

The hydroboration product from 2-hexene prepared as described above, was heated under reflux for three hours (isomerization procedure). The reaction mixture was then treated with 300 mmoles of propionic acid and handled as above. There was obtained 14.7 g. of *n*-hexane, 85% yield.

Acknowledgment.—This investigation was made possible by Contract DA-33-008-ORD-992 supported by the Office of Ordnance Research, U. S. Army. This assistance is gratefully acknowledged.

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RECEIVED JUNE 29, 1959

SOME NEW COMPOUNDS HAVING THE HEXAGONAL BARIUM TITANATE STRUCTURE

Sir:

The structure of hexagonal barium titanate was determined by Burbank and Evans¹ using a single crystal prepared by the method of Matthias.² The procedure, which involves heating the reactants in a platinum crucible, has been repeated in this laboratory to obtain the amber colored crystals. These crystals did not become colorless upon heating for several days in air at 1200°. It seemed likely that the presence of platinum was needed to stabilize this hexagonal structure, especially since the isotopic phase Ba(Ti_{0.75}Pt_{0.25})O₃ has been reported by Blattner.³ The possibility that stabilization could be promoted by other foreign ions has been under investigation here for some time.

It has been found, using X-ray powder patterns as the criterion, that the hexagonal structure was adopted in presence of platinum, iridium, rhodium, ruthenium, cobalt, iron, manganese, chromium, vanadium and even trivalent titanium. The phases were prepared according to the formula BaM_xTi_{1-x}O_{3-z}. Mixtures of barium oxide, titanium dioxide, and the added metal oxide were ground together in an agate mortar and heated in air except those containing Mn₂O₃, Cr₂O₃ and V₂O₃. These mixtures were heated in evacuated sealed silica capsules. X-Ray powder diffraction photographs showed that the patterns of the phases given agreed closely with that of hexagonal barium titanate. Only a slight difference in spacing and intensities of reflections were observed.

BaPt_{0.10}Ti_{0.90}O_{3-z} BaIr_{0.25}Ti_{0.75}O_{3-z} BaIr_{0.50}Ti_{0.50}O_{3-z}
BaRh_{0.25}Ti_{0.75}O_{3-z} BaRu_{0.25}Ti_{0.75}O_{3-z} BaRu_{0.50}Ti_{0.50}O_{3-z}
BaCo_{0.25}Ti_{0.75}O_{3-z} BaFe_{0.25}Ti_{0.75}O_{3-z} BaFe_{0.50}Ti_{0.50}O_{3-z}
BaFe_{0.75}Ti_{0.25}O_{3-z} BaV_{0.50}Ti_{0.50}O_{3-z} BaV_{0.75}Ti_{0.25}O_{3-z}
BaV_{0.90}Ti_{0.10}O_{3-z}

Chemical analyses of these phases have not yet been made. The formulas are derived from starting compositions and from the absence of any evidence for heterogeneity obtained by X-ray and microscopic examination. When the proportion of foreign ion was smaller than the lowest figure shown in the formulas, the pattern of tetragonal barium titanate could be detected in the photo-

- (1) R. D. Burbank and H. T. Evans, Jr., *Acta Cryst.*, **1**, 330 (1948).
- (2) B. Matthias, *Phys. Rev.*, **73**, 808 (1948).
- (3) H. Blattner, H. Gränicher, W. Kanzig and W. Merz, *Helv. Phys. Acta*, **21**, 341 (1948).

graphs. Iridium, ruthenium, iron and vanadium in proportions larger than the highest given in the formulas caused the introduction of extraneous lines in the X-ray diffraction photographs. The limiting compositions of the phases have not yet been determined. The data suggest, however, that these metal ions are incorporated in the lattice of the hexagonal barium titanate.

Magnetic susceptibility measurements have been made on the phases of BaIr_{0.25}Ti_{0.75}O_{3-z}, BaCo_{0.25}Ti_{0.75}O_{3-z}, and BaFe_{0.25}Ti_{0.75}O_{3-z}. While these measurements have been made only at one temperature, they appear to indicate one, two and four unpaired electrons per atom of iridium, cobalt and iron, respectively.

Work is now in progress to determine the permissible range of composition of the phases prepared.

