The moment of the $(CH_3)_3Si{-}C_{aliph}$ group was evaluated from the moment of the dichloromethyltrimethylsilane by considering the moment of this compound to be the vector sum of the two C–Cl moments and the $(CH_3)_3Si{-}C_{aliph}$ moment each acting along the regular tetrahedral bond angle. In order to eliminate as far as possible the effect of inductive interaction of the two chlorine atoms, the moment of the $-CHCl_2$ group, 2.07 *D*, as measured in ethylidene chloride[5] and 1,1-dichloropropane[6] was used in the calculation. This moment was assumed to act along the bisector of the Cl–C–Cl angle. This vector, the resultant of the two C–Cl moment vectors, meets the $(CH_3)_3Si{-}C_{aliph}$ moment at an angle, β, such that

$$\cos \beta = \sqrt{\frac{2\cos^2 109°28'}{1 + \cos 109°28'}} = 0.5772$$

In this manner, a value of 0.32 *D* for the $(CH_3)_3Si{-}C_{aliph}$ group is obtained. While this is in fair agreement with the 0.25 *D* value calculated from the chloromethyltrimethylsilane, it is definitely higher. This can be attributed to the high polarizable character of the silicon atom already noted by Curran.[7] It should be noted that solvent effects, which tend to discredit the significance of dipole measurements performed on compounds in solution, are effectively eliminated by comparing compounds of similar structures measured in the same solvent. Compounds in which silicon is bonded to aromatic carbon may be expected to have varying moments,[4] reflecting the ease with which silicon can be electrically distorted. An investigation of organosilicons of this type is under way.

PITTSBURGH 13, PENNSYLVANIA

RECEIVED JANUARY 22, 1951

---

(5) A. A. Maryott, M. E. Hobbs and P. M. Gross, THIS JOURNAL, **63**, 659 (1941).

(6) P. Gross, *Physik. Z.*, **32**, 587 (1931).

(7) B. C. Curran, R. M. Witucki and P. A. McCusker, THIS JOURNAL, **72**, 4473 (1950).

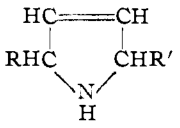
[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

The Structure of Alkyl-Substituted Pyrrolines[1]

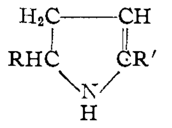
BY GORDON G. EVANS[2,3]

Two isomers each of 2-methyl-, 2,5-dimethyl- and 1,2,5-trimethylpyrroline have been prepared and characterized, and their structures have been established. Each pair of isomers differs only in the position of the double bond in the ring, and in one case the direct conversion of one isomer to the other has been demonstrated. The reduction of homologs of pyrrole with zinc and hydrochloric acid may lead to a mixture of pyrrolines containing the Δ^1- or Δ^2- as well as the Δ^3-isomer, although the product from the reduction of pyrrole itself is homogeneous.

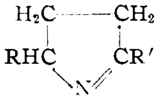
It has long been recognized that, for a pyrroline containing a particular carbon–nitrogen skeleton, various isomers are possible depending on the position of the double bond,[4] but previous work on the preparation of such isomers and the establishment of their structure has been limited to pyrrolines with an aromatic substituent[5] and 1,1-dimethylpyrrolinium salts.[6] The preparation of two isomers each of 2-methyl-, 2,5-dimethyl- and 1,2,5-trimethylpyrroline has now been accomplished.



Ia, $R = R' = H$
Ib, $R = CH_3$, $R' = H$
Ic, $R = R' = CH_3$



IIa, $R = R' = H$
IIb, $R = H$, $R' = CH_3$
IIc, $R = CH_3$, $R' = H$
IId, $R = R' = CH_3$



IIIa, $R = R' = H$
IIIb, $R = H$, $R' = CH_3$
IIIc, $R = CH_3$, $R' = H$
IIId, $R = R' = CH_3$

It has generally been assumed[4] that Δ^3-pyrrolines will be formed in the reduction of pyrroles by zinc and an acid (unless an aromatic substituent is present[5,7]) and this assumption has been verified by Treibs and Dinelli[8] for the unsubstituted compound (Ia). Pyrroline preparations involving closure of the ring, on the other hand, have been supposed to yield compounds with the Δ^2 structure (II) or its Δ^1 tautomer (III).[4,9] On very limited evidence, attempts have been made to establish generalizations differentiating the behavior of the two classes.[10,11] The present work necessitates some modification of these views.

