and 2 g. of acetylacetone, dissolved in 40 cc. absolute alcohol, 15–20 drops of conc. sulfuric acid was added and the solution set aside. After several days crystals of a sulfate separated. These crystals were dissolved in water and the solution treated as described in preceding paragraph. The result is again acetylacetoneurea. Alkalies fail to bring about any condensation whatsoever. The action of acids however favors a saponification here of the amido group just as also of the cyano group in cyanurea. The end result in both cases must be urea and consequently in this condensation, an acetylacetoneurea.

THE IDENTIFICATION OF THE CINCHONA ALKALOIDS BY OPTICAL-CRYSTALLOGRAPHIC MEASUREMENTS.[1]

By EDGAR T. WHERRY AND ELIAS YANOVSKY.

Optical crystallographic methods of identification of crystallized substances have been in recent years of great service in mineralogy and geology, and it has been repeatedly suggested that they should also be useful in connection with synthetic compounds.[2] The senior author has recently applied these methods to some of the problems encountered by the food and drug analyst. The present paper represents the following up of one of the subjects outlined by Dr. Wright.[3]

It was decided first to ascertain the value of these methods in the distinction of alkaloids which occur together or are difficult to recognize by chemical means. Samples of the 4 cinchona alkaloids were purchased on the open market and submitted to purification and recrystallization. This work was carried on by the junior author, who has supplied the chemical data given in the tables. The optical properties were then measured under the microscope by the senior author. As these substances are soluble in the mixtures of oils usually employed for the immersion method of determining refractive indices, solutions of known indices prepared from potassium-mercuric iodide and glycerol were used. The data for each alkaloid are presented first in a standard formal description, and then in tabular form to bring out the differences between them; determinative tables which may be followed in practice are included. The results obtained in the study of mixtures and of a proprietary

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[1] Presented in abstract form at the November, 1917, meeting of the Association of Official Agricultural Chemists.

[2] Compare William H. Fry, "Identification of Commercial Fertilizer Materials," U. S. Dept. Agr., Bull. **97**, 13 pp. (1914); Fred E. Wright, "The Petrographic Microscope in Analysis," THIS JOURNAL, **38**, 1647 (1916); Emile M. Chamot, "Chemical Microscopy," J. Ind. Eng. Chem., **10**, 60 (1916).

[3] Loc. cit.

remedy containing these alkaloids are also outlined. The methods used in making the measurements were those described in works on optical mineralogy. A brief outline of these methods has been published else-where.[1]

I. Formal Descriptions of the Cinchona Alkaloids.

Cinchonine,[2] $C_{19}H_{22}N_2O$.—Free from solvent-of-crystallization. Crystal-lized from alcohol or from benzene; products identical. Monoclinic; usually tabular on base, and elongated along axis b.

Two commercial products were recrystallized from 95% alcohol and their specific rotation in absolute alcohol determined to be $[\alpha]_D^{20} = +223.3°$ in both cases. This value did not change on further recrystalliza-tion. A portion of one sample was crystallized from benzene, and yielded somewhat smaller crystals, agreeing in every respect with those from alcohol. Oudemans found $[\alpha]_D^{17} = +223.3°$, so the material at hand is evidently pure and free from solvent-of-crystallization.

In ordinary light: colorless; in six-sided plates and rods, the angles of which are indicated in Fig. 1, below; shows lengthwise cleavage.

Refractive indices: $[_D^{20°}]$ $\alpha = 1.570$, $\beta = 1.685$, $\gamma = 1.690$, $\gamma - \alpha = 0.120$, all ± 0.003; the directions X, Y and Z, in which each of these indices in turn is shown, are marked on the figure. Most crystals yield index γ lengthwise (*i. e.*, when their long direction is parallel to the vibration plane of the polarizer) but a value lying between α and β, 1.60 to 1.63, crosswise; β is, however, shown by those with the interference figure centered, and α by those with the plane of the optic axes parallel to the face on which they lie, no part of the usual figure being visible.

In parallel polarized light: extinction is parallel in most cases. The double re-fraction of most of the plates is extremely strong, their centers showing pale 4th order colors, with several colored marginal bands. Occasional cleavage fragments, tilted at about 45° from the usual position, show bright colors of the 2nd order. The sign of elongation is +.

