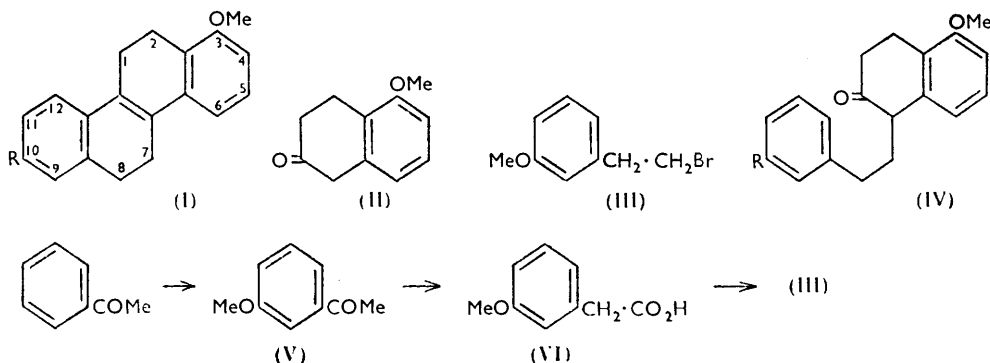


830. The Synthesis of 1:2:7:8-Tetrahydro-3-methoxy- and 1:2:7:8-Tetrahydro-3:10-dimethoxy-chrysenes.

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The synthesis of the hydrochrysenes of the title is described. Light-absorption data for these and the corresponding chrysenes are recorded. A convenient route to *m*-methoxyphenethyl bromide from acetophenone is demonstrated.

IN connection with the synthesis of (\pm)-18:19-bisnor-D-homosteroids,¹ we required an efficient preparation of the previously unknown 1:2:7:8-tetrahydro-3:10-dimethoxy-chrysenes (I; R = OMe). The route selected involved alkylation of the readily available² 5-methoxy-2-tetralone (II) with *m*-methoxyphenethyl bromide (III) and cyclodehydration of the intermediate (IV; R = OMe) to the chrysenes (I; R = OMe).



As a model we treated the sodium derivative of the tetralone (II) with phenethyl bromide in *isopropyl alcohol* and obtained the ketone (IV; R = H) in 33% yield. This was improved somewhat by substituting phenethyl iodide for the bromide and carrying out the reaction in benzene. Cyclodehydration with polyphosphoric acid at 180° furnished the tetrahydrochrysenes (I; R = H) which was dehydrogenated with sulphur at 230° to 3-methoxychrysenes m. p. 188—190°. Cook and Schoental³ gave m. p. 167—168°. Our specimen, purified by chromatography on alumina, had light absorption characteristics similar to those determined⁴ for Cook and Schoental's compound.

For synthesis of the methoxy-analogue (I; R = OMe) an adequate supply of *m*-methoxyphenethyl bromide was necessary. This compound had previously been prepared in quantity from *m*-hydroxybenzaldehyde⁵ or *m*-bromo-⁶ or *m*-iodo-aniline,⁷ all expensive starting materials. We have now devised what is at least as efficient a synthesis from the much cheaper acetophenone. By published procedures, the latter was converted through the *m*-nitro-, *m*-amino- and *m*-hydroxy-derivatives into *m*-methoxyacetophenone (V) in an overall yield of 50%. The Willgerodt reaction (Kindler modification)⁸ then gave *m*-methoxyphenylacetic acid (VI), which was transformed by lithium aluminium hydride into *m*-methoxyphenethyl alcohol and thence by phosphorus tribromide into the bromide (III). This with the potassium derivative of the tetralone (II) in benzene gave >80% yields of product (IV; R = OMe), cyclodehydration of which with polyphosphoric acid at 70° gave the desired tetrahydrochrysenes (I; R = OMe) [*ca.* 50% from (III)]. The

¹ Birch and Smith, unpublished work.

² Cornforth and Robinson, *J.*, 1949, 1855.

³ Cook and Schoental, *J.*, 1945, 288.

⁴ Holiday and Jope, *Spectrochim. Acta*, 1950, 4, 157.

⁵ Rapson and Robinson, *J.*, 1935, 1533.

⁶ Silverman and Bogert, *J. Org. Chem.*, 1946, 11, 34.

⁷ Bachmann and Thomas, *J. Amer. Chem. Soc.*, 1942, 64, 94.

