[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Rearrangement of α-Aminoketones during Clemmensen Reduction. V. Influence of Alkyl Substitution on the α-Carbon[1,2,3]

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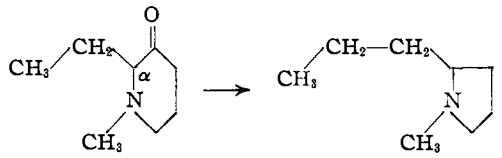
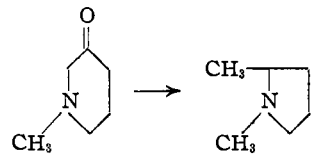
In all previously observed Clemmensen reduction–rearrangements of α-aminoketones, for which the conversion I to II is representative,[3b] the α-carbon has been substituted with one alkyl or alkylene group.[3,4] In order to determine the influence, if any, of α-alkyl substitution on the course of the Clemmensen reduction of α-aminoketones, a series of 1-methyl-3-piperidones has been studied in which the α-carbon was unsubstituted, monoalkyl-substituted, and dialkyl-substituted, The Clemmensen reduction of all of these six-membered ring compounds was found to be accompanied by rearrangement, with the formation of pyrrolidines.



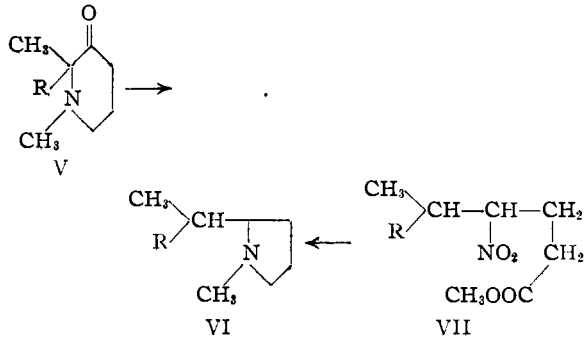
I II

The unsubstituted compound, 1-methyl-3-piperidone (III), which was prepared by the Dieckmann ring-closure method utilized by McElvain and his co-workers,[5,6] underwent conversion to 1,2-dimethylpyrrolidine (IV) in 60% yield when subjected to Clemmensen reduction conditions. The identity of the reduction–rearrangement product was established by direct comparison of its picrate and chloroplatinate with the corresponding derivatives of an authentic sample[7] of 1,2-dimethylpyrrolidine. Wolff–Kishner reduction of III led to the formation of the normal product, 1-methylpiperidine.



III IV

The reduction–rearrangement of a monoalkyl-substituted 1-methyl-3-piperidone, the 2-ethyl compound (I), has already been reported[3b]: 1-methyl-2-*n*-propylpyrrolidine (II) was obtained in 71% yield by the reduction of I under Clemmensen conditions. As an example of a dialkyl-substituted 1-methyl-3-piperidone, the compound 1,2,2-trimethyl-3-piperidone (Va) was subjected to Clemmensen reduction. The rearranged product, 1-methyl-2-isopropylpyrrolidine (VIa), was obtained (in at least 54% yield) and was identified by comparison of its picrate and methiodide with the corresponding derivatives of an authentic sample of VIa. The 1-methyl-2-isopropylpyrrolidine used for the comparison was obtained by the reductive cyclization (hydrogen and copper chromite) of methyl γ-nitroisoheptanoate (VIIa).[8] Similar reductive cyclizations accompanied by N-alkylation have been observed previously in this Laboratory.[3b,8] Wolff–Kishner reduction of Va gave the normal product, 1,2,2-trimethylpiperidine. The preparation of 1,2,2-trimethyl-3-piperidone (Va) was accomplished by a conventional series of reactions, illustrated by VIIIa through Va.



V VI VII

a, R = CH_3; b, R = C_2H_5

While it is a reasonable assumption that the length of the alkyl group attached to the α-carbon atom should not appreciably influence the course of the Clemmensen reduction of α-alkyl- and α,α-dialkyl-α-aminoketones, nevertheless it seemed worthwhile to test another representative of each type. Accordingly, 1,2-dimethyl-2-ethyl-3-piperidone (Vb) was subjected to Clemmensen reduction conditions. Rearrangement again accompanied reduction, and the product, formed in at least 50% yield, was identified as 1-methyl-2-*s*-butylpyrrolidine (VIb). The synthesis of 1,2-dimethyl-2-ethyl-3-piperidone (Vb) was realized by the same series of reactions (VIIIb → Vb) which led to the formation of the homologous

(1) This investigation was supported in part by a grant from the Research Board of the University of Illinois.

