adenine synthesis. The possibility exists that this type of phenomenon may occur in other biochemical mutations.

The initial stocks from which the yeasts used in these experiments were derived were kindly furnished by Dr. Carl C. Lindegren.

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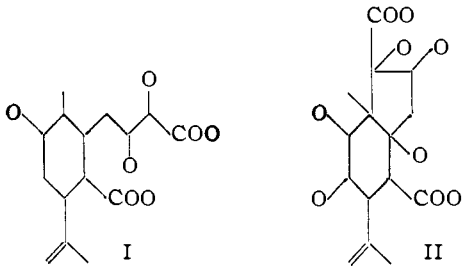
CHICAGO 37, ILLINOIS

RECEIVED MARCH 10, 1951

THE SKELETON OF PICROTOXININ

Sir:

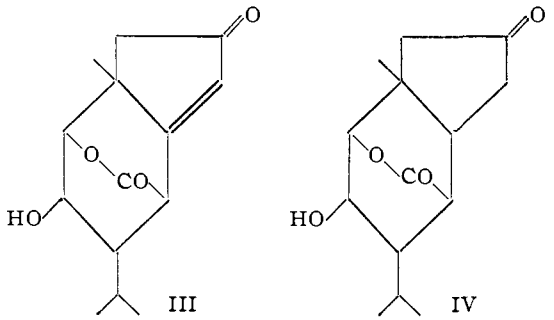
In order to account for the formation of picrotic acid and related substances, Robertson, *et al.*,[1] have proposed the partial carbon skeleton (I) for picrotoxinin, $C_{15}H_{16}O_6$, one of the two components of the amaroid picrotoxin. However picrotoxinin possesses two carbocyclic rings, *i.e.*, one more carbon-carbon bond must be drawn to complete the expression. *Evidence now obtained defines the location of*



I II

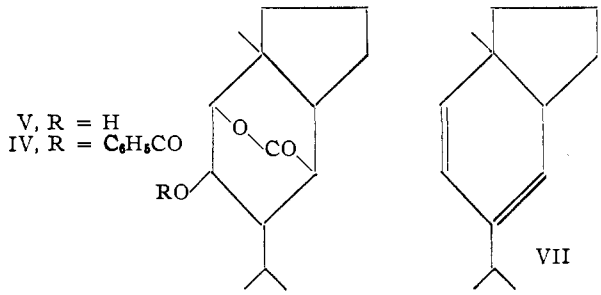
the missing bond and requires that picrotoxinin be assigned the skeleton (II), one which lacks only five carbon atoms of a complete steroid nucleus.

Dihydro-α-picrotoxininic acid[2] underwent smooth pyrolysis with loss of carbon dioxide and water to a new substance, designated picrotoxinide, $C_{14}H_{18}O_4$, not crystalline ($\lambda_{max.}$ 254 mμ, log E 4.0; $\lambda_{max.}$ 2.95, 5.70, 5.84 and 6:20 μ) formulated as (III). Hydrogenation of (III) gave 90% of dihydropicrotoxinide (IV, m.p. 187°; calcd. for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.82; H, 8.11) which formed a 2,4-dinitrophenylhydrazone (m.p. 209° dec.; calcd. for $C_{20}H_{24}O_7N_4$: C, 55.53; H, 5.60.



III IV

Found: C, 55.42; H, 5.55) and a dibenzylidene derivative (m.p. 127–128°; calcd. for $C_{28}H_{28}O_4$: C, 78.48; H, 6.59. Found: C, 78.43; H, 6.74) strikingly similar in infrared and ultraviolet spectra to 2,5-dibenzylidenecyclopentanone.[3] The dihydroxyketo-acid from (IV) reacted with one mole of periodate. Dihydropicrotoxinide (IV) was converted to its ethylene mercaptal (m.p. 250°; calcd. for $C_{16}H_{24}O_3S_2$: C, 58.50; H, 7.36. Found: C, 58.52; H, 7.38) desulfurized with Raney nickel to tetrahydrodesoxypicrotoxinide (V; m. p. 162°; calcd. for $C_{14}H_{22}O_3$: C, 70.55; H, 9.31. Found: C, 70.65; H, 9.41; infrared $\lambda_{max.}$ 5.70 μ). The latter gave a benzoate (VI; m.p. 134°; calcd. for $C_{21}H_{26}O_4$: C, 73.66; H, 7.65. Found: C, 73.56; H, 7.88) which underwent smooth pyrolysis to benzoic acid, carbon dioxide and picrotoxadiene (VII;