In convergent polarized light: biaxial, the plane of the optic axes emerging at an angle of 45° or more from the perpendicular to the majority of the plates, so that only the margin of the interference figure is visible. Cleavage fragments with low order colors show, however, a good interference figure. Axial angle $2E_D = 38 \pm 2°$. Sign —. Dispersion of optic axes marked, with $2E_r < 2E_v$; dispersion of bisectrices hori-zontal, weak.

These data agree well with those of the authors cited; Wright gives, however, plane of optic axes normal to elongation, so must have had crystals of different habit. Some earlier observers recorded this alkaloid as crystallizing rhombic, but, as shown by Täuber, they apparently over-looked the inclination of the prism faces, and there is no evidence that it is dimorphous.

[1] U. S. Dept. Agr., *Bull.* **679** (1918).

[2] A. C. Oudemans, *Ann.*, **182**, 44 (1876) [Specific rotation]; C. Täuber, *Inaug. Diss., Breslau*, **1898**; *Z. Kryst. Min.*, **33**, 78 (1900); F. E. Wright, THIS JOURNAL, **38**, 1655 (1916). (Only articles containing optical-crystallographic data are in general referred to.)

Cinchonidine,[1] $C_{19}H_{22}N_2O$. — Free from solvent-of-crystallization. Crystallized from alcohol. Rhombic; usually tabular on base and elongated along axis a.

A commercial product was found to be pure, as on recrystallization from 95% alcohol the specific rotation remained unchanged. Another attained the same purity after 2 recrystalliza- tions. For a 1% solution in absolute alcohol this value was $[\alpha]_D^{20} = -109.2°$. Oudemans found for a 1.5% solution

Fig. 1.

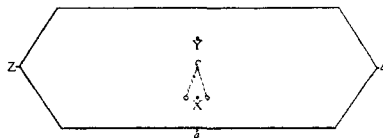$[\alpha]_D^{20} = -109.0°$. Our samples are therefore pure, and free from alcohol.

In ordinary light: colorless; in good-sized plates or rods with lengthwise cleavage; angles shown in Fig. 2, below.

Refractive indices: $\left[\substack{20°\\D}\right]$ $\alpha = 1.610$, $\beta = 1.625$, $\gamma = 1.675$, $\gamma - \alpha = 0.065$, all ± 0.003; the directions X, Y and Z are shown in the figure. Most crystals yield index γ length-wise and β crosswise, but cleavage blades show either the mean of β and α, or α itself.

In parallel polarized light: extinction is parallel. Double refraction is very strong, some grains showing brilliant colors of the 2nd order, although many of the plates are so thin that only 1st order white and yellow are shown. The sign of elongation is +.

In convergent polarized light: biaxial, but no interference figures are visible on most of the plates. Approximate measurements on a few fragments which happened to be broken across the cleavage gave $2E_D = 100 \pm 10°$. Sign +.

These data agree with those of the authors cited, except that Wright's sample was in radial spherulites, and showed a maximum refractive index less than 1.65; the orientation of the crystals with reference to those here studied is however, uncertain, and maximum index he observed may have been β.
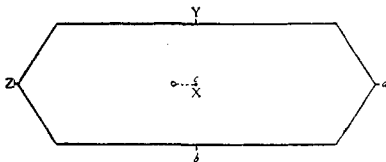

Fig. 2.

Cinchonidine.—With benzene-of-crystallization,[2] $C_{19}H_{22}N_2O.1C_6H_6$.

Rhombic; usually elongated along axis a.

The specific rotation of cinchonidine crystallized from benzene was found to be $[\alpha]_D^{20} = -87.0°$, in good agreement, allowing for one molecule of solvent, with the value of the pure substance given above.

In ordinary light: colorless; in rods with lengthwise cleavage; angles somewhat variable, but averaging as in Fig. 3, below.

Refractive indices: $\left[\substack{20°\\D}\right]$ $\alpha = 1.595$, $\beta = 1.620$, $\gamma = 1.655$, $\gamma - \alpha = 0.060$, all ± 0.003; the directions X, Y and Z are shown in the figure. γ is always shown length-wise and α or β crosswise.

