(at C) and equal in intensity to the ethylenic hydrogen absorption (at A).

The NMR spectra of the hydrocarbons which might be designated as cycloheptatriene,[6] 1,1,4-trimethylcycloheptatriene[7a] and 1,1,3,4tetramethylcycloheptatriene[7b] or the corresponding bicyclic valence tautomers have also been obtained and indicate unequivocally the validity of the cycloheptatriene structures. In each case the ratio of aliphatic to ethylenic hydrogen absorption is that predicted for the monocyclic structure and there is no absorption due to bridge hydrogens.

(6) Kindly provided by Dr. H. L. Dryden, Jr.

(7) Prepared from eucarvone: (a) with sodium borohydride followed by dehydration; (b) with methyllithium followed by dehydration.

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RECEIVED JULY 18, 1955

GONYLEPTIDINE

Sir:

Experiments done by one of us (C. E.) in Montevideo, Uruguay, on the cephalothoracic glands of a South American arachnid of the *Gonyleptidae* family to elucidate the biological significance of the secretion led to the discovery of a volatile antibiotic, named gonyleptidine.

To a drop of protozoan and bacterian culture was added a drop of the substance globally extracted from the secretory pore of the sacciform glands of these gonyleptidae. Cytolysis led us to think of the action being possibly due to proteolytic ferments, but microscopic observation of protozoa and bacteria—in a suspended drop on excavated slides, the bottom of which had a small disc of filter paper soaked in secretion—showed the antimicrobial effect at a distance by emanation. This gave evidence of a volatile antibiotic and not of proteolytic ferments.

Preliminary experiments showed strikingly the action of gonyleptidine on membrane, cytoplasm and nucleus of free cells. Afterwards (Saez and Drets) disturbance was seen in mitosis and meiosis. Isolation of gonyleptidine (M.I.A.) fully confirmed the presence of a volatile antibiotic and allowed quantitative determination of activity. Isolated by distillation from the frozen state, gonyleptidine was characterized as a yellow substance, m.p. 12°, λ^{Water} 255 mμ ($E^{1\%}$ 1400), which gives color reactions characteristic of quinones. It was found (N.P.B.) effective against at least eighteen genera of bacteria and protozoa, for example, against six strains of *Staphylococcus aureus* at concentrations of 3 to 10 γ/ml., various strains of *B. cereus*, *B. subtilis* or *B. anthracis* (2.6 to 64 γ/ml.), *Escherichia coli* strains (3 to 112 γ/ml.), *B. tuberculosis* (100 γ/ml.), *Trypanosoma cruzi* (100 γ/ml.). (C. E., O. Simani, and N. P. B.) Given orally to mice (1 mg./mouse/24 hr.) infected with intestinal parasites, the substance was tolerated perfectly and destroyed the giardias, trichomonas, and hexamites.

While biological studies were continued in Uruguay, a chemical investigation was undertaken at Harvard (L. F. F., M. I. A.). Reduction of yellow aqueous extract with hydrosulfite, acetylation, and chromatography gave, as a derivative of the major but not the sole quinone component, a substance, m.p. 105–106° (C, 64.69; H, 6.46; acetyl, 38.02; mol. wt., 237), identified by mixed melting point determination as 2,3-dimethylhydroquinone diacetate. Polarographic analysis indicated the presence in gonyleptidine, in addition to a dimethylquinone or quinones ($E_0^{25°}$ 0.588–590 v.), of a companion quinone of lower potential, and infrared analysis indicated 2,5-dimethyl- and 2,3,5-trimethyl-1,4-quinone to be the probable companions. Hence methods of fractionation were tested on mixtures of the synthetic models. Finally 115 mg. of gonyleptidine was treated at room temperature with 2,3-dimethylbutadiene for selective conversion of 2,3-dimethyl-1,4-quinone to an adduct. When the unreacted quinones were reduced with hydrosulfite and extracted from ether with alkali, the adduct remained in the neutral fraction and was identified as such and as 2,3,6,7-tetramethyl-1,4-naphthoquinone, m.p. 167°. After reoxidation of the hydroquinones, Thiele acetoxylation of the quinone mixture and steam distillation gave a non steam-volatile residue identical with 2,5-dimethyl-1,3,4-triacetoxybenzene (m.p. 107°; mixed m.p.; infrared) derived from 2,5-dimethyl-1,4-quinone, and a steam-volatile quinone identified as 2,3,5-trimethyl-1,4-quinone by ultraviolet and infrared spectra and mixed m.p. of the hydroquinone (m.p. 170°). The amounts of components accounted for (in the order just mentioned) were 71, 11, and 15 mg. Average activities against representative microörganisms in terms of multiples of the activity of gonyleptidine are (same order): Gram positive: −4, +2, +2; Gram negative: +4, +4, +2. Although a great many quinones have been assayed for bacteriostatic activity, these simple benzoquinones have gone neglected. Actually, data to be presented elsewhere show that they are considerably more promising, with respect to potency and retention of activity *in vivo*, than any quinones previously investigated. Acids resulting from addition of thioacetic and β-thiopropionic acid to the methylbenzoquinones and oxidation to the quinones also have interesting bacteriostatic properties.

