(5 g.) in methanol (50 ml.) was refluxed with a solution of selenium dioxide (2 g.) in water (5 ml.) for 15 hours. The resulting red solution after removal of the selenium gave upon evaporation a red oil. Traces of selenium and selenium dioxide were removed by refluxing the oil with acetone (50 ml.) for one hour and filtering. Concentration of the acetone to 25 ml. gave orange-yellow crystals of the diketone (2.0 g.) melting at 164°.

Anal. Calcd. for $C_{18}H_{14}O_3$: C, 78.60; H, 4.86. Found: C, 78.47; H, 4.99.

The phenazine prepared by refluxing the diketone X (0.5 g.) in absolute ethanol (10 ml.) with *o*-phenylenediamine (0.2 g.) for 30 minutes formed long yellow needles with a greenish tinge, m.p. 163°, yield 0.4 g. A mixture with the diketone started to melt at 120°.

Anal. Calcd. for $C_{25}H_{18}N_2O$: C, 81.30; H, 5.46. Found: C, 81.48; H, 5.44.

β-Phenyl-α-*o*-methoxybenzalglutaconic Acid (XI).—The diketone X (1 g.) and 30% hydrogen peroxide (1 ml.) in ethanol (25 ml.) were treated with 20% sodium hydroxide (5 drops) and allowed to stand for 30 minutes. The resulting solution was poured into water (50 ml.) and extracted twice with 25-ml. portions of ether. The alkaline layer upon acidification gave β-phenyl-α-*o*-methoxybenzalglutaconic acid (XI) melting at 229–230° after four crystallizations from an alcohol–benzene mixture; yield 0.5 g.

Anal. Calcd. for $C_{19}H_{16}O_5$: C, 70.36; H, 4.97. Found: C, 70.03; H, 4.95.

A solution of diethyl β-phenylglutaconate[5] (XII, 2.0 g.), *o*-methoxybenzaldehyde (1.0 g.) and sodium methoxide (1.0 g.) in methanol (20 ml.) was refluxed for 2 hours. Acidification gave a quantitative yield of β-phenyl-α-*o*-methoxybenzalglutaconic acid (XI) melting at 229–230° after recrystallization from an ethanol–benzene mixture. This sample did not depress the melting point of the product obtained by the cleavage of the diketone X and had similar infrared spectra.

5-Isonitroso-3-phenyl-2-cyclopenten-1-one.—A solution of 3-phenyl-2-cyclopenten-1-one[6] (4.5 g.), butyl nitrite (4.4 g.) and concentrated hydrochloric acid (2 ml.) in ethanol (50 ml.) was refluxed for 30 minutes and allowed to stand for one hour. The resulting crystals after five crystallizations from absolute ethanol gave 5-isonitroso-3-phenyl-2-cyclopenten-1-one (3.0 g.) melting at 203°.

Anal. Calcd. for $C_{11}H_9NO_2$: C, 70.58; H, 4.85. Found: C, 69.72; H, 4.98.

4-Phenyl-3-cyclopenten-1,2-dione.—5-Isonitroso-3-phenyl-2-cyclopenten-1-one (10 g.) in acetic acid (50 ml.) was refluxed with 37% formaldehyde (50 ml.) and concentrated hydrochloric acid (2 ml.) for 30 minutes and allowed to stand overnight. The solution was diluted with water (300 ml.) and extracted twice with chloroform (100 ml.). Removal of the chloroform gave orange crystals which were recrystallized four times from benzene; m.p. 185°, yield 1.4 g.

Anal. Calcd. for $C_{11}H_8O_2$: C, 76.73; H, 4.68. Found: C, 76.43; H, 4.83.

Equimolar amounts of the diketone and *o*-methoxybenzaldehyde in ethanol when refluxed with either 10% sodium hydroxide or sodium ethoxide gave a black tar.

