

The androgenic material present in the product is undoubtedly androstenedione,⁴ and the method for separating it from progesterone is based upon a difference in partition coefficients which the two compounds show when divided between petroleum ether (35–40°) and 35% alcohol. Calculations made from the data of Wintersteiner and Allen¹⁰ show that progesterone is about five times as soluble in petroleum ether as in 35% alcohol, while a simple experiment using crystalline material revealed that androstenedione is twice as soluble in 35% alcohol as in petroleum ether. Using these figures, the following procedure was devised.

The sample, containing about 200 units, is taken up in 100 cc. of absolute alcohol, and 42 cc. of water is added. It is extracted with two 50-cc. portions of petroleum ether. The petroleum ether is extracted with 58 cc. of 70% alcohol and discarded. The combined alcoholic extracts are diluted to 400 cc. with water, extracted with five 80-cc. portions of petroleum ether and discarded. The ether is evaporated to 50 cc., 200 cc. of 35% alcohol is added and a total of five extractions with 50-cc. portions of petroleum ether are made. The hormone is stored in alcohol after evaporation of the petroleum ether. There is no loss of progestational activity within the limits of the assay method. A preparation so purified was assayed for androgens. There was no significant result at a dose level of 1 rabbit unit (seminal vesicles averaged 13 mg. in 4 rats), or at 5 units (16 mg., 4 rats). At 10 rabbit units per rat, the vesicles from 4 animals averaged 28 mg.

(10) Wintersteiner and Allen, *J. Biol. Chem.*, **107**, 321 (1934).

Isolation of Progesterone.—For purpose of characterization a sample of progesterone was isolated in crystalline form. About 100 units, purified by the 35% alcohol method, was distilled at 180° (air-bath) at 0.001 mm. pressure, and then crystallized several times from dilute methanol. The top fraction was stout prisms melting at 128°. The second fraction melting at 110–113° appeared to be a mixture of prisms and the lower-melting needle form. This was confirmed by conversion to the common dioxime which darkened at 220° and melted at 238°. The total of recovered crystalline hormone was 14 mg.

Recovery of Cholestenone.—The main by-product is cholestenone which remains in the petroleum ether after the hydrochloric acid extraction. The solvent is washed with water and then evaporated on a steam-bath. The residue is taken up in 25 cc. of acetone and set in the refrigerator to crystallize. About 25 g. of cholestenone is recovered; m. p. 79–80°. Further crystallization is best made from 50% acetone–methanol.

Summary

Detailed directions are given for a simple and inexpensive method of making progesterone from cholesterol. The physiological properties of the product are described.

(11) Allen and Wintersteiner, *Science*, **80**, 190 (1934).

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RECEIVED FEBRUARY 3, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

Rearrangements of Tetraaryldiallenes. XII.¹ The Synthesis of 2,8-Diphenylchrysene

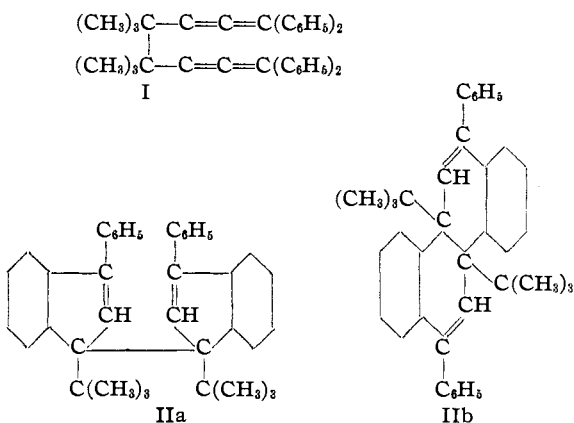
BY C. S. MARVEL AND W. J. PEPPEL

It has been shown² that the tetraaryldiallene, 1,1,6,6-tetraphenyl-1,3-di-*t*-butylhexatetraene-1,2,4,5 (I) is isomerized by acids and by the addition and subsequent removal of sodium to give two new C₃₈H₃₈ hydrocarbons (isomers A and B, respectively) of unknown structures. Neither of these rearrangement products can be the diindenyl^{2d} (IIa) which might be formed by simple ring closure in a manner analogous to the formation of indenes from phenylallenes.³ In the present communication evidence is submitted to show that neither of these rearrangements of the tetraaryldiallene (I) produces the chrysene structure (IIb)

(1) For the eleventh communication in this series see Marvel, Mueller and Peppel, *THIS JOURNAL*, **60**, 410 (1938).

