n_D^{25} 1.6591; *M* calcd. 47.31, obs. 48.02. On distillation the substance behaved as reported by Peratoner,[11] liberating iodine and forming a solid compound.

Tolyl Iodoacetylene.—Eight grams of tolylacetylene was iodinated in the same manner as was phenylacetylene. The dry oil weighed 16.5 g. (99%). Considerable decomposition took place when the material was distilled. The fraction boiling at 135–141° at 16 mm. had the following properties: d^{27} 1.810; n_D^{27} 1.6870; *M* calcd., 52.02, obs. 51.01. The material was apparently impure tolyl iodoacetylene.

Summary

1. Iodine in liquid ammonia has been found to be an effective reagent for the direct iodination of monosubstituted acetylenes.

2. Phenyl, tolyl and vinyl acetylenes react with iodine in ammonia at −34° giving almost theoretical yields of the corresponding iodoacetylene.

3. Ethyl, butyl, amyl and heptyl acetylenes react slowly with ammonia solutions of iodine at −34°. At 25° 15–45% yields of the iodoacetylenes are obtained.

4. At 25° iodine has been found to react completely with liquid ammonia giving ammonium iodide.

5. Amyl iodoacetylene is produced in 28% yield by the action of iodine in ammonia–ether solution on amylacetylene.

6. Sodium amylacetylide is very rapidly iodinated by the action of iodine in ammonia, giving 68% yields of amyl iodoacetylene.

(11) Peratoner, *Gazz. chim. ital.*, [II] **22**, 96 (1892).

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Narcotine and Hydrastine. A Study of the Mechanism of their Conversion into Narceine, Methylhydrasteine and their Derivatives[1]

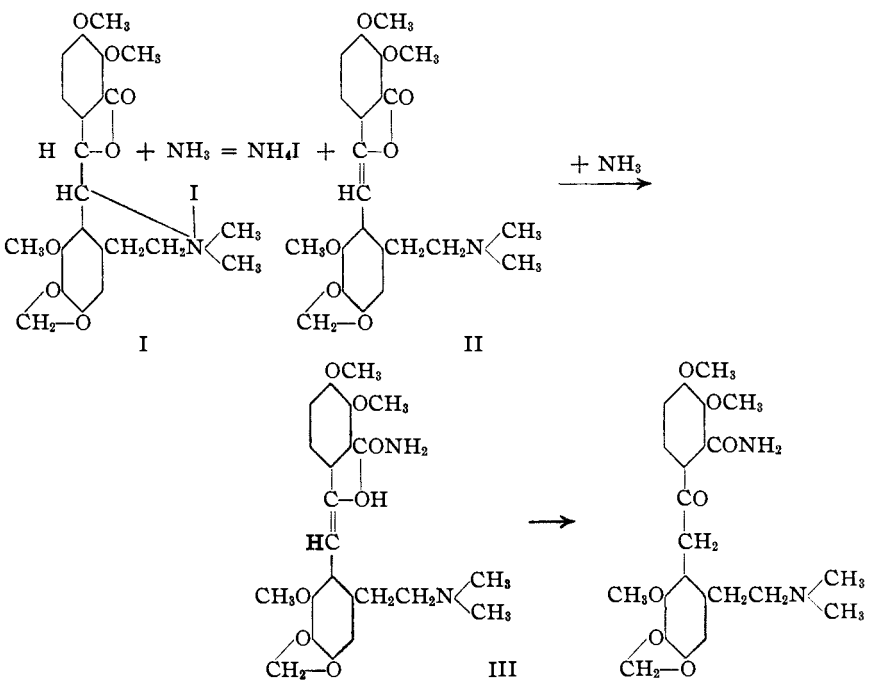
BY C. R. ADDINALL AND RANDOLPH T. MAJOR

The transformation of quaternary narcotine halides into the pseudonarceine studied by Roser[1a] was firmly established when Freund and Frankforter[2] proved the identity of pseudonarceine with opium narceine and demonstrated the close structural relationship of narcotine and narceine. Rabe and McMillian,[3] who regarded narcotine and the closely related hydrastine as the inner esters of 1,2-hydramines, showed that two reactions were involved in the hydrolysis of these alkaloids and that in addition to decomposition by cleavage of the C–C linkage, rearrangement took place. On the contrary the quarternary ammonium compounds of nar-

(1) Presented at the New Orleans meeting of the American Chemical Society, March 29, 1932.
(1a) Roser, *Ann.*, **247**, 167 (1888).
(2) Freund and Frankforter, *ibid.*, **277**, 20 (1893).
(3) Rabe and McMillian, *ibid.*, **377**, 223 (1910).

