sealed in a 3-mm. o.d. Pyrex tube under high vacuum. The sample was then subjected at room temperature to 2.2×10^6 rads (enough to cause 10% decomposition) of γ-radiation from the Co^{60} source. During the 45 minutes which elapsed between removal from the source and placing it in the spectrometer cavity, the sample was kept at $-196°$. An unirradiated control gave no signal response. However, the irradiated sample showed an ESR spectrum with a sharp peak at a g value of approximately 2.0 and the height of the peak corresponded to about one free radical developed for every 10^4 e.v. of energy expended in the sample. The free radical signal was fairly stable at room temperature and decayed with a half-time of about four hours, in good agreement with data of Table III. Work leading to the identification of the free radical is now in progress.

Discussion

The radiation sensitivities of crystalline choline chloride and bromide is a matter of considerable interest since they are the only examples known at present of solid-state free-radical chain mechanisms. A recent investigation into the crystal structure of choline chloride has uncovered,[8] how-

(8) Michael E. Senko. "The Crystal Structure of a Triazole and Choline Chloride," University of California Radiation Laboratory Report No. UCRL-3521, September, 1956.

ever, no unusual features which can account for the radiation instability. The explanation of why the chloride and bromide crystals propagate a chain mechanism, whereas the other analogs do not, must await more detailed comparisons among the various crystal structures.

An interesting facet of choline chloride's great radiation instability was uncovered in the recent work of Serlin.[9] He showed that the crystalline compound is more radiation unstable at 50° than it is at room temperature. Furthermore, and quite unexpectedly, when the temperature is raised to 150° the compound "becomes markedly radiation-resistant." This observation might indicate the presence of a reaction involving the free radicals which competes with the chain mechanism, and that this reaction becomes the predominant one at the higher temperature. It might also mean that the choline chloride had assumed a different crystal form at the higher temperature.

(9) I. Serlin, *Science*, **126**, 261 (1957).

BERKELEY, CALIF.

The Alkaloids of *Tabernanthe Iboga.* VII.[1] Derivatives of Isoquinuclidine

BY L. H. WERNER AND S. RICCA, JR.

A number of N-alkylated derivatives of 3-isoquinuclidone and isoquinuclidine were prepared. They did not show any pharmacological activity of interest. Isoquinuclidine was obtained in a pure form by catalytic debenzylation of N-benzylisoquinuclidine. Hofmann degradation of N-benzylisoquinuclidine methiodide resulted in cleavage at the bridgehead.

Recently[2] it was found that the Tabernanthe alkaloids contain an isoquinuclidine ring as part of their structure. Very few derivatives of isoquinuclidine have been reported, and we therefore considered it of interest to prepare a small series of derivatives (Table I).

3-Isoquinuclidone (II) was prepared by fusion of *cis*-4-aminocyclohexanecarboxylic acid (I) according to Ferber and Brückner[3]; likewise *cis*-methyl 4-aminocyclohexanecarboxylate (III) could be cyclized to 3-isoquinuclidone but at a somewhat lower temperature. Refluxing with 2 N hydrochloric acid cleaved the 3-isoquinuclidone ring again to give the *cis*-4-aminocyclohexanecarboxylic acid. This could be shown by thermal recyclization to 3-isoquinuclidone. The *trans*-acid does not yield 3-isoquinuclidone, even on prolonged heating. Likewise 2-benzyl-3-isoquinuclidone (IV) was cleaved by refluxing with 2 N hydrochloric acid to

(1) Paper VI, H. B. MacPhillamy, R. Dzemian, R. A. Lucas and M. Kuehne, THIS JOURNAL, **80**, 2172 (1958).
(2) Paper IV, M. F. Bartlett, D. F. Dickel and W. I. Taylor, *ibid.*, **80**, 126 (1958).
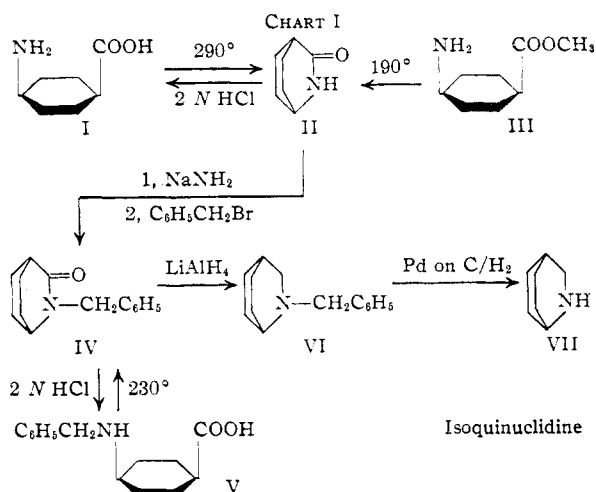(3) E. Ferber and H. Brückner, *Ber.*, **76**, 1019 (1943).

