[CONTRIBUTION FROM THE METCALF LABORATORIES, BROWN UNIVERSITY]

Reactions of 2-Propyl-3-nitroso-4-ethyloxazolidine and Related Compounds

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The behavior of 2-propyl-3-nitroso-4-ethyloxazolidine toward catalytic and chemical reduction has been investigated. Reduction with Raney nickel yields 2-amino-1-butanol (75%), *n*-butylamine (41%) and di-*n*-butylamine (36%). Reduction with lithium aluminum hydride, using an inverse addition procedure, yields the hydrazine, 2-propyl-3-amino-4-ethyloxazolidine (65–85%). The parent oxazolidine, 2-propyl-4-ethyloxazolidine, has been acetylated and benzoylated. In addition to the oxazolidine, 2-(2-ethyl-2-hexenylideneamino)-1-butanol has been identified as a product of the reaction between 2-amino-1-butanol and *n*-butyraldehyde in benzene. This Schiff base is of interest because catalytic hydrogenation with Raney nickel under the conditions given reduces only the C=C bond. Infrared studies suggest a reaction path for the polymerization of 2-propyl-4-ethyloxazolidine.

In a previous communication[2] the preparation of 2-propyl-3-nitroso-4-ethyloxazolidine was reported. Since this represented a new class of compounds[3] it was of interest to investigate some of its reactions, and the results are reported here.

The first reaction studied was reduction, under a variety of conditions. With Adams platinum catalyst at room temperature no hydrogen uptake was observed and the nitroso compound was recovered.

With Raney nickel[4] the reaction was exothermic and hydrogen uptake ceased at 3.5 molar equivalents. The reaction mixture possessed a strong odor of ammonia and the products isolated were 2-amino-1-butanol (75%), *n*-butylamine (41%) and di-*n*-butylamine (36%). If the reduction was stopped when two molar equivalents of hydrogen had been used, 2-propyl-4-ethyloxazolidine (35%) could be isolated. These data are consistent with the route outlined in Fig. 1.

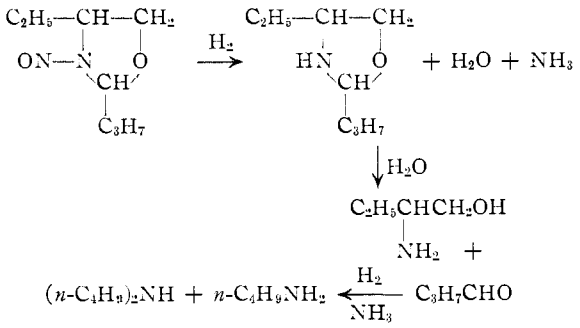

Fig. 1.

Since there were no breaks in the hydrogen uptake *vs.* time curve, it seems reasonable to conclude that the reduction proceeds by simultaneous reduction of the nitroso group, hydrolysis of the resulting oxazolidine and reductive alkylation of ammonia by *n*-butyraldehyde. Paal and Yao[5] have demonstrated that catalytic reduction of nitrosamines, using a palladium catalyst, leads predominantly to the parent amine (diphenylamine from N-nitrosodiphenylamine). Since nitrogen was also a product, they suggested a mechanism involving an intermediate tetrazine. However, a reinvestigation of the reduction of N-nitrosodiphenylamine by Grillot,[6] using platinum or nickel catalysts, indicated that ammonia and diphenylamine were formed. This is in accord with Fig. 1.

That ammonia can be reductively alkylated by *n*-butyraldehyde, in the presence of hydrogen and Raney nickel, has been observed by Grigorovskii and Margolina[7] and Winans and Adkins.[8] The former obtained mixtures of *n*-butylamine, di-*n*-butylamine and tri-*n*-butylamine using alcoholic ammonia and Raney nickel, while Adkins obtained the primary and secondary amines.

The intermediate 2-*n*-propyl-4-ethyloxazolidine was also reduced with Raney nickel[4] and yielded 2-*n*-butylamino-1-butanol as well as 2-amino-1-butanol.[9]

It is particularly interesting that no 2-*n*-butylamino-1-butanol was isolated from the reduction of 2-propyl-3-nitroso-4-ethyloxazolidine. It must therefore be concluded that hydrolysis of the oxazolidine and subsequent reductive alkylation of ammonia by the butyraldehyde are the favored reactions. 2-*n*-Butylamino-1-butanol has been prepared previously by the catalytic reduction of a mixture of 2-amino-1-butanol and *n*-butyraldehyde[10] and by the reaction of 2-amino-1-butanol with *n*-butyl bromide.[11]

Reduction of 2-propyl-3-nitroso-4-ethyloxazolidine was carried out with lithium aluminum hydride using the inverse addition procedure of Poirer and Benington.[12] The resulting pale yellow hydrazine, 2-propyl-3-amino-4-ethyloxazolidine, had basic properties, reduced cold Fehling solution and was obtained in 65–85% yield. This material was sensitive to the atmosphere, and considerable difficulty was encountered in obtaining satisfactory analytical data. The significant infrared maxima occurred at 3.12 μ (NH stretch) and at 6.19 μ (NH_2 deformation). The experimental molar refraction was in good agreement with that calculated for the hydrazine. In most attempts to prepare crystalline derivatives for characterization, oily products were

(1) Brown University Fellow 1952–1953.

