A quartz cell and water having a conductivity of the order of 0.1×10^{-6} were used. The solutions were made up by weight with an error of less than 0.05%.

2. Values at round concentrations have been interpolated from the results upon the three salts. These data may be published in the "International Critical Tables."

3. Extrapolation of the results, on the assumption that the mass-action law is approached as a limiting form at infinite dilution, gives a value of Λ_∞ for tetramethylammonium bromide, 124.34, for tetra-ethylammonium chloride, 109.19 and for tetrapropylammonium iodide, 99.69.

4. Assuming that the value of Λ_∞ at 25° of the chloride ion is 75.10, of the bromide ion 77.44 and of the iodide ion 76.12, the values 46.90, 34.09 and 23.57 for the Λ_∞ of the tetramethyl-, tetra-ethyl- and tetrapropylammonium ions, respectively, are obtained.

5. The $\Lambda_c - \sqrt{C}$ curves of the three alkyl ammonium as well as the two alkyl sulfonium salts of the previous paper are straight lines. This corroborates Kohlrausch's rule which assumes a theoretical significance in the theory of complete ionization of Debye and Hückel.

UNIVERSITY HEIGHTS, NEW YORK

[CONTRIBUTION FROM THE COLLEGE OF AGRICULTURE OF THE UNIVERSITY OF WYOMING]

THE NATURAL OCCURRENCE OF ACONITIC ACID AND ITS ISOMERS

BY O. A. BEATH

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Review of Literature

Aconitic acid has been reported as being obtained from various plant sources. From the data it is obvious that a compound varying in its melting point from 167° to 191° cannot be in every instance the normal acid, but presumably consists of the normal admixed with its isomeric forms.

Wicke[1] reports the isolation of an acid from *Delphinium consolida* having the same composition as normal aconitic acid. The melting point is not given. His evidence is based upon the composition of the silver salt and the ultimate analysis of the free acid. Parsons[2] detected aconitic acid in sorghum juice by means of characteristic salts. Behr[3] appears to have obtained large quantities of the acid from muscovado sugar and molasses, the composition of which he verified by combustion and formation of the characteristic salts. He proved that lime acting upon the invert

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[1] Wicke, *Ann.*, **90**, 98 (1854).

[2] Parsons, *Am. Chem. J.*, **4**, 39 (1882).

[3] Behr, *Ber.*, **10**, 351 (1877).

sugar did not form the acid, so that it was undoubtedly a naturally occurring substance. Samples of sugar-cane juice from Cuba gave a lead and an acid ammonium salt said to be characteristic of the acid. Through an accident the cleanest portion of the acid was lost, but a small fraction, recovered and purified, gave a melting point of 167°. Behr obtained aconitic acid from West India cane that melted at 172–173°; material from *Aconitum napellus* melted at 165°, from citric acid at 187–188°.

v. Lippman[4] reports aconitic acid in sugar beet products. Yoder[5] found aconitic acid in native sugar cane and gave it a melting point of 183–184°. He states that the low value is probably due to incomplete purification. On the other hand Taylor[6] reports having isolated normal aconitic acid from sugar cane juice and found the substance to melt at 191°. Zerban[7] found aconitic acid in cane juice which melted at 178°. From *Aconitum heterophyllum* Jowett[8] isolated a crop of aconitic acid crystals which melted at 191.5°.

Experimental Part

Six species of native Delphiniums, the *Geyeri, Barbeyi, cuculatum, Nelsonii, bicolor, glaucescens;* two species of *Aconitum*, the *columbianum* (native) and U.S.P. official drug (imported), and one commercial sample labeled aconitic acid from a supply house, have been investigated as to the form of acid by the author.

The plants mentioned gave in each instance an acid melting at 172–173°. The procedure followed was the same for all plants. The air-dried material was macerated with water for a day and after filtering treated with basic acetate of lead. The lead was removed in the usual way (H_2S) and the treatment with lead repeated. When the final solution was quite uniformly free from coloring, it was concentrated slowly and finally agitated with anhydrous ether. The residue from the ether was taken up with purified acetone (hot) the minimum solvent being used, and this quickly diluted with an excess of anhydrous chloroform. On chilling, the acid separated in warty magmas. The acid was further purified by recrystallizing from anhydrous alcohol.

Combustions were made on the free acid and the corresponding ethyl esters. The actual percentages compared very favorably with those calculated in each test. To illustrate, the aconitic acid from *D. Geyeri* gave

	C	H	O
Found, %	41.39	3.57	55.04
Calcd. %	41.38	3.47	55.15

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[4] v. Lippmann, *Ber.*, **12**, 1649 (1879).

[5] Yoder, *J. Ind. Eng. Chem.*, **3**, 640 (1911).

[6] Taylor, *J. Chem. Soc.*, **115**, 886 (1919).

[7] Zerban, *J. Ind. Eng. Chem.*, **11**, 1034 (1919).

[8] Jowett, *J. Chem. Soc.*, **69**, 1521 (1896).

The corresponding ethyl ester gave

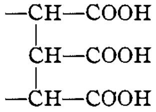
	C	H	O
Found, %	55.63	7.05	37.32
Calcd., %	55.79	7.02	37.19

The conversion of the acid from the ester by acid hydrolysis indicates that the aconitic acid melting at 172–173° is a comparatively stable compound.

