zole ring, forming a methylol derivative with a melting point of 210–215° (uncor.). As shown by the melting point, neither of Neuberger's compounds is the 1:1 mole compound we have isolated. The conditions of the reaction between amino acids and aldehyde no doubt determine whether ring closure takes place resulting in pyridine compounds or whether simple methylol derivatives are formed.

In our work we expect that the 1:1 mole compound is the usual methylol type of derivative of the amino acid. The second mole of aldehyde must link together two molecules of the 1:1 mole compound. This could be accomplished by reaction with two methylol groups— $2R—NHCH_2OH + HCHO \rightarrow R—NHCH_2O—CH_2—OCH_2NH—R + H_2O$ or by reaction of the aldehyde with the imino groups of two imidazole rings. Inasmuch as the second compound is not stable, we are inclined to favor the first alternative as the more probable.

Summary

1. The reaction between solutions of *l*(–)-histidine containing one equivalent of sodium hydroxide and various amounts of formaldehyde has been followed by polariscopic and hydrogen-ion measurements.

2. Under the experimental conditions, histidine forms two compounds, one of the AF type and one of the A_2F_3 type as the aldehyde concentration is increased.

3. The equilibrium constant of the latter reaction has been calculated.

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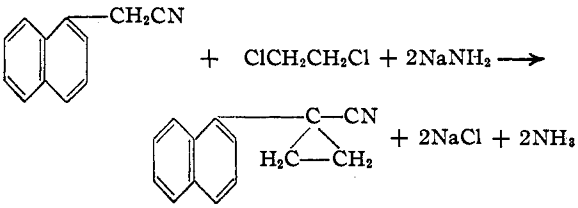
[CONTRIBUTION FROM THE WALKER LABORATORY OF THE RENSSELAER POLYTECHNIC INSTITUTE]

1-α-Naphthylcyclopropanecarbonitrile and Some of its Derivatives[1]

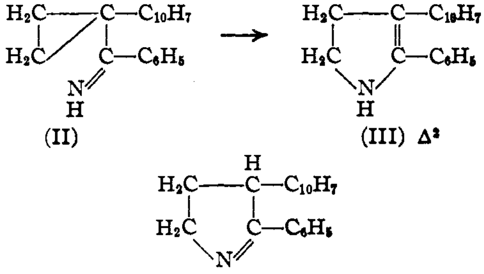
BY JOHN B. CLOKE AND THOMAS S. LEARY

1-α-Naphthylcyclopropanecarbonitrile (I) and some of its derivatives have been made as a part of a general study of compounds containing the cyclopropane ring. Compound (I) was prepared from α-naphthylacetonitrile, ethylene dichloride and sodium amide in liquid ammonia



by methods already reported for similar compounds.[2,3]

The presence of a cyclopropane ring in (I) is supported by its stability in the presence of potassium permanganate, which has been used for the differentiation of cyclopropane from ethylenic nitriles,[3,4] and also by the fact that it will give a ketimine, 1-α-naphthylcyclopropyl phenyl ketimine (II), whose cyclopropane structure is demonstrated by its rearrangement to give the isomeric 1-phenyl-2-α-naphthylpyrroline (III). Whether (III) has the conventional Δ^2 pyrroline structure or the Δ^1 structure or whether these two structures may be in tautomeric equilibrium has not been ascertained.



(II) (III) Δ^2

(III) Δ^1

The use of the cyclopropyl ketimine–pyrroline rearrangement as a test for the presence of the cyclopropane ring in such compounds is based upon considerable work, some of which has already been reported.[2,4,5] The effect of heating on the rearrangement of the ketimine base (II) may be seen in the top curve of Fig. 1, which was obtained by the differential thermocouple method already described.[5] It will be noted that the decomposition of the ketimine (II) is evident at about 144°, becomes more rapid as the temperature rises, and appears to be complete around 196°. The effect of heating on the 1-α-naphthylcyclopropylphenylketimmonium chloride (IV), $\underline{CH_2CH_2C}(C_{10}H_7)—C(=NH_2Cl)C_6H_5$, may be seen in the middle and lowest curves of the figure. A comparison of these curves with those obtained with the simpler phenyl cyclopropyl ketimine, $\underline{CH_2CH_2C}(H)—C(=NH)C_6H_5$,[5] would indicate that the replacement of the hydrogen (H) in the cyclopropane ring by the α-naphthyl group increases the resistance of the compound to rearrangement. The

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[1] The data reported in this paper have been taken from a thesis presented by Thomas Samuel Leary to the Rensselaer Polytechnic Institute in partial fulfillment of the requirements for the degree of Master of Science in 1939.

