conducted for the benefit of the visiting geologists. Three all-day trips, run simultaneously, offered a choice among a wide range of geologic phenomena because of the fact that Harrisburg is exceptionally well located for such observations. Trip A covered the area north and west of Harrisburg and included the Paleozoic stratigraphy from the Ordovician to the Pennsylvanian, Appalachian structures and physiography. It was conducted by Bradford Willard and Frank M. Swartz. Trip B visited the area southwest of Harrisburg to observe the stratigraphy of the Cambrian and Ordovician, the Triassic sediments and volcanics and the pre-Cambrian crystalline complex. This party was in charge of W. O. Hickok, IV, and R. W. Stone. Trip C was in charge of F. T. Moyer, C. W. Cumings and G. L. Adair. This trip toured the region east of Harrisburg covering the Ordovician and Triassic sediments and igneous rocks, the Cornwall iron mines and associated phenomena.

While the field trips were in progress, special entertainment was arranged for the visiting ladies. In the morning those interested met at the Rose Gardens of Dr. J. Horace McFarland. The visit to the gardens was followed by luncheon at the residence of Dr. and Mrs. Bradford Willard. In the afternoon entertainment was provided at the residence of Mr. and Mrs. R. W. Stone. At five o'clock, after the conclusion of the field trips, delegates, invited guests, the ladies and others assembled for a tea at the residence of Dr. and Mrs. George H. Ashley, which event brought the celebration to a close.

Bradford Willard

SPECIAL ARTICLES

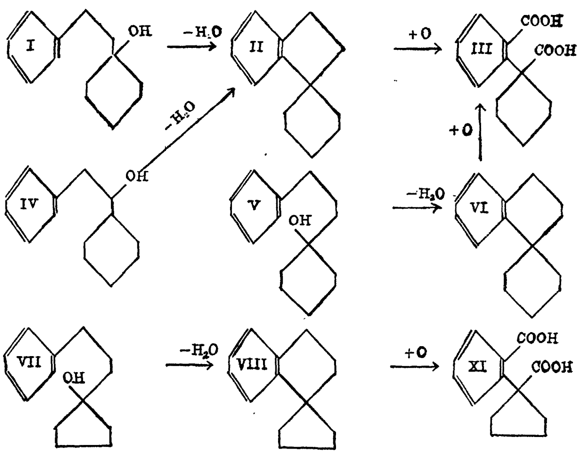
A SPIRANE BY-PRODUCT IN THE PHENANTHRENE SYNTHESIS

Since our preliminary communication[1] announcing the preparation of phenanthrene by the dehydration of 1-phenylethylcyclohexanol-1(I), with subsequent dehydrogenation of the as-octahydrophenanthrene so produced, we have been studying this synthesis, especially from the standpoint of its mechanism and the constitution of the products. The results were submitted last month (May) to the faculty of pure science of Columbia University, in Dr. Perlman's dissertation for the Ph.D. degree. Articles based upon these experiments are now in course of preparation and will be submitted soon for publication in one of our chemical journals.

In the June, 1936, number of the *Journal of the American Chemical Society,* p. 1062, there appears a communciation by van de Kamp and Mosettig showing that they too are investigating this same problem, and it seems desirable therefore that we should announce immediately those of our results which concern the work reported by them.

By repeated distillation, they succeeded in separating the crude as-octahydrophenanthrene into two main fractions; A(20 per cent.), boiling at 135.5–135.7° at 10.5–10.8 mm; and B(70 per cent.), boiling at 142.6–142.8° at 9.2 mm; which they believe to be the two stereoisomeric forms of the octahydrophenanthrene, A having probably the *trans-* and B the *cis-*configuration. Using the Friedel-Crafts reaction, they found that A and B gave different monacetyl derivatives.

Our own experimental results have led us to a quite different conclusion, namely, that the (lower-boiling) by-product is not a phenanthrene derivative at all, but is really the spirane (II), the higher-boiling constituent being the octahydrophenanthrene.



In support of this deduction concerning the constitution of the by-product, we offer the following experimental observations:

(1) On permanganate oxidation, it yielded the *alpha, alpha*-pentamethylenehomophthalic acid (III), whereas under similar conditions the octahydrophenanthrene gave only phthalic acid.

(2) The same spirane (II) was obtained as the by-product when benzyl cyclohexylcarbinol (IV) was used instead of the 1-phenylethylcyclohexanol-1.

(3) The spirane VI, from 1-phenylpropylcyclohexanol-1(V), on oxidation also gave the *alpha, alpha*-pentamethylenehomophthalic acid, one carbon being eliminated in the reaction.

(4) Similarly, the spirane VIII, prepared from 1-phenylpropylcyclopentanol-1(VII), yielded on oxidation the corresponding *alpha, alpha*-tetramethylenehomophthalic acid(IX).