cis-4-benzylaminocyclohexanecarboxylic acid (V). This acid also cyclized readily again on heating. The N-substituted 3-isoquinuclidones given in Table I were obtained by reaction of the sodio derivative of 3-isoquinuclidone with the appropriate alkyl- or aralkyl halide. Reduction of the N-substituted 3-isoquinuclidones with lithium aluminum hydride yielded the corresponding isoquinuclidines. The quaternary bases formed very readily in alcoholic solution at 25° on treatment with an excess of methyl iodide. Isoquinuclidone itself could not be reduced directly to isoquinuclidine (VII); this compound was obtained by lithium aluminum hydride reduction of 2-benzyl-3-isoquinuclidone (IV) to 2-benzylisoquinuclidine (VI), followed by reductive debenzylation. Isoquinuclidine (VII) was found to be a crystalline solid melting and also boiling at 173–175°. Previously,[3] this compound had been isolated only as a picrate and as the N-benzoyl derivative.

It was also of interest to determine the structure of the cleavage product (IXa or b) obtained by the Hofmann degradation of 2-benzylisoquinucli-
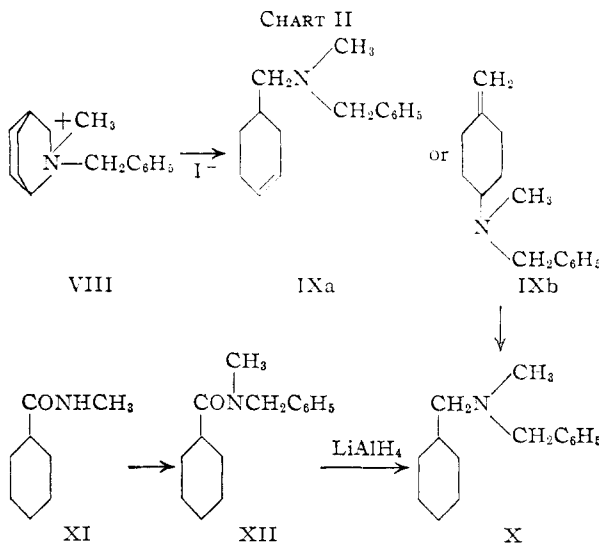
Chart I

Chart II

dine methiodide (Chart II, VIII). On the basis of the infrared absorption band at 1653 cm.$^{-1}$ which indicated a double bond, and the absence of a band at 890 cm.$^{-1}$ which would be characteristic for an exocyclic methylene group ($>C=CH_2$), structure IXa for the cleavage product was more probable than IXb. Hydrogenation with platinum gave the cyclohexane derivative X. This compound was synthesized by benzylation of N-methyl-cyclohexanecarboxamide (XI)[4] followed by reduction with lithium aluminum hydride and was found to be identical with the degradation product X.

In addition 6-ethyl-3-isoquinuclidone (XVII) was prepared by conventional methods (Chart III)[5,6] as a possible approach to one of the degradation products of ibogamine.

It is noteworthy that hydrogenation of 4-amino-3-ethylbenzoic acid (XV) gave a crystalline, homogeneous cis-4-amino-3-ethylcyclohexanecarboxylic acid (XVI) in 46% yield.[7]

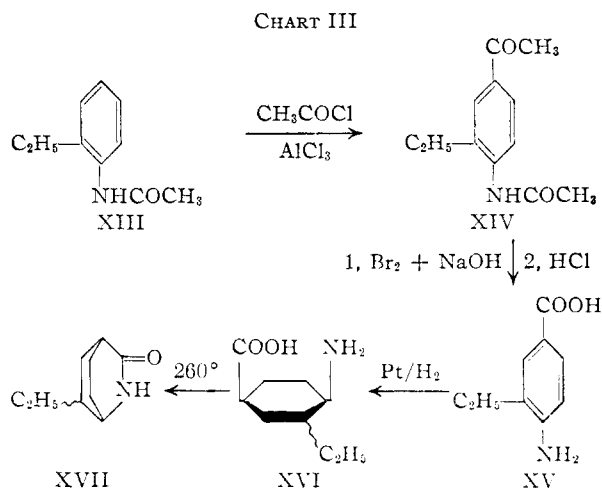(4) K. Bernhard, J. physiol. Chem., **248**, 256 (1937).

