form equivalent experiments with chymotrypsin. The results of these experiments are shown in Table I. Again the sum of the oxidation constants for the accessible histidine and accessible methionine is approximately equal to the observed rate constant of 0.67 min.$^{-1}$ for loss of enzyme activity. These data therefore provide presumptive evidence for analogous involvement of both the histidine and methionine in these two enzymes and hence support the hypothesis[3] that the bond changing or "catalytic" amino acids may be similar in enzymes of widely diverse specificity.

TABLE I

RATE CONSTANTS FOR PHOTOOXIDATION OF CHYMOTRYPSIN

Property assayed	k (min.$^{-1}$)
Enzyme activity[a]	0.67
Accessible histidine	.32
Accessible methionine	.36
Inaccessible histidine	.022
Inaccessible methionine	.037
Tyrosine	.01
Tryptophan	.013

[a] Assayed by rate of hydrolysis of acetyltyrosine ethyl ester.

The inference that the thioether group of a methionyl residue is involved in enzyme catalysis is of particular interest since this group has no significant acidic or basic properties in aqueous solutions, but it is a powerful neighboring group as indicated by the reactivity of mustard gas.[5]

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(5) *Cf.* J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1956.

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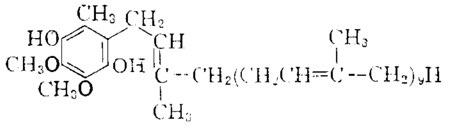
RECEIVED JULY 8, 1960

COENZYME Q. XXI. CONVERSION OF COENZYME Q_{10} INTO THE CORRESPONDING CHROMANOL

Sir:

The reduction of coenzyme Q_{10} to the hydroquinone (1) with subsequent refluxing in acetic acid containing potassium bisulfate has yielded a product which has the properties of the corresponding chromanol II or 7,8-dimethoxy-2,5-dimethyl-2-[3′-methyl-2′-butenyl-oktakis-(3′-methyl-2′-butenylene)methyl]-6-chromanol.



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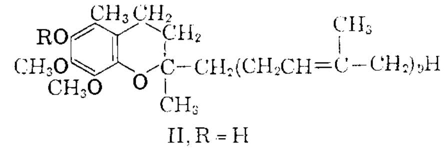

II, R = H
III, R = CH₃CO

Studies on the preparation of this compound, also called ubichromanol, have been summarized,[1,2] but the solutions were examined only by paper chromatography and ultraviolet spectral measurements; we repeated these experiments,[1,3] but were unable to obtain the chromanol. Other reaction conditions successfully converted hexahydrocoenzyme Q_4 to 7,8-dimethoxy-2,5-dimethyl-2-(4′,8′,12′-trimethyltridecyl)-6-chromanol[4]; such conditions with coenzyme Q_{10} apparently gave chromanol formation with concurrent cyclizations of the 10-unit isoprenoid side chain. The product[4] lacked detectable unsaturated isoprenoid units by n.m.r. data. Others[5] attempting to prepare ubichromanol reported materials with unexpected properties, possibly due to side chain cyclization.

A solution of coenzyme Q_{10} hydroquinone in acetic acid containing potassium bisulfate was refluxed one hour and then concentrated. A solution of the residue in Skellysolve B was water-washed and chromatographed on Florisil. Fractions eluted with ether–isoöctane yielded the chromanol II which could also be purified by distillation *in vacuo*. The 60 megacycle n.m.r. spectrum of the oily product in carbon tetrachloride is the most critical criterion of its identity; tau (τ) 4.84 (-OH); 4.96 (HC=); 6.12 and 6.25 (CH_3O—); 7.50 triplet (—CH_2C=); 7.98 (CH_3C= ring); 8.02 (=$C(CH_2)_2C$=); 8.40 (CH_3C=); 8.73 (CH_3—C—O). This spectrum excluded a coumaran nucleus.[6] Ultraviolet spectrum: λ_{max} 292 mμ, $E^{1\%}_{1\,cm.}$ = 38; infrared spectrum, band at 2.85 μ (—OH), no band for C=O in the 6 μ region and a band at 9 μ.

