heated to 1600°, quenched in mercury, and sawed open. The walls had been attacked somewhat, and in the interior of the solidified thorium tetrafluoride a few gray areas of finely divided thorium metal were found.

No evidence for the existence of a lower fluoride of thorium was found. There was some indication however, that thorium dissolves slightly in its fluoride at high temperature, a behavior similar to that of uranium in its tribromide,[6] the alkaline earth metals in their halides,[7] or cerium in its chloride.[8]

Mention should be made of the preparation of thorium(III) and thorium(II) halides[9–11] prepared by reduction of the tetrahalides, especially the iodide, by the metal. These lower iodides were observed to parallel the corresponding halides of zirconium and hafnium in physical and chemical properties. Similarly a brown thorium(III) and silvery thorium(II) sulfide are known[12] whose properties indicate the presence of no f electrons.

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[6] C. D. Thurmond, Plutonium Project Report CC-2522 (Dec. 20, 1944).

[7] D. D. Cubicciotti and C. D. Thurmond, THIS JOURNAL, **71**, 2149 (1949).

[8] D. D. Cubicciotti, *ibid.*, **71**, 4119 (1949).

[9] E. Hayek and Th. Rehner, *Experientia*, **5**, 114 (1949).

[10] E. Hayek, Th. Rehner, and A. Frank, *Monatsh.*, **82**, 575 (1951).

[11] J. S. Anderson and R. W. D'Eye, *J. Chem. Soc.*, (Suppl. Issue No. 2), S 244 (1949).

[12] E. D. Eastman, *et al.*, THIS JOURNAL, **72**, 4019 (1950).

CONTRIBUTION NO. 52 FROM THE
INSTITUTE FOR ATOMIC RESEARCH
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AMES, IOWA

RECEIVED OCTOBER 30, 1951

COMMUNICATIONS TO THE EDITOR

THE REACTION OF DI-ISOPROPYL FLUOROPHOSPHATE WITH TYROSINE

Sir:

We have been engaged for some time on a comparative study of the action of di-isopropyl fluorophosphate (DFP) and di-isopropyl chlorophosphate (DClP) on amino-acids under "physiological" conditions in the hope of finding some clear-cut difference which might parallel the marked difference between the biochemical activities of these two compounds[1] (DFP is toxic and inhibits cholinesterase and other enzymes whereas DClP is not markedly toxic). The appearance of the recent paper of Wagner-Jauregg, O'Neill and Summerson[2] on a similar subject prompts us to make this preliminary communication of our positive findings.

Wagner-Jauregg, O'Neill and Summerson[2] studied the action of non-polar DFP and DClP on a number of amino-acid esters and amines in that DClP is the more reactive solution and uniformly observed the latter to be the more reactive[3]; they were unable to phosphorylate amino-acids in slightly alkaline aqueous media with DFP although they observed, but do not describe in detail, reaction between DFP and phenol in aqueous potassium carbonate.

We have been more fortunate and have been able to demonstrate a marked difference in the reactivity of DFP and DClP toward tyrosine. Using 0.02 *M* halophosphate and 0.005 *M* tyrosine in 0.08 *M* sodium bicarbonate at 38° and following the disappearance of free phenolic hydroxyl by the colorimetric method of Thomas[4,5] we obtained the following results

Time hr.	3	4	9	24
% Reaction of (DFP)	43	49	52	56
phenolic OH. (DClP)	-	7	10	8

Clearly DFP reacts readily, under these conditions, with the phenolic hydroxyl group of tyrosine whereas DClP does not. The reaction product from DFP, O-di-isopropylphosphoryl-tyrosine (I), was isolated from the reaction mixture, by chromatography on deactivated charcoal,[6] as needles, m.p. 158–160° (dec.), from aqueous acetone (Found N, 4.1; $C_{15}H_{24}O_6NP$ requires N, 4.1), and, more easily, as its N-2,4-dinitrophenyl derivative, needles, m.p. 159–160°, from methanol (Found C, 49.4; H, 5.1; N, 7.9; $C_{21}H_{26}O_{11}N_3P$ requires C, 49.3; H, 5.1; N, 8.2). The structure of (I) was confirmed by its chromatographic recognition in the hydrogenation product of its amorphous *p*-bromocarbobenzoxy derivative (Found C, 49.7; H, 5.0; N, 2.8; $C_{23}H_{29}O_2NBrP$ requires C, 49.5; H, 5.2; N, 2.5), obtained by treating DFP similarly with N-*p*-bromocarbobenzoxytyrosine, m.p. 156–157° (Found: C, 51.7; H, 4.1; N, 3.4; $C_{11}H_{16}O_5NBr$ requires C, 51.8; H, 4.1; N, 3.55).

This marked difference in the chemical behavior of the two halophosphates suggests, although it does not prove, that the reaction of DFP with cholinesterase and other sensitive enzymes involves reaction at a tyrosine side-chain; it is of interest that chymotrypsin, which is sensitive to DFP, has been

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[1] E. C. Webb, *Biochem. Soc. Symp.*, **2**, 50 (1948); H. G. Cook, B. C. Saunders and F. E. Smith, *J. Chem. Soc.*, 635 (1949).

[2] T. Wagner-Jauregg, J. J. O'Neill and W. H. Summerson, THIS JOURNAL, **73**, 5202 (1951).

[3] *Cf.* B. C. Saunders and G. J. Stacey, *J. Chem. Soc.*, 695 (1948).

[4] L. E. Thomas, *Arch. Biochem.*, **5**, 175 (1944).

[5] The absorptiometer used was purchased with the aid of a grant from the Central Research Fund of the University of London for which we express our thanks.