(5) Certain of these spiranes were fused with sele-

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[1] Bogert, Science, n. s., 77: 1994, 289, March 17, 1933.

nium at temperatures up to 350°, but no phenanthrenes could be isolated from the fluorescent oily products.

Further, the formation of these spiranes was suspected by us, and their presence in the reaction products predicted, because of our experience with the indanes and ionenes.[2]

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THE OESTROGENIC ACTIVITY OF CERTAIN PHENANTHRENE AND HYDROPHENANTHRENE DERIVATIVES

A SOMEWHAT novel technique of bio-assay has been developed in the course of an investigation of the series of phenanthrene and hydrophenanthrene derivatives listed in Table I. The synthetic substances were prepared by Fieser and his collaborators, as indicated in the preceding note,[*] and their values for the melting points are included in the table.[1,2,3,4]

The oestrogenic activity of the compounds was tested by the intraperitoneal injection of sesame oil solutions into spayed mice at two weeks after ovariectomy. Intraperitoneal injections were employed in order to insure absorption of the oily solutions, since it has been shown[5] that such solutions are retained subcutaneously for long periods. Furthermore, we have observed definite inflammatory reactions against subcutaneous injections of certain of these and related compounds of such a nature that the oily material is eventually walled off by connective tissue overgrowth. There are in addition obvious lymphatic reactions against the subcutaneously injected material.

Various methods of assay were tested, and a standard procedure was evolved, as follows: two intraperitoneal injections of 0.2 cc each were made at twelve-hour intervals and the first vaginal smear was taken at the time of the second injection; at approximately twelve-hour intervals thereafter vaginal smears were taken until a total of nine readings was had on each animal. The animals were taken in groups of five so that a total of forty-five smears were recorded in a routine test. Prooestrus and oestrus smears were recorded as positive and the total positive count was compared with a set of control (sesame oil injected) animals. As our standard of comparison for degree of activity we employed a set of determinations on animals receiving various dosages of crystalline oestrone in sesame oil. The standard oestrone curve is given in Fig. 1. Injections of 0.1 γ and above give a statistically significant increase of positive smears over the control series.

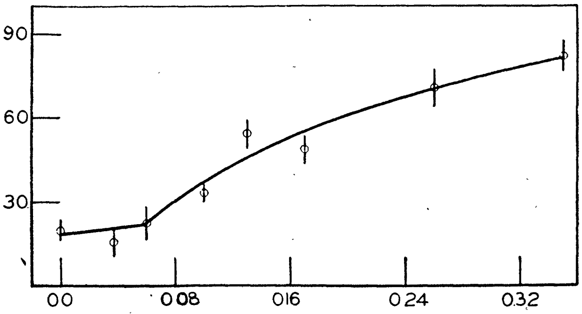

FIG. 1

Abscissa-dosage of oestrone in gamma.

Ordinate—per cent. of positive smears in test mice. The vertical lines at each point are equal to twice the standard error of the measurements.

The synthetic compounds were ordinarily tested in dosages of 100 γ or less, and their activity in terms of oestrone was determined from the standard curve (Table I, column 4). With few exceptions (substances II, III and X) those substances showing no activity in 100 y dosages were not tested further. On the basis of vaginal cornification alone substances II and III showed an activity of about 10,000 to 15,000 mouse units per gram with low dosages, but no significant increase in activity with higher dosages. Using our standard criteria, however, both compounds were inactive in dosages up to 200 γ. Substance XV, on the other hand, by our method of assay showed an exact proportional increase when the minimum effective dosage was quadrupled.

It will be noted that the addition of auxiliary hydroxy and methoxy groups results in a definite increase in activity. Furthermore, the addition of these groups at either position 6 or 7 results in the same degree of enhancement (compare substances XIII, XIV and XVII) and the presence of these groups at both 6 and 7 (substances XV and XVI) results in approximately three times the activity of the compounds with single additions at these positions. Closure of the fourth ring in the 1,2 position (substance V) is about half as effective in enhancing activity as the hydroxy and methoxy additions. This is the position of the cyclopenteno-ring typical of the native oestrogenic hormones. When the ring is in the 3,4 position (substance VI) we do not obtain a corresponding activity.

That the assay procedure we have employed offers a more sensitive indication of activity than ordinary

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[2] *Jour. Am. Chem. Soc.*, 56: 185, 248, 959, etc.

[*] L. F. Fieser and others, SCIENCE, 83: 2162, 558, 1936.

[1] L. F. Fieser and E. B. Hershberg, *Jour. Am. Chem. Soc.*, 57: 1851, 1935.

[2] L. F. Fieser, M. Fieser and E. B. Hershberg, unpublished work.

[3] L. F. Fieser and E. B. Hershberg, *Jour. Am. Chem. Soc.*, 57: 2192, 1935.

[4] L. F. Fieser and E. B. Hershberg, unpublished work.

[5] R. Deansley and A. S. Parkes, *Jour. Physiol.*, 78: 155, 1933.