III.—*On the Constitution of Codeine and its Products of Decomposition.* By THOMAS ANDERSON, M.D.

(Read 15th April 1850.)

During the last few years, great progress has been made in the study of the organic alkalies, and the discovery of methods by which these substances can be artificially produced, and the long train of investigations by which it has been followed, has greatly extended our previous information, and afforded us some definite ideas regarding their constitution. The advance made has, however, related entirely to the volatile bases produced by artificial processes, and our knowledge of the natural fixed alkaloids stands very much where it did some years since, and is still very imperfect, and in regard to many entirely fragmentary; so much so, indeed, that of all the alkaloids of this class described in chemical works, there are not perhaps a dozen of which the constitution can be considered as definitely fixed, and not half that number of which we know the products of decomposition. The fact is, that the interest attaching to the artificial bases has altogether diverted the attention of chemists from the natural alkalies, which have not hitherto proved a very productive field of inquiry; at least the researches to which many of them were subjected ten or fifteen years since, proved comparatively unfruitful in their results. The want of success which attended their investigation at that time, however, is attributable, partly to the imperfections of the method of analysis of such compounds, and partly to our entire ignorance of the constitution of the nitrogenous substances generally. Neither of these difficulties can now be said to exist; and the investigation of the volatile bases has so far elucidated the constitution of these substances generally, that we are now in the condition to return to the examination of the far more complex natural bases with some prospect of ultimate success. Chemists are, accordingly, beginning to turn their attention to this field of inquiry, and during the last few months, several investigations have been published, by which the constitution and products of decomposition of several important bases have been established; and in the present paper I propose communicating to the Royal Society the results of a series of investigations of codeine and its compounds, which has enabled me to add it to the number of those of which the constitution is definitely fixed.

It will be unnecessary for me to premise any observations regarding the history of codeine and its discovery, which are sufficiently well known, further than to refer to the analyses and formulæ given for it by the different chemists by whom it has been examined. Codeine has been analysed by its discoverer, Robiquet, and by Couerbe, Regnault, Will, Gregory, and Gerhardt. All the analyses of these observers I have brought together in the following table, in which, however, the *per centage* results are not those found in the original papers, but have been calculated from the analytical numbers according to the new equivalent of carbon.*

Anhydrous Codeine.

	Robiquet.†	Couerbe.‡		Regnault.§		Gregory.‖	Will.¶
Carbon, .	70·363	71·59	72·10	73·31	72·93	73·18	73·27
Hydrogen, .	7·585	7·12	7·17	7·19	7·23	7·23	7·25
Nitrogen, .	5·353	5·23	...	4·89	4·89	4·82	...
Oxygen, .	16·699	16·06	...	14·61	14·95	14·77	...
	100·00	100·00		100·00	100·00	100·00	

Crystallised Codeine.

	Gerhardt.**	
Carbon, ...	67·77	67·87
Hydrogen, ...	7·59	7·33
Nitrogen, ...	...	...
Oxygen, ...	...	...

From these analyses, four different formulæ have been deduced. Two of these, however, those of Robiquet and Couerbe, do not require particular mention, as they were unsupported by any accurate determination of the atomic weight of the substance, and are now certainly known not to represent its true constitution. That which has been hitherto most generally adopted by chemists is the one founded by Regnault upon his analysis, and represents codeine as $C_{35} H_{20} NO_5$, and the crystallised base as $C_{35} H_{20} NO_5 + 2 HO$; the calculation of which gives

	Anhydrous.	Crystallised.
Carbon, ...	73·94	69·53
Hydrogen, . .	7·04	7·28
Nitrogen, ...	4·92	4·63
Oxygen, ...	14·10	18·50
	100·00	100·00

The analyses of Will and Gregory have usually been quoted in confirmation of this formula. It is clear, however, that the agreement between the calculated and experimental results is by no means satisfactory, either in them or in

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* In the case of Robiquet and Will's analyses, the details of the experiment are not given. I have, therefore, been obliged to convert the per centage of carbon into carbonic acid, according to the old equivalent of carbon, and recalculate it into carbon according to the new equivalent.

† Annales de Chimie et de Physique, vol. li., p 265.

‡ Ibid., vol. lix., p. 158.

§ Ibid., vol. lxviii., p. 136.

‖ Annalen der Chimie und Pharmacie, vol. xxvi., p. 44.

¶ Ibid.

** Revue Scientifique, vol. x., p. 203.

REGNAULT'S own results; the highest amount obtained for the carbon being 0·63 per cent. below the calculation, while the lowest differs by more than one per cent., and the mean of the whole four gives 0·77 too little carbon, involving a loss which could not possibly have occurred in carefully made analyses.

Partly on account of this difference, and partly guided by his views regarding the divisibility of formulæ, GERHARDT was induced to doubt the exactitude of REGNAULT'S formula, which presents three different deviations from his law; the number of equivalents of carbon and of oxygen being uneven, and the sum of the equivalents of hydrogen and nitrogen also indivisible by two. He therefore repeated its analysis, using the crystallised codeine, and obtained the results contained in the table, and deduced from them the formula $C_{36}H_{21}NO_6$ for the anhydrous base, which gives the calculated results:

	Anhydrous.	Crystallised.
Carbon, . . .	72·24	68·13
Hydrogen, . .	7·02	7·25
Nitrogen, . . .	4·68	4·41
Oxygen, . . .	16·06	20·11
	100·00	100·00

and tallies extremely well with his analysis. This formula has, however, been again called in question by DOLLFUS,* who has endeavoured to determine the constitution and atomic weight of the alkaloids by the analysis of their hydrosulphocyanates, and obtained from the codeine salt of that acid; results agreeing with the formula $C_{34}H_{19}NO_5$. Considering the known accuracy of REGNAULT, and of the chemists by whom his formula has been confirmed, I considered it an essential preliminary to my investigation to repeat its analysis with all possible care, so as to determine which of the two represents its true constitution.

I. *Preparation and Analysis of Codeine.*

I have little to add to the information we already possess regarding the preparation of codeine. I have obtained it, as usual, from the mother liquor from which morphia has been precipitated by ammonia. As the codeine forms only from a sixteenth to a thirtieth of the morphia, it is, of course, mixed in this fluid with a corresponding quantity of muriate of ammonia, which must be decomposed by potash, in order to obtain it. Much advantage is gained, however, by first evaporating the fluid to crystallisation, and expressing the crystals deposited, as in this way the greater part of the muriate of ammonia, which is the more soluble salt of the two, is left in solution; and by repeating the crystallisation many

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* Annalen der Chimie und Pharmacie, vol. lxv., p. 218.

times, it may be entirely removed, and crystals obtained which are pure hydrochlorate of codeine. For the preparation of codeine, however, it would be worse than useless to carry the process thus far, as the solubility of hydrochlorates of codeine and ammonia differs so little that much of the former salt would be lost; but by carrying it a certain length, the greater part of the sal-ammoniac may be separated without any material loss of codeine, and the subsequent steps of the process much facilitated. The crystals so obtained being dissolved in boiling water, strong solution of caustic potash is added in excess, when codeine is in part precipitated as an oil, which by-and-by concretes into a solid mass, and is partly deposited in crystals as the solution cools. By evaporating the fluid, another crop of crystals is obtained; and, finally, when the mother-liquor has been concentrated to a very small bulk, it becomes filled on cooling with long silky needles of morphia, which has been retained in solution by the excess of potash. A certain quantity of morphia appears always to remain in solution along with the codeine; at least I have found it in all the mother-liquors I have examined, although its quantity appears to vary considerably. Its presence in this solution has been observed before, and it has been stated that it exists in the form of a double salt with codeine; this, however, is not consistent with my own experience, at least the salt separated from the muriate of ammonia by successive crystallisations contained no morphia, but, as has been already stated, was pure hydrochlorate of codeine.

The crystals of codeine precipitated by potash, in the manner described, are always more or less coloured. They are purified by solution in hydrochloric acid, boiling with animal charcoal, and reprecipitation with a slight excess of potash, and the precipitate obtained finally dissolved in ether, to separate any morphia which may adhere to it. For this purpose hydrous ether is best adapted; and it ought to be free from alcohol, as if any be present, the ether evaporates, and a syrupy fluid is left behind, which refuses to crystallise. When the ether is anhydrous, it dissolves codeine with much greater difficulty, and by evaporation small crystals are deposited, which are anhydrous.

The codeine employed for analysis was dried at 212°. The three first were made with codeine crystallised from hydrous ether, which lost two equivalents of water at 212°; the last was anhydrous codeine in small colourless crystals.