2,5-Dimethylpyrrolines.—The reduction of 2,5-dimethylpyrrole by zinc and hydrochloric acid has been reported by Knorr and Rabe[12] and by Blaise[13] to yield a basic liquid boiling at 106° (736 mm.), whose picrate melts at 107° and which, on treatment with phenyl isocyanate, forms a phenylurea melting at 130°. The present writer, employing

---

(1) Most of the results reported in this paper are taken from a thesis submitted by Gordon G. Evans to the Faculty of Arts and Sciences of Harvard University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, August, 1949.

(2) National Research Council Predoctoral Fellow, 1946–1949.

(3) Department of Chemistry, Tufts College, Medford 55, Mass.

(4) G. Ciamician, *Ber.*, **34**, 3952 (1901).

(5) H. P. L. Gitsels and J. P. Wibaut, *Rec. trav. chim.*, **60**, 50 (1941); J. Dhont and J. P. Wibaut, *ibid.*, **63**, 81 (1944).

(6) R. Lukeš and J. Přeučil, *Coll. Czech. Chem. Comm.*, **10**, 384 (1938).

(7) A. Sonn, *Ber.*, **68B**, 148 (1935); *ibid.*, **72B**, 2150 (1939).

(8) A. Treibs and D. Dinelli, *Ann.*, **517**, 170 (1935).

(9) A. Wohl (*Ber.*, **34**, 1914 (1901)) has claimed the formation of a Δ^1-pyrroline by a ring-closure method, but he adduces no evidence in support of this structure.

(10) G. Ciamician, *ibid.*, **37**, 4246 (1904).

(11) L. Mascarelli and G. Testoni, *Gazz. chim. ital.*, **33II**, 312 (1903).

(12) L. Knorr and P. Rabe, *Ber.*, **34**, 3491 (1901).

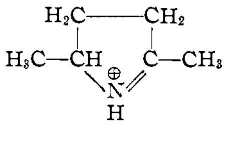
(13) E. E. Blaise, *Compt. rend.*, **158**, 1686 (1914); E. E. Blaise and A. Cornillot, *ibid.*, **178**, 1617 (1924).

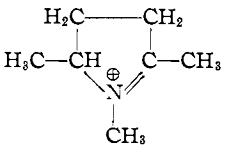
the modified method of Andrews and McElvain,[14] found the product to be a mixture consisting of about 80% of the above base and 20% of an isomeric base, b.p. 110–112°, whose picrate melts at 136° and whose phenylurea melts at 195–205°, depending on the rate of heating.

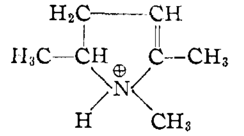
Ozonolysis of the mixture of bases according to Treibs and Dinelli[8] yielded a white solid unequivocally identified as *dl*-α,α'-iminodipropionic acid. Subsequently, the same compound was prepared by ozonolysis of the pure base regenerated from the picrate melting at 107°, and this base therefore has the Δ^3-structure (Ic), with the methyl groups *trans* to the plane of the ring. As would be expected on the basis of this formulation, it decolorizes bromine and potassium permanganate instantly in acid solution, it forms a normal benzoyl derivative in the Schotten–Baumann reaction, and, on treatment with methyl iodide, it yields 1,1,2,5-tetramethyl-Δ^3-pyrrolinium iodide. The infrared absorption spectrum of the carefully dried base shows a band at 3.02 μ which may be assigned to an N–H group (Curve 1). By treatment with Raney nickel in xylene, the compound is converted largely, if not entirely, to the isomeric higher-boiling base; the same change is effected to some extent by hydriodic acid. The latter process is particularly significant in view of the use of hydriodic acid to effect isomerizations in porphyrin derivatives.[15]

The base boiling at 110–112° also possesses the original carbon–nitrogen skeleton, as is shown by the hydrogenation experiments described below, and must therefore have one of the tautomeric structures, IId or IIId. Evidence for the latter is afforded by the infrared absorption spectrum of the carefully dried base, which shows no band at shorter wave lengths than the C–H band at 3.4 μ (Curve 2); hence there appears to be no hydrogen atom attached to nitrogen. The formation of such a structure by the reduction of a pyrrole with aliphatic substituents has not previously been reported.

