scription Macdonald gives of his analytical procedure we feel that the presence of nitrous oxide in the reaction products may not be fully established.

Summary

The photochemical decomposition of nitric oxide has been studied, as a function of the pressure, over the pressure range 0.02 to 7 mm. with irradiation both from the mercury arc and from sparks between electrodes of aluminum, zinc, cadmium, nickel, copper and tin, respectively.

The final products of the reaction are nitrogen and oxygen although the latter is removed by a reaction which takes place during compression of the gas in the McLeod gage. This reaction produces a solid product, probably mercurous nitrite, which decomposes to liberate nitric oxide by a first order process which has a velocity constant of 1.5×10^{-2} hr.$^{-1}$.

The rate of decomposition proves to be directly proportional to the rate of light absorption for light of the effective wave length and is, at very low pressures, directly proportional to the pressure. The absorption of effective radiation follows Beer's law and has, for the reaction with the mercury arc, an extinction coefficient of about 2.9×10^{-2} per millimeter light path per millimeter of pressure. Nitrogen as a diluent does not appreciably influence the rate of decomposition. These results, alone, indicate primary dissociation as the first step in the process.

The use of filters containing solutions of ammonium chloride and of ammonium hydroxide places the effective mercury arc radiation below λ 1900. The use of a water filter indicates that the effective region is in the neighborhood of λ 1830. The strong resonance line at λ 1849 is ruled out, except for a relatively small influence at the higher pressures, by measurement of its absorption coefficient which proves to be one hundred times too small for the observed reaction. The alternative is the weak λ 1832 line of mercury which is strongly absorbed by the (1′,0″) band of the δ-system of nitric oxide. The essential features of this interpretation are confirmed by the measurement of the decomposition under the influence of both filtered and unfiltered radiation from sparks between metal electrodes. The latter owe the greater portion of their effectiveness to a background of continuous radiation below λ 1900.

This interpretation of the primary process, which must be a predissociation since it occurs in a banded region of the spectrum, agrees well with the evidence for predissociation provided by the emission spectrum of nitric oxide.

Possible secondary processes are considered. All are believed ruled out on theoretical or experimental grounds, in comparison with combination of nitrogen and oxygen atoms on the walls.

Macdonald's work with high pressures of nitric oxide has been considered and it is concluded that the mechanism determined for the low pressure decomposition may also be applied to the results at higher pressures. However, predissociation from the upper levels of the β-bands, rather than the δ-bands, provides the primary step at these higher pressures.

COLUMBUS, OHIO RECEIVED JUNE 25, 1935

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

Reduction Studies in the Morphine Series. VII. Pseudocodeinone[1]

BY ROBERT E. LUTZ AND LYNDON SMALL

Pharmacological studies which have been carried out at the University of Michigan coördinate with the chemical investigations at this Laboratory have shown that as regards general physiological action, the four codeine isomers may be grouped in pairs, codeine with allopseudocodeine, and isocodeine with pseudocodeine.[2] This pairing is based primarily upon the relative degree of convulsive and depressant actions exhibited by each of the drugs, upon their toxicity and upon their effective ratios in other respects when toxicity is taken into account. The same relationship holds for the four corresponding isomeric morphines, and suggests that the spatial arrangement of the alcoholic hydroxyl group may be of

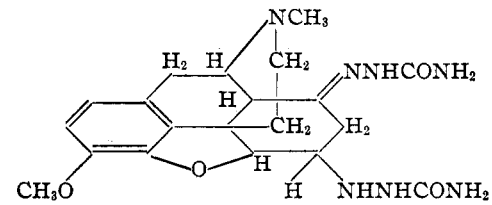
(1) The work reported in this paper is part of a unification of effort by a number of agencies having responsibility for the solution of the problem of drug addiction. The organizations taking part are: The Rockefeller Foundation, the National Research Council, the U. S. Public Health Service, the U. S. Bureau of Narcotics, the University of Virginia and the University of Michigan.

