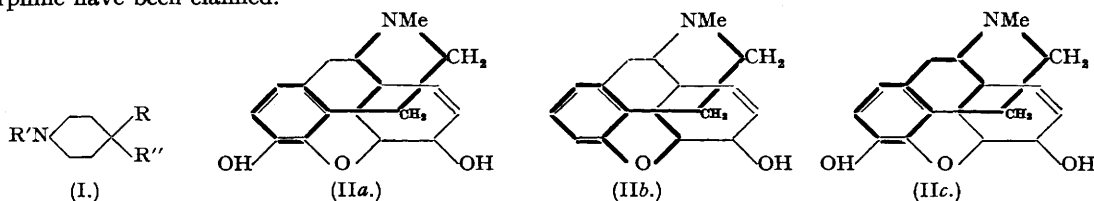


## 240. Experiments in the Piperidine Series. Part II.

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As morphine may be regarded as derived from  $\alpha$ -benzylpiperidine or from  $\gamma$ -phenylpiperidine a number of derivatives of these structures have been prepared as possible analgesics.  $\alpha$ -Benzylpiperidine was converted into a series of derivatives containing alkyl or oxygenated *N*-substituents. Condensation of di- $\beta$ -chloroethylaniline with benzyl cyanide eventually afforded a *N*-phenyl analogue of dolantin and further analogues with oxygenated groupings in the *N*-phenyl residue were similarly obtained. A number of derivatives of 2-phenylpiperidine and 4-piperidine are also described.

SCHAUMANN (*Arch. f. exp. Path. u. Pharm.*, 1940, **196**, 109) examined the pharmacological action of many piperidine derivatives (I; where R = aryl, R' = alkyl, R'' = a derivative of a carboxyl group). Of these dolantin (R = Ph, R' = Me, R'' = CO<sub>2</sub>Et) has been widely used as an analgesic for which advantages over morphine have been claimed.

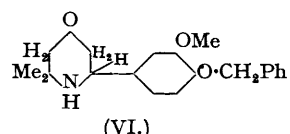
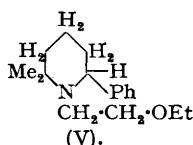
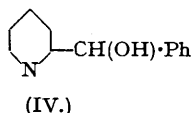
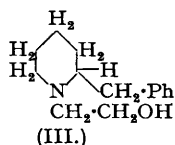


In these laboratories interest in phenylpiperidines had been aroused as a possible development of the many phenylpyridines available from earlier work (*cf. J.*, 1943, 401—419 and earlier papers). For example 2-(4'-carbomethoxyphenyl)-pyridine was readily hydrogenated, but so far no pure product has been isolated. Attention was turned therefore to ring-synthetic and other approaches. Many of the piperidine derivatives here described were tested for analgesic activity in the laboratories of I.C.I. Ltd. (Dyestuffs Division), but no marked potency was disclosed.

The resemblance of the dolantin molecule to certain isolated features of morphine which may also be regarded as containing the skeleton of an arylpiperidine as in (IIa) has been pointed out by Schaumann (*loc. cit.*). There is, however, no more justification for ascribing the analgesic action of morphine to this particular partial structure than to others, and Bergel *et al.* (*J.*, 1944, 261) for example have synthesised possible analgesics modelled upon morphine regarded as a basically substituted coumaran as in (IIb). The experiments described in the present paper were based partly upon (IIa) and also upon (IIc). In addition, some  $\alpha$ -phenylpiperidines have also been examined for comparative purposes. Molecular models of morphine, however, reveal a characteristic which is probably absent in most simple phenyl- and benzyl-piperidines. The piperidine ring in morphine is necessarily maintained at an angle to the phenanthrene skeleton and the molecule exhibits therefore an unusual angularity. It is perhaps significant that this feature is almost certainly present in dolantin as a result of the relative sizes of the phenyl and carbethoxy groupings (R, R'' in I) and further synthetic work based on this conception forms the subject of a separate communication.

