

a little nuchar, the solution was filtered. The yield of colorless quinidine acid tartrate obtained on cooling the solution was 60 Gm., melting point 130–132°. Fifty Gm. of the recrystallized salt were dissolved in hot water and the base was precipitated with ammonium hydroxide. The ammoniacal liquor was poured off and the product was washed with water. It was dissolved in hot alcohol and the solution was filtered. The free base with alcohol of crystallization separated on cooling in colorless crystals. Anhydrous quinidine of constant melting point 170–171° and rotation $[\alpha]_D +262$ in alcohol, was obtained on drying over night at 100°. The yield was 25 Gm. Several Gm. more of base were obtained on concentrating the alcoholic mother liquor.

A comparison of the properties of quinidine thus prepared, with those of a sample of U. S. P. quinidine is shown in Table II. Oxidation experiments per-

TABLE II.—ROTATION AND MELTING POINT OF QUINIDINE.

Sample.	Observed Rotation.*	Solvent.	$[\alpha]_D$.	Melting Point.
U. S. P. quinidine	+ 9.92°	Absolute alcohol	+248.0°	162–163° C.
Quinidine from	+10.48°	Absolute alcohol	+262.0°	170–171° C.
Quinine rearrangement	+12.95°	1.8 HCl solution	+323.8°	

* NOTE: The length of tube was 2 dcm. and the concentration 2 Gm. per 100 cc. of solution in each case.

formed on our U. S. P. material by Dr. Alice G. Renfrew, of this Laboratory, indicated that it contained about 20% hydroquinidine.¹ Some data are available in the literature on the rotation of presumably pure alkaloid. Thus Emde² reported $[\alpha]_D +265^\circ$ in 97% alcohol on a sample of practically pure quinidine supplied by Amsterdamsche Chininefabrik, Amsterdam, while Lewis and his associates³ reported $[\alpha]_D +323.12^\circ$ in dilute hydrochloric acid solution, on a sample containing not more than 0.5% impurity prepared by Blagden and Chick in the laboratory of Howard and Sons, Ilford, England. Our data agree well with these figures.

NIGHT BLUE AS AN INDICATOR FOR USE IN VOLUMETRIC TITRATIONS OF ALKALOIDS WITH SILICOTUNGSTIC ACID.

BY H. L. FEINSTEIN* AND E. O. NORTH.¹

In their study of the use of silicoduodecitungstic acid as a volumetric reagent in the titration of alkaloids, North and Beal (4) used malachite green as an indicator. Malachite green gives a deep bluish green in water, but on the addition of hydrochloric acid the color changes gradually through olive-green, yellow, orange

¹ Hydroquinidine may be estimated by oxidizing at 0° C. with permanganate,⁴ whereby quinidine is destroyed and hydroquinidine is unattacked. Allen, "Commercial Organic Analysis," Philadelphia, Blakiston's Son and Co., 5th Edition, Vol. 7 (1929), 466, 490.

² *Helv. Chim. Acta*, 15 (1932), 574.

³ Lewis, Drury, Wedd and Ilescu, *Heart*, 9 (1922), 207.

⁴ See reference 4, page 412.

* Graduate Assistant, School of Chemistry, University of North Dakota.

¹ Associate Professor of Chemistry, University of North Dakota.

and finally, red. In dilute acid solutions, malachite green gives a dark bluish green precipitate with silicotungstic acid, while from the concentrated solutions the red precipitate is formed. However, malachite green has not proved to be entirely satisfactory. The bluish green color, showing an excess of the silicotungstic acid, might be entirely masked by the yellow of the remainder of the unprecipitated indicator; or various shades of green are obtained by the blending of the green and yellow, making it difficult to titrate to the same end-point each time. North and Beal (4) used a concentration of two Gm. of malachite green in 150 cc. of 6 *N* HCl. Other concentrations have been tried; all give fair results after one has become accustomed to that particular indicator.

The present work was undertaken to check and simplify the previous work of Coleman and Beal (2) who tried out 18 triphenyl-methane dyes. They used starch and fibres to concentrate their colors. The method becomes rather cumbersome for routine analysis. Their analyses of the fluidextract of cinchona, in which they left out sawdust-adsorption and clarification, gave higher results than the U. S. P. method.

In view of the difficulty arising from the changes of color from yellow to green when malachite green is used, other dyes which might give a better range were tried. Night blue gives promise of being a good indicator. When night blue is dissolved in hydrochloric or sulphuric acid of moderate concentration, the solution is brown in color. The characteristic blue color of the dye is restored by the addition of water, or by the addition of a small amount of silicotungstic acid. One drop from a solution containing one drop of 0.01 molar silicotungstic acid in 200 cc. of 0.6 *N* HCl will produce a change of color from brown to blue when mixed on a spot plate with a drop of a dilute solution of night blue in acid.

