ON THE DECOMPOSITION-PRODUCTS OF QUININE, ETC. 189

XXV.—On the Decomposition-products of Quinine and the Allied Alkaloïds.

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Second Paper. Oxidation of Quinine, Quinidine (Conquinine), Cinchonine, and Cinchonidine, with Permanganate.

In our first paper on this subject we published the results of preliminary experiments on the oxidation of quinine. We have since continued those experiments, and extended our investigation to quinidine (conquinine), the isomeride of quinine, and to cinchonine and its isomeride, cinchonidine. All four bases yield on oxidation with potassium permanganate an acid, which, so far as our examination of its physical and chemical characters goes, is one and the same body. In the following paper, however, we have kept our results relating to the acid derived from each base separate, and, for convenience, shall refer to each acid by the name of the base from which it has been derived. The term "mixed acid" we shall use to denote acid obtained from residues containing oxidation products of all four alkaloïds.

The oxidation was conducted in the manner already described; but the following method was found more convenient than that formerly employed for the separation of the acid.

The strongly alkaline liquor, filtered from the manganese oxide, was neutralised with nitric acid, and barium chloride added, which brought down the organic acid in the form of a curdy white precipitate. This precipitate, after thorough washing, was treated with sulphuric acid in quantity insufficient to decompose the whole of the salt. The liquor containing the organic acid was filtered off and evaporated. The residue of barium salt remaining mixed with the sulphate of barium was afterwards treated with excess of sulphuric acid, filtered, and the organic acid in the filtrate precipitated as copper salt, and finally recovered by decomposing that salt with sulphuretted hydrogen. The acid prepared from the barium salt may be purified completely by a few crystallisations. The yield of acid from each base was over 10 per cent.

When pure, the acid crystallises in well formed, transparent, colourless plates, which usually grow together in clusters. For the following description of the cinchonine crystals we are indebted to the kindness of Mr. Baker, of the Owens College :—

"Rectangular plates, whose large faces are somewhat rough and generally curved, and whose edge-faces have an adamantine lustre. No other form was developed. Under the stauroscope no curves or crosses were seen, but the crystal depolarised the polarised light, appearing light on a dark ground.



So that all the interfacial angles are apparently right angles."

The crystals of the other acids are indistinguishable from those of the cinchonine acid.

When heated in a capillary tube in the paraffin bath, all four acids blacken at 200° C., and decompose at 256-257°. This behaviour has been confirmed by numerous experiments.

When dried at 100° for a considerable time, all four acids lose their water of crystallisation.

Cinchonine acid, 1.3597 gram lost 0.1512 gram = 11.1 per cent.

,, ,,	0.7346	,,	,,	0.0702	,,	= 9.55	,,
Quinine acid	0.4360	,,	,,	0.0445	,,	= 10.2	,,
Quinidine acid.	0.3020	,,	,,	0.0333	••	= 11.0	,,
,, ,,	0.0865	,,	,,	0.0992	,,	= 10.63	"

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When the acid is acted upon with sulphuretted hydrogen, it is decomposed, with formation of a red amorphous substance, which is probably a reduction-product, and may be, as we before suggested, identical with Marchand's quinetin. When a mixture of the acid and this red substance is evaporated, at a certain point of concentration a violent action takes place, the red colour is discharged, and carbonic acid is evolved in quantity. It was on account of the decomposing action of sulphuretted hydrogen that the preparation of the acid from the lead salt was abandoned.

Combustion of the acid gave the following results :----

Quinine Acid.

Percentage of C and H. $\cdot 3463$ gram acid gave $\cdot 5869$ gram $CO_2 \cdot 0837$ H₂O = $46 \cdot 27$ 2.65 $\cdot 2440$ ·4143 " ·0602 " ,, = 46.272.73••• ,, Cinchonine Acid. Percentage of C and H. 2595 gram acid gave 4407 gram $CO_2 \cdot 0694$ H₂O = $46 \cdot 28$ 2.93Quinidine Acid. ·3338 gram acid gave ·5697 gram CO_2 ·0780 $H_2O = 46.52$ 2.56Cinchonidine Acid. $\cdot 3330$ gram acid gave $\cdot 5720$ gram $CO_2 \cdot 0764$ H₂O = 46.842.54Mixed Acid. $\cdot 3551$ gram acid gave $\cdot 6010$ gram $CO_2 \cdot 0821$ H₂O = $46 \cdot 16$ 2.56Nitrogen Determinations by Will and Varrentrapp's Process. Quinine Acid. Per cent. N. ·2733 gram acid gave ·1321 gram metallic $Pt = \cdot 01871$ gram N = 6.84·3189 $\cdot 1658$ = .02349,, N = 7.36,, ,, ,, ,, Cinchonine Acid. ·3010 gram acid gave ·1555 gram metallic Pt = ·02203 gram N = 7.32Quinidine Acid. ·3038 gram acid gave ·1547 gram metallic Pt = .02192 gram N = 7.21Cinchonidine Acid. ·3047 gram acid gave ·1658 gram metallic $Pt = \cdot 02349$ gram $N = 7 \cdot 69$ Mixed Acid. ·2931 gram acid gave ·1518 gram metallic $Pt = \cdot0215$ gram $N = 7\cdot33$ $\cdot 3017$ $\cdot 1561$ = .0221,, N = 7.36,, ,, ,, ,,

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Salts of the Acid.

