[CONTRIBUTION FROM THE DIVISION OF CHEMISTRY NATIONAL RESEARCH COUNCIL]

α-Pseudaconitine and α-Veratroylpseudaconine[1]

BY LÉO MARION AND O. E. EDWARDS

Of the previously reported aconite alkaloids two only, bikhaconitine[2] and pseudaconitine[3] yield acetic and veratric acid when hydrolyzed, together with basic fragments designated as bikhaconine and pseudaconine, respectively. A third, indaconitine,[4] yields on hydrolysis, acetic acid, benzoic acid and pseudaconine identical with the alkamine obtained from pseudaconitine.

Two only of the four hydroxyl groups present in pseudaconine are involved in ester linkages in the parent alkaloid and, therefore, several isomers of pseudaconitine are theoretically possible. It is the object of this paper to report one such naturally occurring isomer and a veratroylpseudaconine isomeric with but different from the veratroylpseudaconine produced by the partial hydrolysis of pseudaconitine.

Commercial "Nepaul Aconite Root" is known to contain a varying quantity of *Aconitum Napellus* which is the best source of aconitine. A recent shipment that came to this Laboratory was found to contain no aconitine whatsoever. It has, however, been possible to isolate from the material two new bases which were separated through the different solubilities of their hydrochlorides in chloroform. One of these is isomeric with pseudaconitine and like it on hydrolysis yields acetic acid, veratric acid and pseudaconine. It is proposed to designate it as α-pseudaconitine. The second base yields, when hydrolyzed, veratric acid and pseudaconine but no acetic acid. It is identical with the veratroylpseudaconine obtained as a product of the partial hydrolysis of α-pseudaconitine but different from the veratroylpseudaconine obtained similarly from pseudaconitine.[3] It is, therefore, proposed to designate it as α-veratroylpseudaconine. The formula of pseudaconitine as corrected by Dunstan and Andrews,[4] $C_{36}H_{51}O_{12}N$, is accepted with reserve because of the unusual difficulty experienced in analyzing the alkaloids and their derivatives for nitrogen.

Pseudaconine obtained from both bases is identical with the pseudaconine produced when pseudaconitine is hydrolyzed and it has been identified by analysis, by its properties and by the preparation of its known derivatives. Pseudaconine forms a tetraacetyl derivative which, when heated above its melting point *in vacuo*, loses acetic acid and is converted to triacetylpyropseudaconine.[5] This, in turn, can be saponified to pyropseudaconine. It has now been found that the formation of triacetylpyropseudaconine is accompanied by the production of a small quantity of a second pyrolytic substance which had not previously been observed. Moreover, when pseudaconine was boiled with 10 *N* sulfuric acid it lost one methyl group attached to oxygen plus the elements of methanol and gave rise to des-O-methyldemethoxydehydropseudaconine which contains two methoxyl groups whereas pseudaconine has four. It is already known that one of the methyl groups attached to oxygen is relatively unstable since pyropseudaconitine, on acetylation, yields a compound which contains three acetyl groups but has only five methoxyl groups whereas pyropseudaconitine has six.[5] However, the removal of a second methoxyl group as methanol has not hitherto been observed in the aconitine series.

Like pseudaconitine, α-pseudaconitine pyrolyses readily, but it has not been possible to crystallize pyro-α-pseudaconitine. Furthermore when tetraacetylpseudaconine is pyrolyzed one, and only one, mole of acetic acid is lost. It is, therefore, likely that the acetyl group occupies the same position in the two isomers. Since α-veratroylpseudaconine is not identical with veratroylpseudaconine, it is also likely that α-psuedaconitine differs from pseudaconitine in that the veratroyl group does not occupy the same position in the former as it does in the latter.

It may be mentioned, incidentally, that this case of isomerism is one of the very few of that type noticed so far in the naturally-occurring aconite alkaloids.

