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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Purification of 2,6-Lutidine

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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°.

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Pyrido[3,2-d]thiazoles

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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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