It should be pointed out that since all flasks contained deoxycytidine growth was the same regardless of the B_{12} concentration. Samples of DNA from cells grown with 2 mμg. of B_{12} per ml. and with ribose-1-C^{14} were degraded with sulfuric acid and the deoxyribose converted to levulinic acid which was isolated as the 2,4-dinitrophenylhydrazone.[5] All the C^{14} activity of the original DNA was recovered in this derivative.

The results of these experiments demonstrate that in *L. leichmannii* vitamin B_{12} is required for the conversion of ribose to deoxyribose.

Acknowledgment.—This investigation was supported by research grant A-721, National Institutes of Health, Public Health Service.

(5) M. C. Lanning and S. S. Cohen, *J. Biol. Chem.*, **216**, 413 (1955).

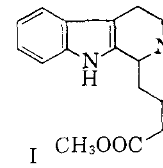
DEPARTMENT OF BIOCHEMISTRY
UNIVERSITY OF ARKANSAS
SCHOOL OF MEDICINE
LITTLE ROCK, ARKANSAS
WILLIAM H. SPELL, JR.
JAMES S. DINNING

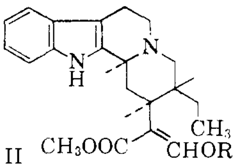
RECEIVED MAY 25, 1959

THE TOTAL SYNTHESIS OF *dl*-DIHYDROCORYNANTHEINE

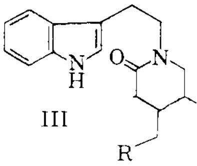
Sir:

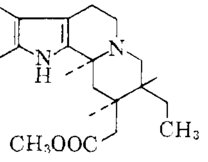
Structural[1] and stereochemical[2] investigations have revealed the characteristic alkaloids (I) of *Pseudocinchona africana* A. Chev. as "missing links" in the biogenetic sequences which involve among other substances, the venerable cinchona and yohimbine bases. We wish to record the first total synthesis of the racemic form of a naturally occurring representative of the corynantheine group, dihydrocorynantheine (II, R = CH_3).


I


II

Nickel-catalyzed reduction of diethyl β-(1-cyano-1-propyl)-glutarate[3] in the presence of excess tryptamine afforded *cis* and *trans* ethyl *dl*-N-(β-3′-indolyl)-5-ethylpiperidone-4-acetates (III, R = C_2H_5OOC-), which were separated as the acids (III, R = COOH) by chromatography on silicic acid (*cis* acid, m.p. 221–223°, C = 69.35; H = 7.54; *trans* acid, m.p. 203–205°, C = 69.78; H = 7.63). These isomers were distinguished stereochemically by correlation of the lower-melting substance with *trans*-N-(β-3′-indolyl)-4,5-diethylpiperidone (III, R = CH_3),[4] achieved by means of this series of transformations: selective reduction with lithium borohydride to the piperidone alcohol (m.p. 145–146°; C, 72.55; H, 8.28); without deliberate purification of intermediates, formation of the O-tosylate, then conversion to the isothiouronium salt, and reductive desulfurization of the latter by means of Raney nickel. Bischler–Napieralski cyclization of *trans* piperidone (III, R = CH_3OOC-), and catalytic reduction over platinum of the resulting imine salt, resulted in formation of the *dl*-tetracyclic ester IV, m.p. 143.5–145.5° (HCl salt, m.p. 274.5–275°; C, 66.29; H 7.47). Treatment of IV with sodium triphenylmethyl then with methyl formate provided the α-hydroxymethylene ester (II, R = H), m.p. 185–186° (dec.) (infrared bands at 2.84 and 6.04μ) (C, 70.68; H, 7.47). Dimethyl sulfate and alkali, or, better, diazomethane in ethanol–ether, effected O-methylation, giving rise to *dl*-dihydrocorynantheine, which was characterized as the crystalline hydrochloride, m.p. 242–243° (C, 64.90; H, 7.17). The infrared spectrum (infrared bands at 2.85, 5.94 and 6.11μ) of the corresponding free base in chloroform solution was identical with the spectrum of *d*-dihydrocorynantheine in the same solvent.


III


IV

Acknowledgment.—This work was supported by a grant from the Research Committee of the University of Wisconsin, with funds supplied by the Wisconsin Alumni Research Foundation.

---

(1) R. H. F. Manske and H. L. Holmes, "The Alkaloids," Vol. II, Academic Press, Inc., New York, N. Y., 1952, p. 420.

(2) (a) E. E. van Tamelen, P. E. Aldrich and T. J. Katz, *Chemistry and Industry*, 793 (1956); THIS JOURNAL, **79**, 6426 (1957); (b) M.-M. Janot, R. Goutarel, A. Le Hir, G. Tsatsas and V. Prelog, *Helv. Chim. Acta*, **38**, 1073 (1955).

