The Mechanism of Reductive Cleavage Reaction of 2, 3-Dimethyl-3-cyanomethylindolenine

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(Received December 1, 1958)

Hoshino and Tamura[1] observed the unexpected formation of 2, 3-dimethylindole(II) by the reduction of 2, 3-dimethyl-3-cyanomethylindolenine(Ia) with sodium and ethanol.

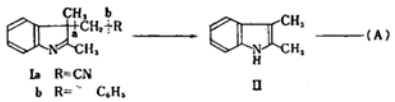

Fig. 1

Recently, we have reported[2] a conversion of 3-alkyl-2, 3-dimethylindolenines into 2, 3-dimethylindole by means of acid, and proposed a mechanism which could not be applied to the explanation of the mechanism of Hoshino's reaction mentioned above.

In some cases, the reductive cleavage of $-CH_2CN$ to CH_3 was reported[3]; however, a search of the literature failed to find analogous reaction[4] to Hoshino's reductive cleavage by the action of sodium and ethanol.

The study of elucidation of the mechanism of this novel reductive cleavage reaction was undertaken with the hope that this might lead to some bits of information which would be able to be applied to the structure determination of the indole alkaloids.

The simplest, but not so attractive, explanation would be the hydrogenolysis of bond a (Fig. 1). Since in many instances, a benzyl group is noticed to be split off very easily under various reductive conditions, 2,3-dimethyl-3-benzylindolenine(Ib) was treated with sodium and ethanol as a model experiment. But, as would be expected, 2, 3-dimethyl-3-benzylindoline, instead of II, was obtained from the reaction mixture, simply as the result of the reduction of indolenine double bond.

To examine another possible route, which would be initiated by an attack of ethoxide anion (Fig. 2. mechanism B), Ia was treated with sodium ethoxide in ethanolic solution.

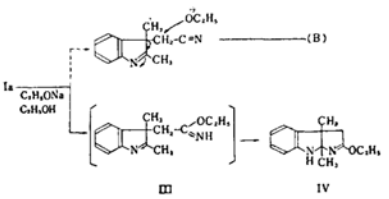

Fig. 2

It was unsuccessful to detect any trace of II, but a crystalline compound, m. p. 148~

1) T. Hoshino and K. Tamura, *Ann.*, **500**, 46 (1933).

2) M. Nakazaki, S. Isoe and K. Tanno, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **76**, 1262 (1955).

3) J. J. Bloch, *Chem. Zentr.*, III, 609 (1919); see also R. B. Wagner and H. D. Zook, "Synthetic Organic Chemistry", John Wiley and Sons, Inc., New York (1953), p. 659.

4) In the case of indole compounds, the vulnerability of bond b (Fig. 1) is noticed, e. g., F. C. Uhle and L. S. Harris, *J. Am. Chem. Soc.*, **79**, 103 (1957); H. R. Snyder and D. S. Mattson, ibid., **79**, 2217 (1957); E. Lecte and L. Marion, *Can. J. Chem.*, **31**, 775 (1953).

149°C, was isolated, the molecular formula of which corresponded to Ia plus one molecule of ethanol. This compound could be prepared also by the action of ethanolic hydrochloric acid onto Ia, and was given the structure IV by the observation of I. R. (see, experimental part) and U. V. spectrum (Fig. 7).

The failure of the conversion of Ia into II only by means of sodium ethoxide indicated that course B must be ruled out, and the reductive condition seems to be imperative for the change Ia→II.

The fact that it was found possible for the compound IV, in turn, to afford II by the action of potasium and *tert*-butanol, led to the conclusion that Ia is not the only compound capable of undergoing Hoshino's reaction. This was confirmed further by the isolation of II, when sodium was added to the ethanolic solution of the indolenine ester V, prepared from Ia by the alcoholysis with ethanol and concentrated sulfuric acid.

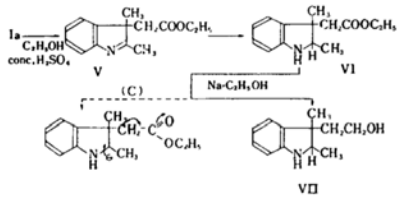

Fig. 3

The complexity encountered in the case of Ia suggested that the compound V appeared to be more suitable than Ia for the further study of Hoshino's reaction[5]. Having two reducible groups in the molecule, at the initial stage of the reaction, the compound V would be attacked by a reduction reagent either on the indolenine nucleus or on the side chain.

