synthesized by inversion of an altrose-2-mesylate and will be the subject of a future paper.

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RECEIVED JUNE 24, 1953

2,6-DI-BUTYLPYRIDINE—AN UNUSUAL PYRIDINE BASE

Sir:

2,6-Di-*t*-butylpyridine was synthesized by the reaction of *t*-butyllithium with 2-*t*-butylpyridine.

Excess *t*-butyllithium, prepared from 0.5 mole of *t*-butyl chloride and 1.0 mole of lithium sand in ethyl ether, was added to 0.2 mole of 2-*t*-butylpyridine in 200 ml. of purified 90–100° petroleum ether. The reactants were maintained at −78° for several hours. The temperature was then raised and solvent removed by distillation until the mixture refluxed at 70°. After seven hours, the mixture was hydrolyzed and the base recovered by distillation. The yield was 18.8 g. (0.099 mole) of 2,6-di-*t*-butylpyridine (b.p. 100–101° at 23 mm., $n^{20}D$ 1.5733).

Anal. Calcd. for $C_{13}H_{21}N$: C, 81.6; H, 11.0; N, 7.3. Found: C, 81.4; H, 10.9; N, 7.5.

The picrate could not be prepared. The chloroaurate melted at 184.2–184.5.

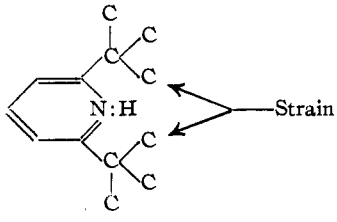
Anal. Calcd. for $C_{13}H_{22}NAuCl_4$: C, 29.4; Au, 37.1. Found: C, 29.7; Au, 36.9.

The base reacts with hydrogen chloride. However, it does not react with methyl iodide or with boron trifluoride. The base thereby permits the quantitative separation of hydrogen chloride from a mixture containing boron trifluoride. For the first time we have a simple method of distinguishing between protonic and Lewis acids.

2,6-Di-*t*-butylpyridine is a relatively weak pyridine base. The pK_a values, measured in 50% aqueous ethanol at 25°, for this and related compounds are

R	Pyridine	2-RC_5H_4N	2,6-$R_2C_5H_3N$
Methyl	4.38	5.05	5.77
Isopropyl	4.38	4.82	5.34
t-Butyl	4.38	4.68	3.58

Thus, 2,6-di-*t*-butylpyridine is weaker than expected by 1.4 pK_a units. We attribute the low pK_a value to steric strain involving the bound proton. The result suggests that the steric requirements of the lone pair on the nitrogen atom must be less than those of the hydrogen atom and its bonding pair.



It follows that the homomorphic molecule, *m*-di-*t*-butylbenzene, should also be strained. This proposal of steric interaction operating between large bulky groups with meta orientation appears capable of accounting for a considerable number of otherwise anomalous data in the literature.

In contrast to other pyridine bases, 2,6-di-*t*-butylpyridine undergoes ready nuclear sulfonation by sulfur trioxide. Identical solutions of sulfur trioxide in liquid sulfur dioxide were prepared. To the solutions (−10°) were added equimolar amounts of pyridine, 2,6-lutidine and 2,6-di-*t*-butylpyridine. After four hours, the solvent was evaporated and the products recovered. Pyridine and 2,6-lutidine formed the sulfur trioxide addition compounds, whereas the 2,6-di-*t*-butylpyridine formed a sulfonic acid, m.p. (dec.) 310°.

Anal. Calcd. for $C_{13}H_{21}NSO_3$: C, 57.6; H, 7.8; N, 5.2. Found: C, 57.5; H, 7.8; N, 5.1.

The S-benzylthiouronium derivative melted at 216.0–216.5°.

Anal. Calcd. for $C_{21}H_{31}N_3S_2O_3$: N, 9.6. Found: N, 9.6.

The product is presumably the 4-sulfonic acid. We are presently attempting to confirm the structure by an independent synthesis. This ready substitution of a pyridine base must result from the blocking of the nitrogen atom. With coördination impossible, the electrophilic reagent readily attacks the heterocyclic nucleus. The result supports the conclusion that the inertness of pyridine rings results primarily from interaction of electrophilic reagent with the lone pair and not from any unusual inertness of the pyridine nucleus.

