

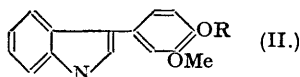
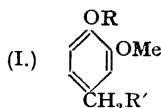
339. *Homovanillin.*

By A. A. L. CHALLIS and G. R. CLEMO.

Homovanillin (I; R = H, R' = CHO) was prepared in 65% yield by ozonolysis of *O*-carbethoxyeugenol, followed by catalytic decomposition of the ozonide, and removal of the hydroxyl-protecting group by mild hydrolysis. Eugenol methyl ether and acetyl- and carbobenzyloxy-eugenol similarly gave the analogously substituted homovanillins.

Homovanillin and its derivatives were used in the Fischer indole synthesis, and the Strecker amino-acid synthesis; and condensation with *cyclohexanone* followed by cyclisation and dehydrogenation provided a new route to substituted phenanthrenes.

HOMOVANILLIN was obtained in poor yield by Harries and Haarmann (*Ber.*, 1915, **48**, 29, 868) by ozonolysis of eugenol and decomposition of the ozonide by zinc and acetic acid. We have found that at 0° and in ordinary freezing mixtures a solution of *O*-carbethoxyeugenol (I; R = CO₂Et, R' = ·CH₂CH₃) in ethyl acetate with excess of ozone gives chiefly *O*-carbethoxyhomovanillic acid, but at -70° 5% ozone is almost completely utilised if the special vessel illustrated in the figure is employed, and if the ozonide is immediately decomposed by shaking with hydrogen and palladised charcoal (cf. Henne and Perilstein, *J. Amer. Chem. Soc.*, 1943, **65**, 2183), good yields of *O*-carbethoxyhomovanillin were produced which could be converted into homovanillin by hydrolysis in dry 2% alcoholic hydrochloric acid. The final product—a viscous pale yellow oil—did not solidify, but gave a *p*-nitrophenylhydrazone, a 2 : 4-dinitrophenylhydrazone, and a semicarbazone, all in 85—90% yield. In the presence of even small amounts of aqueous alkali or acid, the homovanillin polymerised, but otherwise was quite stable.



O-Acetylhomovanillin was prepared in an analogous manner. Oxidation in very dilute potassium permanganate solution containing excess of magnesium sulphate gave *O*-acetylhomovanillic acid; more vigorous conditions gave *O*-acetylvanillic acid. Nitration of *O*-acetylhomovanillin in acetic anhydride with the theoretical quantity of nitric acid for either the mono- or the dinitro-compound gave nitrogenous red oils which would not solidify and could not be distilled.

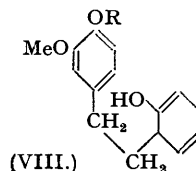
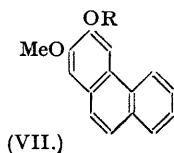
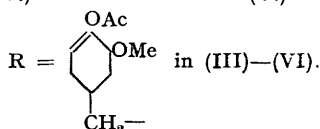
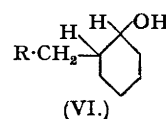
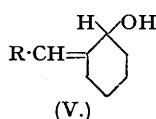
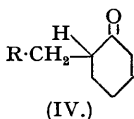
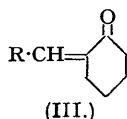
It was found that the ozonide of *O*-carbomethoxyeugenol (I; R = CO₂CH₂·Ph, R' = CH₂CH₃) (Bergmann and Zervas, *Ber.*, 1932, 65, 1194; Olcott, *J. Amer. Chem. Soc.*, 1939, 59, 392) gave only *O*-carbomethoxyhomovanillin (I; R = CO₂CH₂·Ph, R' = CHO) on catalytic reduction. The use of large amounts of catalyst did not result in hydrogenolysis to homovanillin.

Homovanillin phenylhydrazone was used in a Fischer indole synthesis giving 3-4'-hydroxy-3'-methoxyphenylindole (II; R = H). This gave only a slight colour in the Ehrlich rosindole reaction (indoles substituted in position 3 usually give this reaction, and the failure in this case may be due to steric hindrance of the substituent, since neither 2- nor 3-phenylindole gives a colour), but the pine-shaving test was strong, ferric chloride gave a deep red colour, and concentrated sulphuric acid a series of colour changes.

The hydroxyl group of the indole was readily acetylated and benzoylated. These derivatives gave only slight colours in the rosindole test. With the pine-shaving a good violet colour was obtained, but no colour was given with ferric chloride.

