purification was accomplished by ion-exchange chromatography of the acidified filtrate. DHAA was taken up on a column of Amberlite IR-120 (hydrogen form) and was then eluted with 1 *N* sulfuric acid. The quantity of product contained in the various eluate fractions was determined by spectrophotometric assay. Isolation of DHAA from the rich cuts was accomplished by removal of sulfate as barium sulfate and crystallization of the product from the resulting solution by concentrating and cooling. The crude product was recrystallized from glacial acetic acid to give (+)*trans*-**2,3-dihydro-3-hydroxyanthranilic acid,** m.p. (dec.) 190–191°. *Anal.* Found for $C_7H_9NO_3$: C, 53.78; H, 5.95; N, 8.82; neut. equiv., 156; pK_a (water), 8.6; $[\alpha]^{22}D$ (0.5% in water), +445°; ultraviolet absorption, $\lambda_{max.}$ (0.1 *N* hydrochloric acid) 278 mμ, ε 9350; infrared absorption: strong $-NH_3^+$ absorption at 2860–3000 cm.$^{-1}$ (broad), and 2125 cm.$^{-1}$, and $-CO_2^-$ absorption at 1590 and 1390 cm.$^{-1}$.

The infrared spectrum of crystalline DHAA suggested that it was an amino acid. The ultraviolet absorption could be accounted for by the carboxyl and two linearly conjugated double bonds.[3] Catalytic hydrogenation of DHAA resulted in the uptake of two moles of hydrogen to yield **hexahydro-3-hydroxyanthranilic acid,** m.p. (dec.) 270–276°. *Anal.* Found for $C_7H_{13}NO_3$: C, 52.68; H, 8.43; N, 8.59. Thus the original substance, DHAA, was indicated to be a cyclic diene amino acid. Confirmation was seen in the ready conversion under vigorous acidic conditions to anthranilic acid, and under vigorous alkaline conditions to *m*-hydroxybenzoic acid. The presence of acylable amino and hydroxyl groups in DHAA was confirmed by acetylation to **2-acetamido-3-acetoxy-2,3-dihydrobenzoic acid,** m.p. 177–178°. *Anal.* Found for $C_{11}H_{13}NO_5$: C, 55.15; H, 5.54; N, 6.11; acetyl, 35.5. Final proof of the constitution of DHAA as a cyclohexadienoic acid and relative placement of the carboxyl, amino, and hydroxyl groups was found in the very facile catalytic disproportionation of DHAA to 3-hydroxyanthranilic acid and hexahydro-3-hydroxyanthranilic acid. In addition, since DHAA was optically active, gave no ketone reaction with dinitrophenylhydrazine and produced no ammonia on mild alkaline hydrolysis, the structure must be one of the four possible stereoisomeric 2,3-dihydro-3-hydroxyanthranilic acids. The vigorous conditions (4 hours in 12*N* hydrochloric acid at 60°) required for dehydration of DHAA to anthranilic acid strongly suggested a *trans* relationship for the amino and hydroxyl groups.

The possibility that DHAA was involved as an intermediate in the biosynthesis of the tetracyclines was investigated by radiotracer techniques.[4] Labeled DHAA was prepared by an S-652 fermentation of uniformly C^{14}-labeled tobacco starch and was isolated from the mash filtrate by means of preparative paper chromatography. The isolated material was added to a BC-41 fermentation in the active 7-chlorotetracycline (CTC)-producing phase. At the end of the BC-41 fermentation period, CTC was isolated by paper chromatographic means and was shown to contain less than 1% of the total radioactivity added as labeled DHAA. We therefore have concluded that DHAA is not an intermediate in the pathway from carbohydrate to the tetracyclines.[5]

(3) E. A. Braude in "Determination of Organic Structures by Physical Methods," E. A. Braude and F. C. Nachod, Ed., Academic Press, Inc., New York, N. Y., 1955, pp. 131–185.

(4) P. A. Miller, J. R. D. McCormick and A. P. Doerschuk, *Science*, **123**, 1030 (1956).

(5) The close chemical relationship of DHAA to anthranilic acid suggests a possible role for DHAA as an intermediate in the biological conversion of shikimic acid to anthranilic acid (B. D. Davis, "Advances in Enzymology," **16**, 247 (1955); E. L. Tatum, S. R. Gross, G. Ehrensvärd and L. Garnjobst, *Proc. Natl. Acad. Sci.*, **40**, 271 (1954); P. R. Srinivasan, *J. Am. Chem. Soc.*, **81**, 1772 (1959).

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ELECTROPHILIC REACTIONS OF ARGENTOUS AND MERCURIC FLUORIDES WITH FLUOROOLEFINS IN HYDROGEN FLUORIDE

Sir:

We wish to report (1) the addition of mercuric fluoride to 1,1,3,3,3-pentafluoropropene and to hexafluoropropene in hydrogen fluoride to form isopropylmercury derivatives, and (2) the silver fluoride catalyzed addition of hydrogen fluoride to hexafluoropropene and to octafluoro-2-butene. Our results demonstrate electrophilic attack on perfluoroölefins by metal cations and point to electrophilic reactions of π-electron systems as a new area of carbon–fluorine chemistry.

Hexafluoropropene rapidly adds hydrogen fluoride at 25° by reaction with potassium fluoride in formamide with initial nucleophilic attack by fluoride ion[1] but is stable to anhydrous hydrogen fluoride at 200°. Less than 1% CF_3CHFCF_3 was formed from $CF_3CF{=}CF_2$ with excess HF at 200°.[2] Potassium fluoride in HF is ineffective as a nucleophilic reagent. An 8 mole per cent. solution of KF in HF yielded only 8% CF_3CHFCF_3 at 200°; at 125°, less than 1% HF addition took place with $CF_3CF{=}CF_2$ and with $CF_3CF{=}CFCF_3$.[2] The strong solvation of F^- to form $H_nF_{n+1}^-$ ions promotes dissociation but inhibits nucleophilic reaction. Hydrogen fluoride is thus a useful solvent for reactions between metal cations and perfluoroolefins.[3]

Reaction between HgF_2 and the fluoropropenes proceeds smoothly at 85° in hydrogen fluoride without HF addition.[2,4–7] From 16 g. of $CF_3CH{=}$

(1) W. T. Miller, Jr., J. H. Fried and H. Goldwhite, *J. Am. Chem. Soc.*, **82**, 3091 (1960).

(2) Reaction mixtures were heated for 24 hr. in rocker-type stainless steel bombs.

(3) Reactions have also been carried out in aqueous solutions.[4]

(4) The experiments in aqueous solutions and with $CF_3CF{=}CFCF_3$ in HF were carried out by Nathan Edelson.

(5) At 11.9° HgF_2 forms a 0.5% soln. in HF.[6] Equimolar amounts of HgF_2 and $CF_3CF{=}CF_2$ without a solvent gave <5% addition in 12 hr. at 140°.

(6) A. W. Jache and G. H. Cady, *J. Phys. Chem.*, **56**, 1106 (1952).

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 ± 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.

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(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 × 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 ± 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 ∼ +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.