(2) Eddy, *J. Pharmacol.*, **45**, 361 (1932).

more importance for physiological effect than its position (at −6 or −8) on the nucleus.[3] Information on the relative importance of the C-6 and C-8 positions may be expected from the study of derivatives in which the asymmetry at C-6 and C-8 has been destroyed, *i. e.*, compounds whose difference in action must be due to the difference in ring position of the characteristic group present. The present communication deals with the preparation of dihydropseudocodeinone (the "pseudo" analog of Dicodid) and dihydroisomorphinone (the "pseudo"[4] analog of Dilaudid), substances which differ from the well-known drugs cited only in having the keto group at C-8 instead of at C-6. Aside from the practical aspect of the problem, the reduction of pseudocodeinone is of theoretical interest because of the conjugated system involved.

Pseudocodeinone (II) is prepared by oxidation of either pseudocodeine or allopseudocodeine, whereby the secondary alcoholic group at C-8 in these isomers is converted to a carbonyl group, and the stereoisomerism disappears. The location of the carbonyl group at C-8 depends upon the degradation of pseudocodeinone to 3,4,8-trimethoxyphenanthrene.[5] The earlier formulas for pseudocodeine[6] (and hence for pseudocodeinone) placed the alicyclic double linkage at C-13, C-14, whereas the Gulland and Robinson formula[7] locates the unsaturation at C-6, C-7 (formula II). The latter conception is substantiated by the reactions described in the present paper. We have verified the important reaction upon which the Pschorr formula was based, the condensation of pseudocodeinone with benzaldehyde,[8] believed to indicate a methylene group adjacent to the carbonyl. This point of evidence for the Pschorr formula loses most of its weight, however, through our observation that codeine likewise condenses with benzaldehyde under the same conditions.[9]

In favor of the 6,7-position for the pseudocodeinone unsaturation, the reaction with semicarbazide may be advanced. Pseudocodeinone is known to react with semicarbazide to give a monosemicarbazone;[5a] we find that on standing with a large excess of the reagent it reacts with a second molecule in a manner characteristic of α,β-unsaturated ketones[10] to yield a semicarbazino-semicarbazone to which we assign the structure I.



I. Pseudocodeinone semicarbazino-semicarbazone

Hydrogenation of pseudocodeinone in ethanol with a platinum catalyst results largely in formation of the phenolic tetrahydropseudocodeinone,[11] (V), a reaction to be expected from the pseudocodeine type (II) under these conditions. Tetrahydropseudocodeinone still contains the carbonyl group, as is shown by oxime formation.[11] By further reduction, with sodium and alcohol, we obtained only tetrahydropseudocodeine (VI). The diastereomeric tetrahydroallopseudocodeine, whose formation might be anticipated, was not found.

Hydrogenation of pseudocodeinone hydrochloride in glacial acetic acid favors normal saturation of the double linkage, and suppresses reduction of the cyclic ether group. The product consists of nearly equal amounts of the above mentioned tetrahydropseudocodeinone and of the new dihydropseudocodeinone (III).[12] The latter is the desired 8-keto isomer of the 6-keto compound, dihydrocodeinone (Dicodid). In dihydropseudocodeinone the ether bridge is intact, as is shown not only by the lack of phenolic characteristics but also by the reduction (sodium and alcohol) to our previously described non-phenolic dihydropseudocodeine (VII). Through this reduction reaction, as well as by oxime formation, the presence of the carbonyl group in dihydropseudocodeinone is demonstrated. It is notable that the reductions of tetrahydropseudocodeinone and dihydropseudocodeinone are consistent stereochemically in yielding exclusively the reduction product having the pseudocodeine configuration.

(3) Eddy, *J. Pharmacol.*, **51**, 43 (1934).

(4) The prefix *pseudo* cannot consistently be applied to demethylated analogs of pseudocodeine compounds on account of confusion with the dimolecular products of the pseudomorphine series.

(5) Knorr and Hörlein, *Ber.*, **40**, (a) 2032, (b) 3341 (1907).

(6) Pschorr, *ibid.*, **45**, 2212 (1912).

(7) Gulland and Robinson, *Mem. Proc. Manchester Lit. Phil. Soc.*, **69**, 79 (1925).

