

responsible for the oxidation, but we have added large amounts (1 cc. of 2% solution) of hydrogen peroxide to 15 cc. of the dilute indicator solution without observable effect. It is probable that the dissolved oxygen is directly activated by ultrasonic radiation.

Summary

Twelve unbuffered indicator solutions, saturated with air or oxygen, showed color fading when exposed to ultrasonic radiation. Buffered solutions gave the same result. The color of gas-free solutions and solutions saturated with hydrogen did not fade when exposed. These observations show that indicator molecules are permanently destroyed by oxidation under the influence of ultrasonic radiation.

PEIPING, CHINA

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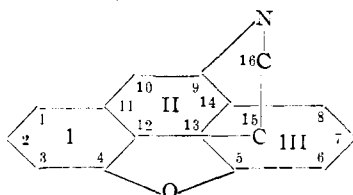
DESOXYCODEINE STUDIES. III. THE CONSTITUTION OF THE SO-CALLED α -DIHYDRODESOXYCODEINE: BIS-DIHYDRODESOXYCODEINE¹

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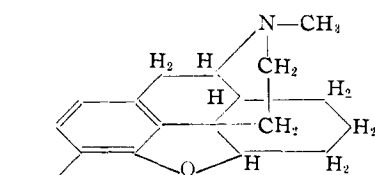
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In the second paper of this series² five isomeric dihydrodesoxycodines were described, of which four are phenolic in nature, and the fifth (dihydrodesoxycodine-D) still contains the codeine cyclic ether structure intact (formula II).



I. Numbering system



II. Dihydrodesoxycodine-D

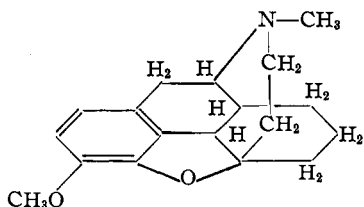
Dihydrodesoxycodine-D represents the only possible non-phenolic member of this class, provided no isomerism appears as a result of steric differences at the asymmetric carbon atoms 5, 9, 13 or 14. Nowhere in morphine chemistry is there any convincing evidence which warrants the expectation of such a stereoisomerism.³

¹ This investigation was supported by a grant from the Committee on Drug Addiction of the National Research Council from funds provided by the Bureau of Social Hygiene, Inc.

² Small and Cohen, *THIS JOURNAL*, **53**, 2227 (1931).

³ Ref. 2, pp. 2231, 2232.

Freund and his co-workers⁴ described in 1921 an amorphous alkali-insoluble base which was obtained by reduction of α -chlorocodide in the presence of colloidal palladium. This substance analyzed approximately for $C_{18}H_{23}O_2N + \frac{1}{2}H_2O$, and although no evidence was advanced to show that the base was homogeneous, it was classified as a dihydrodesoxycodine



III. α -Dihydrodesoxycodine (Freund)⁵

(designated α -) to which Freund assigned the formula III. This is identical with the structural formula which represents dihydrodesoxycodine-D. In view of this apparent contradiction, the present investigation of the so-called α -dihydrodesoxycodine was undertaken. Freund's experiment was

repeated by Mannich,⁶ who confirmed the formation of the amorphous base, and noted traces of crystalline compounds, identical with those obtained by similar reduction of β -chlorocodide.

When α -chlorocodide is hydrogenated in acetic acid solution in the presence of colloidal palladium according to Freund's directions,⁷ a 95% yield of a well-crystallized base of m. p. 107° is obtained. This compound is identical with dihydrodesoxycodine-D. The reduction proceeds slowly (Experiment 9).

With palladium on barium sulfate as catalyst, the result of the reduction is substantially the same, in that dihydrodesoxycodine-D is formed in quantitative yield. In this experiment also the reduction ran slowly (Experiments 1 and 2). When, however, the amount of catalyst is increased (Experiment 3), the speed of reduction is also increased, and dihydrodesoxycodine-D is formed only to the extent of about 40%. As other products were found 5% of tetrahydrodesoxycodine and a 45% yield of an alkali-insoluble amorphous compound which represents the amorphous base described by Freund and Mannich.

