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Syntheses of Pyridine-2-^{13}C and Pyridine-3-^{13}C

BØRGE BAK

Københavns Universitets kemiske Laboratorium, Copenhagen, Denmark and

NIELS CLAUSON-KAAS

Centrallaboratoriet, Sadolin & Holmblad A/S, Copenhagen, Denmark

For the exact determination of interatomic distances in pyridine pyridine-2-^{13}C and pyridine-3-^{13}C have been prepared.

For the exact determination of interatomic distances in pyridine mixtures of isotopic pyridines containing pyridine-2-^{13}C and pyridine-3-^{13}C have been prepared by the series of reactions shown in Fig. 1. Potassium cyanide containing about 20 % of potassium cyanide-^{13}C was used as starting material. It is evident from the syntheses that the mixture containing pyridine and pyridine-2-^{13}C also must contain a minor amount af pyridine-2,6-$^{13}C_2$.

The constitution and the purity of the two pyridines follows from the syntheses, the infrared and microwave spectra and measurements of their vapor pressure. A report on the infrared spectra of all ^{13}C-compounds prepared here and on the microwave spectra of the pyridines will be published later.

EXPERIMENTAL

Diethyl malonate-1-^{13}C. Potassium cyanide [35.0 g (0.538 mole) of a product containing 21.6 % of potassium cyanide-^{13}C] and chloroacetic acid (44.0 g, 0.465 mole) were transformed into 52.5 g (0.328 mole, 61 %) of diethyl malonate after the directions of Vogel [1].

1,3-Dibromopropane-1-^{13}C, cf. Ref.[2] Diethyl malonate-1-^{13}C (52.5 g, 0.328 mole) in ether (500 ml) was added to a stirred mixture of lithium aluminium hydride (21.8 g, 0.575 mole) and ether (700 ml) during 20 min. The reaction mixture was heated under reflux (1 h). Acetic anhydride (700 ml) was added and about 1 100 ml of solvent distilled. Acetic anhydride (150 ml) and acetic acid (50 ml) were added to the residue and the mixture kept in an oil-bath of 125° (4 h). After cooling, ether (1 250 ml) was added and the precipitate of salts removed by filtration (G 3) and washed with ether (200 ml). The

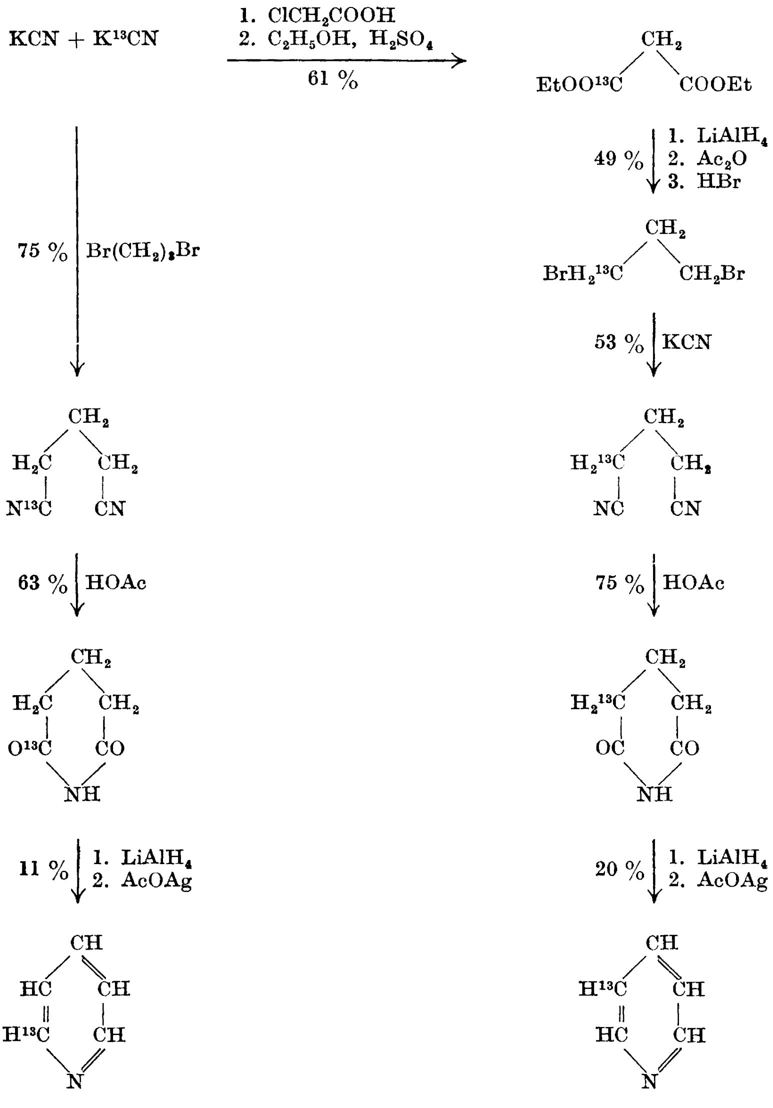

Fig. 1. Routes to pyridine-2-^{13}C and pyridine-3-^{13}C.

solvent was distilled through a small packed column. Ether (100 ml) was added to the semisolid residue and another crop of salts removed by filtration and washed with ether (50 ml). The solution was distilled through the above column, first under atmospheric pressure, then under 15 mm. The fraction boiling at 86—108° (35.0 g) and consisting mainly of 1,3-propanediol diacetate was collected and heated under reflux (7 h) with hydrobromic acid (48 %, 300 ml). About 100 ml of liquid containing dibromopropane was distilled. The dibromopropane layer was separated and washed with the same volume of water, concentrated hydrochloric acid, water, potassium hydrogen carbonate (20 %) and water. Ether was added and the etheral solution dried with magnesium sulfate and distilled. The yield was 32.3 g (0.160 mole, 49 %) of dibromopropane (b.p.$_{760}$ 164–170°).