V, R = H
IV, R = C_6H_5CO

VII

b.p. 213°; λ_{max} 256 mμ, log E 3.6) characterized by its maleic anhydride adduct (m.p. 75°; calcd. for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.51; H, 8.31), the corresponding imide (m.p. 147–148°; $[\alpha]^{20}D$ −78° [chloroform, c = 3.1]; calcd. for $C_{17}H_{23}O_2N$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.63; H, 8.55; N, 5.28) and the N-phenyl imide (m.p. 178°; $[\alpha]^{20}D$ −42° [chloroform, c = 2.5]; calcd. for $C_{23}H_{27}O_2N$: C, 79.04; H, 7.79; N, 4.01; Found: C, 79.57; H, 7.80).

Synthetic *cis*-5-isopropyl-8-methylhydrin-4,6-diene (VII) was obtained by the action of isopropyl lithium on *cis*-8-methylhydrind-6-ene-5-one, (2,4-dinitrophenylhydrazone m.p. 138–139°; calcd. for $C_{16}H_{18}O_4N_4$: C, 58.16; H, 5.49. Found: C, 57.93; H, 5.41) prepared by an unambiguous route from *cis*-2-methyl 2-carboxycyclopentane-1-acetic acid.[4] Although the maleic anhydride adduct of the synthetic diene was not crystalline it gave an infrared spectrum identical with that of the natural adduct, and was converted to the crystalline imide (m.p. 158–159°, mixed m.p. with the natural imide 147–158°; found: C, 74.59; H, 8.36; N, 5.11) and the N-phenyl imide (m.p. 151–152°, mixed m.p. with the natural N-phenyl imide 151–175°; found: C, 79.04; H, 7.83; N, 3.88). Both imides gave infrared spectra identical with those from the corresponding natural derivatives; picrotoxadiene is clearly an optically active form of *cis*-5-isopropyl-8-methyl hydrin-4,6-diene (VII).

DEPARTMENT OF CHEMISTRY
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RECEIVED DECEMBER 19, 1950

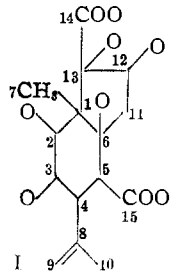
(1) J. C. Harland and A. Robertson, *J. Chem. Soc.*, 937 (1939); D. Mercer, A. Robertson and R. S. Cahn, *ibid.*, 997 (1935).
(2) P. Horrmann, *Ber.*, **46**, 2793 (1913).
(3) D. Vorländer and K. Hobohm, *ibid.*, **29**, 1836 (1896).
(4) K. D. Errington and R. P. Linstead, *J. Chem. Soc.*, 666 (1938).
(5) National Institutes of Health Postdoctoral Fellow.

THE STRUCTURE OF PICROTOXININ

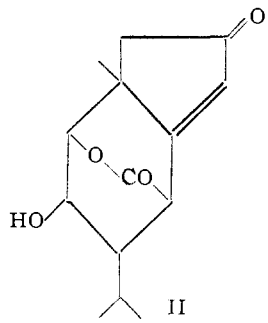
Sir:

The skeleton (I) for picrotoxinin, $C_{15}H_{16}O_6$, has been proposed[1] to account for the formation of

(1) H. Conroy, THIS JOURNAL, **73**, 1889 (1951).



