ton and Overhoff state: "Very numerous attempts were made to condense phthalimidohalogenoacetones with ethyl sodiochloromalonate and indeed with ethyl sodiomalonate itself under various conditions, but all were in vain. The halogenoacetones reacted exothermically with the sodiomalonates with rapid elimination of the sodium halide, but normal condensation did not occur, the products consisting for the most part of highly pigmented resins."

The coupling of III with sodium diethylmalonate was studied in several solvents under various conditions and was found to yield several products. At refluxing temperature in alcohol sodium bromide was formed, but attempts to crystallize a product from alcohol, ether, and chloroform failed. A very small amount of material was crystallized from acetone, but was not studied further. When III was added as a solid to an alcoholic solution of sodium diethylmalonate at room temperature the reaction mixture crystallized spontaneously.

The material (obtained in high yield, but not the desired product) was recrystallized from 95% ethanol in which it is only slightly soluble, m.p. 278–279°. A sample was prepared for analysis by recrystallization from *N,N*-dimethylformamide by addition of water and also from alcohol-water.

The analysis suggested phthalimide (calculated for phthalimide: C: 65.30, H: 3.43, N: 9.52. Found: C: 65.24, H: 3.50, N: 9.10), but the compound differed from phthalimide in several important respects: (1) It melted 44° above phthalimide, (2) its infrared absorption spectrum was different from that of phthalimide, and (3) it was less soluble in alcohol water and *N,N*-dimethylformamide water than phthalimide. When III was allowed to react with sodium ethoxide in *N,N*-dimethylformamide, however, and the product isolated from cold dilute HCl, a considerable yield of phthalimide was obtained. Thus the desired product could not be obtained when the reaction was carried out in alcohol.

By condensing III with sodium diethylmalonate in *N,N*-dimethylformamide in dilute solution at room temperature, the desired product (IV) could be isolated by crystallization from acetone water or more readily from a large volume of petroleum ether. In the course of purification several crystalline products were obtained. The material melting at 83° was shown to be the desired product by analysis, infrared absorption spectrum and its stepwise conversion to VII. Furthermore it yielded the predicted amount of phthalic acid on acid hydrolysis (380 mg. phthalic acid recovered from hydrolysis of 840 mg. of IV, predicted: 386 mg.).

EXPERIMENTAL[12]

Ethyl-α-carbethoxy-γ-oxo-δ-phthalimidovalerate (IV). To a solution of 3.26 g. of sodium in 80 ml. dry ethanol was added 200 ml. of *N,N*-dimethylformamide and 23 ml. diethylmalonate. After allowing this to stand for 15 min. a solution of 40 g. of III in 500 ml. *N,N*-dimethylformamide was added. The temperature gradually rose to 48°. The mixture was allowed to stand overnight and then was evaporated to dryness *in vacuo*. The residue was extracted with chloroform and the NaBr filtered off. The chloroform was evaporated *in vacuo* and the residual oil was crystallized from either acetone water over a period of 4–5 days or more quickly from a large volume of petroleum ether. The 25.5 g. (49.8%) obtained was recrystallized from dilute alcohol and then water, m.p. 84°.

Anal. calcd. for $C_{18}H_{19}NO_7$: C, 59.83; H, 5.30. Found: C, 59.79; H, 5.33.

When the same reaction was carried out with III at twice the concentration reported above, 15 g. of the material melting at 278° was obtained. This was easily separated from the desired product by dissolving the latter in alcohol or petroleum ether, since the high melting side product is only slightly soluble in alcohol and insoluble in petroleum ether.

α-carboxy-γ-oxo-δ-pthalimidovaleric acid (V). Ten g. of IV were suspended in 100 ml. of 48% HBr and allowed to stand at room temperature overnight. It was then heated on the steam bath until all the compound dissolved. The solution was allowed to cool and then evaporated to dryness *in vacuo*. The residue was recrystallized from alcohol or water to yield 7 g. (83.0%) m.p. 171–172° (with evolution of gas).

