[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ILLINOIS INSTITUTE OF TECHNOLOGY]

Chemistry of Ethylenimine. IV. Pyrolysis of 1-Acyl Derivatives of 2,2-Dimethylethylenimine[1]

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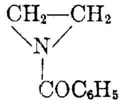
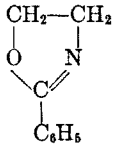
Received July 18, 1957

1-Acetyl-2,2-dimethylethylenimine undergoes a pyrolytic rearrangement to give *N*-(β-methallyl)acetamide in high yield. Further observations on the structural requirements for this reaction provide evidence for a mechanism similar to that proposed for the well-known Chugaev reaction.

In previous studies of the reactions of *N*-acyl derivatives of ethylenimine, ring-expansion, ring-opening, and polymerization reactions have been described. In one of the earliest papers in the field of ethylenimine chemistry, Gabriel and Stelzner[2] reported that 1-benzoylethylenimine (I) (formulated as *N*-vinylbenzamide at that time) was converted upon distillation to 2-phenyl-2-oxazoline (II) plus a resin which is presumably polymeric. They also reported that *N*-(β-chloroethyl)benzamide (III) was formed by the addition of hydrogen chloride to I. The preparation and polymerization of other *N*-acyl ethylenimine derivatives has been described in papers and patents from the I. G. Farbenindustrie laboratories.[3]



I



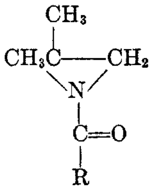
II

$C_6H_5CONHCH_2CH_2Cl$

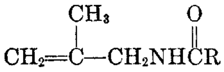
III

The discovery of a novel pyrolytic ring-opening reaction of 1-acyl-2,2-dimethylethylenimines (IV, R = lower alkyl) to give the isomeric *N*-(β-methallyl)amides (V, R = lower alkyl) was recently reported.[1b] In this paper, we present some related observations which provide evidence for the structural requirement and mechanism of the rearrangement.

When IVa, prepared by the treatment of 2,2-dimethylethylenimine with ketene, was heated to the reflux temperature at atmospheric pressure, it was rapidly converted to Va in high yield. The amide Va was characterized by alkaline hydrolysis to β-methallylamine and by acid-catalyzed cyclization to 2,5,5-trimethyl-2-oxazoline (VIa).

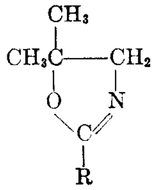


IV, R = lower alkyl
IVa, R = CH_3
b, R = C_2H_5
c, R = C_6H_5

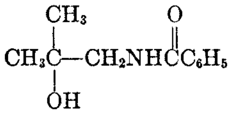


$$CH_2=\overset{CH_3}{\overset{|}{C}}-CH_2NH\overset{O}{\overset{\|}{C}}R$$

V, R = lower alkyl
Va, R = CH_3
b, R = C_2H_5
c, R = C_6H_5

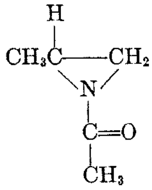


VIa, R = CH_3
b, R = C_2H_5
c, R = C_6H_5



$$CH_3\overset{CH_3}{\underset{OH}{C}}-CH_2NH\overset{O}{\overset{\|}{C}}C_6H_5$$

VII



VIII

$$CH_2=CHCH_2NH\overset{O}{\overset{\|}{C}}CH_3$$

IX

The structural requirements for the rearrangement were further defined by an investigation of the pyrolysis of 1-acetyl-2-methylethylenimine (VIII). This compound did not rearrange readily at the reflux temperature, and on heating under pressure gave predominately a resin, plus a very small yield of volatile material which was not fully characterized, but had some infrared spectral features expected of *N*-allylacetamide (IX).

The *N*-acetyl group is necessary for the rearrangement of the aziridine ring, since 2,2-dimethylethylenimine was recovered unchanged after prolonged heating at the temperature range where rapid rearrangement of IVa occurs.

