[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Preparation and Partial Aromatization of 1,4-Cholestadienone-3 by the Dienone–Phenol Rearrangement[1]

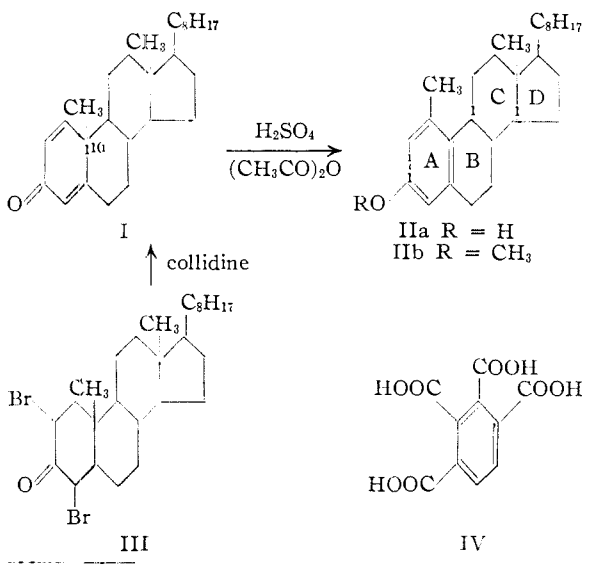
BY A. L. WILDS AND CARL DJERASSI[2,3]

Inhoffen and co-workers[4,5] reported that the unsaturated ketone 1,4-cholestadienone-3 (I) underwent rearrangement to an isomeric phenol, with migration of the angular methyl group at C-10, when treated with sulfuric acid and acetic anhydride at room temperature. They assigned to this product the structure IIa, by analogy to the rearrangement of santonin to desmotroposantonin.[6]

In connection with similar reactions in the androstane series,[5,7,8] we have had occasion to repeat and confirm this work. Substantial improvements in the experimental procedures were developed for preparing the dienone I from cholestanone via the 2,4-dibromo derivative III, and for its transformation into the isomeric phenol IIa. In the dehydrobromination of III by means of collidine, the dienone I was accompanied by a crystalline by-product. This was shown to be a 1:1 molecular compound of 1,4-cholestadienone-3 (I) and 4,6-cholestadienone-3 from the ultraviolet absorption spectrum and by comparison with material prepared from the two pure dienones. The pure 4,6-cholestadienone-3 could be prepared in 41% yield by applying to cholesterol the unusual modification of the Oppenauer oxidation discovered by Wettstein,[9] employing quinone and aluminum *t*-butoxide.[10]

Oxidation of the methyl ether IIb with nitric acid was carried out with the hope of obtaining 5-methoxybenzene-1,2,3-tricarboxylic acid, or a nitro derivative, from ring A. Instead benzene-1,2,3,4-tetracarboxylic acid (IV) was isolated (as the tetramethylester) arising from ring B which was aromatized in the process.[11] Treatment of IIb with boiling alkaline permanganate, a procedure which was successful for preparing the desired methoxy acid from 4-methoxy-2,6-dimethylbenzaldehyde,[12] gave almost no reaction with IIb.

The isolation of the tetracarboxylic acid V would appear to eliminate from consideration a possible (though less probable) structure for the phenol having a seven-membered ring B, and supports formula IIa. The extension of the dienone–phenol rearrangement to a somewhat analogous chrysene derivative, where the structures of both the dienone and the rearrangement product were established by synthesis, affords further support for the course of the rearrangement. This is reported in an accompanying communication.[13]



Experimental[14]

Cholestanol-3 and Cholestanone-3.—Following the procedure of Durland,[15] 30 g. of cholesterol (purified by refluxing in alcohol for twenty-four hours with Raney nickel catalyst and recrystallizing), 75 cc. of anhydrous ether and 8 g. of a special Raney nickel catalyst[16] were shaken in a 270-cc. bomb at 100° and a hydrogen pressure of 2400 lb. per sq. in. for about fifteen hours. Three such runs, test portions of which gave only a faint Liebermann–Burchard test,[17] were combined, centrifuged to remove the catalyst, concentrated and crystallized from alcohol. A total of 72 g. (80%) of cholestanol was obtained, m. p. 142–143° (reported[18] 142–143°).