If the former is the case, the intermediate compound will be the compound VI which would give II, according to the mechanism C shown on Fig. 3. But VI, prepared by catalytic hydrogenation[6] of V with platinum oxide in acetic acid failed to afford II with sodium ethoxide or potassium *tert*-butoxide[7]. The reduction of VI with sodium and ethanol did not afford II either, but an alcohol VII was the sole product isolable from the reaction mixture. This alcohol was proved to be identical with the one prepared from VI by the lithium aluminum hydride reduction.

Thus, mechanism C had to be abandoned, and another conceivable route in which the reduction reagent would attack the side chain first was to be sought. To examine this possibility, an attempt was made to prepare the possible intermediate IX.

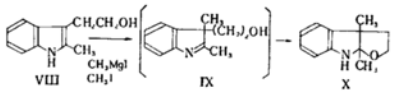

Fig. 4

The reaction of the Grignard complex of VIII with methyl iodide afforded a crystalline product, m. p. 51.5~52.5°C, to which the structure X[8] was assigned because of the lack of OH band but the presence of NH band in its I. R. spectrum, coupled with its indoline type absorption in the U. V. region (Fig. 7). This material again failed to give II, under the Hoshino's condition.

These observations lead one to conclude that: 1. the compounds of the general structure XI[9] (Fig. 5, where X is electronegative atom, such as oxygen or nitrogen.), furnish 2,3-dimethylindole with sodium and alcohol; 2. reduction reagent attacks simultaneously[10] the unsaturated bond of indolenine nucleus and the one on the side chain.

The most plausible mechanism, D, is shown on Fig. 5. A 1,4-biradical XII,

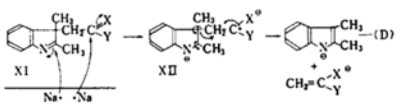

Fig. 5

5) Upon catalytic hydrogenation, V gave the compound VI as the result of the hydrogenation of the indolenine double bond, but in the case of Ia the side chain also would be reduced at the same time.

6) H. L. Holmes, H. T. Openshaw and R. Robinson, *J. Chem. Soc.*, **1946**, 910.

7) The formation of a small amount of *tert*-butyl ester by *tert*-butanolysis was presumed by effervescence of the crude picrate of recovered ester observed at its melting point.

8) T. Hoshino and K. Shimodaira (*Ann.*, **520**, 19 (1935)) succeeded in preparing the first compound which has the same skeleton as X, but they could decide whether their compound has the skeleton IX or X. Since our compound was established to have the structure X (3a, 8a-dihydro-3a,8a-dimethyl-2-furo [2.3-b] indole), their compound is 3a, 8a-dihydro-3a-methyl-2-furo [2.3-b] indole. See the nomenclature in "The Ring Index", by A. M. Patterson and L. T. Capell, Reinhold Pub. Corp., (1940), p. 198.

9) Under the reaction condition, the compound IV would be safely assumed to be converted back to III, which would be cleaved to give II. This causes a shift of equilibrum, and eventually all of IV would be transformed to II.

10) Though not necessarily at the very same instance, the reduction of one of two functional groups should not exceed the other, otherwise it would give either VI or X which can not give II.