(2) The material in this paper was presented at the 116th National Meeting of the American Chemical Society in Atlantic City, New Jersey, September 20, 1949.

(3) For previous papers in this series, see: (a) Leonard and Wildman, THIS JOURNAL, **71**, 3089 (1949); (b) Leonard and Ruyle, *ibid.*, **71**, 3094 (1949); (c) Leonard and Barthel, *ibid.*, **71**, 3098 (1949); (d) Leonard and Wildman, *ibid.*, **71**, 3100 (1949).

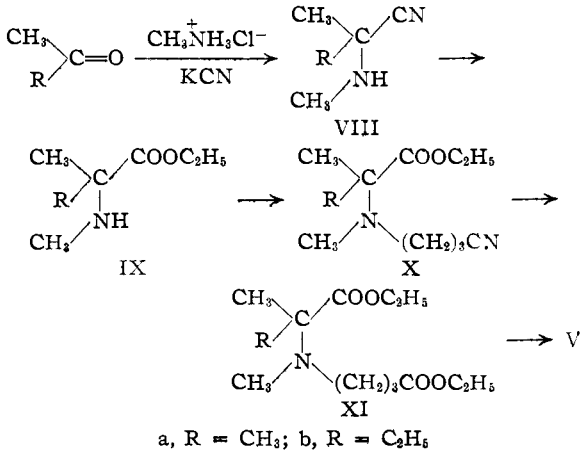
(4) For leading references, see (a) Clemo, Cook and Raper, *J. Chem. Soc.*, 1318 (1938) and (b) Clemo, Raper and Vipond, *ibid.*, 2095 (1949). From the latter reference it is apparent that Clemo and his co-workers have returned to their interesting investigation of this type of anomalous Clemmensen reduction.

(5) Prill and McElvain, THIS JOURNAL, **55**, 1233 (1933).

(6) McElvain and Vozza, *ibid.*, **71**, 896 (1949).

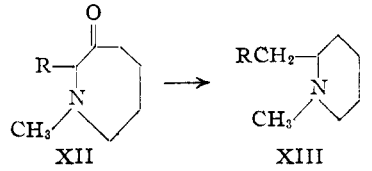
(7) Adams and Mahan, *ibid.*, **64**, 2588 (1942).

(8) Leonard and Beck, *ibid.*, **70**, 2504 (1948).



a, R = CH_3; b, R = C_2H_5

compound, Va. The conversion of 1-methyl-2-ethyl-1-azacycloheptan-3-one (XIIb) to 1-methyl-2-*n*-propylpiperidine (XIIIb) was reported pre-



a, R = CH_3; b, R = C_2H_5

viously,[3c] and it has been established now that the compound with an α-methyl group in place of the α-ethyl group, 1,2-dimethyl-1-azacycloheptan-3-one (XIIa), is similarly rearranged under Clemmensen conditions to give 1-methyl-2-ethylpiperidine (XIIIa).[9,9a]

Experimental[10]

Ethyl Methylaminoacetate.—The method of Staudt[11] was used to prepare the hydrochloride of ethyl methylaminoacetate. A solution of the salt in water was made strongly basic by the slow addition of a saturated solution of potassium hydroxide. The filtered solution was extracted with ether, the ethereal solution was dried, the ether was removed, and the product was distilled *in vacuo*, b. p. 50–55° (17 mm.); $n^{20}D$ 1.4150.

Carbethoxymethyl-γ-cyanopropylmethylamine.—A vigorously stirred mixture of 65.0 g. (0.55 mole) of ethyl methylaminoacetate, 56.9 g. (0.55 mole) of γ-chlorobutyronitrile and 89.5 g. (0.65 mole) of finely powdered potassium carbonate was heated at 100° for twenty-four hours. The cooled reaction mixture was treated with 350 ml. of water, and the whole was extracted with three 100-ml. portions of chloroform. After drying and removal of the solvent, the product was distilled, b. p. 107–108° (1.5 mm.); $n^{21}D$ 1.4440; yield, 76.6 g. (75%).

Anal. Calcd. for $C_9H_{16}N_2O_2$: C, 58.67; H, 8.76; N, 15.21. Found: C, 58.80; H, 8.86; N, 15.35.