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RECEIVED JUNE 12, 1953

THE STRUCTURE OF CHAMAZULENE

Sir:

It has been previously reported that the blue essential oil obtained by steam distillation of *Artemisia absorescens* L. contains an azulene.[1,2] This azulene has now been identified as chamazulene by means of its derivatives (trinitrobenzene complex, m.p. 132°, the melting point was not depressed on admixture with an authentic sample; picrate, m.p. 116°) and its infrared spectrum.

The structure of chamazulene, the azulene from camomile oil,[3] has not as yet been established, but from the spectral measurements of Plattner[4] it has been generally assumed to be 1,5-dimethyl-8-isopropylazulene.[5] During the course of this investigation it has been possible to prove its structure as 1,4-dimethyl-7-ethylazulene.

From the acetone cold extract of the above-mentioned plant a crystalline substance was isolated, the analysis of which corresponded to the formula $C_{15}H_{20}O_3$, m.p. 145°, $[\alpha]^{20}D$ +63° ($CHCl_3$) (*c* 4.24) (*Anal.* Calcd.: C, 72.7; H, 8.1. Found: C, 72.8; H, 8.2).

(1) G. Pellini, *Ann. chim. appl.*, **13**, 97 (1923); *Chem. Zentr.*, **94**, IV, 607 (1923).

(2) A. Weizmann, *Bull. Research Council Israel*, **1**, 92 (1952).

(3) L. Ruzicka and A. J. Haagen-Smit, *Helv. Chim. Acta*, **14**, 1104 (1931).

(4) Pl. A. Plattner, *ibid.*, **24**, 283E (1941).

(5) L. H. Chopard-dit-Jean and E. Heilbronner, *ibid.*, **35**, 2187 (1952).

This new compound, on which details will be given in a later publication, contains a double bond and as functional groups an ether and a lactone group. On dehydrogenation with sulfur it yielded chamazulene.

As dehydrogenation of lactones usually involves decarboxylation,[6] it was inferred that chamazulene might be a C_{14} compound. In fact our analysis of chamazulene and its derivatives agreed with formula $C_{14}H_{16}$ for the azulene, rather than with the generally accepted $C_{15}H_{18}$ formula.

	Calcd. for $C_{14}H_{16}$			Calcd. for $C_{15}H_{18}$			Found		
	C	H	N	C	H	N	C	H	N
Azulene	91.25	8.75		90.85	9.15		91.5	8.5	
TNB	60.45	4.82	10.52	61.31	5.15	10.22	60.1	4.5	10.4
Picrate	58.11	4.63	10.17	59.01	4.95	9.83	58.4	4.5	10.3
Mol. wt.[a]		413.4			427.4			413.3 ± 4	

[a] Determined by titration of the picrate.

Lithium aluminum hydride reduction of the lactone $C_{15}H_{20}O_3$, followed by dehydration, yielded an azulene, which was identified as S-guaiazulene, the constitution of which has been firmly established as 1,4-dimethyl-7-isopropylazulene.[7]

This result indicated that the structures of chamazulene and S-guaiazulene differed only in respect of the substituent in the 7-position, which is the ethyl group in chamazulene and the isopropyl group in S-guaiazulene.

This assumption was confirmed in the following way. 2,8-Dimethylbicyclo[5.3.0]decan-5-one (I) was prepared from guaiol (isolated from guaiacwood oil) by hydrogenation to dihydroguaiol in presence of Raney nickel, followed by chromic acid oxidation. Treatment of the ketone (I) with ethylmagnesium bromide yielded the carbinol (II), b.p. 95–100° at 0.4 mm.; (*Anal.* Calcd. for $C_{14}H_{26}O$: C, 79.9; H, 12.5. Found: C, 80.2; H, 12.8). Upon dehydration and deh drogenation with sulfur at 200°, the carbinol (II) was converted into an azulene, identified by its derivatives and its infrared spectrum as chamazulene.