(5) E. Ferber and H. Brückner, Ber., **72**, 995 (1939).

(6) F. F. Blicke and W. M. Lilienfeld, This Journal, **65**, 2377 (1943).

(7) We wish to acknowledge the able assistance of Mr. E. Mohacsi for this part of the work.

Pharmacological screening of the compounds failed to reveal any interesting activity.

Chart III

Experimental

All melting points were uncorrected. The infrared spectra were taken in Nujol mulls.

3-Isoquinuclidone (II). (a) Cyclization of cis-4-Amino-cyclohexanecarboxylic Acid.—On heating 15.0 g. of cis-4-aminocyclohexanecarboxylic acid in a distillation flask rapidly to 245–290°, water was split off and a melt was obtained. After cooling, the residue was extracted with hot benzene (100 ml.). The benzene solution was filtered and concentrated and the residue recrystallized from hexane; yield 10.1 g. (77%), m.p. 200–202°, infrared absorption band (–CO–NH–) 1680 cm.$^{-1}$.

(b) **Cyclization of Methyl Ester.**—A suspension of 4.3 g. of cis-4-aminocyclohexanecarboxylic acid in 100 ml. of 3 N methanolic hydrogen chloride was refluxed for 3.5 hours. The acid dissolved rapidly. The solution was concentrated in vacuo and the residue recrystallized from isopropyl alcohol; yield 4.1 g. (71%) of cis-methyl 4-aminocyclohexane-carboxylate hydrochloride, m.p. 187–190°.

Anal. Calcd. for $C_8H_{15}NO_2 \cdot HCl$: C, 49.6; H, 8.3. Found: C, 49.9; H, 8.2.

The free ester was obtained by dissolving 1.3 g. of the hydrochloride in 1 ml. of water; 10 ml. of ethyl acetate and 1.3 g. of anhydrous potassium carbonate were added with vigorous stirring. The ethyl acetate solution was separated and the aqueous phase extracted with an additional 10 ml. of ethyl acetate. After drying and concentrating the extracts, 1.0 g. of methyl ester was obtained. The methyl ester was cyclized by heating to 190–200° for 10 minutes. After cooling, the residue was recrystallized from benzene–hexane and yielded 0.55 g. (70%) of 3-isoquinuclidone, m.p. 200–202°. The material gave no depression in a mixed melting point with the 3-isoquinuclidone prepared by direct cyclization of cis-4-aminocyclohexanecarboxylic acid.
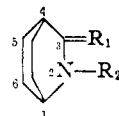
2-Benzyl-3-isoquinuclidone (IV) (General Procedure).— A solution of 5.0 g. (40 mmoles) of 3-isoquinuclidone in 50 ml. of toluene was refluxed with 1.6 g. of sodium amide (40 mmoles) with stirring for 2.5 hours. The reaction mixture was cooled to 25° and 7.2 g. (42 mmoles) of benzyl bromide added. After refluxing for 3 hours, the reaction mixture was cooled, filtered and concentrated in vacuo. On addition of hexane the residue crystallized. After two recrystallizations from hexane 6.4 g. (74%) of 2-benzyl-3-isoquinuclidone, m.p. 95–97°, was obtained; infrared absorption band of –CO–N– group, 1650 cm.$^{-1}$.

