stants relative to cyclohexanecarboxylic acid are given in Table I.

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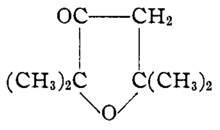
The Dehydration of 4-Hydroxy-2,2,4,5,5-pentamethyltetrahydrofuran (Acetylene Studies, Part VI)[1]

BY MAX SULZBACHER AND ERNST D. BERGMANN

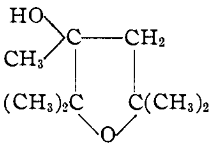
RECEIVED JANUARY 26, 1953

When II, the product of the reaction between 4-keto-2,2,5,5-tetramethyltetrahydrofuran (I) and methylmagnesium iodide, is dehydrated, a compound of the expected composition $C_9H_{16}O$ is obtained. Apart from the normal formulas, III, IV, the structure V is possible for this compound. Indeed, V has been proposed by Bouveault and Locquin,[2] as the same substance is also formed by acid dehydration of 2,3,5-trimethylhexane-2,3,5-triol (VI).

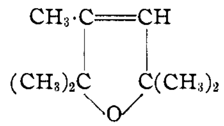
The infrared spectrum of the dehydration product is compatible only with formula V. Whilst it does not show any sign of double bond absorption in the 1620–1700 cm.$^{-1}$ region, the following bands were observed: 980 cm.$^{-1}$ (optical density d = 0.6) cyclobutane[3]; 1099 cm.$^{-1}$ (d = 0.3) isopropyl; 1175 cm.$^{-1}$ (d = 0.8) superposition of the isopropyl and the tetrahydrofuran absorption.[4] The chemical properties of the compound $C_9H_{16}O$ are in accord with formula V. It could not be hydrogenated catalytically to 2,2,4,5,5-pentamethyltetrahydrofuran at ordinary temperature and pressure, and did not decolorize bromine in carbon tetrachloride.



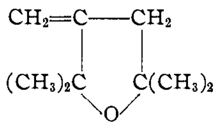
I



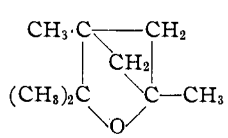
II



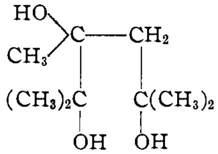
III



IV



V



VI

Experimental

I was prepared in quantitative yield from 1,1,4,4-tetramethyl-2-butyne-1,4-diol and aqueous mercuric sulfate,[5-7] b.p. 150° (760 mm.).

4-Hydroxy-2,2,4,5,5-pentamethyltetrahydrofuran (II).—The reaction of I with 2 moles of methylmagnesium iodide[6] gave II in 63% yield; from diisopropyl ether, m.p. 77°.[8]

Dehydration to V.—The mixture of 80 g. of II and 100 g. of freshly fused and finely ground potassium hydrogen sulfate was heated for six hours at 120°. The liquid product was distilled directly, dried and fractionated; b.p. 132°, yield 68 g. (96%), $d^{27.5}_4$ 0.820 (literature 0.826).

Anal. Calcd. for $C_9H_{16}O$: C, 77.1; H, 11.4. Found: C, 77.0; H, 11.5.

The infrared spectrum was measured in the 950–1200 cm.$^{-1}$ region in carbon disulfide solution (0.015 g. plus 1 cc. of solvent), in the 1600–1700 cm.$^{-1}$ region in carbon tetrachloride (0.016 g. plus 1 cc. of solvent); cell thickness 0.5 mm.[9]

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[1] Part I: THIS JOURNAL, **73**, 4013 (1951); Part II–V, *J. Applied Chem.*, **3**, 39, 42, 97, 145 (1953).

[2] L. Bouveault and R. Locquin, *Ann. chim*,. [8] **21**, 414 (1910).

[3] L. W. Marrison, *J. Chem. Soc.*, 1614 (1951).

[4] H. Tschamler and H. Voetter, *Monatsh.*, **83**, 302 (1952). See also G. M. Barrow and S. Searles, THIS JOURNAL, **75**, 1175 (1953).

[5] G. Dupont, *Compt. rend.*, **152**, 1486 (1911).

[6] G. Dupont, *Ann. chim.*, [8] **30**, 536 (1913).

[7] H. Richet, *ibid.*, [12] **3**, 317 (1948).