We wish to thank Dr. A. Fuerst, Zürich, for kindly supplying a sample of chamazulene trinitrobenzoate. Chuit, Naef Co., Geneva, generously made available the guaiacwood oil.[8]

(6) L. Ruzicka and J. A. van Melsen, *Helv. Chim. Acta*, **14**, 397 (1931).

(7) Pl. A. Plattner, A. Fuerst, L. Marti and H. Schmid, *ibid.*, **32**, 2137 (1949).

(8) Pl. A. Plattner and G. Magyar, *ibid.*, **25**, 581 (1942).

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RECEIVED JUNE 25, 1953

BOOK REVIEWS

Vitamins and Hormones—Advances in Research and Applications. Volume X. By ROBERT S. HARRIS, Professor of Biochemistry of Nutrition, Massachusetts Institute of Technology, Cambridge, Massachusetts; G. F. MARRIAN, Professor of Medical Chemistry, University of Edinburgh, Edinburgh, Scotland; and KENNETH V. THIMANN, Professor of Plant Physiology, Harvard University, Cambridge, Massachusetts (Editors). Academic Press, Inc., 125 East 23rd Street, New York 10, N. Y. 1952. xi + 421 pp. 16.5 × 23.5 cm. Price, $8.00.

This volume contains ten review articles, the great majority of which are concerned with hormone research. The heavy weighting in this direction emphasizes the great interest and effort in this field.

Drawing heavily from clinical observations obtained from prisoner-of-war camps and undernourished populations during World War II, K. Cruickshank, writing on "Dietary Neuropathies," discusses the clinical syndromes and their relationships to nutritional deficiencies. "The Problem of the Absorption and Transportation of Fat-Soluble Vitamins" by A. E. Sobel reviews work mainly concerned with the transport of Vitamin A, as a model of the fat-soluble vitamins, and emphasizes the problem of poor absorption and transport, rather than insufficient intake, as a cause of deficiency. The limited amount of research on "The Nutrition of Crustacea" is indicated by the brevity of this review of E. Beerstecher, Jr., who points out, however, the possibilities of studies in this area in evaluating and applying principles of comparative physiology and biochemistry.

"Nutrition and the Anterior Pituitary with Special Reference to the General Adaptation Syndrome" by B. H. Ershoff is an extensive and excellent review in which are discussed the interrelationships between various nutrients and the endocrine glands. The profound and complex effects of nutrients upon the synthesis, secretion, metabolism and the response of target organs, as well as the converse effects of the endocrine glands on the absorption, utilization, and requirements for specific dietary factors are very well described.

R. Booth and H. de Watteville in "Hormone Assays in Obstetrics and Gynecology" give a critical discussion of the use of hormone assays in gynecological and clinical practice. Specific methods are discussed and not only their usefulness but also their limitations are pointed out. R. P. Ogilvie presents a well organized review of "Experimental Glycosuria, Its Production, Prevention and Alleviation" under the broad classifications of insulin insufficiency, hormones, diet, glycogenolysis and kidney. K. L. Blaxter reviews "Some Effects of Thyroxine and Iodinated Casein on Dairy Cows, and Their Practical Significance." The effects upon the production and composition of milk, and upon the metabolism of the cow are discussed.

The last three articles deal more directly with the metabolism and the effects on metabolism of the steroid hormones. L. T. Samuels and C. D. West review "The Intermediary Metabolism of the Non-Benzenoid Steroid Hormones." Data and conclusions for the metabolism of androgens, progestins and the steroids of the adrenal cortex based upon experiments *in vitro* with various tissues, and also upon *in vivo* studies of urinary excretory products are included. An analysis of the relationship of adrenal cortex action to the central process of energy production of the cell based upon studies of cell enzymes is the subject of the excellent review, "The Influence of Corticoids on Enzymes of Carbohydrate Metabolism" by F. Vezar. The final article, "Steroids and Tissue Oxidation" by R. I. Dorfman, is concerned with steroid-enzyme relationships including effects upon tissue enzyme concentrations and upon specific enzyme systems.

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