This procedure was used for the preparation of all the N-substituted 3-isoquinuclidones. In those cases where a

TABLE I

DERIVATIVES OF ISOQUINUCLIDINE

No.	R₁	R₂	Formula	M.p., °C.	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found
1	O	H	$C_7H_{11}NO$	200–202	67.2	67.3	8.9	8.7
2	H₂	H·HCl	$C_7H_{13}N·HCl$	>300	57.0	57.1	9.6	9.4
3	H₂	H·HO·C₆H₂(NO₂)₃ᵃ	$C_{13}H_{16}N_4O_7$	244–247	45.9	45.6	4.7	4.6
4	H₂	(CH₃)₂I⁻	$C_9H_{18}IN$	>300	40.5	40.3	6.8	6.8
5	O	CH₂C₆H₅	$C_{14}H_{17}NO$	93–95	78.1	78.2	8.0	7.9
6	H₂	CH₂C₆H₅	$C_{14}H_{19}N$	B. 100–103ᶜ	83.5	83.5	9.5	9.7
7	H₂	CH₂C₆H₅·CH₃I⁻	$C_{15}H_{22}IN$	238 dec.	52.5	52.5	6.5	6.3
8	O	CH(C₆H₅)₂	$C_{20}H_{21}NO$	181–184	82.4	82.1	7.3	7.4
9	H₂	CH(C₆H₅)₂	$C_{20}H_{23}N$	150–152	86.6	86.6	8.4	8.3
10	O	CH₂CH₂CH₂N(CH₃)₂ᵇ	$C_{12}H_{22}N_2O$	B. 125ᶜ	68.5	68.2	10.6	10.6
11	O	CH₂CH₂CH₂N⁺(CH₃)₃I⁻	$C_{13}H_{25}IN_2O$	168	44.3	44.0	7.2	7.3
12	H₂	CH₂CH₂CH₂N(CH₃)₂	$C_{12}H_{24}N_2$	B. 72–75ᶜ	73.4	73.2	12.3	12.3
13	H₂	CH₂CH₂CH₂N(CH₃)₂·2HCl	$C_{12}H_{24}N_2·2HCl$	253–257	Cl:26.3	26.0		
14	H₂	CH₂CH₂CH₂N⁺(CH₃)₃I⁻, CH₃I⁻	$C_{14}H_{30}I_2N_2$	295 dec.	35.0	34.9	6.3	6.5
15	O	CH₂CH₂N(C₂H₅)₂ᵇ	$C_{13}H_{24}N_2O$	B. 130ᶜ	69.6	69.1	10.8	10.9
16	H₂	CH₂CH₂N(C₂H₅)₂	$C_{13}H_{26}N_2$	B. 75ᶜ	74.2	74.7	12.5	12.7
17	H₂	CH₂CH₂N(C₂H₅)₂·2HCl	$C_{13}H_{26}N_2·2HCl$	198–202	55.1	54.9	10.0	10.0
18	H₂	CH₂CH₂N⁺(C₂H₅)₂CH₃I⁻, CH₃I⁻	$C_{15}H_{32}I_2N_2$	245 dec.	36.5	36.3	6.5	6.4

ᵃ Calcd.: N, 16.5. Found: N, 16.4. ᵇ These compounds were distilled in a semi-micro flask which permitted only the determination of the bath temperature and not of the actual vapors. ᶜ Boiling point at 1 mm. pressure.

crystalline product was not obtained the material was distilled.

2-Benzylisoquinuclidine (VI) (General Procedure).—To a stirred suspension of 3.0 g. (79 mmoles) of lithium aluminum hydride in 200 ml. of ether, 10.7 g. (50 mmoles) of 2-benzyl-3-isoquinuclidone was added gradually. The reaction mixture was stirred for 20 hours at 25°, then decomposed by addition of 9 ml. of ethyl acetate, 3 ml. of water, 6 ml. of 15% aqueous sodium hydroxide and 9 ml. of water; the solution was filtered, dried and concentrated *in vacuo*. The residue was distilled *in vacuo;* yield 9.0 g. (89%) of 2-benzyl-isoquinuclidine, b.p. 100–103° (1 mm.).

The same ratio of reactants was used in the preparation of the other substituted isoquinuclidines.

2-Benzylisoquinuclidine Methiodide (VIII) (General Procedure).—A solution of 3.6 g. (18 mmoles) of 2-benzyl-isoquinuclidine in 20 ml. of alcohol was treated with 7.8 g. (54 mmoles) of methyl iodide at 25°. After 5 minutes the methiodide began to crystallize. After 3 hours the methiodide was filtered off and recrystallized from alcohol; yield 4.8 g. (78%), m.p. 258°.

