I. If the difference in the free energies of the parent ketone (cation) and the product thiazolium cation is approximately independent of the nature of the solvent, the free energy of the methanolysis differs from the free energy of the hydrolysis by the free energy of hydrolysis of methyl benzoate. The data required to evaluate this latter are lacking. However, Hammett[5] reports that all esterification reactions have nearly the same equilibrium constant. Accordingly it seems reasonable to carry over to methyl benzoate the value cited by Carpenter[6] for the free energy of hydrolysis of ethyl acetate. With these assumptions the free energy of hydrolysis of I to 3,4-dimethylthiazolium ion + benzoate ion at pH 7 should be ~ 7 kcal./mole more negative than the free energy of methanolysis we estimate above.

This high free-energy of hydrolysis of a carbon-carbon bond in a 2-acylthiazolium ion appears to place this type of ketone above adenosinetriphosphate, acetyl phosphate and other classical "high energy" anhydrides.

The instability of 2-acylthiazolium compounds shows that the postulated intermediate 2-acetylthiaminepyrophosphate is able to react with phosphate ion to produce acetyl phosphate and thiamine pyrophosphate in the reaction catalyzed by phosphoketolase.[7]

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[5] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 213.

[6] F. H. Carpenter, *J. Am. Chem. Soc.*, **82**, 1111 (1960).

[7] E. C. Heath, J. Hurwitz, B. L. Horecker and A. Ginsburg, *J. Biol. Chem.*, **231**, 1009 (1958).

[8] We wish to thank the American Cancer Society for generous financial support of this project.

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RECEIVED JULY 10, 1961

SERRATAMOLIDE, A METABOLIC PRODUCT OF *SERRATIA*

Sir:

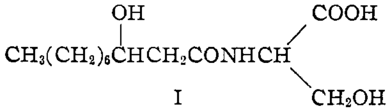
During studies on the pigments produced by *Serratia*[1a,b] we have isolated a neutral metabolite from cultures of strains HY-3,[2a] 9-3-3[2b] and P-1.[2c]

This product, which we name serratamolide, and to which we assign structure II, can be isolated from liquid cultures by methylene chloride extraction, or from cultures grown on agar plates by extraction with acetone. It can be crystallized from ethanol as fine white needles, m.p. 159–160° (uncorr.): $\alpha^{25}{}_D$ + 4.8° (ethanol); *Anal.* Calcd. for $C_{26}H_{46}O_8N_2$: C, 60.68; H, 9.01; N, 5.44; mol. wt., 515. Found: C, 60.90; H, 8.86; N, 5.22; mol. wt., 556 (Rast), 543 (ebullioscopic, acetone).[3]

Serratamolide shows no absorption in the ultraviolet above 200 mμ. It contains two C-methyl groups in Kuhn–Roth analysis, no methoxyl (Zeisel) and no amino nitrogen (Van Slyke). The infrared spectrum shows strong absorption at 5.79, 6.05 and 6.46 as well as a peak at 3.01μ (KBr).

The presence of two hydroxyl groups in the molecule is indicated by the formation of these derivatives: *diacetyl derivative*, m.p. 222.5–223° (dec.), calcd. for $C_{30}H_{50}O_{10}N_2$: C, 60.18; H, 8.42; N, 4.68; mol. wt., 599. Found: C, 60.49; H, 8.49; N, 4.78; mol. wt., 599 (ebullioscopic, $CHCl_3$). *Ditetrahydropyranyl ether* (mixture of isomers), m.p. 140–145°, calcd. for $C_{36}H_{62}O_{10}N_2$: C, 63.31; H, 9.15; N, 4.10; mol. wt., 683. Found: C, 63.64; H, 9.19; N, 4.03; mol. wt., 712 (ebullioscopic, $CHCl_3$). *Ditosyl derivative* (unstable), m.p. 150° (dec.), calcd. for $C_{40}H_{58}O_{12}S_2N_2$: C, 58.37; H, 7.10; N, 3.41; S, 7.79. Found: C, 58.54; H, 7.43; N, 3.62; S, 7.09. *Ditrityl ether*, m.p. 186–187.5°, calcd. for $C_{64}H_{74}O_8N_2$: C, 76.92; H, 7.47; N, 2.80; mol. wt., 999. Found: C, 77.05; H, 7.27; N, 2.65; mol. wt., 900 (thermoelectric).

