

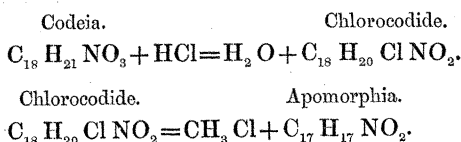
coloured the liquid, it was submitted to distillation. Only a small portion came over below  $40^{\circ}$ ; the thermometer rose rapidly to  $180^{\circ}$ , and nearly the whole of the bromine-compound distilled at  $184^{\circ}$  to  $188^{\circ}$ . This substance is amylene bromide,  $C_5H_{10}Br_2$ ; Wurtz gives the boiling-point of this body at about  $180^{\circ}$ . The portion therefore boiling at  $35^{\circ}$  is mainly amylene.

Exactly similar results were obtained from the portion boiling at  $65^{\circ}$  to  $70^{\circ}$ . This, from its boiling-point, may be either  $C_6H_{12}$  or  $C_6H_{14}$ , or a mixture of both. Bromine disappears instantly on adding it to the carefully cooled liquid, and on distillation by far the greater portion is found to have combined with the halogen. The bromide thus obtained distils with slight decomposition about  $195^{\circ}$ . Pelouze and Cahours found that hexylene bromide,  $C_6H_{12}Br_2$ , boiled at  $192^{\circ}$  to  $198^{\circ}$ .

We are at present engaged in the further investigation of this subject, and hope shortly to lay our results before the Royal Society.

III. "Contributions to the History of the Opium Alkaloids. Part I.—On the Action of Hydrobromic Acid on Codeia." By C. R. A. WRIGHT, D.Sc. Communicated by Professor ROSCOE F.R.S. Received February 6, 1871.

It has been shown by the late Dr. A. Matthiessen, in conjunction with the writer\*, that when codeia is heated with a large excess of strong hydrochloric acid the following reactions successively take place:—



It appeared of interest to examine the action of hydrobromic acid under similar circumstances, and for this purpose Messrs. Macfarlane, of Edinburgh, with their wonted liberality, put a considerable quantity of pure codeia at the writer's disposal.

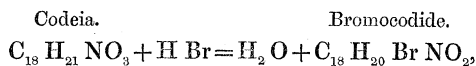
The aqueous hydrobromic acid employed was obtained by the action of  $H_2S$  on  $Br$  in presence of water, and subsequent rectification over pulverized  $KBr$ ; it was free from  $SO_4H_2$  and other sulphur compounds, had a sp. gr. of about 1.5, and contained about 48 per cent. of  $HBr$ .

When codeia is heated with from three to six times its weight of this acid, either on a water-bath or to gentle ebullition over a flame, the liquid, which at first produces no precipitate with solution of carbonate of soda, gradually darkens in colour, and acquires the property of yielding a dense white precipitate with this reagent. No appreciable quantity of methyl

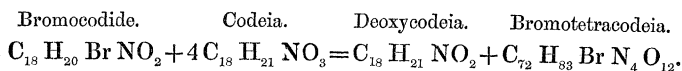
\* Proc. Roy. Soc. vols. xvii. p. 460, xviii. p. 83.

bromide is evolved during the first stages of this change, but subsequently this body is produced in some little quantity.

The precipitate thrown down by carbonate of soda before this further change ensues, appears to consist of a variable mixture of at least three substances, two of which are readily soluble in ether, while the third is but sparingly soluble in that menstruum; all are bases, the one insoluble in ether, and one of those soluble containing bromine: the one apparently first formed is produced by a reaction precisely analogous to that whereby chlorocodide is generated, viz.—



and is therefore termed bromocodide; this base appears to be acted on further with great ease, giving rise ultimately to the other two, the first of which has the constitution of codeia less one equivalent of oxygen, or  $\text{C}_{18}\text{H}_{21}\text{NO}_2$ , and is therefore provisionally named Deoxycodide; whilst the second has the composition of four molecules of codeia coalesced together, one of the 84 H atoms in the product being replaced by Br; it is therefore provisionally termed Bromotetracodide, the simplest mode of representing the simultaneous formation of these two bases being as follows:—



