
COMMUNICATIONS TO THE EDITOR

THE TOXIC PRINCIPLES OF POISON IVY

Sir:

We have investigated the active principles of poison ivy and find that the toxic oil is a complex of at least three active components and several innocuous concomitants.

Hill and his co-workers¹ isolated a toxic yellow oil from poison ivy with the stated boiling point of 210° (0.5 mm.), and presented evidence to prove that it was identical with urushiol, the boiling point of which was quoted as 210° (0.4–0.6 mm.). From this toxic oil they prepared a series of derivatives, identical when crystallizable with those prepared from urushiol, but no yields were reported.

"Urushiol" is a name first applied by Majima² to an extract of Japan lac which boiled over a range of 210–222° ((0.4–0.6 mm.), and, upon redistillation, from 195° to "above 210°." It was shown to consist of four components³ the structures of which were partially elucidated.

Since it is known that plants of the *Anacardiaceae* family, to which both poison ivy and Japan lac belong, elaborate a number of vesicant mono- and dihydric alkyl phenols with fifteen and seventeen carbon side chains, the derivatives prepared by Hill only prove the presence of a compound or compounds with a 3-pentadecacatechol skeleton in the distillate. This is a property it possesses in common with urushiol.

Essentially we followed Hill's method of isolation; our concentrate boiled over a range, the major portion distilling at 185–250° (2 microns) with considerable resinification. Redistillation in a Hickman molecular still yielded three fractions at bath temperatures up to 125°, 165° and 170°, the principal superficial difference being one of color. The products, although containing innocuous concomitants, were all toxic, 0.5 gamma of oil per sq. cm. of hypersensitive skin being sufficient to elicit a strong characteristic poison ivy reaction.

Chromatographed under nitrogen on barium carbonate-Hyflo Super Cel (Johns Mansville Sales Corporation), fraction 1 was separated into

an unsaturated acid (or acids, hydrogenation yielding a solid, m. p. 66–67°, depressed by palmitic but not stearic acid; C, 75.4; H, 12.5; amide m. p. 105–106°, depressed by palmitamide but not stearamide; therefore stearic acid⁴) and a phenolic oil, $\log \epsilon$ 265 $m\mu$ = 3.02, $\log \epsilon$ 273 $m\mu$ = 3.09 in absolute ethanol. In twenty-four hours absorption decreased to $\log \epsilon$ 265 $m\mu$ = 2.72 and the ferric chloride test became negative in the original concentration, 6 mgm./100 cc. This suggests that the presence of drying oils in the vesicant-bearing sap accounts at least in part for the extraordinary stability of the toxic principles in their natural environment.

Chromatographed on alumina (Alorco) deactivated with 90% ethanol, fraction 1 yielded six bands, from the top: orange, four colorless with bright blue-white fluorescence under ultraviolet light, and yellow. One fluorescent band, eluted with 90% ethanol, was phenolic and auto-oxidized with extreme rapidity. The other fluorescent bands could not be removed without major destruction, but were shown to be highly toxic, while the remaining fractions were not. We conclude that at least three toxic components are present, and are engaged in improving this technique and elucidating the structures of the toxic compounds. The exigencies of the day have required this short report at this time.

(4) We are indebted to Dr. Arthur T. Ness for the microchemical analyses.

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RECEIVED OCTOBER 21, 1942

THE MECHANISM OF THE DIELS-ALDER REACTION

Sir:

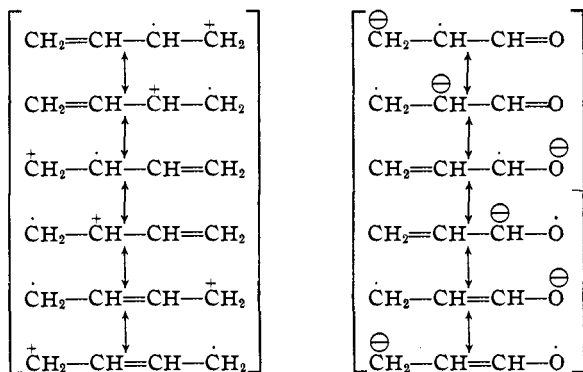
It is noteworthy that in the usual case the Diels-Alder reaction involves, on the one hand, a substance, *e. g.*, a diene, of relatively low ionization potential and, on the other, a molecule of high electron affinity, *e. g.*, an α,β -unsaturated carbonyl compound. We may therefore expect an electron-transfer from the diene to the dienophile with the formation of an ion-pair intermediate of the type recently postulated in general for molecu-

(1) Hill, Mattacotti and Graham, *THIS JOURNAL*, **56**, 2736 (1934).

