termediate in the reaction of xylulose-5-phosphate with phosphate ion to give glyceraldehyde-3-phosphate and acetyl phosphate[4] catalyzed by the enzyme phosphoketolase and the coenzyme, thiamine pyrophosphate.[5]

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

[5] The authors gratefully acknowledge the support of the work by the American Cancer Society.

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RECEIVED JUNE 21, 1960

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## TETRAFLUOROPYRIMIDINE[1]

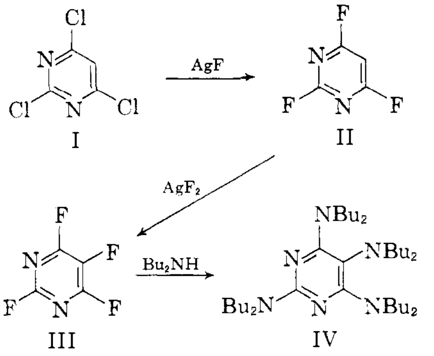
*Sir:*

To date there have been reported only two pseudo-aromatic perfluoro-N-heterocyclic parent compounds, namely, pentafluoropyridine and 2,4,6-trifluoro-s-triazine (cyanuric fluoride). The former compound was synthesized by defluorination of undecafluoropiperidine,[2] while cyanuric fluoride was obtained from cyanuric chloride (1) by means of potassium fluorosulfinate[3] or (2) with $SbF_3Cl_2$ (Swarts mixture).[4,5] Only the latter method led to exclusive formation of the desired perfluorinated triazine compound. Attempts to fluorinate other nuclear chlorinated heterocycles, such as chloropyrimidines, with $SbF_3Cl_2$ resulted in failure.[6]

In connection with an investigation of fluorinated heterocyclic compounds, we were interested in the synthesis of perfluorinated pyrimidine. Using 2,4,6-trichloro-pyrimidine[7] (I) as starting material, we employed silver fluoride (AgF) as the suitable inorganic fluorinating agent for the replacement of the chlorine atoms with fluorine. This selection was based upon the results of a comparative study of the effectiveness of $SbF_3Cl_2$, AgF, $AgF_2$ and $HgF_2$ upon certain chloro-s-triazines.[8] When compound I was refluxed and distilled from fresh AgF three times, 2,4,6-trifluoropyrimidine (II), b.p. 98°, was obtained in a 76% yield.

The conversion of II into tetrafluoropyrimidine (III) required the substitution of the hydrogen atom in 5-position by fluorine which was accomplished by means of silver difluoride ($AgF_2$). The reaction of II with $AgF_2$ either at reflux temperature or at 280° in an autoclave led to an incompletely fluorinated product; however, complete fluorination was achieved by carrying out the reaction in triperfluorobutylamine at 90°. Distillation of the reaction product gave III in 30% yield, b.p. 89°, $n^{25}\mathrm{D}$ 1.3875 (calcd. for $C_4F_4N_2$: C, 31.60; F, 49.98; N, 18.42; found: C, 31.66; F, 49.70; N, 18.25). To our knowledge the direct replacement of hydrogen with fluorine in an aromatic system by means of silver difluoride in the liquid phase without subsequent addition of fluorine to the double bonds constitutes a novel procedure for such fluorination.

The identity of III was established by its reaction with di-*n*-butylamine to give tetra-di-*n*-butylaminopyrimidine (IV), b.p. 196° (0.3 mm.). Compound IV also was obtained from tetrachloropyrimidine. Experimental details and the description of the derivatives of II and III will be the subject of a subsequent publication.



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[1] This article is based on work performed under Project 116-B of The Ohio State University Research Foundation sponsored by the Olin Mathieson Chemical Corporation, New York, N. Y.

[2] J. Burdon, D. J. Gilman, C. R. Patrick, M. Stacey and J. C. Tatlow, *Nature*, **186**, 231 (1960).