cotine and hydrastine showed no tendency to cleave during hydrolysis but gave exclusively rearrangement products. Rabe believed that a definite relationship existed between the valence of the nitrogen atom and the type of hydrolysis and stated that, "the molecules with pentavalent nitrogen were adapted to hydrolytic rearrangement into basic keto-carboxylic acids." In the present work this specific rearrangement has been extended to include the transformation of narcotine (and hydrastine) quaternary salts into the acid salts of narceine (and methylhydrasteine) esters, amide and free acid by the action of HA reagents where A is OR, NH_2 or OH.

Freund and Michaels[4] prepared narceinamide by dissolving narcotine methiodide (I) in a little water and allowing this solution to stand in a liter of alcoholic ammonia for several days. A copious quantity of the amide, m. p. 178°, insoluble in water but soluble in alcohol crystallized out. The mechanism of the reaction was assumed to consist in the formation of a methine (II) by the abstraction of hydrogen iodide, followed by the addition of ammonia to form an unsaturated amide and finally the rearrangement of this compound into the stable, saturated narceinamide (III).



An attempt to repeat this experiment failed, and since the conditions, as stated, were very indefinite, it was decided to pass gaseous ammonia through a boiling solution of the methiodide in absolute ethyl alcohol. While standing overnight at room temperature the solution deposited

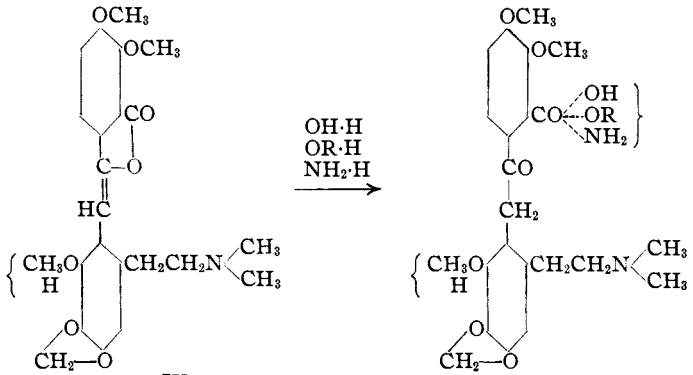
(4) Freund and Michaels, *ibid.*, **286**, 248 (1895).

crystalline material identical with the ethyl ester of narceine hydriodide prepared by the treatment of the ethyl ester of narceine hydrochloride with an aqueous solution of potassium iodide. If it is surmised that this reaction took place by the opening of the two heterocyclic rings of the narcotine methiodide molecule, followed by the mutual linkage of the central pair of free bonds and the addition of the addenda H and OR of the alcohol to the N and C atoms at the ends of the chain thus formed, it is then evident that the reaction mixture used by Freund contained no less than three compounds capable of addition to such a system, *i. e.*, H–OR, H–OH, H–NH_2, which would produce the hydrohalides, respectively, of the ester of narceine, of narceine itself (hydrolyzed to narceine under the conditions of the experiment) and narceinamide. All these compounds have now been produced by various modified procedures and it became necessary to investigate the conditions under which the rings could be opened, the circumstances under which one or other HA compound would add and the general nature of the addition of HA compounds to narcotine methyl salts, $C_{22}H_{23}NO_7 \cdot CH_3X$, to produce salts of narceine derivatives, $C_{22}H_{26}NO_6(COA)HX$.

By continued boiling with distilled water it was found possible to convert the methochloride and methyl methosulfate of narcotine into narceine but it was necessary to use dry ammonia to aid the conversion with the alcohols of the narcotine methohalides into narceine ester hydrohalides. The transformation of narcotine methiodide into narceine methyl ester hydriodide was also brought about by the addition of glacial acetic acid to the methyl alcoholic solution previous to refluxing. This series of conversions under increasingly acidic conditions is contrary to the conception of the elimination of hydrogen iodide in the presence of a base postulated in the Freund mechanism or typical Hofmann degradation.

