theory of valency is reviewed, a definition of resonance is provided which is open to serious objections.

It is implied—particularly in the use of the expression "equilibrium mixture"—that distinct molecular species corresponding to the extreme electronic formulae of resonating compounds are capable of independent existence.

The word resonance undoubtedly suggests some kind of rapid oscillation or vibration to many people. Nevertheless, no such change, quick or slow, is actually present, and a resonating compound is not a mixture. It seems unfortunate to add to the confusion by using the word "vibrator" (p. 259) for a part of a molecule which is capable of resonance.

The reader is cautioned aginst confusing resonance with tautomerism (p. 137), yet a typical tautomeric equilibrium is given in Fig. 6.11c (p. 143) as an example of resonance. Similar confusion is reflected in Fig. 8.41. In Fig. 6.11c, too, the equation purporting to show resonance within the molecule of quinone is obviously incorrect; the dipolar structure shown has two positive charges.

The relationship implied by the caption for Fig. 9.29 is at variance with the text. If the unsymmetrical dye shows a deviation in λ max., it would absorb at some shorter wave-length than the mean of the values of λ max. of the related symmetrical dyes, whereas the caption is so worded that the unsymmetrical dye appears to absorb at *longer* wave-length than either of the symmetrical dyes. Actually none of these curves is that of a dye which contains a thiazole ring; they are the spectra of 1,1′-diethyl-2,2′-, 2,4′- and 4,4′-carbocyanine iodides, taken in the order A, B, C. Incidentally, the term "degeneracy" is used in Fig. 9.30 where "deviation" is meant.

Aside from these criticisms, however, this volume contains such a wealth of material that it may confidently be expected to appeal to a wide circle of readers.

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TEMPERATURE

Temperature Measurement. By ROBERT L. WEBER. Frontisp., x + 171 + 6 pp.; 3 pls. Ann Arbor, Mich.: Edwards Brothers, Inc. $2.50. 1941.

THE scope of the book is considerably broader than the title indicates; it might better have been called "Heat Measurements." There are chapters on heat transfer, radiation, calorimetry, thermal analysis and elementary thermodynamics. From the outside reader's point of view this is a defect, for none of these subjects can be treated in such brief chapters in more than a very condensed and—for the elementary student—inadequate way. On the other hand, the author, who is on the teaching staff of the School of Chemistry and Physics of Pennsylvania State College, may have found that his students were not getting, from other physics courses, a point of view or insight that he wished them to have on some of these subjects, and may have inserted them for local and practical reasons. Thirty pages are devoted to laboratory experiments intended for instruction.

The chapters that do hew to the line cover expansion thermometry, resistance thermometry, thermo-electric pyrometry, radiation (including optical) pyrometry, special methods of temperature measurement, measurement of extreme temperatures, the International Scale, temperature recorders and temperature control. The chapter on control, six pages long, can hardly do more than tell the student that there is such a thing as automatic control and hint at its complexity. It is a subject still badly in need of a good write-up.

The job of offset printing from typescript copy is quite satisfactory with the exception of illustrations of the half-tone variety, which are not well adapted to this method of reproduction.

This looks like a book that will be useful to any teacher or student concerned with measurements of energy and temperature.

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SPECIAL ARTICLES

DESTHIOBIOTIN[1]

DURING the work leading to the proof of structure of biotin,[2] a procedure devised for the hydrogenolysis of organic sulfides[3] was applied to biotin methyl ester.[4] The resulting product was named *desthiobiotin* methyl ester, and was formed from biotin methyl ester by the replacement of the sulfur atom in the molecule

[1] The authors wish to thank Dr. R. T. Major and the Research Staff of Merck and Company, Incorporated, for supplies of biotin. The authors also wish to express their appreciation to Dr. J. R. Rachele and R. C. Funk, Jr., for the microanalyses, and to Miss Carol Tompkins and Mrs. Glenn Ellis for technical assistance in the bioassays.

[2] V. du Vigneaud, SCIENCE, 96: 455, 1942.

[3] R. Mozingo, D. E. Wolf, S. A. Harris, and K. Folkers, *Jour. Am. Chem. Soc.*, 65: 1013, 1943.