Experimental

A dried benzene extract of commercial "Nepaul Aconite Root" (4.55 kg.) obtained from the Fine Chemical Company, Toronto, was used as starting material. The dry material was broken up, stirred into aqueous oxalic acid, the mixture filtered, basified with ammonia and exhaustively extracted with chloroform in continuous liquid-liquid extractors. The combined chloroform extract was distilled to dryness and the residue dissolved in aqueous oxalic acid. The filtered solution was extracted repeatedly with ether, basified with ammonia and again exhausted with chloroform in continuous extractors. The combined chloroform extract was concentrated to about one liter and extracted with three portions of 3 *N* hydrochloric acid, each about one-third the volume of the chloroform solution. There were thus obtained a chloroform solution A of the soluble base hydrochlorides and an aqueous solution B containing the base hydrochlorides insoluble in chloroform.

Isolation of α-Veratroylpseudaconine.—The aqueous solution B was basified with ammonia and the solution thoroughly extracted first with ether and then with chloroform. The chloroform extract was distilled to dryness and the residual bases dissolved in 3 *N* hydrochloric acid, the solution basified again with ammonia and extracted again first with ether and then with chloroform (extract C). The combined ether extract was distilled to dryness and the residual gum dissolved in a little warm methanol. After long standing this solution deposited a few crystals and cautious addition of absolute ether then brought

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(1) Published as N. R. C. No. 1396.

(2) W. R. Dunstan and A. E. Andrews, *J. Chem. Soc.*, **87**, 1636 (1905)

(3) W. R. Dunstan and F. H. Carr, *ibid.*, **71**, 350 (1897).

(4) W. R. Dunstan and A. E. Andrews, *ibid.*, **87**, 1620 (1905)

(5) T. M. Sharp, *ibid.*, 3094 (1928).

down a copious precipitate of the crystalline base. After four recrystallizations from methanol–ether, from which it separated as colorless flat needles, α-veratroylpseudaconine melted at 209–211°[6] when immersed in the bath at 180°; wt. 0.5 g., $[\alpha]_D$ +55° (c = 1.137 in chloroform in micro-tube).

Anal. Calcd. for $C_{34}H_{49}O_{11}N$: C, 63.06; H, 7.57; N, 2.16; 6 OCH_3, 28.75. Found: C, 63.35, 63.14; H, 7.81, 7.66; N, 2.28, 2.20; OCH_3, 28.15, 26.15.

A methanolic solution of α-veratroylpseudaconine was cautiously neutralized with 65% perchloric acid. Crystallization of the perchlorate was induced by the addition of a little absolute ether. After recrystallization from methanol, α-veratroylpseudaconine perchlorate consisted of clusters of colorless rectangular plates sintering at 231° and melting at 232–233° (dec.) when immersed in the bath at 210°.

Anal. Calcd. for $C_{34}H_{49}O_{11}N \cdot HClO_4$: C, 54.59; H, 6.69; N, 1.87; Cl, 4.75. Found: C, 54.57, 54.65; H, 6.70, 6.84; N, 1.79; Cl, 4.79, 4.66.

A solution of α-veratroylpseudaconine in dry methanol was acidified to congo red by the dropwise addition of 40% hydrobromic acid. The addition of absolute ether combined with cooling in a Dry Ice–acetone-bath brought about the crystallization of the hydrobromide which, after several recrystallizations from methanol–ether, was obtained as colorless flat needles melting at 246–247° (dec.) when immersed in the bath at 235°.

Anal. Calcd. for $C_{34}H_{49}O_{11}N \cdot HBr$: Br, 10.98. Found: Br, 10.64.

A small quantity of α-veratroylpseudaconine in dry methanol was converted to the hydriodide by the procedure followed for the hydrobromide. The recrystallized hydriodide which separated as small faintly yellow buttons, melted at 246° (dec.) when immersed in the bath at 210°.

Isolation of α-Pseudaconitine.—The chloroform solution A containing the soluble base hydrochlorides was distilled to dryness, the residue dissolved in 3 *N* hydrochloric acid, the solution washed several times with ether and basified with ammonia. This caused the precipitation of an amorphous base which was filtered. The filtrate was extracted first with ether (extract D) and then with chloroform (extract E).