This compound shows chemical behavior like that of the supposed 2-methyl-Δ^2-pyrroline first prepared by Hielscher[16] and investigated by Mascarelli and Testoni[11] and by Gabriel.[17] In acid solution, it decolorizes permanganate only after five minutes or thereabouts, decolorizes bromine only after an hour or more, and resists ozone for as much as eight hours.[18] Its benzoyl derivative must be formulated as 5-benzamidohexanone-2, $CH_3CH(NHCOC_6H_5)CH_2CH_2COCH_3$, as is shown by its analysis and by the presence in its infrared spectrum (Curve 3) of an absorption band at 5.88 μ which is ascribable to a free carbonyl group. (No such band appears in the spectrum of the benzoyl derivative of the Δ^3-isomer (Curve 4).) It reacts


IV


V


IV

with only one molecule of methyl iodide to give 1,2,5-trimethyl-Δ^1-pyrrolinium iodide[19] (V); this is decomposed by potassium hydroxide to yield 1,2,5-trimethyl-Δ^2-pyrroline, and the latter in turn reacts with another molecule of methyl iodide to form a crystalline substance which may be either 1,1,2,5-tetramethyl-Δ^2-pyrrolinium iodide or 1,2,-3,5-tetramethyl-Δ^1-pyrrolinium iodide.

For purposes of comparison, two of the ring-closure methods for the preparation of pyrrolines were adapted to the formation of the 2,5-dimethyl compound. Bases were obtained by treatment of γ-chlorovaleronitrile with methylmagnesium iodide,[20] and by the conversion of γ-bromovaleryl chloride to 5-bromohexanone-2 with dimethylcadmium, followed by the action of alcoholic ammonia.[16] Both products were identical with the above-described 2,5-dimethyl-Δ^1-pyrroline. Maginnity and Cloke[21] have recently concluded on chemical grounds that the Δ^1-structure is correct for pyrrolines prepared from chloronitriles.

Hydrogenation of the Δ^3-pyrroline over Adams catalyst yielded *trans*-2,5-dimethylpyrrolidine, while the *cis*-pyrrolidine was obtained from both 2,5-dimethylpyrrole and 2,5-dimethyl-Δ^1-pyrroline. Both *cis*- and *trans*-pyrrolidines have been prepared before,[22] but, because of the similarity of the boiling points of the bases and the melting points of the picrates, it was not recognized that they were different.

1,2,5-Trimethylpyrrolines.—The reduction of 1,2,5-trimethylpyrrole by means of zinc and hydrochloric acid leads to a mixture of bases which boils over a considerable range.[12] One of the bases obtained from this mixture, on treatment with methyl iodide, yielded a quaternary salt identical with the 1,1,2,5-tetramethyl-Δ^3-pyrrolinium iodide prepared from 2,5-dimethyl-Δ^3-pyrroline; this base is therefore 1,2,5-trimethyl-Δ^3-pyrroline. The other base, which was obtained in very small amount and in a state of doubtful purity, is probably identical with the 1,2,5-trimethyl-Δ^2-pyrroline mentioned above.

2-Methylpyrrolines.—The reduction of 2-methylpyrrole with zinc and hydrochloric acid

---

[14] L. H. Andrews and S. M. McElvain, THIS JOURNAL, **51**, 887 (1929).

[15] H. Fischer and H. Orth, "Die Chemie des Pyrrols," Vol. II, part 2, Leipzig, 1940, pp. 84, 168.

[16] R. Hielscher, *Ber.*, **31**, 277 (1898).

[17] S. Gabriel, *ibid.*, **42**, 1238 (1909); S. Gabriel and J. Colman, *ibid.*, **42**, 1243 (1909).

[18] This behavior speaks strongly in favor of the presence of a C=N link in the pyrrolinium ion, but cannot be used as an argument for the structure of the free base. Structure IV might well be formed by the addition of a proton to either IId or IIId.

[19] The double bond in this compound is unquestionably in this position, although the analogous 1,2-dimethylpyrrolinium iodide is formulated by Mascarelli and Testoni[11] as a Δ^2-structure. A substance of structure VI would be expected to undergo immediate further methylation, like the Δ^2 isomer.

[20] L. C. Craig, H. Bulbrook and R. M. Hixon, THIS JOURNAL, **53**, 1831 (1931); D. F. Starr, H. Bulbrook and R. M. Hixon, *ibid.*, **54**, 3971 (1932).

[21] P. M. Maginnity and J. B. Cloke, *ibid.*, **73**, 49 (1951).

[22] M. de Jong and J. P. Wibaut, *Rec. trav. chim.*, **49**, 237 (1930).