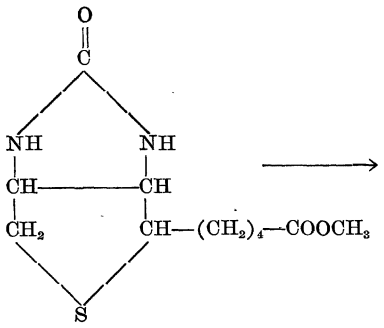
[4] V. du Vigneaud, D. B. Melville, K. Folkers, D. E. Wolf, R. Mozingo, J. C. Keresztesy and S. A. Harris, *Jour. Biol. Chem.*, 146: 475, 1942.

by two hydrogen atoms, as indicated by the accompanying structures.

Vigorous treatment of desthiobiotin methyl ester with acid or alkali yielded ζ,η-diaminopelargonic acid which by treatment with phenanthrenequinone yielded the same quinoxaline derivative as synthetic ζ,η-diaminopelargonic acid.[4]

In line with our study of the relationship of structure to the biological activity of biotin, which we have under way, an investigation of the biological effects of desthiobiotin was undertaken. While all phases of the investigation of this compound are not yet complete, we feel it worthwhile to make a preliminary report at this time, in view of the surprising yeast-growth activity of this compound. We have found that desthiobiotin is equally as effective as biotin in stimulating the growth of *Saccharomyces cerevisiae*, and produces a readily noticeable growth effect in a concentration of less than 1 part in 400,000,000,000.

The previously published method[4] of preparing desthiobiotin methyl ester by refluxing an alcoholic



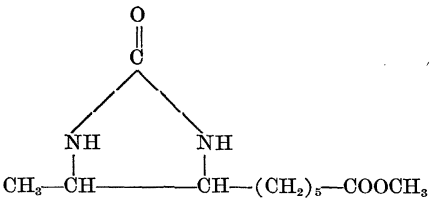
solution of biotin methyl ester with Raney nickel for several hours was found unsatisfactory for the preparation of the pure compound. Various samples of desthiobiotin methyl ester prepared in this manner showed differences in melting point and varying degrees of biological activity. Separation from undesirable side-products was difficult. In no case did we obtain a product with an activity approaching the activity reported here for the pure product. Treatment of biotin (free acid) under the same conditions was equally unsatisfactory.

We have now found that by carrying out the desulfurization of biotin in aqueous *alkaline* solution and for a short period of time, excellent yields of pure desthiobiotin can be obtained. In this way we have prepared desthiobiotin of constant melting point and biological activity. The compound was characterized by analysis and by conversion to ζ,η-diaminopelargonic acid.

50 mg of biotin were dissolved in 15 cc of 0.5 per cent. Na_2CO_3, and approximately 2.5 gm of Raney nickel[3] prepared at 50° were added. The mixture was heated with continuous stirring at 75° for 15 minutes. At the end of this time, the nickel was centrifuged down and washed with 2 cc of 0.5 per cent. Na_2CO_3 solution and twice with 2 cc of water. The combined solutions were acidified to Congo red with HCl and concentrated to 2–3 cc. Fine needles separated from the solution during the last stages of concentration. These were removed and washed with water. This fraction, micro m.p. 152–7°, weighed 36 mg. By concentration of the mother liquors and then continuous ether extraction for 5 hours an additional 6 mg, m.p. 147–152° were obtained. Two recrystallizations of the crude desthiobiotin from water yielded the pure compound, m.p. 157–8°.

$C_{10}H_{18}O_3N_2$	Calculated,	C 56.04,	H 8.47,	N 13.08
214.3	Found,	" 56.30,	" 8.58,	" 13.12

The desthiobiotin was tested for its biotin activity by the yeast-growth method of biotin assay,[5] in which Strain 139 *Saccharomyces cerevisiae* was used. Under our conditions of assay, both biotin and desthiobiotin



produced similar growth curves with a half-maximum growth increase at a concentration of 1 part in 4.75×10^{10}. Desthiobiotin is therefore, on a weight basis, fully as active as biotin for this strain of yeast. On a molarity basis, desthiobiotin, because of its slightly lower molecular weight, is somewhat less effective than biotin as a yeast-growth factor.

In conformity with our hypothesis that the urea grouping of biotin is essential for the combination of biotin with avidin,[6] we find that the yeast-growth activity of desthiobiotin is also inhibited by avidin.

That such a deep-seated change in the structure of the biotin molecule should result in a compound of such a high order of biological activity is indeed surprising. However, that desthiobiotin can not replace biotin in the media for all micro-organisms which require biotin is demonstrated by our finding that desthiobiotin does not stimulate the growth of *Lactobacillus casei*. The effect of desthiobiotin on various other

[5] E. E. Snell, R. E. Eakin and R. J. Williams, *Jour. Am. Chem. Soc.*, 62: 175, 1940.

