either the term "natural proteose" proposed by Wells and Osborne, or the term "natural proteone" be adopted for their designation. The latter term is suggested as an alternate because it is recognized that the allergens have chemical properties similar to those of both proteoses and peptones (*cf.* footnote 10 in reference 5). It is suggested that consideration be given adoption of possibly a more suitable class name for the natural proteoses in any future revision of the protein classification system.

It is recognized that each of the allergens described herein, although immunologically distinct from other allergens and antigens present in the seed, is chemically a complex mixture.[35,17] However, the isolation of carbohydrate-free allergenic proteins from both cottonseed (CS-60C)[16] and castor beans (CB-65A)[17] by prolonged, drastic and varied fractionation has left little room for doubt that the specifically active constituent is protein in nature. Undoubtedly, similar carbohydrate-free allergens could be isolated from the other 1A fractions by application of similar techniques.

The information gained on composition and important chemical and immunological properties that characterize the typical natural proteoses, as represented by the allergenic fractions almond nut-1A, Brazil nut-1A, castor bean-1A, cottonseed-1A, Barcelona filbert nut-1A and -H1B, DuChilly filbert nut-H1B, flaxseed-1A, kapok-1A and mustard-1A, may be summarized as follows. They are soluble in water and in dilute ethanol (up to 25% concentration) at room temperature. They are insoluble in 75% ethanol and organic solvents. The allergens are stable in boiling water and resist drastic chemical treatment; an electrophoretic subfraction CS-51R, from CS-1A, retained allergenic[35] and antigenic[36] properties, although of decreased potency, after being refluxed for 4 hours in 0.1 *N* hydrochloric acid. These substances are not precipitated by basic lead acetate, which is important in the purification procedure. They are partially dialyzable. The allergens are composed of known amino acids and in general are characterized by relatively high proportions of arginine and glutamic acid. They possess potent allergenic activity; positive cutaneous reactions were obtained with dilutions up to $1:10^6$ and positive passive transfer reactions were produced by 0.1 to 100 millimicrograms. They are potent antigens producing sensitization and fatal shock in guinea pigs. These substances are preformed in the seeds and are immunologically distinct from other allergens and antigens in the seeds.

(35) Spies, Bernton and Stevens, THIS JOURNAL, **63**, 2163 (1941).

(36) Coulson and Spies, *J. Immunol.*, **46**, 377 (1943).

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The Acid-catalyzed Conversion of Codeinone to 8-Hydroxydihydrocodeinone

BY STEPHEN P. FINDLAY AND LYNDON F. SMALL

It has been discovered that the α,β-unsaturated ketone, codeinone, dissolved in dilute mineral acids, slowly combines with water. This reaction involves hydration of the ethylenic bond, the product being 8-hydroxydihydrocodeinone. The reaction rate is approximately proportional to the hydrogen ion concentration. Unlike codeinone, the α,β-unsaturated ketone, the bainone, does not react with water in the presence of dilute acids.

During a study of the chromic acid oxidation of codeine chromate,[1] which gives codeinone (II), it was observed that the product was contaminated by considerable quantities of phenolic impurities, but attempts to characterize them failed. Because of the disposition of codeinone to rearrange in hot dilute[2] and hot concentrated[2] hydrochloric acid it was thought that these impurities arose from the action of the acidic reaction medium and that one might establish their identity by ascertaining the action of cold, dilute acids on the isolated ketone. First of all, it was observed that on long standing codeinone, dissolved in normal hydrochloric acid, lost about half its optical rotatory power, but that no morphothebaine, which alone of the two acid-produced rearrangement products of codeinone[2] is optically active, could be recovered from the solution. Instead a new base was discovered which had nearly the same melting point (200°) and specific rotation in alcohol ($[\alpha]^{20}D$ −135°) as morphothebaine but which gave a distinctive color test with concentrated nitric acid[3] and was found by analysis to differ from codeinone (m.p. 184°) by the elements of water