The amorphous precipitate was dried (13 g.), dissolved in methanol and the solution neutralized with 65% perchloric acid. A crystalline salt was precipitated which after recrystallization from methanol began to sinter at 233° and melted at 245° (dec.), wt. 2.5 g.

The ether extract of the basic filtrate (extract D) was concentrated on the steam-bath and dried over anhydrous sodium sulfate. α-Pseudaconitine crystallized from the ether solution and after repeated recrystallization from methanol was obtained as colorless diamond-shaped prisms, m. p. 205–206° (dec.) when immersed at 180°, wt. 1.2 g. $[\alpha]^{25}_D$ +24.7° (c = 2.40 in chloroform). In admixture with α-veratroylpseudaconine it melted at 193–195°.

Anal. Calcd. for $C_{36}H_{51}O_{12}N$: C, 62.70; H, 7.40; N, 2.03; 6 OMe, 27.0. Found: C, 63.03, 63.12; H, 7.73, 7.92; N, 2.44, 2.47; OMe, 26.57, 26.67.

α-Pseudaconitine dissolved in dry methanol was neutralized with 65% perchloric acid. A perchlorate crystallized out which after three recrystallizations from dry methanol and one from acetone, was obtained as colorless diamond-shaped plates which began to sinter at 233° and melted at 246° (dec.) when immersed in the bath at 210° either alone or in admixture with the perchlorate obtained from the above-described amorphous precipitate.

Anal. Calcd. for $C_{36}H_{51}O_{12}N \cdot HClO_4$: C, 54.72; H, 6.58; N, 1.77; Cl, 4.50. Found: C, 54.25, 54.27; H, 6.96, 7.08; N, 1.27; Cl, 4.61, 4.42.

It was not possible to obtain a crystalline hydrobromide from α-pseudaconitine but it formed a hydriodide which crystallized from methanol–ether as clusters of needles melting at 220–220.5° (dec.) when immersed in the bath at 210°.

Anal. Calcd. for $C_{36}H_{51}O_{12}N \cdot HI$: C, 52.88; H, 6.36. Found: C, 52.77, 52.69; H, 6.31, 6.53.

Both the hydrobromide and hydriodide of pseudaconitine contain water of crystallization and melt at 199 and 230°, respectively.[7]

Hydrolysis of α-Pseudaconitine.—α-Pseudaconitine (1.2 g.) was hydrolyzed by boiling with methanolic potassium hydroxide. Most of the methanol was evaporated, water added and the solution extracted repeatedly with chloroform. The combined chloroform extract when distilled to dryness left a basic residue which crystallized from acetone. After two recrystallizations from the same solvent the base was obtained as colorless prisms containing 1 mole of acetone; sintered at 81° and melted at 86° (dec.) $[\alpha]_D$ +38.1° (c = 1.272 in water). Henry and Sharp[7] give for pseudaconine crystallized from acetone, m. p. 93–94°, $[\alpha]^{20}_D$ + 38.7° (in water), whereas Dunstan and Andrews[4] give m. p. 86–87°, $[\alpha]_D$ + 39.0° (in water).

Anal. Calcd. for $C_{25}H_{41}O_8N \cdot C_3H_6O$: C, 62.04; H, 8.69; N, 2.59; 4 OCH_3, 22.92; C_3H_6O, 10.72. Found: C, 62.18, 62.23; H, 8.62, 8.70; N, 2.89, 3.00; OCH_3, 22.76, 22.82; C_3H_6O, 9.94, 10.2.

Pseudaconine can also be crystallized from ethanol from which it separated as colorless prisms containing 1 mole of ethanol which began to sinter at 90° and melted completely at 97°.

Anal. Calcd. for $C_{25}H_{41}O_8N \cdot C_2H_6O$: C, 61.25; H, 8.88. Found: C, 61.58, 61.60; H, 8.68, 9.00.

For pseudaconine crystallized from ethanol, Dunstan and Andrews[4] give m. p. 94–95°.

The aqueous potassium hydroxide solution which had been extracted with chloroform was acidified with sulfuric acid. This caused the precipitation of a crystalline acid which, after cooling, was filtered and washed with a little water. After two recrystallizations from aqueous methanol it consisted of colorless leaflets, m. p. 180–182° either alone or after admixture with an authentic sample of veratric acid.

