salt of β-alanine, to give the corresponding ethyl acetylpantothenate, ethyl carbobenzoxypantothenate and *p*-nitrobenzoylpantothenic acid. *p*-Nitrobenzoylpantothenic acid was inactive in microbiological tests. Ethyl pantothenate and ethyl acetylpantothenate were practically inactive in microbiological tests but were active in rats and chicks.

Evidence is described which shows that when sodium α,γ-dihydroxy-β,β-dimethylbutyrate is acetylated, then treated with thionyl chloride, then treated with β-alanine or its ester, the major mechanism of the formation of the pantothenic acid derivative involves the condensation of α-acetoxy-β,β-dimethylbutyrolactone with β-alanine, while only a minor part of the synthesis is accomplished through the condensation of the diacetyl acid chloride with β-alanine.

Pure α,γ-diacetoxy-β,β-dimethylbutyric acid was made by the treatment of α,γ-diacetoxy-β,β-dimethylbutyramide with amyl nitrite in acetic acid. Subsequent treatment with thionyl chloride and β-alanine ester gave pure ethyl diacetylpantothenate which was saponified to pantothenic acid.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF PENNSYLVANIA]

The Dissociation Constant of Brom Cresol Green in Water[1]

BY MARTIN KILPATRICK

Several determinations have been made of the equilibrium constant for the reaction

Brom cresol green (yellow) + $H_2O \rightleftharpoons H_3O^+$ + Brom cresol green (blue) (1)

and the dissociation constant

$$K_C = C_{H_2O}K_{(A_I.H_2O)} = C_{H_3O^+}C_{B_I}/C_{A_I} \quad (2)$$

at zero ion concentration has been reported by various workers.[2,3,4,5] Since the values vary from 1.03 to 1.20 × 10^{-5}, it has seemed worthwhile to present a summary of a number of determinations made in this Laboratory. The first series involves the colorimetric determination of the equilibrium constant, K_{A_IB}, of the reaction

Brom cresol green (yellow) + Acetate $\rightleftharpoons$ Acetic acid + Brom cresol green (blue) (3)

where

$$K_{A_IB} = \frac{C_A}{C_B}\frac{C_{B_I}}{C_{A_I}} \quad (4)$$

The constant K_{A_IB} may be related to the thermodynamic equilibrium constant $[K_{A_IB}]^0$ by the equation

$$\log K_{A_IB} = \log [K_{A_IB}]^0 + A(Z_A - Z_{A_I})\sqrt{\mu} + B\mu \quad (5)$$

where $\mu = {}^1/_2 \sum CZ^2$ and Z_A and Z_{A_I} are the charges on the buffer acid and indicator acid, re-

TABLE I

THE EQUILIBRIUM CONSTANT AT 25°

Brom cresol green (yellow) + Acetate $\rightleftharpoons$ Acetic acid + Brom cresol green (blue)

Ionic strength, μ	$\log K_{A_IB}$, obsd.
0.00079	$\bar{1}.827$
.00082	$\bar{1}.826$
.00129	$\bar{1}.833$
.00162	$\bar{1}.837$
.00188	$\bar{1}.844$
.00202	$\bar{1}.847$
.00208	$\bar{1}.851$
.00216	$\bar{1}.851$
.00233	$\bar{1}.847$
.00246	$\bar{1}.849$
.00256	$\bar{1}.859$
.00302	$\bar{1}.849$
.00375	$\bar{1}.855$
.00506	$\bar{1}.860$
.00516	$\bar{1}.861$
.00602	$\bar{1}.866$
.00622	$\bar{1}.855$
.00740	$\bar{1}.868$
.00784	$\bar{1}.867$
.00950	$\bar{1}.873$
.01000	$\bar{1}.886$
.01000	$\bar{1}.877$
.01035	$\bar{1}.886$
.01152	$\bar{1}.887$
.01286	$\bar{1}.897$
.01477	$\bar{1}.881$
.01842	$\bar{1}.889$
.02000	$\bar{1}.895$
.02020	$\bar{1}.897$

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(1) Aided by a grant from the Penrose Fund of the American Philosophical Society.

(2) Sendroy and Hastings, *J. Biol. Chem.*, **82**, 197 (1929).

(3) Guggenheim and Schindler, *J. Phys. Chem.*, **38**, 543 (1934).

(4) Kilpatrick, *Chem. Rev.*, **16**, 57 (1935).

(5) Minnick and Kilpatrick, *J. Phys. Chem.*, **43**, 259 (1939).