The potash and soda salts of the acid, prepared by neutralising with potash and soda respectively, are deliquescent bodies very soluble in water, insoluble in alcohol.

Titration of acid with soda gave-

Cinchonine ad	eid.		24·84 per	r cent. Na
Cinchonidine	acid	•••••	24.70	,,
Quinidine	,,	••••	23.54	**

Titration of acid with potash gave-

Cinchonine acid...... 36.1 per cent. K. Quinine acid (two experiments) 36.1 ,,

The ammonia salt was prepared by neutralising the acid with ammonia, and evaporating to dryness.

Mixed Acid.

 $0.4300~{\rm gram}$ gained on evaporation $0.1200~{\rm gram}=21$ per cent. ammonia.

Silver Salts.

Three silver salts exist. When the acid is neutralised with ammonia, and silver nitrate is added to the cold solution, a curdy white precipitate forms immediately.

Mixed Acid.

0.4445 gram of silver salt lost on ignition 0.1774 gram, leaving 0.2671 gram = 60.05 per cent. Ag.

0.4176 gram of silver salt lost on ignition 0.1690 gram, leaving 0.2486 gram = 59.54 per cent. Ag.

From boiling solution containing a little free nitric acid, after addition of $AgNO_3$, a salt containing less silver than the preceding, and crystallising in radiating tufts of long colourless needles, separated out.

Quinidine Acid.

- \cdot 5787 gram salt gave \cdot 3837 gram silver chloride = \cdot 2888 gram Ag = 49.9 per cent. Ag.
- \cdot 4670 gram salt gave \cdot 2995 gram silver chloride = \cdot 2262 gram Ag = 48.4 per cent. Ag.

 \cdot 2790 gram salt gave \cdot 1765 gram silver chloride = \cdot 1327 gram Ag = 47.56 per cent. Ag.

- ·4100 gram salt gave ·3969 gram silver chloride = ·2997 gram Ag = 48.48 per cent. Ag.
- $\cdot 3252$ gram salt gave $\cdot 2090$ gram silver chloride = $\cdot 157$ gram Ag = 48.5 per cent. Ag.

Quinine Acid.

3283 gram salt gave 2087 gram silver chloride = 1576 gram Ag = 48.01. With regard to the first of the seanalyses, it may be well to note that there was no free nitric acid present in the solution. The silver salts decompose suddenly, even when heated up very gradually. On this account it is better to estimate the silver as chloride than as metallic silver after ignition.

The third silver salt, which crystallises in prisms of a faint yellowgreen colour, was obtained from both the quinine and cinchonine acids, by adding to a hot solution containing free nitric acid, silver nitrate in quantity insufficient for the formation of the neutral salt. Our analyses of this salt were unsatisfactory, but sufficed to show that it contained much less silver than the preceding.

Calcium, barium, and strontium all form salts insoluble in cold water, and partially soluble in boiling water.

The *calcium salt*, prepared by adding calcium nitrate to a hot solution of the acid, separates out in beautiful satin-like flakes.

Mixed Acid.

 \cdot 1341 gram salt gave \cdot 0545 calcium carbonate = \cdot 0218 calcium = 16 \cdot 1 per cent. Ca.

The *barium salt*, prepared by adding barium chloride to hot solution of free acid, crystallises in oblong colourless plates. On analysis the salt from mixed acid gave 36.26 per cent. barium. A gelatinous salt, containing a higher percentage of barium, is formed when barium chloride is added to a solution of the acid neutralised with ammonia.

Mixed Acid.

·1461 gram salt gave ·1175 gram barium sulphate = ·06907 Ba = 47.26 per cent.

3618 gram salt gave 2895 gram barium sulphate = 1682 Ba = 46.76 per cent.

The strontium salt, prepared in the same way as the calcium and barium salts, forms thick colourless plates or prisms pointed at both ends.

Quinidine Acid.

 \cdot 3530 gram salt gave \cdot 2050 gram strontium sulphate = \cdot 09775 gram strontium = 27.69 per cent.

Mixed Acid.

'1905 gram salt gave '1100 gram strontium sulphate = '05239 gram strontium = 27.5 per cent.

Another experiment gave 28.07 per cent.

Lead Salt.—When lead nitrate is added to a hot solution of the VOL. XXXV. P

Per cent. Pb.

acid containing a little free nitric acid, the lead salt separates out on cooling in glistening white silky needles.