Using the method described by Bruce,[19] the cholestanol was oxidized to cholestanone in 82% yield, m. p. 129–129.5°.

2,4-Dibromocholestanone-3 (III).[20]—A small amount (1–2 cc.) of a solution of 26.4 g. of bromine in 165 cc. of

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(4) Inhoffen and Huang Minlon, *Naturwissenschaften*, **26**, 750 (1938).

(5) Inhoffen and Zühlsdorff, *Ber.*, **74**, 604 (1941).

(6) See Clemo, Haworth and Walton, *J. Chem. Soc.*, 1110 (1930).

(7) Inhoffen, Zühlsdorff and Huang-Minlon, *Ber.*, **73**, 451 (1940).

(8) Inhoffen and Zühlsdorff, *ibid.*, **74**, 1911 (1941).

(9) Wettstein, *Helv. Chim. Acta*, **23**, 388 (1940).

(10) This affords a simpler method of preparation than that of Dane, Wang and Schulte, *Z. physiol. Chem.*, **245**, 87 (1937).

(11) The theoretical possibility of this acid arising from ring C seems improbable to us.

(12) To be reported in a separate communication.

(13) Wilds and Djerassi, THIS JOURNAL, **68**, 1715 (1946).

(14) All melting points are corrected.

(15) J. R. Durland, Ph.D. Thesis, U. of Wisconsin, 1939.

(16) Pavlic and Adkins, THIS JOURNAL, **68**, **1471** (1946).

(17) Unless this color test for unsaturation was negative or a faint pink, the yield of cholestanone from the subsequent oxidation was lowered.

(18) Diels and Abderhalden, *Ber.*, **39**, 889 (1906).

(19) Bruce, "Organic Syntheses," Coll. Vol. II, 139 (1943).

(20) First described by Ruzicka, Bosshard, Fischer and Wirz, *Helv. Chim. Acta*, **19**, 1151 (1936), as the 2,2-dibromo derivative. For a clarification of the structure see Butenandt, Schramm, Wolff and Kudszus, *Ber.*, **69**, 2779 (1936), and Inhoffen, *ibid.*, **70**, 1695 (1937).

acetic acid was added to 30 g. of cholestanone dissolved in 3000 cc. of acetic acid. The solution was warmed gently until the bromine color disappeared, cooled to room temperature and the remainder of the bromine added from a buret with swirling. After about two hours fine, long needles started to separate. The mixture was allowed to stand at room temperature for twenty-four hours, the precipitate was filtered and washed with 200 cc. of water, allowing the latter to dilute the filtrate. The solid, after drying at 80°, weighed 25 g. and melted at 193.5–194° (dec.), with previous sintering at 189°. A second crop from the filtrate amounted to 10 g., m. p. 189–191° (dec.). Addition of another 600 cc. of water yielded 7.8 g. of crude material which melted below 180°. After two recrystallizations from petroleum ether, using Norit, this gave 4 g. of satisfactory material, m. p. 190.5–191°, bringing the total yield to 39 g. (92%). Recrystallization of a sample of the purest material gave clusters of prismatic needles, m. p. 194–194.5° (dec.); $[\alpha]^{23}D$ + 3 (14.2 mg. in 2 cc. of chloroform). Ruzicka[20] obtained the compound, m. p. 194°, in 71% yield; Inhoffen[20] reported the m. p. 192°; no rotations were reported.