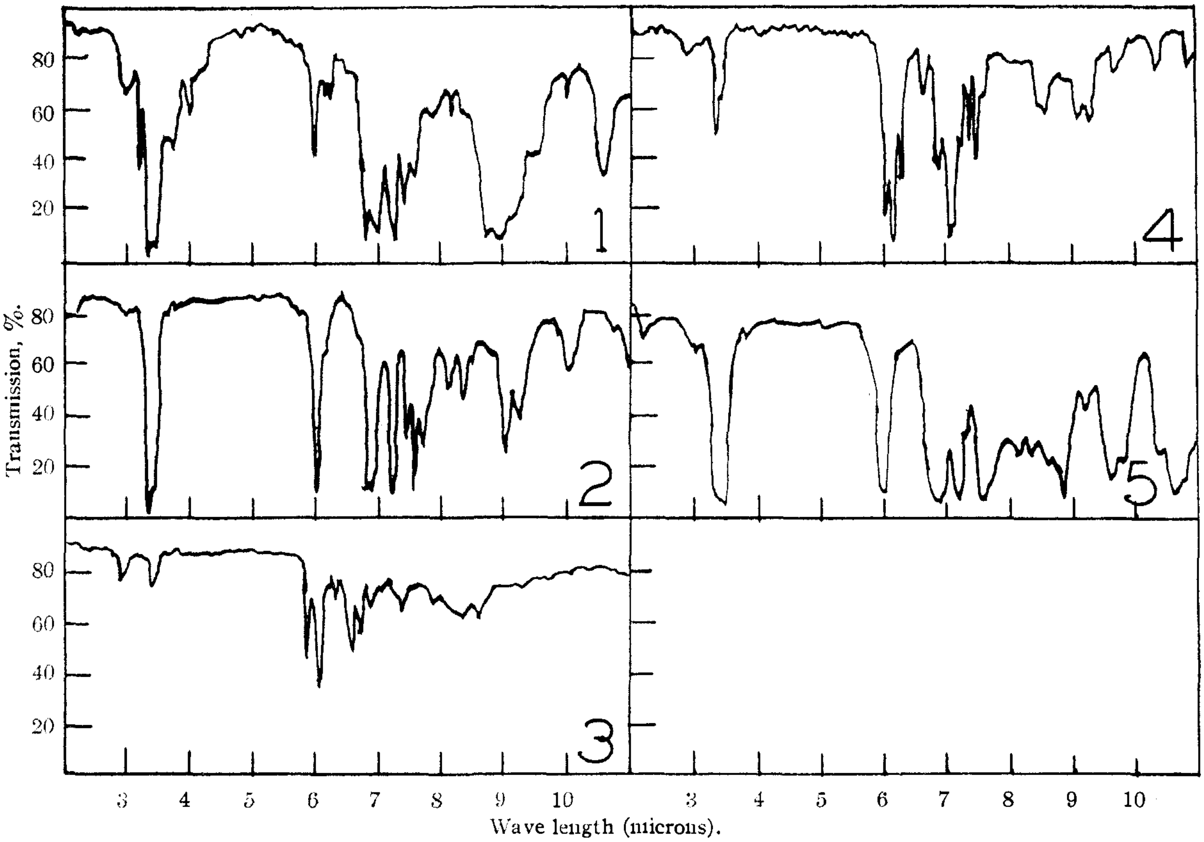


Fig. 1.—Infrared absorption spectra: (1), 2,5-dimethyl-Δ^3-pyrroline; (2), 2,5-dimethyl-Δ^1-pyrroline; (3), 5-benzamidohexanone-2; (4), 1-benzoyl-2,5-dimethyl-Δ^3-pyrroline; (5), 2-methyl-Δ^1(or Δ^2)-pyrroline.

yields a mixture of bases boiling quite sharply but capable of being separated by fractional crystallization of the picrates from *n*-butyl alcohol. One of the resulting picrates, m.p. 121–123°, does not depress the melting point of the picrate of the well-known 2-methylpyrroline first prepared by Hielscher[16,20]; the other, m.p. 124–126°, gives a strong depression. The base corresponding to the latter picrate presumably has structure Ib; the other, unlike its 2,5-dimethyl homolog, appears to consist at least in part of structure IIb rather than IIIb, inasmuch as its infrared absorption spectrum, even after very careful drying, shows a weak band at 3.02 μ (Curve 5). Compounds corresponding to structure IIc or IIIc have not yet been prepared.

Pyrroline.—The unsubstituted pyrroline obtained by the reduction of pyrrole with zinc and hydrochloric acid was converted to the picrate and fractionally crystallized from *n*-butyl alcohol.[23] It appeared to be entirely homogeneous.

Experimental

Microanalyses were performed under the direction of S. Nagy of the Massachusetts Institute of Technology. Infrared absorption spectra were obtained with the help of a Baird Associates Infrared Recording Spectrophotometer, Model B; liquid pyrrolines were diluted with carbon tetrachloride, the solid derivatives were dissolved in chloroform; cell thickness 0.1 mm. Melting points are uncorrected.