(2) H. R. Nace and M. H. Gollis, THIS JOURNAL, **74**, 5189 (1952).

(3) Analogous six-membered ring compounds, N-nitrosotetrahydrometaoxazines, have been prepared by M. Kohn, *Monatsh.*, **25**, 817, 850 (1904); **26**, 951 (1905).

(4) N. L. Drake, *Org. Syntheses*, **21**, 15 (1941).

(5) C. Paal and Wan-Nien Yao, *Ber.*, **63B**, 57 (1930).

(6) G. F. Grillot, THIS JOURNAL, **66**, 2124 (1944).

(7) A. Grigorovskii and R. Margolina, *J. Applied Chem. (U.S.S.R.)*, **18**, 644 (1945); *C. A.*, **40**, 6408[2] (1946).

(8) C. Winans and H. Adkins, THIS JOURNAL, **55**, 2051 (1933).

(9) The formation of 2-amino-1-butanol is apparently due to hydrolysis of the oxazolidine—either by atmospheric moisture or water in the catalyst.

(10) R. C. Elderfield and H. A. Hageman, *J. Org. Chem.*, **14**, 605 (1949).

(11) J. S. Pierce, J. M. Salsbury, W. W. Haden and L. H. Willis, THIS JOURNAL, **64**, 2884 (1942).

(12) R. H. Poirer and F. Benington, *ibid.*, **74**, 3192 (1952).

obtained (these include the hydrochloride, picrate, benzenesulfonamide, ethiodide, benzamide, hydrazones, thiosemicarbazides and semicarbazides). Only the *p*-nitrobenzamide and the oxalate could be crystallized.

Though Bergmann and co-workers[13] have demonstrated that oxazolidines are cleaved to substituted aminoalcohols by a normal lithium aluminum hydride reduction, it is evident that by using equimolar amounts of the reactants and by preventing an excess of lithium aluminum hydride (inverse addition) the oxazolidine ring is not cleaved. This may be accounted for by the increased stability of N-substituted oxazolidines and by the presence of the easily reduced N-nitroso group.

The hydrazine hydrolyzed more slowly than the nitroso compound[2] in acidic 2,4-dinitrophenylhydrazine reagent to give the 2,4-dinitrophenylhydrazone of *n*-butyraldehyde.

Attempts to oxidize 2-propyl-3-nitroso-4-ethyloxazolidine to the corresponding nitramine, using basic 3 and 30% hydrogen peroxide,[14] resulted in recovery of the nitroso compound. Oxidation with nitric acid and hydrogen peroxide[15] was not attempted since the use of nitric acid with the acid sensitive nitroso compound suggested the possibility of a deeper going attack upon the molecule.

In the course of this study, some aspects of the previously reported work[2] were investigated in more detail. The identity of the high boiling product of the reaction between 2-amino-1-butanol and *n*-butyraldehyde in benzene was of interest because of a desire to nitrosate the crude reaction mixture (after removal of benzene and water) in an attempt to improve the yield of nitroso compound, and also to establish whether the separation of Schiff base and oxazolidine isomers was indeed possible in this instance (as suggested by Nace and Gollis[2]). The infrared absorption of this yellow liquid was characterized by a strong band at 6.17 μ. Catalytic reduction, using Raney nickel,[4] yielded a colorless liquid having a strong absorption band at 6.02 μ. The shift in wave length, coupled with the quantity of hydrogen required for reduction, suggested the presence of a conjugated double bond system, —N=C—C=C— only the carbon–carbon double bond of which was reduced under the mild conditions used. In this connection, Bergmann and co-workers[16] have shown that the normal C=N absorption at 6.00 μ is shifted to longer wave lengths by conjugation with a C=C bond.

The reduced material was readily hydrolyzed to 2-amino-1-butanol and 2-ethylhexanal whereas the unreduced material yielded 2-amino-1-butanol and 2-ethyl-2-hexenal. The high boiling product was therefore 2-(2-ethyl-2-hexenylideneamino)-1-butanol (not 2-*n*-butylideneamino-1-butanol[2]) and apparently resulted from an aldol condensation of *n*-butyraldehyde, followed by dehydration and condensation with 2-amino-1-butanol. Little of the isomeric 2-(3-heptene-3)-4-ethyloxazolidine could be present since the infrared spectrum showed strong C=N absorption and the molar refraction displayed an exaltation of 1.3 units above that calculated for the Schiff base. This is in accord with the generalization made by Bergmann[16] that α,β-unsaturated aldehydes tend to form Schiff bases rather than oxazolidines. The infrared spectrum and molar refraction of the reduction product indicated that about 80% was 2-(2-ethylhexylideneamino)-1-butanol (the remaining 20% being the isomeric oxazolidine). It is of interest to note that if the selective reduction of the C=C bond in the conjugated system —N=C—C=C— is general,[17] it offers a method for reducing the C=C bond of an α,β-unsaturated aldehyde without exposing it to acidic reagents (an alternative procedure to the one involving the formation of an acetal may thus be provided).