Owing to the ease with which bromocodide is altered, it is a matter of some difficulty to obtain it in even an approximately pure condition, as the complete separation of deoxycodide appears impracticable when this base has once been produced. The product of the action of three parts 48 per cent. acid on one part codeia on the water-bath for from one to two hours is precipitated by excess of sodium carbonate and the precipitate collected on filters; unaltered codeia is for the most part separated thus, being contained in the filtrate. Extraction of the mass with ether and agitation of the ethereal solution with HBr furnishes crude bromocodide hydrobromate, which may be purified by a repetition of the process, fractional precipitation being resorted to to get rid of traces of colouring-matters: the purified hydrobromate thus obtained was a viscid colourless liquid which utterly refused to crystallize, and dried up to a gum-like mass over  $\text{SO}_4\text{H}_2$ . Dried at  $100^\circ$ , the powdered gum gave these numbers \*:—

0.3500 grm. gave 0.6340  $\text{CO}_2$  and 0.1580  $\text{H}_2\text{O}$ .

0.230 grm, boiled with  $\text{NO}_3\text{H}$  and  $\text{AgNO}_3$  gave 0.1900 Ag Br.

\* All combustions given in this paper were made with lead chromate and finished in a stream of dry oxygen.

Calculated.			Found.	
C <sub>18</sub>	216	48·76	49·40	
H <sub>21</sub> .....	21	4·74	5·01	
Br <sub>2</sub> .....	160	36·12	....	35·08
N .....	14	3·16		
O <sub>2</sub> .....	32	7·22		
C <sub>18</sub> H <sub>20</sub> Br NO <sub>2</sub> HBr .....	443	100·00		

The slight excess of carbon and deficiency in bromine thus found are doubtless due to the presence of a little deoxycodeia, the hydrobromate of which requires 59·34 per cent. carbon and 21·98 per cent. Br. Another specimen of bromocodide hydrobromate, prepared as above from the product of three hours' digestion at 100° of one part codeia and three parts 48 per cent. HBr, yielded numbers indicating 51·6 per cent. carbon, 5·3 and 33·4 per cent. Br; whilst a repetition of the purification process scarcely altered the numbers. Owing to the great difficulty in preparing the pure salt in quantity, no attempt to isolate and analyze the base itself was made, the more so that the precipitate thrown down by carbonate of soda from the pure hydrobromate appeared to tally in every respect with the chlorocodide formerly examined; their qualitative reactions, too, are identical.

The crude bromocodide hydrobromate obtained after five or six hours' digestion of codeia with from three to five times its weight of 48 per cent. HBr deposited, on standing for some days, crystals not readily soluble in cold water; recrystallized several times from boiling water, minute snow-white crystals were ultimately obtained; these slightly darkened on drying over SO<sub>4</sub> H<sub>2</sub>, and more so at 100° and gave the following numbers on analysis:—

0·3565 grm. gave 0·7760 CO<sub>2</sub> and 0·1960 H<sub>2</sub> O.

0·3245 grm. gave 0·7045 CO<sub>2</sub> and 0·1790 H<sub>2</sub> O.

0·2200 grm. burnt with soda-lime gave 0·0570 Pt.

0·1380 grm. boiled with NO<sub>3</sub> H and Ag NO<sub>3</sub> gave 0·0700 AgBr.

These numbers agree with those calculated for deoxycodeia hydrobromate, as the following comparison shows:—

Calculated.			Found.		
C <sub>18</sub> .....	216	59·34	59·36	59·21	
H <sub>22</sub> .....	22	6·05	6·11	6·13	
N .....	14	3·84	....	....	3·69
O .....	32	8·79			
Br .....	80	21·98	....	....	21·59
C <sub>18</sub> H <sub>21</sub> NO <sub>2</sub> HBr	364	100·00			

The yield of this base from the codeia used being but small (about 4 per cent.), no attempt was made to isolate the base itself; carbonate of soda throws down from the hydrobromate solution a white precipitate which is soluble in alcohol, ether, benzol, and chloroform; by exposure to air it rapidly becomes coloured, and finally acquires a very dark green tint. Its qualitative reactions are identical with those of apomorphia; the colour-reactions of the two with  $\text{Fe}_2\text{Cl}_3$ ,  $\text{NO}_3\text{H}$ , and  $\text{SO}_4\text{H}_2 + \text{K}_2\text{Cr}_2\text{O}_7$ , being indistinguishable when examined side by side. Its physiological effects, however, are different; three-tenths of a grain of the hydrobromate administered by the mouth to a dog producing no appreciable effect, whilst a much less dose of apomorphia produces speedy vomiting.

