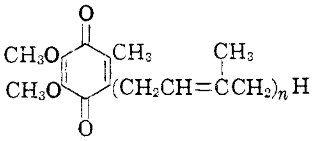
COENZYME Q. II. SYNTHESIS OF 6-FARNESYL- AND 6-PHYTYL-DERIVATIVES OF 2,3-DIMETHOXY-5-METHYLBENZOQUINONE AND RELATED ANALOGS

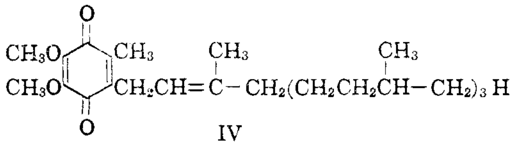
Sir:

Evidence[1,2] was obtained that coenzyme Q is characterized as a group of 2,3-dimethoxy-5-methylbenzoquinones, substituted with homologous isoprenoid chains. A series of such benzoquinones containing isoprenoid substituents in the 6-position was synthesized for comparisons with the coenzyme Q group.

2,3-Dimethoxy-5-methylbenzoquinone[3] was reduced with sulfur dioxide to 2,3-dimethoxy-5-methylhydroquinone, m.p. 77-78°, (*Anal.* Calcd, for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.80; H, 6.71). Reaction of this compound with farnesol and various condensing agents yielded 2,3-dimethoxy-5-methyl-6-farnesylhydroquinone which was oxidized to 2,3-dimethoxy-5-methyl-6-farnesylbenzoquinone, I, red liquid; $\lambda_{\max.}^{\text{isooctane}}$ 272 mμ; ($E_{1\,\text{cm}}^{1\%}$, 328); (*Anal.* Calcd. for $C_{24}H_{34}O_4$: C, 74.57; H, 8.87. Found: C, 74.68; H, 8.87). I also was obtained when the isomeric tertiary alcohol, nerolidol, was substituted for farnesol.



I, $n=3$
II, $n=2$
III, $n=1$



IV

2,3-Dimethoxy-5-methyl-6-geranylbenzoquinone (II)$\lambda_{\max.}^{\text{isooctane}}$ 272 mμ ($E_{1\,\text{cm}}^{1\%}$, 440); (*Anal.* Calcd. for $C_{19}H_{26}O_4$: C, 71.67, H, 8.23. Found: C, 72.08; H, 8.00), and 2,3-dimethoxy-5-methyl-6-(3′-methyl-2′-butenyl)-benzoquinone (III)$\lambda_{\max}^{\text{isooctane}}$ 270 mμ ($E_{1\,\text{cm}}^{1\%}$, 539); (*Anal.* Calcd. for $C_{14}H_{18}O_4$: C, 67.18; H, 7.26. Found: C, 67.64, H, 7.01) were obtained, respectively, when geraniol and 3-methyl-2-buten-1-ol were substituted for farnesol in the condensation reaction. When phytol was used for the alcohol, 2,3-dimethoxy-5-methyl-6-phytylbenzoquinone (IV) was obtained; $\lambda_{\max.}^{\text{isooctane}}$ 272 mμ ($E_{1\,\text{cm}}^{1\%}$,-291) (*Anal.* Calcd for $C_{29}H_{48}O_4$: C, 75.60; H, 10.50. Found: C, 76.31; H, 10.60).

Nuclear magnetic resonance spectra of benzoquinones I and II were consistent with the structures assigned and show a broad resonance region,[4] as expected, with center at +8 c.p.s. ($-C\underline{H}=$), resonance at −34 c.p.s. ($=\overset{|}{C}-OC\underline{H}_3$), a doublet at −63 and −70 c.p.s. ($=\overset{|}{C}-C\underline{H}_2-CH=$), resonance at −113 c.p.s. ($=\overset{|}{C}-C\underline{H}_2C\underline{H}_2CH=$ and ring $=\overset{|}{C}-C\underline{H}_3$, which were not resolved in the spectrum at 40 mc.), and resonance at −125 c.p.s. (chain $=\underset{\underset{C\underline{H}_3}{|}}{C}-$). Benzoquinone III showed similar bands with the exception that the band at −113 c.p.s. was due entirely to ring $=\overset{|}{C}-C\underline{H}_3$. The phytyl analog, IV, showed the above bands and an additional doublet at −154 and −159 c.p.s. due to paraffinic protons. The nuclear magnetic resonance spectra for the coenzyme Q group are fully compatible with those of the synthetic compounds.

The infrared spectra in carbon disulfide of compounds I-IV showed bands at 6.03, 6.18 and 7.9 μ characteristic of 2,3-dimethoxybenzoquinone functionality.

Dr. Frederick L. Crane of the Institute for Enzyme Research of the University of Wisconsin and Dr. David Hendlin of our laboratories have found compounds I, II, and IV above active in replacing coenzyme Q_{10} in the isoöctane-extracted ETP succinoxidase system.[5] Details on the enzymatic activities of these compounds will be published shortly.

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[1] R. L. Lester, F. L. Crane and Y. Hatefi, THIS JOURNAL, **80**, 7451 (1958).

[2] D. E. Wolf, C. H. Hoffman, N. R. Trenner, B. H. Arison, C. H. Shunk, B. O. Linn, J. F. McPherson and K. Folkers, *ibid.*, **80**, 7452 (1958).

[3] W. K. Anslow, J. N. Ashley and H. Raistrick, *J. Chem. Soc.*, 439 (1938).

[4] The bands refer to 40 mc. spectra in carbon tetrachloride. + means at lower fields than water protons while − means at higher fields.

[5] F. L. Crane, Y. Hatefi, R. L. Lester and C. Widmer, *Biochim. Biophys. Acta*, **25**, 220 (1957).

BOOK REVIEWS

Chemistry of the Rare Radioelements. Polonium–Actinium. By K. W. BAGNALL, B.Sc., Ph.D., Atomic Energy Research Establishment, Harwell, Eng. Academic Press Inc., Publishers, 111 Fifth Avenue, New York 3, N. Y. 1957. x + 177 pp. 22 × 14.5 cm. Price, $5.00.

Here is a valuable book on a group of six radioelements, Po, At, Fr, Ra and Ac, atomic numbers 84–89. Few chemists, except those in government institutions, have had the opportunity to investigate the properties of all of these radioelements, especially in weighable amounts. Dr. Bagnall is very well informed, in the chemistry and handling of such elements and has made many important contributions to the chemistry of polonium to which about half the space of the book is devoted. He has written "... with the object of collecting all the published data ... and to give some account of the methods used for the study of their chemistry." While the former aim is somewhat unrealized, the author has, on the whole, accomplished his mission successfully.