When the hydrogenation was carried out with a palladium-calcium carbonate catalyst, the amorphous base was formed to the extent of 95-100%. Crystalline products could be isolated only in traces (Experiments 4 and 5). With platinum oxide as the catalyst, the amorphous base was obtained exclusively (Experiments 6, 7 and 8).

Regarding the catalytic hydrogenation of β -chlorocodide, a stereoisomer

⁴ Freund, Melber and Schlesinger, *J. prakt. Chem.*, **101**, 1 (1921).

⁵ In accordance with the at that time accepted Knorr-Hörlein structure for the morphine series, Freund linked C-15 to C-5. The uncertainty in regard to the morphine structure at this linkage has no bearing upon the isomerism in question.

⁶ Mannich and Löwenheim, *Arch. Pharm.*, **258**, 300 (1920).

⁷ An exact reproduction of Freund's experiment was impossible because of the lack of details given regarding volume of solvent, amount of catalyst and time required for the reduction.

of α -chlorocodide, contradictory statements have appeared in the literature. By reduction in the presence of palladium on charcoal, Mannich obtained as the main product the base which we have named dihydrodesoxycodeine-D, together with small amounts of a second base which Kondo⁸ and Small⁹ have shown to be tetrahydrodesoxycodeine. Speyer and Krauss,¹⁰ on the other hand, reduced β -chlorocodide (at that time believed to be allospseudochlorocodide) using colloidal palladium and obtained what was claimed to be the so-called α -tetrahydrodesoxycodeine (dihydrodesoxycodeine-A).

The reduction of β -chlorocodide with palladium-barium sulfate, which gives substantially the results obtained by Mannich, is described in paper II of this series.² When colloidal palladium is used (Experiment 10) or palladium on calcium carbonate (Experiment 11), the product likewise consists of about 70% dihydrodesoxycodeine-D and 30% tetrahydrodesoxycodeine. With platinum oxide, the reduction runs very rapidly to completion, and results in a quantitative yield of tetrahydrodesoxycodeine, with absorption of three moles of hydrogen (Experiments 12 and 13). The isomers α - and β -chlorocodide behave alike in that both are reduced in the presence of the less active catalysts to dihydrodesoxycodeine-D. They differ under the influence of the more active catalysts; α -chlorocodide gives the amorphous base as end-product, while β -chlorocodide goes to tetrahydrodesoxycodeine with absorption of three moles of hydrogen.

Bromocodide behaves like α -chlorocodide toward catalytic reduction. In the presence of palladium-barium sulfate, it gives a 94% yield of dihydrodesoxycodeine-D (Experiment 14), whereas with palladium-calcium carbonate or platinum oxide yields of 93 and 100%, respectively, of the amorphous base were obtained (Experiments 15 and 16). From evidence in the thiocodide series Pschorr¹¹ concluded that the one known bromocodide must have the same configuration as β -chlorocodide. This question is still not definitely settled. The unexpected similar behavior of α -chlorocodide and bromocodide in our reduction experiments is not necessarily an argument against the above hypothesis.

The one known iodocodide¹² likewise gives the same catalytic reduction products as α -chlorocodide. With a palladium-barium sulfate catalyst 70% dihydrodesoxycodeine-D and 25% amorphous base are obtained.

The Amorphous So-called α -Dihydrodesoxycodeine.—The separation of the reduction products described above was accomplished most expeditiously by sublimation in high vacuum. At the temperature em-

⁸ Kondo and Ochiai, *Ber.*, **63**, 646 (1930); Ochiai, *J. Pharm. Soc. Japan*, **568**, 91 June (1929).

⁹ See following paper, Small and Cohen, *THIS JOURNAL*, **54**, 802 (1932).