[3] D. W. Grisley, Jr., E. W. Gluesenkamp and S. A. Heininger, *J. Org. Chem.*, **23**, 1802 (1958).

[4] A. F. Maxwell, J. S. Fry and L. A. Bigelow, THIS JOURNAL, **80**, 548 (1958).

[5] E. Kober and C. Grundmann, *ibid.*, **81**, 3769 (1959); U. S. Patent 2,845,421.

[6] Unpublished results of E. Kober and H. Ulrich.

[7] M. Langermann and K. C. Banks, THIS JOURNAL, **73**, 3012 (1951).

[8] Unpublished results.

[9] Olin Mathieson Chemical Corporation, New Haven, Connecticut.

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## THE STEREOCHEMISTRY OF THE SUCCINIC DEHYDROGENASE REACTION[1]

*Sir:*

The stereochemistry of the succinic dehydrogenase reaction was examined by Englard and Colowick in 1956.[2] From the data obtained on the exchange of the methylene hydrogen atoms with $D_2O$, it was concluded that the elimination of 2H is either random or *trans*. We now wish to report the results of some recent experiments which show that the elimination is not random, but is *trans* in nature.

Samples of fumaric acid and maleic acid were reduced catalytically with $D_2$ using Pd on charcoal as catalyst and ethyl acetate as solvent. The succinic acid obtained was oxidizied by the Keilin–Hartree preparation of heart sarcosome.[3] An excess of ferricyanide was used to oxidize completely the succinic acid added. Although the sarcosome preparation contained fumarase, this would not affect the result since this enzymatic addition of water to fumarate has been shown to be stereo-

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[1] This investigation was supported in part by a grant from the United States Public Health Service (No. H-4139 (C1)). The authors also wish to acknowledge the invaluable help from Dr. G. O. Dudek of Harvard University in the use of the analytical mass spectrometer.

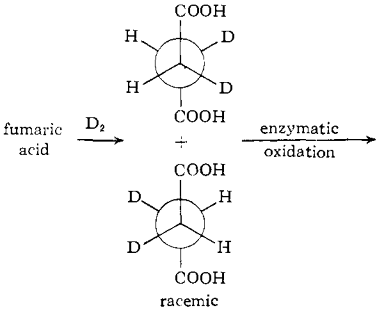
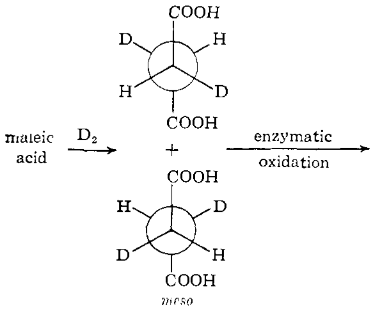
[2] S. Englard and S. P. Colowick, *J. Biol. Chem.*, **221**, 1019 (1956).

[3] D. Keilin and E. F. Hartree, *Proc. Roy. Soc.* (*London*), **B129**, 277 (1940). The grinding in a mortar was replaced by the use of a Waring Blendor.

specific.[2,4] The samples of fumaric acid were isolated by ether extraction after acidification of the solution, purified by column chromatography (Dowex-1-formate), reduced catalytically to succinic acid ($H_2$ + Pd), and esterified with an excess of diazomethane. The dimethyl succinate samples were purified by distillation under reduced pressure and their content of dideuterated molecules analyzed with the use of an analytical mass spectrometer.

The basis of the experimental approach and the results are shown in Table I. Two *meso*-forms are drawn since, although they are identical in solution, they might be expected to be different when bound to the enzyme. The expected presence and absence of di-deuterated molecules in fumarate in excess of normal abundance are shown for the three possible mechanisms of elimination of hydrogen, namely, *cis*, random and *trans*. The value for dideuteriofumarate formed was derived from the per cent. of di-deuterated molecules in the dimethyl succinate samples as determined with the mass spectrometer. The results demonstrated conclusively that the elimination of hydrogen must be *trans*.