$$C_{18}H_{19}NO_3(\text{codeinone}) + H_2O \xrightarrow{H^+} C_{18}H_{21}NO_4$$

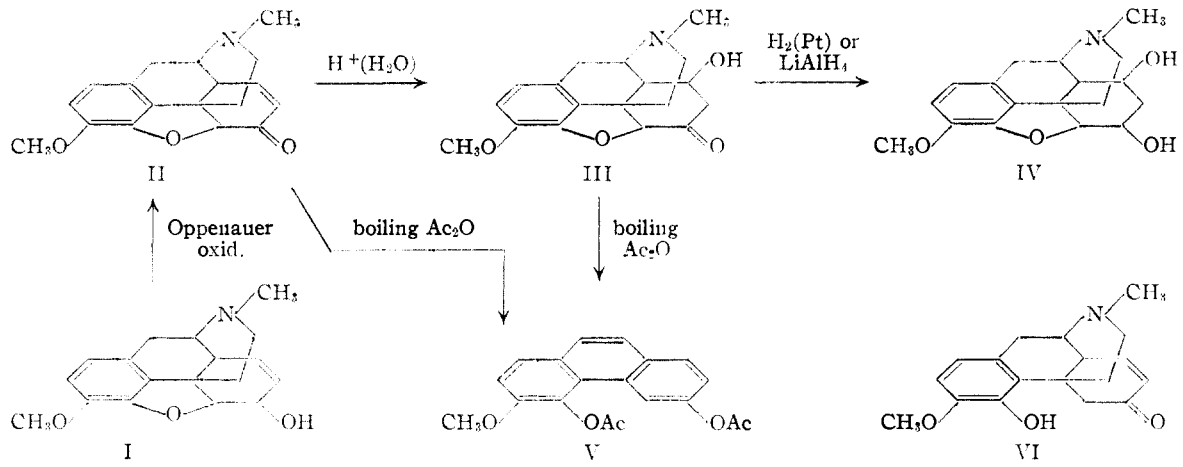
In subsequent experiments it was found that the best yields of the new base were obtained by dissolving codeinone in a large excess of 1.5 *N* hydrochloric acid and keeping three weeks. The new base was also obtained when hydrochloric acid was replaced by dilute sulfuric acid. The rate of hydration of codeinone was approximately proportional to the hydrogen ion concentration.

The new base furnished a crystalline hydrochloride, which, with respect to melting point and water solubility, was similar to codeinone hydrochloride. It reacted readily with hydroxylamine hydrochloride and acidic 2,4-dinitrophenylhydrazine to give the corresponding ketone derivatives. The retention of the keto group indicated that the transformation had involved no rearrangement of the carbon skeleton. It liberated one and a half atoms of ac-

(1) S. P. Findlay and L. F. Small, THIS JOURNAL, **72**, 3247 (1950); *cf.* F. Ach and L. Knorr, *Ber.*, **36**, 3067 (1903).

(2) L. Knorr, *ibid.*, **36**, 3074 (1903).

(3) *Cf.* W. Klee, *Arch. Pharm.*, **252**, 211 (1914).



tive hydrogen per molecule. Dissolved in methanol, it quickly absorbed one mole of hydrogen in the presence of platinum to give a dihydro derivative, which did not react with hydroxylamine hydrochloride or acidic 2,4-dinitrophenylhydrazine, contained two active hydrogen atoms per molecule, yielded a diacetyl derivative, and combined with one molecule of methyl iodide to give a methiodide. Later it was found that the dihydro base was also obtainable by the agency of lithium aluminum hydride.

From these facts it was concluded that, of the four oxygens of the dihydro derivative, two were present as hydroxyl groups and the other two were still bound in ether linkages and that the new base from which it was derived must have been a keto alcohol. Also, since the new base absorbed only one mole of catalytic hydrogen, it could no longer contain an ethylenic bond and hence must have been formed from codeinone by hydration of this linkage. Of the two conceivable modes of addition of water to an α,β-unsaturated ketone, that in which the hydroxyl attaches itself to the β-carbon is the more likely. The other mode was excluded by the observation that the hydrochloride of the dihydro derivative was not cleaved by periodic acid (Malaprade reagent[4]). Therefore, it was concluded that the new base was 8-hydroxydihydrocodeinone (III) and that the dihydro derivative, in accordance with the suggestion of Fieser and Fieser concerning the steric course of catalytic hydrogenations in the morphine series,[5] was 8-hydroxydihydrocodeine (IV).