The **picrate**, formed in ether and recrystallized from 95% ethanol, separated as bright yellow prisms, m. p. 106.5–107.5°.

Anal. Calcd. for $C_{17}H_{19}N_5O_9$: C, 43.58; H, 4.63; N, 16.95. Found: C, 43.80; H, 4.70; N, 16.97.

Carbethoxymethyl-γ-carbethoxypropylmethylamine.—The ethanolysis of the cyanoester described above was accomplished by the method which was effective for the preparation of the homologous α-carbethoxypropyl-δ'-carbethoxybutylmethylamine[3c]; b. p. 110° (1.3 mm.); $n^{20}D$ 1.4382; yield, 70%.

1-Methyl-3-piperidone (III).—The hydrochloride, m. p. 108–110° (reported, 110–111°),[5] was obtained by the usual method of Dieckmann ring-closure[5] followed by hydrolysis of the intermediate with hydrochloric acid.[3c]

Wolff–Kishner Reduction of 1-Methyl-3-piperidone. 1-Methylpiperidine.—A mixture of 3.0 g. (0.02 mole) of 1-methyl-3-piperidone hydrochloride, 4.2 g. (0.074 mole) of potassium hydroxide, 30 ml. of triethylene glycol, and 3 ml. of 85% hydrazine hydrate was refluxed for one hour. The reaction mixture was then distilled while the bath temperature was maintained at 230°. The distillate was extracted with three 20-ml. portions of ether. The residue from the dried ether extracts was distilled at 107–108° (750 mm.); $n^{26}D$ 1.4273; yield, 0.89 g. (45%). The **picrate**, m. p. 149.5–150° (reported for 1-methylpiperidine picrate, 148°[12]), and **chloroplatinate**, m. p. 193–194° (reported for 1-methylpiperidine chloroplatinate, 194°[12]), were made in the usual manner.

Clemmensen Reduction of 1-Methyl-3-piperidone. 1,2-Dimethylpyrrolidine (IV).—Zinc amalgam was prepared by shaking 40 g. of mossy zinc, 4 g. of mercuric chloride, 4 ml. of concentrated hydrochloric acid, and 40 ml. of water for five minutes. The amalgam was washed with distilled water, and 5.4 g. (0.036 mole) of 1-methyl-3-piperidone hydrochloride in 40 ml. of concentrated hydrochloric acid was added to the metal. The mixture was caused to reflux gently and, at two-hour intervals, 15-ml. portions of concentrated hydrochloric acid were added, and after four hours, an additional 20 g. of zinc amalgam was added. Heating was stopped after twelve hours and the solution was concentrated *in vacuo*. The cooled residue was made strongly basic by the addition of a saturated solution of potassium hydroxide, and the alkaline mixture was subjected to steam distillation. The distillate was acidified and evaporated to dryness under reduced pressure, the residue was made alkaline by addition of a saturated solution of potassium hydroxide, and the basic solution was extracted with ether. After drying, the ether was removed through a six-inch, helices-packed column, and the basic product was collected at 93–96° (750 mm.); $n^{20}D$ 1.4246. The best yield obtained was 60%. The **picrate** of the base, formed in ether solution and recrystallized from ethanol, was obtained as yellow needles, m. p. 230°.

Anal. Calcd. for $C_{12}H_{16}N_4O_7$: C, 43.90; H, 4.91; N, 17.07. Found: C, 43.88; H, 5.01; N, 17.33.

The melting point of a mixture of an authentic sample of 1,2-dimethylpyrrolidine[7] picrate (m. p. 229°) and the picrate of the Clemmensen reduction product showed no depression. The **chloroplatinate** was formed by mixing a hydrochloric acid solution of the reduction product with an aqueous solution of chloroplatinic acid. The orange

(9) The Clemmensen reduction results of Clemo, Raper and Vipond[4b] on 1-methyl-2-acetylpiperidine have been duplicated in this Laboratory (Barthel, Ph.D. Thesis, University of Illinois, 1949), and we offer our corroboration of their results in that we also have isolated methyl-*n*-heptylamine as one of the reduction products. It was identified by direct comparison of its picrate, m. p. 96.5–97°, and chloroplatinate, m. p. 174–175°, with the corresponding derivatives of a sample of methyl-*n*-heptylamine made from methylamine and *n*-heptyl iodide.

