The Vitamin E Dimer, a Fluxional System

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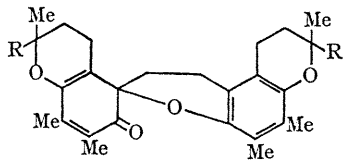
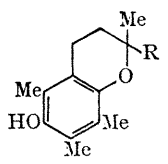
DURING a recent investigation[1] of the biological significance of polymers of vitamin E (IIa) we noted that its oxidation product[1-4] showed the principal molecular ion at *m/e* 858 (dimer -- 2H), rather than 856 (dimer — 4H) as expected for structure (Ia) suggested by Schudel *et al.*[3] Similarly, the model compound from oxidation of (IIb) (m.p. 122—124°)† subjected to g.l.c.–mass spectrometry (source temperature 290°) showed three chromatographic peaks, one exhibiting a parent ion at *m/e* 438 (dimer — 2H), and two at 434 (dimer — 6H), none of which are in accord with structure

† Dimers (Ia) and (Ib) are known to be difficult to purify, and m.p.s of 77—79°,[2] 120·5°,[3] 126—127°[4] are reported for extensively recrystallized material. Our (Ib) was conveniently prepared by re-oxidation of (IIIb), and melted at 122—124°.

(Ib).[3] When a solution of (Ia) was treated with bis(trimethylsilyl)acetamide and the raw reaction mixture investigated by mass spectrometry, a monosilyl derivative was observed at *m/e* 930 (dimer − 2H + Me_3Si). To complicate the picture further, deuterium exchange with D_2O in the mass spectrometer increased the mass of the parent ion of (Ia) to 860 indicating *two* exchangeable protons. The n.m.r. spectrum of (Ib) in chloroform at 30° was unusual (Figure, a) in that the aromatic and olefinic methyl bands were broad‡ and of low intensity compared to the *gem*-dimethyl bands at δ 1·24—1·26.

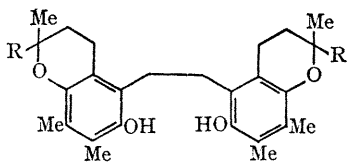


(Ia) R=$C_{16}H_{33}$
(Ib) R=Me



(IIa) R=$C_{16}H_{33}$
(IIb) R=Me

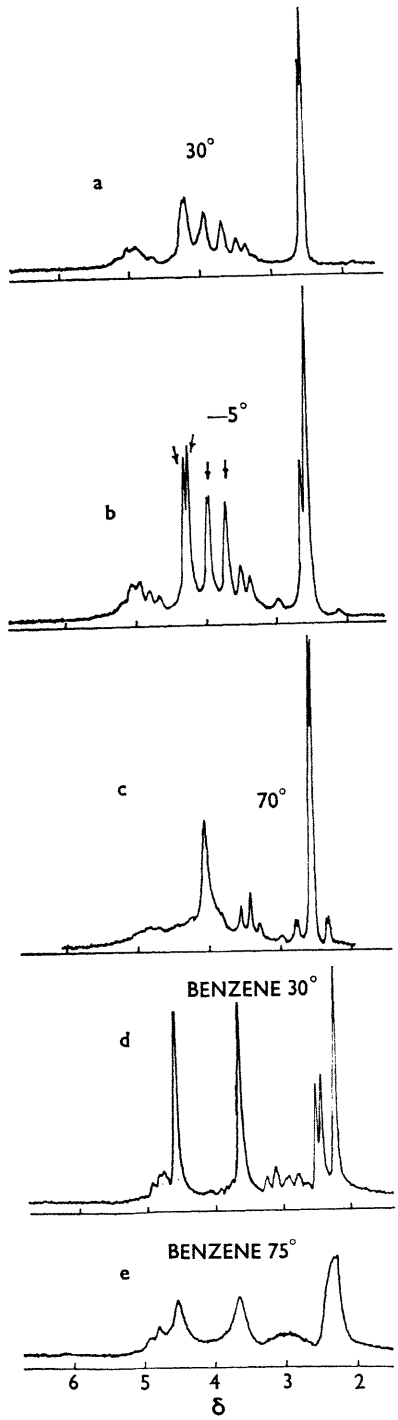
Because of these facts, structures (Ia) and (Ib) were questioned in spite of excellent u.v., i.r., and degradative evidence in their favour.[3] On the other hand, (Ib) has been partially converted into (IIIb) (dimer − 2H) by pyrolysis at 250° through an unusual oxidation–reduction process.[3] Proof that all of our g.l.c.–mass spectral observations were of artifacts based on this process was obtained by observing the mass spectrum of (Ib) at a very low source temperature (150°) for the lifetime of the sample (1 hr.), whereupon only *m/e* 436 was observed, in agreement with structure (Ib). The aforementioned monosilyl derivative (*m/e* 930) was undoubtedly formed in the inlet system of the mass spectrometer and may be the monosilyl ether of (IIIa). The anomalous n.m.r. spectrum of (Ib) was explained when the



