

dine dissolve 10 g. of alpha glucose and the solution is not seeded crystallization will begin in an hour and a half and in 5 hours probably 2.5 g. of material have precipitated. The solution should be allowed to stand at least 24 hours in an ice box, and much better yields are obtained if 25 g. of glucose are used to 25 cc. of pyridine.

The following table gives a résumé of the specific rotations of the alpha glucose used and of the beta glucose obtained from it. It will be noted that the change of rotation of the beta glucose takes place rather slowly in pure water and is complete after 24 hours; extrapolations of the readings to the initial rotations are not given.

Material.	SPECIFIC ROTATIONS OF GLUCOSE.						
	Immediately.	30 min.	1 hr.	2 hrs.	3 hrs.	4 hrs.	24 hrs.
Alpha.....	82.49	65.21	47.94	const.	...
Alpha-2nd.....	Crys., 85.72	74.49	59.94	50.53	49.23	const.	...
Beta-(a).....	35.41	50.63	const.
Beta-(b).....	41.46	48.37	...	50.90	const.
Beta-(c).....	23.84	39.30	...	47.51	51.39
Beta-(d).....	83.65	51.83
Beta-(f).....	23.80	50.70
Beta-(g).....	25.40	50.20
Beta-(h).....	26.90	51.90
Beta-(i).....	25.50	50.60	52.00
Beta-(j).....	25.90	49.30	52.10

Conclusions.

It has been found that alpha glucose dissolves readily in hot pyridine and precipitates out readily as the beta form in combination with one molecule of pyridine, as previously described by Behrend. This molecule of pyridine of crystallization is readily lost in the air, or in a vacuum desiccator containing concentrated sulfuric acid, or in an oven at 105°. When dried thoroughly and dissolved in water the beta glucose has an initial rotation of 20-25 and a final rotation of 50-52 when equilibrium is established. As yields of 70-85% can be obtained easily, Behrend's method is very satisfactory.

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THE INFLUENCE OF VARYING CONCENTRATION OF HYDROGEN ION ON THE OPTICAL ROTATION OF THE ISOMERIC ALKALOIDS, CINCHONINE, CINCHONIDINE AND CINCHOTOXINE.

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Introduction.

The effect of dilution upon the specific rotation of the salt of an optically active base or acid in solution has been studied by several investiga-

tors.¹ The variations in specific rotation appear to be dependent upon the relation between dissociated and undissociated molecules, but to be independent of the inactive ion. As Hädrich² has observed, "The rotatory power not only of salts, but of electrolytes in general, is in solutions giving almost complete dissociation, independent of the inactive ion." The studies of Rimbach³ indicate that the generalization is to be limited to substances which dissociate highly in solution, in so far as it cannot with accuracy be applied in the case of electrolytes of moderate or slight dissociation.

In the study of the conversion of the cinchona alkaloids into their toxines by one⁴ of the writers and his coworkers, it was found necessary to determine the concentration in the various solutions examined of the bivalent alkaloid ion. In the course of the measurements there made, it was noted that the specific rotation increased to a certain extent with increasing concentration of H^+ ion, although no attempt was made at that time to determine the exact relation between the variation of rotation on the one hand and the concentration either of H^+ ion or of alkaloid ion on the other. In view of the fact that the concentration of the bivalent alkaloid ion could be measured with a fair degree of accuracy, it was considered of interest to determine experimentally just what relation the variations in rotation bore to the concentration of the ions in question.

The investigation was of further interest in view of the somewhat inconclusive evidence regarding the effect of electrolytic dissociation in general upon the specific rotation of a substance. The results obtained lead to the conclusion that the specific rotation in the cases studied is independent of the inactive ion, on the one hand, and on the other that the variations in rotation are a direct function of the concentration of the bivalent alkaloid ion. These results are of additional interest in that they enable us to compare the optical behavior in this relation of the three isomeric substances, cinchonine, cinchonidine, and cinchotoxine.

The materials used in the study were Merck's cinchonine and cinchonidine, pure crystals, and cinchotoxine obtained from cinchonine in accordance with the method described by Roques⁵ with some modifications given later on in this paper.

Dissociation Constant of the Bivalent Cinchonine Ion.

In order that an adequate comparison might be made of the variations in optical rotation under variations in concentration of H^+ ion, it was necessary to determine with some degree of accuracy the value

¹ Landolt, *Ber.*, 6, 1077 (1873); Schneider, *Ann.*, 207, 257 (1881).