[8] G. Dupont, *Compt. rend.*, **154**, 601 (1912).

[9] We are greatly indebted to Dr. S. Pinchas, Optics Department, Weizmann Institute of Science, Rehovoth, for the determination of the spectrum.

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cis- and *trans*-Tropine (Tropanol)[1]

BY PIERRE F. SMITH[2] AND WALTER H. HARTUNG[3]

RECEIVED MARCH 5, 1953

Recent papers establish the stereochemical structure of the tropine (tropanol) isomers,[4-6] namely, that in tropine the hydroxyl group and N-methyl bridge are *trans* and that in ψ-tropine they are *cis*. We now submit additional experimental evidence confirming these conclusions.

A study of models suggested that the structure with the –OH and $\rangle NCH_3$ groups in close proximity might be expected, owing perhaps to hydrogen bonding, to exhibit greater pK values in aqueous solution and less change in pH upon titration. Our results, obtained from the titration of 20.00-ml. portions of 0.050 N solutions of the isomeric tropines (purified by sublimation *in vacuo*) with 0.0613 N hydrochloric acid, are summarized in Fig. 1. The pK values at 25°, as estimated from the half neutralization points, are 2.98 for tropine and 3.67 for ψ-tropine. The greater value for ψ-tropine is suggestive of intramolecular hydrogen bonding and therefore a configuration of the –OH *cis* to the $\rangle NCH_3$ group.

Tropine, refluxed for ten minutes with benzoyl chloride in a 1:8 molar ratio, yielded 84.5% of tropine benzoate hydrochloride. ψ-Tropine, identically treated, yielded 79.2% of ψ-tropine benzoate hydrochloride. Regrettably limited amounts of materials did not permit further study of the reactivity of the –OH groups in the isomeric alcohols.

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[1] Experimental work performed at the University of Maryland.

[2] Rutgers University, Newark, N. J.

[3] University of North Carolina, Chapel Hill, N. C.

[4] G. Fodor and K. Nador, *Nature*, **169**, 462 (1952).

[5] B. L. Zenitz, C. M. Martini, M. Priznar and F. C. Nachod, THIS JOURNAL, **74**, 5564 (1952).

[6] A. Nickon and L. F. Fieser, *ibid.*, **74**, 5566 (1952).

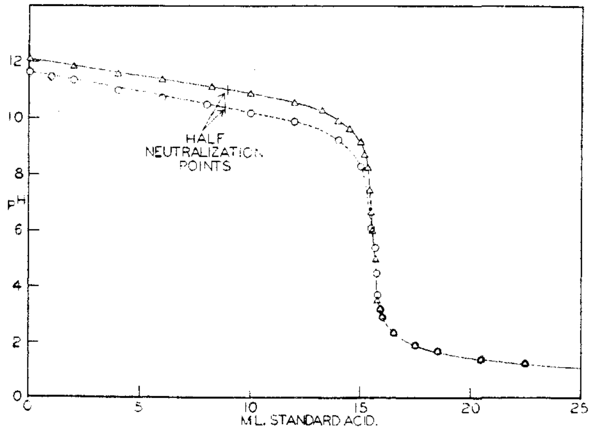
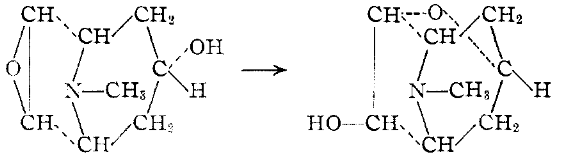


Fig. 1.—Titration curves of tropanol (Δ and solid line) and pseudotropanol (O and dashed line).

It was hoped that the rule of v. Auwers[7] might be applied, although tridimensional models of the molecules reveal that the reference point for *cis–trans* definition is not clear. The densities obtained for liquid tropine and ψ-tropine are $d^{116}{}_{20}$ 1.001 and $d^{116}{}_{20}$ 0.998.

In this connection it may be pointed out that in scopine, I, the basic moiety of hyoscine (scopolamine), the -OH group at position 3 is most probably *trans* to the $>NCH_3$ bridge, since that configuration best explains the easy rearrangement to scopoline, II. Hyoscine frequently occurs together with atropine in various *Atropa* and *Datura* species,[8] suggesting similar stereo-biochemical genesis for the two alkaloids.