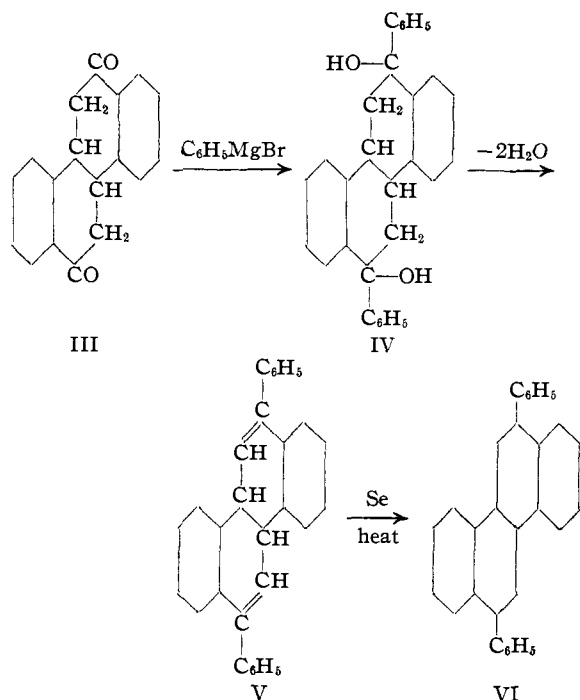
(2) (a) Farley and Marvel, *ibid.*, **58**, 29 (1936); (b) Althausen and Marvel, *ibid.*, **54**, 1174 (1932); (c) Stampfli and Marvel, *ibid.*, **53**, 4057 (1931); (d) Halley and Marvel, *ibid.*, **54**, 4450 (1932); Goebel and Marvel, *ibid.*, **55**, 3712 (1933).

(3) Vorländer and Seibert, *Ber.*, **39**, 1024 (1906); Ziegler, Grabbe and Ulrich, *ibid.*, **57**, 1983 (1924).



by simultaneous closure of two six-membered rings.

2,8-Diphenyl-6b,12b-dihydrochrysene (V) and 2,8-diphenylchrysene (VI) were synthesized by the following reactions.



A molecule with the structure indicated by formula II should show absorption in the ultraviolet which would be almost identical with that shown by 2,8-diphenyl-6b,12b-dihydrochrysene (V) and perhaps not greatly different from that shown by 2,8-diphenylchrysene (VI). Hence the ultraviolet absorption spectra of the two new chrysene derivatives (V and VI) were compared with those

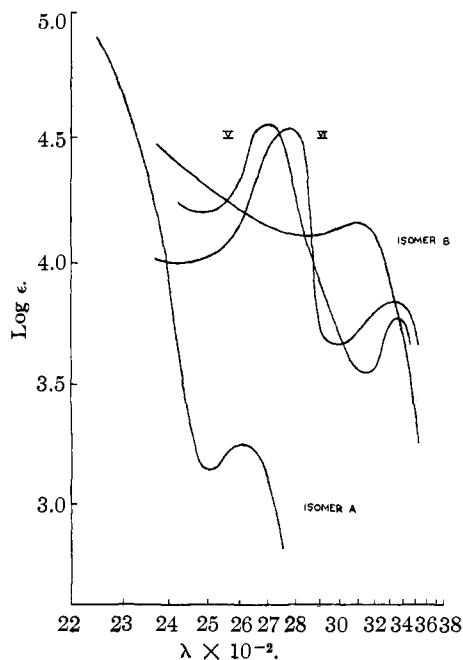


Fig. 1.