The aqueous mother liquor from which veratric acid had first separated was distilled with steam so long as the distillate showed an acid reaction. The distillate was neutralized with 0.1 *N* sodium hydroxide and evaporated to dryness. The solid residue was dissolved in water (2 cc.) and *p*-bromophenacyl bromide (0.2 g.) added together with sufficient ethanol to produce a clear solution which was refluxed for two hours and allowed to cool. Some unchanged *p*-bromophenacyl bromide first separated and then a crop of crystals which after three recrystallizations from aqueous methanol melted at 80–83° either alone or after admixture with an authentic sample of *p*-bromophenacyl acetate (m. p. 85–86°).

Hydrolysis of α-Veratroylpseudaconine.—α-Veratroylpseudaconine (93 mg.) was hydrolyzed by refluxing with methanolic potassium hydroxide. The resulting solution when worked up exactly as above yielded pseudaconine which was crystallized from acetone. Either alone or in admixture with the hydrolytic base obtained from α-pseudaconitine, it began to sinter at 81° and melted at 84° (dec.). The hydrolysis liquor also yielded a small quantity of veratric acid but no acetic acid.

Tetraacetylpseudaconine.—Pseudaconine (70 mg. obtained from α-pseudaconitine) was refluxed for two hours with acetyl chloride (2 cc.), the excess reagent distilled off and the residue dissolved in water. The solution was basified with sodium carbonate and extracted repeatedly with ether. The combined and dried extract when distilled to dryness left a crystalline residue which was crystallized four times from methanol. Tetraacetylpseudaconine formed clusters of colorless needles, m. p. 227–228° (dec.) when immersed in the bath at 210°; wt. 76 mg., $[\alpha]_D$ −8.2° (c = 1.12 in ethanol).

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(6) All melting points are corrected

(7) T. A. Henry and T. M. Sharp, *J. Chem. Soc.*, 1105 (1928).

Henry and Sharp[7] describe tetraacetylpseudaconine as colorless stout needles, m. p. 228° (dec.), $[\alpha]^{20}D$ −8.1° (c = 0.956 in alcohol).

Anal. Calcd. for $C_{33}H_{49}O_{12}N$: C, 60.83; H, 7.53; N, 2.15; 4 OCH_3, 19.05; 4 CH_3CO, 26.42. Found: C, 60.45, 60.70; H, 7.58, 7.55; N, 2.31, 2.35; OCH_3, 19.69, 19.40; CH_3CO, 25.08, 25.58.

The tetraacetyl derivative was also prepared from a small quantity of pseudaconine obtained from the hydrolysis of α-veratroylpseudaconine and found by melting point and mixed melting point to be identical with that described above.

The mother-liquors from the crystallization of α-pseudaconitine and α-veratroylpseudaconine were combined with Extracts C and E and evaporated to dryness. The residual gum was saponified with methanolic potassium hydroxide and the basic product refluxed with acetyl chloride. This yielded tetraacetylpseudaconine, m. p. 227–228°, wt. 6.4 g.

Partial Hydrolysis of α-Pseudaconitine.—α-Pseudaconitine (92 mg.) was dissolved in dilute sulfuric acid, the solution made just neutral by the addition of dilute sodium hydroxide and heated in a sealed pressure tube at 135° for three hours. After cooling sulfuric acid was added and the solution repeatedly extracted with absolute ether. The combined extract on evaporation yielded no veratric acid but a volatile acid which was distilled from a small bulb heated in an air-bath (120–130°). The colorless acid which had a strong odor of acetic acid was converted to the silver salt by shaking with water and silver oxide. The filtered solution when evaporated to a small volume (*ca.* 0.5 cc.) deposited needles of silver acetate, wt. 2 mg. The previous identification of acetic acid in the complete hydrolysis of α-pseudaconitine and the isolation of α-veratroylpseudaconine described below show that this salt must be silver acetate.