[6] V. du Vigneaud, K. Dittmer, K. Hofmann and D. B. Melville, *Proc. Soc. Exp. Biol. and Med.*, 50: 374, 1942.

micro-organisms and on mammals and birds remains to be investigated.

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RATIONS FOR THE STUDY OF THE RELATIVE NUTRITIVE VALUE OF FATS AND OILS

DATA have shown butter fat to have superior growth-promoting value for the albino rat as compared to certain vegetable oils: (1) on a diet of mineralized raw skimmed milk into which the various fats and oils have been homogenized;[1] (2) on a basal diet of ether-extracted mineralized skim milk powder[2]; and (3) on a synthetic type ration containing *lactose 32,* casein (fat free) 28, liver extract 1–20[3] 6, salts 6, fat 28, and vitamins.[2]

Since at the present time there is great interest in the nutritional value of fats, we felt that our data would be of aid to workers in the field. In the present study weanling albino male rats of the Sprague-Dawley strain were given *ad libitum* a basal diet of the following composition: *lactose 48,* casein (fat free) 20, fat 28 and salts IV[4] 4 per cent., respectively. Vitamins added per 100 gm of ration: thiamine 0.5 mg; riboflavin 0.5 mg; nicotinic acid 0.625 mg; pyridoxine 0.625 mg; calcium pantothenate 5.0 mg; p-amino benzoic acid 30.0 mg; inositol 100 mg; choline 250 mg; β-carotene 0.56 mg; α-tocopherol 2.24 mg; calciferol 0.014 mg; and 2-methyl-1, 4-naphthaquinone 0.21 mg. The results recorded in Table 1 show the average number of grams gained during the period of six weeks by rats fed butter fat or corn oil on both the 32 per cent. lactose ration[2] and on the 48 per cent. lactose ration. Rough and discolored fur coats, blood-stained noses and scaly paws (when the humidity was not abnormally high) were noted in the rats fed the 48 per cent. lactose ration containing corn oil. Thus greater differences were found between the nutritive value of butter fat and corn oil in the young rapidly growing rat when the lactose content of the ration was raised from 32 to 48 parts, and the liver concentrate was omitted entirely.

TABLE 1

	32 per cent. lactose ration	48 per cent. lactose ration		
Experiment No.	53, 54, 62	78	81	84
No. of rats on each fat	15	6	6	6
Butter fat. Gain in six weeks	197 gm	164 gm	174 gm	156 gm
Corn oil. Gain in six weeks	168 gm	124 gm.	131 gm	118 gm
Difference	29 gm	40 gm	43 gm	38 gm

TABLE 2

Diet exclusive of fat	Fat	Average gain in gm in six weeks
Skim milk powder 70	Butter fat 30	219*
Skim milk powder 70	Corn oil 30	200*
Difference		19
Skim milk powder 50, lactose 20	Butter fat 30	214
Skim milk powder 50, lactose 20	Corn oil 30	172
Difference		42
Skim milk powder 50, dextrose 20	Butter fat 30	221
Skim milk powder 50, dextrose 20	Corn oil 30	217
Difference		4

* Average of 12 male rats.

Likewise, an increased level of lactose on a skim-milk powder basal ration accentuates the difference in the nutritive value of butter fat and corn oil. The ration was prepared as described,[2] and the experiment set up as shown in Table 2. These data represent the average growth over a six-week period by six male rats, in each group.

It is apparent that lactose has an as yet unknown effect on intestinal conditions which is counteracted by butter fat but not by corn oil.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

THE FRACTIONAL CEPHALIN-CHOLESTEROL FLOCCULATION TEST

IN a recent communication, Bruger[1] proposed a fractional cephalin-cholesterol flocculation test to be used as an index of increasing or decreasing hepatic pathology. The modification consisted in the utilization of increasing dilutions of serum with saline and noting the flocculation according to the procedure originally described by Hanger.[2] The data presented

[1] E. J. Schantz, C. A. Elvehjem and E. B. Hart, *Jour. Dairy Science,* 23: 181, 1940.
[2] R. K. Boutwell, R. P. Geyer, C. A. Elvehjem and E. B. Hart, *Jour. Dairy Science,* 26: 429, 1943.
[1] M. Bruger, SCIENCE, 97: 585, 1943.
[3] A fat-free water extract. One part equals twenty parts of whole fresh liver.
[4] P. H. Phillips and E. B. Hart, *Jour. Biol. Chem.,* 109: 657, 1935.