The aldol condensation of *n*-butyraldehyde creates an excess of 2-amino-1-butanol and may account for the inability of Nace and Gollis[2] to obtain satisfactory analytical data for 2-propyl-4-ethyloxazolidine (since the aminoalcohol and the oxazolidine have similar boiling points).[18] By using the method of Knorr,[19] refluxing the reactants in ether over anhydrous potassium carbonate, the oxazolidine was obtained in good yield (66–77%) and no aldol condensation occurred. The material analyzed satisfactorily and had a lower refractive index than previously reported.[2] The refractive index increased rapidly on standing. The molar refraction of a freshly distilled sample indicated that the oxazolidine structure was predominant (90%). This was borne out by the infrared spectrum which showed only a weak-medium band at 6.04 μ (C=N).

A study of the increase in refractive index of 2-propyl-4-ethyloxazolidine as related to the change in the infrared spectrum revealed some pertinent facts. On standing, the C=N band at 6.04 μ became very broad and bands appeared at 6.10 and 6.16 μ. The latter two eventually became stronger than the 6.04 μ absorption. In addition, the absorption at 9.40 μ (1°-OH deformation) increased as neighboring bands decreased in intensity. Redistillation of a one-month old sample did not regenerate the pure oxazolidine. After standing one year, a sample showed strong absorption at 6.05, 6.13 and 6.43 μ. The 9.40 μ band was the only strong absorption in the 9μ region.

A sample of 2-(2-ethyl-2-hexenylideneamino)-1-butanol that was one year old showed strong absorption at 6.05 and 6.14 μ. The 9.40 μ band was again the only significant one in the 9 μ region.

These data coupled with the known tendency of aliphatic Schiff bases to aldolize[20] lead to a possible explanation of the observed refractive index changes of oxazolidines. Figure 2 outlines the suggested polymerization of 2-propyl-4-ethyloxazolidine.

(13) E. Bergmann, D. Lavie and S. Pinchas, *ibid.*, **73**, 5662 (1951).

(14) E. Bamberger, *Ber.*, **33**, 113 (1900).

(15) F. J. Brackman, D. C. Downing and G. F. Wright, *Can. J. Research*, **27B**, 469 (1949).

(16) E. Bergmann, *et al.*, *Rec. trav. chim.*, **71**, 161 (1952).

(17) No examples could be found in the literature of the use of Raney nickel, at low temperature and pressure, with this type of conjugated system.

(18) The inability of E. Bergmann, E. Gil-Av and S. Pinchas, THIS JOURNAL, **75**, 358 (1953), to obtain pure oxazolidines from propionaldehyde or butyraldehyde and ethanolamine may be caused by the aldolization of the aldehydes in refluxing benzene.

(19) L. Knorr and H. Matthes, *Ber.*, **34**, 3484 (1901).

(20) W. S. Emerson, S. M. Hess and F. C. Uhle, THIS JOURNAL, **63**, 872 (1941).

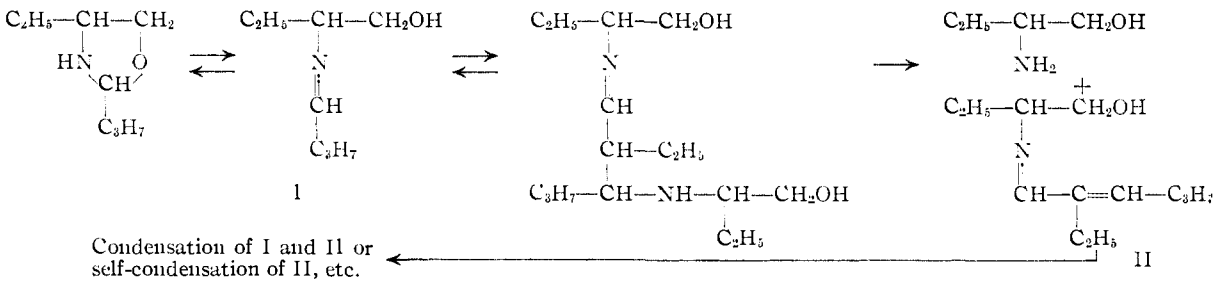

Fig. 2.

The increased unsaturation of the polymerization products gives rise to the observed absorption in the 6 μ region and the bands at 6.43 and 9.40 μ are probably due to the 2-amino-1-butanol formed as the reaction proceeds.

Nitrosation of 2-propyl-4-ethyloxazolidine, according to the method of Nace and Gollis[2] but using acetic acid instead of hydrochloric acid, gave yields of 25–30% of 2-propyl-3-nitroso-4-ethyloxazolidine. Hydrolysis and aldolization also occurred, resulting in the formation of 2-ethyl-2-hexenal. Inverse addition of the reactants (addition of the oxazolidine to the cold nitrous acid solution) gave poorer yields. The crude benzene-free reaction mixture (from 2-amino-1-butanol and *n*-butyraldehyde), when nitrosated with a 10% excess of nitrous acid, yielded up to 56% of the N-nitroso compound (based upon the oxazolidine content of the crude reaction mixture—60% as determined by distillation). Here again 2-ethyl-2-hexenal was a product of the reaction. This procedure and the nitrous acid deamination of 2-amino-1-butanol[2] provide the most satisfactory routes to the N-nitrosoöxazolidine.