(8) Knorr and Hörlein, *Ber.*, **40**, 3341 (1907). See Gulland and Robinson, *J. Chem. Soc.*, **123**, 1001 (1923). *Cf.* Schöpf, *Ann.*, **452**, 212, Note 2 (1927).

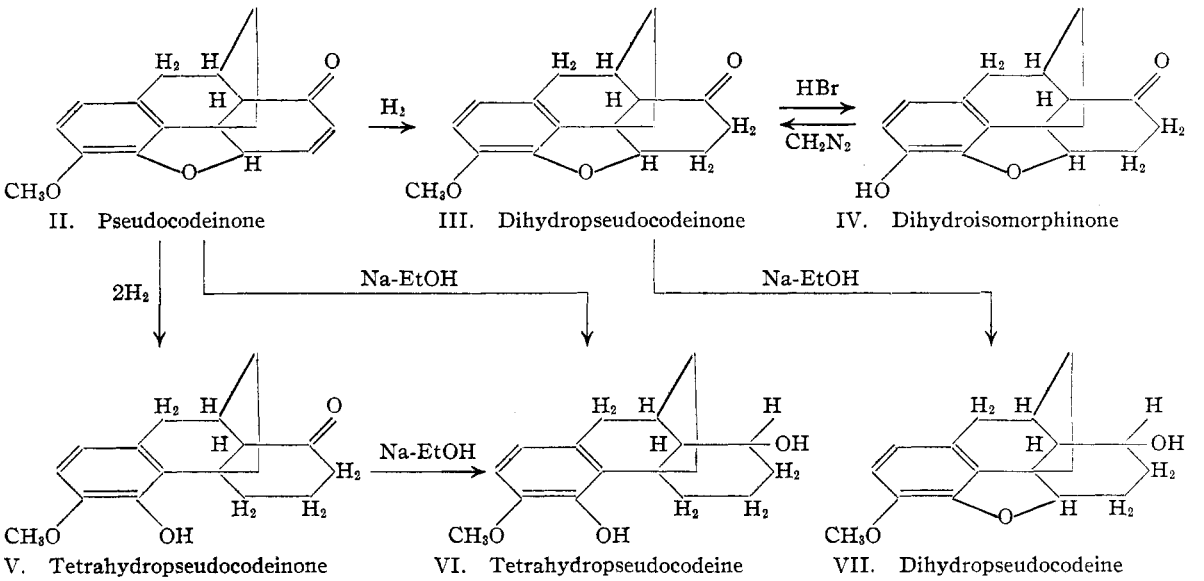
(9) The nature of the reaction is under further investigation.

(10) Houben, "Methoden der org. Chem.," Vol. II, p. 1005.

(11) Karl A. T. Hill, Dissertation, Frankfurt a./M., 1925.

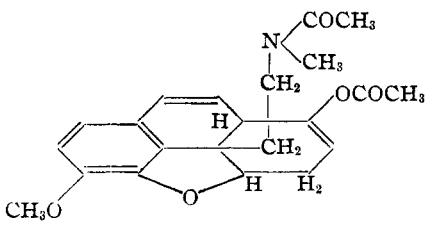
(12) Speyer and Rosenfeld, *Ber.*, **58**, 1117 (1925), obtained from treatment of bromocodeinone with sodium hydrosulfite a compound of formula $C_{18}H_{21}O_3N$, for which they suggested a dihydropseudocodeinone structure. No evidence was advanced to support this suggestion, and the properties of their compound differ from those of our dihydropseudocodeinone.

Sodium and alcohol reduction of pseudocodeinone yields tetrahydropseudocodeine directly, the keto group again being reduced to the favored pseudocodeine configuration as noted above.



Demethylation of dihydropseudocodeinone gives in good yield dihydroisomorphinone (IV), the 8-keto analog of the 6-keto compound, dihydromorphinone. Dihydroisomorphinone is a strongly phenolic base whose structure is sufficiently demonstrated by the reconversion to dihydropseudocodeinone through the action of diazomethane. The synthesis of dihydroisomorphinone here realized is at present not a practicable one on account of the difficulty involved in the preparation of dihydropseudocodeinone.