(9a) ADDED IN PROOF.—It will be noted that Leonard and Ruyle[3b] reported different behavior for 1-methyl-2-propionylpyrrolidine under Clemmensen conditions from that found by Clemo, Raper and Vipond[4b] for the homologous 1-methyl-2-acetylpyrrolidine. This discrepancy has now been resolved by Clemo and Vipond (*Chem. and Ind.*, 856 (1949)), who have shown that the isomeric 5-ethyl-3,4-trimethyleneoxazolidine, rather than 1-methyl-2-propionylpyrrolidine, results from the preparative method of Hess (*Ber.*, **46**, 4104 (1913)), which was followed in this laboratory.[3b] Accordingly, it appears that Leonard and Ruyle[3b] were operating on an oxazolidine rather than an aminoketone, and certain conclusions[3b] based upon the behavior of this compound as an α-aminoketone are therefore invalidated.

(10) All melting points are corrected.

(11) Staudt, *Z. physiol. Chem.*, **146**, 286 (1925).

(12) Haase and Wolffenstein, *Ber.*, **37**, 3228 (1904).

needles melted at 196–198° and the melting point was not depressed on admixture with the chloroplatinate prepared from an authentic sample of 1,2-dimethylpyrrolidine.[7]

In order to test the action of hydrochloric acid alone on 1-methyl-3-piperidone, a solution of 1.0 g. of the amino-ketone hydrochloride in 20 ml. of concentrated hydrochloric acid was refluxed for eight hours. Additional 5-ml. portions of acid were added after the second and fifth hour. Evaporation under reduced pressure left a viscous red residue which was recrystallized from acetone-ethanol. The crystalline product was shown to be 1-methyl-3-piperidone hydrochloride by melting point and mixed melting point; recovery, 0.88 g. (88%).

α-Methylaminoisobutyronitrile (VIIIa).—The general procedure of Immendörfer[13] was used. To a cooled and vigorously stirred mixture of 169 g. (2.5 moles) of methylamine hydrochloride in 200 ml. of water and 550 ml. (7.5 moles) of acetone was added slowly a solution of 168 g. (2.5 moles) of potassium cyanide in 350 ml. of water. When the addition was complete, the mixture was stirred at room temperature for nine hours. The organic layer was separated, and three 100-ml. portions of chloroform were used to extract the aqueous layer. After drying the combined extracts, the solvent was removed and the product was distilled under reduced pressure; b. p. 54° (18 mm.), 133° (747 mm.); $n^{20}D$ 1.4176; yield, 138.9 g. (57%).

Anal. Calcd. for $C_5H_{10}N_2$: C, 61.18; H, 10.27. Found: C, 61.43; H, 10.35.

α-Methylamino-α-methylbutyronitrile (VIIIb).—The same method[13] applied to methyl ethyl ketone gave α-methylamino-α-methylbutyronitrile in 83% yield; b. p. 66–68° (17 mm.); $n^{21}D$ 1.4282; N-benzoyl derivative, m. p. 82–83° (reported, 82°[13]).

Ethyl α-Methylaminoisobutyrate (IXa).—To 1 l. of cold absolute ethanol saturated with dry hydrogen chloride was added 81 g. (0.83 mole) of α-methylaminoisobutyronitrile. After standing at room temperature for two hours, the solution was heated under reflux for three hours. Ammonium chloride was removed by filtration and was washed with ethanol. Filtrate and washings were concentrated *in vacuo*, and the residue was taken up in 100 ml. of water. A solution of 120 g. of potassium hydroxide in 120 ml. of water was added slowly, and the organic product was extracted with five 100-ml. portions of chloroform. The residue after removal of the solvent yielded 20.0 g. (17%) of the colorless liquid, b. p. 51–53° (15 mm.); $n^{20}D$ 1.4185. The **hydrochloride** was prepared by passing dry hydrogen chloride into an acetone solution of the amino ester. Recrystallization from acetone gave colorless plates, m. p. 169.5–170.5°.

Anal. Calcd. for $C_7H_{16}ClNO_2$: C, 46.28; H, 8.88; N, 7.71. Found: C, 46.57; H, 9.02; N, 7.70.

Ethyl α-Methylamino-α-methylbutyrate (IXb).—The ethanolysis of 112 g. (1 mole) of α-methylamino-α-methylbutyronitrile by the same procedure gave 37.6 g. (24%) of IXb; b. p. 77–79° (19 mm.); $n^{22}D$ 1.4272.

