COENZYME Q. XXII. CHROMENOLS CORRESPONDING TO COENZYME Q_{10} AND HEXAHYDROCOENZYME Q_{10}

By C. H. Shunk, F. R. Koniuszy, E. L. Wong, N. R. Trenner
B. H. Arison and K. Folkers

Merck Sharp & Dohme Research Laboratories
Rahway, New Jersey

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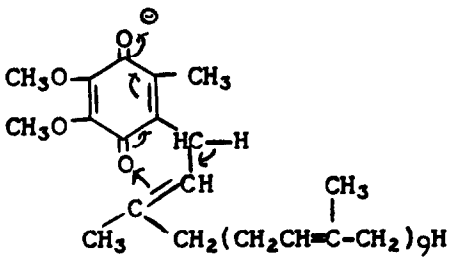
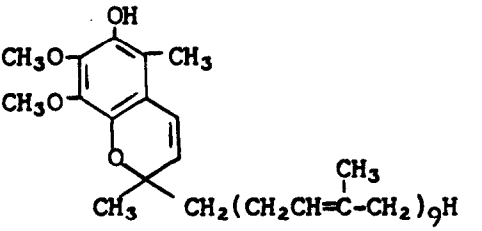
The conversion of ubiquinone-50 (coenzyme Q_{10}) (I) to ubichromenol (II) over alumina and elution with acetone - 10% aqueous hydrochloric acid has been reported (Links, 1960).



I



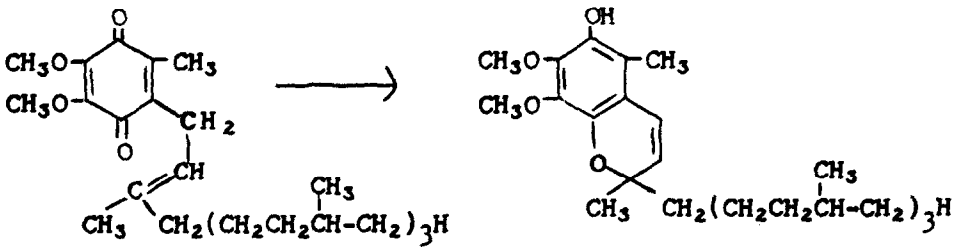
II

Experiments (Green, Edwin, Diplock and McHale, 1960) to repeat this conversion gave no ubichromenol by solvent elution, but perhaps a little on acidic elution; these authors expressed doubt of the intactness of the isoprenoid side chain of their eluted chromenol, and believed that chromenol formation took place only during the acidic elution.

We have confirmed Links' conversion, in principle, and have converted coenzyme Q_{10} (I) into ubichromenol (II) by adsorption on alumina (alkaline) and elution with methanol-ether, i.e.,

without an acidified eluting system. Our sample of ubichromenol exhibited an N.M.R. spectrum which was compatible with the isoprenoid-side chain structure II.

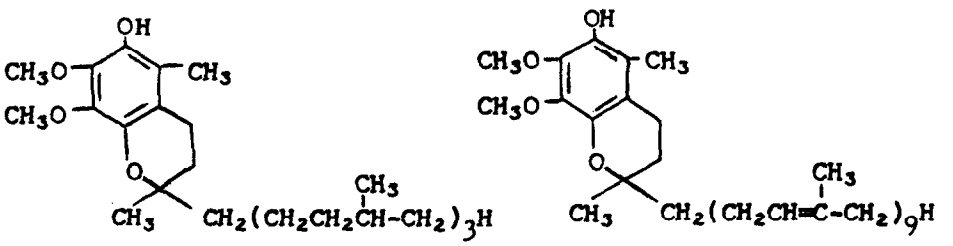
Further, we have passed hexahydrocoenzyme Q_4 (III) over alumina by the same procedure and obtained the corresponding



III IV

chromenol, 7,8-dimethoxy-2,5-dimethyl-2-(4',8',12'-trimethyl-tridecyl)-6-chromenol (IV).

The preparation of the chromanol (V), 7,8-dimethoxy-2,5-dimethyl-2-(4',8',12'-trimethyltridecyl)-6-chromanol, from hexahydrocoenzyme Q_4 (III) has been described (Shunk et al., 1960), and the conversion of coenzyme Q_{10} (I) into the corresponding ubichromanol (VI) has been reported (Hoffman et al., 1960).



V VI

The chromanol V from hexahydrocoenzyme Q_4 was not converted into the corresponding chromenol IV by adsorption on alumina under the conditions of conversion of III to IV.

Hydrogenation of the chromenol (IV) yielded the corresponding chromanol (V) as determined by ultraviolet absorption.