² Hädrich, *Z. physik. Chem.*, 12, 489 (1893).

³ Rimbach, *Ibid.*, 28, 251 (1899).

⁴ Biddle, *THIS JOURNAL*, 37, 2088 (1915).

⁵ Roques, *Bull. soc. chim.*, [3] 13, 1005 (1895).

of the second dissociation constant at the temperature employed. According to the measurements of Veley,¹ the second dissociation constant of cinchonine is to be represented by 3.3×10^{-10} at 15° . Determinations carried out later in this laboratory² pointed to a value of 0.59×10^{-10} . Measurements recently made in this laboratory in conjunction with Dr. E. Q. Adams lead to the conclusion that the value obtained by Veley is more nearly correct.

In the redetermination, as in that earlier made, a colorimetric method was employed, methyl orange being used as indicator. A solution of cinchonine was prepared as given later on, $0.05 M^3$ with respect to the alkaloid and $0.075 M$ with respect to hydrochloric acid. Fifty cc. portions of this solution were transferred to a 100 cc. graduated flask by means of a pipet, together with 20 cc. of a methyl orange solution of definite strength ($0.00005 M$). Further acid of known strength was then added and the flask was filled to the 100 cc. mark.

The solutions thus obtained were compared in a Stammer colorimeter with solutions of acetic acid and potassium acetate containing the same concentration of methyl orange. Two solutions in any case were assumed to have the same concentration of H^+ ion when columns of the same length (15 cm.) gave the same color. In calculating K_2 , the second dissociation constant of the alkaloid, the ratios of the amounts of acetic acid and acetate (added as potassium hydroxide and acetic acid) were employed, with negligible error, as representing the ratios of undissociated acetic acid and acetate ion. Similarly in the case of cinchonine, the ratio of hydrogen chloride above that necessary to form the monohydrochloride to that necessary to form the monohydrochloride alone, was taken to represent the ratio of cinchonine divalent to cinchonine univalent ion. The equation is expressed in the following form:

$$K_2 = \frac{K_w}{K_{ac}} \times \left(\frac{\text{Cin } H_2^{++}}{\text{Cin } H^+} \right) \times \left(\frac{Ac^-}{HAc} \right),$$

where K_{ac} represents the dissociation constant of acetic acid, 1.82×10^{-5} .

TABLE I.
In 100 cc. Solution.

Mols. acid per mol of base.	Stock solution base = 0.05 M; HCl = 0.075 M.	Indicator 0.00005 M methyl orange.	0.5 M HCl.	Comparison solution of acetic acid and potassium acetate.		$K_w/K_2 \times 10^4$.
				0.4 N acetic acid.	0.4 N potassium acetate.	
1.5	50 cc.	20 cc.	...	50.25 cc.	16.25 cc.	5.62
1.7	50 cc.	20 cc.	1.0 cc.	42.95 cc.	7.05 cc.	4.75
1.8	50 cc.	20 cc.	1.5 cc.	47.63 cc.	5.04 cc.	4.30

Mean, 4.89

¹ Veley, *J. Chem. Soc.*, 93, 2114 (1908); 95, 758 (1909).

² Biddle, *THIS JOURNAL*, 37, 2093 (1915).

³ *M* represents molal concentration in this article.

From the mean value of K_w/K_2 , $K_2 = 2.05 \times 10^{-10}$. As already indicated, the value of K_2 as obtained by Veley was 3.3×10^{-10} . In the calculations made in this paper a value was taken for K_2 of 2.5×10^{-10} .

The Salts of Cinchonine.

In the case of cinchonine, as in that of the other two alkaloids studied, the measurements were confined to solutions of 0.025 M concentration with respect to the alkaloid.

Stock solutions were made up of hydrochloric and nitric acids 0.5 N in strength and of acetic acid 0.5 N and 3.0 N , respectively. Also a stock solution of cinchonine of 0.05 M strength was prepared, using 7.35 g. of the alkaloid and 75 cc. of 0.5 N hydrochloric acid in 500 cc. of solution. By this means an acid concentration of 0.075 M was obtained.

50 cc. portions of the stock of cinchonine solution were measured, by means of a pipet, into 100 cc. graduated flasks, the requisite amounts of hydrochloric acid added, from a buret, to give in each case an increasing acid concentration of 0.0025 M (*i. e.*, 0.5 cc. of 0.5 N hydrochloric acid per 0.0025 M increase), and each flask was then filled to the 100 cc. mark. The optical rotation of the solutions thus obtained was measured in a Franz Schmidt and Haensch quartz wedge saccharimeter, a 4 dm. tube being employed. The source of light was a Welsbach burner, a bichromate cell being used as a light filter. The readings are in Ventzke degrees and each represents the average of six independent readings. The temperature was 16°.