Anal. Calcd. for $C_8H_{17}NO_2$: C, 60.34; H, 10.76; N, 8.80. Found: C, 60.17; H, 10.71; N, 8.96.

The **picrate** formed yellow prisms from water, m. p. 91.5–92.5°.

Anal. Calcd. for $C_{14}H_{20}N_4O_9$: C, 43.30; H, 5.19; N, 14.43. Found: C, 43.67; H, 5.35; N, 14.48.

α-Carbethoxy-α-methylethyl-γ'-cyanopropylmethylamine (Xa).—The method of synthesis was similar to that employed for the preparation of α-carbethoxypropyl-γ'-cyanopropylmethylamine.[3b] The product was obtained in 39% yield; b. p. 115–120° (1.5 mm.); $n^{20}D$ 1.4498.

Anal. Calcd. for $C_{11}H_{20}N_2O_2$: C, 62.23; H, 9.50; N, 13.20. Found: C, 62.43; H, 9.34; N, 13.48.

α-Carbethoxy-α-methylpropyl-γ'-cyanopropylmethylamine (Xb).—The condensation between IXb and γ-chlorobutyronitrile was effected in the same way; b. p. 125–130° (1.2 mm.); $n^{20}D$ 1.4483; yield, 50%.

(13) Immendörfer, *Ber.*, **48**, 605 (1915).

α-Carbethoxy-α-methylethyl-γ'-carbethoxypropylmethylamine (XIa).—Ethanolysis of Xa was carried out in the usual manner,[3b] and α-carbethoxy-α-methylethyl-γ'-carbethoxypropylmethylamine was obtained in 58% yield; b. p. 119–121° (1.2 mm.); $n^{20}D$ 1.4455.

Anal. Calcd. for $C_{13}H_{25}NO_4$: C, 60.20; H, 9.72; N, 5.40. Found: C, 60.33; H, 9.74; N, 5.63.

α-Carbethoxy-α-methylpropyl-γ'-carbethoxypropylmethylamine (XIb).—Ethanolysis of Xb gave a 38% yield of α-carbethoxy-α-methylpropyl-γ'-carbethoxypropylmethylamine; b. p. 122–125° (1.0 mm.); $n^{20}D$ 1.4451.

Anal. Calcd. for $C_{14}H_{27}NO_4$: C, 61.51; H, 9.96. Found: C, 61.64; H, 10.26.

1,2,2-Trimethyl-3-piperidone (Va).—The same general method of Dieckmann ring closure followed by hydrochloric acid hydrolysis which has been described previously[3b,5] was used for the preparation of 1,2,2-trimethyl-3-piperidone **hydrochloride** from XIa in 50% yield. The salt separated as colorless prisms when recrystallized from ethanol–ethyl acetate, m. p. 217–218°.

Anal. Calcd. for $C_8H_{16}ClNO$: C, 54.07; H, 9.08; N, 7.88. Found: C, 53.87; H, 9.06; N, 7.69.

The **picrate**, prepared in ether from the free base and recrystallized from ethanol, separated as yellow plates, m. p. 217.5–218.5°.

Anal. Calcd. for $C_{14}H_{18}N_4O_8$: C, 45.41; H, 4.90; N, 15.13. Found: C, 45.67; H, 5.15; N, 15.03.

1,2-Dimethyl-2-ethyl-3-piperidone (Vb).—The same general procedure was used for the preparation of 1,2-dimethyl-2-ethyl-3-piperidone **hydrochloride** from XIb in 46% yield. The salt separated as colorless needles from ethanol–ether, m. p. 151.5–152°.

Anal. Calcd. for $C_9H_{18}ClNO$: C, 56.38; H, 9.46; N, 7.31. Found: C, 56.65; H, 9.57; N, 7.47.

The **picrate** was obtained as yellow plates, m. p. 207.5–208.5°, from ethanol.

Anal. Calcd. for $C_{15}H_{20}N_4O_8$: C, 46.87; H, 5.25; N, 14.58. Found: C, 47.06; H, 5.23; N, 14.57.

The **picrolonate** was obtained as yellow prisms, m. p. 199.5–200°, from ethanol.

Anal. Calcd. for $C_{19}H_{25}N_5O_6$: C, 54.40; H, 6.01; N, 16.70. Found: C, 54.27; H, 6.01; N, 16.53.