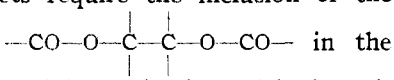
I



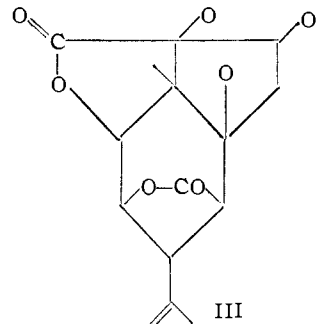
II

picrotoxinide (II) in the pyrolytic decomposition of dihydro-α-picrotoxininic acid. Picrotoxinin has long been suspected[2,3] to be a monohydroxy-dilactone; the remaining oxygen was assumed to be present as an ether linkage, since no carbonyl derivatives could be prepared. The infrared absorption spectrum of picrotoxinin has now been examined, and it is consistent with these views. In addition to an intense, fairly sharp band at 2.90 μ, due to the hydroxyl group, the only carbonyl absorption is a split peak with maxima at 5.57 and 5.63 μ, characteristic of two five-membered lactones.[4]

Picrotoxic acid,[2] $C_{15}H_{18}O_7$, monobasic, formed directly by the action of one mole of base upon picrotoxinin, produces infrared absorption at 5.57 and 5.78 μ. This evidence is consistent with the view that in this acid only the lactone responsible for the 5.63 μ band of picrotoxinin has been opened. The isomeric α-picrotoxininic acid,[2] also monobasic, produces infrared bands at 5.70 and 5.78 μ, with negligible absorption in the 5.6 μ region, evidence consistent with the view that the single lactone system in this acid directly corresponds to neither of those present in the original picrotoxinin.

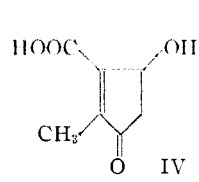
Both of these isomeric, monobasic acids were treated with a known excess of neutral, aqueous sodium periodate solution for an extended period at room temperature, and the remaining periodate determined according to a well known procedure.[5] Neither picrotoxic nor α-picrotoxininic acid reacted to any extent with periodate under these conditions. On the other hand, picrotoxinin dicarboxylic acid,[2] which can be prepared from either α-picrotoxininic acid or picrotoxinin and which shows only carboxyl absorption at 5.8 μ, took up very nearly one mole of periodate under the same conditions. These facts require the inclusion of the structural unit  in the molecule of picrotoxinin, and taken with the evidence for the skeleton (I) indicate the partial formulation (III) for this substance. Any alternative expression would embody either a four-membered or a six-membered lactone, both excluded by the infrared data[4] (*vide supra*).

The oxygen at C6 cannot be present as the oxide function, but instead must represent the single free

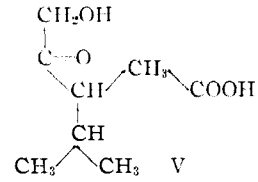


III

hydroxyl, for otherwise the formation (*vide infra*) of the products (IV) and (V) obtained by Sutter and Schlittler[6] would be prohibited. Consequently the

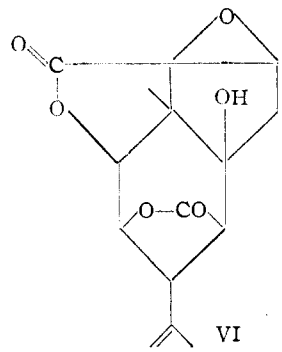


IV

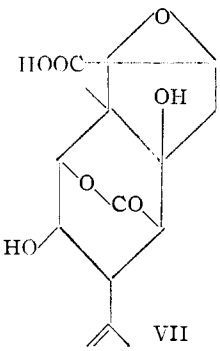


V

complete structure of picrotoxinin may be represented as (VI), while α-picrotoxininic acid is pictured as (VII), a view consistent with its infrared spectrum and with the formation of picrotoxinide[1] in the pyrolysis of the dihydro acid.