2-Benzylpiperidine was prepared by reducing 2-benzylpyridine catalytically (Adkins and Cramer, *J. Amer. Chem. Soc.*, 1930, **53**, 4349), and, after acetylation, separating *N*-acetyl-2-benzylpiperidine from incompletely reduced material. The required base was obtained by hydrolysis of the acetyl derivative. 2-Benzylpiperidine yielded a *methiodide* from which 2-benzyl-1-methylpiperidine (Bryans and Pyman, *J.*, 1929, 549) was obtained. Oxygenated groupings were introduced into the benzylpiperidine unit with the object of conferring some of the physical character of morphine on the molecule. Ethylene bromohydrin and 2-benzylpiperidine reacted spontaneously, and a crystalline salt of 1- $\beta$ -hydroxyethyl-2-benzylpiperidine (III) was obtained from which the *benzoic ester* was prepared. Similarly appropriate bromo-ethers afforded 1- $\beta$ -methoxyethyl- and 1- $\beta$ -ethoxyethyl-2-benzylpiperidine. Finally oxidation of 2-benzylpyridine with mercuric acetate introduced a single hydroxyl group; by analogy with, for example, the oxidation of papaverine (Gadamer, *Arch. Pharm.*, 1915, **253**, 284) the product, characterised as its *picrate*, is regarded as 2-pyridylphenylcarbinol (IV). An attempt was made to introduce hydroxyl groups indirectly into the aromatic grouping. Nitration of 1-acetyl-2-benzylpiperidine gave a dinitro compound, presumably 1-acetyl-2-(2':4'-dinitrobenzyl)-piperidine, but as the preparation was complicated by simultaneous sulphonation the project was not pursued farther.

In the early part of this work attention was directed to the preparation of *N*-aryl analogues of dolantin (I; R' = aryl) and, again, especially those containing oxygenated groupings which might have conferred on



the compounds something of the physical character of morphine. Di-( $\beta$ -chloroethyl)aniline reacted with benzyl cyanide in presence of sodamide to give 4-cyano-1 : 4-diphenylpiperidine (I; R, R' = Ph; R'' = CN). The nitrile was unaffected by ethanolic hydrogen chloride at 130°, whilst concentrated sulphuric acid in ethanol afforded only a sulphonated product. Hydrolysis was finally effected with hydrobromic acid (48%) at 170° and the product esterified to give 4-carbomethoxy-1 : 4-diphenylpiperidine. As Schaumann (*loc. cit.*) showed that among simple dolantin analogues corresponding 4-piperidyl ketones and esters possessed similar activity, 4-cyano-1 : 4-diphenylpiperidine was treated with ethylmagnesium bromide to yield 1 : 4-diphenyl-4-piperidyl ethyl ketone (I; R, R' = Ph; R'' = CO·Et). Experiments were also instituted to obtain compounds of this type but carrying oxygenated groups in one of the phenyl substituents. Thus reaction of *p*-anisidine with ethylene chlorohydrin gave *N*-di-( $\beta$ -hydroxyethyl)-*p*-anisidine, which was converted into *N*-di-( $\beta$ -chloroethyl)-*p*-anisidine, and thence by reactions similar to those above into 4-cyano-1-*p*-methoxyphenyl-4-phenylpiperidine (I; R = Ph; R' = *p*-MeO·C<sub>6</sub>H<sub>4</sub>; R'' = CN), *N*-*p*-methoxyphenylmorpholine being a by-product. On hydrolysis, the former was converted into 4-carboxy-1-*p*-hydroxyphenyl-4-phenylpiperidine which could not be directly esterified with methanolic hydrogen chloride. Moreover by treatment with diazomethane it was converted into 4-carbomethoxy-1-*p*-methoxyphenyl-4-phenylpiperidine. By esterifying the corresponding 1-*p*-acetoxyphenyl compound to produce 4-carbomethoxy-1-*p*-acetoxyphenyl-4-phenylpiperidine and removing the acetyl group the desired 4-carbomethoxy-1-*p*-hydroxyphenyl-4-phenylpiperidine was obtained.