Wolff–Kishner Reduction of 1,2,2-Trimethyl-3-piperidone. 1,2,2-Trimethylpiperidine.—The procedure followed for the reduction of 1-methyl-3-piperidone afforded a 74% yield of $C_8H_{17}N$ base, isolated as the **picrate**, which separated as small yellow prisms from ethanol; m. p. 273°, with decomposition (reported for 1,2,2-trimethylpiperidine picrate, m. p. 270°, with decomposition).[14]

Anal. Calcd. for $C_{14}H_{20}N_4O_7$: C, 47.19; H, 5.66; N, 15.72. Found: C, 47.21; H, 5.69; N, 15.53.

Reductive Cyclization of Methyl γ-Nitroisoheptanoate (VIIa). 1-Methyl-2-isopropylpyrrolidine (VIa).—A solution of 24.5 g. (0.13 mole) of methyl γ-nitroisoheptanoate[8] in 65 ml. of purified dioxane was hydrogenated at 260° and 250 atmospheres in the presence of 16 g. of copper chromite catalyst. The theoretical amount of hydrogen was absorbed in four and one-half hours. The dioxane was removed by distillation through a six-inch Fenske column and the product was collected at 138–140° (744 mm.); $n^{20}D$ 1.4376; yield, 6.3 g. (43%).

The **picrate**, formed in ether and recrystallized from ethanol, separated as yellow plates, m. p. 172–172.5°.

Anal. Calcd. for $C_{14}H_{20}N_4O_7$: C, 47.19; H, 5.66; N, 15.72. Found: C, 47.42; H, 5.87; N, 15.86.

The **methiodide** was prepared by warming the amine, 1-methyl-2-isopropylpyrrolidine, with methyl iodide. Recrystallization from acetone gave colorless prisms, m. p. 238–239°.

Anal. Calcd. for $C_9H_{20}IN$: C, 40.16; H, 7.49; N, 5.20. Found: C, 40.44; H, 7.77; N, 4.79.

(14) Lukes and Grossman, *Coll. Czechoslov. Chem. Commun.*, **8**, 533 (1936).

The **acid oxalate** was formed by combining the theoretical amounts of amine and oxalic acid in ethanol. After recrystallization from acetone, the colorless prisms melted at 90.5–91.0°.

Anal. Calcd. for $C_{10}H_{19}NO_4$: C, 55.28; H, 8.81; N, 6.45. Found: C, 55.48; H, 9.06; N, 6.32.

Clemmensen Reduction of 1,2,2-Trimethyl-3-piperidone.—Eight-tenths of a gram (0.0045 mole) of 1,2,2-trimethyl-3-piperidone hydrochloride was reduced with zinc amalgam and hydrochloric acid, as previously described, affording 0.86 g. (54% yield) of the **picrate** of a $C_8H_{17}N$ base, m. p. 172–172.5°, after recrystallization from ethanol.

Anal. Calcd. for $C_{14}H_{20}N_4O_7$: C, 47.19; H, 5.66; N, 15.72. Found: C, 47.33; H, 5.72; N, 15.74.

The melting point was not depressed when the picrate was mixed with 1-methyl-2-isopropylpyrrolidine picrate.

The **methiodide** of the reduction product was prepared by warming an ethereal solution of the amine with a small amount of methyl iodide. The solid derivative was recrystallized from acetone as slender, colorless prisms, m. p. 240–240.5°. The melting point was not depressed on admixture with 1-methyl-2-isopropylpyrrolidine methiodide.

Anal. Calcd. for $C_9H_{20}IN$: C, 40.16; H, 7.49; N, 5.20. Found: C, 40.44; H, 7.77; N, 4.90.

Clemmensen Reduction of 1,2-Dimethyl-2-ethyl-3-piperidone.—The reduction of 2.0 g. (0.01 mole) of 1,2-dimethyl-2-ethyl-3-piperidone hydrochloride with amalgamated zinc and hydrochloric acid led to a basic product which was isolated as the picrate in a yield of 1.93 g. (50%). The **picrate** was obtained as yellow needles from ethanol, m. p. 125.5–126°.

Anal. Calcd. for $C_{15}H_{22}N_4O_7$: C, 48.64; H, 5.99; N, 15.13. Found: C, 48.80; H, 6.11; N, 15.08.

The identity of the picrate as that of 1-methyl-2-*s*-butylpyrrolidine was confirmed by analogy to its homolog, by analysis, and by melting point (reported for 1-methyl-2-*s*-butylpyrrolidine picrate, m. p. 127°[15]).

