were sufficiently inhibitory even at 10^{-7} M to raise significantly the concentrations of calcium and phosphate required to "seed" collagen with crystals.

It may prove difficult, indeed, to identify the substance or substances present in serum which are inhibitory to the seeding of calcium phosphate crystals by collagen. In any case, the ester phosphate fraction of serum, while too small to serve as a normal substrate, in the conventional sense, is sufficiently large to contain one or several highly inhibitory polyphosphates, hydrolyzable by bone phosphatase. Thus, the present experiments provide an important new function for phosphatase in biological calcification, but do not preclude other functions yet to be established by further investigations.

DEPARTMENT OF RADIATION BIOLOGY
UNIVERSITY OF ROCHESTER HERBERT FLEISCH
SCHOOL OF MEDICINE AND DENTISTRY
ROCHESTER, NEW YORK WILLIAM F. NEUMAN

RECEIVED JUNE 17, 1960

THE CYCLOÖCTATETRAENYL DIANION

Sir:

We wish to report experimental substantiation in a simple unsubstituted carbocyclic system of the theoretical prediction of molecular orbital theory[1] that a high degree of resonance stabilization is associated with a closed shell of $(4n + 2)$ π electrons for $n = 2$.

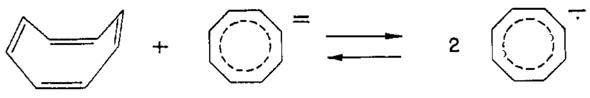
The demonstration that cycloöctatetraene is non-planar[2] has suggested that the strain imposed on the underlying molecular framework might prohibit the preparations of such a system.[2,3,4]

Extensive evidence is available which suggests that cycloöctatetraene has a large affinity for electrons and forms a stable dianion. The reaction of cycloöctatetraene in ether or liquid ammonia solution with alkali metals to form di-alkali derivatives, which on hydrolysis yield cycloöctatrienes and on carbonation yield diacids[7]; the reaction of cyclooctatetraene with sodium triphenylmethyl to form a mixture of hexaphenylethane and a di-alkali derivative which yields cycloöctatrienes on hydrolysis and a *bis*-diol on treatment with benzophenone[8]; the electrolytic reduction of cycloöctatetraene in aqueous ethanolic solution to 1,3,6-cycloöctatriene and the polarographic data which indicate the reaction to be a reversible (the Heyrovsky-Ilkovič equation is obeyed) two electron reduction[9]—all these reactions, well-known for aromatic compounds, but uncharacteristic of olefins, imply that the cycloöctatetraenyl dianion possesses unusual stability.[10]

In tetrahydrofuran solution cycloöctatetraene undergoes a very ready reaction with two moles of potassium metal, and on cooling large, almost colorless, but pale yellow and probably solvated crystals of dipotassium cycloöctatetraenide precipitate. These crystals are difficult to isolate, for on drying and exposure to air they explode. Solutions however, are stable.

The n.m.r. spectrum[12] of dipotassium and dilithium cycloöctatetraenide—a single sharp peak of expected intensity insignificantly displaced from the resonance of cycloöctatetraene itself—is not in accord with the covalent 1,4 structure which usually appears in the literature,[13] nor with rapid exchange averaging among such covalent structures, for in either case the spectrum should be shifted to higher fields than characterize the spectrum of cycloöctatetraene itself. Increased proton shielding would be expected on addition of electrons to the molecule, and in this case must be compensated, if the ring flattens, or aromatizes, by the displacement to low fields characteristics of aromatic molecules, due, at least in part, to the diamagnetic ring current induced in the applied magnetic field.[14] It is this latter representation of a flattened eight-membered ring carrying two negative charges which alone appears in accord with the spectrum.[15]

That the n.m.r. spectrum of the solvent, tetrahydrofuran, is clearly resolved when less than two moles of potassium is allowed to react with cyclooctatetraene proves that large concentrations ($> 10^{-3}$ M) of paramagnetic ions, which would



(1)

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[1] E. Hückel, "Grundzüge der Theorie ungesättigter und aromatischer Verbindungen," Verlag Chemie, Berlin, 1938.

[2] The chemistry of cycloöctatetraene has recently been reviewed: R. A. Raphael, "Non-Benzenoid Aromatic Compounds," D. Ginsburg editor, Interscience Publishers, Inc., New York, N. Y., 1959.

[3] Wilson Baker, "Perspectives in Organic Chemistry," A. Todd editor, Interscience Publishers, Inc., New York, N. Y., 1956, p. 28 ff.; K. Mislow, *J. Chem. Phys.*, **20**, 1489 (1952).

