The n.m.r spectra of I and II exhibit axial–axial splitting for H_1 and H_2 (I, $J_{1a,2a}$ = 7.6 cps.; II, $J_{1a,2a}$ = 8.6 cps.). The resulting absolute configuration at C-1, as indicated in II, agrees with that predicted, according to Hudson's rules, for a sugar in the D-series which mutarotates to a more positive value (*i.e.*, a β-D sugar).[8]

Thus, the second sugar obtained as a degradation product of chalcomycin has been isolated as 6-deoxy-2,3-di-O-methyl-β-D-allose.

(8) C. S. Hudson, "Advances in Carbohydrate Chem.," **3**, 15 (1948).

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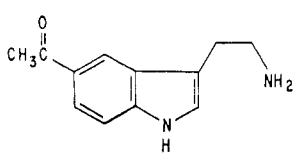
RECEIVED DECEMBER 22, 1961

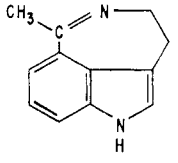
ACYLTRYPTAMINES. I. 5-ACETYLTRYPTAMINE AND RELATED COMPOUNDS

Sir:

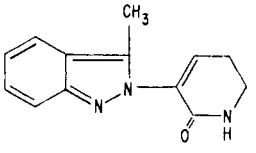
The interest in 5-hydroxytryptamine (serotonin) and the total synthesis of reserpine has resulted in the preparation of a multiplicity of tryptamines for use in biological and synthetic investigations. The results of our efforts in another field led to our preparation of a series of novel tryptamines having acyl groups in the benzene ring. The discovery of the unusual hypotensive[1] properties of 5-acetyltryptamine (I) and some interesting chemical transformations during this extensive synthetic program has prompted us to publish some of our findings at this time.



I



XI



XIII

The Japp-Klingemann reaction of *p*-acetylbenzenediazonium chloride with 2-oxopiperidine-3-carboxylic acid[2] gave the corresponding 3-(*p*-acetylphenyl)hydrazone of 2,3-piperidinedione (II, m.p. 229–231°, λ_{max}^{EtOH} 238 mμ, ε 10,800, 351 mμ, ε 42,000. Calcd. for $C_{13}H_{15}N_3O_2$: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.40; H, 6.28; N, 16.93). Refluxing II with 88% formic acid for four hours gave 6-acetyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]-indol-1-one (III; m.p. 370–372°, λ_{max}^{EtOH} 273 mμ, ε 42,250, 302 mμ, ε 8,800. Calcd. for $C_{13}H_{12}N_2O_2$: C, 68.40; H, 5.30; N, 12.27. Found: C, 68.35; H, 5.33; N, 12.08). Hydrolysis[3] of III in refluxing 2 *N* KOH in 60% aqueous ethanol gave 5-acetyl-2-carboxytryptamine (IV, m.p. 337–343°, λ_{max}^{EtOH} 266.5 mμ, ε 47,000, 303 mμ, ε 8,000. Calcd. for $C_{13}H_{14}N_2O_3 \cdot H_2O$: C, 59.08; H, 6.10; N, 10.60. Found: C, 59.04; H, 6.18; N, 10.77). Decarboxylation of IV in refluxing 20% hydrochloric acid containing 30% by volume glacial acetic acid gave 5-acetyltryptamine (I, m.p. 140–142°, λ_{max}^{EtOH} 254 mμ, ε 34,400, 299 mμ, ε 7,850. Calcd. for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.85. Found: C, 70.99; H, 6.93; N, 14.09).

Reaction of *m*-acetylbenzenediazonium chloride with 2-oxopiperidine-3-carboxylic acid gave the 3-(*m*-acetylphenyl)hydrazone of 2,3-piperidinedione (V, m.p. 204–206°, λ_{max}^{EtOH} 233 mμ, ε 19,500, 312.5 mμ, ε 21,200. Calcd. for $C_{13}H_{15}N_3O_2 \cdot 0.5H_2O$: C, 61.40; H, 6.34; N, 16.53. Found: C, 61.58; H, 6.59; N, 16.87). Refluxing V with 88% formic acid gave a mixture of 5-acetyl and 7-acetyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-ones which were separated by fractional crystallization from absolute ethanol. The less soluble 7-acetyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-one (VI) had the m.p. 283–286°, λ_{max}^{EtOH} 248 mμ, ε 27,100, 315 mμ, ε 23,700. Calcd. for $C_{13}H_{12}N_2O_2$: C, 68.40; H, 5.30; N, 12.27. Found: C, 68.30; H, 5.38; N, 12.45. The more soluble 5-acetyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-one (VII) had the m.p. 241–243°, λ_{max}^{EtOH} 223 mμ, ε 24,500, 258 mμ, ε 11,800, 327 mμ, ε 10,090. Calcd. for $C_{13}H_{12}N_2O_2$: C, 68.40; H, 5.30; N, 12.27. Found: C, 68.62; H, 5.48; N, 12.06.