The complete restoration of this color is dependent on the concentration of the indicator. This is a most important point in the use of night blue with silicotungstic acid, since an increase in the amount of night blue present in a drop containing silicotungstic acid will mask the blue color first formed. It thus becomes necessary to choose the concentration of the dye which would give the best results, and also to control accurately the amount of both dye and acid mixed on the spot plate. This was accomplished by a very simple method described here.

EXPERIMENTAL.

I. Preparation of Indicators and Reagents.—Night Blue. Night blue was dissolved in 7–8 normal H_2SO_4 in the concentration of 1.5 mg. of dye per cubic centimeter of solution. The solution must be prepared fresh daily, since decomposition sets in after about 12 hours.

Silicododecitungstic Acid, $4\text{H}_2\text{O} \cdot \text{SiO}_2 \cdot 12\text{WO}_3 \cdot 4\text{H}_2\text{O}$. This acid was prepared according to the directions of North and Beal (3) and modified by Scroggie (5).

Cinchonine, $\text{C}_{19}\text{H}_{22}\text{ON}_2$, was used to standardize the silicotungstic acid solution.

Quinine Hydrochloride, $\text{C}_{20}\text{H}_{24}\text{O}_2\text{N}_2 \cdot \text{HCl} + 2\text{H}_2\text{O}$. A U. S. P. sample of quinine hydrochloride was used in titrations with silicotungstic acid.

Strychnine alkaloid, $\text{C}_{21}\text{H}_{22}\text{O}_2\text{N}_2$, and *Brucine Sulphate*, $(\text{C}_{23}\text{H}_{26}\text{O}_4\text{N}_2)_2 \cdot \text{H}_2\text{SO}_4 + 7\text{H}_2\text{O}$.

II. Titrations.—A solution of silicotungstic acid approximately 0.01 molar is prepared by dissolving 30 Gm. of the acid in enough water to make a liter of solution. Known amounts of pure cinchonine are dissolved in 5 *N* H₂SO₄ and the solution titrated with the silicotungstic acid solution.

A precipitate first forms with a light colloidal suspension in the supernatant liquid. When the alkaloid is 90% or more precipitated the precipitate becomes flocculent, leaving a clear supernatant liquid. In view of the fact that a mono-alkaloidal salt may be formed and also of the possibility that adsorption by the heavy floc may become excessive, the precipitate is allowed to settle for a half minute or so, and then a drop of the clear supernatant liquid is removed to a spot plate by means of a thick-walled glass tubing having an internal diameter of 1.5 mm. The clear supernatant liquid rises in the glass tubing by capillary attraction to the height of a few centimeters and is then gently blown out on a spot plate. Thus, the size of the drop is controlled accurately. Caley's (1) filtration pipette for spot indicator tests was used during the first part of the investigation but was found to be inadequate. The filter-paper in this pipette is not changed easily, and much time is lost in washing. Also dilution of the filtrate takes place unless the pipette is dried before each trial. The formation of a clear supernatant liquid over a rapidly settling precipitate when the point of neutralization is approached eliminates the need of a special filtering apparatus. The thick-walled capillary tubing serves both as a stirring rod and as a pipette.

A drop of the indicator is then added to the silicotungstic acid on the spot plate by means of a platinum wire loop 2.5 to 3.0 mm. in diameter. The two solutions are then mixed. While the alkaloid is present the color of the drop on the spot plate remains brown. With silicotungstic acid in excess the color becomes blue. The end-point, which is taken at the complete disappearance of the brown color, is sharp and easily reproducible. Using the concentrations and amounts of acid and dye indicated here, the colorimetric end-point coincides with 100.0% precipitation of the cinchonine.

The correctness of the end-point is demonstrated by the fact that filtered portions of the same supernatant liquid now give a slight opalescence with excess of either cinchonine or silicotungstic acid solutions.

The equivalent value of the silicotungstic acid solution in terms of weight of cinchonine per cubic centimeter of acid is thus determined, and the acid solution is then evaluated for quinine, strychnine and brucine. The evaluation of silicotungstic acid solution by evaporation to dryness and ignition is not dependable, since at times free silicic acid or other silicates that were introduced during the synthesis of the silicotungstic acid may be present.

Weighed samples of each of the alkaloids or their salts were titrated with silicotungstic acid using night blue as an indicator, and the recovery calculated. The method of aliquot portions was used to determine the approximate end-point. The method of back-titrating with standard of cinchonine after the end-point is passed can be used but a large excess of the alkaloidal solution must be added and the end-point approached again using only the acid solution. Small amounts of the alkaloidal solution added alternately with the acid disturb the end-point—probably by some adsorption phenomenon.

TABLE I.—VOLUMETRIC TITRATION OF CINCHONINE.

Cinchonine Weighed Out. Gm.	Cinchonine Recovered. Gm.	Per Cent Recovery.
0.0896	0.0895	99.9
0.16835	0.1682	99.9
0.2521	0.2519	99.9
0.0937	0.0937	100.0
0.1426	0.14245	99.9

This titration was undertaken to check the accuracy of the indicator and silicotungstic acid solutions in determining the end-point of the reaction. The accuracy of these titrations is the maximum that can be expected with concentrations of the acid solution used, since the difference between the percentage recovery obtained here and 100% recovery is due to less than $\frac{1}{20}$ cc. of the acid solution.

