cury compounds. Such investigations are in progress in this laboratory.

Additionally, we have found that the cleavage by mercuric bromide of dialkylmercury compounds, which are free of possible complicating stereochemical features, occurs with retention of configuration. In contrast, the reduction of *sec*-butylmercuric bromide by sodium stannite to yield di-*sec*-butylmercury occurs with racemization of *both* R-groups.

The resolution was accomplished through the *sec*-butylmercuric mandelates. The (−)-*sec*-butylmercuric mandelate was recrystallized to constant optical rotation using dioxane as solvent, and then converted to (−)-*sec*-butylmercuric bromide by reaction with sodium bromide. The rotation of (−)-*sec*-butylmercuric bromide thus obtained is $[\alpha]^{22}D$ −25.8° (*C* 5, ethanol), $[\alpha]^{22}D$ −25.9° (*C* 3, acetone) (lit.[2] $[\alpha]^{20}D$ −24.0° (*C* ~5, acetone)).

The cleavage of active *sec*-butylmercuric bromide by bromine to form 2-bromobutane has been studied under various conditions, and the results are similar to those obtained with the *cis*- and *trans*-4-methylcyclohexylmercuric bromides.[4] Depending upon reaction conditions, active or inactive *sec*-butyl bromide is obtained. In pyridine as the solvent, (+)-*sec*-butylmercuric bromide, $[\alpha]^{22}D$ + 3.76°, was treated with bromine to yield D-(+)-2-bromobutane, $[\alpha]^{22}D$ + 4.15°. Since this reaction has been shown to proceed with retention of configuration,[4] the configurational assignment is D-(+)-*sec*-butylmercuric bromide. The rotation of optically pure D-(+)-2-bromobutane is $[\alpha]^{25}D$ + 28.6°.[5] Assuming the bromine cleavage in pyridine is completely stereospecific, the empirically calculated rotation for optically pure D-(+)-*sec*-butylmercuric bromide is $[\alpha]^{22}D$ − 25.9°, which value is identical with the experimental value reported here. This appears to be the most reliable stereospecific method for making active secondary bromides.[5,6]

Using compounds which have more than one asymmetric center[7] and neighboring methoxy group,[8] the cleavage of dialkylmercury compounds by mercuric halides has been reported to occur, respectively, with racemization and with retention of configuration. With simple aliphatic compounds we have found the reaction occurs with retention of configuration. *sec*-Butylmagnesium bromide was added to (−)-*sec*-butylmercuric bromide, $[\alpha]^{22}D$ − 6.49°, to give (−)-*sec*-butyl-(±)-*sec*-butylmercury, $[\alpha]^{22}D$ − 5.52°. The dialkyl compound with mercuric bromide gave (−)-*sec*-butylmercuric bromide (91%), $[\alpha]^{22}D$ − 3.36°. (The rotation of the final product was approximately one-half that of the starting material.)

The stereochemistry of the reduction of 2-methoxycyclohexylmercuric iodide by sodium stannite to yield di-2-methoxycyclohexylmercury has been studied by Traylor and Winstein.[9] Their suggested mechanism implied that only *one* alkyl group loses its configuration in the course of the reaction. We have found that with *sec*-butylmercuric bromide, *both* of the alkyl groups are predominantly racemized. The product (di-*sec*-butylmercury) is optically stable to the reaction conditions. (+)-*sec*-Butylmercuric bromide, $[\alpha]^{22}D$ + 5.4°, was treated with sodium stannite solution to give (+)-di-*sec*-butylmercury, $[\alpha]^{22}D$ + 0.22°, in 87% yield. Cleavage of this compound with mercuric bromide gave (+)-*sec*-butylmercuric bromide, $[\alpha]^{22}D$ + 0.23°.

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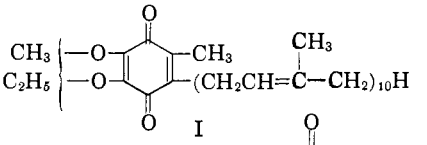
COENZYME Q. VI. ETHOXY HOMOLOGS OF COENZYME Q_{10}. ARTIFACT OF ISOLATION

Sir:

We have characterized ethoxy homologs of coeznyme Q_{10}; an artifact of isolation is evident. Ubiquinone[1,2,3] and these ethoxy homologs are very similar and differ from coenzyme Q_{10}.

Our isolation of coenzyme Q_{10} has been described,[4] and we initially observed no evidence for the presence of related quinones. Continued processing yielded lower melting material. Further purification separated coenzyme Q_{10} from another quinone, m.p. 43–43.5°. *Anal.* Found: C, 82.19; H, 10.34.

Ultraviolet, infrared and nuclear magnetic resonance spectra agree with formula I for this quinone; n.m.r. data were particularly revealing. The n.m.r. spectrum of CH_3CH_2O— was observed as



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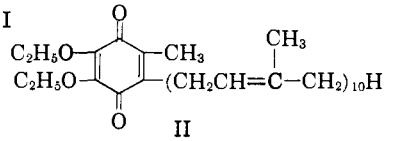

II

two members of the methyl triplet at −144 and −136.5 c.p.s. and three members of the $-CH_2O-$ quartet at −29, −22, and −14.5 c.p.s., the missing members being obscured by the large CH_3- and CH_3O- resonances of the rest of the molecule.

Our isolation included a step using hot ethanolic alkali. It was thought that an alcohol exchange reaction had occurred. When pure coenzyme Q_{10} was subjected to this isolation step in a simulated process, the ethoxy homolog (I) was produced. When methanol was substituted for ethanol in the isolation process, only coenzyme Q_{10} was isolated.