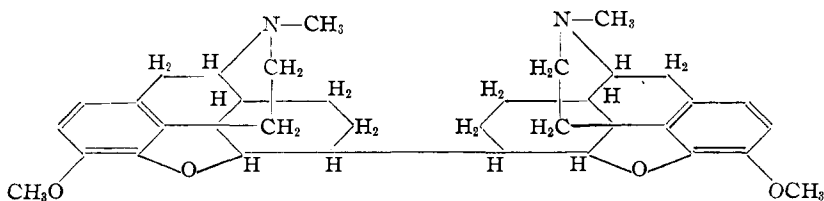
¹⁰ Speyer and Krauss, *Ann.*, **432**, 233 (1923).

¹¹ Pschorr and Rollett, *ibid.*, **373**, 1 (1910); *cf.* Faltis, *Arch. Pharm.*, **255**, 85 (1917).

¹² *Cf.* Small and Cohen, *THIS JOURNAL*, **53**, 2216, 2222 (1931).

ployed the amorphous base was undecomposed, and not at all volatile; the sublimate could be separated by the use of tartaric acid, as described in paper II. The amorphous base which we obtain is obviously the same as that of Freund and Mannich. It seems probable, however, that Freund never obtained the base free from the small amounts of accompanying crystalline compounds (see below).

The amorphous base yielded no crystalline salts. Its very high boiling point, in comparison with the easily distillable hydrogenated desoxycodines, indicated that it could scarcely be a simple dihydrodesoxycodine. It proved in fact to be a dimolecular compound, which was probably formed in a manner analogous to the formation of diphenyl by catalytic dehalogenation of bromobenzene.¹³ The dimolecular nature of the base is shown by the fact that it yielded with methyl iodide a crystalline monomethiodide $(C_{18}H_{22}O_2N)_2CH_3I$, which could be further transformed into a dimethiodide (amorphous), $(C_{18}H_{22}O_2N \cdot CH_3I)_2$. For the amorphous base, which we may call bis-dihydrodesoxycodine, the formula IV seems most probable.



IV. Bis-dihydrodesoxycodine

Freund¹⁴ describes the electrolytic reduction of bis-dihydrodesoxycodine to the so-called α -tetrahydrodesoxycodine. We find pure bis-dihydrodesoxycodine entirely unaffected by prolonged electrolytic reduction, and believe that the product which Freund observed (yield not stated) was actually tetrahydrodesoxycodine,¹⁵ formed through electrolytic reduction of small amounts of dihydrodesoxycodine-D present as an impurity in his amorphous base. As we have shown,² dihydrodesoxycodine-D can be reduced quantitatively to tetrahydrodesoxycodine by the electrolytic method.

With the establishment of the dimolecular nature of the amorphous non-phenolic base, the necessity for the assumption of stereoisomers of formula II is eliminated.

A satisfactory explanation of the different courses taken in the reduction of the halogenocodides cannot be given at present. In the reduction of α -chlorocodide, bromocodide and iodocodide where bis-dihydro-

¹³ Busch and Schmidt, *Ber.*, **62**, 2612 (1929).

¹⁴ Freund, *J. prakt. Chem.*, **101**, 36 (1921).

¹⁵ Ochiai, *J. Pharm. Soc. Japan*, **578**, 58, April (1930), states that he was able to obtain tetrahydrodesoxycodine by electrolytic reduction of the amorphous base, but does not mention the purity of his starting material nor the yield of tetrahydro product.