I. 6·120 grains of codeine, with oxide of copper, gave
16·135 ... of carbonic acid, and
3·888 ... of water.

II. 5·896 grains of codeine, with oxide of copper, gave
15·616 ... of carbonic acid, and
3·737 ... of water.

III. 4·688 grains of codeine, with chromate of lead, gave
12·392 ... of carbonic acid, and
3·015 ... of water.

IV. { 5·858 grains of codeine, with chromate of lead, gave
15·485 ... of carbonic acid, and
3·780 ... of water.

5·395 grains of codeine gave, by Varrentrap and Will's method, 3·79 grains of ammonio-chloride of platinum.

5·898 grains gave, by the same method, 4·32 grains of ammonio-chloride of platinum.

	I.	II.	III.	IV.
Carbon, . . .	71·91	72·02	72·09	72·09
Hydrogen, . .	7·05	7·04	7·14	7·16
Nitrogen, . .	4·41	4·60	4·50	...
Oxygen, . .	16·63	16·34	16·27	...
	100·00	100·00	100·00	

These results confirm, in all respects, the formula $C_{36}H_{21}NO_6$, the calculated results of which are given on a former page. The determination of the atomic weight of codeine by the analysis of its platinum salt, presented considerable difficulties, and at first gave extremely discordant results, the per centage of platinum varying from 18·51 to 20·30. I found, however, that by precipitating in the cold, a salt was obtained, to be afterwards described, which gave sufficiently uniform results. This salt, dried at 212°, retained an equivalent of water. It gave, as the mean of seven experiments, the details of which will be afterwards given, 19·25 per cent. of platinum, while the calculation, according to the above formula, requires 19·19 per cent. These determinations leave no doubt as to the formula of codeine; and they are fully confirmed by the result of the analyses of the substances to be described in the sequel of this paper.

Codeine crystallised from water or hydrous ether is obtained in crystals, often of considerable size, belonging to the right-prismatic system, and presenting a considerable number of modifications. These crystals contain two equivalents of water of crystallisation, as determined by this experiment:—

7·126 grains crystallised codeine lost, at 212°, 0·454=5·66 per cent. water.

The calculated result gives 5·67.

Codeine is an extremely powerful base, rapidly restoring the blue of reddened litmus, and precipitating oxides of lead, copper, iron, cobalt, nickel, and other metals, from their solutions. It is precipitated by potash from its salts; and is generally stated to be insoluble in that alkali, but this is true only of very highly concentrated solutions, as a considerable quantity of strong potash may be added to a saturated solution of codeine in water without producing precipitation; and even when a very large amount of potash is added, a certain quantity of the base is still retained in solution. Codeine is soluble in ammonia, but not more so than in water. 100 parts of a moderately strong solution of ammonia dissolved, at 60°, 1·46 parts of codeine; and according to Robiquet, 100 parts of water, at 59°, dissolve 1·26 parts. Contrary to what is usually stated, I have found that codeine is precipitated from all its salts by ammonia; it does not, however, fall immediately, but is slowly deposited in small transparent crystals.

II. *Salts of Codeine.*

Hydrochlorate of Codeine.—This salt is readily obtained by saturating hot dilute hydrochloric acid with pure codeine. If the solution has been sufficiently concentrated, it becomes nearly solid on cooling, but if more dilute, the salt is deposited in radiated groups of short needles, which, under the microscope, are found to be four-sided prisms terminated by dihedral summits. It is never obtained in large crystals, even when considerable quantities are crystallised. These crystals are soluble in 20 times their weight of water at 60°, and in less than their weight of water at 212°. Codeine is precipitated from the saturated cold solution immediately by potash; ammonia gives no precipitate, but after some time colourless crystals are deposited. The crystallised hydrochlorate of codeine contains water of crystallisation, and presents some curious anomalies in its relations to that fluid. When dried in the air, it retains four equivalents of water, one of which escapes at 212°, but the remaining three are only expelled at 250°, and at the same time the salt loses acid, and acquires an alkaline reaction. It would appear, also, that under certain circumstances, the salt is deposited in anhydrous crystals, as one analysis of it dried at 212°, gave numbers corresponding to the anhydrous salt. I could not, however, again succeed in obtaining it in this condition; but many analyses were made which gave results lying between those of the anhydrous and crystallised salts, and the only means of explaining the discrepancy is by supposing that the two sorts of crystals had been deposited simultaneously and in variable proportions. The following is the analysis of the salt dried at 212°:—

6·035 grains hydrochlorate of codeine gave
13·208 ... of carbonic acid,
3·830 ... of water.

	Experiment.	Calculation.		
Carbon, . .	59·68	59·58	C_{36}	216
Hydrogen, . .	7·08	6.89	H_{25}	25
Nitrogen, . .	...	3·86	N	14
Oxygen, . .	...	19·88	O_9	72
Chlorine, . .	...	9·79	Cl	35·5
		100·00		362·5

10·735 grains of the salt lost, at 212°, 0·31 grains of water=2·88 per cent. One equivalent of water gives by calculation 2·42 per cent. The formula of the air-dried salt is therefore $C_{36} H_{21} NO_6 H Cl + 4 HO$.

The anhydrous salt gave the following results. Of these, No. I. is the salt obtained by direct crystallisation from the morphia mother-liquor; No. II. is that which was got anhydrous at 212°; and No. III. is a portion dried at 250°; it had become strongly alkaline, which accounts for the excess of carbon obtained.

I. { 6·171 grains dried at 250° gave
14·565 ... carbonic acid, and
3·795 ... water.

II. { 4·286 grains dried at 212° gave
10·014 ... carbonic acid, and
2·603 ... water.

III. { 5·740 grains dried at 250° gave
13·667 ... carbonic acid, and
3·467 ... water.

	Experiment.			Calculation.		
	I.	II.	III.			
Carbon,	64·37	64·56	64·93	64·38	C_{36}	216
Hydrogen,	6·83	6·74	6·71	6·55	H_{22}	22
Nitrogen,	...	...	...	4·17	N	14
Oxygen,	...	...	...	14·32	O_6	48
Chlorine,	...	...	...	10·58	Cl	35·5
				100·00		335·5

These results correspond to the formula $C_{36} H_{21} NO_6 H Cl$.

Hydriodate of Codeine is obtained by dissolving codeine in hot hydriodic acid, and allowing the solution to cool. It is deposited in long slender needles, which fill the whole fluid, if it have been sufficiently concentrated. It is of rather sparing solubility in cold water, requiring about 60 times its weight, but is much more soluble in boiling water. Its saturated cold solution is precipitated by ammonia on standing. No difficulty was experienced in its analysis.

I. { 6·336 grains hydriodate, dried at 212°, gave
11·190 ... of carbonic acid, and
3·247 ... of water.

II. { 5·801 grains dried at 212°, gave
10·347 ... of carbonic acid, and
2·977 ... of water.

5·733 grains of hydriodate of codeine gave 2·994 grains of iodide of silver.

	Experiment.		Calculation.		
	I.	II.			
Carbon, . .	48·16	48·64	48·60	C_{36}	216
Hydrogen, .	5·69	5·70	5·40	H_{24}	24
Nitrogen, .	...	...	3·15	N	14
Oxygen, . .	...	...	14·45	O_8	64
Iodine, . .	...	28·22	28·40	I	126·36
			100·00		444·36

The formula of the salt, dried at 212°, is, therefore, $C_{36} H_{21} NO_6 HI + 2 HO$.

Sulphate of Codeine.—Crystallises in radiated groups of long needles, or by spontaneous evaporation in flattened four-sided prisms. It requires for solution 30 times its weight of cold water, but it is very soluble in the heat. When pure, it is neutral to test paper, but it is very liable to retain a small quantity of acid, which can be got rid of by repeated crystallisations. The first analysis was made with the salt which had been only once crystallised, and has therefore given an excess of sulphuric acid.

Analysis of the salt, dried at 212°, gave the following results:—

I. 5·564 grains sulphate of codeine gave
12·536 ... of carbonic acid, and
3·270 ... of water.

II. 5·677 grains of sulphate of codeine gave
12·831 ... of carbonic acid,
3·324 ... of water.

I. 9·540 grains of sulphate of codeine gave
3·265 ... of sulphate of baryta.

II. 10·826 grains of sulphate of codeine gave
3·650 ... of sulphate of baryta.

	Experiment.		Calculation.		
	I.	II.			
Carbon,	61·44	61·64	62·07	C_{36}	216
Hydrogen,	6·52	6·50	6·39	H_{22}	22
Nitrogen,	...	...	4·03	N	14
Oxygen,	...	...	16·03	O_7	48
Sulphuric Acid,	11·75	11·54	11·49	SO_3	40
			100·00		348

27·13 grains of the crystallised salt lost, at 212°, 3·068 grains of water = 11·30 per cent. This corresponds to 5 equivalents of water, the calculated result for which is 11·45.