Glutaronitrile-2-^{13}C. 1,3-Dibromopropane-1-^{13}C (32.3 g, 0.160 mole) and potassium cyanide (25.0 g, 0.384 mole) were transformed into 8.00 g (0.0849 mole, 53 %) of glutaronitrile following the directions of Vogel [3]. The reaction mixture was heated under reflux for 48 h instead of the recommended 35 h and chloroform was used instead of ethyl acetate for extraction of the inorganic salts. An infrared spectrum of the final product showed it to contain certain impurities, but not less than 95 % of glutaronitrile.

Glutarimide-3-^{13}C cf. Ref.[4] Glutaronitrile-2-^{13}C (8.00 g, 0.0849 mole) was dissolved in glacial acetic acid (65 ml) and the solution heated in a sealed tube (210°, 15 h). The solvent was distilled under 15 mm from a water-bath (85°) and the semisolid residue crystallized from ethanol (30 ml). The crystals were washed with ethanol (10 ml) and dried. The yield was 7.19 g (0.0636 mole, 75 %) of glutarimide.

Pyridine-3-^{13}C. Glutarimide-2-^{13}C (7.19 g, 0.0635 mole) was suspended in dry ether (300 ml). Lithium aluminium hydride (8.4 g, 0.22 mole) was added in one portion and the mixture heated with stirring under reflux (8 h). Water (25 ml), followed by a solution of sodium hydroxide (50 g) in water (275 ml), was added dropwise with stirring. The mixture was distilled, first from a water-bath and then by heating with a free flame until the residue solidified. Water (100 ml) was added to the residue and distilled. Acetic acid (30 ml) was added to the combined distillates consisting of ether, water and piperidine. The mixture was distilled from a water-bath (80°), finally under 15 mm. 6.5 g of an oil consisting mainly of piperidine acetate remained.

The oil was dissolved in water (130 ml) and the solution stirred to a paste with silver acetate (130 g), *cf.* Ref.[5] The paste was heated in a glass-lined autoclave under 100 atmospheres of nitrogen (210°, 18 h). The reaction mixture was washed into a 250 ml flask with water (15 ml). A solution of sodium hydroxide (66 g) in water (60 ml) was added together with a large portion of boiling chips, and the mixture distilled by heating with a free flame. After 100 ml of distillate had been collected, water (40 ml) was added to the distilland and another 40 ml distilled. Concentrated hydrochloric acid (14 ml) was added to the combined distillates and the solution evaporated under 20 mm to dryness from a water-bath (70°). The residue was kept in the bath for 3 min under 0.5 mm. The remaining crystals containing pyridine hydrochloride were dissolved in water (20 ml) and a warm solution of mercury chloride (20 g) in water (100 ml) added, *cf.* Ref.[6] The mixture was left standing (1 h) at 0° and the crystals removed by filtration and dried under 0.1 mm. The dry crystals were cooled in liquid air and sodium hydroxide powder (12 g) added rapidly. The solids were mixed thoroughly by shaking with cooling. The mixture was heated slowly under 0.1 mm in an oil-bath to 220°. At 180–200° pyridine and water was evolved rather suddenly and condensed in a receiver containing pulverized sodium hydroxide (2.0 g). The reaction was complete after 20–30 min. The distillate of aqueous pyridine was dried by successive distillations from sodium hydroxide as described previously [7]. The yield was 1.02 g (0.0129 mole, 20 %). The infrared and microwave spectra and the vapor pressure showed the product to be a mixture of pyridine and pyridine-3-^{13}C.

Glutaronitrile-1-^{13}C. 1,3-Dibromopropane (15.5 g, 0.0772 mole) and potassium cyanide [10.0 g (0.154 mole) of a product containing 21.6 % of potassium cyanide-^{13}C] were transformed into 5.45 g (0.0579 mole, 75 %) of glutaronitrile as described above.

Glutarimide-2-^{13}C. Glutaronitrile-1-^{13}C (5.41 g, 0.0574 mole) was transformed into 3.88 g (0.0343 mole, 63 %) of glutarimide as described above.

Pyridine-2-^{13}C. Glutarimide-2-^{13}C (3.88 g, 0.0343 mole) was transformed into 0.30 g (0.038 mole, 11 %) of pyridine as described above. The infrared and microwave spectra and the vapor pressure showed the product to be a pyridine-mixture containing pyridine and pyridine-2-^{13}C. Pyridine-2,6-$^{13}C_2$, which also must be present in the mixture, was not identified.

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