Di-( $\beta$ -chloroethyl)aniline reacted with ethyl malonate producing 4 : 4-dicarbomethoxy-1-phenylpiperidine, which was devoid of analgesic activity despite its angular structure.

Attempts to prepare 3 : 4-dimethoxybenzyl chloride by interreaction of veratrole with trioxymethylene and hydrogen chloride in acetic acid gave a very low yield of veratryl alcohol, and a rather similar approach was made by allowing vanillin to react with benzyl chloride to obtain *O*-benzyl-vanillin which was to have been reduced. These experiments were abandoned when the paper of Schaumann (*loc. cit.*) became available.

6-Phenyl-2 : 2-dimethyl-piperidone could not be reduced by the Clemmensen method, only mixtures of low boiling ketones being recovered. It was, however, reduced satisfactorily to 6-phenyl-2 : 2-dimethylpiperidine by hydrazine in presence of sodium ethoxide. The latter, when allowed to react with ethoxyethyl bromide, was converted into 1- $\beta$ -ethoxyethyl-6-phenyl-2 : 2-dimethylpiperidine (V). Attempts to alkylate the parent piperidone with methyl iodide, ethylene oxide, or ethylene chlorohydrin failed. Nevertheless, it reacted spontaneously with methyl sulphate and 6-phenyl-1 : 2 : 2-trimethyl-4-piperidone was isolated, and an oxygenated analogue, 6-(4'-benzyloxy-3'-methoxyphenyl)-2 : 2-dimethyl-4-piperidone (VI) was prepared from *O*-benzylvanillin and diacetoneamine oxalate. In contrast with the 6<sub>2</sub>phenyl compound, the modified Kishner-Wolff reduction did not reduce the more complex piperidone and, in view of unpromising biological results, attempts at further modification of these piperidones were abandoned.