When codeinone is boiled with acetic anhydride it undergoes a molecular rearrangement with the elimination of the ethaneamine chain and the formation of 3-methoxy-4,6-diacetoxyphenanthrene (V). This propensity of derivatives of morphine having the requisite degree of unsaturation to aromatize with simultaneous expulsion of the ethaneamine chain is significant and led Gulland and Robinson to the most distinctive feature of the morphine ring system, namely, the quaternary nature of C_{13}.[6] Inasmuch as 8-hydroxydihydrocodeinone possesses potentially the same degree of unsaturation as codeinone, one might expect that it too would yield this phenanthrene derivative under the same conditions, an expectation which was realized. The hydration of codeinone in cold, dilute acid has not therefore been accompanied by rearrangement, as happens in hot acids, and little doubt remains that the product is 8-hydroxydihydrocodeinone (III).

The acid-catalyzed hydration of codeinone is analogous to the conversion of crotonaldehyde to aldol under similar conditions.[7] If the unstable β-hydroxyketone, diacetone alcohol, be an intermediate, Claisen's generation of acetone by distilling a mixture of dilute sulfuric acid and mesityl oxide[8] is also an analogous process. Of late the hydration of α,β-unsaturated carbonyl compounds has received systematic study by H. J. Lucas and his collaborators. They have observed that in dilute perchloric acid such compounds as acrolein[9a] and mesityl oxide[9b] are extensively hydrated to the corresponding β-hydroxy derivatives, an equilibrium between the hydrated and unhydrated forms being eventually attained.

Under the conditions used for codeinone, the similar unsaturated ketone, thebainone (VI), was very little affected.

The erroneous conclusion, based upon their reactions with diazosulfanilic acid, that 8-hydroxydihydrocodeinone and its dihydro derivative were phenolic[1] was due in the former compound to changes brought about by the reagent,[9c] and in the latter to traces of phenolic by-products of the catalytic hydrogenation. Although the conditions for the catalytic hydrogenation of such 6-ketones as dihydrothebainone,[10] metathebainone,[11] methyldihydromorphinone,[12] methyldihydrocodeinone[12] and

(4) Malaprade, *Bull. soc. chim.*, [5] **1**, 833 (1934).

(5) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1949, p. 24; K. Freudenberg, "Stereochemie," Franz Deuticke, Leipzig, 1933, p. 638.

(6) J. M. Gulland and R. Robinson, *J. Chem. Soc.*, **123**, 980 (1923).

(7) A. Wurtz, *Bull. soc. chim.*, [2] **42**, 286 (1884).

(8) L. Claisen, *Ber.*, **7**, 1168 (1874); *Ann.*, **180**, 20 (1875).

(9) (a) D. Pressman and H. J. Lucas, THIS JOURNAL, **64**, 1953 (1942); (b) D. Pressman, L. Brewer and H. J. Lucas, *ibid.*, **64**, 1122 (1942). (c) However, this reagent is quite sensitive to phenols having a free para position. Dihydroethebainone is detectable in a dilution of 1:2,000,000. K. Goto, *Bull. Chem. Soc. Japan*, **5**, 311 (1930).

(10) A. Skita, F. F. Nord, J. Reichert and P. Stukart, *Ber.*, **54**, 1560 (1921).

(11) H. Kondo and E. Ochiai, *J. Pharm. Soc. Japan*, No. 549, 913 (1927); L. F. Small and E. Meitzner, THIS JOURNAL, **55**, 4602 (1933).

(12) L. F. Small, H. M. Fitch and W. E. Smith, *ibid.*, **58**, 1457 (1936).

ethyldihydrocodeinone[13] have been rather arbitrarily and unsystematically chosen and make impossible, therefore, a generalization concerning the reducibility of this class of ketones, it is usually true that they are more slowly reduced in neutral than in acidic media. 8-Hydroxydihydrocodeinone is, however, exceptional, being rapidly hydrogenated in neutral solution and very slowly hydrogenated in hydrochloric acid solution. For this reason the relation of 8-hydroxydihydrocodeinone to 8-hydroxydihydrocodeine was at first misunderstood and was finally made unequivocal by infrared absorption spectra. The former compound exhibited a sharp absorption maximum about 5.75 μ (1740 cm.$^{-1}$), which is characteristic of the carbonyl group, whilst the latter compound did not absorb in this region.

