Anal. Calcd. for $C_{22}H_{26}O_6$: C, 68.38; H, 6.78. Found: C, 68.50; H, 6.87.

The compound was insoluble in dilute sodium carbonate which eliminated the possibility of it being a diether.

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NATIONAL CANCER INSTITUTE
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Purification of 2,6-Lutidine

BY JOHN A. CATHCART AND DELBERT D. REYNOLDS

2,6-Lutidine is a very useful reagent in synthetic organic chemistry. It is a stronger base toward hydrogen chloride than is pyridine,[1] and it has less tendency to quaternize than does pyridine or the picolines.[2] The combination of these properties makes it especially useful in the chemistry of the sulfonates, in which quaternization is often an undesirable side reaction.

This note deals with the separation of 2,6-lutidine from the picolines. Commercial 2,6-lutidine contains β- and γ-picolines. Previous methods of separation have depended upon the fractional crystallization of derivatives such as hydrohalides, picrates, dimercurichlorides and oxalates, or upon azeotropic distillation.[3] The method described here is based upon the fact that 2,6-lutidine quaternizes with alkyl sulfonates much more slowly than do the picolines. Thus, when a mixture of 2,6-lutidine and the picolines reacts with an alkyl sulfonate, the picoline forms insoluble, undistillable quaternary salts which may be separated from the 2,6-lutidine by decantation or distillation. The effectiveness of this method is illustrated in the experimental section.

Experimental

The crude 2,6-lutidine was Eastman Kodak Co. Practical grade (m.p. −8.5°). The impurity is not water alone, since distillation over calcium hydride raised the melting point to only −7.6° instead of −5.9° which was the value found for pure 2,6-lutidine by repeated fractional crystallization.[3]

Any of the alkyl sulfonates may be used, but we prefer ethyl *p*-toluenesulfonate because of its availability and because of the rate with which it reacts with the picolines.

Removal of β- and γ-Picolines.—A. One kilogram of 2,6-lutidine (m.p. −8.5°) was mixed with 200 g. of ethyl *p*-toluenesulfonate and heated to reflux for one hour. The reaction mixture was cooled and the upper layer separated and distilled without fractionation. This product was refluxed over 100 g. of calcium hydride and distilled through a 20-inch column packed with glass helices; first fraction: b.p. < 144°, 25 g.; second fraction: b.p. 144°, 741 g., m.p. −6.15°.

B. This example omits the steps in which the quaternized product is separated and the distillation over calcium hydride.

One kilogram of 2,6-lutidine (m.p. −8.5°) was refluxed for one hour with 200 g. of ethyl *p*-toluenesulfonate. The 2,6-lutidine was distilled from the reaction mixture through a 20-inch packed column; first fraction: 24 g., b.p. 64–144°; second fraction: 780 g., b.p. 141°, m.p. −6.4°.

Removal of β-Picoline.—Four hundred and seventy-five grams of 2,6-lutidine (m.p. −6.3°) was mixed with 25 g. (5%) β-picoline. This mixture melted at −9.1°. One hundred grams of ethyl *p*-toluenesulfonate was added, the solution refluxed for one hour and then distilled as above; first fraction: 26 g., b.p. < 144°; second fraction: 350 g., b.p. 144°, m.p. −6.3°.

Redistillation of the second fraction over calcium hydride raised the melting point to −6.2°.

Removal of γ-Picoline.—Four hundred and seventy-five grams of 2,6-lutidine (m.p. −6.5°) was mixed with 25 g. of γ-picoline. The mixture (m.p. −9.1°) was refluxed for 1.5 hours with 100 g. of ethyl *p*-toluenesulfonate. The upper layer was separated and fractionally distilled; first fraction: b.p. < 144°, 18 g.; second fraction: 338 g. b.p. 144°, m.p. −6.3°.

Removal of α-Picoline.—Four hundred and seventy-five grams of 2,6-lutidine (m.p. −6.5°) was mixed with 25 g. of α-picoline. This mixture (m.p. −9.1°) was refluxed one hour with 100 g. of ethyl *p*-toluenesulfonate. The lutidine layer was separated and distilled; first fraction: b.p. < 144°, 42 g., second fraction: b.p. 144, 325 g., m.p. −6.4°.