5-*o*-Methoxybenzal-3-phenyl-2-cyclopenten-1-one.—3-Phenyl-2-cyclopenten-1-one[6] (5 g.) and *o*-methoxybenzaldehyde (4.3 g.) were refluxed with 10% sodium hydroxide (5 ml.) in ethanol (15 ml.) for 2 hours. The mixture after acidification gave 5-*o*-methoxybenzal-3-phenyl-2-cyclopenten-1-one (5.0 g.) which after six crystallizations from ethanol melted at 152–153°.

Anal. Calcd. for $C_{19}H_{16}O_2$: C, 82.58; H, 5.83. Found: C, 81.93; H, 6.00.

IOWA CITY, IOWA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STATE UNIVERSITY OF IOWA]

Studies on the Cyclization of N-Chlorodialkylamines

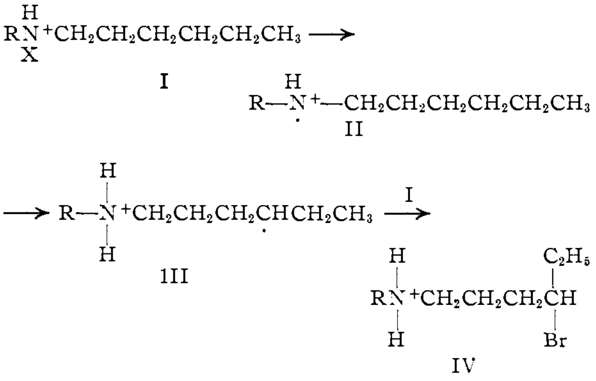
BY S. WAWZONEK AND T. P. CULBERTSON[1,2]

RECEIVED JUNE 4, 1959

Ethylamylamine, methylhexylamine and dihexylamine have been cyclized through their N-chloro derivatives and the resulting tertiary amines have been examined by gas chromatography. Ethylamylamine gave pure 1-ethyl-2-methylpyrrolidine. Methylhexylamine gave a mixture consisting of 80% 1-methyl-2-ethylpyrrolidine and 20% 1-methyl-2-methylpiperidine. Dihexylamine gave 95.6% 1-hexyl-2-ethylpyrrolidine and 4.4% 1-hexyl-2-methylpiperidine.

Secondary aliphatic amines can be converted into pyrrolidines by heating[3] or irradiating[4] the N-bromo or N-chloro derivative in sulfuric acid and treating the resulting solution with alkali. In all the examples of simple aliphatic amines studied only pyrrolidines are reported as final products even when the alkyl groups are extended beyond four carbon atoms.

In the mechanism proposed[4] the ring size depends on the alkyl halide formed during the irradiation of the N-haloamine. This intermediate is a direct consequence of the hydrogen abstraction step II → III.



$$\mathrm{R\overset{H}{\underset{X}{N}}{}^{+}CH_2CH_2CH_2CH_2CH_2CH_3} \longrightarrow \mathrm{R{-}\overset{H}{\underset{\cdot}{N}}{}^{+}{-}CH_2CH_2CH_2CH_2CH_2CH_3}$$

I II

$$\longrightarrow \mathrm{R{-}\overset{H}{\underset{H}{N}}{}^{+}CH_2CH_2CH_2\underset{\cdot}{C}HCH_2CH_3} \xrightarrow{\mathrm{I}} \mathrm{R\overset{H}{\underset{H}{N}}{}^{+}CH_2CH_2CH_2\overset{C_2H_5}{\underset{Br}{C}H}}$$

III IV

Factors determining which hydrogen is abstracted are the stereo configuration of the carbon chain and the relative stability of the carbon free radical formed. The steric factor is the sole one involved in the synthesis of the bicyclic amines, N-methylgranatanine[5] and quinuclidines[6] by this method; piperidine ring formation is favored over that of pyrrolidine rings.

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(1) Abstracted in part from the Ph.D. Thesis of T. P. Culbertson, February, 1959.