The aqueous acid solution which had been extracted with ether was basified with sodium carbonate and thoroughly extracted with chloroform. The base recovered from the combined chloroform extract was dissolved in acetone, the solution concentrated to a thin sirup and allowed to stand. A crystalline base separated which was recrystallized twice from methanol–ether from which it separated as colorless needles, m. p. 207–211°. In admixture with α-veratroylpseudaconine, the m. p. was 208–211°; wt. 62 mg. $[\alpha]_D$ +49° (c = 1.12 in chloroform in a Hilger microtube).[8] Veratroylpseudaconine obtained from pseudaconitine melts at 199° and has $[\alpha]_D$ −38.18° (c = 1.5 in alcohol).[3]

Pyrolysis of Tetraacetylpseudaconine.—Tetraacetylpseudaconine (0.323 g.) was heated for three minutes at 240°/1 mm. when a vigorous reaction took place. After cooling, the residue in the flask (wt. 0.30 g.) was dissolved in warm dry methanol. A small precipitate of fine, colorless needles separated almost immediately. After three recrystallizations from methanol the product sintered at 281° and melted at 284°.

Anal. Found: C, 62.36, 62.19; H, 8.05, 8.07; N, 2.87; OMe, 21.87.

The foregoing substance which had not yet been reported was obtained in too small a yield to permit the preparation of derivatives. Saponification yielded a gum which could not be crystallized. Because of the uncertainty of the nitrogen determinations in pseudaconine and the products derived from it, no attempt is made at suggesting an empirical formula for the product melting at 284°. The original methanolic mother-liquor from which the above compound had separated was concentrated on the steam-bath. On cooling it deposited a second product as colorless six-sided plates, m. p. 154°, $[\alpha]_D$ +157.3° (c = 0.642 in abs. ethanol). Triacetylpyropseudaconine has been described[5] as six-sided plates, m. p. 155–158°, $[\alpha]_D$ +156.4° (c = 1.2 in ethanol).

Anal. Calcd. for $C_{31}H_{45}O_{10}N$: C, 62.94; H, 7.61; N, 2.37. Found: C, 63.13; H, 7.48; N, 2.71.

Hydrolysis of Triacetylpyropseudaconine.—Triacetylpyropseudaconine when hydrolyzed with methanolic potassium hydroxide yields pyropseudaconine which crystallizes from ether as colorless needles, m. p. 170° when immersed in the bath at 155°, $[\alpha]_D$ +227° (c = 0.2736 in abs. ethanol). Sharp[5] describes pyropseudaconine as prismatic needles, m. p. 173–174°, $[\alpha]_D$ +230.1° (c = 1.12 in ethanol).

Anal. Calcd. for $C_{25}H_{39}O_7N$: C, 64.52; H, 8.39. Found: C, 64.30, 64.57; H, 8.61, 8.44.

Pyropseudaconine can also be crystallized from water from which it separated as colorless, prismatic needles containing 2 moles of water, m. p. 92°.

Anal. Calcd. for $C_{25}H_{39}O_7N \cdot 2H_2O$: C, 59.88; H, 8.58. Found: C, 59.58, 59.71; H, 8.42, 8.67.

Des-O-methyldemethoxydehydropseudaconine.—Pseudaconine (0.33 g.) was refluxed for ninety minutes with 10 N sulfuric acid (30 cc.), the solution cooled, basified with sodium carbonate and thoroughly extracted with chloroform (10 times). The combined extract on evaporation yielded a gummy residue which crystallized from water from which it was obtained as colorless needles containing 3 moles of water, which sintered at 108° and melted at 114° (dec.); wt. 0.14 g.

Anal. Calcd. for $C_{23}H_{35}O_7N \cdot 3H_2O$: C, 56.20; H, 8.35; 2 OCH_3, 12.63; $3H_2O$, 11.0. Found: C, 56.44, 56.43; H, 8.22, 8.43; OCH_3, 12.46, 11.88; H_2O, 10.0, 9.55 (*in vacuo* over boiling water).

The base left after heating for two hours at 100° (0.5 mm.) consisted of a white powder which readily absorbed water from the air. Even after prolonged and repeated heating, analysis revealed a trace of water still present.