Methylnarcotine and methylhydrastine, the unsaturated intermediates formulated in the Freund mechanism, were prepared and their conversion into narceine, methylhydrasteine and their derivatives was studied. In that methylnarcotine is difficult to prepare and to purify, the behavior of the unsaturated lactone system was studied more thoroughly by an extended investigation of the more stable analogous methylhydrastine.[5] These methines (IV) were hydrolyzed on treatment with dilute aqueous alkali, the esters were formed by refluxing them with absolute alcohol in the presence of gaseous ammonia and heating with 28% ammonium hydroxide produced the amides. On the other hand, with the pure methylhydrastine and its hydriodide no change was noted on continued refluxing with water, refluxing with alcohols for five days nor on treatment with liquid ammonia. It would therefore seem that the lactone ring is only opened in a strongly alkaline medium. This lactone ring is common to methylnarco-

(5) Schmidt, *Arch. Pharm.*, **231**, 576 (1893).

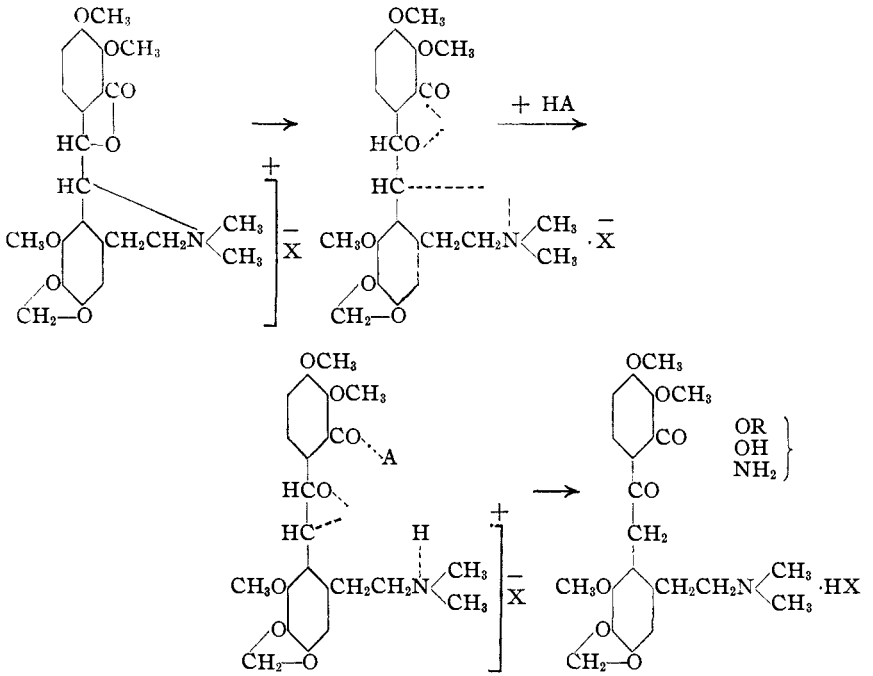


IV

tine, methylnarcotine hydriodide and narcotine methiodide and its stability on the one hand contrasted with its ease of cleavage on the other would lend support to the assumption that the opening of the lactone ring is conditioned by the instability of the remainder of the molecule. This stability in neutral media of the methines which are postulated as intermediates in the Freund mechanism and of the hydriodides which might be formed in the course of the reaction lends further support to the conception, in the proposed alternative mechanism, of a highly unstable intermediate formed by the opening of the two rings of the quaternary ammonium compound in the presence of a polar solvent.

Freund's mechanism of the reaction, involving the use of ammonia and dependent on the elimination of hydrogen iodide, postulates a tertiary amine as a final product whereas experimentally salts are formed except that on the addition of water the salt is hydrolyzed to the free base. These findings, in addition to the difficulty of explaining the transformation of narcotine methyl salts (particularly that of the methyl sulfate which takes place in acidic solution) into narceine by boiling with water, the above-mentioned conversion of narcotine methiodide into narceine methyl ester hydriodide by refluxing with methyl alcohol in the presence of glacial acetic acid, and the known hydrolytic rearrangement of narcotine into nornarceine in the presence of dilute acetic acid led to the devising of another mechanism. Its essential points are these: the opening of the two heterocyclic rings under the influence of a polar solvent without the removal of the H atom in the β position to the N atom as postulated in the Freund mechanism; the addition of the component A to the C atom of the CO group and the maintenance of the positive nature of the ammonium radical by the addition of the positive H ion of the polar solvent to form a new positive radical and finally, the internal compensation of the two central bonds by a 1–2 H shift giving a stable desoxybenzoin structure. By this mechanism as generalized in the following diagram (X = I, Cl, CH_3SO_4; A = OH, NH_2, OR where R = Me, Et, *i*-Pr and Bu) the formation of the hydro-

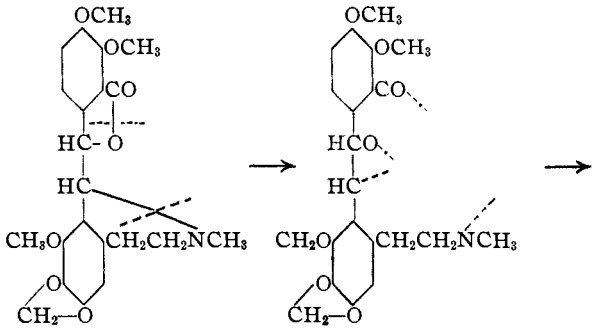
halides of the esters, amide and acid of narceine by the action of alcohols, ammonia and water on narcotine alkyl salts is readily explained.