The greater portion of the codeinone required for this investigation was prepared by the Oppenauer oxidation of codeine (I). Using α-methoxycyclohexanone as hydrogen acceptor, one can thus obtain codeinone in approximately 50% yield.[14] However, pseudocodeine could not be converted to pseudocodeinone by this method; most of the starting material was recovered. Apropos of these results is the recent observation that dihydroallopseudocodeine, but not dihydropseudocodeine, could be oxidized by the Oppenauer method using potassium tertiary butylate as catalyst.[15]

Since thebaine is the methyl enolate of codeinone it was hoped that the former base would serve as an inexpensive substitute for the latter in making 8-hydroxydihydrocodeinone. However, it furnished only amorphous products.

In view of the tenacity with which codeinone oxime prepared in alcohol retains one molecule of alcohol it was considered worthwhile proving that this was solvent of crystallization and not bound chemically during the formation of the oxime in consequence of a process analogous to the hydration reaction. It was established that the oxime prepared in alcohol and crystallized from methanol was identical with that prepared in methanol.

Acknowledgments.—The authors are indebted to Dr. H. L. Holmes of Harvard University who furnished infrared absorption spectra for 8-hydroxydihydrocodeinone and 8-hydroxydihydrocodeine. They are also indebted to Mr. William C. Alford of this Institute for the analytical data reported herein.

Experimental[16]

The Oppenauer Oxidation of Codeine (I) to Codeinone (II).[14]—Codeine (30.0 g.), 675 ml. of toluene and 98 ml. of α-methoxycyclohexanone were heated to reflux temperature and, to dry out the system and the solution, 135 ml. of solvent was distilled out using the condenser (air-cooled) as a fractionating column. Fifty-two ml. of a solution of aluminum tertiary butoxide[17] in toluene (0.15 g. of catalyst per ml.) was added and the mixture refluxed 1.75 hours. Addition of the catalyst caused the solution to change in color from pale yellow to deep orange. The mixture was cooled to about 5° and the toluene solution extracted with two 500-ml. volumes of cold 0.3 *N* sulfuric acid. The combined acid extracts were washed with two 50-ml. portions of chloroform and two 150-ml. portions of ether. To the acid solution were added 130 ml. of a 30% solution of Rochelle salt and then, with stirring, 300 ml. of 1.25 *N* sodium hydroxide. Codeinone separated and was filtered off within ten minutes and dried in air: 17–24 g. (57–80%) of nearly white product. This was crystallized from acid-free ethyl acetate using about 15 ml. of solvent per gram of base: 10–14 g. (33–47%), m.p. 184°.[1] A second crop (5–4 g., m.p. 183°) and also a third (*ca.* 2 g.) could be obtained from the mother liquors.

During the course of several hours a tan product precipitated from the alkaline filtrate (6 g.). It separated from ethyl acetate as a jelly and was quite soluble in alcohol, from which it slowly precipitated as brown warts. No 8-hydroxydihydrocodeinone could be isolated by extracting its solution in chloroform with water. It was not further investigated.

Application to Pseudocodeine.—A mixture of 4.72 g. of pseudocodeine, 200 ml. of toluene, 15 ml. of α-methoxycyclohexanone and 13 ml. of aluminum tertiary butoxide solution (see above) was refluxed four hours and worked up as described before. Only unreacted pseudocodeine (2.9 g., 61%) was recovered.

8-Hydroxydihydrocodeinone (III), $C_{18}H_{21}NO_4$.—Codeinone (12.5 g.) was dissolved in 1250 ml. of 1.5 *N* hydrochloric acid and stored in the dark at room temperature for 20 days. The red solution was made just neutral with anhydrous sodium carbonate (99.5 g.) and any insoluble by-products filtered off. The filtrate was extracted with 100 ml. of chloroform to remove unreacted codeinone, made strongly alkaline with carbonate, and extracted again with chloroform (3 × 300 ml.). The brown extracts were dried and the solvent removed. To eliminate the colored impurities from the residue of crude 8-hydroxydihydrocodeinone, it was dissolved in 150 ml. of chloroform and extracted with five 600-ml. volumes of water, the first containing an amount of hydrochloric acid equivalent to 70% of the weight of crude product. Each aqueous extract was passed through a separatory funnel containing 30 ml. of chloroform. The combined aqueous extracts were made strongly alkaline with carbonate and extracted with chloroform (3 × 300 ml.). The nearly colorless chloroform extracts were dried and the solvent distilled, the last few ml. under reduced pressure: *ca.* 8 g. (60%) of residue. In order to remove color more completely the chloroform extraction process was usually repeated. The yellowish residue was crystallized from acid-free ethyl acetate, using about 20 ml. of solvent per gram of base: *ca.* 4.0 g. (30%), m.p. 200–201°. From the mother liquors 2–3 g. of darker product (m.p. 200°) was obtained. This procedure is an improvement of one described earlier.[1]

It was found that during the course of four days the rate of mutarotation of codeinone at 20° in 1.45 *N* hydrochloric acid was about twice that in 0.73 *N* acid.

