Intermediates.—The compounds 2-acetylthiophene, 2-propionylthiophene, 2-butyrylthiophene, 2-butyrylfuran and 2-acetylfuran were prepared according to Heid and Levine[7] by interaction of thiophene (or furan) with the appropriate acid anhydride in the presence of boron trifluoride. Application of this method was extended to prepare 2,5-dimethyl-3-acetylthiophene,[8] 2,5-dimethyl-3-acetylfuran[9] and 2-butyrylpyrrole[10] in yields of 50, 70 and 16.5%, respectively. The physical constants of these compounds were found to be in agreement with those reported in the literature. Treatment of 2,5-dimethyl-2-acetylfuran with excess aqueous ammonia in a sealed tube at 145° for four hours gave the corresponding pyrrole.[9] Decarboxylation of the appropriate keto acids according to the procedure of Burrus and Powell[11] gave 2-acetylpyridine, 4-acetylpyridine, 3-acetylpyridine and 3-propionylpyridine. Application of this method was extended without modification to prepare 3-butyrylpyridine[12] in approximately 15% yields. Interaction of nicotinoyl chloride and benzene in the presence of aluminum chloride gave good yields of 3-benzoylpyridine.[13] Pyridine-3-carboxaldehyde was prepared by the procedure of Panizzon.[14] Thiophene-2-carboxaldehyde was purchased from the Arapahoe Chemical Co., Boulder, Colorado.

Acknowledgment.—We are indebted to David Regenbogen and Sydney Gister for the preparation of intermediates and to Ruth Becker for microanalytical data.

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[7] J. V. Heid and R. Levine, *J. Org. Chem.*, **13**, 409 (1948).

[8] H. Ruffi, *Ber.*, **20**, 1750 (1887); W. Steinkopf and I. Schubart, *Ann.*, **424**, 1 (1921).

[9] G. Magnanini and T. Bentivoglio, *Gazz. chim. ital.*, **24**, 435 (1894).

[10] B. Oddo, *Ber.*, **43**, 1012 (1910).

[11] H. O. Burrus and G. Powell, THIS JOURNAL, **67**, 1468 (1945).

[12] C. Engler, *Ber.*, **24**, 2541 (1891).

[13] R. Wolffenstein and F. Hartwich, *ibid.*, **48**, 2043 (1915).

[14] L. Panizzon, *Helv. Chim. Acta*, **24**, 24E (1941).

THE RESEARCH LABORATORIES OF THE
NEPERA CHEMICAL CO., INC.
NEPERA PARK, YONKERS, N. Y.
RECEIVED APRIL 25, 1951

Molar Refractions in the Binary System Acetone–Carbon Tetrachloride

BY KENNETH C. BACHMAN[1] AND EDWARD L. SIMONS[2]

In connection with vapor–liquid equilibrium studies of the binary system acetone–carbon tetrachloride, both densities and refractive indices of known solutions covering the entire composition range were made at 25°.[3] In Table I are shown the molar refractions obtained from these data along with those calculated assuming a linear variation with composition.

TABLE I

MOLAR REFRACTIONS IN THE SYSTEM ACETONE–CARBON TETRACHLORIDE

$$[R]_D,\ \text{obsd.} = \left(\frac{n^2 - 1}{n^2 + 2}\right) \times \left(\frac{x_1M_1 + x_2M_2}{d}\right);\ [R]_D,\ \text{calcd.} = 16.167 + 10.280x_2.$$

Mole fraction CCl_4, x_2	Molar refraction $[R]_D$ obsd.	$[R]_D$ calcd.	ΔR
1.000	26.447	(26.447)	
0.8978	24.426	25.396	0.030
.8027	24.461	24.419	.042
.6990	23.394	23.353	.041
.5993	22.371	22.328	.043
.4996	21.345	21.303	.042
.4005	20.309	20.284	.025
.3010	19.292	19.261	.031
.2004	18.250	18.227	.023
.1003	17.212	17.198	.014
.0000	16.167	(16.167)	

In spite of the large positive deviations from ideal behavior indicated by the vapor–liquid equilibrium data, the deviations from additivity of the molar refractions, though varying with composition, never exceed 0.045 cc. This observation is in agreement with the more limited data (0–40 mole per cent. acetone) of Smyth, Engel and Wilson[4] and with the unpublished results of Koenig-Gressman.[5]

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[1] M. W. Kellogg Co., Jersey City, N. J.

[2] General Electric Research Laboratory, Schenectady, N. Y.