Anal. Calcd. for $C_{23}H_{35}O_7N$: C, 63.16; H, 8.01. Calcd. for $C_{23}H_{36}O_7N \cdot 0.5H_2O$: C, 61.88; H, 8.07. Found: C, 61.84, 62.03; H, 8.37, 7.86.

Des-O-methyldemethoxydehydropseudaconine when crystallized from methanol separated as colorless needles which sintered at 127° and melted at 133° (dec.). The crystals contain one mole of methanol which is gradually lost on standing, $[\alpha]_D$ +17.9° (c = 0.488 in dry methanol).

Anal. Calcd. for $C_{23}H_{35}O_7N \cdot CH_4O$: C, 61.41; H, 8.32. Found: C, 61.49, 61.34; H, 8.46, 8.17.

Pseudaconine was not altered by boiling with 28% phosphoric acid but boiling with 65% phosphoric acid produced the same compound as 10 N sulfuric acid.

Summary

1. Two new alkaloids have been isolated. One of these, α-pseudaconitine, is isomeric with pseudaconitine. The other is identical with the base obtained on removal of the acetyl group of α-pseudaconitine by partial hydrolysis and it has been named α-veratroylpseudaconine.

2. On complete hydrolysis α-pseudaconitine, like pseudaconitine, gave rise to acetic acid, veratric acid and pseudaconine whereas α-veratroylpseudaconine yielded veratric acid and pseudaconine.

3. Pseudaconine was identified by its analysis, its properties and the preparation of a number of its known derivatives.

4. It was shown that the pyrolysis of tetraacetylpseudaconine produced besides triacetyl-

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(8) The micro-polarimeter tube used is made so that it gives a positive polarimeter reading which varies with the amount of tightening of the screw-caps This may be due to the strains set up in the cover glass by the screw-cap. A tube filled with pure chloroform gave polarimeter readings of 0.01 to 0.09 depending on the degree of tightening of the screw caps. This obviously lowers the accuracy of the determination.

pyropseudaconine, a small quantity of a hitherto unobserved by-product.

5. The action of 10 *N* sulfuric acid on pseudaconine gave rise to des-O-methyldemethoxydehydropseudaconine.

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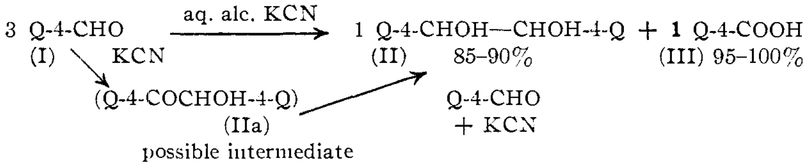
[CONTRIBUTION FROM THE WELLCOME RESEARCH LABORATORIES]

Cinchoninaldehyde: Benzoin and Cannizzaro Reactions

BY ARTHUR P. PHILLIPS

In continuation of our studies with cinchoninaldehyde (I),[1] it has been found that this aldehyde exhibits an unexpected reaction with potassium cyanide. Instead of the usual benzoin type of product (IIa) the hydrobenzoin-type of compound (II) was obtained together with cinchoninic acid (III). The structure of II was established by oxidation with chromic anhydride to form cinchoninic acid, by reaction with benzoyl chloride to form the dibenzoate (IV), and by lead tetraacetate oxidation to produce cinchoninaldehyde, which was isolated as its phenylhydrazone or *p*-nitrophenylhydrazone (V).[2]



$$\underset{\text{(I)}}{3\ \text{Q-4-CHO}} \xrightarrow{\text{aq. alc. KCN}} \underset{\text{(II)}\ \ 85\text{–}90\%}{1\ \text{Q-4-CHOH—CHOH-4-Q}} + \underset{\text{(III)}\ 95\text{–}100\%}{1\ \text{Q-4-COOH}}$$

$$\text{(I)} \xrightarrow{\text{KCN}} \underset{\text{possible intermediate}}{\underset{\text{(IIa)}}{\text{(Q-4-COCHOH-4-Q)}}} \longrightarrow \text{(II)} \qquad \text{Q-4-CHO} + \text{KCN}$$

The results can be explained by considering the benzoin (IIa) to be formed as an intermediate which then undergoes an intermolecular oxidation–reduction (modified Cannizzaro) with more of the aldehyde to give the final products II and III.