⁸ Schwenck and Bloch, *ibid.*, p. 3051.

light-absorption properties of the products (IV; R = H and OMe), the corresponding chrysenes, and 4 : 10-dimethoxychrysene are recorded below.

EXPERIMENTAL

Evaporations were carried out under reduced pressure. Light petroleum without further definition means the fraction of b. p. 60—80°. Absorption spectra were determined by Mr. F. Hastings and Mrs. L. Skatterböl under the supervision of Dr. F. B. Strauss. Ultraviolet absorption spectra in EtOH were determined with a Unicam SP-500 spectrophotometer; those in hexane were determined with a Beckman DU spectrophotometer modified by Mr. A. E. Thompson of this department to a single-beam automatically recording instrument.

5-Methoxy-1-phenethyl-2-tetralone (IV; R = H).—(a) 5-Methoxy-2-tetralone² (10 g.) in isopropyl alcohol was added with stirring to a solution of sodium isopropoxide (from the metal, 1.3 g.) in isopropyl alcohol (50 c.c.) under nitrogen. Phenethyl bromide (10.7 g.) was added and the mixture refluxed with stirring for 12 hr. After cooling, hydrochloric acid (10 c.c.) was added and the mixture extracted with ether. The ether solution was washed with water, dried (Na₂SO₄), and evaporated to an oil which was shaken with saturated aqueous sodium hydrogen sulphite (50 c.c.) for 30 min. The solid was collected and washed thoroughly with ether, and the washings were combined with the ether extract of the filtrate. The ether solution was dried and evaporated. Distillation of the residue gave 5-methoxy-1-phenethyl-2-tetralone as a yellow viscous oil (5.3 g., 33%), b. p. 168—174°/0.05 mm. (Found: C, 81.5; H, 7.4. C₁₉H₂₀O₂ requires C, 81.4; H, 7.1%). Use of phenethyl iodide and a reaction time of 6 hr. raised the yield to 44%. The 2 : 4-dinitrophenylhydrazone was obtained from ethyl acetate as yellow needles, m. p. 137° (Found: N, 11.9. C₂₅H₂₄O₅N₄ requires N, 12.2%).

(b) 5-Methoxy-2-tetralone (8 g.) in benzene (50 c.c.) was added to finely powdered sodium (1.12 g.) in benzene (50 c.c.) under nitrogen, and the solution refluxed with stirring for 1 hr., then phenethyl iodide (10 g.) in benzene (30 c.c.) was added. Refluxing was continued for a further 5 hr. After cooling, the mixture was acidified with 2N-sulphuric acid, and the benzene layer was separated and combined with the benzene extract of the aqueous layer. The benzene solution was washed with water, dried, and evaporated to an oil, distillation of which gave the tetralone (IV; R = H) (4.8 g.), b. p. 180—185°/0.08 mm.

1 : 2 : 7 : 8-Tetrahydro-3-methoxychrysene (I; R = H).—The 2-tetralone (IV; R = H) (2 g.) was added with stirring to a solution of phosphoric anhydride (9 g.) in phosphoric acid (d 1.75; 9 c.c.) at 120° under nitrogen. The mixture was then heated at 180° for 45 min., cooled to 90°, and poured into water. The product was collected with ether, and the ether solution was washed with aqueous sodium hydroxide and water, dried (Na₂SO₄), and evaporated. The residual oil (1.3 g.) was taken up in carbon tetrachloride and adsorbed on activated alumina. Elution with carbon tetrachloride gave 1 : 2 : 7 : 8-tetrahydro-3-methoxychrysene, obtained from light petroleum (b. p. 40—60°) as needles (0.9 g., 51%), m. p. 80° (Found: C, 87.1; H, 7.0. C₁₉H₁₈O requires C, 87.0; H, 6.9%). Light absorption: (a) in EtOH, λ_{max.} 230, 256, 266, 274 (infl.), 299 (infl.), 310, 324, and 340 mμ (10⁻³ε 20.7, 7.9, 9.8, 7.0, 13.6, 19.9, 23.1, and 15.6); (b) in hexane, λ_{max.} 232.2, 238.4 (infl.), 256, 266, 274 (infl.), 299 (infl.), 312, 325, and 340.5 mμ (10⁻³ε 22.1, 19.5, 15.0, 8.3, 11.3, 8.0, 15.0, 22.3, 26.1, and 16.8).