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RECEIVED JULY 18, 1955

SYNTHESIS OF PERCHLOROFULVALENE[1]

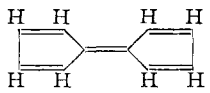
Sir:

The hydrocarbon fulvalene (I), as yet unsynthesized, has been postulated to be a stable compound possessing resonance energy amounting to about 41 kcal./mole.[2] 1,2,3,4-Tetraphenylfulvalene (II) was the first fulvalene derivative reported[3]

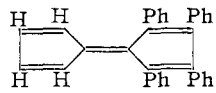
(1) The authors wish to express their appreciation to the Hooker Electrochemical Company for financial support of this investigation.

(2) R. D. Brown, *Trans. Faraday Soc.*, **46**, 146 (1950).

(3) E. C. Schreiber and E. I. Becker, THIS JOURNAL, **76**, 6125 (1954).

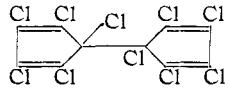


I

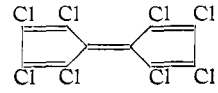


II

wherein the fulvalene nucleus was not an integral part of a fused aromatic system, as, for example, is the case in bis-(biphenylene)-ethylene.[4] However, no compound has been described wherein the fulvalene system represents the only unsaturation present. It should be noted that extensive halogen substitution generally decreases the reactivity of the diene system; for example, hexachlorobutadiene behaves much like a saturated compound.[5] We have synthesized bis-(pentachlorocyclopentadienyl), or perchloro-9,10-dihydrofulvalene, m.p. 121° (III) (λ_{max} 330 mμ, ϵ 2950), by cuprous chloride coupling of hexachlorocyclopentadiene.[6] Compound III was reduced over platinum to give bicyclopentyl, b.p. 188–190°, n^{20}D 1.4650. On being heated to 250°, III lost a mole of chlorine giving compound IV (85%), m.p. 347°. *Anal.* Calcd. for $C_{10}Cl_8$: C, 29.70; Cl, 70.30; mol. wt.,



III



IV

404. Found: C, 29.48; Cl, 70.86; mol. wt., 429 (vapor pressure depression in benzene). Ultraviolet absorption of IV (in cyclohexane) was broad and intense from 200–400 mμ, λ_{max} 267 mμ, ϵ 21,400, λ_{max} 277 mμ, ϵ 23,900, λ_{max} ~ 310 mμ (partially submerged), ϵ ~ 10,000. Hydrogenation of IV in ethanol over copper chromite gave bicyclopentyl, b.p. 60–65° (20 mm.), n^{20}D 1.4653, identical with an authentic sample prepared by sodium coupling of cyclopentyl bromide.[6] This is consistent with the behavior of III and other chlorocarbons possessing the bicyclopentyl carbon skeleton.[6] It is therefore concluded that IV is perchlorofulvalene.

We explain the absence of pronounced color in perchlorofulvalene (it is medium yellow rather than orange or red) on the grounds that steric interaction between the chlorine atoms in the 4- and 5- and the 1- and 8-positions causes rotatory distortion of the 9–10 ethylenic bond forcing the molecule into a "warped" conformation. Our calculations indicate an interference of chlorine radii of about 0.5 Å. The resultant non-planarity would disturb inter-ring resonance in much the same manner as in the *o,o,o',o'*-substituted biphenyls[7,8] and would depress lower energy light absorption (in the visible region). Riemschneider[9] has claimed the synthesis of perchlorofulvalene by zinc-acid reductive coupling of hexachlorocyclopentadiene. In view of a recent report[10] it is now apparent that the product described by Riemschneider was actually 1,2,3,4-tetrachlorocyclopentadiene, m.p. 62°.