Anal. calcd. for $C_{14}H_{11}NO_7$: C, 55.08; H, 3.63; N, 4.58. Found: C, 55.38; H, 3.73; N, 4.39.

δ-Phthalimidolevulinic acid (VI). Four g. of V were heated to 170° at a pressure of 3–4 mm. Hg until the evolution of gas ceased. The glass-like residue was recrystallized from boiling water yielding 3.1 g. (90.7%) m.p. 157–158° (Neuberger and Scott[3] reported 158.5°).

Anal. Calcd. for $C_{13}H_{11}NO_5$: C, 59.76; H, 4.24, N, 5.36. Found: C, 60.01; H, 4.42; N, 5.47.

δ-Aminolevulinic acid hydrochloride (VII). A mixture of 4 g. of VI, 4 cc. of 95% ethanol and 40 cc. of 7*N* HCl was refluxed for 6 hr. and allowed to cool overnight. The phthalic acid was filtered off and the filtrate evaporated to dryness *in vacuo*. The slightly yellow crystals of VII weighed 2 g. (78.2%). It was recrystallized from methanol ethyl acetate m.p. 148°. It had the same ultraviolet absorption spectrum as a sample prepared by another route and also the same RF value in butanol, acetic acid, and water (.11). It was further identified by mixed melting point.

Anal. Calcd. for $C_5H_{10}NO_3Cl$: C, 35.82; H, 6.01; N, 8.35; Cl, 21.15. Found: C, 36.01; H, 6.06; N, 8.07; Cl, 20.73.

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[12] All melting points are uncorrected.

The Crystal and Molecular Structures of Overcrowded Compounds. V.[1] The Double Cyclization of Diphenethylacetic Acids

(MRS.) E. R. CAHANA, G. M. J. SCHMIDT, AND K. H. SHAH[2]

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During our work on the crystal and molecular structures of overcrowded molecules we became

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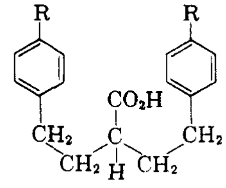
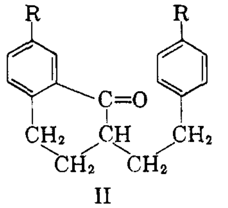
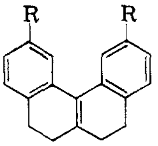
[1] Part IV. F. H. Herbstein and G. M. J. Schmidt, *J. Chem. Soc.*, 3314 (1954).

[2] Weizmann Memorial Fellow 1954–55.

interested in the problem of the 6,7-substituted benzo[*c*]phenanthrenes. Since the several known routes to this ring system do not lend themselves readily to the synthesis of such derivatives, we investigated a novel approach *via* the double cyclization of diphenethylacetic acids (I) to the tetrahydrobenzo[*c*]phenanthrenes (III).


I


II

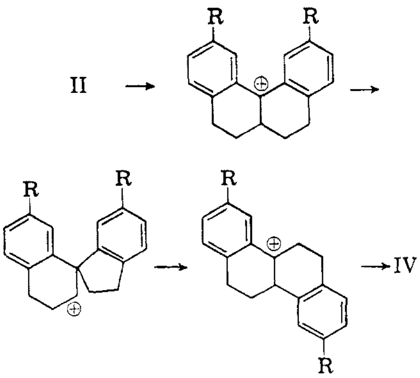

III

The acids I (R = H, OMe) were prepared in good over-all yields by procedures *A* and *B* and

$$A\!: 2ArCH_2CH_2Br + CH_2(CO_2Et)_2 \longrightarrow (ArCH_2CH_2)_2C(CO_2Et)_2 \longrightarrow (ArCH_2CH_2)_2CHCO_2H$$

$$B\!: (ArCH{:}CH)_2CO \longrightarrow (ArCH_2CH_2)_2CHOH \longrightarrow {>}CHOSO_2Me \longrightarrow {>}CHCN \longrightarrow (ArCH_2CH_2)_2CHCO_2H$$

cyclized by HF and polyphosphoric acid; however, under all experimental conditions the reaction failed to produce benzo[*c*]phenanthrenes, but yielded instead the corresponding chrysenes of varying degrees of hydrogenation. Since the 2-phenethyltetralones (II) can be obtained as intermediates under mild conditions of cyclization, we may suppose that the rearrangement reaction takes place, by the mechanism of a double Wagner-Meerwein rearrangement, at the tertiary carbonium ion formed after final cyclization.