These data support some definite conclusions with regard to the mechanism of the rearrangement. Since the amide Va is converted to the oxazoline VIa by treatment with acid, the rearrangement of the *N*-acylimine IVa must be purely pyrolytic and not acid-catalyzed. In this respect it is similar to

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[1] (a) This research was supported in part by a contract with the Aeronautical Research Laboratory, Wright Air Development Center, and was presented in part at the 126th National Meeting of the American Chemical Society in New York, September, 1954. The preparation of the manuscript was aided by a grant from the American Cancer Society. For paper number III in this series, see P. E. Fanta, *J. Chem. Soc.*, 1441 (1957); (b) Disclosed in part by P. E. Fanta, U. S. Patent 2,766,232 (Oct. 9, 1956).

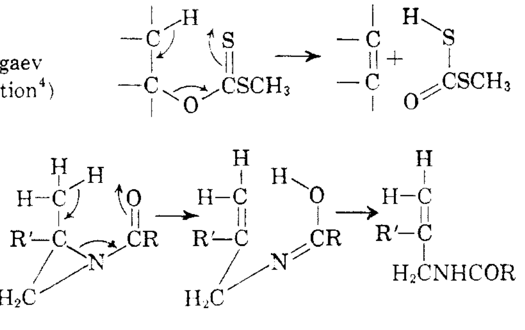
[2] S. Gabriel and R. Stelzner, *Ber.*, **28**, 2929 (1895).

[3] (a) H. Bestian, U. S. Patent 2,339,046 (Jan. 11, 1944); (b) *Ann.*, **566**, 210 (1950).

the well known Chugaev reaction,[4] as illustrated by a comparison of Equations 1 and 2. It is evident that the opening of the aziridine ring provides the driving force for the reaction illustrated in Equation 2. The fact that the rearrangement occurs much more readily when R′ of Equation 2 is methyl than when it is hydrogen may be due to a steric requirement for a sufficiently bulky group at R′ to force the participating methyl group close to the acyl oxygen.

(1) (Chugaev Reaction[4])

(2)



Acetylation and rearrangement may be accomplished in a single operation by heating 2,2-dimethylethylenimine with isopropenyl acetate in a pressure vessel. Since the imine is readily prepared on a large scale from commercially available 2-amino-2-methyl-1-propanol,[5] and *N*-(β-methallyl)acetamide is readily hydrolyzed, the operation of this series of reactions is presented in detail in the experimental part of this paper, as an alternative to the previously reported preparations of β-methallylamine.[6]

In further extension of this reaction, the homologous 1-propionyl-2,2-dimethylethylenimine (IVb) was prepared, as suggested in the literature,[3b] by the treatment of 2,2-dimethylethylenimine with propionyl chloride in the presence of triethylamine. On heating, IVb smoothly rearranged to the isomeric amide Vb, which was cyclized in sulfuric acid to the oxazoline VIb.

An attempted preparation of 1-benzoyl-2,2-dimethylethylenimine by the treatment of 2,2-dimethylethylenimine with benzoyl chloride in aqueous sodium hydroxide gave a mixture of *N*-(β-methallyl)benzamide (Vc), 2-phenyl-5,5-dimethyl-2-oxazoline (VIc) and *N*-(2-hydroxy-2-methylpropyl)benzamide (VII). Amides Vc and VII were both converted to the oxazoline VIc by treatment with concentrated sulfuric acid.

EXPERIMENTAL[7]

Ketene was prepared in a generator similar to the standard laboratory apparatus[8] except that the vertical water-cooled condenser was surmounted by a large, cold-finger trap maintained at −50 to −45°, which effectively reduced the quantity of entrained acetone in the gas stream.

1-Acetyl-2,2-dimethylethylenimine (IVa). Ketene was passed into 123 g. of 2,2-dimethylethylenimine maintained at a temperature of −35 to −20° until the increase in weight corresponded to completion of acetylation. Vacuum distillation of the crude, slightly yellow product gave 155 g. (79%) of colorless liquid, b.p. 61–62.5°/22 mm.: n_D^{25} 1.4324.