The formula of the crystallised salt is therefore

$$C_{36} H_{21} NO_6 HO SO_3 + 5 HO.$$

Nitrate of Codeine.—Is obtained by slowly adding nitric acid, of specific gravity 1·060, to powdered codeine, an excess of nitric acid being carefully avoided, as the base is rapidly decomposed by it with the formation of a product of substitution to be afterwards described. The nitrate is readily soluble in boiling water, and is deposited on cooling in small prismatic crystals. Heated on platinum, it melts, and on cooling, concretes into a brown resinous mass; at a higher temperature it is rapidly decomposed, leaving a bulky coal, difficult of incineration.

6·360 grains of nitrate of codeine, dried at 212°, gave
13·854 ... of carbonic acid,
3·746 ... of water.

These results correspond with the formula $C_{36} H_{21} NO_6 HO NO_5$.

	Experiment.	Calculation.		
Carbon,	59·40	59·66	C_{36}	216
Hydrogen,	6·54	6·07	H_{22}	22
Nitrogen,	...	7·73	N_2	28
Oxygen,	...	26·54	O_{12}	96
		100·00		362

Phosphate of Codeine.—Several phosphates of codeine appear to exist, but I have only examined that which is obtained by saturating tribasic phosphoric acid with codeine in powder. In this way a fluid is obtained, which, when concentrated to a small bulk, refuses to crystallise, but from which crystals are immediately precipitated by the addition of strong spirit. The salt is thus obtained in small scales, or in short thick prisms. It is readily soluble in water, and cannot be obtained in crystals from the solution. Its analysis gave the following results, corresponding with the formula $C_{36} H_{21} NO_6 HO 2 HO PO_5$.

6·343 grains phosphate of codeine, dried at 212°, gave
12·618 ... of carbonic acid,
3·708 ... of water.

	Experiment.	Calculation.		
Carbon,	54·25	54·27	C_{36}	216
Hydrogen,	6·49	6·03	H_{24}	24
Nitrogen,	...	3·52	N	14
Oxygen,	...	18·09	O_9	72
Phosphoric acid,	...	18·09	PO_5	72
		100·00		398

6·911 grains of the crystallised salt lost, at 212°, 0·434 grains of water = 6·27 per cent. Three equivalents of water correspond to 6·35 per cent.; and the formula of the crystallised salt is, consequently, $C_{36} H_{21} NO_6 HO 2 HO PO + 3 HO$.

Oxalate of Codeine.—This salt is deposited, on cooling its saturated hot solution, in short prisms, and sometimes in scales. It requires 30 times its weight of water at 60° for solution, and about half its weight at 212°. Heated to 212° it loses water of crystallisation; at 250° it becomes brown, and at a higher temperature it is entirely decomposed.

6·073 grains oxalate of codeine, dried at 212°, gave
14·739 ... of carbonic acid,
3·608 ... of water.

	Experiment.	Calculation.		
Carbon,	66·19	66·28	C_{38}	228
Hydrogen,	6·60	6·39	H_{22}	22
Nitrogen,	...	4·07	N	14
Oxygen,	...	23·26	O_{10}	80
		100·00		344

10·050 grains of the crystallised oxalate lost, at 212°, 0·704 grains of water = 7·00 per cent., corresponding to three equivalents of water, which requires 7·27 per cent. The formula of the crystallised salt is, therefore, $C_{36} H_{21} NO_6 HO C_2 O_3 + 3 HO$.

Hydrosulphocyanate of Codeine.—This salt has been already examined by Dollfus;[*] but I have prepared it, and repeated the analysis, with results differing somewhat from those obtained by him. It is readily obtained by mixing solutions of hydrochlorate of codeine and of sulphocyanide of potassium, and is slowly deposited in beautiful radiated needles.

6·164 grains of hydrosulphocyanate, dried at 212°, gave
14·285 ... carbonic acid, and
3·543 ... water.

7·444 grains, burnt with nitre and carbonate of soda, gave 4·899 grains of sulphate of baryta.

These results correspond with the formula $C_{36} H_{21} NO_6 H C_2N S_2$, as is shewn by the following per centage calculation, to which I have added the results obtained by Dollfus:—

	Experiment.		Calculation.		
	Dollfus.				
Carbon, . . .	62·30	63·20	63·68	C_{38}	228
Hydrogen, . . .	6·13	6·38	6·14	H_{22}	22
Nitrogen, . . .	...	...	7·82	N_2	28
Oxygen, . . .	...	...	13·43	O_6	48
Sulphur, . . .	...	9·04	8·93	S_2	32
			100·00		358

11·613 grains of the crystallised salt, dried at 212°, lost 0·288 grains of water = 2·47 per cent., corresponding to one equivalent of water, the calculation of which gives 2·45 per cent.

In the analysis of Dollfus, there is manifestly a loss of carbon, as the results are quite incompatible with those of the base and its other salts. In the same paper Dollfus has also determined the amount of sulphocyanogen by precipitation with silver, and the results obtained agree better with the formula given above than with his own.

Chloride of Platinum and Codeine.—When bichloride of platinum is added to a moderately concentrated solution of hydrochlorate of codeine, a pale-yellow, pulverulent precipitate is deposited. If this be allowed to stand for some time in the solution, or still better, if it be collected on a filter and kept moist, it begins to change in its appearance; specks of darker colour appear in it, and it is gradually converted into a mass of crystalline grains of an orange-yellow colour. The fluid which filters off deposits, on standing, a small quantity of larger grains.

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[*] Annalen der Chimie und Pharmacie, vol. lxv., p. 218.

The change which takes place in this manner is not always complete, and the granular crystals are often mixed with unchanged yellow powder. When the chloride of platinum is added to a more dilute solution of hydrochlorate of codeine, precipitation does not take place immediately, but in a short time the salt is deposited in minute tufts of silky needles. The salt is soluble in boiling water, and is deposited on cooling partly in grains, partly as a powder. By this process, however, it is partially changed; and I have ascertained that by ebullition, with excess of chloride of platinum, it is completely decomposed. I have not as yet, however, followed up this observation. I at first attempted to purify the salt by solution in water and alcohol, in which it is also soluble; and a number of analyses were made, which gave extremely contradictory results; but by precipitation in the cold, and without excess of platinum, sufficiently uniform results were obtained.

When dried at 212°, the salt retains an equivalent of water, which is expelled at 250°, but not without occasioning partial decomposition of the substance, which evolves acid, and acquires a brownish colour. The following are the results of analysis:—

I. { 7·240 grains of platinum salt, dried at 212°, gave
11·072 ... of carbonic acid, and
2·925 ... water.

II. { 9·394 grains of platinum salt gave
14·593 ... of carbonic acid, and
3·912 ... of water.

III. { 7·648 grains of platinum salt gave
11·694 ... of carbonic acid, and
3·450 ... of water.

IV. { 6·665 grains of platinum salt gave
10·230 ... of carbonic acid, and
2·835 ... of water.

V. { 7·383 grains of platinum salt gave
11·372 ... of carbonic acid, and
3·304 ... of water.

7·247	grains platinum salt gave	1·400	grains platinum,	=19·31	per cent.
10·030	... ...	1·920	...	=19·14	...
9·775	... ...	1·850	...	=18·92	...
10·471	... ...	2·020	...	=19·32	...
8·428	... ...	1·600	...	=18·98	...
6·790	... ...	1·296	...	=19·08	...
5·052	... ...	0·960	...	=19·00	...

	I.	II.	III.	IV.	V.	VI.	VII.
Carbon, .	41·70	42·36	41·70	41·80	42·00	...	...
Hydrogen, .	4·49	4·62	5·01	4·72	4·97	...	...
Nitrogen, .	...	...	...	...	...	...	...
Oxygen, .	...	...	...	...	...	...	...
Chlorine, .	...	...	...	...	...	...	...
Platinum, .	19·31	19·14	18·92	19·32	18·98	19·08	19·00

These analyses correspond with the formula

$$C_{36}\,H_{21}\,NO_6\,HCl+Pt\,Cl_2+HO.$$

of which the following is the calculated result compared with the mean of experiment:—

	Mean.	Calculation.		
Carbon,	41·91	42·07	C_{36}	216·
Hydrogen,	4·76	4·47	H_{23}	23·
Nitrogen,	...	2·72	N	14·
Oxygen,	...	10·94	O_7	56·
Chlorine,	...	20·61	Cl_3	106·5
Platinum,	19·25	19·19	Pt	98·7
		100·00		514·2

The air-dried salt gave the following results, when dried at 212°:—

14·845 grains lost 0·770 grains of water, =5·11 per cent.
14·546 ... 0·758 ... =5·20 ...