The natural occurrence of ubichromenol (II) (Laidman et al., 1960) has been questioned (Links, 1960; Draper and Csallany, 1960), but its optical activity (Morton, 1960) supports the concept of natural occurrence. The corresponding ubichromanol (VI) has not been established in natural sources.

EXPERIMENTAL

7,8-Dimethoxy-2,5-dimethyl-2-(4',8',12'-trimethyl-tridecyl 6-chromenol (IV). 2,3-Dimethoxy-5-methyl-6-phytylbenzoquinone (hexahydrocoenzyme Q_4, 380 mg.) was dissolved in isooctane and adsorbed on 40 g. of alkaline aluminum oxide (Merck No. 7107, slurry 10:100, pH 10.0-10.5). Development with isooctane, then isooctane-diethyl (1-1) spread the brown color over about one-half of the column. After 20 hrs., the column was washed with 500 ml. of ether-isooctane (1-1), then by 200 ml. of ether. The product was eluted with ether-methanol (1-1). The colored band, collected in a 5 ml.-fraction, yielded 109 mg. of product, $\lambda_{max.}^{isooctane}$ 275 mμ ($E_{1\ cm.}^{1\%}$ 161).

A second run with 400 mg. of hexahydrocoenzyme Q_4 on 40 g. of alkaline aluminum oxide (developed with isooctane-ether (9-1) for 3 hrs., isooctane ether (1-1) for 1 hr., and eluted with methano ether (1-1) to give the colored band in a 10 ml.-fraction) yielded 140 mg. of product; $\lambda_{max.}^{isooctane}$ 275 mμ ($E_{1\ cm.}^{1\%}$ 163).

The combined fractions were chromatographed on 20 g. of Florisil. Elution with 2% ether in isooctane, followed by ultraviolet absorption, yielded the desired product in ca. 300 ml. of eluant. This eluate yielded 120 mg. of 7,8-dimethoxy-2,5-dimethyl-2-(4'8'12'-trimethyltridecyl)-6-chromenol (IV) as an oil. This was evaporatively distilled at ca. 170°/0.01 mm; Anal. Calcd. for $C_{29}H_{48}O_4$; C, 75.60; H, 10.50. Found: C, 74.99; H, 10.21;

$\lambda_{max.}^{isooctane}$ 233 mμ ($E_{1\ cm.}^{1\%}$ 420), 274 mμ ($E_{1\ cm.}^{1\%}$ 177), 282 mμ ($E_{1\ cm.}^{1\%}$ 169), and 331 mμ ($E_{1\ cm.}^{1\%}$ 70). Proton magnetic resonance, as previously determined (Erickson et al., 1959) is consistent with structure IV; shielding numbers (tau) and assignments: 3.51, 3.68, 4.50, 4.67 (ring CH=), 6.13, 6.25 (2 different CH_3O-), 7.98 (ring CH_3C=), 8.75 (CH_3C-O-), 8.88 (CH_2), and 9.21 doublet (CH_3CH-).

Reduction of the chromenol (3.2 mg.) in acetic acid over platinum catalyst with one equivalent of hydrogen yielded the chromanol V (Shunk et al., 1960), based on its ultraviolet absorption spectrum $\lambda_{max.}^{isooctane}$ 292 mμ.

To determine if the chromanol (V) is an intermediate in the conversion of the quinone (III) to the chromenol (IV), a sample (50 mg.) of V was adsorbed on aluminum oxide. After 20 hrs., the material was eluted as above yielding the starting chromanol; $\lambda_{max.}^{isooctane}$ 293 mμ ($E_{1\ cm.}^{1\%}$ 79).

Ubichromenol from Coenzyme Q_{10}. Coenzyme Q_{10} (1.0 g.) was dissolved in 100 ml. of petroleum ether and adsorbed on ca. 100 g. of alkaline aluminum oxide. The column was developed with 300 ml. of ether and, after 18 hrs., eluted as for the phytyl analog. The material (464 mg.) from the ether-methanol eluate was chromatographed on ca. 100 g. of Florisil, and eluted with successive portions of petroleum ether (2 l.), ethyl ether (2 l.) and methanol-ether (1-1, 200 ml.). The methanol-ether eluate yielded 128 mg. of ubichromenol. Paper chromatography of it using vaseline-coated paper developed with 5% water - 95% dimethylformamide, showed only one spot (Emmerie-Engel test); R_f 0.48, identical with a sample of ubichromenol which was kindly furnished by Prof. Morton. Proton magnetic resonance (determined as above) is consistent with structure II; shielding numbers and assignments: 3.50, 3.67, 4.47, 4.64 (ring CH=), 4.95 (side chain CH=), 6.10, 6.22 (2 different CH_3O-), 7.90 (ring CH_3-C=) 8.03 (=C-CH_2CH_2-C=), 8.44 (side chain CH_3C=), and 8.69 (CH_3C-O-).

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