The same ratio of reactants was used for the quaternization of the other derivatives of isoquinuclidine and for the 3-isoquinuclidones with a basic side chain in the 2-position. The derivatives of isoquinuclidine with a basic side chain in the 2-position, were treated with 5 equivalents of methyl iodide to give the bis-methiodides.

Isoquinuclidine (VII).—A solution of 9.0 g. of 2-benzyl-isoquinuclidine in 100 ml. of ethanol was hydrogenated with 1.7 g. of 5% palladium-on-charcoal (hydrogen-uptake 0.97 l., calcd. 1.0 l., 0° (760 mm.)). The solution was filtered, neutralized with alcoholic hydrogen chloride and concentrated *in vacuo*. The crystalline residue was washed with ethyl acetate and recrystallized from an isopropyl alcohol–ethyl acetate mixture. This yielded 5.0 g. (76%), m.p. >300°, of isoquinuclidine hydrochloride.

A solution of 4.45 g. of isoquinuclidine hydrochloride in 10 ml. of water containing 4.2 g. of potassium carbonate was extracted twice with ether. The ether extract (50 ml.) was dried and concentrated; the residue was distilled and yielded 1.8 g. of crystalline isoquinuclidine.

Anal. Calcd. for $C_7H_{13}N$: C, 75.6; H, 11.8; N, 12.6. Found: C, 76.7; H, 11.6; N, 12.3.

Due to the ease with which the sample picked up CO_2 erratic analytical results were obtained, ranging from C, 71.3 to 76.7.

A picrate (Table I) was prepared from 55 mg. of isoquinu-

clidine in alcohol and melted at 244–247°, with decomposition starting at 220°.

Hydrolysis of 3-Isoquinuclidone.—Hydrolysis was carried out by refluxing a solution of 1.0 g. of 3-isoquinuclidone in 10 ml. of 2 N hydrochloric acid for 12 hours. The solution was evaporated to dryness, the residue dissolved in 10 ml. of ethanol and the *cis*-4-amino-cyclohexanecarboxylic acid (0.85 g.) precipitated by addition of triethylamine. After recrystallization from aqueous alcohol it melted over 300°.

Anal. Calcd. for $C_7H_{13}NO_2$: C, 58.7; H, 9.1. Found: C, 58.9; H, 9.1.

Thermal recyclization of 0.8 g. of the amino acid yielded 0.5 g. of isoquinuclidone after recrystallization.

Hydrolysis of 2-Benzyl-3-isoquinuclidone.—A mixture of 2 g. of 2-benzyl-3-isoquinuclidone and 40 ml. of 2 N hydrochloric acid was refluxed for 16 hours. The cooled reaction mixture was extracted with ether which yielded 1 g. of unchanged 2-benzyl-3-isoquinuclidone. The remaining aqueous solution was evaporated to dryness and the *cis*-4-benzyl-aminocyclohexanecarboxylic acid hydrochloride recrystallized from a mixture of alcohol and ether, m.p. 209–212°, yield 1 g. (40%).

Anal. Calcd. for $C_{14}H_{19}NO_2·HCl$: C, 62.3; H, 7.5. Found: C, 62.3; H, 7.6.

On addition of ammonia to a solution of 0.4 g. of the above hydrochloride in 3 ml. of water, the aminoacid precipitated; yield 0.28 g. (80%), m.p. 224–226°.

Anal. Calcd. for $C_{14}H_{19}NO_2$: C, 72.1; H, 8.2. Found: C, 72.1; H, 8.2.

Hofmann Degradation of 2-Benzylisoquinuclidine Methiodide (Chart II).—A solution of 2 g. of 2-benzylisoquinuclidine methiodide in 150 ml. of water was shaken for 1 hour with silver oxide freshly prepared from 4.25 g. of silver nitrate. The reaction mixture was filtered and concentrated *in vacuo* at 50–60°, and transferred to a distillation flask. At 1 mm. and 100–115° bath temperature 0.65 g. (52%) of base IXa distilled.

A sample (0.3 g.) was converted to the hydrochloride and recrystallized from a mixture of isopropyl alcohol–ether; it then melted at 181–183°.

Anal. Calcd. for $C_{15}H_{21}N·HCl$: C, 71.5; H, 8.8. Found: C, 71.8; H, 8.9.