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RECEIVED MAY 21, 1959

ISOLATION OF ALDOSTERONE FROM INCUBATES OF ADRENALS OF THE AMERICAN BULLFROG AND STIMULATION OF ITS PRODUCTION BY MAMMALIAN ADRENOCORTICOTROPIN^{1,2}

Sir:

We wish to report that aldosterone was the most abundant steroid found in incubates of adrenals from the American bullfrog, *Rana catesbeiana*, under the stimulation of bovine adrenocorticotropin. Corticosterone was the second major steroid found in the incubates, with the ratio of aldosterone to corticosterone, 3.6 to 1. No cortisol could be detected, although previous studies have disclosed only cortisol and corticosterone as the major steroids secreted by the adrenals of both mammals³ and cold-blooded animals.^{4,5} The salt metabolism of the frog has been shown to be under the regulation of both the adrenals and the anterior pituitary,⁶ and it is possible that aldosterone may be the adrenal hormone responsible for this regulation.

Adrenal tissue (1218 mg. fresh weight) excised from 37 female bullfrogs (total body weight 13.13 kg.) just prior to their breeding season were cut up into small pieces in isotonic Krebs-Ringer bicarbonate solution containing glucose (200 mg. per 100 cc.) which has been flushed with mixture of 5% CO₂-95% O₂ (final pH, 7.4). After incubation for 30 minutes at 25-26° the medium was discarded and incubation was continued for 2 hours with a new volume of medium containing bovine adrenocorticotropin⁷ (1.09 I.U. per 100 mg. of tissue). This medium then was extracted with dichloromethane and ethyl acetate. The extract was fractionated by partitioning between ethyl

(1) Paper XVIII of the adrenocorticotropin (ACTH) series; for Paper XVII, see C. H. Li, *Bull. Soc. Chim. Biol.*, **40**, 1757 (1958).

(2) This work is supported in part by the U. S. Public Health Service (G-2907) and the Albert and Mary Lasker Foundation.

(3) I. E. Bush, *Schweiz. Med. Wochschr.*, **85**, 645 (1955).

(4) J. G. Phillips and C. Jones, *J. Endocrinol.*, **16**, iii (1957).

(5) D. R. Idler, A. P. Ronald and P. J. Schmidt, *THIS JOURNAL*, **81**, 1260 (1959).

(6) M. A. Fowler and C. Jones, *J. Endocrinol.*, **13**, vi (1956).

(7) C. H. Li and J. S. Dixon, *Science*, **124**, 934 (1956); C. H. Li, J. S. Dixon and D. Chung, *THIS JOURNAL*, **80**, 2587 (1958).

acetate and water and between *n*-hexane and 3% ethanol. The corticosteroid fraction was subjected to reversed phase partition chromatography on purified acetylated filter paper (Schleicher and Schuell) in the system recently developed,⁸ *n*-butyl acetate/23% aqueous ethanol, at 22–25° for 18.5 hours, collecting the overflow for the isolation of aldosterone.

Ultraviolet contact photography of the paper strips showed a spot parallel to corticosterone, but no spots were detected corresponding to cortisone or cortisol; the methanol eluate of the spot gave λ_{\max} , at 240 $m\mu$ (EtOH), with an optical density equivalent to 15.1 μg . of corticosterone. An aliquot of the sample reduced blue tetrazolium,^{9,10} with a typical color development within 40 minutes. When treated with concd. sulfuric acid at 24° for 2 hours,¹¹ another aliquot of the sample showed λ_{\max} , at 287, 375 and 455 $m\mu$ and a shoulder at 330 $m\mu$, and optical density ratios of 1.0/0.30/0.17/0.50. In the Aminco-Bowman spectrophotofluorometer there was a maximum in the activation spectrum at 465 $m\mu$. Activation at this wave length gave a fluorescent spectrum^{12,13} with λ_{\max} , at 510 $m\mu$.

The overflow collected from the chromatogram gave a λ_{\max} , at 239 $m\mu$ (EtOH), equivalent to 54.8 μg . of aldosterone. After the fraction had been rerun for 5 hours in the same system, ultraviolet contact photography showed a single intense spot parallel to standard aldosterone with R_f values different from cortisone, cortisol, epicortisol, and 20 α - and 20 β -hydroxycortisol, run on parallel strips. The eluate of the spot from the paper chromatogram gave a λ_{\max} , at 239 $m\mu$ (EtOH), with an optical density equivalent to 54.6 μg . of aldosterone. An aliquot (12 μg .) treated with 1 ml. of concd. sulfuric acid¹⁴ at 24° for 2 hours gave λ_{\max} , at 288 $m\mu$. After an additional incubation in a water-bath at 90° for one hour the spectrum was characteristically changed, and was identical with that of standard aldosterone eluted from the paper chromatogram, with λ_{\max} , at 245, 285 and 380 $m\mu$ and optical density ratios of 1.0/0.99/0.3. When a 2- μg . aliquot was treated with blue tetrazolium for 40 minutes,¹⁴ it gave a characteristic color, with λ_{\max} , at 520 $m\mu$. Biological assay of the product indicated that it had a sodium-retention activity¹⁵ comparable to that possessed by an authentic sample of *dl*-aldosterone.