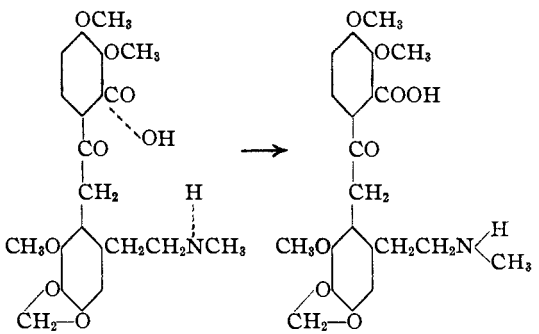
The general nature of the reaction was investigated by the conversion of the methiodide, methochloride and methyl methosulfate of narcotine into the corresponding hydrohalides and methyl hydrosulfates of the esters of narceine by refluxing with the requisite absolute alcohol in the presence of dry ammonia; into the salts of narceinamide by treatment with liquid ammonia, and into narceine by boiling with water. It was found that the reaction between narcotine methyl salts, $C_{22}H_{23}NO_7 \cdot CH_3X$ (X = I, Cl, CH_3SO_4) and HA compounds (A = OH, NH_2 and OR where R = Me, Et, *i*-Pr and *n*-Bu) produces salts of narceine derivatives, $C_{22}H_{26}NO_6$-(COA)HX. The hydrohalide salts of narceine are easily hydrolyzed and so the addition of water to the opened ring system of narcotine methiodide resulted in the elimination of hydrogen iodide and the consequent formation of narceine. The addition of a basic alcohol and the degradation of the postulated ammonium salt to a tertiary amine was demonstrated by the behavior of diethylaminoethyl alcohol as an HOR compound in producing the diethylaminoethyl ester of narceine.

This series of transformations is in agreement with the hydrolysis of narcotine in the presence of acetic acid to form nornarceine. Here the opening of the rings in the presence of a polar solvent and internal com-

pensation by a 1–2 shift form a system to which the addenda OH and H may add to yield the predicted compound as illustrated in the diagram



Narcotine



Nornarceine

The lack of an external ion to unite with the β H atom prevents the application of Freund's mechanism to this particular transformation.

An interesting application of the conversion of a quaternary ammonium compound of narcotine into a derived narceine, similar to the formation of dibenzoylbulbocapnine from bulbocapnine[6] was made by the transformation of the benzoyl chloride addition compound of narcotine into benzoylnornarceine.

Our thanks are due to Mr. Douglass F. Hayman for the microanalyses reported in this paper.

Experimental

Conversion of Narcotine Methyl Salts into Narceine.—Narcotinemeth*iodide* dissolved in water containing a trace of pyridine was completely converted into narceine, m. p. 176–178°. identical with a sample of narceine obtained from opium,[7] when the solution was refluxed for two hours. When an attempt was made to add diethylaminoethyl alcohol to the methiodide the salt was recovered unchanged but contaminated with traces of the basic alcohol. When this material was heated with water in an attempt to recrystallize the iodide it was converted into narceine. Narcotine metho*chloride* was transformed into narceine when refluxed with distilled water for six hours.

(6) Barger and Girardet, *Helv. Chim. Acta*, **14**, 484 (1931).

(7) Hope and Robinson, *J. Chem. Soc.*, **105**, 2100 (1914).