An attempt to prepare an 8-enol-acetate analog of the drug "Acedicon" (acetyldemethylodihydrothebaine, or dihydrocodeinone enol acetate) failed because of the lability of the nitrogen-containing ring in dihydropseudocodeinone. The action of acetic anhydride and sodium acetate on dihydropseudocodeinone results in a substance, $C_{22}H_{25}O_5N$, which contains two acetyl groups and which is no longer basic. These facts are best explained by a des-N-acetyldihydropseudocodeinone enol acetate formula, (VIII). This ring opening of dihydropseudocodeinone on acetylation recalls the behavior of apomorphine[13] and morphothebaine,[14] where the driving force of the reaction appears to be the possibility of forming a completely aromatic nucleus.



VIII. Des-N-acetyldihydropseudocodeinone enol acetate

It has long been known that the carbonyl group in codeinone does not react with the Grignard reagent under ordinary conditions[15] or even at temperatures up to 170°, where decomposition occurs.[16] Dihydrocodeinone is attacked only in small degree, yielding traces of a *phenolic* product, and dihydropseudocodeinone is recovered unchanged after treatment with methylmagnesium iodide. Pseudocodeinone, on the other hand, reacts readily with this reagent to yield a substance provisionally named methyldihydropseudocodeinone, which is of interest because of its peculiar properties. It is a strongly phenolic base, whose empirical formula shows that the elements of methane have been added to the starting material. Accordingly, the ether bridge must be open, and the carbonyl group and a double bond still be present. Nevertheless, the new compound resists all attempts at reduction, whether by catalytic methods, sodium in alcohol or cyclohexanol, or the Clemmensen method. None of the other unsaturated or saturated ketones of the morphine series has been found to offer such resist-

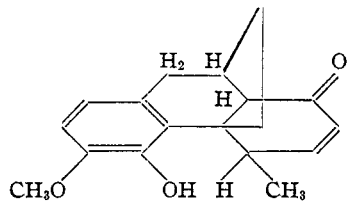
(13) Pschorr, Jaeckel and Fecht, *Ber.*, **35**, 4377 (1902).

(14) Freund, *ibid.*, **32**, 168 (1899); Knorr and Pschorr, *ibid.*, **38**, 3153 (1905).

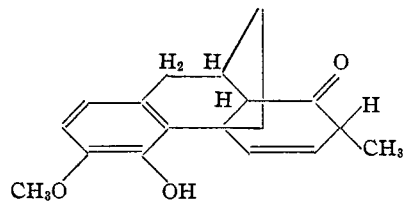
(15) Schneider, Dissertation, Jena, 1906.

(16) Small and Cohen, unpublished results.

ance to reduction at the double linkage or carbonyl group.[17] Furthermore, repeated attempts to prepare an oxime or a semicarbazone failed. We were unable to find any evidence of the presence of either alicyclic double linkage or carbonyl group, although one or both must be present, whatever may be the mechanism by which *one mole* of alkylmagnesium halide adds. We believe that the best interpretation of the reaction is the 1,2- or 1,4-addition of methylmagnesium iodide to the system consisting of an ether linkage and the 6,7-double bond, such as we postulate in the case of desoxycodeine-C and other pseudocodeine types.[18] That the carbonyl group is not involved is not remarkable in view of the indifference of this group in the examples cited above. The structure of methyldihydropseudocodeinone might be expressed by formula IX or X (or a rearranged form of X), of which the α,β-unsaturated ketone formula IX seems the less probable on account of the extraordinary resistance to reduction with sodium and alcohol.