O-Acetylhomovanillin was used in a Strecker synthesis of β-4-hydroxy-3-methoxyphenylalanine [I; R = H, R' = CH(NH₂)·CO₂H]. A slight modification of the general method of Cocker and Lapworth (*J.*, 1931, 1391) was used, but the yield obtained (ca. 30%) does not compare with the 65% by the synthesis of Johnson and Bengis (*J. Amer. Chem. Soc.*, 1913, 35, 1613), who hydrolysed vanillylhydantoin, obtained by the reduction of vanillylidenehydantoin, with barium hydroxide.

O-Acetylhomovanillin was condensed with cyclohexanone in technical pyridine to give the homovanillylidene derivative (III), which crystallised only with difficulty, possibly owing to the presence of geometrical isomers; the dihydro-compound (IV) crystallised fairly readily. This was obtained by reduction of (III) either with sodium amalgam in alcohol-acetic acid, or by catalytic hydrogenation, using Adams's catalyst; it was saturated but still gave an oxime. On prolonged refluxing of a moist ethereal solution of (III) with aluminium amalgam, a compound was obtained which was unsaturated and non-ketonic and was consequently formulated as (V). This compound also was difficult to obtain crystalline and when catalytically hydrogenated gave a non-ketonic saturated dihydro-compound identical with that obtained by action of aluminium amalgam on (IV). The latter gives a benzoyl derivative; and is therefore 2-*O*-acetylhomovanillyl-cyclohexanol (VI).



Attempts to cyclise it by using sodium ethoxide, syrupy phosphoric acid, or phosphoric oxide in benzene all failed. This may be due to the fact that while free rotation about the carbon bonds of the atoms joining the two cyclic systems allows favourable orientation of the hydrogen and hydroxyl groups on the two rings, all three bonds would have to be in definite positions to enable this orientation to take place. The substance (III), however, was found to cyclise in small yield in either a boiling benzene suspension of phosphoric oxide or on standing at room temperature in a chloroform solution of phosphorus oxychloride. With these drastic

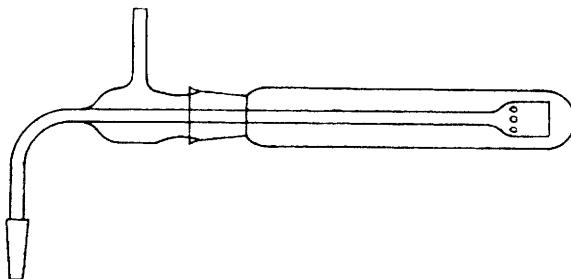
reagents, enolisation and isomerisation of (III) to (VIII) would be expected; this would then cyclise *para* to the methoxy-group and aromatisation would occur to give 3-acetoxy-2-methoxy-9:10-dihydrophenanthrene. This structure was confirmed by a fairly smooth selenium dehydrogenation of the cyclisation product to phenanthrene. Further, less drastic dehydrogenation by heating to 210–220° with palladium-black (Majima and Murahs, *Proc. Imp. Acad. Japan*, 1934, 10, 342) gave 3-acetoxy-2-methoxyphenanthrene (VII, R = Ac; Gilman and Cook, *J. Amer. Chem. Soc.*, 1940, 62, 2816), which was hydrolysed to 3-hydroxy-2-methoxyphenanthrene (VII, R = H; Gilman and Cook, *loc. cit.*); methylation gave 2:3-dimethoxyphenanthrene (VII, R = Me; Pschorr and Buckow, *Ber.*, 1900, 33, 1831).

EXPERIMENTAL.

(All m. p.s and b. p.s are uncorrected. Sodium sulphate was used as the drying agent unless otherwise stated.)

O-Carbethoxyeugenol.—Sodium hydroxide solution (35 g., 40%) was added dropwise with cooling and shaking to a mixture of eugenol (54 g.) and ethyl chloroformate (40 g.). The whole was extracted with ether, the extract washed with water and dried, the ether removed, and the residue distilled in a vacuum (50 g., b. p. 135–138°/1.5 mm.). The distillate solidified to stout rhombs, m. p. 31°.