The rest of the base (0.35 g.) was hydrogenated in 10 ml. of alcohol with platinum (50 mg. of PtO₂). In 10 minutes the calculated amount of hydrogen was taken up and

the reaction was stopped. The solution was filtered, acidified with methanolic hydrogen chloride and evaporated to dryness. The crystalline residue was recrystallized from an isopropyl alcohol–ether mixture and melted at 216–218° (X).

Anal. Calcd. for $C_{15}H_{23}N \cdot HCl$: C, 71.0; H, 9.5; N, 5.5. Found: C, 70.7; H, 9.6; N, 5.5.

N-Cyclohexylmethyl-N-methylbenzylamine (X).—A solution of 7.1 g. (50 mmoles) of N-methylcyclohexanecarboxamide[4] (XI) in 80 ml. of toluene was refluxed with 2 g. (50 mmoles) of sodium amide for 3 hours. After cooling, 8.5 g. (50 mmoles) of benzyl bromide was added and refluxing continued for 3 hours. The reaction mixture was cooled, filtered, concentrated and the residue was distilled *in vacuo;* yield 8.5 g. (74%) of N-benzyl-N-methylcyclohexanecarboxamide (XII), b.p. 146–149° (1 mm.).

Anal. Calcd. for $C_{15}H_{21}NO$: C, 77.9; H, 9.2. Found: C, 77.6; H, 9.1.

To a suspension of 1.7 g. (45 mmoles) of lithium aluminum hydride in 120 ml. of anhydrous ether, 6.95 g. (30 mmoles) of the above amide was added. The reaction mixture was stirred at 25° for 18 hours, then decomposed by adding 5.1 ml. of ethyl acetate, 1.7 ml. of water, 3.4 ml. of 15% aqueous sodium hydroxide and 5.1 ml. of water, filtered and concentrated. The residue was distilled *in vacuo* and yielded 5.2 g. (79%) of N-cyclohexylmethyl-N-methylbenzylamine, b.p. 106–108° at 1 mm. The hydrochloride prepared from this base, after recrystallization from isopropyl alcohol–ether melted at 216–218°.

Anal. Calcd. for $C_{15}H_{23}N \cdot HCl$: C, 71.0; H, 9.5. Found: C, 70.8; H, 9.4.

4-Acetamino-3-ethylacetophenone (XIV).—To a mixture of 50 g. (0.3 mole) of 2-ethylacetanilide,[8] 225 g. (1.69 moles) of aluminum chloride and 125 g. of carbon disulfide, 80 g. (0.78 mole) of acetyl chloride was added gradually. The reaction is exothermic and was completed by warming on a steam-bath for 5 minutes. After distilling off the carbon disulfide and excess acetyl chloride, the red mass was poured on to ice and the reaction product extracted with benzene. After recrystallization from an ethyl acetate–ether mixture the product melted at 113–115°, yield 36 g. (57%).

Anal. Calcd. for $C_{12}H_{15}NO_2$: C, 70.2; H, 7.4. Found: C, 70.2; H, 7.3.

(8) H. Paucksch, *Ber.*, **17**, 767 (1884); J. v. Braun, O. Bayer and G. Blessing, *ibid.*, **57**, 392 (1924).

4-Acetamino-3-ethylbenzoic Acid.—To a cooled solution of 24 g. (0.15 mole) of bromine in 130 ml. of water containing 17.4 g. (0.43 mole) of sodium hydroxide, 10 g. (0.049 mole) of 4-acetamino-3-ethylacetophenone dissolved in 25 ml. of dioxane was added dropwise with stirring at 0°. After 3 hours the reaction mixture was partially neutralized and extracted with chloroform. The aqueous solution was acidified to pH 2 which precipitated the acid. After cooling, the acid was filtered off and recrystallized from isopropyl alcohol; yield 4.0 g. (40%), m.p. 277–280°.

Anal. Calcd. for $C_{11}H_{13}NO_3$: C, 63.7; H, 6.3. Found: C, 63.5; H, 6.3.

4-Amino-3-ethylbenzoic Acid (XV).—A suspension of 15 g. of 4-acetamino-3-ethylbenzoic acid in 50 ml. of concentrated hydrochloric acid was refluxed for 4 hours. After cooling, the amino acid hydrochloride was filtered off and dissolved in alcohol. The solution was adjusted to pH 5 by adding alcoholic sodium hydroxide. After filtering off the sodium chloride the solution was concentrated *in vacuo* and the residue recrystallized from an alcohol–water mixture; yield 6 g. (50%), m.p. 152–154°.