1,4-Cholestadienone-3 (I).—Attempts to repeat the procedure of Butenandt, *et al.*,[21] led to an oily product from which only a small amount of crystalline material could be isolated. By chromatographic adsorption, and utilizing the optimum conditions of time and concentration given in the following procedure, consistent yields were obtained. A mixture of 15 g. of 2,4-dibromocholestanone and 60 cc. of redistilled γ-collidine was refluxed (oil-bath) for eighty minutes. The amount of collidine hydrobromide, determined by filtering and washing with ether, corresponded to 91–93% of the calculated quantity. The excess collidine was removed by distillation under reduced pressure, the residue was extracted with ether, washed with water, dilute hydrochloric acid, dilute potassium hydroxide and dried over sodium sulfate. After removal of the ether the residual oil, which showed little tendency to crystallize, was digested thoroughly with boiling methanol and the latter decanted from 0.73 g. of a black, insoluble oil, which still contained some bromine. The methanol-soluble fraction (11 g.) was dissolved in petroleum ether (b. p. 40–60°) and adsorbed on a column of 150–200 g. of alumina.[22] The material was then fractionally eluted using the free-flow method (no suction) with 100-cc. portions of petroleum ether, petroleum ether–benzene (in the ratios 75/25, 50/50, 25/75), benzene, benzene–ether (75/25, 50/50, 25/75), ether and finally acetone. A given solvent or mixture was used as long as an appreciable amount of material was found to be removed. Crystalline material was usually obtained from all fractions up to benzene–ether (50/50). The melting point varied from 84–100° for the first fractions to as high as 103–111° for the later ones; the total amount of crystalline material was 7.7–8.0 g. (73–76%). Recrystallization from methanol (Norit) gave 5.2–5.6 g. (49–53%) of material satisfactory for subsequent reactions; the m. p. varied in different runs from 98–107° to 108.5–111°. Concentration of the filtrate yielded 0.91 g. (9%), m. p. 68–87° and about 0.85 g. (8%), m. p. 62–68°, which is shown below to contain 4,6-cholestadienone-3 as well as the 1,4-isomer. By aromatization with sulfuric acid in acetic anhydride this material and the oily filtrates were found to contain an additional 10–16% of the 1,4-isomer, indicating the total yield to be about 60–70%.

The analytical sample was obtained by recrystallization from methanol as colorless stout prisms, m. p. 110–112°, $[\alpha]^{24.5}D$ + 31 ± 1.5° (10.2 mg. in 1.3 cc. of chloroform). Inhoffen[23] reported m. p. 111.5–112.5°, $[\alpha]^{23}D$ + 28.1° (chloroform), while Butenandt[21] reported m. p. 108–110°, $[\alpha]^{22}D$ + 31°. The absorption spectrum,[24] measured in absolute alcohol solution, exhibited a single maximum at 245 mμ (log E = 4.15). This is in agreement with that reported by Dannenberg[25a] for Inhoffen's sample (236 mμ, log E = 4.20 in ether) since it has been found, in general, that the maximum of α,β-unsaturated ketones is shifted by about 6 mμ to higher wave lengths in going from ether to alcohol solutions.[25]

Anal. Calcd. for $C_{27}H_{42}O$: C, 84.8; H, 11.1. Found: C, 84.8; 85.0; H, 11.0; 11.2.

Variations in the above procedure, especially in the time and temperature, gave yields which were poorer or unchanged. When the amount of collidine was increased to 15 cc. per gram of dibromo ketone, rather than 4 cc. per gram, the tendency for rearrangement to the 4,6-cholestadienone-3 was increased, and the yield of the pure 1,4-isomer was reduced to 16%.

Identification of the By-product from the Dehydrobromination.—The low melting fractions from several runs (m. p. 68–87°) were combined and recrystallized from dilute acetone, yielding clusters of needles with the m. p. 64–68° and $[\alpha]^{22}D$ + 32° (10.1 mg. in 2 cc. of chloroform). Adsorption of 90 mg. of this material on alumina[22] and elution gave the following fractions:

Fraction A (petroleum ether–benzene, 50/50), 30 mg., m. p. 66–68°: after one recrystallization from dilute methanol this yielded 23 mg. of crystals of m. p. 68.5–70°, $[\alpha]^{22}D$ + 34 ± 0.3° (11.8 mg. in 2 cc. of chloroform). The absorption spectrum, taken in absolute alcohol solution and shown in Fig. 1, exhibited a maximum at 283 mμ (log E = 4.15) and a long plateau at 242–258 mμ. The spectrum resembled that of a synthetic sample of the 1:1 molecular compound of 1,4-cholestadienone-3 and 4,6-cholestadienone-3. A mixed m.p. of the synthetic sample (m.p. 68.5–70°) with that isolated above showed no depression. The material retained solvent rather tenaciously and was dried at 45° (0.2 mm.) for twenty hours before analysis.