This corresponds to three equivalents of water, the calculated result for which gives 4·99 per cent. The crystallised salt is therefore represented by the formula

$$C_{36}\,H_{21}\,NO_6\,HCl+Pt\,Cl_2+4\,HO.$$

Codeine forms many other crystallisable salts, none of which, however, have been examined. The chromate is easily obtained in fine yellow needles. With solution of bichloride of mercury, codeine gives a white precipitate, soluble in boiling water and alcohol, and deposited on cooling in stellated groups of crystals. With chloride of palladium a yellow precipitate is obtained, which is decomposed by boiling, with separation of metallic palladium. Tartrate and hydrocyanate of codeine are uncrystallisable.

PRODUCTS OF DECOMPOSITION OF CODEINE.

III. *Action of Sulphuric Acid.*

Amorphous Codeine.—When codeine is dissolved in an excess of moderately-concentrated sulphuric acid, and the mixture digested on the sand-bath, the fluid gradually acquires a dark colour, and after some time gives a precipitate with carbonate of soda, which the salts of codeine are incapable of doing. The precipitate so obtained is codeine in a modified or amorphous condition, similar to that in which quinine is obtained by a similar treatment with excess of acid. By carefully regulating the temperature of the mixture of codeine and sulphuric acid, the amorphous codeine may be obtained in a state of purity; but it is neither so definite nor so stable a substance as quinoidine. After the action has been prolonged for some time, carbonate of soda is added to the fluid, and the gray precipitate obtained, collected on a filter, washed with water, dissolved in alcohol, and precipitated from the solution by means of water. As thus obtained, it is a gray powder, with a more or less green shade, insoluble in water, readily soluble in alcohol, and precipitated by ether from the solution. It fuses at 212° into a black resinous mass. In acids it is readily soluble, with the formation of salts which are amorphous, and dry up by evaporation into brown resins.

Analysis gave the following results:—

I. 5·400 grains amorphous codeine gave
14·240 ... of carbonic acid, and
3·663 ... of water.

II. 4·532 grains amorphous codeine gave
12·054 ... of carbonic acid, and
2·781 ... of water

	Experiment.		Calculation.
	I.	II.	
Carbon, ...	71·92	72·53	72·24
Hydrogen, ...	7·53	6·84	7·02
Nitrogen, ...	...	...	6·68
Oxygen, ...	...	...	16·06
			100·00

These results correspond sufficiently closely with those of codeine to shew that this substance is represented by the same formula. At the same time it is to be observed, that the action does not stop at the point at which amorphous codeine is formed; for the excess of carbon and deficiency of hydrogen in the second analysis (which occurred also in another analysis from a different preparation), appear to me to shew that some farther change had taken place. Indeed, by continuing the action of sulphuric acid, a deep-green powder was obtained, which contained sulphur, and agreed in its general properties with the sulphomorphide described by ARPPE, and the corresponding sulphonarcotide of LAURENT and GERHARDT.

IV. *Action of Nitric Acid.*

Nitrocodeine.—When strong nitric acid is poured upon codeine, and heat applied, violent action takes place, nitrous fumes are abundantly evolved, and the solution acquires a red colour. If the fluid be evaporated on the water-bath, a yellow resinous acid is left, which dissolves in ammonia and potash solutions, with a red colour.* If the nitric acid be employed in a sufficiently dilute state, a different result is obtained, and a nitrobase is formed, to which I give the name of nitrocodeine.

The preparation of this substance is a matter of some nicety, as by the continued action even of very dilute nitric acid it is rapidly destroyed. The operation succeeds best when the acid employed is of a specific gravity of 1·060. Acid of this density is heated in a flask, but not to ebullition, and finely-powdered codeine is added, and a moderate heat is sustained. In the course of a few minutes a small quantity of the fluid is poured out into a glass, and an excess of ammonia

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* The constitution and properties of this substance will be detailed in a future communication.

added; if no precipitate appears, the heat is kept up for a short time longer, and another quantity is then taken out and tested; and this is repeated until the precipitate, which makes its appearance when the acid is neutralised, ceases to increase. The fluid is then immediately saturated with ammonia, and stirred rapidly, when it becomes filled with a bulky precipitate of nitrocodeine. The action which takes place is extremely rapid, and the whole operation is complete in a few minutes; so that the experimenter requires to be carefully on the watch, in order to hit the right moment for precipitating the fluid. No red fumes are evolved; if they are seen, it is a sure sign that the action has gone too far, and that part of the codeine has been converted into the resinous acid already mentioned. On this account it is better to stop the action before the whole of the codeine is decomposed, the quantity left being easily recovered from the solution; but even with the greatest possible care, the formation of a small quantity of the resinous acid cannot be avoided, and its presence is always indicated by the dark colour which the fluid acquires when saturated by ammonia.

On the addition of ammonia, the nitrocodeine falls in the form of minute silvery plates, with a very slight shade of yellow. It is purified by solution in hydrochloric acid, boiling with animal charcoal and a reprecipitation with ammonia, in order to separate colouring matter and any unchanged codeine which may have been precipitated along with the first crystals. The nitrocodeine is then crystallised by dissolving in dilute alcohol, or a mixture of alcohol and ether.

Nitrocodeine crystallised from alcohol is deposited in the form of slender silky needles of a pale fawn-colour, which, on drying, mat together into a silky mass. From alcohol and ether it is obtained by spontaneous evaporation in small yellowish crystals, which, under the microscope, are seen to be four-sided prisms, terminated by dihedral summits. Nitrocodeine is sparingly soluble in boiling water, from which it is deposited in minute crystals on cooling. It dissolves abundantly in boiling alcohol, and but sparingly in ether. It is soluble in acids, with the formation of salts which are neutral to test-paper, and from which potash and ammonia precipitate the base as a crystalline powder. When heated carefully, it melts into a yellow fluid, which concretes on cooling into a highly-crystalline mass. At a higher temperature, it suddenly decomposes without flame, leaving a bulky charcoal.

Its analysis yielded the following results, of which No. 1 is from the base crystallised from the first precipitate by ammonia, before I had observed its tendency to carry down codeine with it, and which has therefore given a slight excess; the others are from the pure base. Crystallised nitrocodeine is anhydrous.

I. 5·748 grains of nitrocodeine, dried at 212°, gave
13·301 ... of carbonic acid, and
3·128 ... of water.

II. 5·523 ... of nitrocodeine gave
12·724 ... of carbonic acid, and
2·887 ... water.

III. 4·463 grains of nitrocodeine gave
10·226 ... of carbonic acid, and
2·377 ... of water.

	Experiment.			Calculation.		
	I.	II.	III.			
Carbon,	63·10	62·83	62·49	62·79	C_{36}	216
Hydrogen,	6·04	5·80	5·91	5·81	H_{20}	20
Nitrogen,	...	...	...	8·11	N_2	28
Oxygen,	...	...	...	23·29	O_{10}	80
				100·00		344

These results correspond with the formula $C_{36}H_{20}(NO_4)NO_6$, derived from that of codeine by the substitution of NO_4 in place of an equivalent of hydrogen. It is confirmed by the analysis of its platinum salt, which was found to contain 17·88 per cent. of platinum, giving for the atomic weight of the base 345·8: the calculated atomic weight is 344.

Hydrochlorate of Nitrocodeine.—Nitrocodeine dissolves readily in hydrochloric acid, and the solution on evaporation leaves the hydrochlorate in the form of a resinous mass, which cannot be made to crystallise.

Sulphate of Nitrocodeine is obtained in a radiated group of short-pointed needles, which are neutral to test-paper, and very soluble in boiling water.

4·687 grains of the sulphate, dried at 212°, gave 1·383 sulphate of baryta.

This corresponds to the formula $C_{36}H_{20}(NO_4)NO_6\,HO\,SO_3$, which requires

	Experiment.	Calculation.		
Nitrocodeine,	...	...	...	344
Water,	...	...	...	9
Sulphuric acid,	10·13	10·17	...	40
				393

Oxalate of Nitrocodeine.—Crystallises in beautiful yellow short prisms, readily soluble in water.

Platinochloride of Nitrocodeine.—This salt is precipitated from the solution of the hydrochlorate as a yellow powder, insoluble in water and alcohol. Its analysis gave the following results:—

8·113 grains of platinochloride of nitrocodeine, dried at 212°, gave
11·635 ... of carbonic acid, and
2.987 ... of water.

9·392 grains, dried at 212°, gave 1·68 grains platinum.