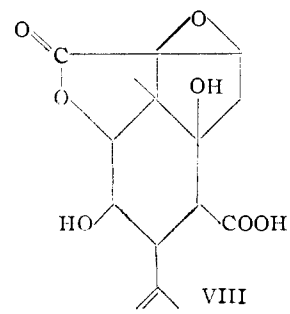


VI



VII

The formation[6] of the products (IV) and (V) of Sutter and Schlittler from either α-dihydropicrotoxinin or dihydro-α-picrotoxininic acid is represented as a base catalyzed dealdolization with cleavage of bonds at C5-C6 and C1-C2, followed by β-elimination of the oxide at C13. Picrotoxic acid, which does not undergo such cleavage, and is unchanged by the continued action of aqueous base, retains one of the original lactones intact, and is formulated as (VIII). The stereochemistry of the structure (VI) as well as possible mechanisms of the transforma-



VIII

(2) P. Horrmann, *Ber.*, **46**, 2793 (1913); **45**, 2090 (1912); *Ann.*, **411**, 273 (1916).

(3) D. Mercer, A. Robertson and R. S. Cahn, *J. Chem. Soc.*, 997 (1935).

(4) R. S. Rasmussen and R. R. Brattain, THIS JOURNAL, **71**, 1076 (1949).

(5) "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 361.

(6) M. Sutter and E. Schlittler, *Helv. Chim. Acta*, **30**, 403 (1947); **30**, 2102 (1947); **32**, 1855 (1949); **32**, 1860 (1949).

tions outlined will be discussed in a subsequent communication.

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CAMBRIDGE 38, MASS.
RECEIVED JANUARY 29, 1951

(7) National Institutes of Health Postdoctoral Fellow.

THE REACTION OF TRIPHENYLMETHYL WITH NITROBENZENE

Sir:

It has been rather generally accepted[1,2,3] that aromatic nitro compounds are activated, relative to their unsubstituted analogs, toward attack by free radicals leading to aromatic substitution. Recent evidence concerning the inhibition of the peroxide induced polymerization of allyl acetate[4] by nitro compounds was taken to indicate that some other mode of reaction must be available to the growing chain radicals. A sequence of reactions involving attack on the nitro function was suggested as a likely alternative to nuclear substitution. We have undertaken a study of the reaction of triphenylmethyl with nitrobenzene in benzene solution and find that this radical and others which may be formed in the course of the reaction react only by abstracting oxygen from the nitro function.

When one mole equivalent of nitrobenzene is added to a benzene solution of triphenylmethyl, the solution immediately develops a red color. If such a solution is allowed to stand exposed to diffuse daylight for 24 hours, nearly a quantitative yield of triphenylcarbinol precipitates. The supernatant liquid is fractionated by adsorption on a a 5:1 Magnesol–Celite mixture followed by elution with mixtures of Skellysolve B, benzene and acetone or ethanol. Products isolated and characterized are unreacted nitrobenzene, azobenzene, azoxybenzene, nitrosobenzene, biphenyl and *p*-terphenyl. The nitrogen balance is quantitative but oxygen and hydrogen have not been entirely accounted for. Phenol is detected as its tribromo derivative in alkaline extracts of the original solutions. When the reaction is carried out in the dark a slower reaction produces a quantitative yield of ditriphenylmethyl peroxide and the same nitrobenzene reduction products. There is no evidence for attack on solvent in the dark reaction. Nitrosobenzene, which is found only in small amounts, reacts rapidly with triphenylmethyl, in separate experiments, to produce azobenzene and a trace of azoxybenzene (substantial amounts are produced from nitrobenzene) along with triphenylcarbinol, biphenyl and terphenyl. Azoxybenzene does not react to any appreciable extent in 72 hours.

