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SYNTHESES WITH STABLE ISOTOPES: PYRIDINE-^{15}N.

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SUMMARY

The acid-catalyzed condensation of either 2-ethoxy-3,4-dihydro-2H-pyran or pentanedial (glutaraldehyde) with ammonium-^{15}N chloride in the presence of methylene blue is a convenient one-step synthesis of pyridine-^{15}N.

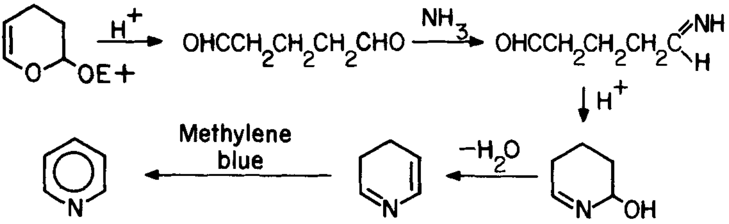
INTRODUCTION

Pyridine-^{15}N was recently required at this Laboratory both as an isotopic tracer in studying molecular rearrangement reactions and for spectroscopic studies. A single preparation of pyridine-^{15}N has been reported -- that of Bak *et al.* [1], who obtained a yield of 5% while noting that the method (condensation of 2-pentenedial with ammonium-^{15}N nitrate) gave yields of 10-13% in preliminary experiments. Colchester and Corran [2] reported the preparation of pyridine in yields of 20-80% from pentanedial or 2-methoxy-3,4-dihydro-2H-pyran and ammonium sulfate in the presence of a number of reducible dyes. We investigated this reaction under conditions in which ammonium ion was not used in excess as a possible method for preparing pyridine-^{15}N.

DISCUSSION

An outline of the condensation of 2-ethoxy-3,4-dihydro-2H-pyran or pentanedial with ammonia to give 3,4-dihydropyridine which is then dehydrogenated to

Scheme I



pyridine by methylene blue is shown in Scheme I. It is preferable to use 2-ethoxy-3,4-dihydro-2H-pyran as an *in situ* source of pentanedial, since the latter tends to polymerize in aqueous solution. The reaction was found to proceed smoothly when stoichiometric amounts of ammonium ion were used, and yields of 60-65% (by uv analysis) could be realized.

Pyridine was conveniently isolated as an aqueous azeotrope after steam volatile substances were removed from the acidic reaction mixture. Anhydrous pyridine was prepared by distilling pyridine from a mixture of anhydrous pyridinium chloride and N,N-dibutyl-1-butanamine (tributylamine) or by treatment of aqueous pyridine with molecular sieve and vacuum transfer of the anhydrous pyridine. The overall conversion of ammonium-^{15}N chloride to anhydrous pyridine-^{15}N could be accomplished in yields of 50-55%.

EXPERIMENTAL

Materials and Methods—Ammonium-^{15}N chloride was obtained from the hydrolysis of calcium nitride-$^{15}N_2$.* Nmr spectra were recorded on a Perkin-Elmer R-24 60 MHz spectrometer using TMS as an internal standard. Ir spectra were recorded on a Perkin-Elmer 710 spectrophotometer. Absorption spectra were measured on a Unicam SP-800 ultraviolet spectrophotometer. Gc analyses were performed using a Varian Aerograph 90-P gas chromatograph with Porpak-Q and FFAP on Chrom. W columns in series using helium as a carrier gas.

Pyridine-^{15}N--A 5-l., three-neck flask equipped with a reflux condenser, addition funnel, and magnetic stirrer was charged with water (1.7 l.), concentrated sulfuric acid (50 ml), methylene blue (157 g, 0.42 mol), and ammonium-^{15}N chloride (22.7 g, 59.8 atom % ^{15}N, 0.42 mol). The solution was brought to gentle reflux, and a solution of 2-ethoxy-3,4-dihydro-2H-pyran (53.8 g, 0.42 mol) in ethanol (50 ml) was added dropwise over a period of 2 hr. After addition of the acetal, the mixture was refluxed gently for 10 hr. After cooling, the reflux condenser and addition funnel were replaced with a distilling head, condenser, and receiver. Additional water (500 ml) was added, and the mixture was distilled until no odor of glutaraldehyde could be detected in the distillate (ca. 1.2 l.). The reaction mixture was allowed to cool and made basic by the gradual addition of 50% sodium hydroxide solution (200 ml) and then distilled until about 500 ml of distillate was collected. Redistillation of the distillate through a short (6-cm) fractionating column packed with glass helices gave a pyridine-water mixture (115 g, ambient to 93°, 580 torr) which contained 20.7 g (62%) pyridine as determined by uv absorption of a suitably diluted aliquot. The pyridine-water mixture was acidified with hydrochloric acid and evaporated to a semisolid mass which was made basic with the minimum amount of 50% sodium hydroxide solution. Molecular sieve (3A, 300 g) was added slowly to the chilled pyridine-water-salt solution, and pyridine was collected from the mixture by bulb-to-bulb vacuum transfer (moderate heating of the molecular sieve was necessary). The pyridine collected in this manner (18.6 g) contained traces of water (by gc) which was removed by a second bulb-to-bulb vacuum transfer from molecular sieve (3A, 10 g) to yield anhydrous pyridine-^{15}N (18.2 g, 55% yield, 88% recovery): nmr (CCl_4)δ 7.1 (2H, m, H-3, H-5), 7.4 (1H, m, H-4), 8.5 (2H, m, H-2, H-6, complex ^{15}N splitting); ir (vapor) 3100, 3060, 1580, 1440, 1420 cm^{-1}.

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