(3) R. P. Evstigneeva, R. S. Livshits, L. I. Zakharkin, M. S. Bainova and N. A. Preobrazhensky, *Doklady Akad. Nauk., U.S.S.R.*, **75**, 539 (1950); N. A. Preobrazhensky, R. P. Evstigneeva, T. S. Leuchenko and K. M. Fedyshkina, *ibid.*, **81**, 421 (1951).

(4) E. E. van Tamelen, P. E. Aldrich and J. B. Hester, Jr., THIS JOURNAL, **79**, 4817 (1957).

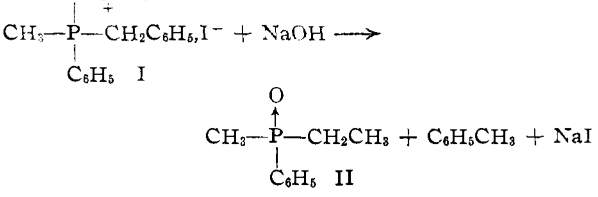
DEPARTMENT OF CHEMISTRY
UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN
EUGENE E. VAN TAMELEN
JACKSON B. HESTER, JR.

RECEIVED JUNE 5, 1959

STEREOSPECIFIC CONVERSION OF METHYLETHYLPHENYLBENZYLPHOSPHONIUM IODIDE TO METHYLETHYLPHENYLPHOSPHINE OXIDE

Sir:

In the following communication[1] data were provided to show that the conversion by the action of sodium hydroxide solution of methylethylphenylbenzylphosphonium iodide (I) to methylethylphenylphosphine oxide (II), with elimination of toluene, is a third order reaction. We also wish to report that the reaction is completely stereospecific.



$$CH_3-\overset{\overset{CH_2CH_3}{|}}{\underset{\underset{C_6H_5}{|}}{\overset{+}{P}}}-CH_2C_6H_5, I^- + NaOH \longrightarrow \quad \text{I}$$

$$CH_3-\overset{\overset{O}{\uparrow}}{\underset{\underset{C_6H_5}{|}}{P}}-CH_2CH_3 + C_6H_5CH_3 + NaI \quad \text{II}$$

Treatment of optically pure levorotatory I[2]

---

(1) M. Zanger, C. A. VanderWerf and W. E. McEwen, THIS JOURNAL, **81**, 3806 (1959).

(2) K. F. Kumli, W. E. McEwen and C. A. VanderWerf, *ibid.*, **81**, 248 (1959).

with aqueous-methanolic sodium hydroxide solution at 100° for 10 hours gave toluene and dextrorotatory II. The latter compound was obtained in 89% yield by distillation *in vacuo*. Its physical constants were found to be: m.p. 47–48° (reported[3a] 50°), $[\alpha]^{25}\text{D}$ $+22.4 \pm 1.0°$ (*c*, 2.184 in water) (reported[3b] +22.8°).

Anal. Calcd. for $C_9H_{13}PO$: C, 64.30; H, 7.73; P, 18.46. Found: C, 64.36; H, 7.84; P, 18.28.

Similar treatment of dextrorotatory I[2] with sodium hydroxide solution gave levorotatory II, $[\alpha]^{25}\text{D}$ $-22.8 \pm 1.0°$ (*c*, 2.168 in water), m.p. 48–49° (*Anal.* Found: C, 64.16; H, 7.90; P, 18.15).

Vapor phase chromatographic examination of the hydrocarbon fraction of a reaction mixture obtained by treatment of racemic I with sodium hydroxide solution revealed that toluene was the only compound present.

Although the reactions cited above are completely stereospecific, it is still an open question whether they proceed with inversion or retention of configuration. In nucleophilic displacement reactions on silicon in optically active silicon compounds, evidence has been provided for both inversion and retention of the configuration of the silicon atom, depending on the reagents.[4] However, it is not possible to draw too close a comparison between the reactions of silicon and phosphorus compounds. For example, whereas displacement of hydride ion by hydroxide ion in a silane is a second order reaction,[5] displacement of a hydrocarbon anion by hydroxide ion in a phosphonium salt is a third order reaction,[1] even though both reactions are presumed to proceed through a transition state in which the central atom (silicon or phosphorus) has a trigonal bipyramidal configuration.

Acknowledgment.—This investigation was supported in part by a research grant, RG-4215, from the National Institutes of Health, Public Health Service.

---

(3)(a) J. Meisenheimer and L. Lichtenstadt, *Ber.*, **44**, 356 (1911); (b) J. Meisenheimer, J. Casper, M. Horing, W. Lauter, L. Lichtenstadt and W. Samuel, *Ann.*, **449**, 213 (1926).