(IIIa) R=$C_{16}H_{33}$
(IIIb) R=Me

sample was cooled to −5°. At this temperature the methyl bands (arrows, Figure, b) sharpen markedly and the spectrum is in good accord with structure (Ib). On the other hand, at 70° (Figure, c) the olefinic methyl peaks coalesce into one broad band while the *gem*-dimethyl signal at δ 1·25 appears as a simple 1 : 1 doublet. In benzene, the system is fixed at 30° (Figure, d) perhaps due to collision complexes with the solvent, but the same broadening of all bands is pronounced at 75° (Figure, e). Mixtures of the two solvents indicated that one of the dienone methyls was most affected by solvent change and on the basis of models (carvone and 3,5-dimethylcyclohex-2-enone) this appeared to be the methyl β to the ketone. The spectrum of (Ib) in hexachlorobutadiene is similar to that obtained in $CDCl_3$.§

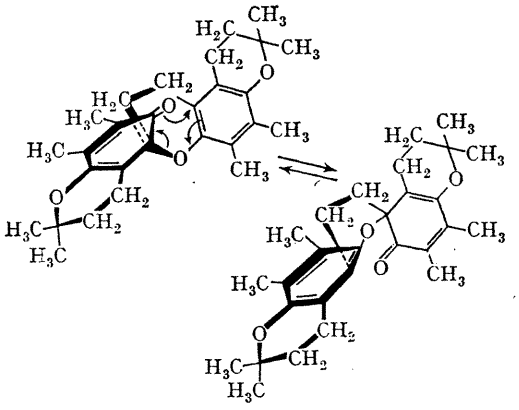
These spectra indicate that a temperature-sensitive "exchange" process is occurring wherein the methyl groups on each ring are losing their separate identity, and we are led to speculate that the molecule possesses a fluxional[5,6]



FIGURE

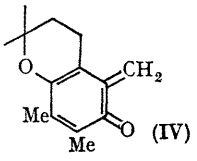
‡ P. Schudel *et al.*[3] also noted the breadth of these bands.
§ On heating to 120° in this solvent the dimer was converted in high yield into the trimer (trimer −6H, m.p. 232—234°).[2]

character brought about by the rearrangement of bonds without significant movement of atoms:



Although the π-orbital overlap usually encountered in such systems[5] is absent, the unshared p-electrons of the carbonyl group may facilitate the process.

The fluxional system depicted above would be optically stable and resolution should be possible as long as dissociation to quinone methide (IV) does not occur. To test for this process a mixture (Ia) and (Ib) was heated at 100° overnight



(IV)

and investigated by t.l.c. No evidence of mixed dimer was found.

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[1] B. S. Strauch, H. M. Fales, R. C. Pittman, and J. Avigan, *J. Nutrition*, 1968, **97**, 194.
[2] W. A. Skinner and P. Alaupovic, *J. Org. Chem.*, 1963, **28**, 2854.
[3] P. Schudel, H. Mayer, J. Metzger, R. Rüegg, and O. Isler, *Helv. Chim. Acta*, 1963, **46**, 636.
[4] D. R. Nelan and C. D. Robeson, *J. Amer. Chem. Soc.*, 1962, **84**, 2963.
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