IX. 5-Methyldihydropseudocodeinone



X. 7-Methyldihydropseudocodeinone

In the cases of phenyldihydrothebaine[19] and the methyldihydrothebaines[20] we have a reluctance toward catalytic hydrogenation similar to that here observed, but it should be noted that methyl, ethyl and cyclohexyl dihydro derivatives of desoxycodeine-C, presumably of structure analogous to that of methyldihydropseudocodeinone, can be hydrogenated without difficulty.[18]

Dihydropseudocodeinone is about one-half as toxic as Dicodid, and shows less convulsant action. Its analgesic effect is much less than that of Dicodid, but in effective doses it causes no emesis and almost no excitement. Its activity in general is about one-tenth that of Dicodid. Dihydroisomorphinone presents a similar picture. In respect to analgesia and respiration it is only one-tenth as effective as the 6-keto isomer, Dilaudid; like dihydropseudocodeinone, it has no emetic and but little exciting action. Convulsions occur only with fatal doses. As far as conclusions are justified by the evidence available, it appears that a functional group in the 6-position exerts much more influence on physiological action than one in the 8-position. Pseudocodeine and γ-isomorphine, because of a favorable configuration of the alcoholic hydroxyl, are effective drugs in spite of the disadvantageous ring position of the group; allopseudocodeine and β-isomorphine, the least active of the isomers, have the hydroxyl unfavorably located both in space and in position. In codeine and morphine, the location of the hydroxyl in the active 6-position is of more importance than the unfavorable spatial arrangement, and in the most effective of the isomers, isocodeine and α-isomorphine, both position and configuration intensify physiological action. These conclusions, although drawn from few examples, are offered as a tentative explanation of the consistent relations (in respect to physiological action) of the codeine and morphine isomers and most of their dihydro derivatives.

Experimental

Pseudocodeinone (II) was prepared by chromic acid oxidation of pseudocodeine according to the method of Knorr and Hörlein.[5a] The product was best isolated by cooling the oxidation mixture through addition of ice, making strongly alkaline with sodium hydroxide, and extracting several times with ether. The yield of pure product seldom exceeded 10 to 15%. The important fact reported by Knorr that allopseudocodeine gives the same ketone on oxidation was verified, the yield in one experiment being 30% of that required by theory. The pseudocodeinone base was purified from butanone; occasionally some unchanged pseudocodeine was found, and was removed by utilizing its very slight solubility in ether.

II-Hydrochloride crystallizes from ethanol or from dilute hydrochloric acid; m. p. 201–203° (corr. with dec.); $[\alpha]^{25}_{D}$ −24° (water, c = 1.0).

Anal. Calcd. for $C_{18}H_{20}O_3NCl + H_2O$: H_2O, 5.1. Found: H_2O, 4.6. Calcd. for $C_{18}H_{20}O_3NCl$: Cl, 10.63. Found (dried at 120° *in vacuo*): Cl, 10.24.

Pseudocodeinone Semicarbazino-semicarbazone (I).—Two grams of pseudocodeinone with 25 cc. of water, 4 cc. of ethanol and 3 g. of semicarbazide hydrochloride went largely into solution on stirring, and a hydrochloride crystallized out; this showed the constants given by Knorr for pseudocodeinone semicarbazone hydrochloride. When allowed to stand for about three hours with occasional shaking in the presence of the excess semicarbazide, the pre-

(17) Compare, for example, the reduction of codeinone, dihydrocodeinone, thebainone, metathebainone, dihydrothebainone, pseudocodeinone, dihydropseudocodeinone, tetrahydropseudocodeinone, hydroxycodeinone, dihydrohydroxycodeinone.

(18) Small, Yuen, Fitch and Smith, unpublished results.

(19) Literature review, Small and Lutz, "Chemistry of the Opium Alkaloids," pp. 332–336.

(20) Small and Fry, unpublished results.

cipitate dissolved. After sixty hours the semicarbazinosemicarbazone was thrown out crystalline by ammonia; yield 1.85 g. It is very slightly soluble in most organic solvents, and was purified from 70% alcohol; m. p. 225–227° (unsharp, dec.).

Anal. Calcd. for $C_{20}H_{27}O_4N_7 + H_2O$: H_2O, 4.0. Found: H_2O, 4.1. Calcd. for $C_{20}H_{27}O_4N_7$: C, 55.91; H, 6.34. Found: C, 55.61; H, 6.46.