O-Carbethoxyhomovanillin.—*O*-Carbethoxyeugenol (10 g.) was dissolved in ethyl acetate (100 c.c.), the solution placed in the ozonolysis vessel (see fig.), and the whole cooled in acetone–Drikold. A



stream of 5% ozone at 50 c.c./min. was passed in for 6 hrs. The cold solution of the ozonide was hydrogenated in the presence of palladised charcoal (2 g.), hydrogen being rapidly absorbed (530 c.c. at 17° and 754 mm. in 40 mins.). The flask was evacuated, air admitted, the flask shaken for 10 mins., the air replaced by hydrogen, and the flask shaken for 5 hrs. The solution was filtered (the catalyst, after being washed with a little alcohol and dried, can be used 10–12 times), and the solvent removed under reduced pressure. The residue was dissolved in ether, the solution washed with saturated sodium hydrogen carbonate solution (washings A, see below), dried, the ether removed, and the residue fractionated in a vacuum: 0.5 g., b. p. 135–140°/2 mm.; 7.5 g., b. p. 150–155°/2 mm.; 1 g., b. p. 170–200°/2–3 mm. The redistilled middle fraction was *O*-carbethoxyhomovanillin (Found: C, 60.7; H, 6.1. C₁₂H₁₄O₅ requires C, 60.5; H, 5.9%); its 2:4-dinitrophenylhydrazone formed short yellow needles, m. p. 129–130° (Found: C, 51.7; H, 4.7. C₁₈H₁₆O₈N₄ requires C, 51.7; H, 4.3%), from alcohol, and its *p*-nitrophenylhydrazone crystallised from alcohol in orange-red rhombs, m. p. 85–86° (Found: C, 57.6; H, 5.0. C₁₈H₁₆O₈N₃ requires C, 57.8; H, 5.1%).

Homovanillin.—Carbethoxyhomovanillin (4.5 g.) was dissolved in absolute alcohol (75 c.c.), and dry hydrogen chloride (1.5 g.) passed in. The whole was heated for 1 hr. at 60°, the alcohol removed under reduced pressure, and the residue dissolved in ether; the ethereal solution was washed with saturated sodium hydrogen carbonate solution, dried, the ether removed, and the residue twice distilled in a vacuum (3.2 g.), b. p. 147–149°/2 mm. (Found: C, 65.5; H, 6.0. Calc. for C₉H₁₀O₃: C, 65.2; H, 6.2%). *Homovanillin* is a pale oil, stable in air, and giving a blue coloration with ferric chloride. Its 2:4-dinitrophenylhydrazone crystallised from alcohol in yellow cubes, m. p. 203°. Its *p*-nitrophenylhydrazone, recrystallised from ethyl acetate, had m. p. 154° (Harries and Haarmann, *loc. cit.*, give m. p. 154–155°). The semicarbazone, recrystallised from alcohol, had m. p. 173° (Harries and Haarmann, *loc. cit.*, give 173°), and the oxime, colourless needles from alcohol, had m. p. 115° (Harries and Haarmann, *loc. cit.*, give 115°).

O-Carbethoxyhomovanillic Acid.—On acidifying the wash liquor (A) from carbethoxyhomovanillin a colourless crystalline solid was precipitated; it recrystallised from water as glistening, colourless, elongated plates of the acid (0.1 g.), m. p. 125–126° (Found: C, 56.5; H, 5.3. C₁₂H₁₄O₄ requires C, 56.7; H, 5.5%).

Homovanillic acid.—*O*-Carbethoxyhomovanillic acid (1 g.) was heated for 2 hours on a water-bath with sodium hydroxide (10%, 6 c.c.), and the product, precipitated by acidification and cooling, was recrystallised from water, forming glistening plates (0.7 g.), m. p. 139° (Harries and Haarmann, *loc. cit.*, give 139°).

O-Acetylhomovanillin.—*O*-Acetyleneugenol (13 g.) was ozonised for 11 hrs. and worked up in the same manner as the carbethoxy-compound (0.6 g., b. p. 130–135°/2 mm.; 9.2 g., b. p. 140–145°/2 mm.; 2 g., b. p. 150–200°/2 mm.). The redistilled middle fraction (Found: C, 63.1; H, 5.6. Calc. for C₁₁H₁₂O₄: C, 63.4; H, 5.8%) gave a 2:4-dinitrophenylhydrazone, which crystallised from alcohol in yellow cubes, m. p. 144–145° (Found: C, 52.8; H, 4.3. C₁₇H₁₆O₇N₄ requires C, 52.6; H, 4.1%).

O-Acetylhomovanillic Acid.—(1) Homovanillic acid (0.5 g.) was dissolved in a solution of sodium hydroxide (0.3 g.) and poured into acetyl chloride (1 c.c.). The product which separated on cooling crystallised from water in glistening plates (0.45 g., m. p. 135–136°) (Harries and Haarmann, *loc. cit.*, give 134°). Hydrolysis gave homovanillic acid, m. p. and mixed m. p. 139°.