Anal. Calcd. for $C_{27}H_{42}O$: C, 84.8; H, 11.1. Found: C, 85.0; H, 11.1.

Fraction B (petroleum ether–benzene, 30/70 to 10/90) weighed 25 mg. and after recrystallization yielded 10 mg. m. p. 77–92°. The absorption spectrum (Fig. 1) indicated it to be richer in the 1,4-isomer than the molecular compound from Fraction A.

Fraction C (benzene and benzene–ether, 80/20) weighed 13 mg. and gave 5 mg. of the nearly pure 1,4-isomer, m. p. 103–107° (see Fig. 1).

4,6-Cholestadienone-3.—The following procedure is based on that of Wettstein for preparing 6-dehydrotestosterone benzoate.[9] A solution of 2 g. of cholesterol and 12 g. of quinone in 120 cc. of dry toluene was concentrated under reduced pressure to 100 cc., 2 g. of aluminum *t*-butoxide was added and the mixture refluxed for forty-five minutes. The solution was then cooled, diluted with water and steam distilled (1.5 l. of distillate). The black residual mixture was cooled in ice, 100 cc. of 1 *N* sulfuric acid added and the mixture was extracted thoroughly with ether. The ether was washed six times with dilute sulfuric acid and six times with water. Then 5% potassium hydroxide was added *without shaking* (to avoid a troublesome emulsion) and the black aqueous layer was separated. This treatment with alkali was repeated until the ether layer was light red, and then it was washed thoroughly by shaking with alkali until no more color was removed from the solution (now yellow). After washing with water and drying over sodium sulfate the ether was removed.

The residual reddish oil, which did not crystallize, was adsorbed from petroleum ether (b. p. 40–60°) on 40 g. of

(21) Butenandt, Mamoli, Dannenberg, Masch and Paland, *Ber.*, **72**, 1617 (1939).

(22) Aluminum Company of America, grade F-20, minus 80-mesh.

(23) Inhoffen and Huang-Minlon, *Ber.*, **71**, 1720 (1938); **72**, 1686 (1939).

(24) The absorption spectra measurements were made using a Beckman quartz photoelectric spectrophotometer; $E = \frac{1}{c} \log \frac{I_0}{I}$ for a 1-cm. cell, where c is the concentration in moles per liter

(25) (a) Dannenberg, *Abhandl. preuss. Akad. Wiss., Math.-nat. Klasse*, no. 21 (1939); (b) Woodward, THIS JOURNAL, **63**, 1123 (1941).

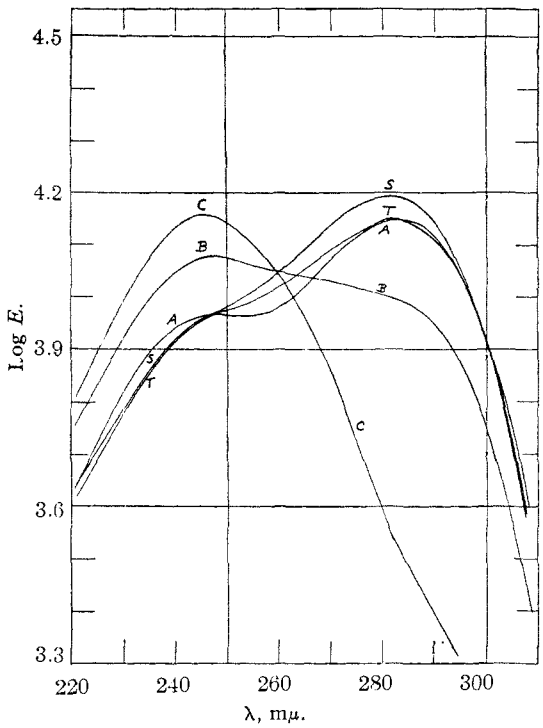

Fig. 1.—Ultraviolet absorption spectra (in absolute alcohol): curve S, synthetic sample of molecular compound of 1,4-cholestadienone-3 and 4,6-chloestadienone-3; curve T, theoretical curve (1:1 ratio) for the molecular compound; curve A, fraction A of chromatogram of the by-product from the preparation of I; curve B, fraction B of by-product; curve C, fraction C of by-product.

alumina.[22] The first eluates, using 200 cc. of petroleum ether–benzene (70/30) and 200 cc. of a 50/50 mixture of these solvents, contained only 40 mg. of an oil and were discarded. The product was then eluted with 500 cc. of petroleum ether–benzene (35/65), 300 cc. of benzene and finally benzene–ether (200 cc. of 80/20 and 100 cc. of 60/40). The total amount of material obtained by evaporation was 0.72 to 0.82 g. (36–41%), m. p. 78–80°.