Anal. Calcd. for $C_{59}H_{92}O_4$: C, 81.89; H, 10.72. Found: C, 82.11; H, 10.50.

The Q_{10} hydroquinone (I) and the chromanol II are not clearly distinguishable by ultraviolet maxima alone in mixtures, and by infrared data, but are differentiated by R_f and n.m.r. comparisons.

The chromanol II in pyridine was treated with acetic anhydride. Subsequent purification by adsorption on silica gel from isoöctane solution and elution by ether in isoöctane gave a chromatographically homogeneous band; λ_{max} 282 mμ, $E^{1\%}_{1\,cm.}$ = 26 in isoöctane. The n.m.r. spectrum is consistent with the chromane acetate structure III.

Anal. Calcd. for $C_{61}H_{94}O_5$: C, 80.75; H, 10.44. Found: C, 80.79; H, 10.24.

Drs. David Green and Robert Lester[7] have tested the chromanol II and reported it to have no coenzymatic activity *in vitro* like that of Q_{10} for electron transfer.

This chromanol II is of current interest[8-10]

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(1) J. Bouman, E. C. Slater, H. Rudney and J. Links, *Biochim. Biophys. Acta*, **29**, 456 (1958).

(2) J. Links, *ibid.*, **38**, 193 (1960).

(3) J. Bouman and E. C. Slater, *ibid.*, **26**, 624 (1957).

(4) C. H. Shunk, N. R. Trenner, C. H. Hoffman, D. E. Wolf and K. Folkers, *Biochem. Biophys. Res. Com.*, **2**, 427 (1960).

(5) D. A. Laidman, R. A. Morton, J. Y. F. Paterson and J. F. Pennock, *Biochem. J.*, **74**, 541 (1960).

(6) I. Cmielewska, *Biochim. Biophys. Acta*, **39**, 170 (1960).

(7) Enzyme Institute, University of Wisconsin.

(8) R. D. Dallam and J. F. Taylor, *Fed. Proc.*, **18**, 210 (1959).

(9) P. J. Russell and A. F. Brodie, *ibid.*, **19**, 38 (1960).

(10) E. E. Jacobs and F. L. Crane, *Biochem. Biophys. Res. Com.*, **2**, 218 (1960).

concerning a possible role for Q_{10} in oxidative phosphorylation mechanisms; also, concerning analyses for vitamin E, since the chromanol II is a methoxy analog of vitamin E. However, the natural occurrence of the chromanol II has not yet been established.

CONTRIBUTION FROM THE
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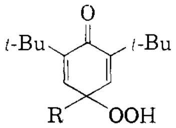
RECEIVED JULY 11, 1960

OXIDATION OF HINDERED PHENOLS TO SEMIQUINONES

Sir:

The reactions between oxygen and hindered phenols in alkaline solution have been reported in several recent papers.[1,2,3,4] The major products at low temperatures are peroxides of structure I which in alkaline solution can decompose[1,2] to II or III or rearrange to IV. Free radicals whose structure has not been explained heretofore have been observed[5,6] in this system by electron spin resonance (e.s.r.) spectroscopy.



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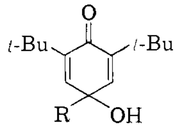

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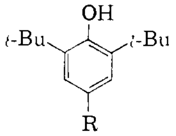

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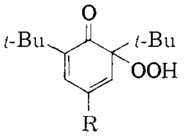
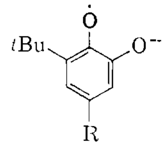


IV

We wish to report an unusual new reaction, isobutene elimination leading to the formation of pyrocatechol semiquinones V which are responsible for the observed e.s.r. spectra (Table I).