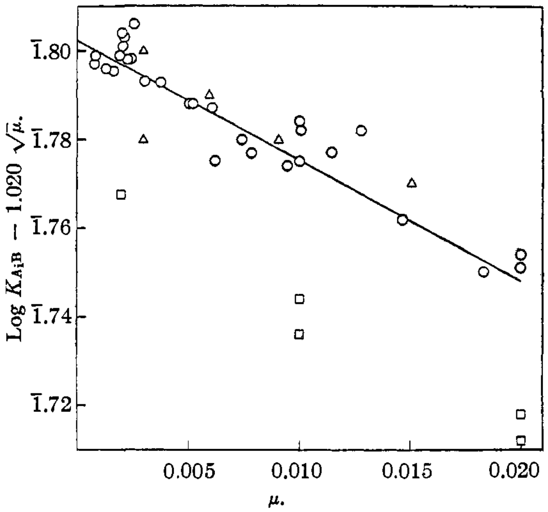

Fig. 1.—△, Hastings and Sendroy; ○, this paper; □, Guggenheim and Schindler.

spectively.[6] Equation (5) offers a convenient method of extrapolation to infinite dilution of results at low ionic strengths. For the solvent water, A has a value 1.020 at 25° and B is a constant based on the assumption that the deviation from the Debye–Hückel limiting law is linear in the concentration of electrolyte. Twenty-nine runs covering the ionic strength range 0.00079 to 0.02020 gave values of $\log K_{A_1B}$ which differ on the average from the values calculated from the following equation by ± 0.005. Figure 1 shows these results graphically as well as the corresponding results of Hastings and Sendroy[2] and Guggenheim and Schindler.[3]

$$\log K_{A_1B} = \bar{1}.802 + 1.020\sqrt{\mu} - 2.7\,\mu \tag{6}$$

$[K_{A_1B}]^0$, the ratio of the thermodynamic dissociation constant of brom cresol green to that of acetic acid, is 0.634 as compared with 0.59 obtained by Guggenheim and Schindler (ref. 3) by a different method of extrapolation. On the basis of the value of 1.754×10^{-5} for the dissociation constant of acetic acid,[7] the dissociation constant of brom cresol green is 1.12×10^{-5}. Hastings and Sendroy[2] report 1.20×10^{-5} for this dissociation constant. These authors found that the dissociation constant of brom cresol green was independent of temperature over the range 20–38°[8,9] and the results in this Laboratory confirm this result, within the experimental error of the measurements, over the range 21–28°. Extrapolation of individual runs at 21, 22, 23, 25, 27 and 28° yields values of the dissociation constant of 1.13, 1.14, 1.10, 1.09, and 1.06×10^{-5}, respectively.[10]

In a second series the equilibrium constant between brom cresol green and benzoate was determined. The results can be represented by the equation

$$\log K_{A_1B} = \bar{1}.241 + 1.020\sqrt{\mu} - 1.2\,\mu \tag{7}$$

and the calculated values agree on the average with the observed values given in Table II within ± 0.005. Combining the value 0.174 for the ratio of the thermodynamic dissociation constant of brom cresol green to that of benzoic acid with the value 6.312×10^{-5} for the thermodynamic dissociation constant of benzoic acid from conductance measurements,[11] the dissociation constant of brom cresol green is found to be 1.10×10^{-5}. This value is in good agreement with 1.12×10^{-5} found from the measurements with acetate buffers.

TABLE II

THE EQUILIBRIUM CONSTANT AT 25°

$$\underset{\text{(yellow)}}{\text{Brom cresol green}} + \text{Benzoate} \rightleftarrows \text{Benzoic acid} + \underset{\text{(blue)}}{\text{Brom cresol green}}$$

Ionic strength, μ	$\log K_{A_1B}$ obsd.
0.00207	$\bar{1}.292$
.00275	$\bar{1}.292$
.00457	$\bar{1}.303$
.00516	$\bar{1}.312$
.00684	$\bar{1}.319$
.01031	$\bar{1}.326$
.01367	$\bar{1}.343$
.01715	$\bar{1}.343$
.02450	$\bar{1}.375$
.02730	$\bar{1}.386$

Summary

The thermodynamic dissociation constant of brom cresol green (yellow to blue) has been found to be 1.11×10^{-5} at 25°.

PHILADELPHIA, PENNA. RECEIVED JULY 22, 1941

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[6] Kilpatrick and Mears, THIS JOURNAL, **62**, 3047 (1940).

[7] Harned and Ehlers, *ibid.*, **55**, 962 (1933).

[8] Hastings and Sendroy, *J. Biol. Chem.*, **61**, 695 (1924).

[9] Hastings, Sendroy and Robson, *ibid.*, **65**, 381 (1925).

[10] These determinations were carried out by Dr. W. H. Mears, Dr. G. L. Lewis, C. Feldman and N. E. White.

[11] Brockman and Kilpatrick, THIS JOURNAL, **56**, 1483 (1934).