The identity of the reaction products obtained was checked by their preparation by known methods: tetrahydrochrysene (IV) was prepared from 1-phenethyltetralone-2; in the methoxy series the chrysene derivatives were prepared *via* the unambiguous double cyclization of the corresponding acyloin by the method developed by Johnson and co-workers.[3] In neither of the two series (R = H, OMe) investigated was any evidence obtained for the formation of the benzophenanthrene alongside the chrysene system. The cyclization of I (R = OMe) yielded, together with 3,9-dimethoxychrysene, small quantities, insufficient for further investigation, of a compound analyzing for a dimethoxyhexahydrochrysene; since it was also obtained from the acyloin on cyclization it is unlikely to be a benzo[*c*]phenanthrene derivative. It would appear that intramolecular compression forces, even within the 5,6,7,8-tetrahydrobenzophenanthrene system, are sufficient to displace equilibrium between the two ring systems completely to the side of chrysene.

We are attempting to provide further evidence for the reaction mechanism by the cyclization of 2,5-dibenzylcyclopentane-1-carboxylic acid and related compounds; however, the preparation of this acid by route *B* from any of the three stereoisomeric cyclopentanols has not yet been successful; attempts to prepare the acid by other methods are under way.

EXPERIMENTAL[4]

Diphenethylacetic acid. Route *A*, according to Leuchs.[5] Route *B*: Dibenzalacetone (23 g.) was reduced in 250 ml. of tetrahydrofuran with 0.5 g. 10% palladium-on-charcoal at an initial pressure of 50 lb./sq. in. After 2 hr. the solution was filtered, the solvent removed, the crude ketone dissolved in methanol and reduced with 6 molar equivalents of sodium borohydride. The product was worked up in the usual way; b.p. 165°/0.8 mm., m.p. 42–43°. (Zechmeister and Rom[6] give m.p. 42–44°.) Yield was 60% based on dibenzalacetone. To 20 g. of the carbinol dissolved in dry pyridine was added 10 g. of freshly distilled methyl sulfonyl chloride; the mixture was kept at 0° for 90 min., poured into ice water, and neutralized with sodium carbonate solution. The mesylate was extracted with ether; the ethereal solution was dried and worked up to give an oil which was dissolved in 150 ml. of dimethylformamide and treated with 3.0 g. of potassium cyanide dissolved in the minimum amount of water. The mixture was kept at 85° for 2 hr. and then poured into water. The product was fractionated, b.p. 157–159°/0.35 mm., yield 62%. The nitrile (5 g.) was added to 70 ml. of 40% sulfuric acid; hydrolysis was complete after 18 hours' refluxing. The acid was recrystallized from petroleum ether (30–60°), m.p. 49°, yield 75%. (Leuchs[5] gives m.p. 49–50°.)

Di(4-methoxyphenethyl)acetic acid. The method of preparation follows essentially the procedure just given. Because of the low solubility of the reduced ketone in methanol, the boron hydride reduction is best carried out in a methanol-tetrahydrofuran mixture, 70% yield of the carbinol, m.p. 80–81°, from methanol. (Straus and Grindel[7] give m.p. 80–81.5°.)

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(3) W. S. Johnson, C. A. Erickson, and J. Ackerman, *J. Am. Chem. Soc.*, **74**, 2251 (1952).

(4) All melting points and boiling points are uncorrected. Microanalyses were carried out by Mr. E. Meier of the Microanalytical Laboratory, The Weizmann Institute of Science.

(5) A. Leuchs, *Ann.*, **461**, 44 (1928).