(2) The bicarbonate wash liquor from acetylhomovanillin gave, on acidification and recrystallisation from water, the same acid (0.2 g., m. p. and mixed m. p. 135–136°).

(3) *O-Acetylugenol* (2 g.) in ethyl acetate (100 c.c.) was ozonised for 12 hrs. at 0°. Removal of the solvent, dissolution of the residue in ether, extraction of the ethereal solution with saturated bicarbonate solution, and acidification of the extract gave acetylhomovanillic acid (1.2 g.), m. p. and mixed m. p. 135–136°.

(4) Acetylhomovanillin (2 g.) in acetone (15 c.c.) was shaken with a solution of potassium permanganate (1 g.) in water (1500 c.c.) containing magnesium sulphate (2 g.) for 24 hrs. The manganese dioxide was filtered off, and the filtrate evaporated to dryness. Hydrochloric acid (6*N*, 13 c.c.) was added, and acetylhomovanillic acid filtered off and recrystallised from water (0.8 g.), m. p. and mixed m. p. 135–136°; a small amount of homovanillic acid was also formed.

Vanillic Acid.—Acetylhomovanillin (1 g.) in acetone (30 c.c.) was shaken with potassium permanganate (1 g.) dissolved in water (100 c.c.), the manganese dioxide filtered off, the filtrate evaporated to dryness, and the residue ground with concentrated hydrochloric acid (5 c.c.) and warmed on the water-bath for 15 mins. The vanillic acid was filtered off, and recrystallised from water as lustreless cubes (0.25 g., m. p. and mixed m. p. 207°).

Nitration of O-Acetylhomovanillin.—Fuming nitric acid (*d* 1.52, 0.36 g.) was added dropwise to a mechanically stirred solution of acetylhomovanillin (2 g.) in acetic anhydride (25 c.c.) in a freezing mixture, and the whole was set aside overnight. Urea (1 g.) was added, the mixture diluted with water (100 c.c.) and extracted with ether, the extract washed with sodium hydrogen carbonate solution (5%), dried, and the ether removed. The residue was a deep red oil which solidified in "Drikold" but melted again at room temperature; it could not be distilled. Use of twice the quantity of nitric acid and warming the reaction mixture on the water-bath gave an apparently identical product.

O-Carbobenzyloxyeugenol.—Carbobenzyloxy chloride (3.5 g.) (Bergmann and Zervas, *loc. cit.*) was added to a suspension of eugenol (3 g.) in water (70 c.c.) containing sodium carbonate (1 g.). The whole was shaken for 48 hrs., the smell of the acid chloride then having almost gone (cf. Olcott, *loc. cit.*). The suspension was extracted with ether, the extract dried, the ether removed, and the residue distilled in a vacuum (5.8 g., b. p. 170–180°/1–2 mm.). On standing, the distillate solidified into stout needles, m. p. 53°.

O-Carbobenzyloxyhomovanillin.—Carbobenzyloxyeugenol (13 g.) was ozonised for 6 hrs. and worked up in the same manner as the carbethoxy-compound except that 6 g. of pallidised charcoal were used. The middle fraction (9 g., b. p. 160–170°/1 mm. Found: C, 67.7; H, 5.5. $C_{17}H_{15}O_3$ requires C, 68.0; H, 5.3%) gave no coloration with ferric chloride.

O-Carbobenzyloxyhomovanillic Acid.—The bicarbonate wash liquor from the last experiment, on neutralisation, gave this acid, which crystallised from water in long lustrous needles (0.8 g., m. p. 107–108°). On refluxing with hydrochloric acid (4*N*, 10 c.c.), this gave homovanillic acid, m. p. and mixed m. p. 139°.