Cinchonine Acid.

'4365 gram salt gave '3115 gram $PbSO_4 = '2128$ gram Pb = 48.7

Quinine Acid.

 $\cdot 1250$ gram salt gave $\cdot 0892$ gram $PbSO_4 = \cdot 0609$ gram Pb = 48.7

Quinidine Acid.

$\cdot 4974$	gram salt	t gave	$\cdot 3530$	gram	$PbSO_4 =$	= ·2411	gram	Pb =	48.67
4863	"	,,	$\cdot 3498$,, =	= · 2389	,,	=	49.1

Zinc forms a beautiful salt, which separates in well-defined colourless crystals, having, when viewed through the microscope, the appearance of rhombohedra of Iceland spar.

Copper sulphate, added to the acid, gives a light blue heavy crystalline precipitate. We used this salt in working up the residues in preference to the lead salt. It is less apt to get into a slimy condition, and is more easily decomposed by sulphuretted hydrogen.

The *ethyl ether* of the acid is a crystalline body. It was prepared by passing hydrochloric acid gas into a solution of the acid in absolute alcohol. We have not yet analysed it.

In attempting to prepare the methyl ether by heating together the acid and methyl iodide, a tarry mass was obtained, which, on distillation, gave off pyridine freely.

An attempt to prepare the chloride by distilling the acid with phosphorous pentachloride gave a very decomposable crystalline substance, but in too small quantity for examination. The formula deducible from the analysis of the acid and its salts is $C_8H_5NO_6 + 1\frac{1}{2}H_2O$. Probably, from the fact mentioned in our first paper, that some of the salts on heating give off pyridine, the acid is tricarbopyridenic acid.

It is obvious from a comparison of the analyses of the salts that the acid is tribasic.

The potash. soda, ammonia, and silver salts, precipitated from neutral solution, are all normal salts, containing three atoms of metal. The following is a comparison of numbers found with those calculated from assigned formula for normal salts :---

Normal salt.	Calculated.	Found.
Soda	24.7	$\begin{cases} 24.84 \\ 24.7 \\ 23.54 \end{cases}$
Potash	35.5	36.1
Ammonia	20.5	21.0
Silver	60.2	$\begin{cases} 60.05 \\ 59.54 \end{cases}$

The gelatinous barium salt is also apparently a normal salt, in which three atoms of barium replace six atoms of hydrogen in two molecules of the acid.

The crystallised salts of barium, strontium, and calcium, as well as the crystallised silver salt, seem to be acid salts, containing one atom of dyad metal or two of monad metal, with one atom of replaceable hydrogen.

The third silver salt obtained by precipitation in hot acid solution probably belongs to the series of acid salts containing two atoms of replaceable hydrogen.

In the research by one of us on the dicarbopyridenic acids from picoline, it was found that the vapour-density of the decomposition-products of the acid, viz., pyridine and CO_2 , corresponded with their decomposition according to the equation :---

$\mathrm{C_5H_3N(\mathrm{COOH})_2} = \mathrm{C_5H_5N} + 2\mathrm{CO_2}.$

We have made a similar experiment with the mixed acid, using the new form of apparatus described v. Meyer in the *Berichte* for 1879, No. 1. The vapour-density from the first determination gave 48.2, and that from a second determination 43.2. Supposing the acid to decompose according to the equation—

$\mathrm{C}_5\mathrm{H}_2\mathrm{N}(\mathrm{COOH})_3 = \mathrm{C}_5\mathrm{H}_5\mathrm{N} + 3\mathrm{CO}_2,$

the vapour-density should be 26.3. On examining the contents of the bulb afterwards, it was noticed that charring had taken place, and that a crystalline substance had sublimed into the cool tube. This substance is not improbably an anhydride, formed by 2 molecules of the acid losing 3 molecules of water. A strong smell of pyridine was observed, showing that partial decomposition had taken place in the manner indicated by the equation.

The result of our investigation so far has been to confirm our hypothesis, that there is a close relation between the cinchona-bark alkaloïds and the bases of the pyridine series; and to prove that the four principal alkaloïds derived from the cinchona bark all yielded on oxidation one and the same acid.

We would draw attention to the fact that our first paper on this subject, in which we pointed out the close relation existing between the oxidation-products of quinine and those of the bases of the pyridine series, was published in March, 1878, in the *Journal of the Chemical Society*.

The Berichte der Deutschen Chemischen Gesellschaft for 11th February, 1879, contains an account (without analyses) by S. Hoogewerff and W. A. van Dorp, of the acid and some of the salts which we have described. We are glad to find that, as regards quinine, the results arrived at by those chemists confirm those which we had independently

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obtained, and we hope that their investigation of the oxidation-products of the allied alkaloïds may also confirm those which we here publish. We are engaged in continuing our investigation of the acid, and of the other decomposition-products of quinine and the allied alkaloïds.

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