Anal. Calcd. for $C_6H_{11}ON$: C, 63.68; H, 9.80; N, 12.38. Found· C, 64.01; H, 9.74; N, 12.00.

Pyrolysis of IVa. Twenty-six grams of IVa was gradually heated in a flask provided with a reflux condenser and a thermometer immersed in the liquid. At 160° refluxing commenced and the temperature of the refluxing liquid rose in a few minutes to 220°, where it remained constant for 5 min. Vacuum distillation yielded 24 g. (92%) of *N-(β-methallyl)-acetamide* (Va), b.p. 123°/21 mm., n_D^{25} 1.4590. The infrared absorption spectrum had a broad NH band at 3.05 μ and distinctive $=CH_2$ bands at 3.26 and 11.22 μ.

Anal. Calcd. for $C_6H_{11}ON$: C, 63.68; H, 9.80; N, 12.38. Found: C, 63.81; H, 9.83; N, 12.32.

Hydrolysis of Va. A mixture of 5.66 g. of Va, 20 ml. of water, and 5.0 g. of sodium hydroxide was refluxed for 2 hr., then distilled until 5 ml. of distillate had been collected. β-Methallylamine was identified in the aqueous distillate by the preparation of four previously reported derivatives[9] using the standard procedures.[10] The picrate melted with decomposition at 202.5–204.5° (lit., 202–206°), the phenylthiourea melted at 78–79° (lit. 78–79°), the *p*-bromobenzenesulfonamide melted at 73.5–75° (lit. 74–76°) and the hydrochloride melted at 189.5–190.5° (lit. 190–191°).

Preparation of β-methallylamine by the isopropenyl acetate procedure. Fifty grams (0.5 mole) of isopropenyl acetate and 35.5 g. (0.5 mole) of 2,2-dimethylethylenimine were placed in a steel high-pressure bomb and heated at 200–220° for 30 min., during which time the pressure rose to 250 lb. p.s.i. Acetone was removed from the crude *N*-(β-methallyl)-acetamide by heating it to 100°/25 mm. and it was then mixed with a solution of 30 g. (0.75 mole) of sodium hydroxide in 60 ml. of water, and 30 ml. of diethylene glycol in a 200-ml. round-bottom flask. The flask was fitted with a 20-cm. Vigreux column attached to a condenser and ice-cooled receiver, and heated so that 60–70 ml. of distillate was collected in 20 to 30 min. During the distillation the temperature at the head of the column rose from 93 to 99°. The distillate was saturated with sodium hydroxide and the non-aqueous layer was dried over fresh sodium hydroxide pellets. Fractional distillation of the crude amine through a short, packed column gave 18.5–20.0 g. (52–56%) of colorless β-methallylamine, b.p. 78–81°, n_D^{25} 1.4285.

2,5,5-Trimethyl-2-oxazoline (VIa). *N*-(β-methallyl)acetamine (20 g.) was added dropwise with stirring over a period

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[4] Evidence with regard to the mechanism of the Chugaev reaction is summarized by E. R. Alexander, *Principles of Ionic Organic Reactions*, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 120.

[5] K. N. Campbell, A. H. Sommers, and B. K. Campbell, *Org. Syntheses*, Coll. Vol. III, 148 (1955); an improved procedure for the Wenker synthesis is reported by Anon., *Modern Plastics*, 26, (November), 130 (1948).

[6] β-Methallylamine has been prepared by heating 1-amino-2-methyl-2-propanol with sulfuric acid, ref. (9); by hydrolysis of *N*-(β-methylallyl)-phthalimide with hydrazine hydrate, ref. (9) and by the reaction of β-methallyl chloride with aqueous ammonia, M. Tamele, C. J. Ott, K. E. Marple, and G. Hearne, *Ind. Eng. Chem.*, **33**, 115 (1941).

[7] Melting points are corrected. Analyses are by Micro-Tech Laboratories, Skokie, Ill. Infrared absorption spectra were determined on thin films of the liquid samples between sodium chloride plates, using a Perkin-Elmer double beam spectrophotometer.

[8] W. E. Hanford and J. C. Sauer, *Org. Reactions*, III, 132 (1946).