(4) L. H. Sommer and C. L. Frye, THIS JOURNAL, **81**, 1013 (1959).

(5) See L. H. Sommer, O. F. Bennett, P. G. Campbell and D. R. Weyenberg, *ibid.*, **79**, 3295 (1957), and earlier references cited there.

DEPARTMENT OF CHEMISTRY KARL F. KUMLI
UNIVERSITY OF KANSAS WILLIAM E. MCEWEN
LAWRENCE, KANSAS CALVIN A. VANDERWERF

RECEIVED MAY 25, 1959

KINETIC STUDY OF THE DECOMPOSITION OF QUATERNARY PHOSPHONIUM HYDROXIDES

Sir:

We wish to report the results of kinetic studies on the reaction of quaternary phosphonium halides with sodium hydroxide to produce phosphine oxides and hydrocarbons. These studies on methylethylphenylbenzylphosphonium iodide and on a series of *p*-Y-benzyltribenzylphosphonium halides (where Y = NO_2, Cl, H, CH_3, or CH_3O) revealed several facts: (1) all of the reactions were third order, with a first order dependence on the concentration of phosphonium cation and a second order dependence on the concentration of hydroxide ion; (2) the relative ease of elimination of the various groups parallels their stability as anions; and (3) the relative ease of the departure of a given group is definitely influenced by the nature of the non-departing groups (see partial rate factors for departure of benzyl group in Table I).

TABLE I

REACTIONS OF $p\text{-Y-}C_6H_4CH_2P(CH_2C_6H_5)_3^+, I^-$ WITH NaOH

Y	k_2 (l./mole-min.)	Toluene, mole %	*p*-Y-Toluene, mole %	Yield, %	Partial rate factor for departure of benzyl group[b]
NO_2	...[a]	0.0	100.0	95	..
Cl	13.80	64.1	35.9	90	2.95
H	2.72	75.0	25.0	90	0.68
CH_3	2.05	82.9	17.1	90	0.57
OCH_3	1.45	93.3	6.7	85	0.45

[a] Too rapid to be measured. [b] Partial rate factor = (k_2 × mole % toluene)/(3 × 100).

For the series *p*-Y-benzyltribenzylphosphonium halides, our kinetic studies were conducted in aqueous dimethoxyethane (1:1) at 38.9° with the phosphonium salt present in twenty-fold molar excess. The specific rate constants, k_2, shown in Table I represent pseudo-second-order constants. Product ratios were determined by vapor phase chromatographic analysis of the hydrocarbon fraction of each reaction mixture.

The kinetic measurements for methylethylphenylbenzylphosphonium iodide were carried out in 1.00 *N* potassium chloride solution at 99.4°. A total of four kinetic determinations were made, the first two with $[OH^-] = 2[R_4P^+]$ and the other two with $[OH^-] = [R_4P^+]$. The average specific rate constant, av. k_3, = 7.90 ± 0.24 $l.^2$/moles^2-hr. The data were completely inconsistent with a second order reaction.

A mechanism consistent with these observations, as applied to tetrabenzylphosphonium iodide, is as proposed[1]

$$\begin{tikzcd}[column sep=large] {}^+P(CH_2C_6H_5)_4 + {}^-OH \arrow[r, "\text{Fast}"] & HOP(CH_2C_6H_5)_4 \arrow[dl, shift left, "{}^-OH\ \text{Fast}"] \\ H_2O + {}^-OP(CH_2C_6H_5)_4 \arrow[ur, shift left] \arrow[r, "\text{Slow}"] & C_6H_5CH_2^- + O\leftarrow P(CH_2C_6H_5)_3 \end{tikzcd}$$

$$C_6H_5CH_2^- \xrightarrow[\text{Fast}]{\text{HOH}} C_6H_5CH_3$$

This mechanism is similar to that postulated by Ingold and co-workers[2] insofar as formation of a pentacovalent phosphorus intermediate (trigonal bipyramidal) is concerned, but differs in that Ingold considered the initial addition of hydroxide ion to phosphorus to be rate-determining. Ingold also supposed, on the basis of product ratio studies alone, that the relative ease of elimination of any specific group was independent of the other groups attached to phosphorus, which is contrary to our findings.

---

(1) Conceivable variations of this general mechanism are (a) synchronous attack of the second hydroxide ion and departure of the benzyl anion and (b) the formation of a transition species with two hydroxide ions bonded to phosphorus (tetragonal bipyramidal structure).

(2) (a) C. W. Fenton and C. K. Ingold, *J. Chem. Soc.*, 2342 (1929); (b) L. Hey and C. K. Ingold, *ibid.*, 531 (1933).