Because of heavy halogen substitution, IV is not a highly reactive compound. In contrast to II, IV does not take part in the Diels–Alder reaction. Under forcing conditions, both III and IV add chlorine to give a rearranged product, perchloro-3a,4,7,7a-tetrahydro-4,7-methanoindene (V), m.p. 220–221°, λ_{max} 224 mμ, ϵ 15,800[6].

(4) P. Karrer, "Organic Chemistry," Fourth English Edition, Elsevier Publishing Co., New York, N. Y., 1950, p. 104.

(5) E. H. Huntress, "Organic Chlorine Compounds," John Wiley and Sons, New York, N. Y., 1948, p. 871.

(6) E. T. McBee, J. D. Idol, Jr., and C. W. Roberts, THIS JOURNAL, **77**, 4375 (1955).

(7) L. W. Pickett, G. F. Walter and H. France, *ibid.*, **58**, 2296 (1936).

(8) R. L. Shriner, R. Adams and C. S. Marvel in Gilman's "Organic Chemistry, An Advanced Treatise," Second Edition, John Wiley and Sons, New York, N. Y., 1943, Vol. I, p. 353 *et seq.*

(9) R. Riemschneider, *Z. Naturforschung*, **6B**, 463 (1951).

(10) E. T. McBee, R. K. Meyers and C. F. Baranauckas, THIS JOURNAL, **77**, 86 (1955).

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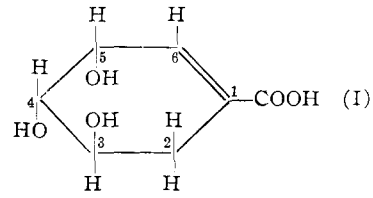
THE ENZYMATIC SYNTHESIS OF SHIKIMIC ACID FROM D-ERYTHROSE-4-PHOSPHATE AND PHOSPHOENOLPYRUVATE[1,2,3]

Sir:

Previous investigations on the biosynthesis of shikimic acid (SA) (I) from labeled glucose by



(I)

intact *Escherichia coli* have indicated that the carboxyl and carbon atoms 1 and 2 of SA are derived from a 3-carbon intermediate of glycolysis, and carbons 3, 4, 5 and 6 from the pentose-sedoheptulose pathway.[4] Furthermore, in cell-free extracts SA or its precursor, DHS, was formed from fructose-6-phosphate or FDP in a 5% yield[5,6] but from SDP almost quantitatively.[7,6] We have now found that E-4-P[8] plus PEP are rapidly and quantitatively converted to DHS (Table I). The present results also indicate that the utilization of SDP is due to its prior conversion to E-4-P and PEP (Table I).

(1) This work was supported by grants from the National Institutes of Health, U. S. Public Health Service, and the Williams–Waterman Fund.

(2) Abbreviations: SA, shikimic acid; DHS, 5-dehydroshikimic acid; E-4-P, D-erythrose-4-phosphate; PEP, phosphoenolpyruvate; SDP, sedoheptulose-1,7-diphosphate; FDP, fructose diphosphate; DHAP, dihydroxy-acetone phosphate; 3-PGA, D-3-phosphoglyceric acid; DPN, diphosphopyridine nucleotide; P_i, inorganic phosphate.

(3) For a review of the role of DHS and SA in the biosynthesis of the aromatic amino acids see B. D. Davis in "Amino Acid Metabolism" (W. D. McElroy and B. Glass, eds.), The Johns Hopkins Press, Baltimore, Md., 1955, pp. 799–811.

(4) P. R. Srinivasan, H. T. Shigeura, M. Sprecher, D. B. Sprinson, and B. D. Davis, manuscript in preparation; D. B. Sprinson, in "Amino Acid Metabolism", (W. D. McElroy and B. Glass, eds.), The Johns Hopkins Press, Baltimore, Md., 1955, pp. 817–825.

(5) E. B. Kalan, B. D. Davis, P. R. Srinivasan and D. B. Sprinson, manuscript in preparation.

(6) Certain of these results appeared in preliminary form (E. B. Kalan and P. R. Srinivasan, in "Amino Acid Metabolism" (W. D. McElroy and B. Glass, eds.), The Johns Hopkins Press, Baltimore, Md., 1955, pp. 826–830).

(7) P. R. Srinivasan, D. B. Sprinson, E. B. Kalan and B. D. Davis, manuscript in preparation.

(8) C. E. Ballou, H. O. L. Fischer, and D. L. MacDonald, THIS JOURNAL, **77**, 2658 (1955).