	Experiment.	Calculation.		
Carbon,	39·11	39·25	C_{36}	215
Hydrogen,	4·09	3·81	H_{21}	21
Nitrogen,	...	5·08	N_2	28
Oxygen,	...	14·58	O_{10}	80
Chlorine,	...	19·35	Cl_3	106·5
Platinum,	17·88	17·93	Pt	98·7
		100·00		550·2

8·670 grains of the precipitated salt, dried by long exposure to the air, lost, at 212°, 0·569 grains of water = 6·56 per cent.

Four equivalents of water require 6·14 per cent. The formula of the salt is, therefore, $C_{36}H_{20}(NO_4)NO_6HCl + PtCl_2 + 4HO$.

When nitrocodeine dissolved in alcohol is treated with hydrosulphuret of ammonia in the water-bath, the solution gradually acquires a dark colour, and sulphur is deposited. When the action is complete, the filtered fluid gives with ammonia a brown amorphous precipitate, which, when dissolved in hydrochloric acid, and boiled with animal charcoal, gives, on precipitation, a pale-yellow base. The substance so obtained is very different from nitrocodeine; it is extremely soluble in alcohol, and is deposited from it as an amorphous powder. Once only did I obtain definite crystals, which were brownish rhomboids, but in too small quantity to admit of examination. The amorphous base did not give satisfactory results; and as its preparation is extremely troublesome, I did not pursue its investigation further. Arguing from what we know of the other bases formed by the same process, its constitution ought to be $C_{36}H_{22}N_2O_6$, and it might be called azocodeine.

V. *Action of Bromine on Codeine.*

Bromocodeine.—In order to obtain this substance, bromine-water is added in small successive portions to finely-powdered codeine. The base is rapidly dissolved, and the solution loses its colour of bromine, but acquires a peculiar and characteristic red shade. After a certain quantity of bromine has been added, small crystals make their appearance, which are hydrobromate of bromocodeine; but these are only observed if the bromine-water has been thoroughly saturated, and are deposited in small quantity only, the remainder being retained in solution. When the whole of the codeine has been got into solution, ammonia is added, and bromocodeine is immediately thrown down as a silvery-white powder. In this state it contains a small quantity of unchanged codeine. It is collected on a filter; washed several times with cold water, and redissolved in hydrochloric acid, from which it is reprecipitated by ammonia, and finally crystallised from boiling spirit. Bromocodeine is scarcely soluble in cold water; but by boiling, a somewhat larger quantity is taken up, and deposited again on cooling in minute prisms, terminated by dihedral summits. It is readily soluble in alcohol, particularly on boiling, and is best crystallised from spirit diluted with its bulk of water. The crystals in which it is deposited are always very small, but brilliantly white. It is scarcely soluble in ether. Exposed to heat, it melts into a colourless fluid, which is destroyed at a temperature slightly above its melting point. It dissolves in cold sulphuric acid, and the solution when heated becomes dark coloured. It is attacked by nitric acid, but much less rapidly than codeine itself.

Considerable difficulty was experienced in getting it absolutely free from codeine; and the first of the following analyses has given an excess in the carbon:—

I. 6·119 grains bromocodeine, dried at 212°, gave
12·941 ... of carbonic acid, and
3·000 ... of water.

II. 5·940 grains bromocodeine gave
12·461 ... of carbonic acid, and
2·910 ... of water.

5·268 grains gave 2·663 grains of bromide of silver.

	Experiment.		Calculation.		
	I.	II.			
Carbon, . . .	57·67	57·21	57·14	C_{36}	216
Hydrogen, . . .	5·44	5·44	5·29	H_{20}	20
Bromine, . . .	...	21·50	21·16	Br	80
Nitrogen, . . .	...	...	3·70	N	14
Oxygen, . . .	...	...	12·71	O_6	48
			100·00		378

The formula is therefore $C_{36} H_{20} Br NO_6$. Bromocodeine is capable of uniting with water in two different proportions, as appears by the determination of the loss by drying.

11·784	crystallised bromocodeine, lost at 212°	0·273,	=2·32 per cent.
9·308	... ...	0·623,	=6·69 ...
7·707	... ...	0·512,	=6·64 ...

The first of these results corresponds exactly to one equivalent of water, the calculated result for which gives 2·32 per cent. The other two give three equivalents, for which the calculation is 6·66. I am unable now to recollect how the bromocodeine used in the first experiment was obtained, but my impression is, that it was prepared in exactly the same manner as the rest.

Hydrochlorate of Bromocodeine is obtained in radiated needles closely resembling those of hydrochlorate of codeine.

Hydrobromate of Bromocodeine.—The crystals, which have been mentioned as making their appearance during the preparation of bromocodeine, are this salt. It is sparingly soluble in cold water, readily soluble in boiling water, and is deposited from the solution in small prismatic crystals. It contains two equivalents of water which are not expelled at 212°.

8·424 grains of hydrobromate, dried at 212°, gave
13·956 ... of carbonic acid, and
3·985 ... of water.

	Experiment.	Calculation.		
Carbon, ...	45·18	45·28	C_{36}	216
Hydrogen, ...	5·25	4·84	H_{23}	23
Bromine, ...	...	33·54	Br_2	160
Nitrogen, ...	...	2·93	N	14
Oxygen, ...	...	13·41	O_8	64
		100·00		477

The formula of the salt is therefore $C_{36}H_{20}BrNO_6HBr+2HO$.

Platinochloride of Bromocodeine is precipitated as a pale-yellow powder, insoluble in water and alcohol.

8·126 grains, dried at 212°, gave 1·380 grains platinum.

	Experiment.	Calculation.		
Carbon, ...	...	36·97	C_{36}	216
Hydrogen, ...	...	3·59	H_{20}	20
Bromine, ...	...	13·70	Br	80
Nitrogen, ...	...	2·39	N	14
Oxygen, ...	...	5·23	O_6	48
Chlorine, ...	...	18·23	Cl	106·5
Platinum, ...	16·98	16·89	Pt	98·7
		100·00		584·2

Tribromocodeine.—By continuing the addition of bromine water beyond the point at which bromocodeine is formed, a further action takes place, and a bright-yellow precipitate makes its appearance, which at first redissolves in the fluid, but after a time becomes permanent, and goes on gradually increasing until a very large quantity of bromine has been employed, when at length a point is reached at which no further precipitate is produced. If the solution be left till next day, however, bromine again causes a precipitate; and if it be added, as long as anything falls, and the solution be again left standing, another precipitate is produced identical in all respects with that before obtained, and this may be repeated day after day for a very considerable time. The yellow precipitate so obtained is the hydrobromate of tribromocodeine. It is collected on a filter, and washed with water, in which it is very sparingly soluble. In order to obtain the base, this substance is dissolved in dilute hydrochloric acid and ammonia added, when the tribromocodeine is immediately precipitated as a flocky powder, which is washed with water, and purified by solution in alcohol, and precipitation with water.

Tribromocodeine is thus obtained as a bulky white precipitate, perfectly amorphous, and when dry, more or less gray in its colour. It is insoluble in water and ether, but readily soluble in alcohol. It is sparingly soluble in hydrochloric acid in the cold, but much more so by boiling. In this process, however, it appears to undergo a partial decomposition, as a small quantity is always left insoluble. Heated on platinum foil it becomes brown, and is entirely decomposed at its melting point, leaving a coal difficult of incineration.

The tribromocodeine employed for analysis was purified by a second solution in alcohol, and precipitation by ether. It gave the following results:—

$$\begin{cases} \text{8·014 grains of tribromocodeine, dried at 212°, gave} \\ \text{11·665 ... of carbonic acid, and} \\ \text{2·645 ... of water.} \end{cases}$$

3·55 grains of tribromocodeine gave 3·727 grains bromide of silver.

	Experiment.	Calculation.		
Carbon, ...	39·69	40·27	C_{36}	216
Hydrogen, ...	3·66	3·35	H_{18}	18
Bromine, ...	44·68	44·72	B_3	240
Nitrogen, ...	...	2·61	N	14
Oxygen, ...	...	9·00	O_6	48
		100·00		536

These results agree sufficiently well with the formula $C_{36} H_{18} Br_3 O_6$ produced by the substitution of three equivalents of bromine; and this formula has been confirmed by the analysis of its platinum salt, which will be given below.

In such cases as have been hitherto examined, the substitution of three equivalents of bromine in a base, has entirely destroyed its basic properties, but tribromocodeine is still a base, though an extremely feeble one. Its salts are all sparingly soluble in water and amorphous; and as there is no possibility of ascertaining their purity, I have not pursued their investigation to any extent.