(2) Knowles and Cloke, THIS JOURNAL, **54**, 2028 (1932).

(3) Murray and Cloke, *ibid.*, **58**, 2014 (1936).

(4) Gotkis and Cloke, *ibid.*, **56**, 2710 (1934).

(5) Cloke, *ibid.*, **51**, 1174 (1929).

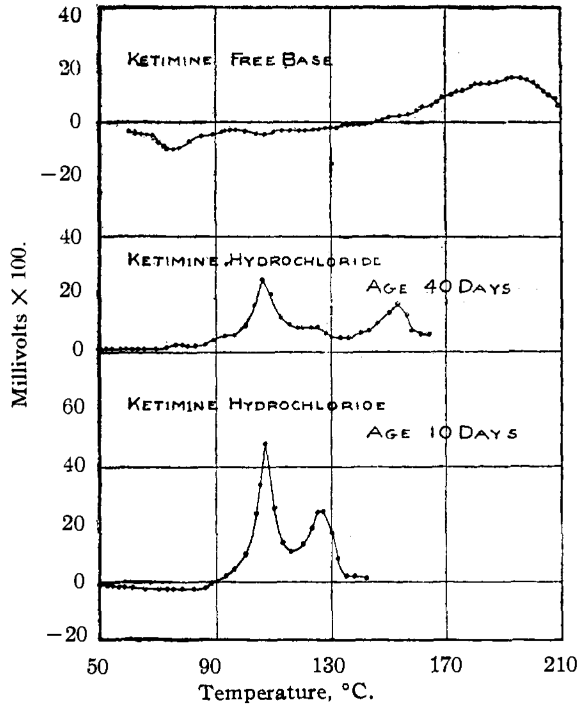

Fig. 1.—Heating curves.

curves also show an aging effect, which we have likewise noted in related compounds.

On account of the slight solubility of the naphthylketimmonium chloride (IV) in water at 0°, its rate of reaction with water to give the corresponding ketone and ammonium chloride was ascertained in 50% aqueous acetone, giving a value for k min.$^{-1}$ of 0.01 in the equation for a unimolecular reaction. Since this value is lower than that ascertained for $\underline{CH_2CH_2C}(H)—C(=NH_2Cl)C_6H_5$ (V) in water at 0° and in 0.05 M solution, *viz.*, 0.0249,[6] and as Pundt[7] found that diphenylketimmonium chloride is more readily saponified by 50% aqueous acetone than by water at 0°, it appears that the replacement of the hydrogen (H) in the cyclopropane ring of (V) by the α-naphthyl group decreases the rate with which the compound is saponified by water. The phenyl group, however, has little effect.[8]

The nitrile (I) may be hydrolyzed to give the amide, $\underline{CH_2CH_2C}(C_{10}H_7)CONH_2$ (VI), and the acid, $\underline{CH_2CH_2C}(C_{10}H_7)CO_2H$ (VII).

Experimental

α-Chloromethylnaphthalene.—The $C_{10}H_7CH_2Cl$ which was first employed in our work was made in 35% yields by the Blanc[9] method as modified by Darzens and Lévy.[10] Later we were more successful with the modification reported by Coles and Dodds,[11] which gave yields up to 60%. These various methods have recently been discussed by Cambron,[12] although we did not see his paper until after our work was done.

α-Naphthylacetontrile.[13]—The $C_{10}H_7CH_2CN$ was prepared from α-chloromethylnaphthalene and sodium cyanide by the same general procedure as that described in "Organic Syntheses" for benzyl cyanide.[14] However, the product was distilled from an anti-creep flask.[15] The compound used by us boiled from 182–186° at 12 mm., and was obtained in yields up to 87%.

