unit tangent to be $-\mathbf{i}\, b \sin\theta + \mathbf{j}\, b\cos\theta + \mathbf{k}\, a/(a^2 + b^2)^{1/2}$. The trigonometric functions in $g^{(0)}$ combine so that the resulting expression is a function of $\theta_{ik} \equiv \theta_k - \theta_i$ only

$$g^{(0)} = \frac{-\alpha^2\beta^2\gamma}{6a^2(1+\gamma^2)^2} \sum_{i>k=1}^{6} f(\theta_{ik}) \qquad (4)$$

where $\gamma \equiv b/a$ and

$$f(x) = \frac{2(1-\cos x) + \gamma^2 x \sin x}{[2(1-\cos x) + \gamma^2 x^2]^{3/2}} \left[1 + \gamma^2\cos x - \frac{3\gamma^2(x - \sin x)^2}{2(1-\cos x) + \gamma^2 x^2}\right] \qquad (5)$$

If a bond length of 1.40 Å. is used, the radius a is 2.42 Å. Lacking an X-ray analysis, we estimated the value of b by assuming the distance between the nearest pair of non-bonded carbon atoms at the ends of the helix to be 3.80 Å., which is the packing distance between neighboring molecules in benzene crystals.[3]

The calculated results are $g^{(0)} = -1.46 \times 10^{-32}$ and $[\alpha]_D = -3010°$. The close agreement between the calculated and experimental rotations demonstrates the applicability of the polarizability theory to compounds which owe their asymmetry to steric interference. The agreement in sign indicates that the molecules of the compound isolated[1] have a left-handed helical configuration.

(3) E. G. Cox, *Proc. Roy. Soc.* (*London*), **A135**, 491 (1932).

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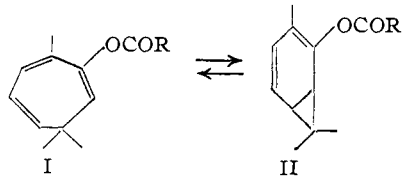
DISTINCTION BETWEEN CYCLOHEPTATRIENE AND BICYCLOHEPTADIENE STRUCTURES BY NUCLEAR MAGNETIC RESONANCE

Sir:

The finding that certain substitution reactions of eucarvone also involve bridging across the ring to form bicyclo[4.1.0]heptene (carene) derivatives[1] prompted us to investigate the possibility that eucarvone enol, eucarvone enolate ion and related structures which are subject to cycloheptatriene ⇄ bicycloheptadiene equilibria may be more stable as the bicyclic than as the monocyclic valence tautomers. This Communication describes the application of nuclear magnetic resonance (NMR) to this hitherto unsolved problem. A complete account of the work together with its bearing on the mechanism of bridging reactions of eucarvone will be presented later.

A number of the enol esters of eucarvone which might have either mono- or bicyclic structures (I or II) were prepared (as models of eucarvone enol) by acylation of sodioeucarvone, *e.g.* the enol



I II

acetate, b.p. 64–66° (1 mm.), $n^{20}D$ 1.4942, λ_{max} 273, 207 mμ (log ε 3.42, 4.09), ν_{max} 1762, 1685, 1649 cm.$^{-1}$. Found: C, 75.10; H, 8.42. These were found to be homogeneous and not subject to a valence tautomeric change upon heating. The NMR spectrum[2] of the enol acetate shows that it is a cycloheptatriene rather than a caradiene type. The ethylenic hydrogen absorption (at A) is well separated from the hydrogen absorption due to CH_3—C(=X)— (at B) and this, in turn, from the *gem*-dimethyl hydrogen absorption (at C).[3] There is no absorption in the place expected for two tertiary bridge hydrogens of a caradiene structure (see below). Furthermore, the ratio of the integrated absorption area for the hydrogens in the *gem*-dimethyl groups (obtained by integration under the curve at C) to that for the ethylenic hydrogens (area under curve at A) is 1.55 in agreement with the cycloheptatriene (calcd. 1.50), but not with the caradiene structure (calcd. 3.0).

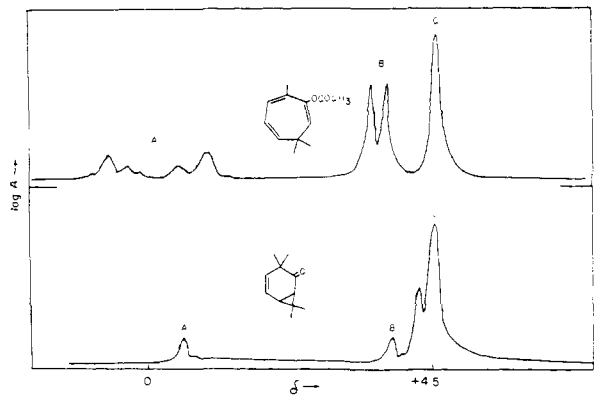


Fig. 1.—A = electromagnetic absorption; δ = change, relative to water as the standard, in magnetic field necessary for hydrogen absorption × $(10)^6$ = structural shift for hydrogen relative to water.

In view of the NMR results which are unambiguous, some of the chemical evidence regarding the structures of the enol esters must be recognized as misleading. Thus, *the enol esters in each case afford upon ozonolysis* (*−70°*) *over 50% yield of cis-caronic acid* which fact, in itself, argues for the caradiene structure. The production of *cis*-caronic acid from a cycloheptatriene structure is unusual, but certainly within the realm of possibility.[4]

The NMR spectrum of Δ²-4-methylcaren-5-one (III),[5] which is formed by methylation of sodioeucarvone, b.p. 70° (5 mm.), $n^{20}D$ 1.4809, λ_{max} 206, 300 mμ (log ε 3.71, 2.89); ν_{max} 1698, 1665, 1007 cm.$^{-1}$. Found: C, 80.34; H, 9.95, shows the absorption of two tertiary bridge hydrogens (at B) well resolved from the methyl hydrogen absorption

(1) E. J. Corey and H. J. Burke, THIS JOURNAL, **76**, 5257 (1954).

(2) All NMR spectra measured by Dr. J. N. Shoolery and staff of Varian Associates, Palo Alto, California on the commercial Varian instrument. We are grateful to Dr. Shoolery and also to Dr. H. S. Gutowsky for their interest in this problem.

(3) See L. H. Meyer, A. Saika and H. S. Gutowsky, *ibid.*, **75**, 4567 (1953).

(4) E. H. Farmer and C. K. Ingold, *J. Chem. Soc.*, **117**, 1362 (1920), have observed the formation of small amounts of caronic acid by oxidation of what is now known to be 4,4-dimethyl-3-carboxy-Δ²-cyclopenten-1-one [N. J. Toivonen, *Chem. Zentr.*, **98**, II, 1248 (1927)].

(5) This structure has been established *inter alia* by ozonolysis to *cis*-caronic acid.

(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).