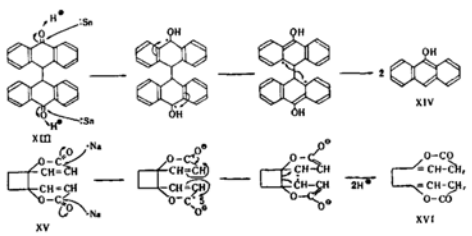

Fig. 6

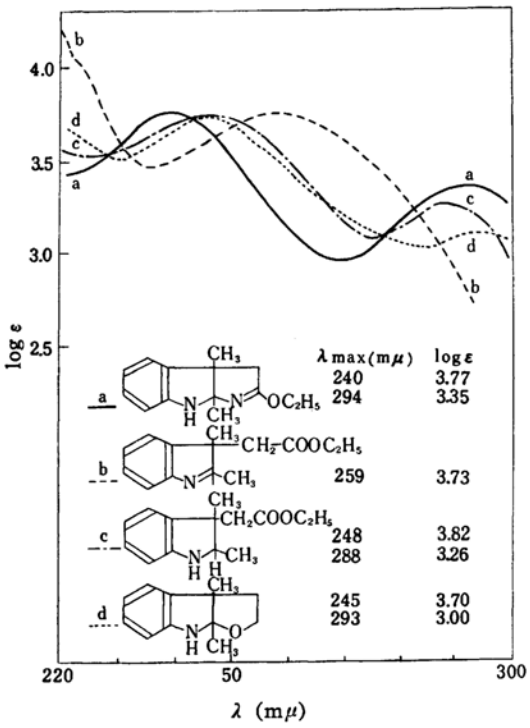

Fig. 7

which is caused by a nucleophilic attack[11] of the electron from sodium, is unstable[12] and suffered cleavage of bond a by the electron migration as indicated with arrows, resulting in end products.

According to this mechanism, in the case of Ia, the side chain split off is probably acetonitrile, which would be reduced further to give ethylamine. The actual isolation of ethylamine as the form of ethyloxamide from the reaction mixture of Hoshino's reaction of Ia, will support this mechanism.

The reductive cleavage of dihydrodianthrone(XIII) to anthrone(XIV)[13] with tin and acetic acid containing hydrochloric acid, and the conversion of anemonine (XV) into dihydroanemonine(XVI)[14] with sodium amalgam and acetic acid in methanolic solution appear to follow the analogous reaction pattern. (Fig. 6).

The driving force of the reaction could be sought in the steric strain of cyclobutane ring in the case of XV, and the tendency to aromatize into stable indole structure would play an important rôle in promoting Hoshino's reaction.

Experimental[15]

2,3-Dimethyl-3-cyanomethylindolenine(Ia).—Ia was prepared following Hoshino and Tamura's procedure[1]. Attempts were made to improve the yield by using methyl bromide in place of the ethyl iodide used in their synthesis or employing "reversed Grignard synthesis". The best result was obtained when chloroacetonitrile was added rather rapidly. Grignard solution prepared from 1.2 g. of magnesium and 8.0 g. of methyl iodide in 30 cc. of absolute ether was cooled and 7.3 g. of 2,3-dimethylindole in 35 cc. of ether was added dropwise onto it.

After the generation of methane subsided, the reaction mixture was stirred for 10 min. at room temperature and refluxed on a water bath for another 30 min. When 4.0 g. of chloroacetonitrile[16] was added during 5 min. into the cooled solution, a yellow viscous precipitate was observed on the wall of the reaction vessel.

After the solution was allowed to stand for 20 min. at room temperature, it was refluxed for 30 min. The Grignard complex was decomposed by the addition of 6 g. of acetic acid and 200 cc. of ice water, and the reaction mixture was thoroughly extracted with ether. Basic material was extracted by shaking with 2 N hydrochloric acid solution from the combined ether extract, and was precipitated from the solution as yellow oil by the addition of excess of 4 N sodium hydroxide solution. The oil was extracted with ether, and the ether extract was washed with water and dried over magnesium sulfate. Evaporation of

11) As for the action of sodium on organic compounds, see an excellent article by A. J. Birch, *Quart. Rev.*, **4**, 69 (1950).

12) R. C. Fuson, "Advanced Organic Chemistry", John Wiley and Sons, New York (1953), p. 72.

13) E. de Barry Barnett and M. A. Mathews, *J. Chem. Soc.*, **123**, 380 (1923).

14) Y. Asahina and R. Fujita, *J. Pharm. Soc. Japan* (*Yakugaku Zasshi*), **448**, 471 (1919); ibid., **455**, 1 (1920). The position of the double bonds of dihydroanemonine (XVI) deduced by this mechanism agrees with the one established by their experimental results.

15) All melting points are uncorrected. All U. V. spectra were measured with an EPS-2 Hitachi Autorecording Spectrophotometer and I. R. spectra on a Perkin Elmer Model 12C. The analyses were performed in the microanalytical laboratory of the Institute of Polytechnics, Osaka City University.