α-Carbethoxyethyl-δ'-cyanobutylmethylamine.—A mixture of 24 g. (0.18 mole) of ethyl α-methylaminopropionate, b. p. 42–43° (7 mm.), $n^{20}D$ 1.4128 (obtained by treatment of α-methylaminopropionitrile[16] with ethanol and hydrogen chloride), 29.2 g. (0.18 mole) of δ-bromovaleronitrile and 25 g. (0.18 mole) of potassium carbonate was heated at 110–115° for twenty-four hours and the product was worked up in the usual manner[3c]; b. p. 125–127° (2.5 mm.); yield, 17.3 g. (45%).

Anal. Calcd. for $C_{11}H_{20}N_2O_2$: C, 62.23; H, 9.50; N, 13.20. Found: C, 61.99; H, 9.51; N, 13.11.

α-Carbethoxyethyl-δ'-carbethoxybutylmethylamine.—Ethanolysis of the cyanoester was carried out in the usual manner to give a 59% yield of the diester, b. p. 120–122° (0.5 mm.); $n^{20}D$ 1.4421.

Anal. Calcd. for $C_{13}H_{25}NO_4$: C, 60.20; H, 9.72; N, 5.40. Found: C, 60.19; H, 9.86; N, 5.33.

1,2-Dimethyl-1-azacycloheptan-3-one (XIIa).—Compound XIIa was obtained by the same procedure used for the preparation of the 2-ethyl homolog (XII b.).[3c] A 46% yield of crude hydrochloride was obtained. A **picrate**, made from an ethereal solution of the free base, crystallized from ethanol as yellow needles, m. p. 174°.

Anal. Calcd. for $C_{14}H_{18}N_4O_8$: C, 45.41; H, 4.90; N, 15.13. Found: C, 45.64; H, 4.99; N, 15.03.

Clemmensen Reduction of 1,2-Dimethyl-1-azacycloheptan-3-one.—The Clemmensen reduction of XIIa was carried out as described above, and the product was converted to the **picrate**, which was recrystallized from water; m. p. 174–175°. An authentic sample of 1-methyl-2-ethylpiperidine (XIIIa) was prepared by catalytic hydrogenation of 2-vinylpyridine in two steps to 2-ethylpiperidine followed by N-methylation. A picrate formed from this sample of 1-methyl-2-ethylpiperidine crystallized from water as yellow needles, m. p. 174.5–175° (reported 170–171°,[17] 175–176°,[18,19] 173°[4b]). Melting points of mixtures of the two picrates were not depressed.

(15) Men'shikov, *J. Gen. Chem.* (*U. S. S. R.*), **7**, 1632 (1937).

(16) Zelinsky, Annenkoff and Kulikoff, *Z. physiol. Chem.*, **73**, 459 (1911).

Summary

It has been established that Clemmensen reduction of 1-methyl-3-piperidones is accompanied by ring contraction no matter whether the 2-position (α-carbon) is unsubstituted, monoalkyl-substituted, or dialkyl-substituted.

(17) Hess and Corleis, *Ber.*, **54**, 3010 (1921).

(18) Lipp, *ibid.*, **33**, 3513 (1900).

(19) Heidrich, *ibid.*, **34**, 1889 (1901).

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Conversion of Ketone Enol Esters to β-Diketones by Intramolecular Thermal Rearrangement and by Intermolecular Acylations using Boron Fluoride

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Various ketone enol esters have been converted to β-diketones by passing the ester through a tube at 500°.[3] By recycling the enol ester, excellent yields (70–85%) of β-diketones have generally been obtained, the process being used for the commercial preparation of acetylacetone.

$$CH_3C(OCOCH_3)=CH_2 \xrightarrow{500^\circ} CH_3COCH_2COCH_3$$

(1) Carbide and Carbon Chemicals Corp. Fellow, 1949.

(2) Carbide and Carbon Chemicals Corp. Fellow, 1946–1948.

(3) Boese and Young, U. S. Patent 2,395,800 (1946); *C. A.*, **40**, 3130 (1946).

The conversion of the enol acetate of cyclohexanone to 2-acetylcyclohexanone by boron fluoride at low temperatures has also been reported,[4] but the details have not been available.

In the present investigation, evidence is presented that the thermal conversion involves an intramolecular rearrangement and the conversion by boron fluoride, an intermolecular acylation. The scope of the latter conversion has been extended considerably and certain analogous acylations

(4) Kastner, in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, p. 289.