3,4'-Hydroxy-3'-methoxyphenylindole.—Homovanillin (2.2 g.) and phenylhydrazine (1.5 g., freshly distilled) were refluxed in alcohol (25 c.c.) for 3 hrs., and the alcohol distilled off. Fresh alcohol (25 c.c.) was added and the solution saturated with dry hydrogen chloride and refluxed for 1 hr. The alcohol was distilled off, alcohol (25 c.c.) added, and the whole saturated with dry hydrogen chloride at 0° and set aside overnight, then refluxed for 1 hr. and the alcohol distilled off. The residue was extracted with hot benzene, and the extract cooled, filtered, and the benzene removed. The residual oil (0.5 c.c.), dissolved in benzene (0.7 c.c.), was poured dropwise into well-stirred light petroleum (b. p. 40–60°). The creamy-white precipitate was filtered off and washed with a little light petroleum, then recrystallised from benzene–light petroleum (b. p. 80–100°) (0.5 g., m. p. 117°, softening at 100°) (Found: C, 75.1; H, 5.4. $C_{17}H_{15}O_3N$ requires C, 75.3; H, 5.45%). The *indole* is soluble in alcohol, benzene, acetone, acetic anhydride, and sodium hydroxide solution, and slightly soluble in hot light petroleum. It gives no coloration in the Ehrlich test, but gives a red-violet pine-shaving reaction, and with concentrated sulphuric acid, a blood-red colour, changing to purple and brown. 3-Phenylindole also gives no Ehrlich test, but with concentrated sulphuric acid it gives a yellow colour, changing to red and brown.

The *O-acetyl* derivative, had m. p. 96° (softening at 90°) (Found: C, 70.9; H, 5.1. $C_{17}H_{15}O_3N$ requires C, 71.4; H, 5.6%), and the *O-benzoyl* derivative m. p. 133° (softening at 130°) (Found: C, 76.2; H, 4.5. $C_{22}H_{17}O_3N$ requires C, 76.9; H, 4.95%), both from benzene light petroleum (b. p. 80–100°).

Both compounds were soluble in organic solvents, but almost insoluble in sodium hydroxide solution or water; neither gave an Ehrlich reaction, but both gave a violet colour in the pine-shaving test.

β-4-Hydroxy-3-methoxyphenylalanine.—*O-Acetylhomovanillin* (20 g.) was dissolved in liquid hydrogen cyanide (40 c.c.), and after 10 mins. the solution was slowly added with stirring to a solution of ammonia (20 g.) in water (25 c.c.) cooled to –70°. The result was sealed, and the mixture set aside overnight and then slowly added to a mechanically stirred solution of sulphuric acid (1200 c.c., 40%), heated to 125° for 3 hrs., and poured into water (2 l.). The solution was heated to boiling and barium hydroxide (700 g.) added. Superheated steam was passed through the boiling solution, while barium carbonate was added in small portions till no more ammonia was evolved (*ca.* 250 g. required). Dilute sulphuric acid was added until the solution showed the presence of sulphate ion, and the barium sulphate was filtered off and well washed, and the combined filtrate and washings concentrated to 100 c.c. The hot solution was treated with lead carbonate until effervescence ceased (*ca.* 10–12 g.); it was not acid to Congo-red. The whole, after standing overnight, was filtered and the filtrate saturated with hydrogen sulphide, allowed to stand, and refiltered. After being boiled with charcoal (3 g.), the filtered solution was concentrated to 20 c.c. and set aside. The crystals (5 g., and a further 1.4 g. obtained on concentration) melted at 228–229°. Recrystallisation from water afforded colourless needles (4 g.), m. p. 254–255° (decomp.), after losing water of crystallisation (Johnson and Bengis, *loc. cit.*, report a dihydrate, m. p. 255–256°, decomp.).

The anhydrous hydrogen cyanide used was conveniently stored in an equal volume of glacial acetic acid. No heat was evolved on mixing, and the solution was kept in an ordinary well-stoppered bottle without deterioration. The pure cyanide was obtained by distilling the solution from a bath at 30–40°.

2-O-Acetylhomovanillylidencyclohexanone (III).—Acetylhomovanillin (13 g.) and cyclohexanone (8 g.) in dry technical pyridine (80 c.c., b. p. 135°) were heated under reflux for 8 hrs., the solvent evaporated off, and the residue poured into water (180 c.c.). The mixture was acidified and extracted with warm benzene, the extract washed (dilute hydrochloric acid; dilute sodium hydroxide solution; water), dried, and refluxed for 0.5 hr. with active charcoal (2 g.). The hot solution was filtered and concentrated to 40 c.c., the residue poured dropwise into well-stirred cold light petroleum (b. p. 40–60°), and the creamy-white precipitate of the compound (III) (18 g.) filtered off, washed with a little petroleum, and recrystallised from benzene–light petroleum or dilute alcohol (10 g.), m. p. 84° (Found: C, 70.5; H, 7.3. $C_{17}H_{20}O_4$ requires C, 71.0; H, 7.0%). The oxime formed needles, m. p. 106°, from alcohol.