#### EXPERIMENTAL.

**2-Benzylpiperidine Derivatives.**—2-Benzylpyridine (46 g.; b. p. 146°/12 mm.) was hydrogenated in dioxan (300 c.c.) at 150°/95 atm. over Raney nickel (6 g.); 75% of the calculated amount of hydrogen was absorbed. The crude product was distilled and the distillate (46 g., b. p. 135°/12 mm.) treated with acetic anhydride (28 g.) for 1 hour at 90° and poured into water (300 c.c.). Unchanged benzylpyridine and other unacetylated products (10 g.) were removed from the oil by washing with *N*-HCl (250 c.c.) and 1-acetyl-2-benzylpiperidine distilled as an oil, b. p. 189°/12 mm. (Found : N, 6.6. C<sub>14</sub>H<sub>18</sub>ON requires N, 6.45%). It was almost unaffected by refluxing with concentrated hydrochloric acid for 90 minutes, and was hydrolysed by heating the oil (30 g.) with concentrated hydrochloric acid (40 c.c.) at 150° for 18 hours (sealed tube); on basifying the resulting solution, 2-benzylpiperidine, b. p. 128°/12 mm. (19 g.), was obtained. The picrate separated from acetone in prisms, m. p. 155° (Tshitschibabin, *J. Russ. Phys. Chem. Soc.*, 1901, **33**, 249, gives m. p. 156—157°). The methiodide solidified on rubbing with ether and was recrystallised from methanol when it formed prisms, m. p. 226° (Found : I, 40.0. C<sub>13</sub>H<sub>20</sub>NI requires I, 39.3%). Treatment of the methiodide with sodium hydroxide liberated an oil which was distilled under reduced pressure; 2-benzyl-1-methylpiperidine, b. p. 128°/12 mm., was obtained (Found : C, 82.8, H, 10.0. Calc. for C<sub>13</sub>H<sub>19</sub>N : C, 82.5; H, 10.1%). Ethylene bromohydrin (5.6 g.) and 2-benzylpiperidine (7.8 g.) were heated at 100° for 10 minutes; when the product was mixed with dioxan the quaternary salt solidified after some time; it was recrystallised from dioxan. 1- $\beta$ -Hydroxyethyl-2-benzylpiperidine hydrobromide had m. p. 133° (Found : Br, 26.9. C<sub>14</sub>H<sub>22</sub>ONBr requires Br, 26.6%). Liberation of the base with sodium hydroxide and distillation gave 1- $\beta$ -hydroxyethyl-2-benzylpiperidine as an oil, b. p. 130°/4 mm. (Found : C, 76.0; H, 9.9. C<sub>14</sub>H<sub>21</sub>ON requires C, 76.6; H, 9.7%). The base was heated at 100° for two hours with excess of benzoyl chloride, excess acid chloride removed by extracting an acid digest of the product with ether, and the benzoylated base liberated; 1- $\beta$ -benzyloxyethyl-2-benzylpiperidine was an oil, b. p. 160°/0.005 mm. (Found : C, 78.0; H, 7.9. C<sub>21</sub>H<sub>25</sub>O<sub>2</sub>N requires C, 78.0; H, 7.8%). 2-Benzylpiperidine (17 g.), water (160 c.c.), mercuric acetate (32 g.) and sufficient acetic acid to give a clear solution were warmed at 70° for 2 hours. The suspension was filtered and the filtrate freed from mercury salts with hydrogen sulphide in the usual way. The base, 2-piperidylphenylcarbinol, was liberated from the final filtrate with aqueous sodium carbonate and obtained as an oil (12 g.), b. p. 103°/3 mm.; it gave a picrate which separated from cyclohexanone in prisms, m. p. 167° (decomp.) (Found : C, 52.4; H, 3.6. C<sub>18</sub>H<sub>14</sub>O<sub>8</sub>N<sub>4</sub> requires C, 52.2; H, 3.4%). 2-Benzylpiperidine was heated

with an equimolecular quantity of  $\beta$ -bromoethyl methyl ether and the base liberated with sodium hydroxide; 1- $\beta$ -methoxyethyl-2-benzylpiperidine formed an oil, b. p. 180°/14 mm. (Found: C, 77.4; H, 9.95.  $C_{15}H_{23}ON$  requires C, 77.25; H, 10.0%). 1- $\beta$ -Ethoxyethyl-2-benzylpiperidine, b. p. 185°/14 mm., was prepared in a similar way (Found: C, 77.65; H, 10.5.  $C_{16}H_{25}ON$  requires C, 77.7; H, 10.2%).