(6) I. Zechmeister and P. Rom, *Ann.*, **468**, 126 (1929).

(7) F. Straus and H. Grindel, *Ann.*, **439**, 306 (1924).

The mesylate of this carbinol is a solid, m.p. 56–58°, which gives, in an over-all yield from the carbinol of 52%, the nitrile, m.p. 92–94° from methanol.

Anal. Calcd. for $C_{20}H_{23}NO_2$: C, 77.66; H, 7.44; N, 4.53. Found: C, 77.24; H, 7.24; N, 4.48.

The acid, obtained in 72% yield from the nitrile, has m.p. 69–70° recrystallized from petroleum ether (60–80°).

Anal. Calcd. for $C_{20}H_{24}O_4$: C, 73.17; H, 7.31. Found: C, 73.12; H, 7.49.

Monocyclization of I (R = H) with zinc chloride and acetic anhydride. Five grams of I, 30 ml. of glacial acetic acid, 20 ml. of acetic anhydride, and 0.4 g. of freshly fused zinc chloride were refluxed for 2 hr. and then poured onto ice; the mixture was made strongly alkaline with potassium hydroxide and extracted with ether; the ether extract was worked up in the usual way to give, in 95% yield, 2-phenethyltetralone identified as the semicarbazone, m.p. 166–167° (Leuchs[5] gives 166–167°) and 2,4-dinitrophenylhydrazone, m.p. 158–160°.

Double cyclization of I (R = H) with polyphosphoric acid. Two grams of I and 40 g. of polyphosphoric acid were heated with stirring for 3 hr. in an oil bath kept at 125°, allowed to cool, and poured into ice water. Tetrahydrochrysene (1.5 g.) (IV) was collected which, after recrystallization from methanol, melted at 105°. (Salzer[8] gives m.p. 105°.) No other compound could be isolated. The compound was found identical with an authentic sample of IV prepared according to Salzer[8] from 1-phenethyltetralone-2. It was smoothly dehydrogenated to chrysene on heating to 300° with 10% palladium-on-charcoal.

Anal. Calcd. for $C_{18}H_{16}$: C, 93.10; H, 6.90. Found: C, 93.24; H, 6.84.

Cyclization of I (R = H) with hydrofluoric acid. Three grams of I was treated with approximately 150 ml. of anhydrous hydrofluoric acid. After 48 hr. the semisolid residue was extracted with boiling methanol: the residue, 0.3 g., was chrysene, identified by mixed m.p.; the methanol solution deposited on cooling 0.5 g. of IV. From the methanol solution 2.0 g. of II were isolated, identified as the 2,4-dinitrophenylhydrazone.

Cyclization of I (R = OMe). Three grams of I was treated with approximately 50 ml. of anhydrous hydrofluoric acid. After 24 hr. the acid was evaporated and the remaining oil taken up in benzene and chromatographed through activated alumina. The column was washed with a mixture of benzene and petroleum ether (60–80°); except for a very small fraction of impure high-melting material, a colorless solid (2.4 g.) was obtained which, after recrystallization from methanol, melted at 85–86°, and which was identified as the 7-methoxy-2-(4-methoxyphenethyl)tetralone-1.

Anal. Calcd. for $C_{20}H_{22}O_3$: C, 77.42; H, 7.10. Found: C, 77.86; H, 7.17.

Dinitrophenylhydrazone, m.p. 163°, from benzene and ethanol.

Anal. Calcd. for $C_{26}H_{26}N_4O_6$: N, 11.4. Found: N, 11.5.

Cyclization of I (R = OMe) with polyphosphoric acid. A mixture of 1 g. of I with 60 g. of polyphosphoric acid and 1 g. of phosphorus oxychloride was stirred and heated to 120° (bath temperature) for 90 min., left to cool, poured into cold water, and filtered. The residue was boiled with methanol and filtered hot. The remaining solid (0.79 g.) was recrystallized from a mixture of benzene and methanol, m.p. 235–238°. Its ultraviolet spectrum in dioxane solution showed it to be a chrysene derivative: maxima at 375, 357, 340, 325, 310, 278 mμ (log ϵ 3.52, 3.52, 3.34, 4.14, 4.16, 4.6).