TABLE I

| | Dideuterio-fumarate expected | | | % of dideuterated molecules in | |
|---|---|---|---|---|---|
| | *cis* | Random | *trans* | Succinate used | Fumarate formed |
|  | + | + | − | 2.4 | 0.1 |
|  | − | + | + | 2.9 | 1.4 |

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(4) H. F. Fisher, C. Frieden, J. S. M. McKee and R. A. Alberty, THIS JOURNAL, **77**, 4436 (1955).

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RECEIVED JUNE 8, 1960

## THE PREPARATION OF A VOLATILE POLONIUM FLUORIDE[1]

*Sir:*

Polonium might be expected to form a volatile fluoride, by analogy with the sixth column elements, S, Se, Mo, Te, W and U, which form hexafluorides. However, neither heating $^{210}$Po in fluorine nor treatment of it with liquid $BrF_3$ have succeeded in preparing a volatile compound.[2,3]

In studies with the unstable, radioactive hexafluoride of plutonium, $PuF_6$, it was discovered that this material could be stored successfully in the vapor phase without decomposition if a small excess of $F_2$ was added to the system; in sharp contrast, $PuF_6$ is found to decompose from the $\alpha$-radiation at the rate of 1.5% per day when stored as solid.[4] It therefore seemed worth while to investigate the formation of $PoF_6$ with subsequent storage as vapor in the presence of excess fluorine. For these experiments we had available 0.563 curie (0.96 mg.) of $^{208}$Po,[5] half-life 2.93 yr., as compared with the $^{210}$Po, half-life 138 days, used by the previous workers.

Of the material used 75% was deposited on two strips of Pt gauze each approximately 3 inches long and 25% on a dozen small, approximately $^1/_4$ inch square, Pt foils. These were loaded into the bottom of a 15.7 cm. long by 1.05 cm. radius i.d. nickel tube with the gauzes remaining upright. The nickel tube then was connected to a filling valve and a pressure gauge. Prior to starting the reaction the fast neutron yield from the F ($\alpha$,n) reaction was studied as a function of $F_2$ pressure and the position of the Po relative to a 1.75 inch diameter scintillation counter button.[6] The total neutron yield was approximately proportional to the fluorine pressure at 335–800 mm. pressure, which corresponded to the $\alpha$-range for the most part being greater than the reactor dimension. At 1600–2405 mm. pressure the total neutron yield appeared to approach a maximum value, which suggested that the $\alpha$-particles were largely being stopped within the reactor.[7] As expected the maximum neutron intensity occurred when the central region of the platinum gauzes was approximately opposite to the center of the Hornyak button.

Figure 1 summarizes similar neutron yield and distribution measurements made with the intention of demonstrating the formation of a volatile Po compound. Curve A corresponds to the Po on the Pt. Curve B was measured after heating the

[1] Based on the work performed under the auspices of the U. S. Atomic Energy Commission.

[2] F. Leitz, Jr., and L. Coulter reported by H. V. Moyer, editor, "Polonium," TID-5221 (1956), Office of Technical Services Department of Commerce, Washington 25, D. C.

[3] Emeleus, Maddock, Miles and Sharpe, *J. Chem. Soc.*, 1991 (1948).

[4] B. Weinstock and J. G. Malm, *J. Inorg. Nucl. Chem.*, **2**, 380 (1956).

[5] We are indebted to Dr. D. T. Vier of the Los Alamos Scientific Laboratory for the use of this material.

[6] We are indebted to Jerome L. Lerner for the use of his Hornyak button scintillation fast neutron counter. In order to use this equipment for our experiment an unfavorable geometric arrangement was used in which the nickel tube was about 1 inch from the edge of the button rather than directly in front of it.

[7] James H. Roberts, "Neutron Yields of Several Light Elements Bombarded with Polonium Alpha Particles," MDDC-731 declassified Jan. 7, 1947.