2-Propyl-3-acetyl-4-ethyloxazolidine was prepared by acetylation of the oxazolidine with acetic anhydride in dry pyridine. The colorless liquid was characterized by analysis, molar refraction and infrared spectrum (no –NH or –OH stretching frequencies in the 3 μ region and a strong —C=O band at 6.05 μ[21]).

Depending upon the reaction conditions employed and the purity of the oxazolidine, benzoylation of 2-propyl-4-ethyloxazolidine yielded 2-propyl-3-benzoyl-4-ethyloxazolidine or a mixture of this compound and N,O-dibenzoyl-2-amino-1-butanol. Freshly distilled oxazolidine (prepared in ether) gave only the oxazolidine benzamide whereas an older sample (having a higher refractive index) yielded both the oxazolidine benzamide and the dibenzoylated aminoalcohol. The amide and amide-ester were easily separated by extraction with heptane, in which the latter was insoluble. The yield of amide-ester was increased by allowing the reaction mixture to stand at room temperature rather than at 0°. 2-Propyl-3-benzoyl-4-ethyloxazolidine was a colorless liquid having an infrared spectrum similar to that of the N-acetyl compound (except for absorption due to the benzene ring). The acetyl and benzoyl oxazolidines are quite stable as compared with the parent oxazolidine.

(21) The —C=O of 3° amides absorbs in this region.

Experimental[22]

2-Propyl-4-ethyloxazolidine. (a) Ether Method.—According to the method of Knorr,[19] 14.4 g. (0.2 mole) of *n*-butyraldehyde, 17.8 g. (0.2 mole) of 2-amino-1-butanol, 30.0 g. of anhydrous potassium carbonate and 100 ml. of ether were heated under reflux for 2.5 hours. Distillation gave 18.8 g. (66%) of 2-propyl-4-ethyloxazolidine; b.p. 77–79° (19 mm.), $n^{25}D$ 1.4381, d^{25}_4 0.8968, M_D 41.94, calcd., 42.20.

Another run gave a 77% yield of the oxazolidine. The refractive index of this material was lowered by redistillation; b.p. 78.5–79° (18 mm.), $n^{25}D$ 1.4361.

Anal. Calcd. for $C_8H_{17}NO$: C, 67.08; H, 11.96; N, 9.78. Found: C, 67.33; H, 12.15; N, 9.62.

The refractive index changed on standing: (initial value of $n^{25}D$ 1.4383), 1 day—1.4397, 3 days—1.4416, 4 days—1.4431, 5 days—1.4444, 13 days—1.4498. Infrared maxima: 3.02 μ (shoulder, –OH stretch), 3.18 μ (medium-weak, –NH stretch), 6.04 μ (medium-weak, C=N stretch), 8.67 μ (medium), 9.07 μ (medium), 9.40 μ (medium).

(b) Benzene Method.—According to the procedure used by Nace and Gollis,[2] 72 g. (1 mole) of *n*-butyraldehyde, 89 g. (1 mole) of 2-amino-1-butanol and 200 ml. of benzene were refluxed for 18 hours under a constant water separator. Distillation yielded two major fractions. The first, 2-propyl-4-ethyloxazolidine, weighed 79 g. (55%); b.p. 74–80° (14–15 mm.), $n^{25}D$ 1.4442.

The second fraction, 2-(2-ethyl-2-hexenylideneamino)-1-butanol (previously referred to as 2-butylideneamino-1-butanol[2]), weighed 33 g. (17% based upon aminoalcohol); b.p. 112–117° (4–5 mm.). Redistillation gave a fraction boiling at 108–109° (2 mm.); $n^{25}D$ 1.4828, d^{25}_4 0.8938, M_D 63.08, calcd. 61.70. Infrared maxima: 3.00 μ (medium, –OH stretch), 6.17 μ (strong, C=N stretch), 9.40 μ (strong, 1° –OH deformation).

Anal. Calcd. for $C_{12}H_{23}NO$: C, 73.04; H, 11.75; N, 7.10. Found: C, 70.66; H, 11.64; N, 7.48.[23]

Reduction of 2-(2-Ethyl-2-hexenylideneamino)-1-butanol.—A 500-ml. Pyrex bottle was charged with 60 ml. of dry methanol, 1 g. of Raney nickel[4] and 7.15 g. (0.036 mole) of 2-(2-ethyl-2-hexenylideneamino)-1-butanol. After shaking for 3 hours, at 1–2 atm. of hydrogen, the hydrogen uptake ceased and one molar equivalent of hydrogen had been consumed. The catalyst was separated by centrifugation, washed with methanol and the methanol distilled from the combined methanol solutions. The residue was distilled through a semi-micro column[24] to give 5.05 g. (70%) of 2-(2-ethylhexylideneamino)-1-butanol; b.p. 110–118° (8 mm.). An analytical sample was prepared by redistillation; b.p. 75° (0.16 mm.), $n^{25}D$ 1.4520, d^{25}_4 0.8721, M_D 61.75, calcd. 62.17. Infrared maxima: 3.18 μ (medium, –NH and –OH

(22) Melting points are corrected; boiling points are uncorrected. The infrared spectra were determined with a double beam spectrophotometer, described by D. F. Hornig, G. E. Hyde and W. A. Adcock, *J. Optical Soc. Am.*, **40**, 497 (1950), using a sodium chloride prism. Liquid film samples, formed by pressing between polished calcium fluoride plates, were used. Microanalyses were performed by Mr. S. M. Nagy and associates, Microchemical Laboratory, Mass. Institute of Technology, Cambridge, Mass.