Narcotine methyl *methosulfate* produced by the heating of 6 g. of narcotine with 2 g. of dimethyl sulfate in a stoppered flask was boiled for thirty hours with water. The cold solution was filtered and rapidly neutralized with ammonia. Acetic acid was then added to slight acidity and the dense precipitate which formed was recrystallized from boiling water and identified as narceine by conversion into the hydrochloride, m. p. 192°, and chloroplatinate, m. p. 195–196°.[8]

The Action of Alcohols on Narcotine Methyl Halides.—Attempts to cleave narcotine methyl halides and form the esters of narceine hydrohalides in the absence of organic bases or of ammonia were fruitless. The deeply colored iodide solutions became colorless during the refluxing operation but it was not found possible to isolate crystalline materials from the end-products. By refluxing the requisite narcotine quaternary ammonium salt with an absolute alcohol in the presence of a slow stream of dry ammonia the salt was gradually converted into the salt of a narceine ester. The general nature of the reaction was shown by the preparation of the methyl esters of narceine hydrochloride, hydriodide and methosulfate, the ethyl ester of narceine hydrochloride and hydriodide in addition to the isopropyl and butyl esters of narceine hydriodide. In the case of the preparation of narceine ethyl ester hydriodide the experiment was repeated in 95% alcohol with a result similar to that when absolute alcohol was employed. On refluxing the iodide in 90% alcohol saturated with ammonia quantitative conversion of the salt into narceine took place. Narcotine methiodide was transformed into narceine methyl ester hydriodide by refluxing it for twelve hours with methyl alcohol containing glacial acetic acid.

ESTERS OF NARCEINE HYDROHALIDES

Formula	M. p., °C.	Analyses, % Calcd. C	Calcd. H	Found C	Found C	Found H	Found H
$C_{23}H_{26}(CH_3)NO_8 \cdot HI$[a]	181–182	49.06	5.11	49.08	49.25	4.81	5.24
$C_{23}H_{26}(CH_3)NO_8 \cdot HCl$[b]	150–151						
$C_{23}H_{26}(CH_3)NO_8 \cdot CH_3HSO_4$	213–214	52.54	5.78	52.53	52.70	5.79	5.75
$C_{23}H_{26}(C_2H_5)NO_8 \cdot HI$	212–213	49.92	5.33	50.03	50.05	5.21	5.40
$C_{23}H_{26}(C_2H_5)NO_8 \cdot HCl$[c]	208–210						
$C_{23}H_{26}(C_3H_7)NO_8 \cdot HI$	224–225	50.73	5.53	50.69	50.64	5.45	5.30
$C_{23}H_{26}(C_4H_9)NO_8 \cdot HI$[d]	185–186	51.51	5.71	51.47	51.47	5.45	5.65

[a] Identified by mixed melting point determinations with a specimen prepared by heating the methyl ester of narceine hydrochloride, produced by the esterification of narceine with methyl alcohol in the presence of hydrochloric acid, with aqueous potassium iodide. [b] Converted into the hydriodide on treatment with hot aqueous potassium iodide solution. Previously obtained by Freund and Frankforter, *Ann.*, **277**, 31 (1893). [c] Identified by mixed melting point determinations with material prepared by the direct esterification of narceine according to the method of Freund and Frankforter,[b] and also by conversion into the hydriodide by heating with aqueous potassium iodide. [d] Recrystallization from methyl alcohol yielded a product containing alcohol of crystallization which parted with the alcohol on heating at 120° for thirty minutes and gave a white crystalline powder slightly soluble in water and very soluble in methyl alcohol.

The Action of Ammonia on Narcotine Methyl Halides. Narceinamide Hydriodide from $C_{22}H_{23}NO_7 \cdot CH_3I$ and Liquid Ammonia.—Narcotine methiodide (5 g.) was introduced into a 250-cc. long-necked Florence flask provided with a spiral tubulature of about twelve turns around the neck. The flask was connected with soda-lime and calcium chloride towers to prevent the entrance of moisture from the air. Ammonia dried by passage over soda-lime was passed into the flask which was then immersed in a mush

(8) Freund and Frankforter, *Ann.*, **277**, 20 (1893).

of solid carbon dioxide and ethyl alcohol. The flask was shaken at intervals until about 75 cc. of liquid ammonia was present and was then connected with guard tubes and allowed to stand in the hood until all the ammonia had evaporated. Recrystallization of the white granular solid remaining in the flask from hot water gave a microcrystalline material, softening on heating at 182° with evolution of gas, resolidifying and melting at 216–218° to a red gum.

Anal. Calcd. for $C_{23}H_{28}N_2O_7 \cdot HI$: C, 48.25; H, 5.07. Found: C, 48.04; H, 4.97.

This material was identical with the narceinamide hydriodide prepared by heating narceinamide with ammonium iodide in aqueous solution. Repeated recrystallization from boiling water yielded the more stable *narceinimide hydriodide*, in rhomboidal prisms, m. p. 228°.

Anal. Calcd. for $C_{23}H_{26}N_2O_6 \cdot HI$: C, 49.82; H, 4.88. Found: C, 49.93; H, 5.14.