Hydrochlorate of Tribromocodeine.—It is obtained by dissolving the base in hot dilute hydrochloric acid, and is deposited on cooling as an amorphous powder.

Hydrobromate of Tribromocodeine.—This is the substance deposited during the preparation of tribromocodeine. It is a bright-yellow powder, perfectly amorphous, and very sparingly soluble in cold water. On boiling, however, a larger quantity is taken up, and deposited unchanged on cooling.

Its analysis gave the following results:—

I. 7·501 grains hydrobromate, dried at 212°, gave
8·868 ... of carbonic acid, and
1·915 ... of water.

II. 6·840 grains hydrobromate, from another preparation, gave
8·072 ... of carbonic acid, and
1·767 ... of water.

3·762 grains hydrobromate gave 4·865 grains bromide of silver.

	Experiment.		Calculation.		
	I.	II.			
Carbon, . .	32·24	32·18	32·84	C_{72}	432
Hydrogen, . .	2·83	2·86	2·96	H_{39}	39
Bromine, . .	...	55·03	54·75	Br_9	720
Nitrogen, . .	...	...	2·12	N_2	28
Oxygen, . .	...	...	7·33	O_{12}	96
			100·00		1315

These results approach most nearly to the formula:—

$$2\ (C_{36}\ H_{18}\ Br_3\ N\ O_6) + 3\ H\ Br.$$

They present, however, a certain deficiency, both in the carbon and hydrogen, and an excess in the bromine; but no other formula can be found at all approximating to the experimental numbers, and the recurrence of the results, in portions prepared at different times, leaves no doubt that this is their real constitution; and, in all probability, the error may be due to the salt retaining a small excess of hydrobromic acid. The constitution is therefore remarkable, and I am not aware of any similar salt having been before observed.

Platinochloride of Tribromocodeine.—Bichloride of platinum throws down from solution of tribromocodeine, in hydrochloric acid, this salt, in the form of a brownish-yellow powder soluble in water and alcohol.

5·142 grains of platinum salt, dried at 212°, gave 0·669 grains of platinum.

	Experiment.	Calculation.		
Carbon, . .	...	29·10	C_{36}	216
Hydrogen, . .	...	2·55	H_{19}	19
Bromine, . .	...	32·33	Br_3	240
Nitrogen, . .	...	1·88	N	14
Oxygen, . .	...	6·57	O_3	48
Chlorine, . .	...	14·34	Cl_3	106·5
Platinum, .	13·07	13·29	Pt	98·7
		100·00		742·2

I have reason to believe that the action of bromine upon codeine does not terminate with the production of the base now described; but its further action did not appear to afford any products of a sufficient interest to induce me to prosecute the investigation in this direction. There must also no doubt exist a *dibromocodeine*, $C_{36}\,H_{19}\,Br_2\,N\,O_6$, but I did not meet with it in the course of my experiments, and have not made any special attempts to obtain it.

VI. *Action of Chlorine upon Codeine.*

We might anticipate that the action of chlorine upon codeine should be exactly similar to that of bromine; but this is not the case, as in place of a simple and definite action complex products are immediately obtained. When a current of chlorine is passed through an aqueous solution of codeine, the fluid immediately acquires a brown colour, which soon becomes very deep, and eventually almost black. From this solution ammonia throws down an amorphous, resinous base. With chlorine-water the solution also becomes rapidly brown, and a similar precipitate is obtained. As there was no method of determining in either of these cases when the action was complete, I did not attempt to examine the product. I succeeded better, however, by the action of chlorate of potash, and obtained a base corresponding to bromocodeine.

Chlorocodeine.—For the preparation of chlorocodeine a sufficient quantity of codeine is dissolved in an excess of dilute hydrochloric acid, at the temperature of about 150° or 160°. Finely-powdered chlorate of potash is then added, and the solution agitated. In the course of a few minutes a small quantity of the fluid is tested with ammonia, in order to see whether a precipitate is formed; and the action is allowed to go on until this is obtained, and the chlorocodeine is then precipitated by a slight excess of ammonia. The successful performance of this experiment requires exactly the same precautions as the preparation of nitrocodeïne; and, unless the action is stopped at the right moment, further products of decomposition are obtained. The reaction which takes place is represented by this equation:—

$$3\,(C_{36}\,H_{21}\,NO_{36}\,H\,Cl) + 3\,H\,Cl + KO\,Cl\,O_5 = K\,Cl + 6\,HO + 3\,(C_{36}\,H_{20}\,Cl\,NO_6\,H\,Cl).$$

The chlorocodeine is precipitated in the form of a silvery crystalline powder, closely resembling bromocodeine; it has generally a yellowish colour, and the fluid from which it has deposited is coloured dark-red by the presence of a small quantity of some products of the further action of chlorine. It retains also a small quantity of codeine, from which it is purified by dissolving in hydrochloric acid, boiling with animal charcoal, and reprecipitating with ammonia; and it is finally obtained in crystals from its solution in boiling spirit.

In its general properties chlorocodeine closely resembles bromocodeine; so much so, indeed, that they may be easily confounded with one another. It is sparingly soluble in boiling water, and deposited, on cooling, in minute prisms exactly similar to, and apparently isomorphous with, those of bromocodeine. It is readily soluble in strong alcohol, especially with heat, and sparingly soluble in ether. It dissolves in sulphuric acid in the cold without change, but the solution is charred by heating. Nitric acid dissolves it, and the solution is decomposed by boiling, but not by any means so readily as codeine. Red fumes are evolved along with a peculiar and excessively pungent vapour.

Analysis gave the following results:—

I. { 6·425 grains of chlorocodeine, dried at 212°, gave
15·315 ... of carbonic acid, and
3·601 ... of water.

II. { 6·162 grains of chlorocodeine gave
14·597 ... of carbonic acid, and
3·372 ... of water.

5·030 grains of chlorocodeine gave 2·100 grains chloride of silver.

	Experiment.		Calculation.		
	I.	II.			
Carbon, . . .	65·00	64·62	64·76	C_{36}	216
Hydrogen, . .	6·22	6·08	5·99	H_{20}	20
Chlorine, . .	...	10·32	10·64	Cl	35·5
Nitrogen, . .	...	...	4·19	N	14
Oxygen, . .	...	...	14·42	O_6	48
			100·00		333·5

The crystallised base contains water which is expelled at 212°.

7·67 grains chlorocodeine lost 0·551 grains water, =7·18 per cent.
9·82 ... ... 0·740 ... =7·53 ...

The calculated number for three equivalents of water is 7·48 per cent.: and the formula of the crystallised base is therefore $C_{36} H_{20} Cl NO_6 + 3 HO$.

The salts of chlorocodeine are exactly similar in their properties to those of bromocodeine; so much so, that I have not thought it necessary to examine more than one or two of them.

Hydrochlorate of Chlorodeine.—Crystallises in groups of needles, readily soluble in water.

Sulphate of Chlorocodeine is deposited from its hot solution in radiated groups of short prisms, which dissolve abundantly in boiling water and alcohol.

10·874 grains of the crystallised salt, dried at 212°, gave 0·953 grains of water, and 3·078 grains of sulphate of baryta.

	Experiment.	Calculation.		
Chlorocodeine,	79·34	79·63	Base.	333·5
Sulphuric acid,	11·90	11·75	$HOSO_3$	49·0
Water,	8·76	8·662	4 HO	36·0
	100·00	100·00		418·5

Platinochloride of Chlorocodeine is obtained in the usual way, as a pale-yellow precipitate scarcely soluble in water. Its analysis gave the following results:—

7·212 grains platinochloride, dried at 212°, gave
10·658 ... of carbonic acid, and
2·655 ... of water.

8·793 grains platinochloride gave 1·608 grains platinum.

	Experiment.	Calculation.		
Carbon,	40·30	40·02	C_{36}	216
Hydrogen,	4·09	3·89	H_{21}	21
Nitrogen,	...	2·59	N	14
Oxygen,	...	8·91	O_6	48
Chlorine,	...	26·31	Cl_4	142
Platinum,	18·29	18·28	Pt	98·7
	100·00			539·7

VII. *Action of Cyanogen on Codeine.*

Dicyanocodeine.—When a current of cyanogen is passed into a solution of codeine in the smallest possible quantity of alcohol, the gas is rapidly absorbed, and the fluid acquires, first a yellow, and, by continued action, a brown colour. If the solution be then left to itself for some time, the smell of cyanogen disappears, and is replaced by that of hydrocyanic acid, and crystals are gradually deposited. In order to obtain the new compound in sufficient quantity, it is best to keep up a continuous slow current of cyanogen, by which means crystals are deposited during the action in considerable abundance. These are collected on a filter, and washed with a small quantity of alcohol; and the filtrate, on being again exposed to the action of cyanogen, yields an additional quantity of crystals inferior in purity to those obtained in the first part of the operation. The product is purified by solution with the aid of heat, in a mixture of alcohol and ether, from which it is deposited in crystals, which are colourless, or slightly yellow. Obtained in this way, however, they are apt to retain a small quantity of codeine; and it is, therefore, advantageous to pass cyanogen into the mixture to be used for their solution, by which means the last traces of codeine are converted into the new compound.