Crystallized from ethyl acetate to constant rotation, 8-hydroxydihydrocodeinone has $[\alpha]^{20}D$ −136 (*c*, 1.0) and melts at 201°. When pure it separates from this solvent as large white sheaves which electrify readily. It is somewhat soluble in water and more so in methyl and ethyl alcohol. It is much less readily colored by light than codeinone and appears to be indefinitely stable in the dark. Although it is not phenolic, with diazosulfanilic acid in the presence of alkali it gives a red dye.[18] With concentrated nitric acid it gives a pale yellow color.[3] It reduces both Fehling solution and Tollens reagent.

The hydrochloride was obtained by dissolving the base in warm dilute hydrochloric acid and cooling to 0°. The salt was crystallized from a little water: tiny prisms, m.p. 186–189° (shrinks at 179°). It gives a negative ferric chloride reaction, but yields a red dye with diazosulfanilic acid. At 110° *in vacuo* it lost 7.18% of its weight.

Anal. Calcd. for $C_{18}H_{21}NO_4 \cdot HCl \cdot 1.5H_2O$: C, 57.1; H, 6.65; Cl, 9.36; H_2O, 7.13. Found: C, 57.2; H, 6.79; Cl, 9.30.

Warm solutions of 8-hydroxydihydrocodeinone hydrochlo-

(13) L. Small, S. G. Turnbull and H. M. Fitch, *J. Org. Chem.*, **3**, 204 (1938).

(14) This procedure, together with a generous supply of α-methoxycyclohexanone, was kindly given to us by Drs. A. H. Homeyer and G. B. DeLaMater of the Mallinckrodt Chemical Works. A modification of it appears in the experimental section.

(15) H. Rapoport, R. Naumann, E. R. Bissell and R. M. Bonner, *J. Org. Chem.*, **15**, 1103 (1950).

(16) All melting points are corrected and all measurements of optical rotation are for solutions in 95% alcohol.

(17) Prepared according to Fieser's directions, see "Experiments in Organic Chemistry," Second Edition, D. C. Heath and Company, Boston, Mass., 1941, p. 445.

(18) L. Rosenthaler, "Der Nachweis organischer Verbindungen," Ferdinand Enke, Stuttgart, 1923, p. 239.

ride and 2,4-dinitrophenylhydrazine in hydrochloric acid[19] were mixed and the yellowish-orange **2,4-dinitrophenylhydrazone hydrochloride** was crystallized twice from absolute alcohol: red prisms, m.p. 220–230°. After 66 hours at 1–2 mm. over P_2O_5 this derivative had lost 11.54% of its weight; calculated for one molecule of alcohol and one and one-half of water, 12.1%. The dried salt was too hygroscopic to be conveniently analyzed. The retention of two solvents together is unusual, but it is reported that conchairamine contains both alcohol and water of crystallization.[20]

Anal. Calcd. for $C_{24}H_{25}N_5O_7 \cdot HCl \cdot 1C_2H_5OH \cdot 1.5H_2O$: C, 51.6; H, 5.83; N, 11.57; Cl, 5.86; RO, 12.6. Found: C, 51.6; H, 5.79; N, 11.28; Cl, 5.99; RO, 10.2.

The **oxime hydrochloride** precipitated almost immediately when a solution of 0.16 g. of hydroxylamine hydrochloride in 10 ml. of absolute alcohol was mixed with a solution of 0.50 g. of base and boiled. It was crystallized twice from absolute alcohol: colorless prisms, m.p. 261.2–261.9° (261.5° *in vacuo*). It was dried 5 hours at 130° *in vacuo* for analysis.

Anal. Calcd. for $C_{18}H_{22}N_2O_4 \cdot HCl$: C, 58.9; H, 6.32; Cl, 9.67. Found: C, 58.8; H, 6.42; Cl, 9.51.