of isomers A and B. In Fig. 1 the four ultraviolet absorption curves are given. It can be seen readily that neither of the rearrangement products of the diallene has an absorption curve that resembles those of the chrysene derivatives. Further evidence that neither isomer A nor B was a substituted dihydrochrysene was obtained from dehydrogenation experiments. Ramage⁴ has prepared 6b,12b-dimethyl-1,2,6b,7,8,12b-hexahydrochrysene and has shown that dehydrogenation with selenium at 360° gives chrysene together with either mono- or dimethylchrysene due to migration of the angular methyl groups. Neither isomer A nor B gave chrysene when similarly treated.

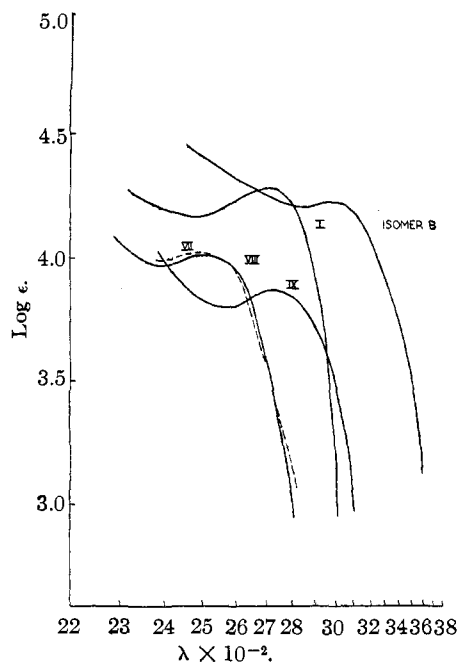
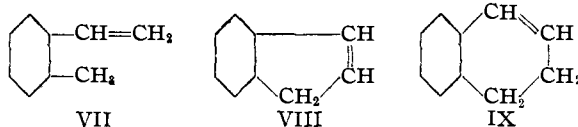


Fig. 2.

The ultraviolet absorption curve of isomer B is very similar to that of the diallene (I) but the absorption is shifted to the region of the longer wave lengths (Fig. 2). Ramart and Hoch⁵ have shown that this shift is characteristic of the change from an open chain unsaturated molecule such as *o*-methylstyrene (VII) or a five-membered ring with one double bond such as indene (VIII) to a six-membered ring with one double bond such as Δ^1 -dihydronaphthalene (IX) (Fig. 2).

(4) Ramage, *J. Chem. Soc.*, 397 (1938).(5) Ramart and Hoch, *Bull. soc. chim.*, [5] 5, 848 (1938).

Reasoning from analogy it may be suggested that isomer B is formed from the diallene by closure of one six-membered ring to give a dihydronaphthalene derivative. For this to happen some other structural change also would have to occur. Hence, much work must yet be done to test this suggestion experimentally.

Experimental

Isomer A ($C_{38}H_{38}$, m. p. 173°)^{2b} and isomer B ($C_{38}H_{38}$, m. p. 181°)^{2c} were prepared by methods previously described.

Dehydrogenation of Isomer A and Isomer B with Selenium.—A 1.0-g. sample of isomer A was mixed with 3–4 g. of selenium and heated at 300° for twenty hours. By extracting the cold reaction mixture with benzene most of the starting material was recovered unchanged. Heating to 375° for the same period yielded only a small amount of a non-crystalline residue. When isomer B was heated with selenium at 300° for twelve hours a dark, viscous residue was obtained from which nothing could be isolated.

With Platinum-Charcoal Catalyst.—A 0.2-g. sample of isomer A was mixed with 0.1 g. of 30% platinum-charcoal catalyst prepared according to the directions of Zelinsky and Turowa-Pollak⁶ and heated to 300° for about six hours. The original hydrocarbon was recovered unchanged by extraction with acetone. When a similar mixture was heated to 400° decomposition occurred and no product could be isolated.