desoxycodeine or dihydrodesoxycodeine-D are the main products, it must be assumed that the first step in the reduction is elimination of the halogen atom. This can take place in two ways: removal of halogen as hydrogen halide, with simultaneous linking of two molecules of base to the dimolecular product, or formation of hydrogen halide and saturation of the valence at C-6 with hydrogen. As a second step in both cases, apparently, saturation of the double linkage still present in Ring III gives the end-products, bis-dihydrodesoxycodeine and dihydrodesoxycodeine-D, respectively. Attempts to isolate the hypothetical intermediate product resulting from the first step failed; when the reduction was stopped after one mole of hydrogen had been absorbed, oily, undistillable products were obtained. It is significant, however, that in every such case the whole reduction product was completely soluble in water. None of the bases in the halogenocodide or desoxycodeine series are soluble in water; therefore the whole of the first mole of hydrogen must have gone to form hydrogen halide as hypothesized above, which united with the base to give the water-soluble salt. That a dihydrohalogenocodide cannot be the first product could also be shown by direct experiment, for it was found impossible to eliminate the halogen from chlorodihydrocodide (*ex* dihydrocodeine) by catalytic reduction.¹⁶ Whether α -chlorocodide reduces to bis-dihydrodesoxycodeine or to dihydrodesoxycodeine-D depends to a certain extent upon the speed of reduction. A large amount of catalyst or a more active catalyst favors formation of the dimolecular product.

β -Chlorocodide behaves in quite a different manner. Whereas in the case of the α -isomer tetrahydrodesoxycodeine appears only in traces (maximum 5%), under the same conditions β -chlorocodide yields about 30% of the tetrahydro product, and in the case of a very active catalyst, as platinum oxide, tetrahydrodesoxycodeine is the only product of the reduction. In no case could the dimolecular base be detected.

The fact that dihydrodesoxycodeine-D cannot be further reduced catalytically shows that the formation of tetrahydrodesoxycodeine does not take place through the reduction of this as an intermediate, but that the two products are formed by two different independent reduction processes. This is further supported by the experimental fact that the reduction which at completion would yield tetrahydrodesoxycodeine alone, with absorption of three molecules of hydrogen, when stopped after one mole of hydrogen had been used, yielded two-thirds unchanged β -chlorocodide and one-third tetrahydrodesoxycodeine hydrochloride.

It is not possible to give a plausible explanation of the different courses taken by the reduction in the cases of α - and β -chlorocodide. Speculations in regard to a reaction mechanism can have but little value until some direct evidence can be found to show whether or not the halogen in the α - and

¹⁶ Cf. Ref. 6, p. 298.

TABLE I

CATALYTIC REDUCTION OF THE HALOGENOCODIDES

The time shown in this table is that required for complete reduction. In those cases where platinum oxide was used as the catalyst the reduction proceeded very rapidly and was practically complete in one-third of the time shown. During the remainder of the time indicated, the absorption was very slow, and finally stopped completely.

Bxpt.	Base	Amount, g.	Catalyst	Amount, g.	Solvent	Amount, cc.	Moles H ₂ ab- sorbed	Time in hours	Di- hydro-D, %	Tetra- hydro- %	Bis-di- hydro- %
1	α -Chlorocodide	15.0	Pd-BaSO ₄	4.0	Dil. HCl, slight excess	150	2.0	5.0	97
2	α -Chlorocodide	7.0	Pd-BaSO ₄	2.5	Dil. HCl, slight excess	100	2.0	2.0	90	5	Trace
3	α -Chlorocodide	5.0	Pd-BaSO ₄	3.0	Dil. HCl, slight excess	100	1.9	1.2	40	5	45
4	α -Chlorocodide	2.0	Pd-CaCO ₃	0.5	Ethyl alcohol	30	1.9	1.5	Trace	Trace	95
5	α -Chlorocodide	2.0	Pd-CaCO ₃	.5	Ethyl alcohol	30	2.0	1.0	100
6	α -Chlorocodide	5.0	PtO ₂	.2	Ethyl alcohol	35	1.85	0.5	95
7	α -Chlorocodide	10.0	PtO ₂	.3	Ethyl alcohol	100	1.80	1.3	93
8	α -Chlorocodide	10.0	PtO ₂	.3	Ethyl alcohol	100	1.80	1.3	95
9	α -Chlorocodide	1.0	Pd colloidal	.06	Dil. HCl, slight excess	25	2.0	2.0	95
10	β -Chlorocodide	3.0	Pd colloidal	.06	Dil. HCl, slight excess	30	2.25	5.6	73	22	...
11	β -Chlorocodide	2.0	Pd-CaCO ₃	1.0	Ethyl alcohol	30	2.30	0.7	70	30	...
12	β -Chlorocodide	3.2	PtO ₂	0.1	Ethyl alcohol	30	3.0	1.0	..	100	...
13	β -Chlorocodide	1.0	PtO ₂	.1	Methyl alcohol	25	3.0	0.6	..	100	...
14	Bromocodide	3.0	Pd-BaSO ₄	.75	Dil. HCl, slight excess	50	1.95	3.5	94	Trace	...
15	Bromocodide	3.0	PtO ₂	.15	Ethyl alcohol	30	2.1	6.0	100
16	Bromocodide	3.0	Pd-CaCO ₃	.7	Ethyl alcohol	30	1.9	1.5	93
17	Iodocodide	2.0	Pd-BaSO ₄	.5	Dil. HCl, slight excess	35	2.2	2.0	70	...	25