(2) Ethyl Corporation Fellow, 1957–1958.

(3) (a) G. H. Coleman and G. E. Goheen, THIS JOURNAL, **60**, 730 (1938); (b) G. H. Coleman, G. Nicholas and T. F. Martens, *Org. Syntheses*, **25**, 14 (1945).

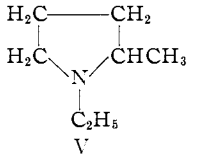
(4) S. Wawzonek and T. P. Culbertson, THIS JOURNAL, **81**, 3367 (1959).

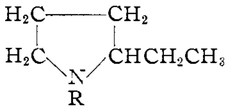
(5) S. Wawzonek and P. J. Thelen, *ibid.*, **72**, 2118 (1950).

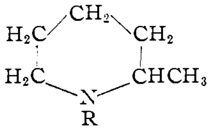
(6) S. Wawzonek, M. F. Nelson, Jr., and P. J. Thelen, *ibid.*, **73**, 2806 (1951).

To determine the importance of these factors in the cyclization of the halo derivative of simple amines, studies were carried out with ethylamylamine, methylhexylamine and dihexylamine and the resulting tertiary amines were examined by gas chromatography.

The tertiary amine produced from ethylamylamine gave only one peak and proved to be pure 1-ethyl-2-methylpyrrolidine (V). 1-Ethylpiperidine, prepared from ethyl iodide and piperidine,[7] when added to the pyrrolidine V gave a distinctly different peak on the gas chromatogram.


V


VIa, R = CH_3
b, R = C_6H_{13}


VIIa, R = CH_3
b, R = C_6H_{13}

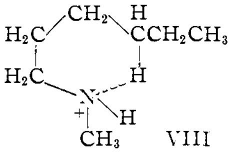
These results indicate that the formation of a secondary free radical is the important factor in the cyclization of amylamines.

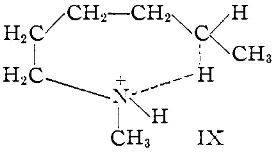
Gas chromatography of the tertiary amine fraction obtained from methylhexylamine gave two separate peaks which were not resolved completely. The curve was duplicated by using a tertiary amine mixture consisting of 80% 1-methyl-2-ethylpyrrolidine (VIa) and 20% 1,2-dimethylpiperidine (VIIa). The amines used in the known mixture were synthesized in an unambiguous manner from 2-ethylpyrrolidine[8] and 2-methylpiperidine,[9] respectively.

Analysis of the product from the cyclization of dihexylamine by the same procedure showed it to be a mixture of 95.6% 1-hexyl-2-ethylpyrrolidine (VIb) and 4.4% of 1-hexyl-2-methylpiperidine (VIIb). These amines were likewise prepared by unambiguous methods from 2-ethylpyrrolidine[10] and 2-methylpiperidine.[9] The methiodide of the cyclized product, when recrystallized twice from ethyl acetate, had the same melting point as the product obtained from 1-hexyl-2-ethylpyrrolidine.

In the last cyclization the intermediate 4-chlorodihexylammonium bisulfate separated from the sulfuric acid during the irradiation and could be isolated and characterized.

The results obtained indicate that the steric factor is all important with hexylamines and causes a preferential abstraction of the hydrogen by the aminium ion II from the fourth carbon rather than the fifth carbon atom. The stability of the free radicals involved would be approximately the same since secondary free radicals are produced at both carbon atoms. The transition state involving a six-membered ring (VIII) must be therefore favored over the seven-membered ring (IX). Models support this observation best if the nitrogen atom shows some tetrahedral character. A planar structure gives a better overlap of orbitals if the transition state is a seven-membered ring. This postulation is also in agreement with the behavior observed with dihexylamine. Substituting the larger hexyl group for methyl would favor a tetrahedral structure over a planar one for the nitrogen and would give more of the six-membered ring transition state and ultimately more of the pyrrolidine as was observed.