(23) The unsatisfactory analytical data are probably due to the instability of the substance. Extensive decomposition was noted during distillation and polymerization occurred readily on standing at room temperature.

(24) C. W. Gould, Jr., G. Holzman and C. Niemann, *Anal. Chem.* **20**, 361 (1948).

stretch), 6.02 μ (medium, C=N stretch), 9.45 μ (strong, 1° -OH deformation).

Anal. Calcd. for $C_{12}H_{25}NO$: C, 72.30; H, 12.64; N, 7.03. Found: C, 72.10; H, 12.63; N, 7.43.

Hydrolysis of 2-(2-Ethyl-2-hexenylideneamino)-1-butanol.—To 1.6 g. (0.008 mole) of a freshly distilled sample of 2-(2-ethyl-2-hexenylideneamino)-1-butanol was added 45 ml. of 10% hydrochloric acid. The mixture was refluxed 1 hour, allowed to stand overnight, and the oil that formed was extracted with ether. The aqueous layer was saved.

The ether was removed on a steam-bath and the residue was taken up in 5 ml. of ethanol. One half of this solution was added to 15 ml. of 2,4-dinitrophenylhydrazine reagent[25] and the resulting red derivative was recrystallized from ethanol, m.p. 121.5–124°, mixed m.p. with the 2,4-dinitrophenylhydrazone of 2-ethyl-2-hexenal[26] (m.p. 119.5–123.5°) 121.5–124.5°. The other half of the ethanol solution was used to prepare a semicarbazone derivative,[27] m.p. 148.5–150.5°, mixed m.p. with the semicarbazone of 2-ethyl-2-hexenal (m.p. 149.5–153°) 148.5–153.5°.

The aqueous solution was evaporated to 5 ml. and a benzenesulfonamide was prepared by the Hinsberg method, m.p. 81–83°, mixed m.p. with the benzenesulfonamide of 2-amino-1-butanol (m.p. 84–85.5°) 81–83.5°.

Hydrolysis of 2-(2-Ethylhexylideneamino)-1-butanol.—The above hydrolytic procedure was used with 0.5 g. (0.0025 mole) of 2-(2-ethylhexylideneamino)-1-butanol and 15 ml. of 10% hydrochloric acid. An orange-yellow 2,4-dinitrophenylhydrazone was obtained and recrystallized from ethanol, m.p. 116–117.5°, mixed m.p. with the 2,4-dinitrophenylhydrazone of 2-ethylhexanal[28] 116–117.5°.

The aqueous solution yielded a benzenesulfonamide melting at 80–82°, mixed m.p. with the benzenesulfonamide of 2-amino-1-butanol (m.p. 84–85.5°) 81–83.5°.

Reduction of 2-Propyl-4-ethyloxazolidine.—A 500-ml. Pyrex bottle was charged with 14.3 g. (0.1 mole) of 2-propyl-4-ethyloxazolidine, 5 g. of Raney nickel[4] and 100 ml. of dry methanol. After shaking for 6 hours at 1–2 atm. of hydrogen, 0.057 mole of hydrogen had been used. The catalyst was separated by centrifugation, washed with methanol, and the solvent removed from the combined methanol solutions. The residue was carefully fractionated through the semi-micro column[24] and 7 fractions, in the range 70–100° (8 mm.), were collected. Refractionation separated the mixture into two components.

The first was a water soluble 1° amine, identified as 2-amino-1-butanol; b.p. 71–80° (major portion at 73–76°) (8 mm.), $n^{25}D$ 1.4489 (5.20 g., 58%). The benzenesulfonamide, prepared by the Hinsberg method, melted at 79.5–81.5°, mixed m.p. with the benzenesulfonamide of 2-amino-1-butanol (m.p. 84–85.5°) 81–83.5°.

The other component was a water insoluble 2° amine, identified as 2-*n*-butylamino-1-butanol (6.57 g., 45%), b.p. 88–95° (8 mm.), $n^{25}D$ 1.4455. This material crystallized on standing, m.p. 38.5–39.5°, mixed m.p. with 2-*n*-butylamino-1-butanol[29] 37–40°. Infrared maxima: 3.20 μ (medium, -NH and -OH stretch), 9.38 μ (strong, 1° -OH deformation).

Anal. Calcd. for $C_8H_{19}NO$: C, 66.15; H, 13.19; N 9.64. Found: C, 66.44; H, 13.26; N, 9.33.