1-α-Naphthylcyclopropanecarbonitrile (I).—A two-liter, three-necked, round-bottomed flask was fitted with a dropping funnel, a reflux condenser provided with a lime tower, and an efficient mechanical stirrer which operated through a mercury seal. One and a half liters of liquid ammonia was run into the flask followed by the addition of 2 g. of bright sodium. The stirrer was set in motion and one gram of hydrated ferric chloride was added; then 46 g. (2 moles) of sodium, in the form of small chips, was added over the course of thirty minutes. The reaction mixture was then stirred until the initial deep blue color of the sodium solution had disappeared, denoting the complete conversion of the sodium into sodium amide.[3]

At this stage, 167 g. (1 mole) of α-naphthylacetonitrile was added cautiously to the sodium amide solution over a period of an hour, when 700 cc. of anhydrous isopropyl ether was added at approximately the same rate as that at which the liquid ammonia evaporated. The reaction mixture was then allowed to attain room temperature, when it was refluxed gently on a steam pot, giving a dark brown viscous liquid.

At this point, the reaction mixture was cooled to −10° in a salt and ice-bath, when 99 g. (1 mole) of ethylene chloride was added during the course of an hour to the stirred mixture. The stirring was continued overnight while the temperature of the bath rose to that of the room, at which time the mixture was refluxed gently for two hours. Here water was added, the solution was acidified with acetic acid and the ether layer separated and dried over anhydrous sodium sulfate. The distillation of the extract in an anti-creep flask gave 118 g. of a fraction of b. p. 153–159° at 3 mm. and a residue. The distillate came over as a light yellow oil which solidified in the receiver. The crystallization of the compound from 95% alcohol gave 100 g. of a pure white crystalline solid of m. p. 84–85°. Further recrystallizations failed to raise the melting point of the product, which was obtained in a 52% yield.

The sublimation of a small sample of compound also gave crystals of m. p. 85°. Likewise, when some of the product was ground up with potassium permanganate in water, followed by the removal of the permanganate with bisulfite and the recrystallization of the residual nitrile from alcohol, it melted at 84°.

Anal. Calcd. for $C_{14}H_{11}N$: C, 87.01; H, 5.74; N, 7.25. Found: C, 86.6; H, 5.63; N, 7.31.

1-α-Naphthylcyclopropanecarbonamide (VI).—When 2 g. of the nitrile (I) was treated with hydrogen peroxide by the modified Radziszewiski method[16] a small amount of amide was obtained. When this was recrystallized from dilute alcohol, white crystals of m. p. 144° were obtained.

Anal. Calcd. for $C_{14}H_{13}NO$: N, 6.63. Found: N, 6.32.

A poor yield of lower melting compound was obtained

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(6) Cloke, THIS JOURNAL, **62**, 117 (1940).

(7) Pundt, "Thesis," Rensselaer Polytechnic Institute, 1933.

(8) Knowles, "Thesis," Rensselaer Polytechnic Institute, 1931.

(9) Blanc, *Bull. soc. chim.*, **33**, 313 (1923).

(10) Darzens and Lévy, *Compt. rend.*, **202**, 73 (1936).

(11) Coles and Dodds, THIS JOURNAL, **60**, 853 (1938).

(12) Cambron, *Can. J. Research*, **17**, 10 (1939); Fuson and McKeever, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., 1942, p. 70.

(13) Wislicenus, *Ber.*, **38**, 507 (1905).

(14) Adams and Thal, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., p. 101.

(15) "Synthetic Organic Chemicals," Vol. VI, No. 4, Eastman Kodak Co., 1933.

(16) Murray and Cloke, THIS JOURNAL, **56**, 2751 (1934).

by the hydrolysis of the nitrile with equal volumes of water, sulfuric acid and acetic acid for four hours at the boiling point of the mixture.[3]

1-α-Naphthylcyclopropanecarboxylic Acid (VII).—A small quantity of the acid (VII) was obtained by boiling 2 g. of the amide (VI) for two hours with 10 cc. of concentrated hydrochloric acid and also by a twenty-hour boil with alcoholic potassium hydroxide. A very small amount of (VII) was also obtained directly from the nitrile (I) by boiling it for twenty hours with concentrated hydrochloric acid.