In parallel polarized light: extinction is parallel. Double refraction is very strong, the colors being mostly 2nd order. Sign of elongation +.

[1] Oudemans, *op. cit.*, p. 46 [Specific rotation]; V. Von Lang, *Sitzb. Akad. Wiss., Wien*, 102 (IIa), 845 (1893); G. Wyrouboff, *Ann. chim. phys.*, [7] 1, 81 (1894); F. E. Wright, *Loc. cit.*

[2] Not previously studied optically.

In convergent polarized light: biaxial, but figures very rarely obtained, and it can merely be stated that the axial angle is large and the sign $+$.

These properties are similar to those of the substance free from solvent, the indices being lower to about the extent which would be predicted from the presence of $1/4$ part of a uniformly distributed substance (benzene) with an index of 1.55.

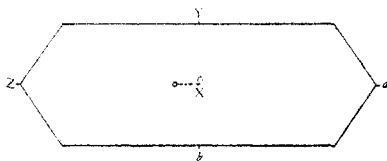**Quinine,**[1] $C_{20}H_{24}N_2O_2$.— Free from solvent-of-crystallization.

Rhombic(?); habit needle-like.

Fig. 3.

Commercial quinine was purified as described under the next heading. On evaporating solutions of this in alcohol they ultimately became viscous, and on standing yielded densely packed needle-like crystals. These were found to have the melting point $172°$ and the specific rotation $[\alpha]_D^{15} = -165.4°$; as Oudemans found $[\alpha]_D^{20} = -166.6°$, our material is free from solvent.

In ordinary light: colorless; in irregular masses, crowded with fine needles.

Refractive indices: $\alpha = 1.620$, $\beta = 1.625$, $\gamma = 1.630$, $\gamma - \alpha = 0.010$, all ± 0.003; α is usually shown lengthwise, β or γ crosswise.

In parallel polarized light: extinction is parallel. Double refraction is weak, the interference colors being first order white, yellow or orange; or in part an intense blue color, the so-called "ultra-blue," which is connected with strong dispersion. Sign of elongation is —.

In convergent polarized light: grains too minute for study.

The weak double refraction and the negative elongation distinguish this from the other alkaloids of the group, which, at least in our preparations, are all $+$ and more strongly doubly refracting.

Quinine.[2]—With benzene-of-crystallization; stable form, $C_{20}H_{24}N_2O_2$.-$1C_6H_6$.

Rhombic; much elongated (along a?).

A commercial sample of quinine was recrystallized twice from benzene, using "norit" as a decolorizing agent. A 1.4% solution in absolute alcohol gave the specific rotation: $[\alpha]_D^{20} = -134.3°$, which corresponds, since one molecule of the solvent is taken up, to $-166.6°$ for the solvent-free alkaloid. Oudemans found for a 2% solution exactly the same figure. The product was therefore pure.

In ordinary light: colorless; in needles and fine rods, without definite terminations.

Refractive indices: $[_D^{20°}]$ $\alpha = 1.608$, $\beta = 1.611$, $\gamma = 1.615$, $\gamma - \alpha = 0.007$, all ± 0.003; directions X, Y and Z are shown in figure. γ is always shown lengthwise and α or β crosswise.

In parallel polarized light: extinction is parallel. Double refraction is weak, the colors being rarely anything but yellow of the first order. Sign of elongation $+$.

[1] Wright, *Loc. cit.*

[2] Oudemans, *Op. cit.*

In convergent polarized light: biaxial, but figures are very rarely obtainable; the axial angle appears to be large and the sign +.

The weak double refraction distinguishes this from the other alkaloids of the series crystallized from benzene, and the + sign of elongation from quinine crystallized from alcohol.

Quinine.—With benzene-of-crystallization; unstable form,[1] $C_{20}H_{24}N_2O_2$.-$1C_6H_6$.

Rhombic(?); roughly equidimensional.