V

The isobutene evolved has been identified by gas-liquid chromatography and mass spectrometry. Two of the suspected pyrocatechols, 3-*tert*-butyl-5-methylpyrocatechol and 3,5-di-*tert*-butylpyrocatechol, have been prepared. The e.s.r. spectra of the semiquinones of these two compounds are identical with the spectra observed on oxidation 2,6-di-*tert*-butyl-4-methylphenol and 2,4,6-tri-*tert*-butylphenol, respectively.

TABLE I

PROPERTIES OF ELECTRON SPIN RESONANCE SPECTRA OF SEMIQUINONES OBTAINED BY OXIDATION OF 2,6-DI-TERT-BUTYL-4-R PHENOL

R	Approx. int. ratios of hyperfine lines	Coupling constants, gauss α_1	α_2
Methyl	1:1:3:3:3:3:1:1	5.2	2.5
Benzyl[a]	1:1:2:2:1:1	4.1	2.5
Isopropyl[a]	1:2:1	2.4	2.4
tert-Butyl	1:1	..	2.5

[a] Provided by the courtesy of Dr. F. C. Davis and Dr. G. C. Coppinger of Shell Development Company.

If I ($R = CH_3$) is allowed to decompose in alkaline solution, the characteristic e.s.r. spectrum of the corresponding semiquinone appears in about four hours. If an equimolar solution of I and III ($R = CH_3$) or an equimolar solution of cumene hydroperoxide and II is made alkaline, a strong e.s.r. spectrum appears immediately. Gersmann and Bickel[2] have suggested that an orthoquinone formed by the decomposition of IV may be responsible for the autocatalytic behavior of the main oxidation reaction. The present work indicates that orthoquinones almost certainly are produced. The mechanism of the olefin elimination reaction giving rise to the orthosemiquinones and orthoquinones is obscure. It is probably significant that the product is an orthosemiquinone rather than a parasemiquinone even if R = *t*-butyl.

Acknowledgment.—It is a pleasure to acknowledge helpful discussions with staff members of this laboratory and particularly with Dr. S. I. Weissman of Washington University and Dr. G. M. Coppinger of Shell Development Company.

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RECEIVED MAY 31, 1960

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(1) M. S. Kharasch and B. S. Joshi, *J. Org. Chem.*, **22**, 1439 (1957).

(2) H. R. Gersmann and A. F. Bickel, *J. Chem. Soc.*, 2711 (1959).

(3) G. G. Yohe, et al., *J. Org. Chem.*, **24**, 1251 (1959).

(4) A. Fairbourn and E. A. C. Lucken, *Proc. Chem. Soc.*, 67 (1950).

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(6) J. K. Becconsall, S. Clough, and Gerald Scott, *Proc. Chem. Soc.*, 308 (1959).

OPTICALLY ACTIVE VINYL POLYMERS. II. THE OPTICAL ACTIVITY OF ISOTACTIC AND BLOCK POLYMERS OF OPTICALLY ACTIVE α-OLEFINS IN DILUTE HYDROCARBON SOLUTION

Sir:

Although the existence of spiralized conformations of the macromolecules of many vinyl polymers in the solid state has been recognized since 1954,[1] no experimental evidence for the existence of such types of conformations in the liquid phase has been reported.

The data given here seem to support the hypothesis that, in the case of poly-α-olefins, helical conformations can exist above the melting point and in dilute solution.[2]

As we have reported recently,[3] the crystalline isotactic and block polymers of (+)(S)-3-methyl-1-

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(1) G. Natta and co-workers, *Nuovo Cimento*, [X], Suppl. **15**, 1–158 (1960).

(2) G. Natta, *et al.* (private communication) have obtained some evidence for the existence of helical conformations of poly-α-olefins in solution from infrared spectra. Similar evidence has been obtained by H. Tadokoro, S. Nozakura, T. Kitazawa, Y. Yasuhura and S. Murahashi, (*Bull. Chem. Soc. Japan*, **31**, 313–315 (1958)).

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