Throughout this work, the organic bases were isolated from neutral or acid aqueous solution by the gradual addition, with cooling, of a large excess of anhydrous potassium carbonate, as was done by de Jong and Wibaut[22]; the presence of undissolved solid interfered with the subsequent extraction and was avoided. The upper layer was separated, and the lower aqueous layer was extracted with three portions of alcohol-free ether; the combined organic layers were shaken with solid potassium hydroxide for 15 minutes, decanted (through glass wool, if necessary) onto Drierite or anhydrous magnesium sulfate, filtered (preferably with the use of pressure rather than suction), and distilled.

All the pyrroline picrates are readily soluble in ethyl alcohol and are more or less unstable in water; they were prepared in alcohol-free ether (a little water to increase the solubility of picric acid was permissible) and recrystallized from *n*-butyl alcohol or a mixture of the latter with *n*-butyl ether.

The chloroaurates of the pyrrolines are not satisfactory derivatives; they tend to decompose, leaving a residue of metallic gold, when allowed to stand for a few days or when warmed in an attempt at recrystallization. Attempts to use 2,4-dinitrochlorobenzene to form derivatives of these substituted pyrrolines were also unsuccessful, although the reagent has been recommended for pyrroline itself[8] and one pyrrolidine derivative was prepared.

Reduction Products of 2,5-Dimethylpyrrole.—Thirty-seven grams of 2,5-dimethylpyrrole[24] was reduced with zinc dust and hydrochloric acid as described by Andrews and McElvain.[14] The liquid was filtered to remove excess zinc, treated with a solution of 400 g. of sodium hydroxide in 800 ml. of water, and steam-distilled until 200 ml. of distillate had been collected. The pyrroline was recovered from the distillate as described above; it amounted to 17.6 g. of colorless liquid, b.p. 103–110°.

Forty-five grams of a similar pyrroline distillate was treated with an ethereal solution of 106.9 g. of recrystallized picric acid. The resulting solid was recrystallized five times from *n*-butyl alcohol and yielded 24.5 g. of a picrate m. 135–137°; concentration of the various mother liquors and addition of *n*-butyl ether to reduce the solubility of the picrate yielded a total of 87.5 g. of a picrate m.p. 104–108°.

---

[23] Michael L. Graffeo, M.S. Thesis, Tufts College, 1950.

[24] D. M. Young and C. F. H. Allen, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 219.

Anal. Calcd. for $C_{12}H_{14}N_4O_7$: C, 44.18; H, 4.33; N, 17.18. Found for 136° picrate: C, 44.14; H, 4.39; N, 17.06. Found for 107° picrate: C, 43.82; H, 4.63; N, 16.95.

Thirty grams of the latter picrate was suspended in 350 ml. of water and treated with 33 ml. of concentrated hydrochloric acid; enough ether was added to dissolve all the precipitated picric acid, and the aqueous layer was separated and extracted with six further 50-ml. portions of ether. The acid solution was treated with potassium carbonate and the product was worked up as usual; yield 5.7 g. liquid, b.p. 103–105°. The picrate of this liquid m.p. 110°, a figure which could not be attained by recrystallization of the original picrate. The other reduction product could be regenerated similarly: from 9.5 g. of the higher-melting picrate there was obtained 1.6 g. of liquid, b.p. approximately 110–112°. Unlike 2-methyl-Δ^2-pyrroline,[16] neither base underwent decomposition on distillation at atmospheric pressure.

Reactions of 2,5-Dimethyl-Δ^3-pyrroline.—Five and three-tenths grams of the pyrroline mixture prepared by the reduction of 2,5-dimethylpyrrole was dissolved in 53 ml. of water, made just acid with hydrochloric acid, and ozonized until the solution no longer decolorized bromine in glacial acetic acid.[8] Sixteen ml. of 30% hydrogen peroxide was added, and on the following day the solution was evaporated to dryness at 35° *in vacuo.* The resulting sticky mass was transferred to a vacuum desiccator, with the help of a little water, and dried over phosphorus pentoxide. When the residue was dissolved in absolute alcohol and warmed for a few minutes, the originally clear solution turned first yellow and then cloudy, and finally there appeared a white precipitate which was recrystallized by suspending it in a little hot absolute alcohol, adding water dropwise until solution was complete, filtering, and adding more absolute alcohol. The resulting white crystals melted at 256° (dec.) when inserted in a bath a few degrees below this temperature. This substance gave a negative Beilstein test and dissolved readily in water to form a strongly acid solution; the latter gave only a faint turbidity with silver nitrate solution. The compound is therefore *dl*-α,α'-iminodipropionic acid itself rather than the hydrochloride. Karrer and Appenzeller[25] report a m.p. of 252–253° (cor.) for *dl*-α,α'-iminodipropionic acid and 237–238° (cor.) for the *meso*-isomer.