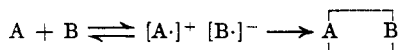
(2) Majima, *Ber.*, **42**, 1418 (1909).

(3) Majima, *et al.*, *ibid.*, **55B**, 172 (1922).

lar compound formation by Weiss.¹ Both components, after the electron exchange, will be hybridized, *viz.*, in the simplest case, the reaction between butadiene and acrolein,



We thus arrive at a mechanistic picture in which collision results in electron transfer followed by formation of a dipolar aggregate, held together



by ionic forces (and possibly further by interparticular overlapping of the orbitals of the non-bonded electrons in each half; in this event, the link could be described as an *intermolecular semipolar bond*,² *cf.* $[A^+]:[B^-]$). Stereochemically, the

(1) Weiss, *J. Chem. Soc.*, 245 (1942).

(2) (Note added in proof, November 25, 1942.) This concept is a logical extension (or modification) of the theory of molecular complex formation which is not implied in Weiss' paper.¹ I intend to develop these ideas further; meanwhile, I note that Dr. L. C. Bateman (*Chemistry and Industry*, 61, 433 (1942), received November 23) has independently proposed a similar picture during a discussion at the Chemical Society (London) on October 15, 1942. On this side these ideas were first embodied in Dr. J. J. Leavitt's Dissertation, "Some Properties and Reactions of Unsaturated γ -Lactones," Harvard University, September 1, 1942.

aggregate would consist of two parallel charged (usually flat) surfaces, oriented in such wise as to take maximum advantage of electrostatic attractive forces. The first step is probably in most cases rapid and reversible, the rate-controlling process being the usually (but not always) substantially irreversible rearrangement of the ion-pair complex to the product $\boxed{A \quad B}$ above.

This picture is in complete conformity with the large body of observed phenomena attendant upon the reaction. There may be cited: (i) transient color formation, (ii) steric course of the reaction, (iii) effect of substituents of divers electrical character on the ease of reaction both of the diene and the dienophile, (iv) observed molecular compound formation preceding reaction in certain cases, (v) the occasional abnormal course of the reaction (notably in the case of heterocyclic nitrogen bases, and ketenes), (vi) solvent effects.

The procession of the reaction by the above course further indicates the possibility of catalysis by donor or acceptor molecules which cannot themselves participate in the diene-addition reaction. Preliminary experiments designed to test this possibility give some qualitative indication that dimethylaniline and 1,3,5-trinitrobenzene exert such an accelerating effect.

The situation will be considered in detail in a forthcoming publication.

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RECEIVED NOVEMBER 12, 1942

NEW BOOKS

Elementary Physical Chemistry. By MERLE RANDALL, Professor of Chemistry in the University of California, and LEONA ESTHER YOUNG, Professor of Chemistry in Mills College. Randall and Sons, 2512 Etna St., Berkeley, California, 1942. (Photolith reproduction.) xiv + 455 pp. Illustrated. 15.5 × 23.5 cm. Price, \$4.50.

Physical Chemistry. By FRANK THOMSON GUCKER, JR., Associate Professor of Chemistry, Northwestern University, and WILLIAM BUELL MELDRUM, Professor of Chemistry, Haverford College. American Book Company, 88 Lexington Avenue, New York, N. Y., 1942. xii + 683 pp. 262 figs. 14.5 × 22.5 cm. Price, \$4.00.

As physical chemistry has advanced beyond its historic preoccupation with aqueous solutions of electrolytes, an

adequate grasp of its subject matter has become increasingly difficult to obtain in a single year-course. An "introductory" course in the third, or even second, year of college is a frequent answer to this problem as well as to the needs of students majoring in other sciences or preparing for medicine. Such a course, covering one or two semesters, is the province of the two text-books with which we are concerned. They both deal mainly with "classical" principles; both stress experimental facts and the deductive approach, with a minimum of mathematics and thermodynamics. Parallel or previous study of the calculus would be desirable but not essential. In both cases the problems of beginning students have been kept clearly in mind; extensive use of illustrations, graphs, exercises and applications should go far to stimulate interest and