When a concentrated solution of quinine in hot benzene was allowed to cool slowly and quietly, a few crystals of equidimensional habit separated at first, but they were soon enveloped in a dense mass of needles of the stable form previously described. The dried material showed a few corroded grains of this unstable form remaining scattered through the needles. The specific rotation of this mixture was the same
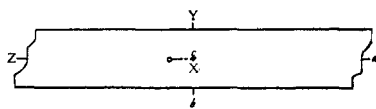

Fig. 4.

as that for the pure needles, so it is concluded that quinine with benzene-of-crystallization is dimorphous. On attempting to pick out the unstable crystals separately from the solution, they became opaque and crumbled, changing into the stable form. The properties here recorded were therefore necessarily obtained on the grains scattered through the dry mass of needles.

In ordinary light: colorless; cleavage distinct; outline various, but rarely elongated in any one direction. No definite angles measurable.

Refractive indices: $[_D^{20}]$ $\alpha = 1.525$, $\beta = 1.630$, $\gamma = 1.655$, $\gamma - \alpha = 0.130$, all $\doteq 0.010$, measurements being rendered uncertain by the corroded surfaces of the grains, as well as superficial alteration to the other form; X, Y and Z are shown in the figure; the grains lie in various positions, so that intermediate values are usually obtained.

In parallel polarized light: extinction is uncertain because there are no definite crystallographic directions recognizable; it appears, however, to be parallel to a cleavage structure sometimes visible. Double refraction is extremely strong, the colors being of high orders. Sign of elongation in the few grains with definite elongation +.

In convergent polarized light: biaxial, and portions of the interference figure frequently visible. Axial angle large, and though not accurately measurable because of the irregularities in the surface of the grains, is roughly $2E_D = 110 \pm 10°$. Sign —. Dispersion marked with $2E_r < 2E_v$.

This modification is not likely to be met with in practice, since dilute solutions are used, and its properties are merely recorded for completeness.

Quinidine.—With alcohol-of-crystallization,[2] $C_{20}H_{24}N_2O_2 \cdot 1C_2H_5OH$.

Rhombic; elongated along axis *c*.

A commercial product was recrystallized from 95% alcohol, decolorized

[1] Not previously described.

[2] Oudemans, *Op. cit.*, p. 44 [Specific rotation]; Wyrouboff, *Op. cit.*, p. 40; Wright, *Loc. cit.*

with "norit," and gave in absolute alcohol the specific rotation $[\alpha]_D^{20}$ = +220.9°, which corresponds to +252.2° for alcohol-free alkaloid.   Another

sample was heated gently to remove alcohol and gave: $[\alpha]_D^{20}$ = +252.5°. Oudemans found $[\alpha]_D^{17}$ = +255.4°, which agrees reasonably well, so our material was pure.
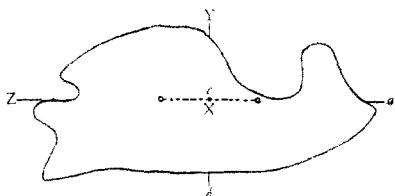

Fig. 5.

In ordinary light: colorless; in rods and irregular masses, sometimes showing rounded hexagonal outlines; cleavage lengthwise, distinct.   The angles are shown in the figure.

Refractive indices: $[_D^{20°}]$ α = 1.550, β = 1.570, γ = 1.690, $\gamma - \alpha$ = 0.140, all ±0.003; the directions X, Y and Z are shown in the figure.   Most crystals yield index γ lengthwise and a value intermediate between α and β crosswise, but occasional flakes with low order polarization colors show α and β.

In parallel polarized light: extinction is parallel.   Double refraction is extremely strong in most grains, the colors being 3rd or 4th order, and only in a few irregular masses are low order colors shown.   The sign of elongation is +.

In convergent polarized light: biaxial, but interference figures are obtained only on flakes with irregular outlines and low polarization colors.   Measurements gave $2E_D$ = 80 ± 5°.   The sign is +. $2E_r < 2E_v$.

These data agree with those of Wyrouboff.   The difficulty in obtaining interference figures, and their much greater axial angle, distinguishes this at once from cinchonine, which the slides resemble at first glance.   It may be noted here that the quinidine described by Wright in the paper cited had different properties, but it was probably crystallized from acetone.
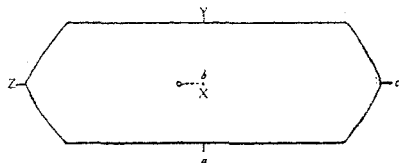

Fig. 6.