16) Since trimethylbenzene recommended as solvent is not easily accessible, the procedure described in "Organic Syntheses" (Vol. **30**, 22 (1950)) was simplified as follows. An intimate mixture of finely powdered chloroacetamide (1 mol.) and phosphorus pentoxide (2.5 mol.) was placed in oil bath heated at 200~220°C beforehand, and the resulting chloroacetonitrile was distilled off at 80~100 mm. collected in a receiver chilled by a freezing mixture. Purification by further distillation gave a yield of 76%. ("Organic Syntheses": 61~70%).

the solvent furnished a yellow viscous residue which gave 2.6 g of Ia (28% yield), b. p. 140~145°C/1 mm. (literature[1]: b. p. 150°C/1 mm., 15% yield).

This compound has a characteristic odor of indolenine compound and solidified on standing to give m. p. 75~76°C after sublimation in vacuo.

Anal. Found: C, 78.41; H, 6.69; N, 15.17. Calcd. for $C_{12}H_{12}N_2$: C, 78.23; H, 6.57; N, 15.21%.

The picrate was recrystallized to give yellow crystals, m. p. 175~178°C. (literature[1]: 177~178°C).

Anal. Found: N, 16.99. Calcd. for $C_{12}H_{12}N_2 \cdot C_6H_3O_7N_3$: N, 16.94%.

2,3-Dimethyl-3-benzylindoline.—To a stirred solution of 1.8 g. of Ib in 25 cc. of absolute ethanol, 2.1 g. of sodium was added in five portions. After the sodium disappeared, water was added and the reaction mixture was extracted with ether. The ether extract gave, after removal of the solvent, 1.8 g. of crystals which melted at 80~82°C after recrystallization from ethanol-water. I. R. spectrum[17]: 3.10 μ (NH). U. V. spectrum[17]: λ_{max} 273 mμ (log ε 3.35) in ethanol.

Anal. Found: C, 85.86; H, 8.10. Calcd. for $C_{17}H_{19}N$: C, 86.03; H, 8.07%.

The picrate was recrystallized to yield yellow needles, m. p. 177~179°C.

Anal. Found: C, 58.86; H, 4.87. Calcd. for $C_{17}H_{19}N \cdot C_6H_3O_7N_3$: C, 59.22; H, 4.75%.

1,2-Dehydro-2-ethoxy-9-methyldinordesoxyeseroline (IV).—*By the action of ethanolic hydrochloric acid on Ia.*—A solution of 4.35 g. of Ia in 45 cc. of absolute ethanol was cooled at −10°C, and saturated with dry hydrogen chloride. After the solution was kept at room temperature overnight, ethanol was removed by distillation in vacuo, and the residue was neutralized with 5% sodium carbonate solution to afford crystals, m. p. 151~152°C (4.2 g.) after recrystallization from water-ethanol. I. R. spectrum: 3.2 μ (NH), 6.33 μ (CN). U. V. spectrum: λ_{max} 240 mμ (log ε 3.77), 294 mμ (log ε 3.35) in methanol.

Anal. Found: C, 72.85; H, 7.70; N, 12.25. Calcd. for $C_{14}H_{18}ON_2$: C, 73.01; H, 7.80; N, 12.17%.

The picrate was recrystallized to give yellow needles, m. p. 174~175°C.

Anal. Found: C, 52.95; H, 4.96; N, 15.09. Calcd. for $C_{14}H_{18}ON_2 \cdot C_6H_3O_7N_3$: C, 52.28; H, 4.61; N, 15.25%.

By the action of sodium ethoxide on Ia.—To a solution of sodium ethoxide prepared from 0.2 g. of sodium and 20 cc. of absolute ethanol, 0.38 g. of Ia was added with 1 cc. of ethanol. After the solution was refluxed for 1 hr., the reaction mixture was subjected to steam distillation, but 2,3-dimethylindole could not be detected in the steam distillate.

The residue of the steam distillation afforded a pale yellow precipitate which was purified by recrystallization from ethanol-water to give crystals, m. p. 148~149°C, undepressed m. p. on admixture with that prepared by the method described above.