[9] R. Adams and T. L. Cairns, *J. Am. Chem. Soc.*, 61, 2464 (1939).

[10] R. L. Shriner and R. C. Fuson, *The Systematic Identification of Organic Compounds*, 3rd ed., John Wiley and Sons, Inc., New York, N. Y., 1948.

of 10 min. to 35 ml. of concentrated sulfuric acid maintained at 30–40°. After standing for 10 min., the solution was poured onto 200 g. of ice, 60 g. of sodium hydroxide was added and the reaction mixture was cooled and extracted with ether. The extract was dried with sodium hydroxide and distilled to give 10 g. (50%) of colorless *2,5,5-trimethyl-2-oxazoline*, b.p. 120–121°, n_D^{25} 1.4188, which was characterized at the crystalline, yellow picrate, m.p. 160–161° after recrystallization from ethanol.

Anal. Calcd. for $C_{12}H_{14}N_4O_8$: C, 42.11; H, 4.12; N, 16.37. Found: C, 42.24; H, 3.86; N, 16.81.

Pyrolysis of 1-acetyl-2-methylethylenimine (VIII). As claimed in the Bestian patent,[3a] VIII was obtained in good yield by the reaction of 2-methylethylenimine with ketene. The procedure described above for the preparation of IVa was used and the product, obtained in 70% yield, had b.p. 47.5–48°/20 mm., n_D^{25} 1.4312. No change in the refractive index of VIII occurred when it was refluxed (147°) at atmospheric pressure for 10 min. On heating to 220° for 10 min. in a sealed glass ampule, VIII gave a viscous, red oil with a green fluorescence. In a vacuum sublimator at 0.2 mm., the crude product gave a drop of volatile, colorless liquid which instantly decolorized dilute aqueous potassium permanganate and had an infrared absorption spectrum in agreement with *N*-allylacetamide: broad NH band at 3.08 μ, $=CH_2$ band at 3.30 μ.

Non-rearrangement of 2,2-dimethylethylenimine. The boiling point (70–72°) and refractive index (n_D^{25} 1.4062) of a 35.1-g. sample of 2,2-dimethylethylenimine were unchanged after heating in a glass-lined steel bomb for 1 hr. at 205°. The refractive index should be a sensitive criterion for possible isomerization to β-methallylamine, since the latter compound has n_D^{25} 1.4285.

1-Propionyl-2,2-dimethylethylenimine (IVb). A solution of 46.2 g. (0.50 mole) of propionyl chloride in 150 ml. of petroleum ether was added dropwise to an ice-cooled, vigorously stirred solution of 35.5. g. (0.50 mole) of 2,2-dimethylethylenimine and 55.5 g. (0.55 mole) of pure, dry triethylamine in 200 ml. of petroleum ether. During the addition, which required 45 min., a copious, white precipitate of triethylamine hydrochloride was formed, which interfered with stirring and cooling, so that the temperature rose to 25°. The reaction mixture was filtered on a 12-cm. Buchner funnel and the precipitate was washed with two 100-ml. portions of petroleum ether. Distillation of the combined filtrate and washings gave 25.3 g. (40%) of colorless IVb, b.p. 74–78°/25 mm., n_D^{25} 1.4350.

Anal. Calcd. for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.01. Found: C, 66.53; H, 10.32; N, 11.27.

Pyrolysis of IVb. 1-Propionyl-2,2-dimethylethylenimine (20.4 g.) was heated in a Claisen flask at atmospheric pressure. Boiling commenced at 170° and an exothermic reaction occurred which subsided after a few minutes. Heating was resumed until the reflux temperature rose and remained constant at 231° (uncorrected). The crude product was a light red oil which was distilled to give 19.6 g. (96%) of colorless *N-(β-methallyl)propionamide*, Vb, b.p 142°/30 mm., n_D^{25} 1.4604.

Anal. Calcd. for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.01. Found: C, 66.12; H, 10.21; N, 11.28.