VIII


IX

These studies indicate that cyclization of secondary amines with alkyl groups larger than amyl by means of the N-chloro derivative will produce mainly pyrrolidines. The amount of isomeric piperidine formed will depend upon the substituent present upon the nitrogen and will become smaller as the substituent becomes larger.

Experimental[11]

N-Formylhexylamine.—Hexylamine (101 g.) was refluxed with 90% formic acid (100 g.) and benzene (70 ml.) for 18 hours using a Dean–Stark collector to remove the water. After removing the excess formic acid by atmospheric distillation, the product, N-formylhexylamine, was distilled at reduced pressure; b.p. 100–101° (2 mm.), n^{21}_{D} 1.4485, d^{20}_{4} 0.896, yield 115.7 g.

Anal. Calcd. for $C_7H_{15}ON$: C, 65.07; H, 11.70. Found: C, 64.76; H, 11.67.

Methylhexylamine.—A solution of N-formylhexylamine in 200 ml. of absolute ether was added in the course of two hours to lithium aluminum hydride (25.0 g.) in 150 ml. of absolute ether. The mixture was stirred for one hour and then decomposed with water (75 ml.) and 15% sodium hydroxide (25 ml.). The ether layer upon removal of the solvent, gave methylhexylamine (40.9 g.) which distilled at 138–140°, n^{20}_{D} 1.4186. The literature[12] reports a boiling point of 141–142°.

Cyclization of N-Chloro-N-methylhexylamine.—N-Chloro-N-methylhexylamine was prepared by the method of Coleman[3b] from methylhexylamine (33.0 g.) in a 99.5% yield. Extraction from the hexane solution with 175 ml. of 85% sulfuric acid was followed by irradiation with ultraviolet light for 40 hours at room temperature. The irradiated solution was poured onto ice, made basic with 40% sodium hydroxide and steam distilled into 25 ml. of concentrated hydrochloric acid. The distillate (1.5 l.) after concentration to 200 ml. was made alkaline. A Hinsberg separation gave N-methyl-N-hexylbenzenesulfonamide (13.02 g.) and a tertiary amine fraction which distilled at 121–122° (747 mm.), yield 12.33 g.

The tertiary amine fraction was chromatographed on a Perkin–Elmer Vapor Fractometer model 154 using a Perkin-Elmer column E (tetraethyleneglycol dimethyl ether) at 60° using a flow rate of 57 ml. per minute of helium at a pressure of 15 p.s.i. Two peaks separated with times of 24.2 and 26.6 minutes, respectively, from the air peak. The relative areas were approximately 80 and 20%.

A mixture of 80% 1-methyl-2-ethylpyrrolidine and 20% 1,2-dimethylpiperidine under the same conditions gave peaks with times of 24.1 and 27.0 minutes, respectively.

1-Methyl-2-ethylpyrrolidine.—2-Ethylpyrrolidine (4.75 g.)[8] was heated with 13 ml. of 90% formic acid and 13 ml. of 37% formaldehyde at 100° for 11 hours. The resulting solution was treated with concentrated hydrochloric acid (8 ml.) and concentrated to an oil. A Hinsberg separation gave 1-methyl-2-ethylpyrrolidine (3.6 g.) which distilled at 124–126°. The picrate melted at 174–175° after recrystallization from ethanol. The literature reports a

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[7] H. T. Clarke, *J. Chem. Soc.*, **101**, 1807 (1912).

[8] D. T. Warner and O. A. Moe, THIS JOURNAL, **74**, 1064 (1952).

[9] S. M. McElvain, *ibid.*, **49**, 2837 (1937).

[10] A. Muller and E. Feld, *Monatsh.*, **58**, 12 (1931).

[11] Melting points are corrected; boiling points are not.