Hydrolysis of VI in refluxing 2 *N* KOH in 60% aqueous ethanol gave 6-acetyl-2-carboxytryptamine (VIII, m.p. 240–243°, λ_{max}^{EtOH} 249 mμ, ε 25,300, 309 mμ, ε 21,700. Calcd. for $C_{13}H_{14}N_2O_3 \cdot H_2O \cdot 0.5 \cdot C_2H_5OH$: C, 58.52; H, 6.66; N, 9.75. Found: C, 58.74; H, 6.40; N, 9.73). Decarboxylation of VIII in refluxing 20% hydrochloric acid gave 6-acetyltryptamine[4] (IX, m.p. 148–150°, λ_{max}^{EtOH} 233 mμ (shoulder), ε 15,500, 253 mμ, ε 21,400, 301 mμ, ε 12,900. Calcd. for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.85. Found: C, 71.38; H, 7.18; N, 14.08).

Hydrolysis of VII in refluxing 2 *N* KOH in 60% aqueous ethanol gave 4-acetyl-2-carboxytryptamine (X, m.p. 314–317°, λ_{max}^{EtOH} 216 mμ, ε 30,000, 245–52 mμ (shoulder), ε 13,900, 260 mμ, ε 15,000. Calcd. for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.59; H, 5.99; N, 11.46). Decarboxylation of X in refluxing 20% hydrochloric acid containing 30% by volume glacial acetic acid gave 3,4-dihydro-6-methyl-1H-azepino[5,4,3-cd]-indole[5] (XI, m.p. 272–277°, λ_{max}^{EtOH} 241 mμ, ε 18,250. Calcd. for $C_{12}N_{12}N_2$: C, 78.22; H, 6.57; N, 15.21. Found: C, 77.98; H, 6.59; N, 15.36).

Reaction of *o*-acetylphenyldiazonium chloride with 2-oxo-piperidine-3-carboxylic acid gave the 3-(*o*-acetylphenyl)hydrazone of 2,3-piperidinedione (XII, m.p. 231–234°, λ_{max}^{EtOH} 230 mμ, ε 17,300, 254 mμ, ε 11,700, 312.5 mμ, ε 14,700, 369 mμ, ε 13,200.

(1) We thank Dr. Max Ben of the Department of Pharmacology for the observation of this hypotensive activity in the dog.

(2) R. A. Abramovitch and D. Shapiro, *Chem. and Ind.*, 1255 (1955); *J. Chem. Soc.*, 4589 (1956).

(3) S. Keimatsu, S. Sugasawa and G. Kasuya, *J. Pharm. Soc.* (Japan), **48**, 762 (1928); *Chem. Abstr.*, **23**, 834 (1929).

(4) This compound showed pressor activity in the dog, according to Dr. M. Osborne of the Department of Pharmacology.

(5) This compound represents the first of a series of derivatives of the novel ring system 1H-azepino[5,4,3-cd]indole.

Calcd. for $C_{13}H_{15}N_3O_2$: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.90; H, 6.42; N, 17.15). Refluxing XII with 88% formic acid gave *inter alia* a basic material having the m.p. 196–197°, λ_{max}^{EtOH} 275 mμ, ε 7,000, 293 mμ, ε 6500.[6] On the basis of spectral and degradative data this material has been tentatively assigned the structure XIII, 3-methyl-2-(1,2,5,6-tetrahydro-2-oxo-3-pyridyl)-2H-indazole.[7]

The preparation of these and other synthetic variants of acyltryptamines and related compounds will be described in detail in our forthcoming papers.

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RECEIVED DECEMBER 28, 1961

(6) V. Rousseau and H. G. Lindwall, *J. Am. Chem. Soc.*, **72**, 3047 (1950), report $\lambda_{max}^{H_2O}$ 275 mμ, ε 5800, 293 mμ, ε 5900 for 2-methylindazole. Elemental analyses of XIII for nitrogen done in three independent laboratories fail to agree although carbon and hydrogen values are consistent.

(7) The details of the structure elucidation of XIII and related compounds will be described in future publications.