I
Scopine

II
Scopoline

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(7) K. v. Auwers, *Ann.*, **410**, 287 (1915); **420**, 84 (1920).

(8) T. A. Henry, "The Plant Alkaloids," The Blakiston Co., Philadelphia, Pa., 1949, p. 65.

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Simultaneous Dissociation of Two Protons. The Acid–Base Equilibria of Porphyrins[1]

BY ROBERT IRVING WALTER[2]

RECEIVED FEBRUARY 19, 1953

The four nitrogen atoms of the porphyrin ring system can participate in a series of acid–base equilibria which can be written (PH_2 is the neutral porphyrin molecule)

$$PH_4^{++} \rightleftarrows PH_3^+ + H^+ \qquad (1)$$

$$PH_3^+ \rightleftarrows PH_2 + H^+ \qquad (2)$$

$$PH_2 \rightleftarrows PH^- + H^+ \qquad (3)$$

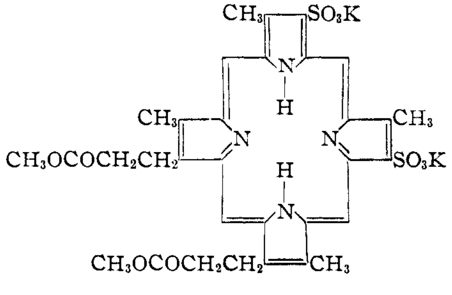
$$PH^- \rightleftarrows P^= + H^+ \qquad (4)$$

A potentiometric study of equilibria (1) and (2) was reported by Conant, *et al.*,[3] who observed only a single inflection in the titration curve for the addition of two equivalents of acid to PH_2. They assumed $pK_1 = pK_2$, and reported values averaging 2.5 for five porphyrins in glacial acetic acid. A colorimetric study of equilibria (1) and (2) was reported by Aronoff and co-workers,[4] who found only one absorption curve for each of three porphyrins in various sulfuric acid–pyridine mixtures. From the absence of a spectrum intermediate between those of PH_4^{++} and PH_2, they concluded that PH_3^+ could exist over only a limited pH range, and assumed that K_1 and K_2 were very nearly equal.

Equilibria (3) and (4) have been studied colorimetrically by McEwen,[5] who found that no difference in acid strength could be detected for the first and second ionization steps of PH_2. He assigned $pK_3 = pK_4 = 16$ for both steps of the ionization of etioporphyrin in methanol.

The authors quoted[3–5] apparently intended to express the conclusions that reactions (1) and (2) occur with equal ease and, similarly, that reactions (3) and (4) occur with equal ease. If this is the case, it is *not* true that $K_1 = K_2$ and $K_3 = K_4$. Instead, due to statistical factors arising in the conventional definition of the dissociation constants, $K_1 = 4K_2$ and $K_3 = 4K_4$[6] (if PH_4^{++} and PH_2 be assumed to dissociate as independent dibasic acids). In such a reaction, the intermediate (PH_3^+ or PH^-) would attain a maximum concentration, when the reaction was half completed, equal to half that of the total porphyrin present.

These results on a number of different porphyrins in a variety of solvents are not strictly comparable, but they suggest an unusual situation in which a tetrabasic acid loses two protons more or less simultaneously in each of two widely separated stages on the pK scale. Accordingly, equilibria (1) and (2) have been investigated in an effort to detect the presence of PH_3^+. The water soluble porphyrin chosen for study was the dipotassium salt of 1,3,5,8-tetramethylporphyrin-6,7-dipropionic acid methyl ester-2,4-disulfonic acid



The formula given is thus the species PH_2.

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[1] This material was presented before the Organic Section at the 119th meeting of the American Chemical Society, Cleveland, April, 1951.

[2] School of Chemistry, Rutgers University, New Brunswick, New Jersey.

(3) J. B. Conant, B. F. Chow and E. M. Dietz, THIS JOURNAL, **56**, 2185 (1934).

(4) (a) S. Aronoff and C. A. Weast, *J. Org. Chem.*, **6**, 550 (1941); (b) S. Aronoff and M. Calvin, *ibid.*, **8**, 205 (1943).

(5) W. K. McEwen, THIS JOURNAL, **58**, 1124 (1936).

(6) J. Greenspan, *Chem. Revs.*, **12**, 339 (1933).