TABLE II.

Cinchonine concentration molal.	Hydrochloric acid concentration molal.	Rotation Ventzke degrees positive at 16°.	Hydrogen- ¹ ion concentration $\times 10^{-4}$.	Bivalent ¹ cinchonine-ion concentration.
0.025	0.0375	19.40	0.40	0.0125
0.025	0.0400	19.95	0.59	0.0149
0.025	0.0425	20.40	0.92	0.0174
0.025	0.0450	21.00	1.54	0.0199
0.025	0.0475	21.30	3.15	0.0222
0.025	0.0500	21.55	9.80	0.0240
0.025	0.0525	21.85	...	0.025
0.025	0.0550	21.85	...	0.025

Under Table III are given the results obtained by using acetic acid instead of hydrochloric. It was found necessary here to use a concentration 0.10 M with respect to the acid in preparing the cinchonine stock solution to facilitate the dissolving of the alkaloid. Also larger increments of acid were employed in preparing the successive solutions.

¹ For determination of concentrations of H^+ ion and bivalent cinchonine ion, respectively, see THIS JOURNAL, 37, 2088 (1915).

TABLE III.

Cinchonine concentration molal.	Acetic acid concentration molal.	Rotation Ventzke degrees positive at 16°.	Hydrogen-ion concentration $\times 10^{-4}$.	Bivalent cinchonine-ion concentration.
0.025	0.050	18.40	0.11	0.0054
0.025	0.075	18.91	0.22	0.0089
0.025	0.100	19.38	0.32	0.0111
0.025	0.125	19.61	0.42	0.0128
0.025	0.150	20.00	0.51	0.0140
0.025	0.300	20.56	1.07	0.0182
0.025	0.450	20.91	1.62	0.0201
0.025	0.600	21.21	2.16	0.0211
0.025	0.750	21.48	2.71	0.0218
0.025	0.900	21.43
0.025	1.050	21.50
0.025	1.200	21.48

The Salts of Cinchonidine and Cinchotoxine.

Solutions of cinchonidine in hydrochloric acid and in nitric acid were prepared as in the case of cinchonine. The results of the measurements obtained are given under Tables IV and V. No measurements in this case were made in solutions of acetic acid.

TABLE IV.

Cinchonidine concentration molal.	Hydrochloric acid concentration molal.	Rotation Ventzke degrees negative at 16°.	Hydrogen-ion concentration $\times 10^{-4}$.	Bivalent cinchonidine-ion concentration.
0.025	0.0375	13.85	0.40	0.0125
0.025	0.0400	14.30	0.59	0.0149
0.025	0.0425	14.70	0.92	0.0174
0.025	0.0450	15.00	1.54	0.0199
0.025	0.0475	15.45	3.15	0.0222
0.025	0.0500	15.65	9.80	0.0240
0.025	0.0525	15.75	0.025
0.025	0.0550	15.80	0.025
0.025	0.0575	15.80	0.025

TABLE V.

Cinchonidine concentration molal.	Nitric acid concentration molal.	Rotation Ventzke degrees negative at 16°.	Hydrogen-ion concentration $\times 10^{-4}$.	Bivalent cinchonidine-ion concentration.
0.025	0.0375	13.85	0.40	0.0125
0.025	0.0400	14.35	0.59	0.0149
0.025	0.0425	14.70	0.92	0.0174
0.025	0.0450	15.10	1.54	0.0199
0.025	0.0475	15.45	3.15	0.0222
0.025	0.0500	15.65	9.80	0.0240
0.025	0.0525	15.75	0.025
0.025	0.0550	15.75	0.025
0.025	0.0575	15.75	0.025

In the conversion of either cinchonine or cinchonidine there is always a slow racemization effect. In the preparation of this alkaloid, consequently, care was taken to reduce as far as possible the racemization of

the product, a second preparation being made as a check. In the first instance the directions of Roques were followed carefully; in the second the prescribed atmosphere of hydrogen was omitted. In both cases the product obtained gave a rotation corresponding to that first observed by Roques, being somewhat lower than that noted in his later work.