Mild hydrolysis of serratamolide in 1 *N* NaOH at room temperature yielded an acid, m.p. 137–138° (dec.), in nearly quantitative yield, which proved identical in m.p., mixture m.p., and infrared spectra with serratamic acid[4] recently isolated by Cartwright from several strains of organisms of the *Serratia* group, and shown to be I.



$$CH_3(CH_2)_6CH(OH)CH_2CONHCH(COOH)CH_2OH$$

I

As would be expected from Cartwright's findings, more vigorous hydrolysis of serratamolide in hot concentrated hydrochloric acid yielded serine, identified by ion exchange chromatography,[5] and an oily acid-insoluble component, which was shown to be 3-hydroxydecanoic acid by comparison of its ethyl ester with synthetic ethyl 3-hydroxydecanoate. Thus, serratamolide and serratamic acid (I) are related as shown in the equation

$$C_{26}H_{46}O_8N_2 + 2H_2O \longrightarrow \underset{\text{I}}{2C_{13}H_{25}O_5N}$$

The generation of two molecules of I, containing free hydroxyl and carboxyl groups from the neutral serratamolide as represented above must involve the hydrolysis of a dilactone such as II, III, or IV (see formula).

Of these possibilities, structure IV, containing four different carbonyl groups, is in poor agreement with the infrared evidence,[6] while structure II, in

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[1] (a) H. H. Wasserman, J. E. McKeon, L. Smith and P. Forgione, *J. Am. Chem. Soc.*, **82**, 506 (1960); (b) H. H. Wasserman, J. E. McKeon and U. V. Santer, *Biochem. and Biophys. Research Commun.*, **3**, 146 (1960).

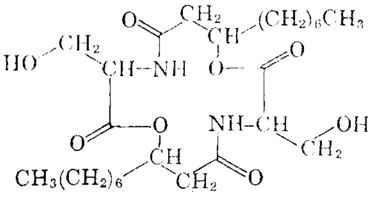
[2] (a) Strain HY-3 was provided by Dr. Mary I. Bunting. See E. L. Labrums and M. I. Bunting, *J. Bacteriol.*, **65**, 394 (1953); (b) U. V. Santer, Ph.D. Dissertation, Yale University, 1958; (c) M. T. M. Rizki, *Proc. Natl. Acad. Sci., U.S.* **40**, 1057 (1954).

[3] It is possible that serratamolide may be the same substance as the colorless product, m.p. 153°, isolated by O. M. Efimenko, G. A. Kuznetsova and P. A. Yakimov from *B. prodigiosus* cultures and assigned the molecular formula $C_{34}H_{62}O_{10}N_3$: *Biokhimiya*, **21**, 416 (1956). See also the report of a colorless compound $C_{24}H_{42-44}O_7N_2$, m.p. 154.3–156°, isolated from the Z-4 strain of *Serratia marcescens* by A. J. Castro, A. H. Corwin, F. J. Waxham and A. L. Beilby, *J. Org. Chem.*, **24**, 455 (1959).

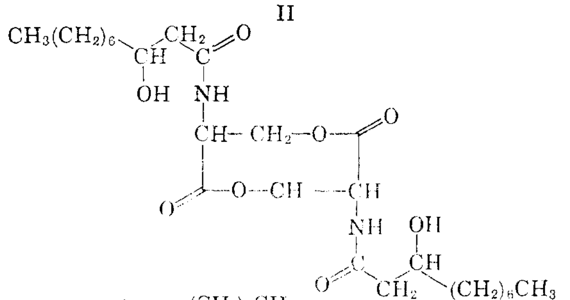
[4] N. J. Cartwright, *Biochem. J.*, **60**, 238 (1955); *ibid.*, **67**, 663 (1957). We thank Dr. Cartwright for an authentic sample of serratamic acid for comparison.

[5] Beckman/Spinco Amino Acid Analyzer, Model MS.

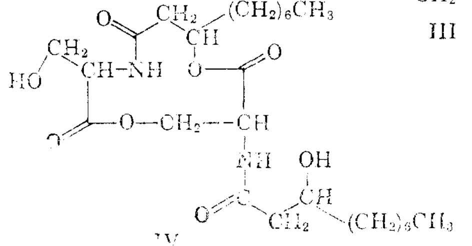
[6] In the depsipeptide, valinomycin, related to II (H. Brockmann and G. Schmidt-Kastner, *Ber.*, **88**, 57 (1955); H. Brockmann and H. Geeren, *Ann.*, **603**, 216 (1957)) the main infrared peaks in KBr are found at 5.75, 6.02 and 6.50 μ. Prof. Brockmann kindly sent us a sample of valinomycin for the infrared comparison.



II



III



IV

which both hydroxyl groups are primary, is favored by the ready formation of a ditrityl derivative.