The picrate salt, prepared in ethanol–water, melted at 87–89°, mixed m.p. with 2-*n*-butylamino-1-butanol picrate[29] 87–89°.

Acetylation of 2-Propyl-4-ethyloxazolidine.—A solution of 14.3 g. (0.1 mole) of 2-propyl-4-ethyloxazolidine in 30 ml. of dry pyridine was cooled in an ice-bath and 15.3 g. (0.15 mole) of acetic anhydride added with stirring. The reaction mixture was allowed to stand at room temperature for 3 days. After the addition of 200 ml. of water, the solution was made strongly basic with 10% sodium hydroxide solution and a yellow oil salted out with potassium carbonate. The oil was extracted with three 50-ml. portions of ether and the ether solution was washed with 10% hydrochloric acid, water, and then dried over anhydrous magnesium sulfate. The ether was distilled and the residue was distilled through the semi-micro column.[24] 2-Propyl-3-acetyl-4-ethyloxazolidine was collected at 115–128° (12 mm.); (5.93 g., 32%), $n^{25}D$ 1.4608, d^{25}_4 0.9889, M_D 51.39, calcd. 51.66. Infrared maxima: 6.05 μ (strong, 3° amide C=O stretch). A sample for analysis was obtained by redistillation, b.p. 87–90° (0.15 mm.), $n^{25}D$ 1.4604.

Anal. Calcd. for $C_{10}H_{19}NO_2$: C, 64.83; H, 10.34; N, 7.56. Found: C, 65.05; H, 10.17; N, 7.56.

Benzoylation of 2-Propyl-4-ethyloxazolidine.—A solution of 5.00 g. (0.035 mole) of 2-propyl-4-ethyloxazolidine (freshly prepared by the ether method) in 15 ml. of dry pyridine was cooled in an ice-bath and 5.10 g. (0.036 mole) of benzoyl chloride added dropwise with thorough mixing. The cold solution was allowed to warm to room temperature and was then kept at 0° for 20 hours. After pouring the reaction mixture on ice, the oil that separated was extracted with three 20-ml. portions of ether. The ether solution was washed with saturated sodium bicarbonate solution and water and was dried over anhydrous magnesium sulfate. The ether was removed on a steam-bath and the residue[30] was distilled through the semi-micro column.[24] 2-Propyl-3-benzoyl-4-ethyloxazolidine was collected at 143–145° (1.5–2 mm.) and weighed 2.81 g. (32%); $n^{25}D$ 1.5162, d^{25}_4 1.0429, M_D 71.65, calcd. 71.15. Infrared maxima: 6.11 μ (strong, 3° amide C=O stretch).

An analytical sample was prepared by redistillation; b.p. 128.5° (0.05 mm.), $n^{25}D$ 1.5168.

Anal. Calcd. for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 73.04; H, 8.58; N, 5.78.

A sample of oxazolidine that was several weeks old was benzoylated as above. The ether residue was only partially soluble in heptane. The soluble material, the N-benzoyl oxazolidine, was obtained by distillation of the heptane solution, 2.4 g. (28%). The insoluble material crystallized on standing to give 1.6 g. (30%) of N,O-dibenzoyl-2-amino-1-butanol. Several recrystallizations from hexane–ethyl acetate afforded an analytical sample, m.p. 93–93.5°, mixed m.p. with a sublimed sample of N,O-dibenzoyl-2-amino-1-butanol[31] (m.p. 103°) 101.5–104.5°.

Anal. Calcd. for $C_{18}H_{19}NO_3$: C, 72.70; H, 6.44; N 4.71. Found: C, 72.81; H, 6.50; N, 4.90.

Attempted Preparation of the Hydrochloride of 2-Propyl-4-ethyloxazolidine.—To a cooled solution of 7.15 g. (0.05 mole) of 2-propyl-4-ethyloxazolidine in 75 ml. of ether was added 20 g. of 10% ethanolic hydrogen chloride. Additional ether was put in and the white precipitate filtered off. This material was identified as 2-amino-1-butanol hydrochloride; (6.0 g., 98%) m.p. 87.5–88.5° after recrystallization from ethanol–ether, mixed m.p. with 2-amino-1-butanol hydrochloride (m.p. 88–89.5°) 86.5–90°.

Nitrosation of 2-Propyl-4-ethyloxazolidine.—2-Propyl-4-ethyloxazolidine was nitrosated according to the procedure of Nace and Gollis,[2] using 5.72 g. (0.04 mole) of oxazolidine, 3.00 g. (0.05 mole) of glacial acetic acid in 15 ml. of water and 3.45 g. (0.05 mole) of sodium nitrite in 25 ml. of water. 2-Propyl-3-nitroso-4-ethyloxazolidine was collected at 84–89° (2–3 mm.) and weighed 1.99 g. (29%): $n^{20}D$ 1.4614, $n^{25}D$ 1 4596.

Another experiment, using 38.1 g. (0.27 mole) of the ox-

(25) 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, p. 171.