The oxime was recrystallized from alcohol: tiny prisms, m.p. 274° (*in vacuo*). A satisfactory analysis for this derivative was not obtained.

8-Hydroxydihydrocodeine (IV)[1] (a) Catalytic Hydrogenation.—A solution of 1.0 g. of 8-hydroxydihydrocodeinone in 75 ml. of methanol was hydrogenated with 50 mg. of Adams catalyst. When about one equivalent of hydrogen had been absorbed, the consumption of gas became negligible. The catalyst-free solution was evaporated to dryness and the residue (1.0 g.) crystallized from ethyl acetate: 0.46 g. (46%), m.p. 206°. From the mother liquors an additional quantity of product (0.3 g.) was recovered. Recrystallized from ethyl acetate to constant rotation, it had $[\alpha]^{20}D$ −115 (*c*, 0.7) and melted at 207°.

Anal. Calcd. for $C_{18}H_{23}NO_4$: C, 68.2; H, 7.32; active H, 0.63. Found: C, 68.1; H, 7.39; active H, 0.63.

When 1.0 g. of 8-hydroxydihydrocodeinone dissolved in 50 ml. of normal hydrochloric acid was hydrogenated using 50 mg. of platinum oxide, hydrogen absorption was quite sluggish; consumption of the theoretical quantity of hydrogen required about 45 hours, and the yield of 8-hydroxydihydrocodeine was lower.

8-Hydroxydihydrocodeine was not dehydrated or otherwise affected when boiled 2 hours in 6 *N* hydrochloric acid. Heating 2 hours with hydroxylamine hydrochloride in absolute alcohol at 50–60° did not result in an oxime. Likewise, the base failed to react with Brady reagent.[17]

8-Hydroxydihydrocodeine hydrochloride, prepared in and purified from absolute alcohol, melted at 238.5–240°. It was a convenient means of separating the dihydro base from phenolic by-products of the catalytic hydrogenation. These impurities in amounts insufficient to affect the melting point or specific rotation of 8-hydroxydihydrocodeine produce a red dye with diazosulfanilic acid and were responsible for an earlier misstatement concerning its properties.[1] The salt lost 4.6% of its weight on drying (calculated for 1 molecule of water, 4.85%); the anhydrous salt is hygroscopic.

Anal. Calcd. for $C_{18}H_{23}NO_4 \cdot HCl$: C, 61.11; H, 6.84. Found: C, 61.19; H, 7.03.

8-Hydroxydihydrocodeine methiodide was prepared in ethyl acetate and crystallized from methanol–ethyl acetate; fine needles, m.p. 250°.

Anal. Calcd. for $C_{19}H_{26}INO_4$: C, 49.7; H, 5.71. Found: C, 49.5; H, 5.54.

The diacetyl derivative, **8-acetoxyacetyldihydrocodeine**, was obtained by boiling 8-hydroxydihydrocodeine either with a 50% mixture of acetyl chloride in acetic acid or with acetic anhydride containing a trace of fused zinc chloride. The reaction mixtures were made basic and the derivative taken up in ether. The yellowish gum remaining after removal of the ether crystallized on long standing. It was quite soluble in the common organic solvents and was best purified from ethyl acetate; square tablets, m.p. 149.5–150.5°.

Anal. Calcd. for $C_{22}H_{27}NO_6$: C, 65.82; H, 6.79; CH_3CO, 21.42. Found: C, 65.74; H, 6.89; CH_3CO, 21.25.

(19) O. L. Brady, *J. Chem. Soc.*, 756 (1931).

(20) O. Hesse, *Ann.*, **225**, 247 (1884); A. Weissberger, "Technique of Organic Chemistry," Vol. III, Interscience Publishers, Inc., New York, N. Y., 1950, p. 473.

8-Hydroxydihydrocodeine hydrochloride (0.0949 g.) was dissolved in a small volume of water, 5.00 ml. of ~0.5 *N* sodium periodate added, and the mixture diluted to 25.00 ml. After 4.5 hours 5.00 ml. of this solution required 6.05 ml. of 0.1000 *N* standard iodine solution; the blank required 5.80 ml. After 22 hours these requirements had not changed appreciably. This consumption (0.25 ml. of the iodine solution) corresponds to 0.23 mole of sodium periodate per mole of hydrochloride; the theoretical requirement is 1.00 mole per mole of hydrochloride. It was concluded that the hydroxyl groups of the hydrochloride were not on adjacent carbon atoms. From the untitrated portion 30 mg. of unreacted base was recovered.