Anal. Calcd. for $C_{20}H_{16}O_2$: C, 83.33; H, 5.56; methoxyl, 10.4. Found: C, 83.23; H, 5.59; methoxyl, 10.2.

From the hot methanol solution a very small quantity of another material separated which, after recrystallization from petroleum ether (60–80°), melted at 166–167°.

Anal. Calcd. for 3,9-dimethoxy-5,6,11,12,13,14-hexahydrochrysene (?): $C_{20}H_{22}O_2$: C, 81.63; H, 7.48; methoxyl, 10.2. Found: C, 81.62; H, 7.47; methoxyl, 10.3.

3,9-Diacetoxychrysene. One gram of 3,9-dimethoxychrysene was boiled for 4 hr. with 57% hydriodic acid; the cold solution was poured into water and filtered, m.p. of crude dihydroxy compound 320°. The diphenol was boiled with 5 ml. of acetic anhydride in 50 ml. of pyridine for 2.5 hr. A solid separated which, after recrystallization from nitromethane, melted at 242–243°.

Anal. Calcd. for $C_{22}H_{16}O_4$: C, 76.74; H, 4.65. Found: C, 76.72; H, 4.79.

Preparation of 1,6-di(4-methoxyphenyl)hexanone-3-ol-4. The methyl ester of 4-methoxyphenylpropionic acid was prepared from methyl 4-methoxycinnamate by hydrogenation in ethyl acetate with 10% palladium-on-charcoal; b.p. 111–112°/0.6 mm. The acyloin was prepared according to Johnson and coworkers[3]: to a suspension of 9.5 g. of powdered sodium in 170 ml. of xylene kept at 105–110°, was added, over 0.5 hr., a solution of 20 g. of methyl 4-methoxyphenylpropionate in 170 ml. of xylene, the reaction being carried out in an atmosphere of pure nitrogen. Heating was continued for a further 0.75 hr., after which the mixture was allowed to cool and sufficient methanol added to destroy the remaining sodium; water was added and the xylene layer separated. After several washings with water the xylene solution was steam-distilled; the yellow oil was extracted with ether, dried over magnesium sulfate, and the ether removed *in vacuo*. The yield of acyloin was 12 g. (75%).

Cyclization of the acyloin with hydrofluoric acid. Five grams of acyloin were treated with approximately 150 ml. of hydrofluoric acid for 24 hr., when the acid was evaporated and the residue dissolved in ether. From the ethereal solution a yellow oil was obtained which was induced to crystallize by trituration with ethyl acetate. The solid (2.5 g.) after recrystallization from ethyl acetate, melted at 235–237°, and proved to be identical with the dimethoxychrysene of m.p. 235–238°, obtained by the polyphosphoric acid cyclization of I (R = OMe). The ethyl acetate solution was concentrated when it yielded a very small amount of a material, m.p. 168–169° after recrystallization from petroleum ether (60–80°) which showed no depression of m.p. with the second material, m.p. 166–167° obtained by the polyphosphoric acid cyclization of I (R = OMe).

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[8] W. Salzer, *Z. physiol. Chem.*, **274**, 39 (1942).

Mesityl Mesitoate

G. W. THIESSEN AND W. N. FARR

Received September 9, 1958

Mesityl mesitoate does not appear in the chemical literature. The compound was made for comparison with an unidentified material from a Kolbe electrolysis, by way of the Schotten-Baumann reaction.

EXPERIMENTAL

Mesitoic acid,[1,2] 5 g. (0.030 mole), m.p. 153°, was converted to mesitoyl chloride by adding 4 ml. of thionyl chloride and refluxing over a water bath for 30 min. The sodium salt of mesitol was prepared by mixing 4 g. (0.037 mole) of

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(1) D. M. Bowen, *Org. Syntheses*, **Coll. Vol. III**, 553 (1955).

(2) Prepared by B. T. Shawver, Monmouth College.