2-Homovanillylidencyclohexanone.—(1) The above ketone (0.5 g.) was shaken with sodium hydroxide solution (6%, 25 c.c.) at 100° for 0.5 hr., then heated at this temperature for 1 hr. After cooling, the solution was extracted with ether, acidified, and extracted with benzene. The benzene extract was dried and boiled under reflux with active charcoal (0.2 g.) for 0.25 hr. The extract was filtered, concentrated to 4 c.c., and poured dropwise with stirring into cold light petroleum (b. p. 40–60°). The creamy-white precipitate was filtered off and washed with a little petroleum, then recrystallised from benzene–light petroleum or dilute alcohol (0.3 g., m. p. 105°).

(2) *O*-Acetylhomovanillin (3.5 g.) and cyclohexanone (2 g.) were refluxed in absolute alcohol (50 c.c.) containing sodium (2.5 g.) for 4 hrs. Glacial acetic acid (6.5 c.c.) was added, and the alcohol removed. The residue was poured dropwise into well-stirred ice-water, and the precipitate collected, washed, dried, dissolved in benzene (50 c.c.), and worked up as above, giving 3 g., m. p. and mixed m. p. with the above 105°.

2-O-Acetylhomovanillylcyclohexanone (IV).—(1) 2-Acetylhomovanillylidencyclohexanone (3 g.) was dissolved in alcohol (25 c.c.), and the solution vigorously stirred while sodium amalgam (4%, 40 g.) was added in small portions. The solution was kept just acid by gradual addition of glacial acetic acid (4.5 c.c.). The temperature towards the end of the reaction was kept between 50° and 60°. The whole was made slightly basic (sodium hydroxide) and evaporated to dryness. The residue was extracted with hot benzene, the extract washed with a little water, dried, refluxed with active charcoal (0.8 g.) for 0.3 hr., filtered, concentrated to 8 c.c., and poured dropwise into well-stirred cold light petroleum (b. p. 40–60°). The colourless precipitate was collected, washed with a little petroleum, and crystallised from benzene–light petroleum or dilute alcohol (2.5 g., m. p. 134°).

(2) The same ketone (30.13 mg.) was quantitatively hydrogenated in glacial acetic acid (10 c.c.) with freshly reduced Adams's catalyst (3 mg.), 2.30 c.c. of hydrogen at N.T.P. being absorbed in 20 mins. (0.985 double bond). The solution was filtered and concentrated to 1.5 c.c., water (20 c.c.) was added, and the precipitate recrystallised from benzene–light petroleum, giving 0.02 g., m. p. and mixed m. p. with the above 134°. The compound was saturated and gave an oxime, needles (from alcohol), m. p. 83°.

2-O-Acetylhomovanillylidencyclohexanol (V).—2-Acetylhomovanillylidencyclohexanone (3 g.), dissolved in moist ether (150 c.c.), was heated under reflux for 12 hrs. with freshly prepared aluminium amalgam (4 g.), the mixture filtered, and the alumina and excess of amalgam washed with ether; the filtrate and washings were dried, the ether removed, and the residual oil dissolved in benzene (8 c.c.) and poured dropwise into well-stirred cold light petroleum. The precipitate was collected, washed with a little petroleum, and recrystallised from benzene–light petroleum. The compound (2.4 g., m. p. 151°) was unsaturated and did not form an oxime, but was soluble in sodium hydroxide.

2-O-Acetylhomovanillylcyclohexanol (VI).—(1) The above hexanol (36.41 mg.) was quantitatively hydrogenated in glacial acetic acid solution (10 c.c.) with freshly reduced Adams's catalyst (5 mg.); 2.76 c.c. of hydrogen at N.T.P. were absorbed in 15 mins. (0.982 double bond). The solution was filtered and concentrated to 1.3 c.c., water (20 c.c.) was added, and the precipitate recrystallised from benzene–light petroleum (0.02 g., m. p. 171°).

(2) 2-Acetylhomovanillylcyclohexanone (3 g.), treated with aluminium amalgam and worked up exactly as in the preparation of (V), gave 2.58 g., m. p. and mixed m. p. with preparation (1) 171°; the compound (VI) was saturated and non-ketonic (Found: C, 70.0; H, 8.0. $C_{17}H_{24}O_4$ requires C, 70.0; H, 8.2%). This gave a benzoate, m. p. 156° (Found: C, 72.4; H, 6.9. $C_{24}H_{28}O_5$ requires C, 72.7; H, 7.1%), from benzene–light petroleum.