Reductive Cleavage of IV with Potassium and *tert*-Butanol.—To a solution of 0.8 g. of IV in 30 cc. of *tert*-butanol, 1.8 g. of potassium was added in small portions. After the solution was refluxed on a water bath for 2 hr., the reaction mixture was subjected to steam distillation. The crystals which separated on the condenser weighed 0.2 g., and melted at 101~104°C after recrystallized from petroleum ether (b. p. 50~70°C). This compound was proved identical with 2,3-dimethylindole by the mixed m. p. (101~103°C) with an authentic specimen (m. p. 104~105°C).

Anal. Found: C, 82.81; H, 7.42; N, 9.41. Calcd. for $C_{10}H_{11}N$: C, 82.72; H, 7.64; N, 9.65%.

Ethyl 2,3-Dimethylindolenine-3-acetate (V).—Ia (4.6 g.) was ethanolyzed by boiling with 20 cc. of 94% ethanol and 10 cc. of concentrated sulfuric acid for 8 hr. The cooled reaction mixture was poured onto a stirred solution of 40g. of sodium carbonate in 100 cc. of water and 100 cc. of ether which formed an upper layer. The ether extract, after being washed with water and dried over magnesium sulfate, was concentrated to give a yellow brown liquid which was distilled to afford 4.2 g. of pale yellow viscous oil with green-yellowish fluorescence, b. p. 120~130°C/6 mm. I. R. spectrum: 5.75 μ (ester carbonyl), 6.30 μ (indolenine C=N). U. V. spectrum: λ_{max} 259 mμ (logε 3.75), λ_{min} 235 mμ (log ε 3.49) in ethanol.

Anal. Found: N, 6.01. Calcd. for $C_{14}H_{17}O_2N$: N, 6.06%.

The picrate was recrystallized to furnish yellow needles, m. p. 141~143°C.

Anal. Found: C, 52.47; H, 4.61; N, 12.22. Calcd. for $C_{14}H_{17}O_2N \cdot C_6H_3O_7N_3$: C, 52.17; H, 4.38; N, 12.17%.

Reductive Cleavage of V.—To a solution of 0.589 g. of V in 13 cc. of absolute ethanol, 1.0 g. of sodium was added in three portions as rapidly as the capacity of the condenser allowed, and after the disappearence of sodium the solution was heated on a water bath for 30 min. To the reaction mixture, 20 cc. of water was added and ethanol was removed to give a turbid solution from which a crystalline material (0.14 g.) precipitated. After recrysallization from petroleum ether (b. p. 50~70°C), this crystal showed m. p. 97~100°C, the identity of which with 2,3-dimethylindole was established by mixed m. p. determination with an authentic sample. Its picrate melted at 152~153°C alone and admixed with an authentic specimen.

Ethyl 2,3-Dimethylindoline-3-acetate (VI).—On catalytic hydrogenation of V (2.1 g.) with 69 mg. of platinum oxide in 10 cc. of acetic acid, the theoretical hydrogen up-take was completed after 2 hr. After the catalyst was filtered, the filtrate was poured onto a solution of 20 g. of sodium carbonate in 150 cc. of water, and extracted with ether. The ether extract,

17) Cf. M. Nakazaki and S. Isoe, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nipon Kagaku Zasshi*), **76**, 1161 (1955).

18) After the nomenclature of "The Ring Index", p. 196, this can be named as 3a, 8a-dihydro-1,2-dehydro-2-ethoxypyrrolo [2.3-b] indole.

after removal of the solvent, afforded a pale yellow oil, which gave 1.64 g. of (78% yield) VI, b. p. 153~154°C/6 mm. No fluorecence was observed. I. R. spectrum: 2.95 μ (NH), 5.76 μ (ester carbonyl). U. V. spectrum: λ_{max} 288 mμ (log ε 3.26), 248 mμ (log ε 3.82) in ethanol.

Anal. Found: C, 70.96; H, 8.24; N, 5.84. Calcd. for $C_{14}H_{19}O_2N$: C, 72.07; H, 8.21; N, 6.00%.

The picrate was recrystallized from ethanol to give yellow needles, m. p. 153°C.

Anal. Found: C, 51.95; H, 4.85; N, 12.12. Calcd. for $C_{14}O_{19}O_2N \cdot C_6H_3O_7N_3$: C, 51.95; H, 4.80; N, 12.12%.