[12] F. F. Blicke and B. F. Zienty, THIS JOURNAL, **61**, 771 (1939).

boiling point of 122–123° (762 mm.) and a picrate melting at 170°.[13]

1,2-Dimethylpiperidine was prepared by the methylation of 2-methylpiperidine[9] with formaldehyde and formic acid by the procedure used for 1-methyl-2-ethylpyrrolidine and boiled at 124–125°. The picrate melted at 240–242°. The literature reports values of 126–127° (720 mm.) and 240–241°, respectively.[14]

Cyclization of N-Chlorodihexylamine.—N-Chlorodihexylamine, prepared from dihexylamine (37 g.), was irradiated for 24 hours in 150 ml. of 85% sulfuric acid. The mixture separated into two layers. The upper layer (97.3 g.) at 0°, when poured into water at 0°, gave a white waxy precipitate. A yield of 12 g. was obtained from 30 g. of the layer after one crystallization from acetone. The compound, after two further crystallizations from acetone, melted at 158–159° and analyzed for 4-chlorodihexylammonium bisulfate.

Anal. Calcd. for $C_{12}H_{28}O_4NSCl$: C, 45.34; H, 8.88; S, 10.07; neut. equiv., 159. Found: C, 46.31; H, 9.14; S, 10.64; neut. equiv., 156.

The upper layer (36.1 g.), when cyclized in the usual manner, gave N,N-dihexylbenzenesulfonamide (6.0 g.), b.p. 164–168° (1.5 mm.), and a tertiary amine fraction (6.25 g.) boiling at 104° (14 mm.), $n^{24.5}$D 1.4465.

The methiodide of the tertiary amine fraction, after two crystallizations from ethyl acetate containing a little ethanol, gave prisms melting at 97.5–99°.

Anal. Calcd. for $C_{13}H_{28}NI$: C, 48.00; H, 8.68; N, 4.30. Found: C, 47.82; H, 8.47; N, 4.58.

The lower layer (320 g.), when cyclized in the usual way, gave N,N-dihexylbenzenesulfonamide (2.68 g.) and 0.7 g. of a tertiary amine fraction.

A second run starting with 37.0 g. of dihexylamine, when cyclized without separating the layers, gave 14.8 g. of tertiary amines boiling at 105–107° (14 mm.).

The tertiary amine, when chromatographed on a polypropylene oxide column using a Perkin–Elmer model 154 Vapor Fractometer at 140° and a flow rate of 51 ml./min. of helium at a pressure of 20 p.s.i. gave two peaks. The peaks separated with times of 33.4 and 35.7 minutes from the air peak and had relative areas of 95.6 and 4.4%, respectively. Addition of pure 1-*n*-hexyl-2-methylpiperidine increased and shifted the second peak at 37.3 minutes. At low concentration the peak occurred at 36 sec. Dihexylamine, when added, caused a third peak to appear at 51.1 minutes.

1-Hexyl-2-ethylpyrrolidine.—A mixture of 2-ethylpyrrolidine[10] (12.6 g.), hexyl bromide (25.1 g.) and potassium carbonate (10.7 g.) was heated at 140° with stirring for five hours. The mixture was added to dilute hydrochloric acid and the excess hexyl bromide removed with ether. The amine, when liberated with alkali, gave 1-hexyl-2-ethylpyrrolidine (14.5 g.) boiling at 104–105° (14 mm.), $n^{24.5}$D 1.4473.

Anal. Calcd. for $C_{12}H_{25}N$: C, 78.69; H, 13.66. Found: C, 78.05; H, 12.90.

The methiodide melted at 97–98° and did not depress the melting point of the product obtained by cyclizing dihexylamine.

1-Hexyl-2-methylpiperidine.—A mixture of 2-methylpiperidine[9] (9.9 g.), hexyl bromide (16.5 g.) and powdered potassium carbonate (13.8 g.) was heated for five hours at 140°. The product, when treated in a manner similar to that given for 1-hexyl-2-ethylpyrrolidine, gave 12.0 g. of 1-hexyl-2-methylpiperidine, b.p. 104° (14 mm.), $n^{21.0}$D 1.4581.