The substance so obtained is a new base, to which I give the name of Dicyanocodeine. It is soluble in boiling absolute alcohol, or a mixture of alcohol and ether, and is deposited on cooling in thin six-sided plates, with a brilliant lustre. It is difficultly soluble in water, but on the addition of alcohol it is dissolved; nothing, however, is deposited from the solution on standing, and by evaporation it is decomposed, and crystals of codeine are left behind. With hydrochloric acid, it is converted into a crystalline salt, but decomposition takes place immediately; for on the addition of potash to the fluid, ammonia escapes, and if it be left for four-and-twenty hours, hydrocyanic acid is evolved. With sulphuric and oxalic acid, it likewise gives somewhat sparingly soluble compounds, which decompose rapidly with the evolution of ammonia and hydrocyanic acid. The crystals deposited from alcohol and ether are anhydrous. Their analysis gave the following results :—

I. { 4·552 grains, dried in vacuo, gave
11·388 ... of carbonic acid, and
2·431 ... of water.

II. { 4·325 grains, dried in vacuo, gave
10·790 ... of carbonic acid, and
2·405 ... of water.

4·954 grains gave by Warrentrap and Will's method 9·320 grains of platinochloride of ammonium.

5·310 grains gave by the same method 9·890 grains of platinochloride.

	Experiment.		Calculation.		
Carbon, . .	68·22	68·04	68·37	C_{40}	240
Hydrogen, . .	5·93	6·17	5·97	H_{21}	21
Nitrogen, . .	11·81	11·50	11·68	N_3	42
Oxygen, . .	14·04	14·27	13·97	O_6	48
	100·00	100·00	100·00		351

These results correspond exactly with the formula $C_{40} H_{21} N_3 O_6$. The method of its formation, however, indicates unequivocally, that its rational formula must be $C_{36} H_{21} NO_6 2 C_2 N$, representing it as formed by two equivalents of cyanogen coupled with one of codeine, and belonging to the same class of compounds as cyaniline. It differs, however, from that substance, in containing two equivalents of cyanogen; and owing to this circumstance, I was at first inclined to take a different view of its constitution, and to consider it as the hydrocyanate of a cyanocodeine formed by substitution, and represented by the formula $C_{36} H_{20} Cy NO_6 + H Cy$, according to which its formation could obviously be equally well explained, and I considered the evolution of hydrocyanic acid, by treating it with acids, as favourable to this view. Attentive observation, however, convinced me, that though hydrocyanic acid always is produced by heating it with strong acids, it is never evolved immediately, as it necessarily must be, if it existed as such; but that it only makes its appearance after the lapse of some time, and that only as the result of an advanced decomposition; for long before it is observed, the addition of potash to the acid solution causes an abundant evolution of ammonia.

The ease with which dicyanocodeine is decomposed has prevented my examining any of its compounds. I attempted to prepare a platinum salt by rapid solution in hydrochloric acid, and precipitation by bichloride of platinum; but the instant the latter substance was added, evolution of hydrocyanic acid was observed, and the results obtained were, as might be expected, wholly incongruous and unsatisfactory. The decompositions of dicyanocodeine evidently afford several different substances; but I have not attempted to follow them out, as their investigation seemed to present some difficulties, among which, not the least was that of obtaining the base itself in sufficient quantity.

VIII. *Action of Alkalies on Codeine.*

Codeine, when treated at moderate temperatures with potash, yields more than one volatile base, according to the circumstances in which the experiment is made. I have found that similar results are obtained by the use of hydrate of potash, or of potash-lime, or soda-lime prepared in the usual way. The method employed in the experiment was to mix codeine with four or five times its weight of potash-lime or soda-lime, and introduce the mixture into a retort with a tubulated receiver, having a doubly-bent tube attached to its tubulature, the end of which passed into a small flask containing hydrochloric acid, in order to retain any of the very volatile base which might not be condensed in the receiver. The retort was introduced into an oil-bath, and kept at a uniform temperature of 250° Fahr. As soon as this temperature is reached, a slight peculiar odour is observed, which soon becomes more powerful, and a small quantity of water, retaining the bases in solution, collects in the receiver. The decomposition at 250°, however, is excessively slow, and even after many days, bases are evolved apparently in undiminished quantity, but I retained the mixture steadily at this point, in hopes of obtaining the product free from ammonia, which my preliminary trials had shewn to be produced at higher temperatures; but I found that even with this low heat it was evolved always in appreciable, and, in some experiments, even in considerable quantity. I therefore gradually raised the temperature to about 350°, when a larger quantity of base was obtained; and after the heat had been sustained for some time, small crystals made their appearance, which deposited themselves in a line round the retort, just above the level of the oil in the bath, but which soon rose into and collected in the neck of the retort.

These crystals resemble benzoic acid in their external appearance, and are at first perfectly colourless, but soon acquire a brownish shade by exposure to light and air. They are a base, and rapidly restore the colour of reddened litmus. They are sparingly soluble in water, but readily in acids, and give a precipitate with bichloride of platinum. The quantity of this substance obtained was excessively minute; and though considerable quantities of codeine were operated upon, all that was obtained served only to make the few qualitative experiments now detailed.

The watery fluid which collected in the receiver possessed a pungent and peculiar smell; it restored the colour of reddened litmus with great rapidity, and gave abundant fumes with hydrochloric acid. On the addition of solid potash, a highly volatile and pungent oily base collected as a layer on the surface of the fluid, and at the same time a gaseous base escaped along with ammonia. From the small quantity of these substances which I was able to obtain, I could not attempt to prepare either of them in a pure state. I was therefore under the necessity of determining their constitution by the analysis of their platinum salts, which can be separated from one another, though not without difficulty. In order to prepare these salts, the basic fluid was saturated with hydrochloric acid, and evaporated to dryness in the water-bath, when it left behind a beautifully crystalline mass, highly soluble in water, and deliquescent in moist air. This was dissolved in absolute alcohol, to separate ammonia, and the filtered solution mixed with an alcoholic solution of bichloride of platinum, when the platinum salts were immediately thrown down as a pale-yellow powder, very sparingly soluble in absolute alcohol, but readily dissolved on the addition of water. The separation of the two bases is best effected by heating the washed precipitate with boiling absolute alcohol, and adding water in small quantities until the whole is dissolved. The crystals which deposit on cooling are one of the salts in a state of purity, if the process have been properly managed, or, at all events, only require a repetition of the process to make them absolutely pure. The salt thus obtained is scarcely soluble in absolute alcohol or ether, but is readily soluble in water and dilute spirit, and is thrown down from the latter solution by ether in the form of fine yellow scales. Its analysis gave the following results:—

8·723 grains, dried at 212°, gave
1·753 ... of carbonic acid, and
2·090 ... of water.

9·880 grains, dried at 212°, gave 4·100 grains of platinum.
7·734 ... ... 3·196 ... ...

	Experiment.		Calculation.		
	I.	II.			
Carbon, . . .	5·48	...	5·06	C_2	12
Hydrogen, . .	2·66	...	2·52	H_6	6
Nitrogen, . .	...	...	5·90	N	14
Chlorine, . .	...	...	44·91	Cl_3	106·5
Platinum, . .	41·49	41·32	41·61	Pt	98·7
			100·00		237·2

The formula of the salt is therefore $C_2 H_5 N H Cl Pt Cl_2$; and the base is, consequently, the methylamine of Wurtz, with whose description of that substance and its platinum salt it perfectly agrees.

The preparation of the platinum salt of the other base was attended with much greater difficulty; and I did not succeed in obtaining it quite free from methylamine. In order to obtain it, the fluid which had deposited the methylamine salt was evaporated to a small bulk, the salt which separated filtered off, and ether added to the mother-liquor. Immediately a precipitate is obtained, generally in the form of minute yellow-needles, but sometimes in scales. It is sparingly soluble in alcohol and ether, and highly soluble in water, from which it crystallises in long needles, and with such facility, that a few drops evaporated on a watch-glass leave the salt they contain in the form of five or six needles crossing the whole space occupied by the solution. The quantity of this salt which I had at my disposal was too small to admit of my carrying its purification by recrystallisation as far as was to be desired, and, consequently, a small quantity of methylamine remained in those subjected to analysis.

