CF_2, 47 g. of HgF_2 and 45 g. of HF was recovered 16.7 g. of $(CF_3CHCF_3)_2Hg$,[9] m.p. 38.8–39.0°, b.p. 154° (738 mm.), (Hg calcd. 39.9, found 40.1%; mol. wt., calcd. 503, found 510) bromine at *ca.* 150° yielded $CF_3CHBrCF_3$, b.p. 31°, reported b.p. 31.5–32.5°[10] (mol. wt., calcd. 231, found 230).

Reaction of 42 g. of $CF_3CF{=}CF_2$, 47 g. of HgF_2 and 57 g. of HF yielded 51.5 g. of $(CF_3CFCF_3)_2Hg$,[11,12] b.p. 116–117, after redistn., b.p. 116.6° (740 mm.), d^{20}_4 2.545, $n^{20}D$ 1.3271 (Hg, calcd. 37.2, found 37.2%; mol. wt., calcd. 539, found 559) iodine at *ca.* 140° yielded CF_3CFICF_3, b.p. 40.6° (740 mm.), f.p. $-61 \pm 2°$, d^{20}_4 2.0990, $n^{20}D$ 1.3283, reported b.p. 40°, $n^{20}D$ 1.327[13] (I, calcd. 42.9, found 43.3%; mol. wt., calcd. 296, found 302).

A mixture of 42 g. of $HgCl_2$ and 35 g. of HgF_2 with 18 g. of $CF_3CF{=}CF_2$ and 52 g. of HF gave 26.3 g. of $(CF_3CFCF_3)HgCl$, m.p. 77°, after recrystn., m.p. 77.7–78.1° (Hg, calcd. 49.5, found 49.6%; Cl, calcd. 8.8, found 8.6%; mol. wt., calcd. 405, found 399). Mercuric chloride and $(CF_3CFCF_3)HgCl$ did not react with $CF_3CF{=}CF_2$ and HF at 85°.[2]

Silver fluoride promotes the addition of HF to $CF_3CF{=}CF_2$ and to $CF_3CF{=}CFCF_3$. A 10 mole per cent. solution of AgF in HF yielded 47% CF_3CHFCF_3 and 28% $CF_3CHFCF_2CF_3$ at 125°.[2,4] Under comparable conditions KF is unreactive. Both salts are dissociated in HF.[14]

The above experiments show that although perfluoroölefins resist protonation by as strong an acid as anhydrous HF, H_0 *ca.* -10,[15] they nevertheless can react with silver and mercury ions at moderate temperatures. We postulate addition of metal ion to olefin followed by reaction with $H_nF_{n+1}^-$. The resulting branched chain fluoroalkylmercury compounds, which have not been prepared by other methods, are stable thermally and to HF, but the silver alkyls react to yield HF addition compounds.

Acknowledgment.—This work was supported in part by a grant from the National Science Foundation for which grateful acknowledgment is made.

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RECEIVED SEPTEMBER 5, 1961

(7) The addition of HgF_2 in AsF_3 to fluoroethylenes has been reported recently by Krespan.[8] The mechanism of addition was considered ionic, but was not investigated.

(8) C. G. Krespan, *J. Org. Chem.*, **25**, 105 (1960).

(9) First isolated from the reaction of $CF_2{=}CHCCl_2F$ with HgO and HF. J. H. Fried, Ph.D. Thesis, Cornell University, Sept., 1955.

(10) E. T. McBee, U. S. Patent 2,644,845; *Chem. Abs.*, **48**, 7044 (1954).

(11) First isolated by Middleton, who was following our procedure, and utilized for the preparation of thioketones.[12] We obtained $(CF_3CFCF_3)HgCl$ from our initial experiments with $CF_3CF{=}CF_2$, presumably, due to the presence of impurities or reaction of $(CF_3CFCF_3)HgF$ with CH_2Cl_2.

(12) W. J. Middleton, E. G. Howard and W. H. Sharkey, *J. Am. Chem. Soc.*, **83**, 2589 (1961); U. S. Patent 2,970,173.

(13) M. Hauptschein and M. Braid, *ibid.*, **83**, 2383 (1961).