Quinidine.—With benzene-of-crystallization,[1] $C_{20}H_{24}N_2O_2.^1/_3C_6H_6$.

Rhombic; roughly equidimensional.

Somewhat less quinidine than could be taken up was dissolved in benzene and the solution allowed to evaporate spontaneously.   A mass of crystals separated, which yielded the specific rotation in 0.6% solution in absolute alcohol, $[\alpha]_D^{20}$ = +238.8°.   This corresponds to the presence of somewhat less than $^1/_3$ molecule of benzene-of-crystallization, slight efflorescence having taken place before making this observation.

In ordinary light: colorless; in irregular grains, with some cleavage.

Refractive indices: $[_D^{20°}]$ α = 1.575, β = 1.595, γ = 1.685, $\gamma - \alpha$ = 0.110, all ±0.003; the directions X, Y and Z are shown in the figure.   The grains lie in various positions, so that intermediate values are usually obtained.

In parallel polarized light: extinction is parallel with reference to the cleavage and occasional long sides of grains.   Double refraction is extremely strong, the colors being 3rd order in many grains, 2nd in some.   Sign of elongation +.

[1] Wyrouboff, *Op. cit.*, p. 68.

In convergent polarized light: biaxial, and at least partial interference figures are usually visible. Axial angle $2E_D = 85 \pm 2°$. Sign $+$. Dispersion distinct, with $2E_r < 2E_v$.

These data agree with those of Wyrouboff. The much larger axial angle distinguishes this at once from cinchonine.

Quinidine.—Free from solvent-of-crystallization,[1] $C_{20}H_{24}N_2O_2$. Crystallized rapidly from benzene.
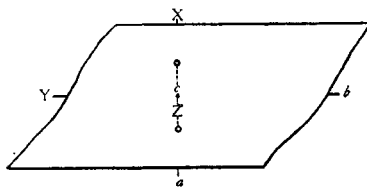
Fig. 7.

Rhombic; elongated (along axis c?).

When hot benzene was saturated with quinidine and allowed to cool, crystallization began very soon, and hemispherical masses of radiating needles were formed. These are free from solvent, as shown by their specific rotation: for a 1% solution in absolute alcohol $[\alpha]_D^{20} = +251.6°$, agreeing closely with the result obtained on the product crystallized from alcohol, but heated to drive out solvent, noted above: $[\alpha]_D^{20} = +252.5°$. This was confirmed by heating, practically no loss taking place.

In ordinary light: colorless; in needles and rods, with some lengthwise cleavage; ends either terminated by a plane at right angles, or frayed.

Refractive indices: $[_D^{20°}]$ $\alpha = 1.580$, $\beta = 1.665$, $\gamma = 1.690$, $\gamma - \alpha = 0.110$, all ± 0.003; the directions X, Y and Z are shown in the figure. Most crystals yield γ lengthwise, and α crosswise.

In parallel polarized light: extinction is parallel. Double refraction is extremely strong in most grains, the colors being 3rd order, although those in which the direction Y lies parallel to the slide show 2nd order. The sign of elongation is $+$.

In convergent polarized light: biaxial, and interference figures are occasionally seen on grains with low polarization colors. The 2 axes are rarely in the field simultaneously, but measurements on a few fair crystals showed the axial angle to be rather large, $2E = 100 \pm 10°$. The sign is $-$.

In this case the absence of solvent makes considerable difference in the optical properties, although the maximum and minimum indices show a normal increase. Wyrouboff gave no optical data, but his description shows that he had the same form.
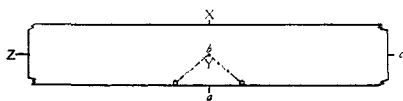
Fig. 8.

II. Tabulations of the Data.

TABLE I.—PROPERTIES OF THE FOUR CINCHONA ALKALOIDS.

Solvent, Alcohol.

Substance.	Cinchonine.	Cinchonidine.	Quinine.	Quinidine.
Solvent taken up.......	None	None	None	1 molecule
Crystal system.........	Monoclinic	Rhombic	Rhombic(?)	Rhombic
Cleavage..............	Lengthwise	Lengthwise	Lengthwise	Lengthwise
Habit.................	Plates, rods	Plates, rods	Fine needles	Rods, lumps
Refractive indices α....	1.570	1.610	1.620	1.550
β....	1.685	1.625	1.625	1.570

[1] Wyrouboff, *Op. cit.*, p. 68.