Anal. Calcd. for $C_{12}H_{25}N$: C, 78.68; H, 13.75. Found: C, 78.53; H, 13.46.

The methiodide melted at 188–189°.

Anal. Calcd. for $C_{13}H_{28}NI$: C, 48.00; H, 8.68. Found: C, 47.78; H, 8.35.

Cyclization of N-Chloro-N-ethylamylamine.—N-Chloro-N-ethylamylamine prepared from ethylamylamine[15] (28.8 g.) after irradiation in 135 ml. of 85% sulfuric acid at 25° for 24 hours, gave after treatment with alkali and a Hinsberg separation, a tertiary amine fraction (10.85) distilling at 118–120°. The picrate melted at 192–193.5°. The literature[16] reports values of 119–120° and 193–194°, respectively, for 1-ethyl-2-methylpyrrolidine.

The product when chromatographed on a tetraethylene glycol dimethyl ether column at a temperature of 60° using a flow rate of 51 ml./min. of helium at a pressure of 15 p.s.i., gave only one sharp peak at 18.6 minutes after the air peak.

1-Ethylpiperidine[7] had a migration time of 21.2 minutes at 70° while 1-ethyl-2-methylpyrrolidine gave a value of 14.0 minutes at this temperature.

IOWA CITY, IOWA

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[13] K. Löffler, *Ber.*, **43**, 2035, 2047 (1910).

[14] A. Lipp, *Ann.*, **289**, 229 (1895).

[15] E. J. Schwoegler and H. Adkins, THIS JOURNAL, **61**, 3499 (1939).

[16] H. Adkins and F. Signaigo, *ibid.*, **58**, 709 (1936).

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF IOWA STATE COLLEGE]

Benzyl Tosylates. VII. Capture of Intermediates by Foreign Anions

BY GEORGE S. HAMMOND,[1] JOHN PELOQUIN, FABIAN T. FANG AND JAY K. KOCHI

RECEIVED MARCH 5, 1959

Solvolysis of benzyl tosylates in the presence of nitrate or chloride ions does not result in release of the theoretical amount of acid. Since the rates of destruction of the tosylates are not accelerated by the anions in question, the result is attributed to capture of intermediate carbonium ions by the foreign anions. This behavior is observed with *m*-halotosylates, indicating that the non-linear relationship between log *k* and σ^+ is not due to the appearance of a non-carbonium ion mechanism, with the less reactive compounds.

The first-order hydrolysis of *m*- and *p*-substituted benzyl tosylates does not follow either the Hammett equation[2-4] or a modified version of the equation using Brown's σ^+-parameter.[4-6] Brown and Okomoto[5] suggested that the failure of the rate data to correlate with σ^+ might be due to the operation of two distinctly different solvolytic mechanisms. The more reactive compounds, which react at rates which can be fitted to a σ^+-plot with only modest curvature, were believed to react by a carbonium ion mechanism. The less reactive compounds might react by a "direct displacement" mechanism, presumably a reaction between water and the substrate analogous to the second-order,

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[1] Gates and Crellin Laboratories, California Institute of Technology, Pasadena, Calif.

[2] J. K. Kochi and G. S. Hammond, THIS JOURNAL, **75**, 3445 (1953).

[3] F. T. Fang, J. K. Kochi and G. S. Hammond, *ibid.*, **80**, 563 (1958).

[4] G. S. Hammond, C. E. Reeder, F. T. Fang and J. K. Kochi, *ibid.*, **80**, 568 (1958).

[5] H. C. Brown and Y. Okomoto, *ibid.*, **79**, 1913 (1957); Y. Okomoto and H. C. Brown, *J. Org. Chem.*, **22**, 485 (1957).

[6] H. C. Brown and Y. Okomoto, THIS JOURNAL, **80**, 4979 (1958).