It is not our intention to consider the mechanisms of these transformations in detail at this time since further study is in progress. However, certain important conclusions are apparent. It is clear that at least one radical, triphenylmethyl, is capable of effecting the reduction of nitrobenzene without bringing about nuclear substitution. The presence of phenol along with biphenyl and terphenyl suggests strongly that phenyl radicals are also produced and that they, too, abstract oxygen rather than attacking the nucleus of the nitro compounds. This is an entirely unexpected result in the light of previous work which indicates that phenyl radicals produced in the thermal decomposition of benzenediazoacetate[5] and benzoyl peroxide[6] attack nitrobenzene to give *p*-nitrobiphenyl. This difference in behavior may be taken to indicate that pairs of radicals produced in unimolecular decompositions are capable of making a concerted attack on solvent molecules in the short time interval in which they are held in the same cavity in the solution. A similar discrepency involving the fate of benzoate radicals[7] produced in different reactions has recently been observed.

This research was carried out under a contract with the Office of Naval Research.

(1) W. A. Waters, "The Chemistry of Free Radicals," Oxford University Press, Oxford, 1946, p. 151.

(2) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Co., New York, N. Y., 1940, p. 383.

(3) G. W. Wheland, "Advanced Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1949, p. 670.

(4) G. S. Hammond and P. D. Bartlett, *J. Polymer Sci.*, in press.

(5) W. S. M. Grieve and D. H. Hey, *J. Chem. Soc.*, 1803 (1934).

(6) D. F. DeTar and H. J. Scheifele, *Abstracts, Chicago Meeting of Am. Chem. Soc.*, September, 1950.

(7) G. S. Hammond, J. T. Rudesill and F. J. Modic, THIS JOURNAL, manuscript submitted.

CHEMICAL LABORATORY
IOWA STATE COLLEGE GEORGE S. HAMMOND
AMES, IOWA ABRAHAM RAVVE
RECEIVED MARCH 14, 1951

RADIATION CHEMISTRY OF FERROUS SULFATE SOLUTIONS

Sir:

Emphasis has been placed recently on R, the yield ratio, $Fe^{+++}_{(O_2)}/Fe^{+++}_{vac}$, obtained by X-ray or γ-ray irradiation of dilute aqueous solutions of ferrous sulfate in the presence and absence of air.[1,2] These values vary from 2.55 to 4.0, as is shown in Table I.[1,2,3,4] The present communication demonstrates that theoretical values less than 4.0 are possible on the basis of the accepted ferrous sulfate oxidation mechanism.

According to present concepts reaction (1) occurs on the passage of ionizing particles through water. Reaction (2) also proceeds through free radical intermediates and occurs where the rate of energy loss is high and results from pairwise recombination of hydrogen atoms and hydroxyl radicals in zones of high free radical concentration. The mechanism for ferrous sulfate oxidation is:

$$H_2O = H + OH \quad (1)$$
$$H_2O = {}^1/_2H_2 + {}^1/_2H_2O_2 \quad (2)$$
$$H + O_2 = HO_2 \quad (3)$$
$$Fe^{++} + OH = Fe^{+++} + OH^- \quad (4)$$
$$Fe^{++} + HO_2 = Fe^{+++} + HO_2^- \quad (5)$$
$$HO_2^- + H^+ = H_2O_2 \quad (6)$$
$$Fe^{++} + H_2O_2 = Fe^{+++} + OH + OH^- \quad (7)$$
$$H + H = H_2 \quad (8)$$

In the absence of air the oxidation follows reactions (1), (2), (4), (7) and (8) and in the presence of

(1) N. Miller, *J. Chem. Phys.*, **18**, 79 (1950).

(2) F. H. Krenz and H. A. Dewhurst, *ibid.*, **17**, 1337 (1949).

(3) H. Fricke and S. Morse, *Am. J. Roent. and Rad. Ther.*, **18**, 430 (1927); H. Fricke and E. J. Hart, *J. Chem. Phys.*, **3**, 60 (1935).

(4) N. A. Shishacow, *Phil. Mag.*, **14**, 198 (1932).