2-Ethyl-5,5-dimethyl-2-oxazoline, VIb. *N*-(*β*-Methallyl)-propionamide (18.3 g.) was added with stirring to 25 ml. of concentrated sulfuric acid at 30–35°. The light red solution was allowed to stand for 10 min., then poured onto 200 g. of ice. An excess of sodium hydroxide was added and the solution was cooled and extracted with ether. The ether extract was dried with sodium hydroxide and distilled to give 8 g. (44%) of colorless VIb, b.p. 141°, n_D^{25} 1.4225.

Anal. Calcd. for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.01. Found: C, 65.66; H, 10.26; N, 11.29.

The picrate of VIb, prepared by adding VIb to half-saturated picric acid in ethanol, formed yellow needles from ethanol, m.p. 147–149°.

Anal. Calcd. for $C_{13}H_{16}N_4O_8$: C, 43.82; H, 4.53; N, 15.73. Found: C, 43.88; H, 4.48; N, 15.67.

Attempted preparation of 1-benzoyl-2,2-dimethylethylenimine. A solution of 80 g. (2.0 moles) of sodium hydroxide and 71.1 g. (1.0 mole) of 2,2-dimethylethylenimine in 500 ml. of water was stirred with cooling at −10° while 140 g. (1.0 mole) of benzoyl chloride was added dropwise. The reaction mixture was extracted with two 150-ml. portions of ether and the combined extracts were dried over magnesium sulfate and distilled. The fraction boiling at 80–140°/0.5 mm. was redistilled, giving a center cut of pure *2-phenyl-5,5-dimethyl-2-oxazoline* VIc,[11] b.p. 109–119°/0.5 mm., n_D^{25} 1.5326.

Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 8.00. Found: C, 75.66; H, 7.42; N, 8.23.

The *picrate* of VIc melted at 206.5–207° (lit.[11] 198–199°).

Anal. Calcd. for $C_{17}H_{16}N_4O_8$: C, 50.49; H, 3.99; N, 13.86. Found: C, 50.42; H, 4.01; N, 13.76.

A higher-boiling fraction from the benzoylation was collected at 140–190°/0.5 mm. and solidified to waxy material on standing. Chromatography of a benzene solution of this crude fraction on alumina gave *N-(β-methallyl)benzamide*, Vc, (eluted with benzene) and *N-(2-hydroxy-2-methylpropyl)benzamide*, VII (eluted with 80% benzene–20% methanol).

Recrystallization of Vc from petroleum ether containing a little benzene gave fine, flat needles, m.p. 69.5–70.5°. An authentic sample having the same m.p. and mixed m.p. was obtained by the benzoylation of β-methallylamine in the usual manner.[10] A dilute, aqueous solution of Vc decolorized aqueous potassium permanganate instantaneously.

Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 8.00. Found: C, 75.43; H, 7.52; N, 7.39.

Recrystallization of VII from benzene gave large, thick prisms, m.p. 104–104.5° (lit.[12] 105.5–107°). A dilute, aqueous solution of VII did not decolorize aqueous potassium permanganate.

Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.36; H, 7.82; N, 7.25. Found: C, 68.87; H, 7.72; N, 6.85.

Cyclization of Vc *or* VII. Either Vc or VII was dissolved in an excess of concentrated sulfuric acid at room temperature. After 2 min. the clear, colorless solution was poured on ice and an excess of sodium hydroxide was added. Oily drops of 2-phenyl-5,5-dimethyl-2-oxazoline separated, which was extracted with ether and identified as the crystalline picrate.

Acknowledgments. Dr. M. L. Bender assisted in the interpretation of the infrared absorption spectra. Some experiments were suggested by Dr. George Richards and members of the staff of G. D. Searle and Co. The Division of Experimental Chemotherapy, Sloan-Kettering Institute for Cancer Research, accepted a sample of 1-acetyl-2,2-dimethylethylenimine for screening in the cancer chemotherapy program.

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(11) H. Dersin, *Ber.*, **54B**, 3158 (1921).

(12) J. C. Sheehan and G. D. Laubach, *J. Am. Chem. Soc.*, **73**, 4376 (1951).