[3] K. C. Bachman and E. L. Simons, *Ind. Eng. Chem.*, Jan. (1952).

[4] C. P. Smyth, E. W. Engel and E. B. Wilson, Jr., THIS JOURNAL, **51**, 1736 (1929).

[5] M. L. Koenig-Gressman, Thesis, University of Munich, 1938. Data obtained through courtesy of Prof. K. Fajans.

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The Failure of Crystalline Vitamin B_{12} to Exchange with Co^{60} in Acidic and Neutral Aqueous Solutions

BY R. R. BALDWIN, J. R. LOWRY AND R. V. HARRINGTON

Because of the recent availability and interest in the growth-promoting characteristics and metabolism of vitamin B_{12}, it was decided to determine whether a radioactive form of the vitamin could be prepared for study by simple exchange with Co^{60}, over a period of several weeks. Fantes, Page, Parker and Smith[1] have shown that this exchange does not occur over a period of two hours at room temperature in 0.1 *N* acid or alkali, or by boiling for one hour at *p*H 7. However, the possibility of exchange on prolonged contact has not been examined.

The possibility of such an exchange was indicated by application of paper chromatography. $Co^{60}SO_4$ in solution with B_{12} was observed to migrate with B_{12}, while a control spot of $Co^{60}SO_4$ did not migrate. To determine whether this is an actual exchange or simply a weak complexing or surface action, the following experiment was performed.

The approximate analysis of the cobalt content of B_{12} is 4%.[2] An aqueous solution was prepared containing 0.1 mg./ml. crystalline Merck vitamin B_{12}. Approximately ten times the amount of cobalt present in the B_{12} was added in the form of $Co^{60}SO_4$. The mixture was allowed to stand at room temperature for five weeks at a *p*H of about 2. This B_{12} cobalt mixture exhibited growth stimulation on *Lactobacillus leichmannii* (ATC 4797). Model experiments had indicated that B_{12} could be salted out of water and into *n*-butanol by the addition of solid ammonium sulfate. Cobalt under these conditions remained in the aqueous phase. Repeated application of the salting-out procedure to the radioactive mixture resulted in a final butanol phase, strongly colored by the vitamin but exhibiting no radioactivity. This procedure was repeated with a neutral solution of B_{12} and $Co^{60}SO_4$ with the same negative results.

The experimental results are recorded in Table I.

A thin-window counting tube was employed in the measurements. Accordingly, under the above conditions, vitamin B_{12} does not exchange with radioactive cobalt, and the conclusions of Fantes, *et al.*, concerning the strong coördinate

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[1] K. H. Fantes, J. E. Page, L. F. J. Parker and E. L. Smith *Proc. Roy. Soc.* (*London*), [B]**136**, 592 (1949).

[2] E. L. Rickes, N. G. Brink, F. R. Koniuszy, T. R. Wood and K. Folkers, *Science*, **108**, 134 (1948).

complexing of the cobalt in vitamin B_{12} have been substantiated under considerably more rigorous conditions.

TABLE I

DISTRIBUTION OF RADIOACTIVITY DURING SEPARATION PROCEDURE

	$Co^{60}SO_4$-control		B_{12}–Co^{60}, pH 2		B_{12}–Co^{60}, pH 7	
Fractionation step	Butanol counts/min.	$(NH_4)_2SO_4$ counts/min.	Butanol counts/min.	$(NH_4)_2SO_4$ counts/min.	Butanol counts/min.	$(NH_4)_2SO_4$ counts/min.
1	49	3400	2400	30,000	2350	30,000
2	1	30	75	2,100	80	2,260
3			4	55	2	60

CENTRAL LABORATORIES
GENERAL FOOD CORP.
HOBOKEN, N. J.

RECEIVED JUNE 21, 1951

The Isolation of Metanethole from the Sponge, *Spheciospongia Vesparia*[1]

BY WERNER BERGMANN AND WILLIAM J. MCALEER[2]