Recrystallization from methanol gave needles with the m. p. 80.5–81.5°, $[\alpha]^{24}D$ + 33° (10.8 mg. in 2 cc. of chloroform). The absorption spectrum in absolute alcohol showed a single maximum at 284 mμ (log E = 4.42) and a minimum at 221 mμ (log E = 3.33). The physical constants reported previously are: m. p. 83°,[10] 80–81°[26]; 79.5–81°[27]; $[\alpha]^{25}D$ +33.4,[26] 35 ± 2°[27] (chloroform); max. 285 mμ in alcohol (log E = 4.4).[26]

The **molecular compound**, prepared by recrystallizing 100 mg. each of the 4,6- and 1,4-isomers from methanol containing a few drops of water, crystallized as clusters of needles, m. p. 68.5–70°, $[\alpha]^{24}D$ + 33 ± 0.2° (8.5 mg. in 2 cc. of chloroform); see Fig. 1 for the absorption spectrum.

Anal. Found: C, 84.3; H, 11.0.

3-Hydroxy-1-methyl-10-norcholestatriene-1,3,5 (IIa).—When the procedure of Inhoffen, *et al.*,[5] was used, the product was oily, due to incomplete hydrolysis of the intermediate acetate. The following procedure was found to be more reliable. A solution of 0.5 g. of 1,4-cholestadienone (m. p. 106–110°) in 12.5 cc. of warm acetic anhydride was cooled to room temperature and a solution of 0.1–0.2 g. of concentrated sulfuric acid in 1 cc. of acetic anhydride was added dropwise. The dark green solution was allowed to stand at room temperature for three hours, 0.1 g. of sulfuric acid in 0.5 cc. of acetic anhydride added and allowed to stand for another hour. The mixture was poured slowly with stirring into 20 cc. of ice-cold 45% aqueous potassium hydroxide solution, extracted with ether, and the oily residue left after evaporation of the ether was hydrolyzed by refluxing for fifty minutes with 2 cc. of 45% potassium hydroxide and 15 cc. of methanol. Dilution with water and scratching gave 0.44 g. (88%) of the colorless phenol, m. p. 143–145°. Recrystallization from petroleum ether (b. p. 40–60°) raised the m. p. of the colorless needles to 145.5–146°, $[\alpha]^{24.5}D$ + 161 ± 1° (10.9 mg. in 1.2 cc. of chloroform). Inhoffen and Zühlsdorff[5] reported 145–146°. The phenol could be chromatographed on alumina and eluted with benzene or benzene–ether.

With less pure cholestadienone (m. p. 98–107°) the yield of the pure phenol was 74–83%. Even when non-crystalline mixtures were used the crystalline phenol was readily isolated.

3-Methoxy-1-methyl-10-norcholestatriene-1,3,5 (IIb). (a) **From the Phenol IIa.**—A warm solution of 0.5 g. of the phenol (m. p. 143–145°) in 17 cc. of alcohol was treated alternately with 1.8 cc. of sodium hydroxide solution (6 g. in 10 cc. of water) and 2.5 cc. of dimethyl sulfate, and the process was repeated four times. After standing for fifteen minutes the solution was diluted, cooled in ice, filtered and the product dried; yield 0.48 g. (93%), m. p. 103.5–105°. Recrystallization of a sample from alcohol gave colorless prisms, m. p. 104.5–105°, $[\alpha]^{24}D$ +165 ± 0.2° (9.7 mg. in 2 cc. of chloroform); reported[5] m. p. 104–105°.