RESEARCH LABORATORY
EASTMAN KODAK COMPANY
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Pyrido[3,2-d]thiazoles

BY SCOTT J. CHILDRESS[1] AND R. L. MCKEE

At the time of this work, previous reports of pyridothiazoles had been confined to the [2,3-d][2] and the [2,1-b][3] series. As a background for future research, the formation of the pyrido[3,2-d]thiazole system has been briefly investigated. During the course of this work, other examples of this system have appeared[4] and certain intermediates have been reported.[5]

The preparation of 5-methylpyrido[3,2-d]thiazole was accomplished by simultaneous reduction and cyclization of 5-methyl-3-nitro-2-pyridinethiol by means of iron filings and formic acid. The 2,5-dimethyl analog, similarly prepared, was not obtained in a pure condition.

Experimental

5-Methyl-2-nitraminopyridine was prepared from 1.0 g. of 2-amino-5-methylpyridine, 4.6 ml. of concentrated sulfuric acid and 0.7 ml. of concentrated nitric acid maintained below 10°. One gram of light yellow needles melting with decomposition at 181° was obtained.

Anal. Calcd. for $C_6H_7N_3O_2$: N, 27.4. Found: N, 27.3, 27.5.

2-Amino-5-methyl-3-nitropyridine was prepared as recently described.[5] The present authors were unable to obtain a yield greater than 36% of a dark yellow powder melting at 192–194°.

Anal. Calcd. for $C_6H_7N_3O_2$: N, 27.4. Found: N, 27.5.

5-Methyl-3-nitro-2-pyridol.—A. Following the procedure of Lapin and Slezak,[5] a crude yield of 55% was obtained. The purified product melted at 251–253.5°. B. The procedure of Hawkins and Roe[6] when applied to 2-amino-5-methylpyridine produced a crude yield of 40% of the desired compound melting at 250–252°.

Anal. Calcd. for $C_6H_6N_2O_3$: N, 18.2. Found: N, 18.2.

2-Chloro-5-methyl-3-nitropyridine.—The action of 50 ml. of phosphorus oxychloride under reflux for six hours upon 9.5 g. of 5-methyl-3-nitro-2-pyridol followed by treatment with crushed ice resulted in a crude yield of 94% of the desired compound melting at 49–51°. For analysis, a portion

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was recrystallized from methanol and sublimed *in vacuo* to give a white crystalline product, m.p. 50–51°.

Anal. Calcd. for $C_6H_5ClN_2O_2$: N, 16.2. Found: N, 16.2.

5-Methyl-3-nitro-2-pyridinethiol.—To a solution of 10 g. of potassium hydroxide in 100 ml. of methanol and saturated with hydrogen sulfide, 10 g of 2-chloro-5-methyl-3-nitropyridine was added in portions. After the vigorous reaction had subsided, the mixture was allowed to stand for five minutes, cooled, treated with 100 ml. of water, acidified with acetic acid, and thoroughly chilled. The product which separated at this point was contaminated with sulfur and hence was dissolved in hot, dilute ammonium hydroxide, filtered, and reprecipitated with acetic acid to give 2.5 g. of a yellow powder. The filtrate slowly deposited 0.1 g. of an orange substance melting at 240°, presumably the disulfide (see below). Recrystallized from 95% ethanol, the thiol appeared as fine yellow needles which decomposed slowly above 170°. On rapid heating, it was completely melted at about 200°.

Anal. Calcd. for $C_6H_6N_2O_2S$: N, 16.5; S, 18.8. Found: N, 16.5; S, 19.0

Five tenths of a gram of this disulfide was dissolved in 10 ml. of 5% sodium hydroxide and treated with a solution of 0.4 g. of iodine in alcohol to form 0.2 g. of **bis-(5-methyl-3-nitro-2-pyridyl) disulfide** an orange compound melting at 246° with decomposition after crystallization from benzene.

Anal. Calcd. for $C_{12}H_{10}N_4O_4S_2$: N, 16.6; S, 18.7. Found: N, 16.6; S, 18.9.

5-Methylpyrido[3,2-d]thiazole.—A suspension of 400 mg. of 5-methyl-3-nitro-2-pyridinethiol in 12 g. of 85% formic acid containing 3 g. of iron filings was boiled vigorously for 1.5 hours, cooled, made basic, and extracted with ether. The ether was evaporated and the residue sublimed *in vacuo* to yield 90 mg. of pale yellow crystals melting at 85–87°. A solution of the compound in methanol after treating with Norite, evaporating, and resubliming gave rise to white crystals melting at 85.5–87.5°. The compound had an odor resembling that of quinoline and turned yellow after standing for a few days.

Anal. Calcd. for $C_7H_6N_2S$: N, 18.7; S, 21.3. Found: N, 18.6; S, 21.4.