[4] Indirect solutions to related problems have been successfully devised by Sondheimer[5] and also by Allinger.[6]

[5] F. Sondheimer and R. Wolovsky, *Tetrahedron Letters*, No. **3**, 3 (1959); F. Sondheimer, R. Wolovsky and Y. Gaoni, THIS JOURNAL, **82**, 755 (1960); F. Sondheimer and R. Wolovsky, *ibid.*, **81**, 4755 (1959).

[6] N. L. Allinger and G. A. Youngdale, *Tetrahedron Letters*, No. **9**, 10 (1959).

[7] (a) W. Reppe, O. Schlichting, K. Klager and T. Toepel, *Ann.*, **560**, 1 (1948); (b) A. C. Cope and F. A. Hochstein, THIS JOURNAL, **72**, 2515 (1950).

[8] G. Wittig and D. Wittenberg, *Ann.*, **606**, 1 (1957).

[9] R. M. Elofson, *Anal. Chem.*, **21**, 917 (1949); J. H. Glover and H. W. Hodgson, *Analyst*, **77**, 473 (1952); L. E. Craig, R. M. Elofson and I. J. Ressa, THIS JOURNAL, **75**, 480 (1953).

[10] The ready equilibria between metallic derivatives of cyclooctatrienes and cycloöctatetraenes[11] are also reminiscent of hydroquinone-quinone systems. The facile base-catalyzed isomerization of 1,3,6-cycloöctatriene[7b] might also have a common origin with the above reactions.

[11] A. C. Cope and M. R. Kinter, *ibid.*, **73**, 3424(1951); A. C. Cope and H. O. van Orden, *ibid.*, **74**, 175 (1952).

[12] Accompanying communication, T. J. Katz, *ibid.*, **82**, 3785 (1960).

[13] W. Reppe, O. Schlichting, K. Klager and T. Toepel, *Ann.*, **560**, 1 (1948); R. A. Raphael, "Chemistry of Carbon Compounds," E. H. Rodd, editor, Elsevier Publishing Company, New York, N. Y., 1953, Vol. IIA, p. 261; E. E. Royals, "Advanced Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1954, p. 545.

[14] J. A. Pople, W. G. Schneider and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Company, Inc., New York, N. Y., 1959, pp. 180–183, 247 ff.

[15] In this connection, the known spectra of the cyclopentadienyl anion,[16] the tropylium ion,[16] and allylmagnesium bromide[17] offer pertinent orientational references.

[16] J. R. Leto, F. A. Cotton and J. S. Waugh, *Nature*, **180**, 978 (1957).

[17] J. E. Nordlander and J. D. Roberts, THIS JOURNAL, **81**, 1769 (1959).

obliterate the spectrum completely, are not present. Thus, the equilibrium must lie to the left.

The analogous equilibria in derivatives of polynuclear aromatic hydrocarbons have always been found to lie to the right.[18] The reversal of this equilibrium in the cycloöctatetraene system must be attributed to geometrical considerations: On the right of reaction (1) two molecules are flat, while on the left only one is so. That the electron affinity of the monoanion exceeds that of the hydrocarbon implies that the energy required to flatten the molecule when the first electron enters exceeds the extra coulombic energy the second must overcome. This conclusion, which will be discussed in detail in the future, has also been derived from two other independent experimental sources: (1) polarographic data, the reversible one-step two-electron reduction of cycloöctatetraene contrasting with the two-step one-electron reductions of polynuclear aromatic hydrocarbons in aprotic solvents[18,19,20]; and (2) electron spin resonance data, the cycloöctatetraenyl anion-radical[21] being directly observable.

The above and other data[12,21] make clear that the eight-membered ring with ten π electrons unlike the parent hydrocarbon must be highly resonance stabilized and flat, either due to the increased delocalization energy to be gained by aromatization in the new reference frame or to the relief of an unfortunate effect associated in a hypothetically planar symmetric cycloöctatetraene molecule with a formal partial occupancy of a degenerate pair of non-bonding molecular orbitals.[22]

[18] G. J. Hoijtink, E. De Boer, P. H. van der Meij and W. P. Weijland, *Rec. trav. chim.*, **75**, 487 (1956); N. S. Hush and J. Blackledge, *J. Chem. Phys.*, **23**, 514 (1955).

[19] S. Wawzonek, E. W. Blaha, R. Berkey and M. E. Runner, *J. Electrochem. Soc.*, **102**, 235–242 (1955); A. C. Aten, C. Büthker and G. J. Hoijtink, *Trans. Faraday Soc.*, **55**, 324 (1959); P. H. Given, *J. Chem. Soc.*, 2684 (1958).

