The Preparation of sec-Butylphenylketimine-^{15}N; Di-n-butylketimine-^{15}N and an Improved Synthesis of Aliphatic Cyanides Using Potassium Cyanide.[1]

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sec-Butylphenylketimine-^{15}N was prepared and the proton nitrogen-15 coupling of two isomers was observed. Di-n-butylketimine-^{15}N was prepared. n-Butyl cyanide and sec-butyl cyanide was prepared from n-butyl chloride and sec-butyl chloride respectively using potassium cyanide. An improvement in yield with the addition of sodium acetate is noted.

In order to obtain proton exchange data from nitrogen-15 substituted ketimines as found previously by J. B. Lambert[2]

(2) J. B. Lambert, W. L. Oliver, and J. D. Roberts, J. Am. Chem. Soc., 87, 5085 (1965).

an aliphatic phenyl ketimined had to be found. The basic synthesis developed by Pickard and Tolbert[3] used anhydrous methanol

(3) P. L. Pickard and T. L. Tolbert, J. Org. Chem., 26, 4886 (1961).

to decompose nitrile Grignard reagent complexes. Of the ketimines tried, the n-butylphenyl and the n-propylphenyl derivatives were made in too small a yield to be practical and the isopropylphenyl compound seemed to polymerize into a yellow oil. However the sec-butylphenyl-ketimine was made in reasonable yields, 70-80%. The problem of preventing the ketimine from hydrolysing to the ketone was solved by keeping the apparatus rigorously dry and by using specially dried methanol.

Without exchange, the spectrum of the proton on the nitrogen of sec-butylphenylketimine-^{15}N would be a doublet because of the coupling between the proton and the nitrogen-15. This was observed at temperatures of -35° to -45° in a five percent pentane solution. The doublet ($J_{^{15}NH}$ = 50 cps) was observed at about 7.5 p.p.m. downfield from tetramethylsilane and at the same point where the broad peak was observed from a similar nitrogen-14 product. At -45° the spectrum consisted of four peaks which

indicates the two isomers of sec-butylphenylketimine (figure 1). The pair of doublets was shifted about 10 cps. As the temperature is raised the peaks coalesce indicating a proton spin exchange. The explanation of the mechanism is given by Lambert[1].

figure 1

The di-n-butylketimine-^{15}N was prepared in the same manner as above. This synthesis necessitated the preparation of n-butyl cyanide-^{15}N from potassium cyanide-^{15}N. The general synthesis required an aliphatic halogen to be added to either potassium or sodium cyanide in a solvent of dimethyl sulfoxide. According of Friedman and Shechter, the yields with sodium cyanide are much higher than with potassium cyanide. In order to increase the yield with potassium cyanide, a quantity of sodium acetate was added to the reaction mixture. Using sec-butyl chloride and potassium cyanide with sodium acetate, the yield was 55 percent, which is considerably better than was reported[4]. Using the sodium

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(4) L. Friedman and H. Shechter, J. Org. Chem., 25, 877 (1960).

salt the yield reported is 64 percent while the potassium salt gives a yield of only 42 percent[4]. It was observed that potassium chloride, a product in the reaction, is considerably more soluble in dimethyl sulfoxide than is sodium chloride. Thus the cyanide reaction seems to be inhibited by free chloride ions.

Experimental

NMR spectra were taken on the Varian Associates Model A-60 spectrometer. Thanks are due Drs. S. L. Manatt and D. D. Elleman of the Jet Propulsion Laboratory, Pasadena, California for the use of an A-60 equipped with temperature probe. Special thanks are due Drs. J. B. Lambert and J. D. Roberts for their advice.