(14) K. Fredenhagen and G. Cadenbach, *Z. physik. Chem.*, **A146**, 245 (1930).

(15) H. H. Hyman, M. Kilpatrick and J. J. Katz, *J. Am. Chem. Soc.*, **79**, 3668 (1957).

MECHANISM OF THIAMINE ACTION: A NEW TYPE OF "HIGH ENERGY" BOND

Sir:

In order to learn more about the function of thiamine pyrophosphate in the transfer of energy[1,2] in biological reactions, we have prepared 2-benzoyl-3,4-dimethylthiazolium iodide (I) and measured its heat of reaction with methanol to produce methyl benzoate and 3,4-dimethylthiazolium iodide. Compound I can be prepared in low yields from 2-benzoyl-4-methylthiazole and methyl iodide in dimethylformamide. Crystallization from acetonitrile gives crystals which decompose 159–162°.

Anal. Calcd. for $C_{12}H_{12}INOS$: C, 41.75; H, 3.50; I, 36.76; N, 4.06; S, 9.29. Found: C, 41.80; H, 3.65; I, 36.82; N, 4.23; S, 9.19.

The calorimetric measurements were made by using a ten-junction copper–constantan thermel to observe the temperature changes when an evacuated glass bulb containing 100–300 mg. of solid sample was shattered in a specially constructed, miniature Pyrex dewar flask containing 30.0 ml. of purified methanol at 25.0°. The validity of the calorimetric method was checked by obtaining a value for the heat of solution of potassium chloride in water which was in good agreement with the value given recently by Sacconi *et al.*[3] As a preliminary to the solvolysis measurements we determined the heat of solution of 2-(α-hydroxybenzyl)-3,4-dimethylthiazolium iodide (II) in methanol over the mole-fraction range 4–10 $\times$ 10^{-4}. We find this process to be endothermic by 7.3 ± 0.2 kcal./mole of II.

The thermal measurements on the reaction of I with methanol over the same mole-fraction range show clearly the endothermic solution process followed immediately by the exothermic solvolysis. Because of the rounded top of the time–temperature curves, some uncertainty, at most 1 kcal./mole of solid, attaches to the values we assign to the separate steps in the process. In our estimation the heat of solution of the ketone in methanol is $+9.9 \pm 0.1$ kcal./mole and the heat of methanolysis is -13.2 ± 0.3 kcal./mole of solid. By using the Parks and Huffman[4] table of group entropies, we estimate the entropy change in the reaction to be $\sim +5$ e.u. Thus the over-all free-energy change in the methanolysis of I is approximately -15 kcal./mole. It should be emphasized that this figure is an approximation to the free energy of reaction when all solute species are at infinite dilution in methanol. It is not necessarily the "standard" free energy of reaction, since this term is most commonly reserved for thermochemical measurements performed when all solute species are at unity activity. In our judgment the dilute-solution result is the more significant from a biochemical standpoint.

An even more interesting quantity is the free-energy change accompanying the hydrolysis of

(1) R. Breslow and E. McNellis, *J. Am. Chem. Soc.*, **82**, 2394 (1960).

(2) F. G. White and L. L. Ingraham, *ibid.*, **82**, 4114 (1960).

(3) L. Sacconi, P. Paoletti and M. Ciampolini, *ibid.*, **82**, 3828 (1960).

(4) G. S. Parks and H. M. Huffman, "The Free Energies of Some Organic Compounds," Chemical Catalog Co., New York, N. Y., 1932.

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 $\sim$ 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]

(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:

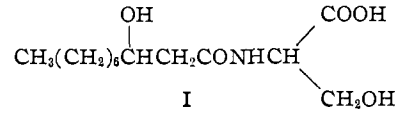
During studies on the pigments produced by *Serratia*[1a,b] we have isolated a neutral metabolite from cultures of strains HY-3,[2a] 9-3-3[2b] and P-1.[2c]

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.



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

$$C_{26}H_{46}O_8N_2 + 2H_2O \longrightarrow 2C_{13}H_{25}O_3N$$
$$\text{I}$$

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

(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 $C_{34}H_{62}O_{10}N_2$: *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.