1 cc. acid = 0.0057 Gm. cinchonine.

Molecular weight, cinchonine, $C_{19}H_{22}ON_2 = 294.19$.

Molecular weight, cinchonine silicotungstate, $2H_2O \cdot SiO_2 \cdot 12WO_3 \cdot 2C_{19}H_{22}ON_2 \cdot 2H_2O = 3504.9$.

TABLE II.—VOLUMETRIC TITRATION OF QUININE HYDROCHLORIDE.

Quinine Weighed Out. Gm.	Quinine Recovered. Gm.	Per Cent Recovery.
0.0820	0.0824	100.48
0.2152	0.2145	99.7
0.0974	0.0972	99.8
0.0855	0.0856	100.1
0.0621	0.0623	100.3
0.1464	0.1460	99.7

Molecular weight, quinine hydrochloride, $C_{20}H_{24}O_2N_2 \cdot HCl + H_2O = 396.70$.

Molecular weight, quinine silicotungstate, $2H_2O \cdot SiO_2 \cdot 12WO_3 \cdot 2C_{20}H_{24}O_2N_2 = 3528.9$.

Therefore, 1 cc. acid = $\frac{396.70}{294.19} \times 0.0057 = 0.0077$ Gm. quinine hydrochloride.

TABLE III.—VOLUMETRIC TITRATION OF BRUCINE SULPHATE.

Brucine Weighed Out. Gm.	Brucine Recovered. Gm.	Per Cent Recovery.
0.3092	0.4051	131
0.1257	0.1722	137
0.1181	0.1591	133
0.0529	0.0708	134
0.1627	0.2148	132
0.1474	0.1975	135
0.0823	0.1095	133

Molecular weight, brucine sulphate, $(C_{23}H_{26}O_4N_2)_2 \cdot H_2SO_4 + 7H_2O = 1012.64$.

Molecular weight, brucine silicotungstate, $2H_2O \cdot SiO_2 \cdot 12WO_3 \cdot 4C_{23}H_{26}O_4N_2 = 4457.9$.

Therefore, 1 cc. acid = $\frac{1012.64}{294.19} \times 0.0057 = 0.01262$ Gm. brucine sulphate.

The accuracy of the recoveries was further rigorously checked by having samples weighed out by one member, and the titrations carried out by the other. The values for the recovery of strychnine and brucine are high but are in substantial agreement with the results of North and Beal (4).

TABLE IV.—VOLUMETRIC TITRATION OF STRYCHNINE SULPHATE.

Strychnine Weighed Out. Gm.	Strychnine Recovered. Gm.	Per Cent Recovery.
0.1381	0.1594	115.4
0.2379	0.2807	118.0
0.0752	0.0879	117.0
0.0832	0.0978	117.6
0.1331	0.1556	116.9
0.1083	0.1268	117.1

Molecular weight, strychnine sulphate, $C_{21}H_{22}O_2N_2 = 334.19$.

Molecular weight, strychnine silicotungstate, $2H_2O \cdot SiO_2 \cdot 12WO_3 \cdot 4C_{21}H_{22}O_2N_2 = 4217.5$.

Therefore, 1 cc. acid = $\frac{2 \times 334.19}{294.19} \times 0.0057 = 0.01295$ Gm. strychnine silicotungstate.

SUMMARY.

1. Night blue has been found to serve as an excellent indicator for the silicotungstic titrations of alkaloids.
2. The method developed here is rapid and useful in routine analysis. If the method for the analysis of cinchona bark suggested by North and Beal (4) and modified by Coleman and Beal (2) is accepted as official, the analysis would be simplified by the use of this indicator.
3. The method developed is applicable to the analysis of other amines which form insoluble precipitates with silicotungstic acid.
4. All phases of the discussion presented in this paper are being further investigated.

LITERATURE CITED.

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UNIVERSITY OF NORTH DAKOTA,
GRAND FORKS.

GASOMETRIC ANALYSIS OF SODIUM NITRITE IN COATED TABLETS, IN THE PRESENCE OF A BICARBONATE AND NITRATE.*

BY LESTER C. DICK.

Powder a sufficient number of tablets in a mortar, equivalent to about ten grains of sodium nitrite. Extract the powdered material with water until 250 cc. has been collected, testing to make certain that all sodium nitrite has been extracted. This solution will contain the bicarbonate, nitrate and the sodium nitrite.

Twenty-cc. aliquots are used for the determination, transferred to a small beaker and the bicarbonate neutralized with $N/2$ hydrochloric acid using methyl orange as the indicator.

The above solution is carefully transferred to the measuring cup of a Lunge nitrometer and introduced into the measuring tube. Follow this with 5 cc. of dilute

* Scientific Section, A. PH. A., Toronto meeting, 1932.