The third base is conveniently obtained, as hydrobromate, by treating codeia with three times its weight of 48 per cent.  $\text{HBr}$  for two hours on the water-bath, precipitating the product (diluted with water) by excess of carbonate of soda, collecting on filters, and well draining from the mother-liquors, and finally extracting with ether until scarcely anything more is taken up; care must be taken to have as little watery fluid as possible present, otherwise the insoluble substance forms a sort of lather, on agitation from which the ether will not separate. The insoluble substance is then dissolved in the least possible quantity of weak hydrobromic acid and fractionally precipitated by cautious addition of stronger acid; the second precipitate is dissolved up in water, in which it is readily soluble, and a few drops of carbonate-of-soda solution added. The filtrate from this yields, with strong  $\text{HBr}$ , nearly white flakes, which are wholly void of crystalline character under the microscope. These remain solid at  $100^\circ$  if previously completely dried over  $\text{SO}_4\text{H}_2$ ; but if warmed while moist, become a more or less coloured tar. Dried at  $100^\circ$ , the following numbers were obtained:—

0·3440 grm. gave 0·6810  $\text{CO}_2$  and 0·1740  $\text{H}_2\text{O}$ .

0·3425 grm. gave 0·6685  $\text{CO}$  and 0·1680  $\text{H}_2\text{O}$ .

0·5615 grm. burnt with soda-lime gave 0·1310  $\text{Pt}$ .

0·3200 grm. boiled with  $\text{NO}_3\text{H}$  and  $\text{AgNO}_3$  gave 0·1330  $\text{AgBr}$ .  
and 0·0315  $\text{Ag}$ .

Calculated.			Found.		
$\text{C}_{72}$ .....	864	54·03	53·99	53·23	
$\text{H}_{87}$ .....	87	5·44	5·61	5·45	
$\text{N}_4$ .....	56	3·50	....	....	3·33
$\text{O}_{12}$ .....	192	12·01			
$\text{Br}_5$ .....	400	25·02	....	....	24·97
<hr/>			<hr/>		
$\text{C}_{72}\text{H}_{83}\text{BrN}_4\text{O}_{12}, 4\text{HBr}$	1599	100·00			

Carbonate of soda throws down from the hydrobromate a nearly white

precipitate, which rapidly darkens, and finally turns a deep green, nearly black. Dried at 100° rapidly, the product gave the following numbers, which fall below those required for the formula  $C_{72}H_{83}BrN_4O_{12}$ , but which agree with those required for a similar formula but containing more oxygen :—

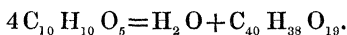
0·3810 grm. gave 0·8460  $CO_2$  and 0·2080  $H_2O$ ,

0·4430 grm. boiled with  $AgNO_3$  and  $NO_3H$  gave 0·059  $AgBr$ .

Calculated			Found.	
$C_{72}$ .....	864	60·89	60·56	
$H_{83}$ .....	83	5·85	6·07	
$Br$ .....	80	5·64	....	5·67
$N_4$ .....	56	3·95		
$O_{21}$ .....	336	23·67		
<hr/> $C_{72}H_{83}BrN_4O_{12} + O_9$			1419	100·00

It hence appears that the free base rapidly absorbs oxygen. In confirmation of this, 0·11 grm. of the hydrobromate treated with caustic potash and injected by a pipette into 15 cubic centims. of air over mercury absorbed 0·9 cubic centim. in the course of an hour, or 6 per cent. of the total volume of the air; the salts, however, when dry, may be kept without alteration, and only slowly darken by exposure to air when moist.