[20] Preliminary experiments (with Mr. William Bahary) in this laboratory have confirmed the reversibility of the reduction in aqueous media by use of a.c. methods, while polarographic experiments in anhydrous acetonitrile indicate that protonation is not involved.

[21] T. J. Katz and H. L. Strauss, *J. Chem. Phys.*, **32**, 1893 (1960).

[22] H. C. Longuet-Higgins, "Theoretical Organic Chemistry. Papers presented to the Kekule Symposium organized by the Chemical Society, London, 1958," Butterworths Scientific Publications, London, 1959, p. 9 ff.; D. P. Craig, Chapt. I in ref. 2.

DEPARTMENT OF CHEMISTRY
COLUMBIA UNIVERSITY
NEW YORK 27, NEW YORK
THOMAS J. KATZ

RECEIVED JUNE 6, 1960

THE CHEMICAL INTERACTION OF THE CYCLOOCTATETRAENYL ANIONS

Sir:

Experiments employing high resolution n.m.r. methods have uncovered a number of significant aspects of the chemistry of the cycloöctatetraenyl anions: the divalent anion[1] and the anion radical.[2]

In tetrahydrofuran solution 0.6 molar in cyclooctatetraene the resonance due to the eight cyclooctatetraene hydrogen nuclei appears as a single sharp peak 125.35 cps. to lower applied field than the lowest of the two solvent bands. As increasingly larger amounts of potassium metal are allowed to dissolve in this solution, the observations summarized in Fig. 1 are made: thus, (1) the sharp resonance line of cycloöctatetraene is seen to decrease in intensity without concomitant broadening; (2) when the peak has decreased to less than about 10% of its initial intensity a very broad band becomes superimposed directly on the initial peak, which itself remains sharp; (3) the initial sharp peak disappears as the broad peak narrows; and (4) finally, this latter peak narrows to a single sharp line of identical intensity to the resonance of the original cycloöctatetraene. In the course of these events, exactly two moles of potassium are observed to dissolve, and if more potassium is initially present, this excess remains at the end.

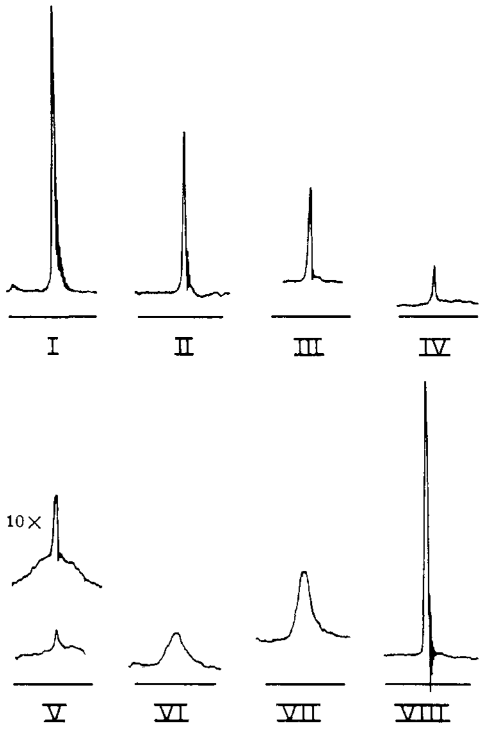

Fig. 1.—Cycloöctatetraene (0.6 formal, in THF) treated with increasing amounts of potassium, from I, no K to VIII, two moles; chemical shifts (from lower solvent band), half-width, and relative areas integrated over a 30-cycle range follow: I, 125.32 cps., <1 cps., 1.0; II, 126.50, <1 cps., 0.7; III, 127.20, <1 cps., 0.5; IV, 127.69; ?, ?; V, 127.94, ~ 18, 0.6; VI, 124.90, 8, 0.7; VII, 125.06, 4, 1.0; VIII, 125.00, <1, 1.0. Spectra were determined on a Varian 60 mc. high resolution n.m.r. spectrometer equipped with superstabilizer.

The resonance spectrum of the solvent remains throughout unchanged and exceedingly well resolved: The two tetrahydrofuran proton resonances are observed as complex spin-spin multiplets of over a dozen peaks each. Although the concentration of paramagnetic species must, therefore, be small ($< 10^{-3}$ M), the presence of the cyclooctatetraenyl anion-radical in low concentrations (2.6×10^{-5} M at half-reaction[3]) has been demon-

[1] T. J. Katz, THIS JOURNAL, **82**, 3784 (1960).

[2] T. J. Katz and H. L. Strauss, *J. Chem. Phys.*, **32**, 1893 (1960).

[3] T. J. Katz and H. L. Strauss, unpublished results.