Dihydropseudocodeinone (III).—A suspension of 13.8 g. of pseudocodeinone hydrochloride in 50 cc. of glacial acetic acid with 0.1 g. of platinum oxide absorbed 1270 cc. (corr.) of hydrogen, or 1.4 moles. The filtered solution was diluted with ice water, made ammoniacal under ether and extracted several times. The oily base thus obtained was dissolved in acetone, from which nearly pure tetrahydropseudocodeinone separated on cooling. Dilution of the filtrate with a little water yielded a second crop of the same product; yield 34%. The acetone solution, partially evaporated in an air blast, gave dihydropseudocodeinone as an oily precipitate, which slowly solidified, m. p. 93–100°, yield 46%. Reduction of pseudocodeinone in alcohol with platinum gave tetrahydropseudocodeinone with only traces of dihydropseudocodeinone.

Dihydropseudocodeinone crystallizes from ethyl acetate or ethyl acetate–ligroin mixtures as balls of rectangular prisms or plates, m. p. 113° (corr.). It may also be purified through the hydriodide. In high vacuum it distils as a colorless glass; $[\alpha]^{25}_D$ +37° (ethanol, c = 0.62).

Anal. Calcd. for $C_{18}H_{21}O_3N$: C, 72.20; H, 7.07. Found: C, 72.19; H, 7.15.

Dihydropseudocodeinone hydrochloride was prepared in acetone with alcoholic hydrogen chloride, and purified from acetone–alcohol mixture. It melts at 172–173° (corr.), and has $[\alpha]^{26}_D$ +13° (water, c = 0.65).

Anal. Calcd. for $C_{18}H_{22}O_3NCl + H_2O$: H_2O, 5.1. Found: H_2O, 4.9. Calcd. for $C_{18}H_{22}O_3NCl$: Cl, 10.57. Found (dried *in vacuo* 120°): Cl, 10.09.

Dihydropseudocodeinone hydriodide crystallizes from water, melts at 250–255° (corr., with dec.), and shows $[\alpha]^{25}_D$ +8.1° (water, c = 0.56).

Anal. Calcd. for $C_{18}H_{22}O_3NI$: I, 29.72. Found (dried *in vacuo* 120°): I, 29.98.

Dihydropseudocodeinone forms a well-crystallized tartrate (from water), m. p. 199–200°, $[\alpha]^{25}_D$ +20° (water, c = 0.91) which gave on analysis values approximating the formula of the acid tartrate.

Dihydropseudocodeinone oxime was prepared by boiling 0.2 g. of base in 2 cc. of water with 1 g. of hydroxylamine hydrochloride; yield nearly quantitative. It was purified from ethanol, and melted at 244–245° (corr.).

Anal. Calcd. for $C_{18}H_{22}O_3N_2$: C, 68.75; H, 7.06. Found: C, 68.69; H, 6.98.

Reduction of dihydropseudocodeinone with sodium in alcohol gave 78% yield of dihydropseudocodeine-A (VII).[21]

Des - N - acetyldihydropseudocodeinone Enol Acetate (VIII).—A solution of 0.5 g. of III in 5 cc. of acetic anhydride with 0.5 g. of sodium acetate, heated for three hours at 100°, gave a nearly quantitative yield of the non-basic product VIII. This crystallized from ethanol as thin six-sided scales of m. p. 191.5–192° (corr.).

Anal. Calcd. for $C_{22}H_{25}O_6N$: C, 68.90; H, 6.57. Found: C, 68.83; H, 6.58.

Tetrahydropseudocodeinone (V).—The physical properties of this compound differ considerably from Hill's description.[11] It behaves like a cryptophenol; it is not readily soluble in dilute sodium hydroxide, and is largely extracted by ether from its solution in alkali. Crystallized from ethanol or acetone it separates as the hemihydrate m. p. 137–138.5° (unsharp, corr.). It sublimes in a high vacuum, yielding the anhydrous form, m. p. 170–171° (corr.); $[\alpha]^{30}_D$ +8.0° (ethanol, c = 0.55).

Anal. Calcd. for $C_{18}H_{23}O_3N + 0.5H_2O$: C, 69.63; H, 7.80. Found: C, 69.64; H, 7.88. Calcd. for $C_{18}H_{23}O_3N$: C, 71.72; H, 7.70. Found (sublimed sample): C, 71.68; H, 8.01.