(b) $LiAlH_4$ **Reduction.**—8-Hydroxydihydrocodeinone (1.0 g.) was reduced with 5.0 ml. of 1.8 *N* lithium aluminum hydride in 150 ml. of ether in the customary manner.[21,22] The crude product (0.80 g., m.p. 195.5–198.5°) was converted to the hydrochloride which was purified from alcohol; m.p. 236–239°.

Infrared Absorption Spectra.—Measured by a Baird Associates Infrared spectrophotometer, the infrared spectrum of 8-hydroxydihydrocodeinone had pronounced maxima at 3.0, 3.48 and 5.75 μ corresponding to the alcoholic hydroxyl group, the carbon–hydrogen bond, and the keto group, respectively. 8-Hydroxydihydrocodeine had maxima corresponding to the alcoholic hydroxyl group and carbon–hydrogen bond but none to the keto group.

3-Methoxy-4,6-diacetoxyphenanthrene (V).—8-Hydroxydihydrocodeinone (1.20 g.) was refluxed three hours with 15 ml. of acetic anhydride. The reaction mixture turned red almost immediately. The boiling solution was treated cautiously with water and the orange, aqueous mixture extracted with ether. The orange ether extract was washed with water and bicarbonate, dried, and distilled. The brown residue was crystallized twice from ethyl acetate and once from alcohol. From the latter solvent it separated as small prisms, m.p. 164.5–165.5° (reported 162–163°[22]). Mixed with the product (m.p. 164–165°) prepared in like manner from codeinone, it melted at 164–165°.

Anal. Calcd. for $C_{19}H_{16}O_5$: C, 70.4; H, 4.97. Found: C, 70.5; H, 5.05.

This phenanthrene derivative did not furnish a molecular compound with alcoholic picric acid.

Thebainone (VI).—Bromocodide was converted to β-ethylthiocodide,[8,23] and this was hydrolyzed with hot, dilute hydrochloric acid according to the directions of Morris and Small.[7] Thebainone as the hydrochloride was purified from alcohol; m.p. 261°, $[\alpha]^{20}D$ −24° (*c* 1.7, alcohol).

Anal. Calcd. for $C_{18}H_{21}NO_3 \cdot HCl$: C, 64.4; H, 6.61; Cl, 10.6. Found: C, 64.4; H, 6.43; Cl, 10.7.

Thebainone hydrochloride (1.0 g.) was dissolved in 100 ml. of 2 *N* hydrochloric acid and stored at 20° for 31 days. The mixture was then made strongly alkaline with carbonate, extracted with chloroform. The residue was dissolved in absolute alcohol and treated in the cold with dry hydrogen chloride. Thebainone hydrochloride (0.75 g.) slowly precipitated; m.p. 260°, mixed m.p. with the authentic salt, 260°. Additional salt was recovered from the mother liquors. It was concluded that thebainone, unlike codeinone, does not combine readily with water in acid solution.

Codeinone Oxime Methanolate.—A mixture of 0.50 g. of codeinone, 0.15 g. of hydroxylamine hydrochloride and 30 ml. of methanol was refluxed 1.5 hours, treated with ammonia, concentrated to 15 ml., and chilled. The crystals which separated were crystallized twice from methanol; shiny flakes, m.p. 218° (221.5° *in vacuo*). The melting point (212°) of the oxime prepared in ethanol was raised to 221° *in vacuo* by recrystallization from methanol. After drying at 125° (2 mm.) for 12 hr. it had reached constant weight; weight loss, 9.30%; calculated for 1 molecule of methanol, 9.30%.

Anal. Calcd. for $C_{18}H_{20}N_2O_3$: C, 69.2; H, 6.47; CH_3O, 9.90. Found: C, 69.3; H, 6.44; CH_3O, 10.1.

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(21) R. F. Nystrom and W. G. Brown, THIS JOURNAL, **69**, 1197 (1947).

(22) P. Karrer, C. H. Eugster and P. Waser, *Helv. Chim. Acta*, **32**, 2381 (1949).

(23) R. Pschorr and A. Rollet, *Ann.*, **378**, 1 (1910).