β -isomers actually is located at the same point in the molecule. The relative inactivity usually shown by the chlorine atom in β -chlorocodide¹⁷ is not displayed in the catalytic reductions described in this paper.

Experimental

The α - and β -chlorocodides and iodocodide used in these experiments were prepared and purified as described in the first paper of this series.¹⁸ The bromocodide was prepared according to the method of Schryver and Lees¹⁹ from codeine and phosphorus tribromide, and showed the melting point 162°. The catalysts used, platinum oxide, colloidal palladium, palladium on barium sulfate and palladium on calcium carbonate were prepared by the usual methods.²⁰ The dihydrodesoxycodeine-D used as a test substance was prepared from β -chlorocodide by Mannich's procedure, and purified through the acid tartrate. The melting point of the free base, 106–107°, was not changed by distillation in high vacuum.

Anal. Calcd. for $C_{18}H_{23}O_2N$: C, 75.74; H, 8.12. Found: C, 75.85; H, 7.97.

The tetrahydrodesoxycodeine used for comparison was obtained from the catalytic hydrogenation of desoxycodeine-B.²¹ It sintered at 131–132°, melted at 145–147° and evolved gas at 151°. The anhydrous form obtained from it by sublimation melted sharply at 157°.⁹

Experiments 1, 2, 9 and 14, in which dihydrodesoxycodeine-D was the chief product of reduction: the reaction mixtures were freed of the catalyst, treated with excess of dilute ammonia and the oily base extracted with ether. The ether yielded on distillation a nearly colorless oil, which solidified on standing to a mass of white crystals. The crude product was converted to the sparingly soluble acid tartrate by treating with a concentrated solution of the calculated amount of tartaric acid and adding boiling water until solution was complete. On cooling the solution slowly, the salt separated as fine white needles. The pure free base was obtained by treating the salt with ammonia and extracting into ether, and melted at 105–107°. It was identified in every case by mixed melting point, rotation ($[\alpha]_D^{20}$ -80.0° to -80.8°), and by the rotation of its acid tartrate ($[\alpha]_D^{25}$ -37.5° to -38.4°). In Experiment 2 a small amount of tetrahydrodesoxycodeine was recovered from the filtrate from the preparation of the acid tartrate.

Experiments 4, 5, 6, 7, 8, 15 and 16, in which bis-dihydrodesoxycodeine was the principal product of reduction: the reaction mixture was freed from catalyst, the alcoholic solution distilled, and the oily residue dissolved in 50 cc. of water. The base was liberated with a slight excess of dilute ammonia and extracted into ether, which left a light yellow oil on distillation. Small test portions in each experiment were heated to 200° in high vacuum, but only in the case of Experiment 4 did any material distill. This was small in amount and appeared to be a mixture of dihydrodesoxycodeine-D and tetrahydrodesoxycodeine.

Experiments 3, 10, 11 and 17, in which mixtures of two or three products were obtained: the mixed bases were liberated and brought into ether solution as described

¹⁷ See for example, Small and Cohen, *THIS JOURNAL*, **53**, 2216, note 13 (1931).

¹⁸ Ref. 17, p. 2214.

