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COENZYME Q. I. STRUCTURE STUDIES ON THE COENZYME Q GROUP

Sir:

The discovery of a quinone, Q-275, has been reported,¹ and characterizing chemical and physical properties, oxidative degradation and hydrogenation are reported in an accompanying com-munication.² Four closely related quinones having similar coenzymatic activity have been isolated from microbial sources.² All five new quinones are designated as members of a coenzyme Q group, *i.e.*, coenzyme Q_6 , Q_7 , Q_8 , Q_9 and Q_{10} .

We now have extended these observations. Formula I agrees with our structural data for coenzyme Q₁₀ (beef heart) and II and III correspond to Q_9 , Q_8 , etc.

$$\begin{array}{c} CH_{3}O\\CH_{3}O\\CH_{3}O\\O\end{array} \begin{array}{c} CH_{3}CH_{3}\\CH_{2}CH_{2}CH=C-CH_{2})_{n}H \end{array} \begin{array}{c} I, n=10\\II, n=9\\III. n=8, \text{ etc.} \end{array}$$

Our isolated Q_{10} (yellow) melted at 49.5–50.5°. Found: C, 81.98, 82.05; H, 10.38, 10.31. Hydrogenation of Q10 resulted in an absorption of about 11 moles of hydrogen. Oxidation of the resulting hydroquinone yielded eicosahydro-coen-zyme Q_{10} ; $\lambda_{\text{max}}^{\text{isocetans}}$ 278 m μ , $E_{1\,\text{em}}^{1\%}$ 187. Found: C, 80.30; H, 12.36.

Proton type	C.p.s. <i>ª</i>	Rela- tive band areas	No. of protons based on 2CH:O/ mole	No. of protons caled, for Cs9H90- O4 and struc- ture I
HC=	+8	5	10	10
CH₃O—	-34	3	6	6
=CCH:CH=	-64, -69	1	2	2
$\int = C - C \underline{H}_2 - C \underline{H}_2 - C =$	-113	20	40	∫36
CH₁C=(nucleus)				3
CH ₂ C=(chain)	-125	16.5	33	33
			91	90

" The bands refer to 40 mc. spectra in carbon tetrachloride, + means at lower fields than water protons while - means at higher fields.

Coenzyme Q₁₀ appears to be a 2,3-dimethoxybenzoquinone derivative. Its absorption spectrum with maxima at 275 m μ and 405 m μ is in good agreement with that of aurantiogliocladin, (maxima at 275 and 407 m μ) identified as 2,3-dimethoxy-5,6dimethylbenzoquinone³.

We have studied the nuclear magnetic resonance spectra at 40 mc. of Q_{10} and many synthetic model compounds, and Dr. James N. Shoolery (Varian Associates) has kindly determined the spectrum of Q₁₀ at 60 me. These data characterize the protons of Q_{10} : these data show convincingly that Q_{10} has two CH_3O —, one CH_3 — and one isoprenoid chain of 10 units attached to a benzoquinone nucleus, but do not define the position of the ring substituents. N.m.r. data exclude the presence of

aromatic proton, $-\dot{C}=C\underline{H}_2$ and $-C\underline{H}_2C\underline{H}_3$, and assign the ten double bonds in the isoprenoid side chain as in I. The n.m.r. spectrum of eicosahydrocoenzyme Q_{16} shows the one =CCH₃ nucleus group at -111.5 c.p.s. While this group is not clearly resolved from $=C-CH_2CH_2C=$ in the spectrum of Q_{10} at 40 mc., it is at 60 mc.

Reduction and methylation of Q10 with dimethyl sulfate, gave a colorless crystalline tetramethoxy derivative (IV), m.p. 38-39°, $[\alpha]$ D 0° (chloroform). Found: C, 81.85; H, 10.82, OCH₃, 14.2.

Oxidation of IV with about a 4-fold excess of aqueous alkaline permanganate at 100° yielded tetramethoxyphthalic anhydride (V) (after sub-limation), m.p. 138-139° not depressed by admixture of synthetic tetramethoxyphthalic anhydride.



Oxidation of IV in acetone with the stoichiometric quantity of permanganate for ten double bonds gave after partition chromatography, 2methyl-3,4,5,6-tetramethoxyphenylacetic acid (VI) m.p. 75-76°, identical by melting point behavior and infrared spectra with a synthetic sample. The presence of levulinic and succinic acids as oxidation products was confirmed.²

The chemical and physical properties of synthetic 2,3-dimethoxy-5-methyl-6-farnesylbenzoquinone⁴ and analogs⁴ are closely similar to those of Q10. Ubiquinone, reported by Morton, et al., from animal organs (m.p. range $33-41^{\circ}$)⁵ and yeast (yellow oily fractions)⁶ is clearly related to the coenzyme Q group.

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