**Phenylpiperidine Derivatives.**—Powdered sodamide (7 g.) was slowly added to a solution of di-( $\beta$ -chloroethyl)aniline (15 g.) and benzyl cyanide (8 g.) in toluene (50 c.c.) at ~45°, the reaction being completed by refluxing for 1 hour. Decomposition with water, removal of toluene in steam and distillation of the residue at 95° in high vacuum gave 4-cyano-1:4-diphenylpiperidine which solidified and was recrystallised from methanol, forming prisms, m. p. 97° (yield, 6.9 g.) (Found: C, 82.8; H, 7.1; N, 10.4.  $C_{18}H_{19}N_3$  requires C, 82.5; H, 6.9; N, 10.7%). Attempted hydrolysis with sulphuric acid was complicated by sulphonation, and no pure product was isolated. The cyanide (8.5 g.) was heated for 12 hours at 170° with hydrobromic acid (48%; 60 c.c.). Hydrogen bromide was removed under reduced pressure and the crude acid precipitated by bringing an alkaline solution of the residue to pH = 2; 1:4-diphenylpiperidine-4-carboxylic acid crystallised from ethanol in small prisms, m. p. 223° (Found: C, 76.8; H, 6.8.  $C_{18}H_{19}O_2N$  requires C, 76.9; H, 6.9%). The acid was esterified with diazomethane in ethereal suspension. 4-Carbomethoxy-1:4-diphenylpiperidine crystallised from ligroin containing a little chloroform in needles, m. p. 88° (yield, 6.3 g.) (Found: C, 77.1; H, 7.1.  $C_{19}H_{21}O_2N$  requires C, 77.3; H, 7.2%). The cyanide (11 g.) in isoamyl ether (70 c.c.) was added to a Grignard reagent prepared from magnesium (4 g.), ethyl bromide (18 g.) and isoamyl ether (100 c.c.) and the whole kept at 100° for 20 hours. Ice followed by 20% sulphuric acid (60 c.c.) was added and the resulting solid collected. This was 1:4-diphenyl-4-piperidyl ethyl ketone hydrobromide which was recrystallised from ethanol and from acetic acid; it had m. p. 256° (yield, 11.3 g.) (Found: C, 63.8; H, 6.3.  $C_{20}H_{21}ONBr$  requires C, 64.1; H, 6.5%). Treatment with sodium hydroxide gave the base which crystallised from methanol in small needles, m. p. 77° (Found: C, 82.0; H, 7.5.  $C_{20}H_{23}ON$  requires C, 81.9; H, 7.9%).