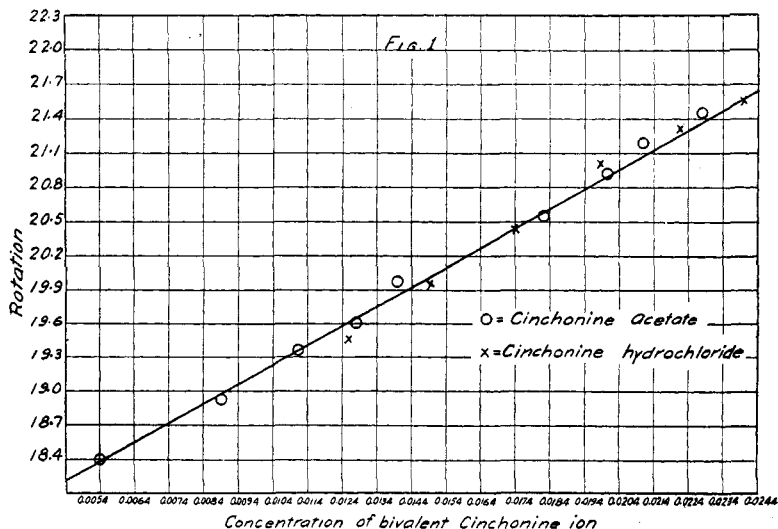
The variations in optical rotation of cinchotoxine due to increasing concentration of acid are, within the limits of the concentrations employed in the case of cinchonine and cinchonidine, so slight as to be negligible under the conditions studied. The results with one acid only (hydrochloric) are recorded in Table VI.

TABLE VI.

Cinchotoxine concentration molal.	Hydrochloric acid concentration molal.	Rotation Ventzke degrees positive at 16°.
0.025	0.0375	2.55
0.025	0.0425	2.57
0.025	0.0475	2.57
0.025	0.0575	2.57

Discussion.

From a consideration of the foregoing tables it is readily seen that in all cases, with the possible exception of the salts of cinchotoxine, there is an increase in rotation with increasing concentration of the bivalent alkaloid ion. It will be noted further that the increase in rotation is directly proportional to the concentration of the bivalent ion, on the one hand, and on the other is independent of the inactive acid ion. These results will be somewhat more readily seen in the accompanying graph (Fig. 1) taken from Tables I and II and affording a direct comparison



of the rotatory power of cinchonine hydrochloride and cinchonine acetate, respectively, with increasing concentration of bivalent alkaloid ion.

By extrapolation the rotatory power of the univalent cinchonine ion in the concentration and at the temperature used may be given as 17.45° Ventzke and that of the bivalent ion as 21.48° Ventzke. The specific rotation of the two ions, in circular degrees under these conditions, would then be $[\alpha] = 205.6^\circ$ and $[\alpha] = 253.1^\circ$, respectively. The corresponding values for the univalent and bivalent cinchonidine ions are -11.94° Ventzke and -15.75° Ventzke. From these values the specific rotation in circular degrees at the temperature employed may be represented as $[\alpha] = -141.1^\circ$ and $[\alpha] = 185.6$.

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THE CONSTITUTION OF XANTHOGALLOL.

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Xanthogallol was discovered by Stenhouse¹ who in 1875 prepared it by the action of bromine and water upon tribromopyrogallol, and afterward more conveniently by the action of the same reagents upon pyrogallol. He also prepared one or two derivatives and made an analysis on the basis of which he assigned to xanthogallol the empirical formula $C_{12}H_4O_6Br_{14}$.

In 1888 Theurer,² working in Zincke's laboratory, made an extensive investigation of the substance, with the express object of determining whether a simpler formula (perhaps $C_6HO_2Br_5$) might not be admissible. His analyses, however, confirmed those of Stenhouse, and he provided additional evidence in favor of the latter's formula by preparing a whole series of derivatives whose genetic relationships he interpreted on the same basis. Some of these interpretations appeared a little forced, but the composition of the derivatives seemed so well borne out by analytical data that Theurer's article has remained essentially the last word upon the subject. It included a tentative structural formula for which, however, the author made no claim for accuracy in matters of detail. This appears below in the modified form suggested by Zincke's foot-note.

Of this formula it may be said that, on the one hand, it harmonized fairly well with the experimental results described by Theurer, and, on the other, that the task of establishing its details with accuracy promised more labor than profit. This is perhaps the reason why the subject has since been so much neglected.

¹ *Ann.*, 177, 191 (1875).

² *Ibid.*, 245, 327 (1888).