Anal. Calcd. for $C_6H_{11}O_4N$: C, 44.71; H, 6.88; N, 8.69; equiv. wt., 161. Found: C, 44.49; H, 7.06; N, 8.60; equiv. wt. (by electrometric titration), 162.

Ozonolysis by the same technique of the base regenerated from the 107° picrate yielded the same substance, as shown by a mixed m.p. determination.

The benzoyl derivative was prepared from the regenerated pyrroline by the Schotten–Baumann method and purified by vacuum distillation and crystallization from petroleum ether at 0°; m.p. 74°.

Anal. Calcd. for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found: C, 78.11; H, 7.79; N, 6.74.

A portion of the pyrroline was refluxed for one hour with methyl iodide in absolute alcoholic solution; distillation of solvent and excess methyl iodide and recrystallization of the residue from absolute ethyl or isopropyl alcohol gave snow-white crystals of 1,1,2,5-tetramethyl-Δ^3-pyrrolinium iodide, melting sharply at 280° (dec.). For analysis, this was converted to the perchlorate by reaction with the equivalent amount of silver perchlorate in aqueous solution, filtration, evaporation *in vacuo*, and recrystallization from absolute alcohol.

Anal. Calcd. for $C_8H_{16}NClO_4$: N, 6.21; Cl, 15.71. Found: N, 6.20; Cl, 15.52.

Two and one-half grams of regenerated 2,5-dimethyl-Δ^3-pyrroline was refluxed with *ca.* 0.3 g. of Raney nickel in 35 ml. of xylene for one-half hour.[26] The mixture was cooled, filtered and extracted with 38 ml. of 1 *N* hydrochloric acid; the extract was worked up as usual, and yielded 0.9 g. of colorless liquid boiling at 105–116°. The crude picrate prepared from this melted at 120–132°, a figure which was raised to 133.5–136° by a single recrystallization, while the once-recrystallized phenylurea melted at 191–194.5°. A mixed m.p. determination on the picrate confirmed that the base had been converted to its Δ^1-isomer. The starting base was recovered unchanged after one-half hour refluxing in xylene alone.

One and six-tenths grams of the same regenerated pyrroline was mixed with 85 ml. of glacial acetic acid and 5 ml. of hydriodic acid (sp. gr. 1.7).[15] After standing ten minutes at room temperature, the mixture was poured into 200 ml. of water containing 15 g. of sodium acetate. Despite some mechanical loss, it was possible to obtain a very small amount of picrate which, after two recrystallizations, melted at 129–134°; this product did not depress the melting point of the picrate of 2,5-dimethyl-Δ^1-pyrroline.

Reactions of 2,5-Dimethyl-Δ^1-pyrroline.—Application of the Schotten–Baumann reaction to regenerated 2,5-dimethyl-Δ^1-pyrroline yielded a product which, after recrystallization from ethanol, melted at 111–114°. For analysis, it was recrystallized from *n*-butyl ether. Its composition corresponded to that calculated for 5-benzamidohexanone-2.

Anal. Calcd. for $C_{13}H_{17}NO_2$: C, 71.20; H, 7.82. Found: C, 70.74; H, 7.59.

This benzoyl derivative formed a semicarbazone, m.p. 195–197°.

The pyrroline was converted to the methiodide and methoperchlorate as described above. Analysis supported the formulation of the product as 1,2,5-trimethyl-Δ^1-pyrrolinium perchlorate.

Anal. Calcd. for $C_7H_{14}NClO_4$: Cl, 16.75. Found: Cl, 16.59.

The above methiodide was treated with an excess of aqueous potassium hydroxide; the resulting organic layer was separated, combined with three ether extracts of the aqueous layer, and dried as usual. Distillation yielded a little light-yellow liquid, b.p. about 132°; a test portion was converted to the picrate, m.p. 174–178.5°, and the rest was treated with methyl iodide as before. Analysis of the picrate agreed with the formulation of this base as 1,2,5-trimethyl-Δ^2-pyrroline.

Anal. Calcd. for $C_{13}H_{16}N_4O_7$: C, 45.88; H, 4.74; N, 16.47. Found: C, 46.03; H, 4.81; N, 16.52.

The new methiodide in turn was converted to the perchlorate and analyzed.

Anal. Calcd. for $C_8H_{16}NClO_4$: N, 6.21; Cl, 15.71. Found: N, 6.32; Cl, 15.91.