The acid from the Aconite sources was not found to vary from that obtained from the native Delphiniums. The commercial sample of aconitic acid was, when purchased, presumed to be the normal acid melting at 191° but upon examination gave a sharp melting point of 173°.

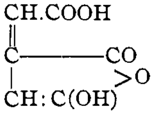
The conductivity value of the commercial sample was approximately the same as that of the acid from the Delphiniums.

Comparative Data.—Rogerson and Thorpe[9] studied the constitution of aconitic acid and concluded that this acid-like glutaconic acid is incapable of existing in forms corresponding to maleic and fumaric acids and that in all probability this property is exhibited by only those derivatives which contain two substituting groups on the methylene carbon atom. Bland and Thorpe[10] prepared labile aconitic acid from the hydroxy-anhydro acid which melted at 173°. The derived acid resembled the normal form in many respects but differed markedly in its behavior on dehydration.



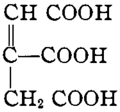
$$\begin{array}{l} \text{—CH—COOH} \\ \quad | \\ \ \ \text{CH—COOH} \\ \quad | \\ \text{—CH—COOH} \end{array}$$

Normal acid



$$\begin{array}{l} \text{CH.COOH} \\ \| \\ \text{C————CO} \\ | \qquad\qquad >\text{O} \\ \text{CH:C(OH)} \end{array}$$

Hydroxy-anhydro acid



$$\begin{array}{l} \text{CH COOH} \\ \| \\ \text{C—COOH} \\ | \\ \text{CH}_2\text{ COOH} \end{array}$$

Labile acid

From the structure of aconitic acid two isomeric forms ought to exist, being geometric isomers. Since Bland and Thorpe have established the structure of one isomeric form of aconitic acid melting at 172–173° it seems logical to conclude that the acid occurring in nature having the same characteristics is an identical compound.

The labile aconitic acid prepared by Bland and Thorpe was found by them to resemble the normal acid in most respects but differed markedly upon dehydration with acetyl chloride, being converted into hydroxy-anhydro acid.

Rather and Reid[11] prepared a phenylacyl ester of the normal aconitic acid which melted at 90–91°. Several attempts were made by the writer to obtain a corresponding ester from the isomeric acid isolated from the *Delphinium* and *Aconite* species, but negative results were obtained. This suggests an additional difference between the normal and the isomeric aconitic acids.

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[9] Rogerson and Thorpe, *J. Chem. Soc.*, **89**, 631 (1906).

[10] Bland and Thorpe, *ibid.*, **101**, 1490 (1912).

[11] Rather and Reid, *Arkansas Exptl. Sta. Bull.*, **156** (1918).

Conclusions and Summary

1. The variation in melting points given in the literature for naturally occurring aconitic acid is presumably due to admixtures of two or more definite forms of aconitic acid.

2. Repeated success in the recovery of an acid melting at 172–173° from several species of native plants, and its recovery in the same form from esters point rather clearly to the natural occurrence of an isomeric aconitic acid.

LARAMIE, WYOMING

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

THE RELATIONSHIP BETWEEN HYDROGEN-ION CONCENTRATION AND CHEMICAL CONSTITUTION IN CERTAIN LOCAL ANESTHETICS

BY ELMER B. VLIET AND ROGER ADAMS

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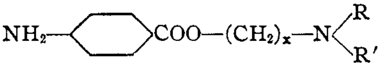
During the past twenty years a considerable number of local anesthetics of the general type (I), where R and R′ are alkyl or allyl groups and where x is any number greater than one, have been described and several have appeared on the market.



I

In an attempt to correlate the relationship between structure, physical properties and anesthetic efficiencies in these compounds, a large number of anesthetics of this type have been prepared.[1] They will be described in subsequent papers.

From recent work[2] it appears that in any study of the efficiency of local anesthetics, the hydrogen-ion concentrations of their aqueous solutions must be considered. Gros[3] found that the anesthetic efficiency of local anesthetics increases markedly as the hydrogen-ion concentration decreases and recent reports corroborate his findings.

In view of this effect of hydrogen-ion concentration on anesthetic efficiency, the hydrogen-ion concentrations of equimolecular solutions of the anesthetics were determined and are described in this communication. It was hoped that such data might incidentally be of some value as a means

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[1] The authors are indebted to The Abbott Laboratories for kindly furnishing quantities of β-diethylaminoethyl-*p*-aminobenzoate hydrochloride and borate, γ-di-*n*-butylaminopropyl-*p*-aminobenzoate hydrochloride and borate and the borates of β-diethylaminopropyl-*p*-aminobenzoate and β-*n*-butylallylaminoethyl-*p*-aminobenzoate.

[2] Copeland, *Brit. Med. J.*, **1925**, II, 547. Regnier, *Bull. sci. pharmacol.*, **31**, 513 (1924); **32**, 513 (1925). Abelin, *Biochem. Z.*, **141**, 458, 470 (1923). Protz, *Arch. exp. Path. Pharmakol.*, **86**, 238 (1920).

[3] Gros, *Arch. exp. Path. Pharmakol.*, **63**, 80 (1910); **67**, 127, 130 (1912).