This welding together of four molecules is not wholly without parallel in the history of the opium alkaloids; and their derivatives thus opianic acid heated\* furnishes a body containing four times as much carbon as the original acid; thus



The qualitative reactions of bromotetracodeia appear to be identical with those of bromo- and chlorocodide. The base itself, when freshly precipitated, is slightly soluble in water, being thrown down again by addition of strong brine; in ether and benzol it is almost insoluble, and in alcohol but sparingly soluble.

When crude bromotetracodeia, got by extraction with ether of the mixture of bases thrown down by carbonate of soda, is dissolved in weak hydrochloric acid, and precipitated twice or thrice by excess of stronger acid, nearly white flakes are ultimately obtained, resembling in all their physical properties the bromohydrobromate of tetracodeia. These flakes, however, contain no bromine, the absence of this element being ascertained by the negative results obtained on examining with chlorine-water and ether the acidified solutions of the lime-salts got by combustion with quicklime, and of the sodium-salts got by boiling with  $NO_3H$  and  $AgNO_3$ , and fusing with carbonate of soda the silver-salts thus got. Dried over  $SO_4H_2$  and finally at 100°, this body gave numbers indicating a base of constitution

\* Matthiessen and Wright, Proc. Roy. Soc. vol. xvii. p. 341.

analogous to that of bromotetracodeia; it may therefore be termed chlorotetracodeia.

Specimen A.—0·3880 grm. gave 0·1970 AgCl.

0·3645 grm. gave 0·8395 CO<sub>2</sub> and 0·2120 H<sub>2</sub>O.

0·3940 grm. burnt with soda-lime gave 0·1080 Pt.

Specimen B.—0·4460 grm. gave 1·0150 CO<sub>2</sub> and 0·2560 H<sub>2</sub>O.

0·2350 grm. gave 0·1250 AgCl.

Calculated.				Found			
				Specimen A.		Specimen B.	
C <sub>72</sub> .....	864	62·77		62·81	....	62·07	
H <sub>97</sub> .....	87	6·32		6·46		6·38	
N <sub>4</sub> .....	56	4·07		....	3·90		
O <sub>12</sub> .....	192	13·94					
Cl <sub>5</sub> .....	177·5	12·90		12·56	....	....	13·16
<hr/> C <sub>72</sub> H <sub>97</sub> ClN <sub>4</sub> O <sub>12</sub> , 4HCl				1376·5	100·00		

Specimen A had been three times precipitated by HCl in large excess, while specimen B had only been thrown down twice, and probably retained a trace of bromotetracodeia.

Specimen A converted into platinum-salt gave the following numbers after drying at 100°.

0·4215 grm. gave 0·0810 Pt = 19·22 per cent.

The formula C<sub>72</sub> H<sub>97</sub> ClN<sub>4</sub> O<sub>12</sub>, 4HCl, 2PtCl<sub>4</sub> requires 19·18 per cent.

Like bromotetracodeia, the free base appears to absorb oxygen with avidity. Dried as rapidly as possible at 100°, the precipitate thrown down by carbonate of soda gave these numbers:—

0·3880 grm. gave 0·9190 CO<sub>2</sub> and 0·2230 H<sub>2</sub>O.

0·3100 „ 0·0330 AgCl.

Calculated.				Found.	
C <sub>72</sub> .....	864	64·74		64·59	
H <sub>97</sub> .....	83	6·22		6·38	
N <sub>4</sub> .....	56	4·20			
O <sub>18½</sub> .....	296	22·18			
Cl .....	35·5	2·66		....	2·64
<hr/> C <sub>72</sub> H <sub>97</sub> ClN <sub>4</sub> O <sub>12</sub> + O <sub>6½</sub>				1334·5	100·00

In all its physical and chemical properties chlorotetracodeia closely resembles bromotetracodeia: their qualitative reactions are identical; they have an intense bitter taste and apparently but slight physiological action, at any rate in small doses.

My thanks are due to Mr. J. L. Bell, in whose laboratory the above experiments were carried out.