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Research Article

Synthesis of ^{13}C-labelled cinnamonitrile

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Summary

^{13}C-labelled cinnamonitrile, a compound that possesses both the aromatic functionality of styrene and the nitrile functionality of acrylonitrile has been synthesized in one step using β-bromostyrene and potassium [^{13}C]cyanide. The preparation of a target material using ^{13}C -labelled cinnamonitrile may provide a cost-effective method for producing nitrogen-13 via proton irradiation for Positron Emission Tomography. Copyright © 2002 John Wiley & Sons, Ltd.

Key Words: cinnamonitrile; nitrogen-13; Positron Emission Tomography (PET)

Introduction

In an effort to prepare an improved carbon-rich target material for the accelerator production of [^{13}N]ammonia for use in Positron Emission Tomography (PET), poly(styrene/divinylbenzene) and poly(acrylonitrile) materials have been evaluated.[1–3] ^{13}N-Ammonia is generally produced by proton bombardment of oxygen-16 and/or carbon-13 enriched target materials.[4,5] While the current production of ^{13}N-ammonia derives mainly from the >10 MeV proton reaction with an oxygen-16 target,[5] development of low cost, low energy (4–7 MeV) accelerator alternatives has been pursued by a number of manufacturers of PET accelerators. This reduction in energy demands new target

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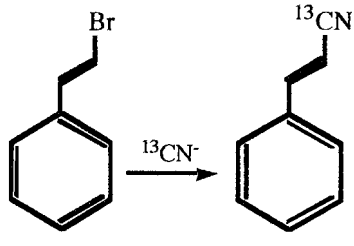
development to accommodate the higher beam currents required, and limits the targets to those that utilize nuclear reactions that are available at these energies, hence the proton reaction with carbon-13, and not the proton reaction with oxygen-16. Current target materials used for production of nitrogen-13 are problematical due to their physical instability and low yields of ammonia.[1] For the purpose of improving nitrogen-13 production for use in medical imaging, pyrolyzed ^{13}C-enriched sulfonated poly(styrene/divinylbenzene) has been under investigation. Preliminary cyclotron studies involving the deuteron irradiation of naturally abundant carbon-12 pyrolyzed poly(styrene/divinylbenzene) derivatives have demonstrated the formation of pure [^{13}N]ammonia in yields consistent with theory.[1,2] At the present time, yields of [^{13}N]ammonia have been limited due to the inability of the generated nitrogen-13 particles to escape the carbon matrix of polymer beads produced by suspension polymerization. Advances have been made in our laboratory by investigating emulsion polymerization techniques that are used for creating porous polymers.[6] The initial attempts at emulsion polymerization have been favorable.

A second approach has been the investigation of a carbon-13 rich porous carbon source made from poly(acrylonitrile). Samples of porous carbon have been irradiated with protons using the natural abundance of carbon-13 and results indicate this target to be very promising.[3]

It was anticipated that a material having the structural properties of styrene and acrylonitrile may provide a porous, carbon-rich target for nitrogen-13 production for PET. Cinnamonitrile possesses both the aromatic ring of styrene and the nitrile group of acrylonitrile. It can be prepared in a one step reaction of β-bromostyrene with potassium cyanide.[7,8] Since [^{13}C]potassium cyanide is readily available, incorporation of the label into cinnamonitrile can be easily accomplished as shown in Scheme 1.



Scheme 1.

Experimental

General

Benzene was freshly distilled over lithium aluminum hydride. All other reagents were obtained in high purity from Aldrich Chemical Co. and opened just prior to use. Glassware was thoroughly flame-dried, and cooled under nitrogen before the start of the experiment. NMR spectra were recorded on a Bruker Avance 300 MHz NMR spectrometer. Mass spectrum was obtained from Mid-South Analytical Labs, Inc., Bossier City, LA. Column chromatographic separation was accomplished using Aldrich 70–270 mesh, 60 Å silica gel with 100% hexanes followed by 100% ethyl acetate as solvents. GC analysis was performed on a Gow-Mac Gas Chromatograph Series 350 Thermal Conductivity Detector using a 20% DC 200 on Chrom. –P 80/100 mesh column.

[1-^{13}C]-Cinnamonitrile

To a 25-ml round-bottomed flask equipped with magnetic stirbar and condenser, and containing benzene (8.3 ml) was added *trans*-β-bromostyrene (1.41 g, 7.7 mmol), potassium [1-^{13}C]cyanide (1.00 g, 15.4 mmol), tetrakis(triphenylphosphine) palladium (0.27 g, 0.23 mmol) and 18-crown-6 (0.15 g, 0.57 mmol). The mixture was allowed to stir at room temperature for 20 min under nitrogen and was then heated to reflux for 7 h. The resulting mixture was poured into deionized water (50 ml) and ether (50 ml). The organic layer was separated, concentrated *in vacuo*, and purified via column chromatography to afford 0.18 g of [1$-^{13}$C]-cinnamonitrile (18% yield, 100% GC pure); ^{1}H NMR ($CDCl_3$): δ 7.40 (m, 5H, aromatic H's), 7.35 (d, 1H, H *geminal* to ring), 5.85 (d, 1H, H *cis* to ring, $J_{trans} = 18$ Hz); ^{13}C NMR ($CDCl_3$): δ 150.94, 133.91, 131.64, 129.54, 127.78, 118.58, 96.76; mass spectrum, $m/z = 130$ (M^+, 100), 129, 103, 102, 63, 51, 50.

Conclusion

[1-^{13}C]-cinnamonitrile has been prepared in adequate yield. It was found that longer reaction times as well as the use of high purity reagents did not allow for an improvement in the yield. Since the source of label is relatively inexpensive, [1-^{13}C]-cinnamonitrile can easily be prepared in

sufficient quantity, and it is anticipated that a markedly porous material will result from emulsion polymerization of cinnamonitrile. Pyrolysis of the resulting polymer may provide a carbon-rich target material for application in PET.

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