Attempted Cyclisations.—(1) *2-Homovanillylcyclohexanol.* 2-Acetylhomovanillylcyclohexanol (0.3 g.), dissolved in absolute alcohol (10 c.c.) containing sodium (0.2 g.), was heated under reflux for 2 hrs. Glacial acetic acid (1 c.c.) was then added, and the whole evaporated to dryness. The residue was extracted with ether, and the extract washed (sodium carbonate), and dried. The ether was removed, and the oily residue dissolved in benzene (1.5 c.c.) and poured into cold, well-stirred light petroleum (b. p. 40–60°). The precipitate, recrystallised from benzene–light petroleum (0.14 g.), had m. p. 161–163° and was probably *2-homovanillylcyclohexanol* (Found: C, 72.1; H, 8.5. $C_{16}H_{22}O_3$ requires C, 72.0; H, 8.8%).

(2) The cyclohexanol (0.5 g.) was stirred into syrupy phosphoric acid (3 c.c.) and set aside for 10 hrs. The whole was poured into water, basified (sodium hydroxide), and extracted with ether. This extract contained only a trace of material. The aqueous solution was acidified and extracted with ether, and the extract worked up like the ethereal extract in (1), giving 0.3 g., m. p. and mixed m. p. with the starting material 171°.

(3) The cyclohexanol (0.5 g.) was stirred into syrupy phosphoric acid (3 c.c.) and warmed on the water-bath for 1 hr. Considerable tar was formed. Working up as in (2) afforded only 0.1 g. of starting material.

(4) To the cyclohexanol (0.3 g.) refluxing in benzene (10 c.c.), phosphoric oxide (0.6 g.) was added in small portions during 1.5 hrs. Water (25 c.c.) was added to the cooled reaction mixture, and the whole worked up as above. Only impure starting material (0.1 g.) was obtained.

3-Acetoxy-2-methoxy-9:10-dihydrophenanthrene. (1) 2-O-Acetylhomovanillylidencyclohexanone (10

g.) and benzene (100 c.c.) were heated under reflux while phosphoric oxide (10 g.) was added in small portions during 3 hrs. The mixture was decomposed with water (200 c.c.), and the whole basified (sodium hydroxide) and extracted with ether (extract *A*). The aqueous solution was acidified and extracted again with ether (extract *B*). Extract *A* was washed with water, dried, and the ether removed. The residue, recrystallised several times from dilute alcohol, gave needles (0.18 g.), m. p. 174° (Found: C, 75.9; H, 5.65. $C_{17}H_{14}O_2$ requires C, 76.1; H, 6.0%). Extract *B* similarly gave 0.049 g. of leaflets from dilute alcohol, m. p. 147° (compound *H*).

(2) The cyclohexanone (5 g.) was dissolved in chloroform (40 c.c.), and phosphorus oxychloride (6 c.c.) added. The whole was kept overnight, shaken with water, and then with sodium carbonate solution. The chloroform layer was filtered and dried, the chloroform removed, and the residue (*ca.* 1 g.) dissolved in a little alcohol. The crystals deposited on standing were recrystallised from dilute alcohol, affording needles (0.2 g.), m. p. and mixed m. p. with the above 174°.

The above compound, m. p. 174° (0.05 g.), was heated at 290–300° with selenium (0.1 g.). The sublimate (*ca.* 0.03 g.), resublimed in a vacuum, had m. p. and mixed m. p. with phenanthrene, 99°; picrate (from alcohol), m. p. 141°.

3-Acetoxy-2-methoxyphenanthrene (VII; R = Ac).—(1) The above dihydro-compound (0.1 g.) was mixed with palladium-black (0.1 g.) and heated at 210–220° until no further change was visible. Alcohol (2 c.c.), was added, the whole warmed and filtered, the filtrate concentrated to 0.3 c.c., and hot water (1 c.c.) added. The crystals which separated on cooling, recrystallised from dilute alcohol, formed needles (0.02 g.), m. p. 144°.

(2) The dihydro-compound (0.3 g.) was heated under reflux for 5 hrs. with maleic acid (0.8 g.), palladium-black (0.25 g.), and water (6 c.c.), diluted with alcohol (12 c.c.), filtered hot, and the filtrate evaporated to dryness. The residue was warmed and stirred with sodium carbonate solution (12 c.c.) and extracted several times with ether, the extract dried, and the ether removed. The residue recrystallised from alcohol in stout, colourless needles (0.2 g.), m. p. 144° (Gilman and Cook, *loc. cit.*, give 146–147°) (Found: C, 74.6; H, 5.6. Calc. for $C_{17}H_{14}O_2$: C, 74.9; H, 5.3%).