*p*-Anisidine (40 g.) and ethylene chlorohydrin (26 g.) were kept at 130° for 3 hours, a vigorous reaction taking place during the first few minutes. Addition of water (300 c.c.) and excess of sodium hydroxide gave an oil which was taken up in ether and fractionated under reduced pressure. Di-( $\beta$ -hydroxyethyl)-*p*-anisidine (32 g.) was collected at 242°/12 mm.; when crystallised from methanol it formed prisms, m. p. 73° (Found: C, 62.4; H, 8.3.  $C_{11}H_{13}O_3N$  requires C, 62.5; H, 8.2%). Di-( $\beta$ -hydroxyethyl)-2-anisidine (35 g.) in chloroform (200 c.c.) was treated slowly with phosphorus oxychloride (25 g.), the solution kept for 1 hour at 90°, and decomposed with aqueous sodium carbonate. The oil was taken up in chloroform and distilled under reduced pressure; di-( $\beta$ -chloroethyl)-*p*-anisidine had b. p. 158°/4 mm., and separated from methanol in prisms, m. p. 51° (yield 30 g., 75%) (Found: C, 53.1; H, 5.9.  $C_{11}H_{13}ONCl_2$  requires C, 53.2; H, 6.1%). The chloro-compound (12.5 g.) was condensed with benzyl cyanide (6 g.) as in the case of di-( $\beta$ -chloroethyl)aniline above. Unchanged chloro-compound and a substituted morpholine (6.1 g.), b. p. 140°/2 mm., were recovered and 4-cyano-1-*p*-methoxyphenyl-4-phenylpiperidine (7 g.) collected at 210°/2 mm.; the cyanide crystallised from ethanol in prisms, m. p. 96° (Found: C, 77.7; H, 6.7.  $C_{19}H_{20}ON_2$  requires C, 77.6; H, 6.9%). The lower boiling fraction solidified and was crystallised from light petroleum, separating in prisms, m. p. 73–74°; this material contained no halogen but was soluble in dilute hydrochloric acid and was evidently *N*-*p*-methoxyphenylmorpholine (Found: C, 68.4; H, 7.85.  $C_{11}H_{15}O_3N$  requires C, 68.4; H, 7.85%). The above 4-cyano-1-*p*-methoxyphenyl-4-phenylpiperidine (2.9 g.) was heated for 15–16 hours at 170° (sealed tube) with hydrobromic acid (48%; 20 c.c.). The solid hydrobromide was dissolved in aqueous sodium hydroxide, the solution acidified and the precipitate sublimed at 200° in high vacuum; 4-carboxy-1-*p*-hydroxyphenyl-4-phenylpiperidine had m. p. 284° (decomp.) (yield, 97%) (Found: C, 72.65; H, 6.45.  $C_{19}H_{19}O_3N$  requires C, 72.6; H, 6.45%). This acid (7.3 g.) was acetylated with acetic anhydride (10 c.c.) and pyridine (15 c.c.) and reaction completed on the steam-bath for 1 hour. Addition of water precipitated crude 4-carboxy-1-*p*-acetoxyphenyl-4-phenylpiperidine (6 g.) which crystallised from ethanol in microscopic prisms, m. p. 216° (Found: C, 70.7; H, 6.25.  $C_{20}H_{21}O_4N$  requires C, 70.8; H, 6.25%). Excess of diazomethane in ether (200 c.c.) containing a little methanol was added to the foregoing compound (4.7 g.) and the mixture left overnight; the solvent was removed and the ester (4.7 g.) recrystallised from ethanol. 4-Carbomethoxy-1-*p*-acetoxyphenyl-4-phenylpiperidine crystallised in prisms, m. p. 115–117°, and could be sublimed in high vacuum at 140° (Found: C, 70.8; H, 6.55.  $C_{21}H_{23}O_4N$  requires C, 71.4; H, 6.6%). This ester (4 g.) was shaken for 2 hours at 40° with sodium hydroxide (2 g.) in water (20 c.c.) and ethanol (30 c.c.), the solution acidified, the filtrate neutralised with sodium bicarbonate and the precipitate so obtained (3.1 g.) extracted with ether. The ester, obtained from the ethereal solution, could be sublimed at 110° in high vacuum and separated from ethyl acetate in microscopic needles, m. p. 172° (Found: C, 73.3; H, 6.5.  $C_{19}H_{21}O_3N$  requires C, 73.3; H, 6.8%). 4-Carboxy-1-*p*-hydroxyphenyl-4-phenylpiperidine was left for some hours with excess of ethereal diazomethane containing a little methanol. After removing the solvents, the residue, dissolved in carbon tetrachloride, was chromatographed on alumina and the material recovered from the eluate recrystallised from a ligroin-carbon tetrachloride (10:1). 4-Carbomethoxy-1-*p*-methoxyphenyl-4-phenylpiperidine separated in small needles, m. p. 146° (Found: C, 73.65; H, 6.9.  $C_{20}H_{23}O_3N$  requires C, 73.85; H, 7.1%).

Ethyl malonate (10 g.), molecular sodium (1.5 g.) and di-( $\beta$ -chloroethyl)aniline (13.7 g.) were heated in toluene (50 c.c.) for 24 hours at 100°. Addition of water and distillation of the toluene layer gave 4:4-dicarbomethoxy-1-phenylpiperidine as an oil, b. p. 140°/4 mm., which solidified and crystallised from methanol in prisms, m. p. 53° (Found: C, 66.8; H, 7.2.  $C_{17}H_{20}O_4N$  requires C, 66.9; H, 7.6%).