TABLE I (*continued*).

Substance.	Cinchonine.	Cinchonidine.	Quinine.	Quinidine.
Refractive indices γ....	1.690	1.675	1.630	1.690
$\gamma - \alpha$	0.120	0.065	0.010	0.140
Refractive indices, usually seen.........	γ & mean of α & β	γ & mean of α & β	α & mean of β & γ	γ & mean of α & β
Extinction............	Parallel	Parallel	Parallel	Parallel
Usual order of colors....	4	2 (or 1)	1	4
Double refraction......	Extremely strong	Very strong	Weak	Extremely strong
Sign of elongation......	+	+	—	+
Class................	Biaxial	Biaxial	Biaxial(?)	Biaxial
Interference figure seen.	Frequently	Rarely	Not seen	Occasionally
Axial angle (2E).......	Small, 38°	Large, 100°	Indeterminate	Medium, 80°
Optical character (sign)	—	+	Indeterminate	+
Dispersion............	$r < v$	Weak	Strong	$r < v$

TABLE II.—PROPERTIES OF THE FOUR CINCHONA ALKALOIDS.

Solvent, Benzene.

Substance.	Cinchonine.	Cinchonidine.	Quinine, stable.	Quinine, unstable.	Quinine.	Quinidine.
Solvent taken up...	None	1 molecule	1 molecule	1 molecule	1/3 molecule	None
Crystal system.....	Monoclinic	Rhombic	Rhombic	Rhombic (?)	Rhombic	Rhombic
Habit.............	Plates, rods	Rods	Rods, needles	Lumps	Lumps, rods	Needles
Cleavage.........	Lengthwise	Lengthwise	Lengthwise	Present	Present	Lengthwise
Refractive indices α	1.570	1.595	1.608	1.525	1.575	1.580
β	1.685	1.620	1.611	1.630	1.595	1.665
γ	1.690	1.655	1.615	1.655	1.685	1.690
$\alpha - \gamma$	0.120	0.060	0.007	0.130	0.110	0.110
Refractive indices, usually seen.....	γ & mean of α & β	γ & mean of α & β	γ & mean of α & β	Means	Means	γ & α
Extinction.........	Parallel	Parallel	Parallel	Parallel	Parallel	Parallel
Usual order of colors	4	2	1	4	3	3
Double refraction..	Extremely strong	Very strong	Weak	Extremely strong	Extremely strong	Extremely strong
Sign of elongation...	+	+	+	+	+	+
Class.............	Biaxial	Biaxial	Biaxial	Biaxial	Biaxial	Biaxial
Interference figure seen............	Frequently	Rarely	Rarely	Frequently	Frequently	Occasionally
Axial angle (2E)...	Small, 38°	Large	Large	Large, 110°	Medium, 85°	Large, 100°
Optical character (sign)...........	—	+	+	—	+	—
Dispersion of optic axes............	$r < v$	?	?	$r < v$	$r < v$	?

TABLE III.—DETERMINATIVE TABLE FOR THE FOUR ALKALOIDS STUDIED, CRYSTALLIZED FROM ALCOHOL.

Immerse in liquid 1.680 and examine with polarizing nicol in and diaphragm partly closed.

Crystals mostly needles

Refractive indices all much lower than liquid; between crossed nicols shows first order yellow colors and — elongation.......... QUININE

Crystals mostly rods or plates

Refractive index lengthwise slightly lower than that of liquid; between crossed nicols shows colors of first and second orders; elongation +; in convergent light (high power objective and eyepiece out) shows no definite interference figures.............. CINCHONIDINE

Crystals mostly plates or irregular grains

Refractive index lengthwise higher than that of liquid; between crossed nicols shows colors of third or fourth orders, rarely lower; elongation +; in convergent light often shows at least partial interference figures...................................... CINCHONINE or QUINIDINE

Immerse another sample in liquid 1.570.