2,5-Dimethyl-Δ^1-pyrroline from γ-Chlorovaleronitrile.—Twenty grams of 4-bromobutene-1[27] was mixed with 25 ml. of 95% ethyl alcohol, saturated with dry hydrogen chloride at 0°, sealed in a glass tube and placed in an oven at 60° for 41 hours. Two layers formed. The upper layer was treated with 100 ml. of water and extracted with three 40-ml. portions of ether; the extracts were combined with the lower layer, washed successively with water, potassium bicarbonate solution, and water, and dried overnight over 15 g. of anhydrous sodium sulfate. Repeated fractionation yielded 8.6 g. (34%) of 1-bromo-3-chlorobutane, b.p. 151–156°.

The bromochlorobutane was converted in 67% yield, according to the procedure of Allen,[28] to γ-chlorovaleronitrile, b.p. 88–90° (20 mm.), n^{25}D 1.4398, d^{25}_{25} 1.051.

Alternatively, γ-chlorovaleramide[29] was dehydrated by mixing with 1.5 times its weight of phosphorus pentoxide and distilling. From 13.6 g. of amide there was obtained 4.7 g. of nitrile, b.p. 86–91° (20 mm.); another fractionation afforded liquid of b.p. 88.5–89° (21 mm.), n^{25}D 1.4391, d^{25}_{25} 1.033.

Anal. Calcd. for C_5H_8NCl: N, 11.92; Cl, 30.16. Found: N, 11.77; Cl, 30.13.

Fifteen grams of γ-chlorovaleronitrile was treated with the equivalent amount of methylmagnesium iodide under nitrogen according to Starr, Bulbrook and Hixon.[20] The xylene solution of the reaction product was stirred with 25 ml. of water, to which, after the evolution of heat had subsided, was added 20 ml. of 20% hydrochloric acid previously used to extract the ether-xylene distillate. The acid layer was separated, a second extraction, with very dilute acid, was made, and the combined acid layers were treated cautiously with potassium carbonate. The magnesium carbonate was filtered off and washed repeatedly, and the filtrate and washings were worked up for pyrroline in the usual way. The

---

[25] P. Karrer and R. Appenzeller, *Helv. Chim. Acta*, **25**, 595 (1942).

[26] R. N. Chakravarti and R. Robinson, *J. Chem. Soc.*, 78 (1947).

[27] R. P. Linstead and H. N. Rydon, *ibid.*, 1995 (1934).

[28] C. F. H. Allen, "Organic Syntheses," Coll. Vol. I, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 156.

[29] H. Wohlgemuth, *Ann. chim.*, [9] **2**, 298 (1914).

melting point of the picrate of this product could not be brought above 129–133° by repeated recrystallization, but it did not depress the m.p. of the 136° picrate prepared from the reduction products of 2,5-dimethylpyrrole. A mixture of the phenylureas likewise showed no m.p. depression.[30]

2,5-Dimethyl-Δ¹-pyrroline from 5-Bromohexanone-2.—A Grignard reagent was prepared from 15.8 g. of magnesium and the necessary amount of methyl bromide in 300 ml. of dry ether, and was treated with 60 g. of anhydrous cadmium chloride.[31] Next, 64.1 g. of γ-bromovaleryl chloride was dropped in, and the solution was refluxed for 1 hour after addition was complete. The mixture was cooled in ice and decomposed with cracked ice and 15% sulfuric acid; the ether layer was separated and dried over anhydrous sodium sulfate. After removal of the ether, the residue was distilled in the vacuum of a mechanical pump, and 37.5 g. (65%) of 5-bromohexanone-2 was collected. This liquid discolored in the receiver even before the distillation was completed.[32]

Thirty-seven grams of 5-bromohexanone-2 was dissolved in 170 ml. of absolute alcohol and 12 g. of anhydrous ammonia was added.[16] After a week, the crystals of ammonium bromide were filtered off and washed with absolute alcohol, and the filtrate and washings were acidified with hydrochloric acid and evaporated to dryness *in vacuo*. The residue was dissolved in water, treated with an aqueous solution of 35 g. of sodium hydroxide and steam-distilled; from the distillate, after the usual working-up, there were obtained a picrate and a phenylurea which melted at 132.5–134.5° and 196–201°, respectively, and which did not depress the melting points of the corresponding derivatives obtained starting from 2,5-dimethylpyrrole.

Hydrogenation.—Hydrogenations were carried out at approx. 3 atm. pressure and room temperature over Adams catalyst in glacial acetic acid. From 2,5-dimethyl-Δ³-pyrroline, there was obtained a base (*trans*-pyrrolidine) boiling about 104°; picrate m.p. 128–130°; phenylurea m.p. 144–146°. From the Δ¹-pyrroline, there was obtained a base (*cis*-pyrrolidine) boiling at 106°; picrate m.p. 120–121°; phenylurea m.p. 119°; 2,4-dinitrophenyl derivative m.p. 127°. The latter pyrrolidine was also obtained from 2,5-dimethylpyrrole, the identity being confirmed by mixed m.p. determinations.