Formation of the hydrobenzoin directly in the benzoin condensation (and other evidence) led the author to suspect that cinchoninaldehyde might undergo the Cannizzaro reaction more readily than many aromatic aldehydes. The reaction

$$\underset{\text{(I)}}{2\text{Q-4-CHO}} \xrightarrow{\text{aq. KOH}} \underset{\text{(III)}}{\text{Q-4-COOH}} + \underset{\text{(VI)}}{\text{Q-4-CH}_2\text{OH}}$$

was effectively quantitative over a range of alkali concentrations, though with a very dilute solution the neutral (alcohol) fraction was found to contain nearly equal amounts of VI and the hydrobenzoin II. The quinolyl-4-methanol was further characterized by preparation of the phenyl and α-naphthyl urethans.

In an attempt to correlate this facile Cannizzaro reaction with the results in the benzoin reactions, an experiment was tried using a base of the same order of base-strength as potassium cyanide but one which does not produce the benzoin condensations. Such a base should be sodium metaborate ($NaBO_2$) since the acidic dissociation constants of hydrocyanic and boric acids are very nearly the same. Using this base, no isolable amounts of the quinoline acid or alcohol products were obtained and most of the aldehyde was recovered. This would suggest that bases of the strength of potassium cyanide or sodium metaborate do not readily produce the Cannizzaro reaction with cinchoninaldehyde itself, but does not necessarily preclude the possibility that such bases could cause a mixed intermolecular oxidation–reduction as suggested for the benzoin reaction.

Acknowledgment.—The author takes this opportunity to express his appreciation to Mr. Samuel W. Blackman for the microanalyses here reported, and to Dr. Richard Baltzly and Mr. Walter S. Ide for helpful advice.

Experimental[3]

A. Benzoin Condensation with Cinchoninaldehyde.—Cinchoninaldehyde monohydrate, 1.5 g., was dissolved in 25–30 cc. of hot absolute methanol and 3 cc. of aqueous potassium cyanide solution (containing 0.9 g. of potassium cyanide) was added. The solution turned a deep blood red color at once and was heated on the steam-bath for one hour. A solid had started to precipitate within two or three minutes, and after heating for one hour the mixture was cooled, the precipitate filtered and washed with water and alcohol. After crystallization from aqueous pyridine, the yield of II was 0.8 g. (90% according to the disproportionation equation shown above), m. p. 204–205° (dec. to red oil).

Anal. Calcd. for $C_{20}H_{16}O_2N_2$: C, 75.92; H, 5.10; N, 8.86. Found: C, 75.91, 75.78; H, 5.17, 5.13; N, 8.50.

To the filtrate from the above precipitate was added 10 cc. of water and all alcohol was removed from the solution by evaporation on the steam-bath. The hot aqueous solution was filtered and then made neutral to congo red paper with concentrated hydrochloric acid. Cooling gave a white crystalline precipitate of cinchoninic acid (III); yield 0.5 g. (100% according to the disproportionation equation), m. p. 254–255°. A mixture with authentic cinchoninic acid showed no depression of the melting point.

Chromic Anhydride Oxidation of II.—A solution of 1.0 g. of II in 10 cc. of acetic acid was treated with 1 g. of chromic anhydride and heated two hours on the steam-bath. The resulting dark solution was filtered and evaporated to dryness *in vacuo*. After dilution of the residue with water, excess ammonium hydroxide was added and the precipitate was removed by filtration. The aqueous filtrate was evaporated to a small volume *in vacuo* and made neutral to congo red paper with dilute hydrochloric acid. Cooling gave 0.85 g. (80%) of white crystals, m. p. 254–255°. There was no melting point depression when a sample of the product was mixed with authentic cinchoninic acid.

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[1] Phillips, THIS JOURNAL, **67**, 744 (1945).

[2] Kwartler and Lindwall, *ibid.*, **59**, 524 (1937).

[3] All melting points are uncorrected.