3-Hydroxy-2-methoxyphenanthrene. (1) The above acetoxy-compound (0.16 g.) was heated for 2 hrs. with sodium hydroxide solution (8%, 3 c.c.), and the solution acidified, allowed to cool, and filtered. The precipitate recrystallised from dilute alcohol in short needles (0.11 g.), m. p. 143° (Gilman and Cook, *loc. cit.*, give 145–146°) (Found: C, 80.3; H, 5.6. Calc. for $C_{15}H_{12}O_2$: C, 80.5; H, 5.35%).

(2) Compound *H* (above) (0.03 g.) was refluxed for 4 hrs. with maleic acid (0.1 g.), palladium-black (0.05 g.), and water (1.2 c.c.), and the product worked up as above; it gave 0.01 g. of needles, m. p. and mixed m. p. with the above, 143°.

2:3-Dimethoxyphenanthrene. The above hydroxy-compound (0.1 g.) was dissolved in sodium hydroxide solution (3 c.c., 2%), and the solution heated on the water-bath. Methyl sulphate (0.1 c.c.) was added with stirring, and after 0.25 hr., sodium hydroxide solution (3 c.c., 4%) was added, and the whole heated for a further 0.25 hr. The reaction mixture when cold was extracted with ether, and the extract dried. The ether was removed, and the residue recrystallised from dilute alcohol in leaflets (0.08 g.), m. p. 130–131° (Pschorr and Buckow, *loc. cit.*, and Pschorr, *Annalen*, 1912, **391**, 39, give m. p. 131°) (Found: C, 80.5; H, 5.7. Calc. for $C_{15}H_{14}O_2$: C, 80.7; H, 5.9%). The picrate separated in yellow needles, m. p. 125–126° (Pschorr, *loc. cit.*, gives 127°).

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NOTES.

Derivatives of Indene and of Butyric Acid. By J. S. H. DAVIES and D. S. MORRIS.

THE work of various authors (*Chem. Reviews*, 1945, **37**, 481) has shown that certain derivatives of 6-hydroxy-2-*p*-hydroxyphenylindene and of 6-hydroxy-2-*p*-hydroxyphenyl-3:4-dihydronaphthalene possess oestrogenic activity. Our programme to extend the work of these authors, although well advanced, was anticipated by the publication of Silverman and Bogert (*J. Org. Chem.*, 1946, **11**, 34).

The present note deals with two similar indenenes, not previously described, and also with unsuccessful attempts to prepare $\alpha\gamma$ -diphenylbutyric acid and $\alpha\gamma$ -di-*p*-methoxyphenylbutyric acid from ethyl $\alpha\gamma$ -diphenylacetoacetate and its di-*p*-methoxy-derivative respectively, as intermediates in an alternative route to 2-phenyltetralone and 7-methoxy-2-*p*-methoxyphenyltetralone.

6-Methoxy-2-*p*-methoxyphenylindene.—The 6-methoxy-2-*p*-methoxyphenylindanone required was prepared by the route independently used by Silverman and Bogert (*loc. cit.*). The indanone (1 g.) was hydrogenated at ordinary temperature and pressure in ethyl alcohol in presence of Raney nickel (2 g.). The residue obtained after filtration and removal of solvent was stirred with concentrated sulphuric acid (1 drop), warmed for a few minutes on the water-bath, and extracted with benzene. The indene formed small needles, m. p. 194° from alcohol (Found: C, 80.2; H, 6.2. $C_{17}H_{14}O_2$ requires C, 81.0; H, 6.3%).

6-Methoxy-2:3-di-*p*-methoxyphenylindene.—The above indanone (1.5 g.) in toluene (14 c.c.) was added to the Grignard reagent prepared from *p*-anisyl bromide (2.1 g.), magnesium (0.27 g.), and ether (28 c.c.). After the ether had been removed, the toluene solution boiled for 1 hour, and the complex decomposed, the residue from the toluene was dissolved in a mixture of light petroleum (b. p. 40–60°) and benzene (1:1 by vol.) and chromatographed (alumina). Pure 6-methoxy-2:3-di-*p*-methoxyphenylindene (0.7 g.) was obtained as small needles, m. p. 129–130° (Found: C, 80.0; H, 6.4. $C_{24}H_{22}O_2$ requires C, 80.4; H, 6.1%).

β -Hydroxy- $\alpha\gamma$ -diphenylbutyric Acid.—Ethyl $\alpha\gamma$ -diphenylacetoacetate (28.2 g.), prepared by the