(b) **From 2,4-Dibromocholestanone-3 (III) without Isolation of Intermediates.**—A solution of 8 g. of the dibromo ketone III in 35 cc. of collidine was heated at reflux for eighty minutes and the mixture worked up as before. The methanol-soluble oil (4.8 g.) was not chromatographed but was aromatized directly by treating a solution in 100 cc. of acetic anhydride with 2.3–2.5 g. of concentrated sulfuric acid in 14 cc. of acetic anhydride. After standing for four hours, the mixture was hydrolyzed with methanolic alkali and the crude phenol isolated as before (2.94 g., or 52% yield, m. p. 134–138°). Methylation of this material in 100 cc. of warm alcohol with five portions each of 11 cc. of sodium hydroxide solution (36 g. in 60 cc. of water) and 15 cc. of dimethyl sulfate (cooling when the reaction became too vigorous), gave 2.37 g. (41% overall yield) of the methyl ether, m. p. 101–103°, with sintering at 98°. One recrystallization from alcohol (using Norit) gave 1.74 g. (30%) of material of m. p. 104–105° and 0.26 g. (4%) of m.p. 97–100°. Although the over-all yield by method (*b*) was not quite as high for material of comparable purity as by the longer procedure of chromatographic separation and isolation of the unsaturated ketone I, the procedure was less time-consuming.

Nitric Acid Oxidation of the Methyl Ether IIb.—A mixture of 400 mg. of the methyl ether (m. p. 104–105°), 3 cc. of concentrated nitric acid and 8 cc. of water was heated in a sealed tube at 190° for twenty-four hours. The clear yellow solution was evaporated to dryness, water was added and evaporated, and the process repeated with water and then methanol. The product was dried in a vacuum desiccator (weight 80 mg., melting point indefinite), treated with an excess of ethereal diazomethane (from 1 g. of nitrosomethylurea), allowed to stand for a day and the methylation repeated. The ether was evaporated and the product dissolved in acetone, filtered and crystallized from petroleum ether (b. p. 60–68°) containing a few drops of acetone to give 71 mg. (23% yield) of crystals melting at 118–126.5° (sint. at 113°). Sublimation at 120–140° and 0.15 mm. and two recrystallizations gave 40 mg. (13%) of colorless needles, m. p. 129–130°, of the tetramethyl ester of benzene-1,2,3,4-tetracarboxylic acid. A mixed m. p. with an authentic sample (m. p. 130–131°; kindly furnished by Dr. W. S. Johnson) prepared by oxi-

(26) Bergstrom and Wintersteiner, *J. Biol. Chem.*, **143**, 503 (1942); Wintersteiner and Ruigh, THIS JOURNAL, **64**, 2453 (1942).

(27) Hardegger, Ruzicka and Tagmann, *Helv. Chim. Acta*, **26**, 2217 (1943).

dation of 1-ketotetrahydrophenanthrene[28] showed no depression (m. p. 129.5–130.5°).

Anal. Calcd. for $C_{14}H_{14}O_3$: C, 54.2; H, 4.5. Found: C, 54.0; H, 4.9.

Summary

The synthesis of 1,4-cholestadienone-3 (I) and its rearrangement to the isomeric 1-methyl phenolic compound (IIa), first reported by Inhoffen and co-workers, has been confirmed and substantial improvements made in certain of the experimental procedures.

(28) Johnson and Goldman, THIS JOURNAL, **66**, 1034 (1944).

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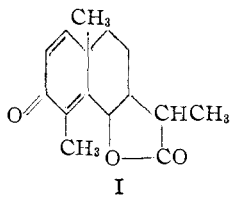
The Dienone–Phenol Rearrangement Applied to Chrysene Derivatives. The Synthesis of 3-Hydroxy-1-methylchrysene and Related Compounds[1]

BY A. L. WILDS AND CARL DJERASSI[2,3]

In an accompanying communication, the rearrangement by acid of 1,4-cholestadienone-3 to 3-hydroxy-1-methyl-10-norcholestatriene-1,3,5 is considered.[4,5] This reaction, which may be termed the dienone-phenol rearrangement, is analogous to the well-known rearrangement of santonin (I) to desmotroposantonin (II),[6] and



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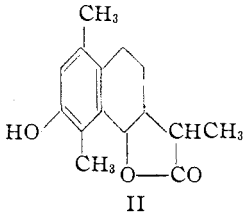

II

also bears a formal resemblance to the rearrangement of quinols[7] and of semibenzenes[8] to the corresponding aromatic structures.