The trinitrobenzene complex separated from ethanol as orange needles, m. p. 177—178° (decomp.) (Found: C, 53.7; H, 3.6; N, 11.7. C₁₉H₁₈O₂C₆H₃O₆N₃ requires C, 54.1; H, 3.5; N, 12.2%).

3-Methoxychrysene.—1 : 2 : 7 : 8-Tetrahydro-3-methoxychrysene (400 mg.) was heated with sulphur (115 mg.) at 180—230° during 2 hr. On cooling, the solid was extracted with benzene-light petroleum (1 : 1), and the solution evaporated to a crystalline residue (390 mg.), m. p. 184—186°, which was purified by percolating its solution in benzene through a column of activated alumina (5 g.). Recrystallisation from benzene-light petroleum (1 : 1) (Norit) gave 3-methoxychrysene as plates, m. p. 188—190° (Cook and Schoental give m. p. 167—168°) (Found: C, 88.2; H, 5.3. Calc. for C₁₉H₁₄O: C, 88.4; H, 5.4%). Light absorption: (a) in EtOH, λ_{max.} 229, 262, 270, 292, 305, 315, 327.5, 347, and 365 mμ (10⁻³ε 31.5, 63.3, 72.4, 8.5, 13.2, 10.4, 10.1, 3.0, and 1.8); (b) in hexane, λ_{max.} 229.6, 261, 270, 292, 304.5, 317, 330, 345, and 362 mμ (10⁻³ε 31.5, 60.5, 69.8, 8.5, 14.0, 11.8, 10.4, 2.9, and 2.9). Holiday and Jope⁴ give for hexane solutions: λ_{max.} 270.5, 291.2, 303.5, 316.9, 328.7, 345.6, and 363.2 mμ (10⁻³ε 106, 10.0, 15.9, 13.8, 11.6, 2.9, and 3.1).

m-Methoxyacetophenone.—m-Nitroacetophenone, prepared by Cobb's method,¹⁰ was reduced

² Birch and Smith, *J.*, 1951, 1882.

¹⁰ Cobb, *Proc. South Dakota Acad. Sci.*, 1945, 23, 64; *Chem. Abs.*, 1946, 40, 7180.

with iron filings and dilute acetic acid to *m*-aminoacetophenone¹¹ which was converted into *m*-hydroxyacetophenone by a conventional diazotisation procedure.¹² The crude *m*-hydroxyacetophenone was methylated directly with 30% aqueous potassium hydroxide and methyl sulphate in methanol, and the product was purified by steam-distillation and fractionation to give *m*-methoxyacetophenone, b. p. 125°/14 mm. (73% from *m*-aminoacetophenone; ca. 50% from acetophenone).

m-Methoxyphenethyl Bromide.—*m*-Methoxyacetophenone (50 g.), sulphur (16 g.), and morpholine (36 g.) were refluxed for 8 hr. Sodium hydroxide (42 g.) in ethanol (420 c.c.) was added and the solution was refluxed for a further 15 hr. The alcohol was distilled off and the residue acidified with hydrochloric acid (ice-cooling). The precipitate was collected and recrystallised from water, to give *m*-methoxyphenylacetic acid as plates (27.8 g.), m. p. 65° (lit.,¹³ m. p. 68°). A further crop (5.5 g.) was obtained by concentrating the mother-liquors. The foregoing acid was reduced with lithium aluminium hydride to *m*-methoxyphenethyl alcohol,¹⁴ which was converted by Bachmann and Thomas's method⁷ into *m*-methoxyphenethyl bromide b. p. 135—138°/9 mm. (35—38% from *m*-methoxyacetophenone).

5-Methoxy-1-*m*-methoxyphenethyl-2-tetralone (IV; R = OMe).—5-Methoxy-2-tetralone (8.9 g.) in benzene (40 c.c.) was added with stirring to finely powdered potassium (1.97 g.) in benzene (80 c.c.) under nitrogen, and the mixture was refluxed for 1.5 hr., whereafter *m*-methoxyphenethyl bromide (9.9 g.) in benzene (25 c.c.) was added. The stirring and refluxing were continued for a further 21 hr., and a little methanol was added to the cooled mixture to decompose any unchanged potassium. 2*N*-Sulphuric acid (40 c.c.) was added and the mixture was extracted with ether (4 × 10 c.c.). The combined extracts were washed with water, dried, and evaporated. Distillation of the residual oil gave 5-methoxy-1-*m*-methoxyphenethyl-2-tetralone (10.9 g., 81%), b. p. 208°/0.05 mm. A sample was redistilled for analysis (Found: C, 77.4; H, 7.1. C₂₀H₂₂O₃ required C, 77.4; H, 7.1%).