[6] Schramm and J. Primosigh, *Ber.*, **76**, 373 (1943).

stated[7] to require a tyrosine side-chain for activity. We are at present engaged in studying the action on tyrosine of other choline-esterase inhibitors and in attempts to isolate O-phosphorylated tyrosine from the reaction products of suitable choline-esterase inhibitors with chymotrypsin and other sensitive enzymes. Full details of our work will be published elsewhere in due course.

[7] I. W. Sizer, *J. Biol. Chem.*, **160**, 547 (1945).

IMPERIAL COLLEGE OF
SCIENCE AND TECHNOLOGY, R. F. ASHBOLT
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RECEIVED JANUARY 14, 1952

THE EXCHANGE REACTION BETWEEN COBALTOUS AND COBALTIC IONS IN PERCHLORIC ACID SOLUTION

Sir:

Previous investigators[1] found that under their conditions the rate of electron transfer between cobaltous and cobaltic ions was complete within the time of separation. Since the possibility existed that their results were due to exchange induced by the separation method, we have reinvestigated the exchange using a non-precipitation method.

We find that, at low cobalt concentrations, the rate is measurable. In our experiments, separation of the cobaltous and cobaltic species was effected by adding the exchange mixture to an ammoniacal solution of sodium Versenate,[2] acidifying the resulting solution with HNO_3, adding NH_4CNS and extracting the cobalt (II) with methylisobutyl ketone. Each fraction was then converted to a cobalt (III) "Versenate" complex for gamma counting and spectrophotometric analysis. Early experiments established that the separation method gave satisfactory activity and material balances (100 ± 5%) when both fractions were examined. In later work, only the specific activity of the Co (III) fraction was measured since this, together with the infinite time specific activity is sufficient to determine the fraction exchange. About 30 or 40% of the Co(III) was reduced to Co(II) during the separation, but a negligible amount of reduction occurred in the exchange mixture before separation. The amount of induced exchange was large (*ca.* 20%) but fairly reproducible.

Co^{+3} was prepared by electrolysis of a perchloric acid solution of cobaltous perchlorate.

The tracer was Co^{60} obtained from Oak Ridge. Experiments were usually done with cobaltous tracer, but one experiment using cobaltic tracer gave results which were consistent with the other data.

The exchanges reported in Table I were carried out in the dark, although experiments showed that no appreciable effects were caused by light of ordinary laboratory intensity.

An experiment done in a vessel packed with glass beads indicated that catalysis by glass surfaces is negligible.

The data for several of our experiments are given in Table I. All runs were made at 0° and in 1 *M* $HClO_4$. The reaction obeyed the usual exponential rate law with four or five points on each curve. The constancy of the product of half-time and total cobalt concentration shows the reaction to be second order, presumably first order in each of the two cobalt ions. The average bimolecular rate constant is calculated to be 46 liter-mole^{-1} min.$^{-1}$.

TABLE I

ELECTRON TRANSFER BETWEEN COBALTOUS AND COBALTIC IONS AT 0° AND 1 *M* $HClO_4$

Co(molarity × 10^3) Total	 Co^{+2}	 Co^{+3}	$T_{1/2}$ (min.) (±0.5 min.)	$T_{1/2}$ × total Co(× 10^2)
0.717	.124	.593	22.0	1.58
1.33	.14	1.19	11.5	1.53
1.47	...	...	10.8	1.59[a]
2.93	.27	2.66	4.8	1.41
3.03	~1.5	~1.5	4.8	1.45[b]
				Av. 1.51

[a] Glass beads added. [b] Tracer added as Co^{+3}.

Experiments are under way to investigate the induced exchange and to study the kinetics of the reaction in detail.

DEPARMENT OF CHEMISTRY
CORNELL UNIVERSITY NORMAN A. BONNER
ITHACA, NEW YORK JOHN P. HUNT

RECEIVED FEBRUARY 25, 1952

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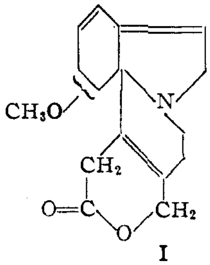
[1] S. A. Hoshowsky, O. G. Holmes and K. J. McCallum, *Can. J. Research*, **27B**, No. 4, 258 (1949).

[2] The sodium salt of ethylenediaminetetracetic acid, manufactured by Bersworth Chemical Co.

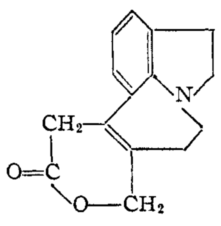
THE STRUCTURES OF β-ERYTHROIDINE AND APO-β-ERYTHROIDINE[1]

Sir:

Previously we have suggested partial structures for apo-β-erythroidine and certain other derivatives.[2,3] Additional evidence, which we are now presenting, makes it possible to assign structures I and II to β-erythroidine and apo-β-erythroidine, respectively.



I



II

Apo-β-erythroidine, a dihydroindole derivative, contains a δ-lactone ring, has no terminal methyl group and yields 7-carboxyisatin on oxidation.[2] These results indicate a tricyclic nucleus having fused five-, six- and seven-membered rings. Hofmann degradation studies have now demonstrated the presence of *two* —CH_2—CH_2— groups attached to the nitrogen atom, making it necessary to place the lactone ring as shown. The evidence for this is the appearance in the Hofmann degradation products of the characteristic absorption peaks in the infrared associated with the —CH═CH_2

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[1] Aided by a grant from the United Cerebral Palsy Association.

[2] M. F. Grundon and V. Boekelheide, THIS JOURNAL, in press.

[3] V. Boekelheide and E. Agnello, *ibid.*, **73**, 2286 (1951).