The amide hydriodide was converted, by boiling in absolute methyl alcohol, into an imide hydriodide containing methyl alcohol of crystallization, thin platelets, m. p. 216° with decomposition.

Anal. Calcd. for $C_{23}H_{26}N_2O_6 \cdot HI \cdot CH_3OH$: C, 49.14; H, 5.29. Found: C, 49.02; H, 5.26.

Narceinamide Hydrochloride from $C_{22}H_{23}NO_7CH_3Cl$ and Ammonia.—By a repetition of the above procedure employing narcotine methochloride a white dry powder was formed which on crystallization from water gave hexagonal plates, m. p. 237°, of $C_{23}H_{28}N_2O_7 \cdot HCl$,[9] converted by treatment with potassium hydroxide into narceinamide.

Narceinamide from Narcotine Methyl Salts and 28% Ammonia.—(a) From $C_{22}H_{23}NO_7 \cdot CH_3$ by heating 20 g. of narcotine methiodide with a large excess of 28% ammonium hydroxide there was an almost immediate formation of about 10 g. of crude narceinamide and about 10 g. of narceine, melting at 178° and 176–178°, respectively, after recrystallization. (b) From $C_{22}H_{23}NO_7 \cdot (CH_3)_2SO_4$ by shaking the oily resin formed by heating 6 g. of narcotine with 2 g. of dimethyl sulfate together with an excess of cold 28% ammonium hydroxide a good yield of narceinamide was produced; recrystallized from benzene in large prisms, m. p. 178°.

Anal. Calcd. for $C_{23}H_{28}N_2O_7$: C, 62.16; H, 6.31. Found: C, 62.05; H, 6.24.

(c) **Narceinamide,** $C_{23}H_{28}N_2O_7 \cdot H_2O$.—To a solution of 25 g. of narcotine methiodide dissolved in 750 cc. of 96% alcohol was added 75 cc. of 28% ammonia. The mixture was heated until it was refluxing gently and 250 cc. more of 28% ammonia was gradually added. The solution was then boiled for one hour and after standing overnight deposited 18 g. of pale green crystalline material. Repeated crystallization from benzene and later from dilute alcohol gave the amide, containing water of crystallization, m. p. 178° (softening at 125° and resolidifying).

Anal. Calcd. for $C_{23}H_{28}N_2O_7 \cdot H_2O$: C, 59.74; H, 6.49; N, 6.06. Found: C, 60.06, 60.03; H, 6.36, 6.39; N, 6.11, 6.23.

Diethylaminoethyl Ester of Narceine, $C_{23}H_{26}(C_8H_{14}N)NO_8$.—On heating 5 g. of narcotine methiodide with an excess of diethylaminoethyl alcohol a red solution was formed which gave a precipitate when diluted with water. Recrystallization from methyl alcohol produced long prismatic crystals, halogen-free, m. p. 203°.

Anal. Calcd. for $C_{23}H_{26}(C_8H_{14}N)NO_8 \cdot CH_3OH$: C, 64.00; H. 7.33. Found: C, 64.23, 64.31; H, 7.53, 7.31.

The Reactions of Hydrastine Methyl Iodide

(a) **The Addition of HOH. Formation of Methylhydrasteine Hydriodide,** $C_{22}H_{25}NO_7 \cdot HI$.—From hydrastine methiodide[10] after refluxing with distilled water for two

(9) Freund and Michaels, *Ann.*, **286**, 248 (1895).

(10) Freund and Rosenberg, *Ber.*, **23**, 404 (1890).

hundred hours a crystalline material was isolated which on recrystallization from absolute ethyl alcohol melted at 216–217°. Previous to analysis the material was dried at 100° for one hour.

Anal. Calcd. for $C_{22}H_{26}NO_7I$: C, 48.62; H, 4.79. Found: C, 48.74, 48.69; H, 4.97, 4.71.

(b) **The Addition of Ammonia. The Action of Liquid Ammonia with Formation of Methyl Hydrastamide Hydriodide,** $C_{22}H_{26}N_2O_6 \cdot HI$.—Treatment of hydrastine methiodide with liquid ammonia yielded a crystalline compound, m. p. 233–235°. A mixed melting point determination with a sample of methylhydrastimide hydriodide,[11] m. p. 235–237° showed a depression to 231°.

Anal. Calcd. for $C_{22}H_{27}N_2O_6I$: C, 48.71; H, 4.98. Found: C, 48.96, 48.74; H, 4.81, 4.87.