The Action of Potassium *tert*-Butoxide on VI.—To a solution of potassium *tert*-butoxide prepared from 0.08 g. of potassium and 6 cc. of *tert*-butanol, a solution of 0.33 g. of VI in 2 cc. of *tert*-butanol was added. After the reaction mixture was heated for 1 hr. on a water bath, the solvent was removed under reduced pressure. After the residue was dissolved in water and saturated with sodium chloride, the solution was extracted with ether. The ether extract was shaken with 2 N hydrochloric acid solution to separate neutral and basic fractions. From the ether layer, after the usual work-up, there could not be detected anything but a faint smell of *tert*-butanol. The hydrochloric acid solution was made strongly basic, and the separated oily material was extracted with ether. The ether extract gave, after evaporation of the solvent, 0.25 g. of liquid which was converted into picrate directly. The crude picrate melted at 145~151°C with a little effervescence, but after two more recrystallizations from ethanol, its m. p. was 152~153°C and proved identical with the picrate of VI.

The Action of Sodium on the Ethanolic Solution of VI.—To a solution of 0.47 g. of VI in 9 cc. of absolute ethanol, 0.7 g. of sodium was added in three portions. After the sodium disappeared, the solvent was removed on a water bath, and water was added to the residue. The basic and neutral fractions were separated as mentioned above. From the neutral fraction, no 2,3-dimethylindole was found. The basic fraction gave 0.221 g. of a pale yellow liquid which afforded a yellow prismatic picrate melting at 152~154°C after recrystallization from ethanol. The mixed m. p. with the picrate of VII (m. p. 151~153°C) was 151~154°C.

Anal. Found: C, 51.84; H, 5.16; N, 13.23. Calcd. for $C_{12}H_{17}ON \cdot C_6H_3O_7N_3$: C, 51.42; H, 4.80; N, 13.33%.

β-(2, 3-Dimethylindolinyl)-ethanol (VII).—To a suspension of 0.15 g. of lithium aluminum hydride on 20 cc. of absolute ether, a solution of 0.909 g. of VI in 10 cc. of ether was added dropwise over a period of 30 min. After the reaction mixture was heated on a water bath for 1 hr., the excess of the reduction reagent was destroyed by the addition of ethyl acetate, and the resulting white voluminous precipitate was dissolved in 2N sodium hydroxide. Continuous extraction with ether (10 hr.) gave, after removal of the solvent, 0.635 g. of a viscous liquid, which was distilled at 136~145°C (air bath temperature) under 3 mm. to yield 0.53 g. of viscous oil. This solidified to give colorless needles, m. p. 100~101°C, after recrystallization from ethanol-petroleum ether.

Anal. Found: C, 75.63; H, 9.14; N, 7.38. Calcd. for $C_{12}H_{17}ON$: C, 75.35; H, 8.96; N, 7.32%.

The picrate was recrystallized to produce yellow crystals, m. p. 151~153°C.

2-Methyltryptophol (VIII).—To a slurry of 1.75 g. lithium aluminum hydride in 130 cc. of absolute ether, a mixture of 10 g. of ethyl 2-methylindole-3-acetate[19] in 50 cc. of ether was added dropwise at such a rate as to keep the ether boiling.

Stirring and refluxing was continued for 30 min., and 15 cc. of ethyl acetate was added to destroy the excess of the reduction reagent followed by the addition of dilute sulfuric aid. The aqueous layer was thoroughly extracted with ether, and ether extract was washed with water and dried over anhydrous magnesium sulfate. After the removal of the solvent, the ether extract gave a viscous liquid, which was purified by distillation in vacuo resulting in 6.0 g. of liquid (75% yield), b. p. 143~144°C/10^{-3} mm.[20]

3a, 8a-Dihydro-3a, 8a-dimethyl-2-furo(2.3-b)-indole (X).—A solution of 5 g. of VIII in 30 cc. of ether was added dropwise onto a stirred cold Grignard solution prepared from 2.08 g. of magnesium and 15.3 g. of ethyl iodide in 15 cc. of ether.