Although the course of the dienone–phenol rearrangement has been fairly well established, it has not been fully confirmed as far as we are aware, by means of an example in which the structures of both the dienone and the phenol were proved by synthesis. The recent claim of a synthesis of santonin (I) by Paranjape, Phalnikar, Bhide and Nargund[9a] must be discounted for the present, since the total asymmetric synthesis of *l*-santonin and related compounds is claimed,[9b] without the use of any optically active reagents.[10]

We therefore decided to synthesize the dienone VI, and subject it to rearrangement. This dienone was selected because it seemed probable that most of the intermediates in its preparation would be solids, thus facilitating development of the steps of the synthesis. Moreover, the structure of the rearrangement product VIIa might be established through dehydrogenation to 3-hydroxy-1-methylchrysene (VIIIa) and synthesis of the latter by a method similar to that used earlier for 3-hydroxychrysene.[11] For preparing the dienone VI, we employed the ingenious method reported by Paranjape, *et al.*,[9a] for the synthesis of compounds with the santonin-type structure, although with significant modifications in the experimental procedures.

1-Keto-1,2,3,4-tetrahydrophenanthrene was condensed with ethyl formate and sodium methoxide, by the procedure of Johnson and Shelberg,[12] to give the 2-hydroxymethylene derivative III in 96% yield. Preliminary experiments on the methylation of this hydroxymethylene ketone resulted in mixtures of the C- and O-methyl derivatives, and revealed that the C-methylated product was quite sensitive to cleavage with loss of the formyl group. A search of the literature for similar alkylations failed to reveal instances in which a C-methylated formyl ketone of established purity had been described. Sen and Mondal[13] found in the case of 2-hydroxymethylenecyclohexanone that some C-alkylation must have occurred, using sodium in benzene or sodium ethoxide in alcohol along with the alkyl halide, since they were able to isolate the semicarbazones of the corresponding 2-alkylcyclohexanones after cleavage of the product. However, they were unable to isolate pure intermediates,[14] and the relative importance of C- and O-alkylation or of cleavage cannot be determined from their work. Pure products were not isolated by Paranjape, *et al.*,[9] in their syntheses. The recent work by Cornforth, *et al.*,[10] did result in an analytically pure, methylated 2-formylcyclohexanone, although the

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(4) Wilds and Djerassi, THIS JOURNAL, **68**, 1712 (1946); see formulas I → IIa for this reaction.

(5) Inhoffen and Huang-Minlon, *Naturwissenschaften*, **26**, 756 (1938); Inhoffen and Zühlsdorff, *Ber.*, **74**, 604 (1941).

(6) See Clemo, Haworth and Walton, *J. Chem. Soc.*, 1110 (1930).

(7) Bamberger and Rising, *Ber.*, **33**, 3636 (1900); Bamberger and Brady, *ibid.*, **33**, 3642 (1900).

(8) v. Auwers and Ziegler, *Ann.*, **425**, 217 (1921).

(9) (a) Paranjape, Phalnikar, Bhide and Nargund, *Current Sci.*, **12**, 150 (1943); *Rasayanam*, **1**, 233 (1943); (b) *Nature*, **153**, 141 (1944).

(10) For unsuccessful attempts to repeat the asymmetric synthesis of 2-formyl-2-methylcyclohexanone, also reported, see Cornforth, Cornforth and Dewar, *Nature*, **153**, 317 (1944), and O'Gorman, THIS JOURNAL, **66**, 1041 (1944).

(11) Wilds and Shunk, *ibid.*, **65**, 469 (1943).

(12) Johnson and Shelberg, *ibid.*, **67**, 1750 (1945).

(13) Sen and Mondal, *J. Indian Chem. Soc.*, **5**, 609 (1928).

(14) *Cf.* also Robinson and Walker, *J. Chem. Soc.*, 1532 (1935).