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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RECEIVED MARCH 10, 1951

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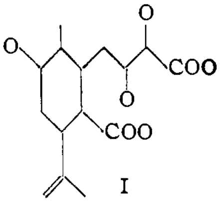
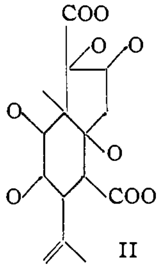
## THE SKELETON OF PICROTOXININ

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

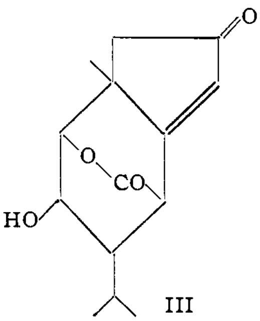


I

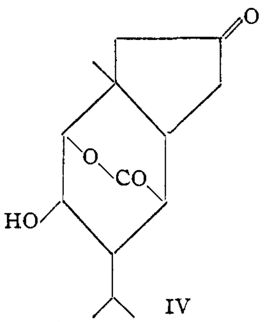


II

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. 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; b.p. 213°; $\lambda_{max}$ 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).

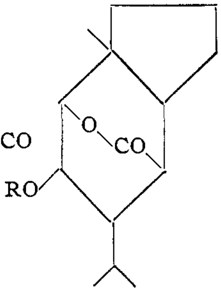


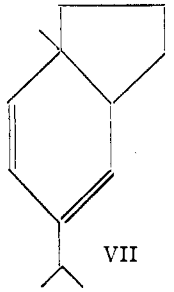
III



IV

V, R = H
IV. R = $C_6H_5CO$




VII

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).

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[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.

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## 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

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