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The reaction of coenzyme Q_{10} with ethanol and sodium ethoxide gave a product, m.p. 34.5–35.5°. *Anal.* Found: C, 82.02; H, 10.44. Its n.m.r. spectrum corresponds to the diethoxy homolog (II).

The name ubiquinone was proposed by Morton, *et al.*,[2,3] "for a substance" which melted at 33–34°, 36°, and 41° ("melting points sharp"). These melting points are significantly lower than that for coenzyme Q_{10} (m.p. 48–49°)[5] and correspond closely to those of the diethoxy and the ethoxy homologs. Furthermore, the infrared spectra[1,2] of ubiquinone appear to correspond to the ethoxy derivatives rather than to that of coenzyme Q_{10}; spectra of carbon disulfide solutions were compared.

An infrared band at 10.55 μ for coenzyme Q_{10} is absent from the spectrum of the ethoxy product (I), and the latter has new bands at 10.10 and 11.18 μ. The 8.30, 8.67 and 10.55 μ bands of coenzyme Q_{10} are not in the spectrum of the diethoxy product (II), and the latter exhibits new bands at 8.51, 10.20 and 11.05 μ. The infrared spectrum[1] of the "best fraction" of ubiquinone (SA) appears identical to that of the diethoxy homolog (II). The infrared spectrum[1] for a second component of ubiquinone (SA) shows bands at 10.20 and 11.1 μ and no band at 10.55 μ; this spectrum is different from that of coenzyme Q_{10} and closely resembles that of the ethoxy homolog (I). Morton and co-workers[1] in their isolation of these ubiquinone preparations used hot ethanolic alkali for the saponification of tissues.

The first published description of a crystalline quinone melting at 48–49° was by Crane, *et al.*,[5] in 1957; it was later designated as coenzyme Q_{10}.[6] In 1958, Morton and co-workers[7,8] and Bouman, *et al.*,[9] described the same quinone. These investigators have now used the expression ubiquinone, not as originally defined,[2,3] but synonymously with coenzyme Q_{10}.

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STEROIDS. CXVII.[1] 6α-FLUORO-16α-HYDROXY CORTICAL HORMONES

Sir:

Among the most recent advances in the cortical hormone field have been the reversal[2] of salt retention of 9α-fluoro steroids by 16α-hydroxylation,[2,3] albeit with somewhat lowered anti-inflammatory activity,[4a,b] the potentiation of activity (with retention of desirable mineral effects) by 16,17-acetonide formation,[4b] and the potentiation of activity by 6α-fluoro[5a,b] substitution.

We now wish to report the synthesis of a number of representative 6α-fluoro-16α-hydroxy cortical hormone analogs in which the combination of several such substituents has been accomplished.

$\Delta^{5,16}$-Pregnadiene-3β,21-diol-20-one 21-acetate[6] on successive treatment with potassium permanganate[7] and acetone–perchloric acid gave Δ^5-pregnene-3β,16α,17α,21-tetrol-20-one 16,17-acetonide 21-acetate (m.p. 215–216.5°, $[\alpha]_D$ +8°.[8] Found for $C_{26}H_{38}O_6$: C, 70.02; H, 8.58; O, 21.74) and thence by means of monoperphthalic acid the 5α,6α-oxide (m.p. 195–196°, $[\alpha]_D$ ±0°. Found for $C_{26}H_{38}O_7$: C, 67.42; H, 8.16; O, 23.96). Fission with boron trifluoride[9] in ether–benzene yielded the 5α-hydroxy-6β-fluoro compound (m.p. 224–226°, $[\alpha]_D$ +30°. Found for $C_{26}H_{39}FO_7$: C, 64.10; H, 8.13; F, 4.11) which was converted to 6α-fluoro-16α-hydroxy-"S"-16,17-acetonide-21-acetate (m.p. 295–296°, $[\alpha]_D$ +104°, λ_{max}^{EtOH} 236 mμ, log ε 4.19. Found for $C_{26}H_{35}FO_6$: C, 66.74; H, 7.62; F, 4.26) by chromium trioxide oxidation followed by treatment with anhydrous hydrogen chloride in acetone. Cleavage of the acetonide function with 60% formic acid and then saponification gave 6α-fluoro-16α-hydroxy-"S" (m.p. 228–230°, $[\alpha]_D$ +64° (dioxane). Found for $C_{21}H_{29}FO_5$: C, 66.04; H, 7.81) which on incubation with bovine adrenals[10] yielded 6α-fluoro-16α-hydroxyhydrocortisone (I) (m.p. 233–235°, λ_{max}^{EtOH} 237 mμ, log ε 4.18. Found for $C_{21}H_{29}FO_6$: C, 63.47; H, 7.42). Alternatively, I was prepared by fermentation of 6α-fluorohydrocortisone[5] with *Streptomyces roseochromogenus*, Rutgers Collection No. 3689.[3] The 16,17-acetonide 21-acetate of I, II (m.p. 261–263°, $[\alpha]_D$ +135°, λ_{max}^{EtOH} 237 mμ, log ε 4.18. Found for $C_{26}H_{35}FO_7$: C, 65.08; H, 7.13) furnished on oxidation with selenium dioxide[11] 6α-fluoro-16α-hydroxy-prednisolone 16,17-acetonide 21-acetate (III) (m.p. 267–269° $[\alpha]_D$ +97°, λ_{max}^{EtOH} 241 mμ, log ε 4.16. Found for $C_{26}H_{33}FO_7$: C, 65.78; H, 7.12). Further, micro-

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