The base does not react with diazomethane. With acetic anhydride in pyridine (100° for thirty minutes) it forms a monoacetyl derivative which distils as a colorless glass in a high vacuum.

Anal. Calcd. for $C_{18}H_{22}O_3N(COCH_3)$: $COCH_3$, 12.5. Found: $COCH_3$, 12.3.

V-Oxime, crystallized from ethanol, melts at 218–219° (corr.). *Cf.* Hill, m. p. 137° (dec.).

Anal. Calcd. for $C_{18}H_{24}O_3N_2$: C, 68.31; H, 7.65; N, 8.86. Found: C, 68.26; H, 7.81; N, 8.98.

V-Hydrochloride crystallizes hydrated from ethanol, m. p. 165–166° (corr.) with frothing; $[\alpha]^{25}_D$ −6.2° (water, c = 1.29).

Anal. Calcd. for $C_{18}H_{24}O_3NCl + 2H_2O$: H_2O, 9.6; Cl, 9.54. Found: H_2O, 9.7; Cl, 9.36. Calcd. for $C_{18}H_{24}O_3NCl$: Cl, 10.50. Found: Cl, 10.09.

V-Hydriodide crystallizes hydrated from water, m. p. 154–155° (corr.), $[\alpha]^{25}_D$ −5.9° (water, c = 0.85).

Anal. Calcd. for $C_{18}H_{24}O_3NI + H_2O$: H_2O 4.0. Found: H_2O, 3.8. Calcd. for $C_{18}H_{24}O_3NI$: I, 29.58. Found: I, 29.41.

Tetrahydropseudocodeine (VI).—Reduction of either pseudocodeinone or tetrahydropseudocodeinone (0.5 g.) in 50 cc. of absolute alcohol with 5 g. of sodium (nitrogen atmosphere) gave 62% yield of tetrahydropseudocodeine, identified by its two melting points and the melting point of its characteristic methine derivative. Sodium amalgam in dilute acetic acid gave the same product.

Dihydroisomorphinone (IV).—Demethylation of dihydropseudocodeinone with hydriodic acid was unsatisfactory. A solution of 4.5 g. of III in 20 cc. of 48% hydrobromic acid was refluxed for fifteen minutes. An oily base was obtained from ether, and crystallized when digested with ethyl acetate; yield 2.45 g., m. p. 198° (corr.), $[\alpha]^{26}_D$ +46° (ethanol, c = 0.44). The base is soluble in sodium hydroxide, and precipitates on addition of ammonium chloride. The ferric chloride test is intense cobalt blue. IV-Perchlorate crystallizes in rectangular plates; the hydrochloride, hydriodide and tartrate are not crystalline. The base sublimes in a high vacuum at 200°.

Anal. Calcd. for $C_{17}H_{19}O_3N$: C, 71.54; H, 6.72. Found: C, 71.22; H, 6.98.

Methyldihydropseudocodeinone.—Treatment of 12 g. of pseudocodeinone in 1000 cc. of absolute ether with 100 cc. of 1.9 molar methylmagnesium iodide gave an oily base

(21) Lutz and Small, THIS JOURNAL, **54**, 4715 (1932).

which partly crystallized from ethanol; yield, 3.3 g. It was purified from isopropyl alcohol, m. p. 213.5–214.5° (corr.).

Anal. Calcd. for $C_{19}H_{23}O_3N$: C, 72.82; H, 7.40. Found: C, 72.96, 72.48; H, 7.62, 7.49.

Methyldihydropseudocodeinone was unaffected by treatment with sodium in alcohol or in boiling cyclohexanol, by catalytic hydrogenation in alcohol, acidified alcohol or glacial acetic acid, by zinc and hydrochloric acid (seven hours under reflux), or by hydroxylamine or semicarbazide under various conditions.

The use of ethylmagnesium iodide in the above reaction gave non-crystalline products.

Summary

1. Pseudocodeinone can be reduced under proper conditions to a non-phenolic dihydropseudocodeinone. The relationship of this to dihydropseudocodeine-A establishes its structure.