Evidence which served to distinguish unambiguously among the above structures was provided by the following sequence of reactions: (i) Treatment of serratamolide with methanesulfonyl chloride in pyridine gave the unstable dimethanesulfonyl derivative, m.p. 125–127° (dec.), which was converted rapidly with lithium bromide in methyl ethyl ketone to the neutral dibromo derivative, m.p. 170° (dec.). Calcd. for $C_{26}H_{44}O_6N_2Br_2$: C, 48.76; H, 6.92; N, 4.37; Br, 24.96. Found: C, 49.13; H, 6.75; N, 4.48; Br, 24.40. (ii) Hydrogenation of the dibromo derivative[7] (Pd/methanol/NaOH) yielded a debrominated product (not isolated) which was immediately hydrolyzed with concd. HCl, producing a mixture of acids. As a result of these changes (—OH → —O—Mesyl → —Br → —H), II would yield alanine and 3-hydroxydecanoic acid, III would yield serine and decanoic acid, while IV would give rise to all four of the above acids.

Examination of the aqueous acidic hydrolyzate by both paper chromatography and ion-exchange chromatography[5] showed alanine (67%) as the only amino acid present in more than trace amounts. A control hydrolysis of serratamolide under the same conditions gave serine in 92% yield. The other acidic product of the sequence outlined in (i) and (ii) above, obtained by ether extraction of the hydrolysate, was methylated with diazomethane and was shown by vapor phase chromatography to be the methyl ester of 3-hydroxydecanoic acid. No peak corresponding to methyl decanoate was detected.

Structure II is thus unique in accommodating all of the properties of serratamolide, which differs from the depsipeptides[8] such as valinomycin and the enniatins in that it contains β-hydroxy acid, rather than α-hydroxy acid residues.

This work was supported in part by Grant P-64 of the American Cancer Society and by USPH Grant E-1729.

[7] *Cf.* reduction of chloroserratamic acid to deoxyserratamic acid, N. J. Cartwright, *Biochem. J.*, **67**, 668 (1957).

[8] See the review of depsipeptides by M. M. Schemjakin, *Angew Chem.*, **72**, 342 (1960).

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RECEIVED AUGUST 18, 1961

OXAZAHYDROBORATE IONS

Sir:

We wish to report the preparation of three members of a new class of hydroborate ions which apparently contain the oxaza (NO) group. These anions were obtained by the reaction of nitrogen dioxide with the perhydrodecaborate ($B_{10}H_{10}^{-2}$) ion,[1,2] or by the reaction of this ion with nitric oxide in the presence of ferric ion. These conditions suggest that an oxidation-reduction reaction is involved. Molecular weights and magnetic properties have not been determined as yet and thus only the simplest empirical formulas are reported.

Addition of 0.010 mole NO_2 in 100 ml. of methylene chloride to a solution of 0.010 mole of triethylammonium perhydrodecaborate in 100 ml. of 10% aqueous acetonitrile at 0° produced a dark blue solution from which $B_{14}H_{12}NO(NHEt_3)_2$ was isolated in 60–65% yield, as purple crystals.

Anal. Calcd. for $C_{12}H_{44}B_{14}N_3O$: C, 36.21; H, 11.14; B, 38.06; N, 10.56. Found: C, 36.26; H, 11.36; B, 37.36; N, 10.46.

The compound also could be obtained when ferric ion and nitric oxide were employed instead of nitrogen dioxide. However, the presence of by-products made the purification more difficult. The oxaza group readily was reduced by Raney nickel-catalyzed hydrogenation to the corresponding amino hydroborate salt, $B_{14}H_{13}NH_2(NHEt_3)_2$. Its infrared spectrum showed N-H stretch (2.80μ) and deformation (6.42μ) in addition to the —NH stretch of the cation (3.22μ).

Anal. Calcd. for $C_{12}H_{47}B_{14}N_3$: C, 37.43; H, 12.30; B, 39.34; N, 10.91. Found: C, 37.51; H, 11.96; B, 39.30; N, 10.30.

Two other oxazahydroborate ions were formed when gaseous nitrogen dioxide was introduced into a 10% aqueous acetonitrile solution of perhydrodecaborate ion. In this case compounds were obtained which contained more than one NO group per hydroborate ion. These materials were red crystalline solids which had compositions $[B_{10}H_6(NO)_2 \cdot N(CH_3)_4]$ (calcd.: C, 20.67; H, 7.80; B, 46.56; N, 18.08. Found: C, 20.38; H, 7.61; B, 46.27; N, 17.93); and $[B_{10}H_4(NO)_3 \cdot N(CH_3)_4]$(calcd.: C, 17.38; H, 5.83; B, 39.14;

[1] M. F. Hawthorne and A. R. Pitochelli, *J. Am. Chem. Soc.*, **81**, 5519 (1959).

[2] W. N. Lipscomb, A. R. Pitochelli and M. F. Hawthrone, *ibid.*, **81** 5833 (1959).