When isomer B or its dihydro derivative, $C_{38}H_{40}$,^{2b} was heated with the catalyst at 300° for about eight hours, decomposition was observed. The residue was distilled under reduced pressure and a few drops of an oil obtained. This crystallized from alcohol by adding a little water, m. p. 141 – 143° . The amount was too small for further study.

The hydrocarbon $C_{38}H_{40}$ when subjected to dry distillation yielded a liquid mixture of hydrocarbons which could not be separated and identified because of the small amount available.

2,8-Diphenyl-6b,12b-dihydrochrysene (V).—Seven grams of *trans*-2,8-diketo-1,2,6b,7,8,12b-hexahydrochrysene (III), prepared by the method of Ramage and Robinson,⁷ was added in 1-g. portions to a solution of phenylmagnesium bromide prepared from 23 g. of bromobenzene and 3.8 g. of magnesium in a mixture of 100 cc. of dry ether and 50 cc. of dry benzene. The mixture was stirred about twenty-four hours until the solid diketone had completely gone into solution. The reaction mixture

was decomposed with dilute hydrochloric acid and ice in the usual manner. The ether layer was separated, dried over sodium sulfate, filtered and evaporated. The residue was taken up in 15 cc. of hot benzene and an equal volume of petroleum ether (b. p. 80 – 100°) was added. On cooling, a yellowish crystalline solid separated.

This diol (IV) was dehydrated readily and was not obtained in a pure form for analysis. The crude product was suspended in 100 cc. of glacial acetic acid and the mixture was boiled under a reflux condenser for one hour. The mixture was cooled and filtered and the product was recrystallized from benzene. The hydrocarbon separated in small white plates which turned yellow on exposure to the light; m. p. 265 – 266° (corr.).

Anal. Calcd. for $C_{30}H_{22}$: C, 94.21; H, 5.79; mol. wt., 382. Found: C, 94.30; H, 5.40; mol. wt. (Rast), 378.

2,8-Diphenylchrysene (VI).—One gram of the above dihydrochrysene derivative was mixed with 3 g. of selenium and the mixture was heated in a Pyrex tube at 275 – 300° for six hours. The cold mixture was then powdered and extracted with hot benzene. Concentration of the extract followed by cooling gave about 0.5 g. of product. This material was purified by sublimation. The pure product was white and melted at 285° (corr.).

Anal. Calcd. for $C_{30}H_{20}$: C, 94.73; H, 5.27; mol. wt., 380. Found: C, 94.60; H, 5.18; mol. wt. (Rast), 389.

Ultraviolet Absorption Spectra.—The ultraviolet absorption spectra were taken on a Bausch and Lomb ultraviolet spectrograph. A hydrogen discharge tube operating at 15,000 volts was used as the ultraviolet source. The H_α , H_β and H_γ lines were observed and the wave length scale calibrated. A slit opening of $60\mu \times 5$ mm. and a 1-cm. cell was employed throughout. The samples were dissolved in hexane and 10^{-2} molar stock solutions were used with dilution down to 10^{-6} molar. The absorption coefficient was determined by comparison with the blackness of a trace obtained from a 10^{-4} molar solution of naphthalene.

Summary

1. 2,8-Diphenyl-6b,12b-dihydrochrysene and 2,8-diphenylchrysene have been synthesized.

2. Comparisons of the ultraviolet absorption spectra of these two products with the ultraviolet absorption spectra of the rearrangement products of 1,1,6,6-tetraphenyl-3,4-di-*t*-butylhexatetraene-1,2,4,5 show no similarity. This is evidence that chrysene derivatives do not form in the known rearrangements of this tetraaryldiallene.

(6) Zelinsky and Turowa-Pollak, *Ber.*, **58**, 1292 (1925).

(7) Ramage and Robinson, *J. Chem. Soc.*, 607 (1933).