After being kept at room temperature for about 20 min., the reaction mixture was refluxed on a water bath for 1 hr. To this solution 9.3 g. of methyl iodide was added during 3 hr., and the mixture was kept at room temperature overnight. The Grignard complex was decomposed with acetic acid and water, and extracted with ether. From the ether extract the basic material was transferred into 1 N hydrochloric acid. The oily material, liberated by the addition of 2 N sodium hydroxide solution to the hydrochloric acid extract, was again extracted with ether. Distillation of the residue, after evaporation of ether, at a reduced pressure gave 0.94 g. of viscous oil, b. p. 125~126°C/5 mm.

This compound solidified gradually, and recrystallization from petroleum ether (b. p. 50~70°C) gave prismatic crystals, m. p. 51.5~52.5°C. I. R. spectrum: 3.00 μ (NH). U. V. spectrum: λ_{max} 245 mμ (log ε 3.7), 293 mμ (log ε 3.0).

Anal. Found: C, 76.29; H, 8.26. Calcd. for $C_{12}H_{15}ON$: C, 76.15; H, 7.99%.

The picrate gave yellow prisms from ethanol, m. p. 137~139°C.

Anal. Found: C, 52.01; H, 4.61; N, 13.39. Calcd. for $C_{12}H_{15}ON \cdot C_6H_3O_7N_3$: C, 51.67; H, 4.34; N, 13.39%.

The Action of Sodium on the Ethanolic Solution of X.—One gram of sodium was added in three portions to a solution of 0.26 g. of X in

19) M. V. Bulloch and S. W. Fox, *J. Am. Chem. Soc.*, **73**, 5156 (1951).

20) T. Hoshino and K. Shimodaira, *Ann.*, **520**, 19 (1935) prepared this alcohol by the Bouveault-Blanc reduction in a yield of 32%, b. p. 198°C/3.5 mm. and m. p. 55~56°C.

20 cc. of absolute ethanol. After the reaction was complete, water was added to the reaction mixture and saturated with sodium chloride. The solution was thoroughly extracted with ether, but the test of 2,3-dimethylindole was negative on the small amount of residue remaining after removal of the solvent.

Reductive Cleavage of Ia. Isolation of Ethylamine.—In a 100 cc. three-necked flask, provided with an inlet tube for dry nitrogen, a reflux condenser carrying a glass tubing which reached the bottom of a Erlenmeyer flask containing 10 cc. of 4 N hydrochloric acid solution, and an inlet tude for sodium, were placed 2.09 g. of Ia and 45 cc. of absolute ethanol. While nitrogen from a cylinder was passed through the flask, 3.5 g. of sodium was added in five portions as rapidly as the capacity of the condenser allowed. Volatile material was swept with nitrogen gas into the hydrochloric acid solution. After completion of the reaction, cooling water for the condenser was cut off, and about 5 cc. of ethanol was distilled through the condenser into the Erlenmeyer flask contaning the acid solution. Another 15 cc. of ethanol was distilled into the same receiver by the usual downward distillation.

Water was added to the residue which remained in the three-necked flask and the turbid solution was distilled with steam. From the distillate, 0.5 g. of 2, 3-dimethylindole was obtained, and identified by mixed m. p. determination with an authentic sample and as in the form of picrate.

The hydrochloric acid solution containing the basic material, was concentrated in vacuo to give a crystalline product which was soluble completely in absolute ethanol. The amine generated by the addition of 10 cc. of 4 N sodium hydroxide solution onto the above mentioned amine hydrochloride, was distilled with water into a flask containing 0.2 g., of diethyl oxalate and 1 cc. of water. The crystals separated from the cold solution, were washed with a small amount of cold water and dried in a desiccator to give 10 mg. of colorless needles, m. p. 178~179°C, which did not depress the mixed m. p. with an authentic sample of ethyloxamide (m. p. 178~180°C[21]). Their I. R. spectra could overlap in every respect.

Anal. Found: C, 50.28; H, 8.85: N, 19.40. Calcd. for $C_6H_{12}O_2N_2$: C, 49.98; H, 8.39; N, 19.43%.

On a control experiment using the same method, 65 mg. of ethyloxamide was isolated by the reduction of 600 mg. of acetonitrile with sodium-ethanol.

The author is very gratiful to Messrs. Kohei Tanno, Masaru Tamura and Munesuke Sato for their skillful technical assistance.

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21) S. P. Mulliken, "A Method for the Indentification of Pure Organic Compounds," Vol. II, John Wiley Inc., New York (1922), p. 132.