Reduction Products of 1,2,5-Trimethylpyrrole.—Forty-one grams of 1,2,5-trimethylpyrrole, prepared analogously to the procedure of Ajello and Cusmano,[33] was reduced with zinc and hydrochloric acid as described earlier for 2,5-dimethylpyrrole. Two fractionations through a column yielded *ca.* 2 g. boiling up to 108°; 10.4 g., b.p. 108–116°; 2.4 g., b.p. 116–128°; and 3.0 g., b.p. 128–140°. From the second fraction there was obtained a picrate which, after recrystallization, decomposed on slow heating but showed a fairly sharp instantaneous melting point of 210°; it had the composition of 1,2,5-trimethylpyrroline picrate.

Anal. Calcd. for $C_{13}H_{16}N_4O_7$: C, 45.88; H, 4.74; N, 16.47. Found: C, 45.70; H, 4.86; N, 17.14.

The free base was regenerated from the picrate as usual. In acid solution, it instantly decolorized bromine in acetic acid. On treatment with methyl iodide, a quaternary salt was formed, m.p. 276–278° (dec.); a mixture of this with 1,1,2,5-tetramethyl-Δ³-pyrrolinium iodide (*v. supra*) melted at 280–281° (dec.), and the infrared absorption spectra of the two samples were identical.

After several crystallizations from *n*-butyl and isopropyl alcohols, the picrates from the two higher-boiling fractions amounted to 5.8 g., m.p. 186–188°; the pyrroline regenerated from this, however, was not homogeneous and could be separated by distillation into 0.4 g. of liquid, b.p. 109–115°, undoubtedly more of the 1,2,5-trimethyl-Δ³-pyrroline, and a few drops of yellow liquid whose b.p. was roughly determined as 142°. The latter liquid was reconverted to the picrate, recrystallized (m.p. 173–179° with previous softening), and analyzed.

Anal. Calcd. for $C_{13}H_{16}N_4O_7$: C, 45.88; H, 4.74. Found (corrected for 1.93% ash): C, 45.52; H, 4.82.

Reduction Products of 2-Methylpyrrole.—Eight and nine-tenths grams of 2-methylpyrrole[34] was reduced with zinc and hydrochloric acid as before. There was obtained 4.6 g. of a pyrroline mixture, b.p. 50–52° (131 mm.), which was converted to the picrate; five recrystallizations from *n*-butyl alcohol yielded 1.6 g. of a picrate, m.p. 121–122.5°, while from the mother liquors there was obtained a total of 8.7 g., m.p. 121–126°. A mixture of the two picrates showed a strong depression of the m.p. A portion of the latter picrate was recrystallized again from butyl alcohol–butyl ether and analyzed.

Anal. Calcd. for $C_{11}H_{12}N_4O_7$: C, 42.31; H, 3.88; N, 17.95. Found: C, 42.79; H, 4.11; N, 17.47.

For comparison, 2-methylpyrroline was prepared from γ-chlorobutyronitrile and methylmagnesium bromide[20] and converted to the picrate. This picrate, m.p. 121.5–122.5°, depressed the m.p. of the latter picrate of the foregoing paragraph but not that of the former. The free base regenerated from this was dried over anhydrous magnesium perchlorate, filtered under pressure of dry air into a carefully dried, all-glass distilling apparatus, and distilled at reduced pressure into a bulb which was sealed off. The bulb was not opened until the time of filling the infrared absorption cells.

Acknowledgments.—The author wishes to express his sincere gratitude to Professor R. B. Woodward for his valuable counsel, and to the National Research Council for financial support.

CAMBRIDGE, MASSACHUSETTS RECEIVED MAY 14, 1951

---

[30] The correct formulation of the compounds obtained by the action of phenyl isocyanate on Δ¹-pyrrolines is not clear. There is in the literature[11] a brief note to the effect that the products obtained from phenyl isocyanate and the pyrrolines derived from 2,4- and 2,5-dimethylpyrrole are abnormal in composition, and in the present work satisfactory analytical values were not obtained for the product from 2,5-dimethyl-Δ¹-pyrroline. Whatever its structure may be, however, it is a well-defined crystalline substance suitable for identification purposes.

[31] H. Gilman and J. F. Nelson, *Rec. trav. chim.*, **55**, 518 (1936).

[32] *Cf.* A. Lipp, *Ber.*, **22**, 1196 (1889).

[33] *Cf.* T. Ajello and S. Cusmano, *Gazz. chim. ital.*, **69**, 207 (1939).

[34] C. D. Nenitzescu and E. Solomonica, *Ber.*, **64**, 1924 (1931).