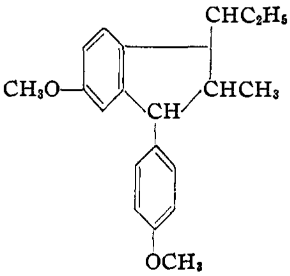
The odor of the majority of species of fresh sponges is not unpleasant, as is generally believed, but often rather aromatic and reminiscent of anise oil and similar products. The first clue to the probable nature of these odoriferous products was secured during a systematic fractionation of the unsaponifiable matter of the sponge, *Spheciospongia vesparia*.[2] In the present work, there was isolated from a fraction, consisting chiefly of hydrocarbons, a small amount of a nicely crystalline material of m.p. 135° and the empirical formula $C_{20}H_{24}O_2$. The compound failed to react positively with reagents for hydroxyl and carbonyl groups, and the absence of such groups was also noticed in its infrared absorption spectrum. The latter, however, showed that the two oxygen atoms were present as methoxyl groups. This was verified by a methoxyl determination according to Zeisel. The presence in the compound of two isolated aromatic rings was suggested by the low hydrogen content and the ultraviolet absorption spectrum. The compound reacted readily with bromine under evolution of hydrogen bromide to afford a nicely crystalline dibromide, $C_{20}H_{22}O_2Br_2$, m.p. 138°. It was also easily nitrated to a dinitroderivative, $C_{20}H_{22}O_6N_2$, m.p. 190°.

The properties of this sponge product were found to be in excellent agreement with those of metanethole (III), the dimerization product of anethole (I). The structure of metanethole, first proposed by Baker and Enderby[3] and supported by Müller and Richl[4] has recently been substantiated through the work of Doering and Berson[5] on the analogous di-isohomoeugenol.

Convincing proof for the identity of the sponge product with metanethole was established by direct comparison of the two compounds. Metanethole was prepared from p-methoxy-α-methylcinnamic acid according to Baker and Enderby.[3] The physical properties of the two products, including their absorption spectra, and their reactions with bromine and nitric acid which afford characteristic derivatives, were identical.

I, anethole

II, methylchavicol



III, metanethole

Like the synthetic material, the sponge product is optically inactive. This lack of activity in spite of the presence of three asymmetric carbon atoms suggests that the sponge product is an artifact. Its immediate precursor was in all probability anethole (I), a constituent of many essential oils, such as anise oil, in which upon long standing it dimerizes to give metanethole.[6] The possibility, however, is not excluded that the material present in fresh sponges is methylchavicol (II) rather than anethole. While it is true that methylchavicol does not readily dimerize to metanethole,[7] it will rearrange to anethole in an alkaline medium. It is not inconceivable that such rearrangement has taken place during the saponification of the original fatty extract of the sponge. The results of the present study therefore indicate that the odor of many sponges is due to the presence of small amounts of anethole, methylchavicol or other related substances. Such compounds which are not uncommon in many plants do not appear to have previously been observed in animals.

Experimental

All melting points are corrected.

The unsaponifiable matter of the sponge, *Spheciospongia vesparia*,[2] from which the bulk of the sterols had been removed by crystallization, was rapidly distilled from a small retort at about 0.02 mm. pressure. The fraction boiling below 230° was dissolved in hot acetone. Upon cooling, the solution deposited a small amount of a solid hydrocarbon mixture consisting chiefly of heptacosane. The mother liquor was then evaporated to dryness, and the residue (15 g.) was dissolved in hexane (50 ml.). The solution was then passed through a column of alumina, and the chromatogram was developed first with hexane and subsequently with hexane containing 20% of benzene, when four distinct zones appeared. The eluate containing the fastest moving zone upon evaporation afforded a yellowish oil (1.5 g.) interspersed with crystalline material. The latter (100 mg.) was readily separated from the oil by several recrystallizations from acetone. It melted at 135° and gave no depression of the melting point when mixed with synthetic metanethole.[3]

Anal. Calcd. for $C_{20}H_{24}O_2$: C, 81.05; H, 8.15; CH_3O, 20.9. Found: C, 81.16; H, 8.70; CH_3O, 20.6.

Dibromometanethole.—About 10 mg. of the sponge product was treated with 1 ml. of 10% solution of bromine in glacial acetic acid. Solution took place rapidly with the evolution of hydrogen bromide. After standing overnight, the crystalline dibromide was collected, washed with acetic acid and acetone, and recrystallized from acetone; m.p.

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(1) Contributions to the study of marine products. XXIX.

(2) F. R. Valentine and W. Bergmann, *J. Org. Chem.*, **6**, 452 (1941).

(3) W. Baker and T. Enderby, *J. Chem. Soc.*, 1094 (1940).

(4) A. Müller and Richl, *Ber.*, **76**, 1119 (1943).

(5) W. von E. Doering and J. A. Berson, THIS JOURNAL, **72**, 1118 (1950).

(6) E. H. Polak and R. M. Hixon, *J. Am. Pharm. Assoc.*, **34**, 240 (1945).

(7) L. S. Glichitch, *Bull. soc. chim.*, [4] **35**, 1160 (1924).