(26) 2-Ethyl-2-hexenal was prepared by the methods of C. Weizmann and S. F. Garrard, *J. Chem. Soc.*, 324 (1920), and S. G. Powell and D. A. Ballard, THIS JOURNAL, **60**, 1914 (1938). The latter procedure gave a greater yield of purer product, b.p. 67° (20 mm.), $n^{22}D$ 1.4500, 50% yield.

(27) Reference 23, p. 170.

(28) The 2-ethylhexanal derivative was prepared from 2-ethyl-2-hexenal by refluxing equimolar amounts of the aldehyde and ethylene glycol in benzene with a trace of *p*-toluenesulfonic acid (under a constant water separator). The resulting dioxolane (b.p. 98–101° (20 mm.), $n^{25}D$ 1.4510) was reduced with Raney nickel[4] at room temperature and 1–2 atm. of hydrogen. 2,4-Dinitrophenylhydrazine reagent hydrolyzed the saturated dioxolane and yielded the 2,4-dinitrophenylhydrazone of 2-ethylhexanal, m.p. 116.5–118° after recrystallization from ethanol–water.

(29) 2-*n*-Butylamino-1-butanol was prepared in 63% yield by the method of Pierce and co-workers[11]; b.p. 58° (0.1 mm.), $n^{25}D$ 1.4452. Though reported previously only as a liquid, this material crystallized when seeded with a crystal of the reduction product of 2-propyl-4-ethyloxazolidine and had m.p. 37–39°. The picrate salt was prepared in ethanol–water and melted at 86–87.5°.

(30) This material was completely soluble in heptane, hence none of the aminoalcohol amide-ester was present (see following section).

(31) This compound was prepared by Dr. L. B. Clapp of this Laboratory and appears to exhibit dimorphism.

azolidine and 0.35 mole of the nitrosating agents, afforded a 25% yield of the N-nitroso compound and 10 g. (59%) of 2-ethyl-2-hexenal; b.p. 30–40° (0.3 mm.), $n^{25}D$ 1.4500. The aldehyde yielded a 2,4-dinitrophenylhydrazone that melted at 124.5–126.5°, mixed m.p. with an authentic sample (m.p. 121.5–124°) 122–124°.

Nitrosation of 75 g. of a reaction mixture, obtained by removing benzene from equimolar amounts of 2-amino-1-butanol and *n*-butyraldehyde after azeotroping off the water, yielded 21 g. of 2-ethyl-2-hexenal (identified by mixed m.p. of the 2,4-dinitrophenylhydrazone with an authentic sample) and 28 g. (56% based upon estimated 3:2 ratio of 2-propyl-4-ethyloxazolidine to 2-(2-ethyl-2-hexenylideneamino)-1-butanol in the reaction mixture) of 2-propyl-3-nitroso-4-ethyloxazolidine, $n^{25}D$ 1.4597. Inverse addition of the reactants (reaction mixture added to acetic acid–sodium nitrite solution at 5°) resulted in a lower yield of the desired nitroso compound (30%).

Catalytic Reduction of 2-Propyl-3-nitroso-4-ethyloxazolidine.—When 8.6 g. (0.05 mole) of the nitroso compound in 100 ml. of ethanol was shaken with 50 mg. of prereduced Adams platinum catalyst at 1–2 atmospheres of hydrogen, no hydrogen uptake was observed and the starting material was recovered.

A 500-ml. Pyrex bottle was charged with 17.2 g. (0.1 mole) of 2-propyl-3-nitroso-4-ethyloxazolidine, 5 g. of Raney nickel[4] and 100 ml. of dry methanol. The bottle was shaken for 5.5 hours at 1–2 atm. of hydrogen and 0.35 mole of hydrogen was used. The reaction was exothermic for the first hour of reduction. The catalyst was removed by centrifugation, washed with methanol and the combined methanol solutions were distilled. The first few drops possessed a strong ammoniacal odor, whereas the greater part of the methanol had an amine-like odor. When the solvent had been removed, the residue was distilled through the semi-micro column[24] and two major fractions were collected.

The lower boiling fraction was di-*n*-butylamine (2.3 g., 36%); b.p. 48–54° (18 mm.), 140–141° (760 mm.), $n^{25}D$ 1.4179. The picrate was prepared in ethanol–water and melted at 63–64° after two recrystallizations from ethanol–water, mixed m.p. with di-*n*-butylamine picrate (m.p. 62.5–65°) 62.5–65°. The phenylthiourea[32] melted at 83–84.5°, mixed m.p. with the phenylthiourea of di-*n*-butylamine (m.p. 82.5–84°) 82.5–84°.

The second fraction, 2-amino-1-butanol, weighed 6.7 g. (75%); b.p. 83–87° (18 mm.). The benzenesulfonamide melted at 80–81°, mixed m.p. with the benzenesulfonamide of 2-amino-1-butanol (m.p. 84–85.5°) 82–84.5°. A picrate was prepared in ethanol–water, m.p. 128–130.5°, mixed m.p. with 2-amino-1-butanol picrate[33] (m.p. 130.5–132.5°) 128.5–131°.