To prevent confusion of this compound with a possible hydrated form of the corresponding imide, the material was dried at 105–115° for two hours.

Anal. Calcd. for 100 $H_2O/C_{22}H_{26}N_2O_6 \cdot HI$: 3.32. Found: 0.4.

Slight decomposition had evidently taken place but there was no change to the imide. Treatment of the hydriodide of the amide with dilute ammonia yielded methylhydrastimide, m. p. 192°, which had also been produced in an attempt to catalyze the hydrolysis of hydrastine methiodide by using extremely dilute ammonia. On recrystallization from aqueous ammonium iodide the imide was converted into microscopic cubical crystals of methyl hydrastimide hydriodide; m. p. 235–237°.

Anal. Calcd. for $C_{22}H_{25}N_2O_5I$: C, 50.38; H, 4.77. Found: C, 50.50, 50.53; H, 4.90, 5 05.

This was apparently the compound prepared by Schmidt[11] by the treatment of hydrastine methiodide with 10% ammonia in alcohol (probably 95%). The closeness of the melting points of the hydrohalides of the amide and the imide caused some confusion in differentiating between the two products and enhanced the difficulties at this period of the investigation.

Treatment of powdered hydrastine methiodide with 28% ammonia gave methyl hydrastamide, m. p. 180°,[12] which was also prepared by the continued agitation of methyl hydrastine with 28% ammonia and by the addition of 28% ammonia to a solution of methyl hydrastine in dioxane and water.

(c) **The Addition of HOR. Methylhydrasteine Ethyl Ester Hydriodide,** $C_{22}H_{24}(C_2H_5)NO_7 \cdot HI$.—Hydrastine methiodide was refluxed with absolute ethyl alcohol in a stream of ammonia for four hours. The crude crystalline material formed on the concentration of the solution was recrystallized three times from boiling water. It contained halogen and was difficult to burn; yellow rhomboidal platelets, m. p. 235–236°.

Anal. Calcd. for $C_{24}H_{30}NO_7I$: C, 50.44; H, 5.25. Found: C, 50.70, 50.42; H, 5.11, 5.05.

Methylnarcotine.—The procedure detailed by Rabe and McMillian[13] was carefully followed and from 4 liters of ether a canary yellow substance, m. p. 115°, was isolated. Attempts to repeat the preparation according to the method of Tambach and Jaeger[14] failed. The substance was converted into the known methylnarcotine methiodide, m. p. 260°[15] by warming together the two components.

Opening of the Lactone Ring.—(a) On attempting the addition of methyl iodide to the methine in the presence of methyl alcohol the lactone ring was opened and by the

(11) Schmidt, *Arch. Pharm.*, **231**, 576 (1893).
(12) Freund and Heim, *Ber.*, **23**, 2897 (1890).
(13) Rabe and McMillian, *Ann.*, **377**, 223 (1910).
(14) Tambach and Jaeger, *ibid.*, **349**, 185 (1906).
(15) Ref. 13, p. 257.

addition of H and the group CH_3O–, followed by ketonization to the desoxybenzoin structure, narceine methyl ester methiodide,[16] m. p. 211°, was formed. (b) Long continued boiling with water completely decolorized the yellow solution with the formation of narceine but since the unsaturated crude compound contained a little free base this may contribute to the cleavage. (c) Though this trace of free base may act in the conversion of the unsaturated compound to the methyl ester of narceine on refluxing with methyl alcohol, the transformation was more rapidly effected in the presence of dry ammonia. The ester was identified by freeing the reaction mixture from alcohol, taking up the residue in water and adding hydrochloric acid. Crystals of $C_{23}H_{26}(CH_3)NO_8 \cdot HCl$, m. p. 149°,[17] were formed. (d) Boiling the unsaturated compound with 28% ammonia gave narceinamide, m. p. 178°, after recrystallization from benzene.

Methylhydrastine. (a) **Hydrolysis.**—Although treatment with aqueous alkali gave methyl hydrasteine, m. p. 151–152°, no such change was found to have taken place after continued refluxing with distilled water. Eventually the compound decomposed and yielded a reddish-orange liquid from which, however, methyl hydrasteine could not be recovered.

(b) **Alcoholysis.**—By refluxing with methyl alcohol in the presence of dry ammonia for three to five hours white crystalline methyl hydrasteine methyl ester, $C_{22}H_{24}(CH_3)NO_7$, m. p. 175°, was formed.

Anal. Calcd. for $C_{23}H_{27}NO_7$: C, 64.34; H, 6.29. Found: C, 64.36, 64.38; H, 6.23. 6.31.