6-Phenyl-2:2-dimethyl-4-piperidone (Kleintz, *Annalen*, 1878, 192, 63) (10 g.) was warmed to 100° for 10 minutes with dimethyl sulphate (6.3 g.). The solid product was dissolved in ethanol and poured into excess aqueous sodium hydroxide and the organic base extracted with ether and distilled. 6-Phenyl-1:2:2-trimethyl-4-piperidone (5 g.) had b. p. 163°/12 mm.; it solidified and crystallised from ligroin in stout prisms, m. p. 77° (Found: C, 77.7; H, 8.7.  $C_{14}H_{19}ON$  requires C, 77.4; H, 8.8%). 6-Phenyl-2:2-dimethyl-4-piperidone (26 g.) was added to sodium methoxide (65 g.) and ethanol (100 c.c.) followed by 98% hydrazine hydrate (15 g.) and the whole heated (autoclave) at 200° for 15 hours. Ethanol was removed at 100°, the residue diluted with water to 700 c.c. and the base extracted with ether. 6-Phenyl-2:2-dimethylpiperidine (22.5 g.) was collected as a liquid, b. p. 127°/12 mm. (Found: C, 82.95; H, 9.85.  $C_{13}H_{18}N$  requires C, 82.5; H, 10.1%); its *picrate* separated from ethyl acetate-ligroin in needles, m. p. 173° (Found: C, 54.0; H, 5.5.  $C_{18}H_{22}O_7N_4$  requires C, 54.0; H, 5.3%); its *hydrobromide* crystallised from ethanol in prisms, m. p. 293° (Found: C, 58.1; H, 7.5.  $C_{13}H_{20}NBr$  requires C, 57.8; H, 7.4%). When the preceding base (22.5 g.) was heated with ethoxyethyl bromide (21 g.) at 170° for 5 hours (sealed tube) much of it escaped reaction and was recovered as hydrobromide, but from the mixture of liquid products 1-ethoxyethyl-6-phenyl-2:2-dimethylpiperidine (11.8 g.) was isolated by fractionation as a liquid, b. p. 172°/23 mm. (Found: C, 78.25; H, 10.5.  $C_{17}H_{23}ON$  requires C, 78.15; H, 10.40%); its *picrate* was not suitable for characterisation but it formed a *perchlorate*, m. p. 165°, which crystallised from ethanol in small prisms (Found: C, 56.2; H, 7.6.  $C_{17}H_{23}O_5NCl$  requires C, 56.4; H, 7.8%).

Diacetonamine oxalate (20 g.), vanillin (16 g.) and ethanol (100 c.c.) were refluxed for 2 hours, the filtrate and hot ethanol washings (50 c.c.) concentrated to 100 c.c. and refluxing continued for 12 hours; the solid was collected and the filtrate again refluxed for 4 hours. The solid products (18 g.) were shaken with ether and sodium bicarbonate so that the aqueous phase was at pH = 7.4 and the ethereal extracts were concentrated. 6-(4'-Hydroxy-3'-methoxy-phenyl)-2:2-

*dimethyl-4-piperidone* (10.3 g.) so obtained was recrystallised from carbon tetrachloride-benzene in prisms, m. p. 108° (Found: C, 67.3; H, 7.5.  $C_{14}H_{19}O_3N$  requires C, 67.45; H, 7.7%). Vanillin (50 g.) in ethanol (100 c.c.) was added slowly with shaking to ethanol (100 c.c.) containing sodium (7.7 g.) followed by benzyl chloride (44 g.) and sodium iodide (3 g.) and the whole refluxed for 6 hours. The cold solution was filtered and concentrated and the benzyl ether crystallised (total yield, 69 g.). *4-Benzyl-oxy-3-methoxybenzaldehyde* had b. p. 185°/2 mm. and separated from methanol in prisms, m. p. 67° (Found: C, 74.55; H, 5.95.  $C_{15}H_{14}O_3$  requires C, 74.4; H, 5.8%). Diacetonamine oxalate (49 g.), benzylvanillin (105 g.) and ethanol (200 c.c.) were refluxed for 40 hours, the solid which separated being removed in stages (total yield of the piperidone oxalate, 70 g.). Treatment of the solid with aqueous sodium hydroxide gave 6-(4'-benzyloxy-3'-methoxy-phenyl)-2:2-dimethyl-4-piperidone which separated from ethanol in prisms, m. p. 123° (yield 53 g.) (Found: C, 74.0; H, 7.5.  $C_{21}H_{26}O_3N$  requires C, 74.3; H, 7.45%).

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