¹⁹ Schryver and Lees, *J. Chem. Soc.*, **79**, 563 (1901).

²⁰ Platinum oxide, Adams and Shriner, *THIS JOURNAL*, **45**, 2171 (1923); colloidal palladium, Skita, *Ber.*, **45**, 3579 (1912); palladium on barium sulfate, Schmidt, *ibid.*, **52**, 409 (1919); Rosenmund, *ibid.*, **51**, 585 (1918); palladium on calcium carbonate, Busch and Stöve, *ibid.*, **49**, 1064 (1916).

²¹ Small and Cohen, *THIS JOURNAL*, **53**, 2225 (1931).

above, and the residue from distillation of the ether was distilled in high vacuum at 140–150°. Dihydrodesoxycodeine-D and tetrahydrodesoxycodeine distilled together as a colorless oil, and were separated by treatment with tartaric acid. The non-volatile residue consisted of bis-dihydrodesoxycodeine, which was identified in every case by conversion to the monomethiodide.

Experiments 12 and 13, in which tetrahydrodesoxycodeine was the only product: the free base obtained from distillation of the ether was dissolved in boiling alcohol, and water added until crystallization started. The yield of pure tetrahydrodesoxycodeine was in each case quantitative.

Bis-dihydrodesoxycodeine.—The amorphous base, the α -dihydrodesoxycodeine of Freund, was obtained from the reductions described above as a pale yellow, glass-like solid, exceedingly soluble in ether and in most organic media excepting petroleum ether and ligroin. It dissolved readily in acids and was precipitated unchanged by addition of alkali. From no solvent could it be obtained crystalline, nor did it yield any crystalline salts with a great variety of acids. In alcoholic solution it showed the rotation $[\alpha]_D^{25} -113.3^\circ$; $c = 3.344$, $l = 1$, $\alpha = -3.79^\circ$. The monomethiodide was the only crystalline derivative which could be prepared. The amorphous product from the reduction of 10 g. of α -chlorocodide was dissolved in 50 cc. of boiling benzene, the solution cooled, and 10 g. of methyl iodide added, with constant stirring. An amorphous precipitate began to form immediately, with evolution of heat. The precipitation was complete in ten minutes and the amorphous methiodide was filtered out and washed with benzene. The yield was 11.2 g. The crude methiodide is unstable toward heat and decomposes to a black tar when warmed in most organic solvents. It was dissolved in cold alcohol and 10 volumes of acetone added; after the solution had stood for several days, long white needles separated. The monomethiodide softens and turns red at 200–230°, and melts with decomposition at 246–250°.

Anal. Calcd. for $C_{37}H_{47}O_4N_2I$: C, 62.51; H, 6.67; I, 17.87. Found: C, 62.69; H, 6.73; I, 18.08, 18.37, 17.83, 17.98 (samples for iodine determination were derived from four different experiments). In alcoholic solution the monomethiodide showed the rotation $[\alpha]_D^{25} -8.6^\circ$; $c = 2.256$, $l = 2$, $\alpha = -0.39^\circ$.

On treatment with silver chloride the monomethiodide yielded the monomethiodide in the form of a yellow, glass-like solid which could not be crystallized.

Bis-dihydrodesoxycodeine dimethiodide was prepared by heating 2 g. of the monomethiodide in a sealed tube with 6 cc. of methyl iodide at 100° for two hours. The product was a reddish oil which gradually hardened to a glass, and could not be obtained crystalline. Like the monomethiodide, it decomposed when heated in solvents, but could be purified by dissolving in warm ethyl alcohol and precipitating with acetone. It separated as a fine white powder, which was apparently not crystalline, and melted at 230–250° with gradual decomposition.

Anal. Calcd. for $C_{38}H_{50}O_4N_2I_2$: C, 53.51; H, 5.91; I, 29.77. Found: C, 53.71; H, 5.97; I, 29.43, 29.40. In benzyl alcohol the dimethiodide showed the rotation $[\alpha]_D^{25} -71.5^\circ$; $c = 1.776$, $l = 1$, $\alpha = -1.27^\circ$.