1 : 2 : 7 : 8-Tetrahydro-3 : 10-dimethoxychrysenes (I; R = OMe).—A solution of phosphoric anhydride (32.7 g.) in phosphoric acid (*d* 1.75; 49 c.c.) at 75° was rapidly added with stirring to the foregoing 2-tetralone (IV; R = OMe) (10.9 g.) at the same temperature under nitrogen. The temperature was maintained at 75—80° for 20 min. The cooled mixture was decomposed with ice and thoroughly extracted with ethyl acetate-ether (1 : 1). The extract was washed with water, dried, and evaporated to a gum which was dissolved in warm ether (50 c.c.) from which the 1 : 2 : 7 : 8-tetrahydro-3 : 10-dimethoxychrysenes separated as needles (5.86 g.), m. p. 119—120°. The residual gum from the mother-liquors was taken up in benzene (30 c.c.) and adsorbed on alumina (75 g.). Elution with benzene-light petroleum (1 : 1) gave a further crop (0.75 g.), m. p. 121—122°. A portion recrystallised for analysis had m. p. 122—123° (Found: C, 81.9; H, 7.1. C₂₀H₂₀O₂ requires C, 82.2; H, 6.9%). Light absorption in EtOH: λ_{max}, 230, 267, 315, 330, and 345 mμ (10⁻³ε 15.1, 4.4, 19.0, 21.4, and 15.0). The trinitrobenzene complex was obtained from ethanol as red needles, m. p. 162° (decomp.) (Found: C, 53.6; H, 3.8; N, 11.7. C₂₀H₂₀O₂, 2C₆H₃O₆N₃ requires C, 53.4; H, 3.6; N, 11.8%).

3 : 10-Dimethoxychrysenes.—1 : 2 : 7 : 8-Tetrahydro-3 : 10-dimethoxychrysenes (400 mg.) was heated with 30% palladised charcoal (80 mg.) at 250° for 10 min. The temperature was raised to 300° during 2 hr. The cooled mixture was extracted with benzene (5 × 25 c.c.), and the solution concentrated to 5 c.c. and percolated through alumina (5 g.). The product was thrice recrystallised from benzene-light petroleum, to give 3 : 10-dimethoxychrysenes (120 mg.), m. p. 200° (Found: C, 83.1; H, 5.5. Calc. for C₂₀H₁₆O₂: C, 83.3; H, 5.5%). Johnson and his co-workers¹⁵ give m. p. 198.5—200°. Light absorption: (a) in EtOH, λ_{max}, 231, 262, 274, 310, 327, 350, and 365 mμ (10⁻³ε 26.0, 62.5, 85.0, 16.7, 9.4, 2.2, and 1.8); (b) in hexane, λ_{max}, 231.8, 261.9, 274.9, 308, 327, 348, and 364 mμ (10⁻³ε 25.9, 57.6, 75.3, 17.0, 10.1, 3.2, and 2.3). Light absorption of 4 : 10-dimethoxychrysenes⁹ in EtOH: λ_{max}, 255, 265, 275, 296, 306, and 317 mμ (10⁻³ε 33.0, 64.3, 125.1, 19.1, 15.4, and 7.7).

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¹¹ Simpson, Atkinson, Schofield, and Stephenson, *J.*, 1945, 653.

¹² Cf. Icke, Redemann, and Burnett, *Org. Synth.*, 1949, 29, 63.

¹³ Chakravarti, Haworth, and Perkin, *J.*, 1927, 2265.

¹⁴ Hunter and Hogg, *J. Amer. Chem. Soc.*, 1949, 71, 1918.

¹⁵ Johnson, Banerjee, Schneider, Gutsche, Shelberg, and Chinn, *J. Amer. Chem. Soc.*, 1952, 74, 2832.