Refractive index crosswise equal to or higher than that of liquid; in the inteference figure, the axial angle is small and sign —......... CINCHONINE

Refractive index crosswise equal to or less than that of liquid; in the interference figure the axial angle is large and sign +............ QUINIDINE

TABLE IV.—DETERMINATIVE TABLE FOR THE FOUR ALKALOIDS STUDIED, CRYSTALLIZED FROM BENZENE.

Immerse in liquid 1.670 and examine with polarizing nicol in and diaphragm partly closed.

Crystals mostly needles

Refractive indices all much lower than that of liquid; between crossed nicols shows first order colors........................ QUININE

Crystals mostly rods or plates

Refractive index lengthwise less than that of liquid; between crossed nicols shows second order colors; in convergent light no definite interference figures................................ CINCHONIDINE

Crystals mostly plates or rods

Refractive index lengthwise higher than that of liquid; between crossed nicols shows mostly third or fourth order colors; in convergent light often shows at least partial interference figures.... CINCHONINE or QUINIDINE

Immerse another sample in liquid 1.690.

Refractive index lengthwise equal to that of liquid; in the interference figure the axial angle is small......................... CINCHONINE

Refractive index lengthwise equal to or slightly lower than that of liquid; in the interference figure the axial angle is large........... QUINIDINE

NOTE.—The unstable form of quinine would come out at this place in the table, but is not likely to be met with in practice; it has one index below 1.530.

III. Data on Mixtures of the Cinchona Alkaloids.

The properties of these 4 alkaloids having been determined, attention was turned to mixtures of them such as are likely to be met with in drug

work. Equal parts by weight of the 4 substances were mixed and heated with enough 95% alcohol to dissolve them completely, about 100 parts being required. On cooling a crystalline mass separated, which was filtered out, dried, and examined under the microscope (1). The mother liquor was evaporated at room temperature until more crystals appeared, which were treated similarly (2); and the process was repeated until practical dryness was reached (3, 4, 5). An exactly similar procedure was followed using benzene as the solvent, several hundred parts being used. The following tables show the results obtained:

TABLE V.—SOLUBILITY OF THE FOUR ALKALOIDS.

Alkaloid.	Solubility in alcohol (95%) at 20°.	Solubility in benzene at 20°.
Cinchonine	in 125 parts	slightly soluble
Cinchonidine	in 20 parts	moderately soluble
Quinine	in 1 part	soluble in 200 parts
Quinidine	in 25 parts	fairly soluble

TABLE VI.—ALKALOIDS FOUND IN FRACTIONS CRYSTALLIZED FROM ALCOHOL.

No.	Bulk of crystals.	Considerable amount.	Small amount.
1	Cinchonine	......	Quinidine
2	Cinchonidine	Quinidine	Cinchonine
3	Cinchonidine	Quinidine	Cinchonine
4	Quinidine	Cinchonidine	......
5	Quinine	Quinidine	Cinchonidine

TABLE VII.—ALKALOIDS FOUND IN FRACTIONS CRYSTALLIZED FROM BENZENE.

No.	Bulk of crystals.	Considerable amount.	Small amount.
1	Cinchonine	Cinchonidine	......
2	Cinchonidine	Cinchonine	Quinine
3	Cinchonidine	Quinine	Cinchonine
4	Quinine	Cinchonidine	......
5	Quinidine	Cinchonidine	Quinine

There is thus evidently no difficulty likely to be encountered when mixtures of these alkaloids are being examined; they can be partially separated by recrystallization, and the observations made on the simplified materials.

IV. Examination of Medicinal Preparations for these Alkaloids.

The following experiments were made with a view toward drawing up instructions for procedure in the case of medicinal products in which the presence of these alkaloids is to be proved. Variations in the preliminary treatment will of course be necessary from one substance to another, but the latter parts of the directions are probably generally applicable.

A few pills of a proprietary remedy presumably containing the alkaloids as sulfates were rubbed with potassium carbonate to free the alkaloids, suspended in water, and stirred with chloroform to dissolve them. The chloroform layer was separated from the aqueous one in a small separatory

funnel, and allowed to stand at ordinary temperature until completely evaporated. The residue was non-crystalline, consisting of whatever alkaloids were present in the original material, along with considerable nondescript gummy matter.