Benzamide-^{15}N. Two 200-ml three-necked round-bottomed flasks were used. One, used for the generation of ammonia, was equipped with an inlet tube for prepurified nitrogen, a dropping funnel, and an outlet through a water condenser leading to two potassium hydroxide drying tubes and the reaction flask. The latter flask had an inlet for the nitrogen and ammonia and an outlet to a 10 percent hydrochloric acid trap and was equipped with a mechanical stirrer. The ammonia was made from 7.1046 g. of ammonium chloride-^{15}N in aqueous solution which was added dropwise to 11 g. of sodium hydroxide in 25 ml of water. The reaction flask was thoroughly dried before the reaction was initiated. This flask was charged with 10.72 g. of benzoyl chloride in 120 ml of anhydrous ether and cooled in a dry ice-acetone bath. When the ammonia was slowly bubbled through

the benzoyl chloride, a white precipitate formed after about 30 minutes. After being heater under reflux for three hours, the flask was stoppered with a calcium chloride drying tube and allowed to stand overnight. The mixture was filtered twice with a sintered glass filter and washed with three 18-ml portions of absolute ethanol and three 20-ml portions of acetone. The solvent was evaporated until crystals formed, then 75 ml of benzene was added. This was heated and filtered, with the residue washed with hot benzene. The benzene was removed by rotatory evaporation until crystallization. The product was collected on filter paper with the concentration of the mother liquer yielding two more crops. All of the residue was washed with acetone and recrystallized from benzene. The excess ammonium chloride was recovered quantitatively (3.2 g.). The yield of benzamide-^{15}N was 6.4 g. (0.053 mole, 80.0%), m.p. 121-123° (lit., m.p. 121-123°).

Benzonitrile-^{15}N. Benzamide-^{15}N (6.4 g., 0.053 mole) and sodium aluminum chloride were mixed in a 50-ml round-bottomed flask carrying a distillation head. This was heated to 190° in a silicone oil bath until effervescence ceased. Heating was continued with a flame until the distillation was completed. The yield of benzonitrile-^{15}N was 1.69 g. (0.016 mole, 32.3%).

sec-Butylphenylketimine-^{15}N. sec-Butyl magnesium bromide was prepared in a 200-ml three-necked round-bottomed flask equipped with a reflux condenser and a dropping funnel.

4.50 g. (0.033 mole) of sec-butyl bromide was added dropwise to 0.77 g. (0.014 g.-atom) of magnesium, in 35 ml of anhydrous ether. The mixture was refluxed for 45 minutes and then 1.60 g. (0.0154 mole) of benzonitrile in 10 ml of ether was added dropwise. The mixture was refluxed for six hours. Anhydrous methanol (3.8 g.) was added dropwise. A semi-gum formed which was stirred for 30 minutes until it became crystalline. After filtration, the product was distilled. The yield of ketimine was 1.34 g. (0.0104 mole, 74.3%).

sec-Butyl Cyanide. A sample of 0.090 g. (0.1 mole) of potassium cyanide was dissolved in 30 ml of dimethyl sulfoxide in a three-necked round-bottomed flask equipped with a water condenser, dropping funnel, and thermometer and then 1.0 g. (0.1 mole) of sodium acetate was dissolved in the solution. The mixture was heated to 120° and 3 g. of sec-butyl chloride added dropwise over a period of one hour. The mixture was refluxed for 15 hours. About 100 ml of water was added to the cooled mixture which was shaken with two portions of ether. The ether solution was shaken with 6N hydrochloric acid to hydrolyze any isocyanate present. The ether was removed and the product was dried over calcium chloride and distilled over phosphorus pentoxide. The yield of sec-butyl cyanide was 0.63 g. (0.076 mole, 55%).

Potassium Cyanide-^{15}N was obtained from the Volk Radiochemical Laboratories.

n-Butyl cyanide was prepared in the same manner as sec-butyl cyanide (vide supra) from n-butyl chloride, 1.09 g. (0.0165 mole) of potassium cyanide-^{15}N, and 1.0 g of sodium acetate. The yield of n-butyl cyanide-^{15}N was 1.01 g. (0.0120 mole, 72.7%).

Di-n-butylketimine was prepared in the same manner as sec-butylphenylketimine-^{15}N (vide supra) from 3.0 g. (0.022 mole) of n-butyl bromide, 0.50 g. (0.0091 g.-atom) of magnesium, 1.01 g. (0.0120 mole) of n-butyl cyanide-^{15}N, and 3.2 g. of anhydrous methanol. The yield of the ketimine was 0.533 g. (0.00375 mole, 41.2%).