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).

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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.

(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 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(× 10^3)
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.

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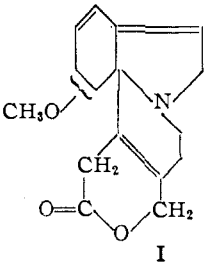
RECEIVED FEBRUARY 25, 1952

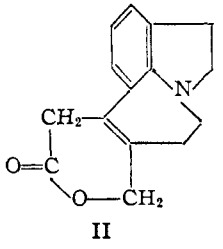
THE STRUCTURES OF β-ERYTHROIDINE AND APO-β-ERYTHROIDINE[1]

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

(1) Aided by a grant from the United Cerebral Palsy Association.

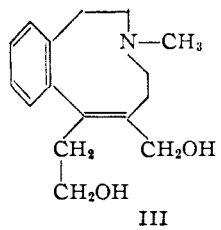
(2) M. F. Grundon and V. Boekelheide, THIS JOURNAL, in press.

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

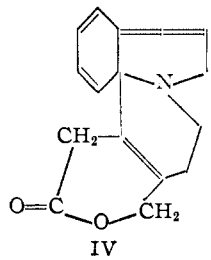
group.[4,5] Thus, des-N-methyl-apo-β-erythroidine, $C_{16}H_{17}NO_2$ (m.p. 167.5–169°, found C, 75.06; H, 6.71) gives formaldehyde on ozonolysis and shows a peak at 10.82 μ which is absent in its dihydro derivative, $C_{16}H_{19}NO_2$ (m.p. 130–130.5°, found C, 74.95; H, 7.71; —C—CH_3, 5.58). Likewise, the Hofmann degradation product of the dihydro derivative (found C, 74.92; H, 7.98) has a peak at 11.00 μ which is absent in its hydrogenation product, $C_{17}H_{23}NO_2$ (found C, 74.22; H, 8.46).

Structure I for β-erythroidine can be deduced from new evidence establishing III as the structure of the Hofmann degradation product of dihydro-β-erythroidinol.[3] This product undergoes slow hydrogenolysis of the allylic hydroxyl to yield a desoxy derivative, $C_{16}H_{23}NO$ (m.p. 89–90.5°, found C, 78.24; H, 9.36; —C—CH_3, 2.66). Further Hofmann degradation of the desoxy derivative gives an oil, $C_{17}H_{25}NO$ (found C, 78.48; H, 9.64), having peaks at 10.03 and 11.02 μ which are absent in the corresponding dihydro derivative, $C_{17}H_{27}NO$ (found C, 77.99; H, 10.50). This dihydro derivative, on a further Hofmann degradation, yields a nitrogen-free product, $C_{15}H_{20}O$ (found C, 82.78; H, 9.24) having peaks at 10.01 and 11.10 μ which are again absent in its hydrogenated derivative, $C_{15}H_{22}O$ (found C, 82.30; H, 10.19). Ozonolysis of this final hydrogenation product yields methyl ethyl ketone, whose identity is established by comparison of its 2,4-dinitrophenylhydrazone with an authentic sample. The presence of two —CH_2—CH_2— groups attached to the nitrogen supports the conclusion made previously with apo-β-erythroidine, and the isolation of methyl ethyl ketone shows the arrangement of the lactone ring with respect to the nitrogen.

Finally, when des-N-methyl-dihydro-β-erythroidinol (III) is subjected to exhaustive methylation without prior hydrogenation, a nitrogen-free product, $C_{15}H_{18}O_2$ (m.p. 84–86°, found C, 78.18; H, 7.58) results which readily gives a tetrahydro derivative, $C_{15}H_{22}O_2$ (found C, 76.79; H, 9.56). Permanganate oxidation of this tetrahydro derivative gives *o*-ethylbenzoic acid, identified by comparison of its infrared spectrum with that of an authentic sample, and establishes III as the correct structure.



III



IV

Since β-erythroidine serves as precursor for both II and III, structure I would appear to be the only logical possibility for it. This formulation shows for the first time the close chemical relationship between β-erythroidine and the other erythrina alkaloids.[6] Recent suggestions[7,8a,b] regarding the structure of β-erythroidine find no support in our experiments.[9]

(4) D. Barnard, L. Bateman, A. J. Harding, H. P. Koch, N. Sheppard and G. B. Sutherland, *J. Chem. Soc.*, 915 (1950).

(5) Because apo-β-erythroidine and certain of its derivatives show absorption in the 10 μ region, only the terminal methylene peak in the 11 μ region is informative for the Hofmann degradation products of this series.

(6) G. W. Kenner, H. G. Khorana and V. Prelog, *Helv. Chim. Acta*, **34**, 1969 (1951); M. Carmack, B. C. McKusick and V. Prelog, *ibid.*, **34**, 1601 (1951).

(7) C. Lapiére and R. Robinson, *Chem. and Ind.*, **30**, 650 (1951).

(8) (a) F. Koniuszy and K. Folkers, THIS JOURNAL, **73**, 333 (1951); (b) **72**, 5579 (1950).

(9) Although the methylation and oxidation experiments on desmethoxy-β-erythroidine reported by Koniuszy and Folkers (ref. 8b) are not in accord with our formulation, we have repeated their experiments and, in our hands, phthalic acid was isolated in 36% yield as the only oxidation product. Since desmethoxy-β-erythroidine, to which we assign structure IV, would be expected to undergo Hofmann degradation under the conditions employed for methylation, phthalic acid is a rational product of oxidation.

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RECEIVED MARCH 13, 1952

PHOSPHONOUS AND PHOSPHONIC CATION EXCHANGE RESINS

Sir:

Cation exchange resins available up to the present time have consisted of three major types—those in which sulfonic, carboxylic, or phenolic acid groups have served as the source of the exchangeable cations. There have now been developed in this laboratory phosphonous[1] and phosphonic[1] cation exchange resins which show certain desirable chemical characteristics that are not found in any of the older exchangers.

Figure 1 shows the titration curve as obtained in 1 *N* sodium chloride solution by the "Direct Titration" method of Gregor and Bregman,[2] for a phosphonic exchanger having a total capacity of 8.8 meq./g. dry resin. It can be seen that the first ionization occurs at a *p*H slightly higher than that of a sulfonic acid resin, while the second one is at a *p*H intermediate between the carboxylic and phenolic types.[2] The *pK* valuesin dicated from this curve compare favorably with those found by Rumpf and Chavane[3] for aliphatic phosphonic acids. The phosphonous resins show titration curves identical with the first portion of the phosphonic type.

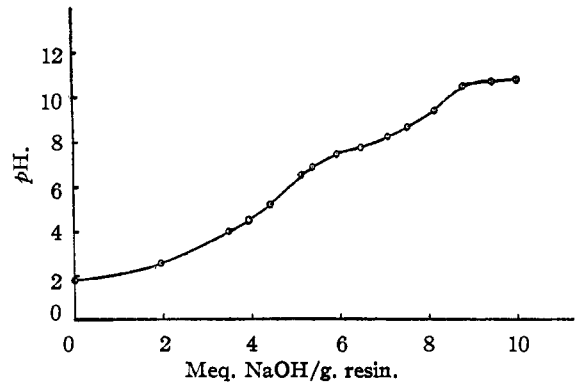

Fig. 1.—Titration curve of phosphonic acid cation exchange resin.

(1) Nomenclature follows that of Chemical Abstracts.

(2) H. P. Gregor, and J. I. Bregman, THIS JOURNAL, **70**, 2370 (1948).

(3) P. Rumpf, and V. Chavane, *Compt. rend.*, **224**, 919 (1947).