I. 5·521 grains of platinum salt, dried at 212°, gave
2·485 ... of carbonic acid, and
1·800 ... of water.

10·475 grains platinum salt, gave 3·951 grains platinum.
6·475 ... ... 2·432 ... ...

	Experiment.		Calculation.		
	I.	II.			
Carbon, . . .	12·27	...	13·57	C_6	36
Hydrogen, . .	3·62	...	3·77	H_{10}	10
Nitrogen, . .	...	...	5·27	N	14
Chlorine, . .	...	...	40·18	Cl_3	106·5
Platinum, . .	37·71	37·56	37·21	Pt	98·7
			100·00		265·2

These results approach most closely to the formula $C_6\ H_9\ N\ H\ Cl\ Pt\ Cl_2$; and though the carbon is very deficient, and the platinum considerably in excess, there can be no doubt that this is due to the imperfect separation of the methylamine, and that this is its true formula; and that of the base itself $C_6\ H_9\ N$. The base, then, obviously belongs to the same series as methylamine, and forms the term of the series corresponding to metacetonic acid, and, in accordance with the system of nomenclature adopted by WURTZ, it receives the name of metacetamine. I have not attempted the examination of the salts of this base, as I did not obtain it in sufficient quantity for that purpose; but I take the opportunity of stating, that before I had obtained it from codeine I had ascertained its existence among the products of destructive distillation of animal substances, and that I shall, at a future period, detail the properties of its compounds.*

The residue in the retort after these bases have been evolved, is dark cinnamon-brown, and slightly coherent; it dissolves in water, with a dark-brown, almost black colour, and gives with acids a flocculent brown precipitate of a humus-like substance, and perfectly amorphous, which I have not thought it necessary to examine. It still contains nitrogen; and by exposure to a heat gradually raised to low redness, it gives an additional quantity of volatile bases, among which ammonia becomes more and more abundant as the temperature rises. A non-basic oil also makes its appearance, but only in very small quantity.

Since these experiments were made, I have received the February number of the *Annalen der Chimie und Pharmacie*, which contains a preliminary notice of an investigation by WERTHEIM of the action of soda-lime on certain organic bases. He has obtained metacetamine from narcotine, and methylamine from morphia; and considering these substances to be directly eliminated from the bases, he expects to obtain the residual atoms in the form of a definite compound. I entertained a similar idea with regard to codeine, until I detected the formation of two different bases, which seemed to me rather to indicate that these substances appear as the result of a true destructive distillation; and that possibly by varying the circumstances of the experiment, other bases may be obtained.

I have also observed another remarkable decomposition of codeine, by which volatile bases are obtained. I have already mentioned the formation, by the action of nitric acid, of a resinous acid, with the examination of which I am still engaged. This acid, which is insoluble in water, dissolves readily in dilute potash, with a red colour; and the solution on boiling evolves a volatile base in

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* I may at the same time mention, that I have convinced myself that the petinine described by me two years since as existing in bone-oil, is represented by the formula $C_8\ H_{11}\ N$, and not by $C_8\ H_{10}\ N$, which I then gave for it. Indeed, my analysis of the platinum salt, which is most to be depended upon, tallies equally well with either formula. I have also ascertained the existence of ethylamine and methylamine in bone-oil. The details of these experiments will be contained in the second part of my paper on the Products of the Destructive Distillation of Animal Matters.

great abundance. I have not yet determined the whole circumstances under which this change takes place, but reserve this for a future communication.*

I have likewise examined the action of iodine on codeine, which yields a magnificent crystalline compound presenting the phenomena of pleochroism in a remarkable manner. Difficulties connected with the analysis have, however, prevented my hitherto completing its investigation.

The following is a Tabular View of the constitutions of the substances described in this paper:—

Codeine,	$C_{36} H_{21} NO_6$.
... crystallised,	$C_{36} H_{21} NO_6 + 2 HO$.
Hydrochlorate,	$C_{36} H_{21} NO_6 HCl + 4 HO$.
Hydriodate,	$C_{36} H_{21} NO_6 HI + 2 HO$.
Sulphate,	$C_{36} H_{21} NO_6 HO SO_3 + 5 HO$.
Nitrate,	$C_{36} H_{21} NO_6 HO NO_5$.
Phosphate,	$(C_{36} H_{21} NO_6 HO) 2 HO PO_5 + 3 HO$.
Oxalate,	$C_{36} H_{21} NO_6 HO C_2 O_3 + 3 HO$.
Hydrosulphocyanate,	$C_{36} H_{21} NO_6 HC_2 NS_2 + HO$.
Platinum salt dried at 212°,	$C_{36} H_{21} NO_6 HCl Pt Cl_2 + HO$.
... crystallised,	$C_{36} H_{21} NO_6 HCl Pt Cl_2 + 3 HO$.
Amorphous codeine,	$C_{36} H_{21} NO_6$.
Nitrocodeine,	$C_{36} H_{20} (NO_4) NO_6$.
Sulphate,	$C_{36} H_{20} (NO_4) NO_6 HO SO_3$.
Platinum salt,	$C_{36} H_{20} (NO_4) NO_6 HCl Pt Cl_2 + 4 HO$.
Bromocodeine,	$C_{36} H_{20} Br NO_6$.
... hydrate,	$C_{36} H_{20} Br NO_6 + HO$.
... terhydrate,	$C_{36} H_{20} Br NO_6 + 3 HO$.
Hydrobromate,	$C_{36} H_{20} Br NO_6 HBr + 2 HO$.
Platinum salt,	$C_{36} H_{20} Br NO_6 HCl Pt Cl_2$.
Tribromocodeine,	$C_{36} H_{18} Br_3 NO_6$.
Hydrobromate,	$2 (C_{36} H_{18} Br_3 NO_6) 3 HBr$.
Platinum salt,	$C_{36} H_{18} Br_3 NO_6 HCl Pt Cl_2$.
Chlorocodeine,	$C_{36} H_{20} Cl NO_6$.
... terhydrate,	$C_{36} H_{20} Cl NO_6 + 3 HO$.
Sulphate,	$C_{36} H_{20} Cl NO_6 HO SO_3 + 4 HO$.
Platinum salt,	$C_{36} H_{20} Cl NO_6 HCl Pt Cl_2$.
Dicyanocodeine,	$C_{36} H_{21} NO_6 2 C_2 N$.
Metacetamine,	$C_6 H_9 N$.

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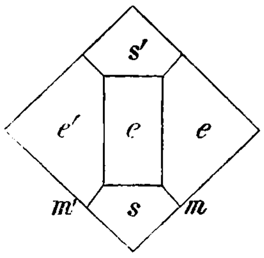
* The action of nitric acid on the organic alkalies, in this point of view, is now under investigation in my laboratory. Narcotine has been found to undergo a precisely similar change, yielding a compound, which gives off a volatile base by ebullition with potash, and a whole series of other substances, the constitution of which will be detailed so soon as the investigations are completed.

SUPPLEMENT.

While engaged with the investigation of codeine, I sent to Professor **Miller**, of Cambridge, some crystals of the base and its sulphate for crystallographic measurement. Owing to Professor **Miller**'s other avocations, he was unable to furnish me with the results in sufficient time to admit of their being incorporated with the foregoing paper. I have, therefore, introduced them here in the shape of a supplement, as they form a valuable addition to the observations contained in the paper.

Codeine.—Prismatic. The symbols of the simple forms are, *c* 001, *s* 011, *e* 101, *u* 102, *m* 110. The angles between normals to the faces are:

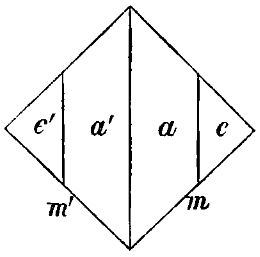
Fig. 1.



	°	′
m c	90	0
s c	38	37
s s′	77	14
e c	39	46
e e′	79	32
u c	22	35
u u′	45	10
m m′	87	40
e m	63	42
s m	63	15
s e	53	3

Cleavage, *c*.

Fig. 2.



The faces *m m′* are usually of very unequal magnitude. The faces *s s′* were not observed upon the same crystals. The form *s* is probably hemihedral.

Fig. 1. Codeine crystallised from alcohol.

Fig. 2. Codeine crystallised from water.

The agreement of the different observations is not very good, so that the above measures must be considered as approximations only.

Sulphate of Codeine.—Prismatic. Symbols of the simple forms, *a* 100, *e* 101, *m* 110.

The angles between normals to the faces are:

	°	′
e a	66	15
e e′	46	30
m a	75	36
m m′	28	48

Cleavage, *a*.

Fig. 3.