BOOK REVIEWS

The Determination of Stability Constants and Other Equilibrium Constants in Solution. By FRANCIS J. C. ROSSOTTI and HAZEL ROSSOTTI, Department of Chemistry, University of Edinburgh. McGraw-Hill Book Co., Inc., 330 West 42nd Street, New York 36, N. Y. 1961. xiv + 425 pp. 16 × 23.5 cm. Price, $12.50.

The last two decades have seen an enormous increase in the study of complexes and the measurement of complex stabilities. This volume summarizes the many methods that have been used to determine stability, describes in detail the often intricate calculations, and gives a remarkably thorough bibliography of work in this field. It concerns itself with ionic and molecular association in all their forms. Quite properly, the emphasis is on methods of determination rather than on the compilation of data. The authors believe that experiments to determine stability constants have heretofore often been ill-designed and that the experimental data are not always subjected to a sufficiently rigorous mathematical analysis. They have accordingly devoted considerable space to the many ingenious methods, many of them graphical, for deriving accurate stability constants from the experimental data. Much of the latter material derives from the British and Scandinavian schools of coördination chemistry, with both of which the authors have been closely identified.

In principle, any property which varies with the degree of complex formation can be used to determine the position of equilibrium. The most useful techniques for measuring these properties are outlined. The methods described in detail are potentiometry, polarography and amperometry, solubility, liquid–liquid partition, ion exchange, freezing point, boiling point, vapor pressure, optical and spectroscopic methods, and reaction kinetics. Fifteen of the 18 chapters are devoted to mononuclear complexes formed with only a single type of ligand. The remaining three chapters consider polynuclear systems and mixed complexes.

This new book provides a welcome degree of systematization to the field of coördination chemistry. The reactions considered are always those for the *formation* of the complex species; hence, the terms "instability constant," "dissociation constant," and "ionization constant" are unnecessary and are not used. Nevertheless, in the reviewer's opinion, it is rather artificial to classify weak acids with metal complexes. A great majority of common solvents are protogenic or protophilic in some degree; hence, the dissociation of acetic acid, for example, is generically quite a different process from that by which the ammine complex of copper is broken into its constituent parts. The suggestion that the electron may be regarded as a ligand in oxidation–reduction equilibria will be regarded by many as an instance of carrying systematization a step too far.

For practical reasons, many, if not most, stability constants are neither activity quotients nor thermodynamic constants, but rather are concentration constants determined in a constant ionic medium, usually of high ionic strength. The various types of stability constants and the basic principles upon which their determination is based are very capably described. It is further evident that the authors are aware of the limitations of the "constant medium" procedure and of the unfortunate fact that stabilities determined in different constant ionic media cannot strictly be compared.

Nevertheless, it should not be implied (as on p. 29) that "in the presence of high concentrations of background salt . . . the activity coefficient of the solute may . . . be assumed to approach that of the bulk electrolyte," in other words, that through its mere preponderance, electrolyte B is able to impose its properties on electrolyte A. This is demonstrably untrue. In a mixture of 0.01 *M* hydrochloric acid and 2.99 *M* sodium chloride, the activity coefficient of sodium chloride is 0.714. According to this postulate, the activity coefficient of the hydrochloric acid should also be 0.714 in the mixture, but experiment shows it to be 1.062. Although the activity coefficients of different cations (whatever they may be) can possibly be rendered constant by this means, it seems certain that they cannot be made equal. Furthermore, a "swamping electrolyte" without a common ion (*e.g.*, sodium perchlorate) can likely do no better.

The large number of symbols employed (105, drawing heavily on the English, Greek and German alphabets, are listed and defined in the front of the book) assures the rigor of the treatment but detracts somewhat from the readability. The book is exceedingly well written, carefully edited, and attractively printed. The discussion is thorough and authoritative; very few errors of fact were noted and none of typography. This volume should be a part of the library of anyone concerned with the determination of stability constants.

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Probability and Experimental Errors in Science. An Elementary Survey. By LYMAN G. PARRATT, Professor of Physics, Chairman of the Department of Physics, Cornell University, Ithaca, New York. John Wiley and Sons, Inc., 440 Park Avenue South, New York 16, N. Y. 1961. xv + 255 pp. 15.5 × 23.5 cm. Price, $7.25.

Nearly thirty-five years have passed since Sir Ronald A. Fisher wrote "Statistical Methods for Research Workers" to show experimenters how their traditional but inadequate machinery for summarizing measured data can be replaced with a rigorous statistical methodology based on logical relationships between small-sample statistics and population parameters.

Sir Ronald developed this methodology in collaboration with research workers in the biological sciences, and it has been adopted in many fields of applied science and technology since that time. Research workers in the physical sciences have been slow to replace the traditional treatment with small-sample statistical methods; and very