Electrolysis of Bis-dihydrodesoxycodeine.—The sample used in this experiment was obtained by catalytic reduction of α -chlorocodide in the presence of platinum oxide. A small test portion yielded no trace of distillable material when heated in high vacuum at 200°. Eight and one-half grams of the base was dissolved in 120 cc. of 20% sulfuric acid and electrolyzed, using a current of 13 amp. and an electrode of 60 sq. cm. The temperature was maintained between 10 and 20°, and the electrolysis continued for eight hours. The clear yellow solution was cooled to 0°, ether added, and a slight excess of ammonia. From the ether a reddish oil was obtained, which gave off no volatile bases at 200° in high vacuum. This excludes with certainty the presence of any di-

hydrodesoxycodine-D or tetrahydrodesoxycodine. The product from the attempted electrolytic reduction was unchanged bis-dihydrodesoxycodine, for with methyl iodide it gave a monomethiodide identical with that described above. In alcohol, $[\alpha]_D^{24} -8.4^\circ$; $c = 2.190$, $l = 2$, $\alpha = -0.37^\circ$.

Anal. Calcd. for $C_{27}H_{47}O_4N_2I$: I, 17.87. Found: I, 18.16.

Partial Reduction of α -Chlorocodide.—Three grams of α -chlorocodide in 30 cc. of ethyl alcohol was hydrogenated in the presence of 0.05 g. of platinum oxide. In twelve minutes one mole of hydrogen was absorbed and the reduction was interrupted. The solution was filtered, and the alcohol removed on the water-bath. The brown oily product obtained was completely soluble in water, and therefore must have consisted entirely of the hydrochloride of a new base. Treatment with ammonia and ether yielded a light yellow oil which slowly hardened to a glassy solid. It could not be obtained crystalline and gave no crystalline salts. It did not distil up to 200° at 1 mm., and at higher temperatures it decomposed.

Partial Reduction of β -Chlorocodide.—One gram of β -chlorocodide in 25 cc. of methanol was hydrogenated with 0.03 g. of platinum oxide as catalyst. In five minutes one mole of hydrogen was absorbed, and the experiment was stopped. The solution was filtered and two-thirds of the alcohol evaporated off. Slow addition of water to the hot solution precipitated a mass of large flake-like crystals. These proved to be pure β -chlorocodide, and weighed 0.6 g. The water-soluble portion from the reaction was treated with ammonia and ether, and yielded 0.25 g. of tetrahydrodesoxycodine. The precipitation of one alkaloid exclusively from the alcoholic solution indicates that the two alkaloids must be of widely differing basicity. This is found to be the case by direct experiment. When water is added to an alcoholic solution of two moles of β -chlorocodide, one mole of tetrahydrodesoxycodine and one mol of hydrochloric acid, the β -chlorocodide base is precipitated quantitatively and the tetrahydrodesoxycodine remains in solution as the hydrochloride. Furthermore, when an ethereal solution of equimolecular amounts of β -chlorocodide and tetrahydrodesoxycodine is extracted with sufficient hydrochloric acid to react with only one of the bases, only tetrahydrodesoxycodine is extracted. The comparatively strong basic nature of tetrahydrodesoxycodine may account in some degree for the peculiarity shown by its phenolic hydroxyl group.

Summary

1. The contradiction presented in the supposed existence of the isomeric non-phenolic bases dihydrodesoxycodine-D and α -dihydrodesoxycodine has been removed with the discovery that the latter substance is dimolecular; it has been renamed bis-dihydrodesoxycodine.

2. The catalytic hydrogenation of the halogenocodides has been studied. α -Chlorocodide yields principally dihydrodesoxycodine-D or bis-dihydrodesoxycodine, depending upon the catalyst. β -Chlorocodide yields only dihydrodesoxycodine-D and tetrahydrodesoxycodine. Bromocodide and iodocodide behave like α -chlorocodide.