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RECEIVED JUNE 11, 1959

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(15) We are indebted to Dr. J. J. Chart of Ciba, Inc., Summit, New Jersey, for the biological data.

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THE STRUCTURES OF DELTALINE AND DELPHELINE Sir:

We wish to suggest Structure I (I, $R^1 = -\text{OAc}$, $R^2 = -\text{OH}$) for deltaline and II (II, $R^1 = -\text{OH}$, $R^2 = -\text{H}$) for delpheline.¹ I and II embody a perhydrophenanthrene skeleton differing slightly but importantly from the ring system proposed for lycoctonine derivatives.² We believe that a rearrangement of the Wagner-Meerwein type occurs during acidic hydrolysis of the cyclic acetal groups and converts the perhydrophenanthrene skeleton into the lycoctonine skeleton.^{1,2}

The tertiary hydroxyl group of I reacts sluggishly with acetyl chloride to yield *acetyldeltaline* (III, $R^1 = -\text{OAc}$, $R^2 = -\text{OAc}$), $\text{C}_{29}\text{H}_{43}\text{NO}_9$, m.p. 155–156°, $[\alpha]_D^{25} -31.0^\circ$ (CHCl_3).^{3a} Pyrolysis of III at 210–220° and dehydrohalogenation of chloroacetyldelpheline (IV, $R^1 = -\text{OAc}$, $R^2 = -\text{Cl}$)¹ in refluxing collidine both gave *dchydrodesoxydeltaline* (V, $R^1 = -\text{OAc}$, R^2 absent, $>\text{C}_{13} = \text{C}_5<$), $\text{C}_{27}\text{H}_{39}\text{NO}_7$,^{3b} m.p. 148.5–150.0°, $[\alpha]_D^{25} -136.0^\circ$ (MeOH), ν_{\max} , 832 cm^{-1} . Catalytic hydrogenation of V over platinum in ethanol gave acetyldelpheline (VI, $R^1 = -\text{OAc}$, $R^2 = -\text{H}$).⁴ The two new routes from deltaline to delpheline strengthen our assumption that no skeletal rearrangement occurred during the previous interconversion.¹

Saponification of I in refluxing alcoholic potassium hydroxide gave *deltamine* (VII, $R^1 = -\text{OH}$, $R^2 = -\text{OH}$),⁵ $\text{C}_{25}\text{H}_{39}\text{NO}_7$, m.p. 239–240°, $[\alpha]_D^{33} -19.25^\circ$ (MeOH).^{3b} Hydrolysis of the acetal function of VII with hot 10% sulfuric acid yields formaldehyde and *demethylenedeltamine* (VIII, $R^1 = -\text{OH}$, $R^2 = -\text{OH}$, $R^3 = -\text{OH}$, $R^4 = -\text{OH}$) as the *dihydrate*, $\text{C}_{24}\text{H}_{39}\text{NO}_7 \cdot 2\text{H}_2\text{O}$,⁵ m.p. 95–97° (dec.), $[\alpha]_D^{25} +27.0^\circ$ (MeOH).^{3b} Demethylenedeltamine (VIII) consumed two moles of periodic acid⁶ to give a diseco-acid, not isolated, which spontaneously formed a γ -lactone (IX), $\text{C}_{24}\text{H}_{35}\text{NO}_7$,^{3b} m.p. 215.0–216.2°, $[\alpha]_D^{24} -64.3^\circ$ (MeOH), ν_{\max} , 1780 and 1712 cm^{-1} .

γ -Lactonization established the relationship of the tertiary hydroxyl group of I with respect to the carbon atom which eventually becomes a carboxyl during the periodate oxidation of VIII. If no rearrangement had occurred during the acidic genesis of VIII, I would then be expected to possess Structure X ($R^1 = -\text{OAc}$, $R^2 = -\text{OH}$, $R^3 = -\text{R}^4 = -\text{O-CH}_2\text{-O-}$)⁶ on the basis of the interconversion to desoxylycoctonine. Placement of the OH group at the bridgehead position, R^2 , in X is not, however, consonant with the chemical behavior of this function. Treatment of deltaline under mild conditions with SOCl_2 gives chloroacetyldelpheline, which reacts nearly instantaneously with ethanolic

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