When refluxed with absolute alcohols no definite products were isolated. After five days the substance began to decompose, the solution gradually changing in color from greenish-yellow to red. By dissolving the methine in aqueous alcohol Schmidt[18] prepared methylhydrasteine ethyl ester (m. p. 95–96°) together with methylhydrasteine. Not only did the repetition of this experiment with the pure methine fail to give these results but on refluxing the unsaturated compound with absolute ethyl alcohol in the presence of ammonia there was produced an ester, m. p. 194–195°; chloroplatinate, m. p. 210° (dec.), identical with that derived from methylhydrasteine ethyl ester hydriodide, m. p. 194–195°; mixed m. p. 194–195°.

Anal. Calcd. for $C_{24}H_{29}NO_7$: C, 65.01; H, 6.55. Found: C, 65.30, 65.18; H, 6.84, 6.69.

(c) **Ammonolysis.**—Heating with 28% ammonium hydroxide yielded methylhydrastamide, m. p. 180°, but treatment with liquid ammonia gave no reaction and the methine was recovered unchanged.

Methylhydrastine Hydriodide.—The base was dissolved in an excess of 57% hydriodic acid from which the hydriodide crystallized out on standing. After air drying the material was recrystallized from very dilute ethyl alcohol in small rod-like prisms; m. p. 257–258°. It was moderately soluble in hot water but difficultly soluble in ethyl alcohol.

Anal. Calcd. for $C_{22}H_{23}NO_6 \cdot HI$: C, 50.23; H, 4.57. Found: C, 50.00; H, 4.66.

(a) **Hydrolysis.**—Continued refluxing for twelve hours of an aqueous solution caused no alteration. The solution was evaporated and the crystalline material was recovered unchanged in appearance and melting point.

Anal. Calcd. for $C_{22}H_{23}NO_6 \cdot HI$: C, 50.23; H, 4.57. Found: C, 50.32; H, 4.72.

(b) Alcoholysis.—No change was noted after continuous refluxing with absolute ethyl alcohol. The very dilute solution yielded unchanged material. On bubbling

(16) Freund, *Ber.*, **40**, 194 (1907).
(17) Freund and Frankforter, *Ann.*, **277**, 31 (1893).
(18) Schmidt, *Arch. Pharm.*, **228**, 243 (1890).

dry ammonia through the alcoholic suspension the hydriodide gradually dissolved. After refluxing for six hours the alcohol was removed *in vacuo*. The dry amorphous material was powdered, air dried and on recrystallization from dilute ethyl alcohol yielded yellow rhomboidal platelets of methylhydrasteine ethyl ester hydriodide, m. p. 235–236°, identical with the compound previously described.

(c) **Ammonolysis.**—About 0.5 g. of the finely divided recrystallized hydriodide was suspended in 50 cc. of liquid ammonia. The mixture was allowed to stand protected from moisture until all the ammonia had slowly evaporated. The material was recovered unchanged.

Anal. Calcd. for $C_{22}H_{23}NO_6 \cdot HI$: C, 50.23; H, 4.57. Found: C, 50.47; H, 4.77.

Benzoylnornarceine.—A solution of narcotine in benzoyl chloride was heated for two hours on the steam-bath and was then treated with 10% sodium hydroxide. An oil formed which soon solidified and later dissolved to give an orange solution. This was neutralized with dilute acetic acid and yielded a solid insoluble in water. Recrystallization from a mixture of methyl alcohol and water gave a white crystalline compound, $C_{29}H_{29}NO_9 \cdot CH_3OH$, m. p. 174–175°.

Anal. Calcd. for $C_{30}H_{33}NO_{10}$: C, 63.49; H, 5.82. Found: C, 63.50, 63.65; H, 5.92, 6.00.

Summary

1. A mechanism is advanced to account for the formation of narceine, and the hydriodides of the ethyl ester of narceine and narceinamide in the course of the preparation of narceinamide by the action of alcoholic ammonia on narcotine methyl iodide.

2. This mechanism has been extended to the conversion of narcotine and hydrastine derivatives to those of narceine and methylhydrasteine, and the hydrolysis of narcotine to nornarceine.

3. Experiments in support of the mechanism have led to the production of the hydrohalides of several esters of narceine and of narceinamide and the hydriodides of methylhydrasteine, its amide and ethyl ester.

4. The transformations of methylnarcotine, methylhydrastine and its hydriodide in the presence of water, ethyl alcohol and ammonia have been studied.

5. Benzoylnornarceine has been prepared.

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