2,5-Dimethylpyrido[3,2-*d*]thiazole.—The reduction of 5-methyl-3-nitro-2-pyridinethiol with iron or zinc or of bis-(5-methyl-3-nitro-2-pyridyl) disulfide with iron followed by treatment with acetic anhydride apparently gave rise to the desired compound, but repeated crystallization and sublimation failed to give a product of satisfactory melting point or analysis. Thus, 1.0 g. of 5-methyl-3-nitro-2-pyridinethiol, 25 g. of acetic acid, 1.0 ml. of concentrated hydrochloric acid and 3 g. of iron filings were refluxed for 1.5 hours. After adding 11 g. of acetic anhydride, the mixture was boiled for an additional 15 minutes. The product was obtained by making the solution basic, distillation with steam, and extraction of the distillate with ether. Sublimation afforded 0.1 g. of white crystals which softened at 55° and melted from 63 to 66°. The most pure product obtained after resublimation softened at 63° and melted at 67.5–69.5° and retained an odor resembling that of quinoline.

Anal. Calcd. for $C_8H_8N_2S$: N, 17.1; S, 19.5. Found: N, 16.9; S, 18.9.

THE VENABLE CHEMICAL LABORATORY
THE UNIVERSITY OF NORTH CAROLINA
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The Nature of the Vapor State of Hydrazine Monohydrate and Ethylenediamine Monohydrate

BY LOWELL V. COULTER

Experimental investigations of the vapor state of hydrazine monohydrate have led to contradictory conclusions regarding the extent of association in the vapor phase. Scott[1] has reported vapor densities at 99°, 367 mm. pressure and 138°, 744 mm. pressure that correspond to molecular weights of 31.8 and 25.0, respectively. These observations have been explained by Yost and Russell[2] by the dissociation equilibrium

$$N_2H_4 \cdot H_2O(g) \rightleftharpoons N_2H_4(g) + H_2O(g)$$

Infrared absorption spectrum measurements[3] indicate, however, that no monohydrate species is present since the spectrum consists of the superposition of the spectra of hydrazine and water.

In view of the opportunity this system might afford for a study of the energy of a gaseous N····H-O hydrogen bond system, an exploratory study of vapor densities was conducted. Within the limits of error of these measurements it appears that the earlier observation, indicating association of water and hydrazine in the gas phase, was in error because of adsorption of vapors on the walls of the apparatus or the lack of complete volatilization of the sample in the Victor Meyer procedure. The results of this research indicate no appreciable association between hydrazine and water or ethylenediamine and water in the gas phase. The latter system was also selected for investigation because of the similarity of the two systems.

Experimental

Hydrazine monohydrate was prepared from the commercial product (National Biochemical Co.) by high vacuum distillation at room temperature and the addition of water to give an equimolecular solution of hydrazine and water. Analysis by acid titration and the iodate method[4] indicated 64.54 and 64.25% hydrazine, respectively (64.01% theoretical). The freezing point of the hydrazine monohydrate was −51.1°, which we compare with −51.7° reported by Mohr and Audrieth[5] for the freezing point. The ethylenediamine monohydrate was prepared from a purified commercial product by the quantitative addition of water. Anhydrous ethylenediamine was obtained by drying over calcium oxide both before and after fractional distillation. The anhydrous product froze at 11.1°, to be compared with 11.0° reported by Wilson.[6] By acid titration the monohydrate analyzed 0.5013 mole fraction diamine.

The experiments involved the determination of pressure-temperature relationships at constant vapor densities. The apparatus consisted of a calibrated glass bulb with an attached Bodenstein gage,[7] sensitivity 0.2 mm., that was employed as a null instrument for pressure measurements with a mercury manometer and cathetometer. The glass bulb and attached gage were completely thermostated in an oil-bath with temperature control usually better than 0.01°.

Samples of the hydrates were transferred to the apparatus with the aid of high vacuum techniques and inert protective gases thereby avoiding exposure of the preparations to atmospheric oxygen, water and carbon dioxide. In each isochore determination the vapor pressure of the liquid was determined prior to complete vaporization in order to ascertain the sharpness of the discontinuity at the point of complete vaporization. The $P-T$ curves are presented in Fig. 1 for hydrazine monohydrate at two different pressure ranges and for ethylenediamine monohydrate at one pressure range. In drawing the vapor pressure curves of the liquid the steepness of the slope near the saturation pressure has been exaggerated in order to reveal the maximum deviation possible of observed pressures from the extrapolated curves (dotted portions).

On the basis of the pressure temperature curves it appears unlikely that any association between hydrazine or

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