The residue was covered with dil. sulfuric acid, shaken to hasten solution, and filtered. To the filtrate dil. ammonium hydroxide was added and a gray precipitate of alkaloids separated. Examination of this under the microscope showed it to be in part very minutely crystalline, but mostly apparently amorphous. Several cc. of benzene was added, and thoroughly stirred in, when the precipitate was dissolved by the benzene. The benzene layer was separated by funnel, and allowed to evaporate slowly at ordinary temperature. When it had become very concentrated, a large drop was placed on a microscope slide, left until it had nearly evaporated, and a cover glass was placed over it to halt the evaporation. Crystals soon formed all around the edge of the cover glass.

On examination under the microscope 3 entirely distinct crystalline substances could be recognized with the greatest readiness. There were, first, radiating groups of very long, slender needles showing between crossed nicols first order colors; this was evidently quinine. Then there were many bunches of rods or plates showing first and second order colors, but no interference figures in convergent light; these were obviously cinchonidine. Finally a few plates could be seen, usually single, and much more coarsely crystallized than the other two. These showed high order polarization colors, distinct partial interference figures; and on a few of them the optical sign could be determined as negative, showing them to be cinchonine.

To make the matter as certain as possible, several drops of the benzene solution were allowed to evaporate slowly to dryness under covers on separate slides, and the crystals immersed in the liquids of known refractive indices as described in Table IV. The features noted in this table for the first 3 alkaloids listed were exhibited very clearly, even by the rather minute crystals obtained, and the presence of these three alkaloids in the pills was thus definitely established.

Summary.

The value of optical-crystallographic measurements for the identification of synthetic substances is pointed out, and the application of this method to the cinchona alkaloids is described. The properties observed are presented first in formal descriptions, and then in tabular form. Determinative tables are given, by following which the identity of an unknown alkaloid of this group can be rapidly ascertained. The results obtained with mixtures are then described, and the possibility shown of partially separating the alkaloids by fractional crystallization. The

method of treatment of a medicinal preparation containing these sub-
stances is then outlined, and the success obtained in their identification
pointed out.

WASHINGTON, D. C.

NITROSO-TRIPHENYLAMINE AND COLORS OF THE SECOND ORDER.

BY JEAN PICCARD AND MORRIS KHARASCH.[1]
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Theoretical Part.

It is a well-known rule[2] that the color of a yellow dye changes with in-
crease of molecular weight to orange, red, violet, blue, and finally to green.
Each one of these colors is called lower than the preceding one, and higher
than the following one.   Generally, we can lower the color by the intro-
duction of alkyl or aryl radicles into the auxochromic or chromophoric
groups of the dye.

The spectroscopic explanation of this behavior of dyes is that a yellow
dye has an absorption band in the violet, and any increase in the mole-
cular weight decreases the number of vibrations corresponding to this ab-
sorption band causing the band to shift toward the red end of the spectrum.
When the absorption band is in the blue the compound appears orange,
and as the absorption band goes through green, yellow, orange to red, the
color of the respective compounds successively changes to red, violet, blue,
and green.   A compound has the color complementary to that of its maxi-
mum absorption.   On the other hand, if in the molecule of a yellow dye
we make such changes as generally tend to produce a higher color, then the
absorption bands shift into the ultra-violet part of the spectrum, the com-
pound becoming colorless.

Absorption colors have very much in common with interference colors.
The colors of Newton, for instance, are also produced by an absorption
band going through the spectrum in the same direction in which the ab-
sorption bands of chemical compounds shift with increase of molecular
weight.   Thin layers of any oil, soap bubbles and glass, are first yellow
in reflected light, and as the thickness of the layer increases, the color be-
comes orange, red, violet, blue and green.   The last color has an absorp-
tion band in the red, but in the violet end of the spectrum there appears
a new band.   If the layer becomes still thicker, the first band (in the red)
shifts into the ultra red, and we have only the second band, which is in
the violet.   Our layer is now again yellow but yellow of the second order.

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[1] A part of this work was done in collaboration with E. H. Fleck.
[2] Nietzki. *Verh. des Vereins zur Förderung des Gewerbefleisses*, **58**, 231 (1879).