The reduction was repeated as above and the resulting methanolic solution was carefully fractionated at atmospheric pressure through a 200-mm. Vigreux column. The odor of ammonia was again evident in the first drops of the distillate. A fraction at 68–91° was refractionated to afford a major portion at 75–78°, $n^{25}D$ 1.3820. The yield of this material, identified as *n*-butylamine, was estimated from the refractive indices of several close fractions and was 3.0 g. (41%). The picrate was prepared in water and recrystallized from water, m.p. 144.5–149°, mixed m.p. with *n*-butylamine picrate (m.p. 145.5–147.5°) 145.5–148.5°. The yields of di-*n*-butylamine and 2-amino-1-butanol were comparable to those obtained in the first run.

(32) Prepared according to N. D. Cheronis and J. B. Entrikin, "Semimicro Qualitative Organic Analysis," Thomas Y. Crowell Co., New York, N. Y., 1947, p. 261.

(33) The picrate salt of 2-amino-1-butanol was unstable and decomposed on standing.

Reduction of 3.44 g. (0.02 mole) of the nitroso compound in 40 ml. of dry ethanol (using 1 g. of Raney nickel[4]) was stopped when 2 molar equivalents of hydrogen had been used. After removal of the catalyst and solvent, the residue was distilled through the semi-micro column.[24] The fraction at 29–35° (3 mm.) was redistilled to give 2-propyl-4-ethyloxazolidine (1.00 g., 35%); b.p. 60–65° (11 mm.), $n^{25}D$ 1.4392. The benzenesulfonamide was prepared by the Hinsberg method and melted at 49–50° after three recrystallizations from ethanol–water,[34] mixed m.p. (1:1, 3:1, 1:3) with the benzenesulfonamide of 2-propyl-4-ethyloxazolidine[35] 61–62.5°.

Lithium Aluminum Hydride Reduction[12] of 2-Propyl-3-nitroso-4-ethyloxazolidine.—A solution of 11.60 g. (0.067 mole) of the nitroso compound in 50 ml. of dry ether was introduced into a flask equipped with a stirrer, thermometer, dropping funnel, calcium chloride drying tubes and an ice-bath. The temperature was kept below 10° during the addition of 2.70 g. (0.071 mole) of lithium aluminum hydride in 100 ml. of dry ether. After stirring for 1 hour at 0°, 125 ml. of a 30% sodium potassium tartrate solution was added. The ether layer was separated and combined with two 40-ml. ether washings of the aqueous layer. The ether solution was washed with water, dried over magnesium sulfate and the ether distilled. The residue was distilled through the semi-micro column[24] to give three fractions in the range 65–70° (0.05 mm.) (7.01 g., 66%). The middle fraction was analyzed; b.p. 68–69° (0.05 mm.), $n^{25}D$ 1.4570, d^{25}_4 0.9370, M_D 45.99, calcd. 45.96. Infrared maxima: 3.12 μ (medium, –NH stretch), 6.19 μ (weak, $-NH_2$ deformation).

Anal. Calcd. for $C_8H_{18}N_2O$: C, 60.71; H, 11.47; N, 17.70. Found: C, 60.99; H, 11.86; N, 16.92.

In further experiments yields up to 85% were obtained.

The *p*-nitrobenzamide was prepared in pyridine and melted at 137–138° after several recrystallizations from ethanol–water. Infrared maxima: (Nujol mull) 3.20 μ (weak, –NH stretch), 6.05 μ (medium, 2° amide C=O stretch), 6.29 μ (medium-weak, phenyl ring stretch), 6.42 μ (weak, N=O stretch), 6.62 μ (medium, phenyl ring stretch).

Anal. Calcd. for $C_{15}H_{21}N_3O_4$: C, 58.61; H, 6.89; N, 13.67. Found: C, 58.18; H, 7.30; N, 13.61.

An oxalate melted at 113–114° after recrystallization from absolute ethanol but did not give a satisfactory analysis. This derivative was sensitive to contact with the atmosphere and yellowed on standing.

Anal. Calcd. for $C_{10}H_{20}N_2O_5$: C, 48.37; H, 8.12; N, 11.29. Found: C, 47.39; H, 8.87; N, 11.22.

Attempted Oxidation of 2-Propyl-3-nitroso-4-ethyloxazolidine.—A mixture of 4.30 g. (0.025 mole) of the nitroso compound, 100 ml. of 3% hydrogen peroxide and 10 ml. of a 10% sodium hydroxide solution was stirred vigorously for 25 hours at room temperature. After standing an additional 2 days, 2.80 g. of the starting material was recovered, $n^{25}D$ 1.4601. The nitroso compound was characterized by its infrared spectrum.

A mixture of 4.30 g. (0.025 mole) of 2-propyl-3-nitroso-4-ethyloxazolidine, 10 ml. of 30% hydrogen peroxide and 1 ml. of a 10% sodium hydroxide solution was stirred for 2 hours, heated on a steam-bath for 10 minutes and stirred 1 hour longer. Three grams of the starting material was recovered unchanged, $n^{25}D$ 1.4593, and was characterized by the infrared spectrum.

PROVIDENCE, RHODE ISLAND

(34) This melting point could not be raised by further recrystallization.

(35) Prepared by M. Gollis of this Laboratory, m.p. 62–63°.