A much better yield of acid (VII) was obtained by heating 12 g. of residual nitrile (I) from the hydrochloric acid treatment with a solution prepared from 25 g. of concentrated sulfuric acid, 25 cc. of glacial acetic acid and 10 cc. of water for about thirty-two hours at a temperature of 120°. The mixture was then poured into water, the solid collected on a filter and dissolved in ammonia water. The solution was extracted with ether in order to remove (I) and (VI) and then treated with sufficient hydrochloric acid to precipitate the acid (VII), which was again collected on a filter and recrystallized from a large quantity of water containing about 15% alcohol, whereby 7.6 g. of acid of m. p. 187–189° was obtained.

Anal.[17] Calcd. for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.92; H, 6.00.

1-α-Naphthylcyclopropyl Phenyl Ketimine (II).—A Grignard reagent was prepared from 14.2 g. of magnesium, 90 g. of bromobenzene and 400 cc. of dry ether in the usual way. A solution of 38.6 g. of the nitrile (I) in 500 cc. of dry ether was then added during the course of a half-hour to the well-stirred Grignard solution, and the mixture was refluxed gently for about eight hours. The mixture was then run into 500 cc. of liquid ammonia in a 1-liter Dewar flask, the ammonia was allowed to evaporate and the residue was extracted with ether. The evaporation of the filtered ethereal solution under diminished pressure gave a light yellow oil, which solidified and darkened on standing. This method of making ketimines has been considered at greater length elsewhere.[6]

Anal. Calcd. for $C_{20}H_{17}N$: N, 5.16. Found: N, 4.89.

Ketimmonium Chloride (IV).—The addition of dry hydrogen chloride to an ethereal solution of the ketimine base gave a white crystalline precipitate of the hydrochloride. The salt was washed with dry ether with the usual precautions[6] and dried over sodium hydroxide and phosphorus pentoxide in a vacuum desiccator; it melted at 126–128° on a Klein stage.

Anal. Calcd. for $C_{20}H_{18}NCl$: N, 4.55; Cl, 11.52. Found: N, 4.64; Cl, 11.49.

Rate of Reaction of Ketimmonium Chloride with 1:1 Water–Acetone.—On account of the slight solubility of the 1-α-naphthylcyclopropylphenylketimmonium chloride in water at 0°, it was impractical to determine its rate of reaction with this solvent alone. Accordingly, a 55-cc. portion of 0.05 M solution in 50% aqueous acetone was prepared and maintained at 0° in an ice-bath. The rate of reaction was ascertained by the analysis of 10-cc. portions of the reacting solution by the titrimetric method described elsewhere.[6] The graphical computation of the results of two runs, using the equation $k = 1/t \ln [a/(a - x)]$, gave the following values of k, min.$^{-1}$: 0.0099, 0.0101; av. k, 0.01.

The 1-α-naphthylcyclopropyl phenyl ketone formed by the hydrolysis of the foregoing ketimmonium chloride in water–acetone solution was separated and recrystallized twice from dilute alcohol giving white crystals of m. p. 94–95°.

2-Phenyl-3-α-naphthylpyrroline (III).—The residues from the thermal rearrangement of the 1-α-naphthylcyclopropyl phenyl ketimine (II) were leached with hot dilute hydrochloric acid, the solution was filtered and the pyrroline base liberated by the addition of sodium hydroxide to the ice-cold solution. The recrystallization of the white solid precipitated in this way gave the pyrroline of m. p. 75–77°. Insufficient material was available to ascertain whether this base was a pure compound or a mixture of isomers.

Anal. Calcd. for $C_{20}H_{17}N$: N, 5.16. Found: N, 4.89.

When ethereal hydrogen chloride was added to an ether solution of the pyrroline, a light yellow oil separated. The addition of aqueous picric acid to a water solution of this oil gave a yellow solid of m. p. 91–93°.

Summary

1-α-Naphthylcyclopropanecarbonitrile may be obtained in a 52% yield by the reaction of ethylene dichloride with α-naphthylacetonitrile in the presence of sodium amide. The compound may be hydrolyzed to give the corresponding amide and acid. It reacts with phenylmagnesium bromide to give 1-α-naphthylcyclopropyl phenyl ketimine, which rearranges on heating to give an isomeric pyrroline, a fact which constitutes evidence for the presence of the cyclopropane ring in the related compounds. The rate of reaction of the ketimmonium chloride in 50% aqueous acetone also has been ascertained.

TROY, N. Y. RECEIVED MAY 11, 1945

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[17] The authors are indebted to Mr. B. I. Vanisky for this microanalysis.