2. Demethylation of dihydropseudocodeinone results in dihydroisomorphinone, the 8-keto analog of Dilaudid.

3. Dihydropseudocodeinone is indifferent to methylmagnesium iodide, but pseudocodeinone reacts to give a phenolic dihydromethylpseudocodeinone. This product is remarkable in the complete passivity of its carbonyl group and double linkage toward the usual reagents affecting such structures.

4. Comparison of the physiological action of dihydropseudocodeinone and dihydroisomorphinone with that of Dicodid and Dilaudid, and that of the codeine and morphine isomers indicates that morphine derivatives with the functional group at C-6 are more effective than those with the same group at C-8, but that spatial relationships are also very important.

UNIVERSITY, VIRGINIA RECEIVED OCTOBER 11, 1935

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Vinyldiazomethane

BY CHARLES D. HURD AND S. C. LUI

Recently, Adamson and Kenner[1] described vinyldiazomethane as if it were new. Nirdlinger and Acree,[2] however, prepared it in 1910. They synthesized it from allylnitrosourethan whereas Kenner employed allyl (acetyl-*t*-butyl)-nitrosamine. In the present work, done in 1933–1934, it was studied to learn whether allyl, cyclopropyl or propenyl esters would be formed during reaction with acids. Actually, it was the ally ester which resulted: $C_6H_5COOH + CH_2{=}CHCHN_2 \longrightarrow N_2 + C_6H_5COOCH_2CH{=}CH_2$. The isomerization of vinyldiazomethane to pyrazole, reported by Adamson and Kenner, was observed. In fact, it was found to isomerize appreciably even during the distillation of the diazo compound.

Vinyldiazomethane was prepared by Nirdlinger and Acree's method, namely, by adding a solution (20%) of potassium hydroxide in methanol to a solution of the nitroso compound (A) in ether (B). When a 1:15 or 1:20 ratio of A:B was maintained, a 22–25% yield of vinyldiazomethane resulted. With a 1:9 ratio, the yield dropped to 13%.

Allylurethan and allylnitrosourethan were prepared by methods closely adapted from those given for methylurethan and methylnitrosourethan in "Organic Syntheses" [Vol. XII, p. 38; XIII. p. 84], the difference being that allylamine was taken instead of methylamine. The yields, respectively, were 81 and 94%. This preparation of allylnitrosourethan is new. Nirdlinger and Acree, who made it from nitrogen trioxide and allylurethan, mentioned no yield and gave no analysis. In the present work, the nitroso compound was analyzed after being thoroughly washed, dried and freed from solvent ether: d^{15}_{15} 1.051 d^{20}_{20} 1.047, d^{25}_{25} 1.044. Decomposition attended efforts to distil it (a red oil) at 3 mm.

Anal. Calcd. for $C_6H_{10}O_3N_2$: N, 17.7. Found: N, 17.4.

To estimate the yields, 10.00 cc. of the ether solution of vinyldiazomethane was mixed in a stoppered flask with a solution of 0.500 g. of *p*-nitrobenzoic acid in 25 cc. of dry ether. When the solution became colorless in 15–25 minutes it was back-titrated with 0.1 *N* barium hydroxide. When the reaction period was extended to twenty-four hours the results were but slightly higher; *e. g.*, a 22.3% value changed to 23.1%. With 2,4,6-trinitrobenzoic acid decolorization occurred immediately and gave quantitative values (23.0% in the case cited) if back-titrated at once.

For comparison of *p*-nitrobenzoic acid and benzoic acid, duplicate experiments were performed with reaction times of one-half, one and twenty-four hours. The yields, respectively, from *p*-nitrobenzoic acid were 22.3, 22.8, 23.1%; from benzoic acid, 12.1, 15.2, 16.2%.

Allyl Benzoate.—Vinyldiazomethane (1.855 g.) and benzoic acid (10 g.) were mixed in 360 cc. of dry ether and left for two days. Then the ether and excess acid were removed. The ester which remained distilled at 228°; yield, 2.90 g. or 65.7%. Two grams of this ester was hy-

(1) Adamson and Kenner, *J. Chem. Soc.*, 286 (1935).

(2) Nirdlinger and Acree, *Am. Chem. J.*, **43**, 381 (1910).