Anal. Calcd. for $C_9H_{11}NO_2$: C, 65.4; H, 6.7. Found: C, 65.7; H, 6.6.

***cis*-4-Amino-3-ethylcyclohexanecarboxylic Acid (XVI).**—Hydrogenation of 8.3 g. (50 mmoles) of 4-amino-3-ethylbenzoic acid in 100 ml. of water with 1.0 g. of platinum oxide (hydrogen uptake 2.71 l. in 24 hours, calcd. 3.36 l.), after removal of the water, gave a sirupy residue. On addition of alcohol, crystals separated. After recrystallization from water–alcohol 4.0 g. (46%) of a *cis*-4-amino-3-ethylcyclohexanecarboxylic acid, m.p. 253–255°, was obtained.

Anal. Calcd. for $C_9H_{17}NO_2$: C, 63.1; H, 10.0. Found: C, 63.2; H, 9.8.

6-Ethyl-3-isoquinuclidone (XVII).—The *cis*-4-amino-3-ethylcyclohexanecarboxylic acid (2.5 g.) was cyclized to 6-ethyl-3-isoquinuclidone by heating to 250° for 3 minutes. After cooling, the melt was dissolved in benzene, filtered and evaporated to dryness. The residue was recrystallized from hexane; yield 2.0 g., m.p. 77–80°; infrared absorption band of –CO–NH– group 1707 cm.$^{-1}$.

Anal. Calcd. for $C_9H_{15}NO$: C, 70.6; H, 9.9. Found: C, 70.4; H, 9.6.

SUMMIT, NEW JERSEY

The Structure of the Antibiotic Puromycin[1,2]

BY PETER W. FRYTH, COY W. WALLER, BRIAN L. HUTCHINGS[3] AND JAMES H. WILLIAMS

The oxidation of puromycin with alkaline permanganate yielded anisic acid. The cleavage of puromycin with alcoholic hydrogen chloride gave 6-dimethylaminopurine dihydrochloride, the ester of *p*-methoxy-L-phenylalanine hydrochloride and 3-amino-3-deoxy-D-ribose hydrochloride. From the chemical and physical data on the antibiotic and its fragments, puromycin was shown to be 6-dimethylamino-9-[3-deoxy-3-(*p*-methoxy-L-phenylalanylamino)-β-D-ribofuranosyl]-β-purine.

Porter and co-workers[4,5] of these laboratories reported the isolation of a new antibiotic from the

substrate of a new species of actinomycete, *Streptomyces albo-niger*.[6] Since the partial structure of this antibiotic[7] showed it to be a purine derivative, puromycin was assigned as its generic name. Porter, *et al.*,[4,5] found that puromycin inhibited the growth of both gram positive and gram negative bacteria *in vitro*. Hewitt and co-workers[8] reported that the antibiotic had curative properties in mice and rabbits infected with *Trypanosoma*

(1) Puromycin is the generic name for Stylomycin, which is the American Cyanamid Co. trademark for puromycin. The trademark Achromycin, associated in some earlier publications with puromycin, has been reassigned as the trademark for the non-related antibiotic tetracycline.

(2) Presented at the Meeting-in-Miniature of the New York Section of the American Chemical Society, New York, February, 1954, and at the 126th Meeting of the American Chemical Society, New York, September, 1954.

(3) To whom inquiries should be addressed.

(4) J. N. Porter, R. I. Hewitt, C. W. Hesseltine, G. Krupka, J. A. Lowery, W. S. Wallace, N. Bohonos and J. H. Williams, *Antibiotics & Chemotherapy*, **2**, 409 (1952).

(5) J. N. Porter, G. C. Krupka and N. Bohonos, U. S. Patent 2,763,642.

(6) C. W. Hesseltine, J. N. Porter, N. Deduck, M. Hauck, N. Bohonos and J. H. Williams, *Mycologia*, **46**, 16 (1954).

(7) C. W. Waller, P. W. Fryth, B. L. Hutchings and J. H. Williams, THIS JOURNAL, **75**, 2025 (1953).

(8) R. I. Hewitt, W. S. Wallace, A. R. Gumble, E. R. Gill and J. H. Williams, *Am. J. Trop. Med. and Hyg.*, **2**, 254 (1953).