

## Research Article

# Synthesis of Phenyl- $^{13}\text{C}_6$ -ethene

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## Summary

In an effort to prepare an improved carbon-rich target material for the accelerator production of  $^{13}\text{N}$  labelled ammonia for use in positron emission tomography (PET), sulfonated poly(styrene/divinylbenzene) has been evaluated. The preparation of this target material using naturally abundant carbon-12 compounds was investigated in an effort to optimize conditions for the preparation of the analogous carbon-13 target material which may provide a cost-effective method for producing nitrogen-13 labelled ammonia via proton irradiation. As part of this study, phenyl- $^{13}\text{C}_6$ -ethene was synthesized in three steps starting from benzene- $^{13}\text{C}_6$ . Copyright © 2001 John Wiley & Sons, Ltd.

**Key Words:** phenyl- $^{13}\text{C}_6$ -ethene; styrene; positron emission tomography

## Introduction

For the purpose of improving ammonia- $^{13}\text{N}$  production for use in medical imaging, pyrolyzed carbon-13 enriched sulfonated poly(styrene/divinylbenzene) is under investigation. In order to prepare the carbon-13

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enriched polymer, the corresponding monomer was synthesized in three steps starting from benzene-13C6 (Scheme 1).<sup>1-3</sup>

Optimization of the phenylethene synthesis was carried out using naturally abundant carbon-12 reagents.<sup>4,5</sup> For the preparation of phenyl-13C6-ethene, bromobenzene-13C6, produced from reaction of benzene-13C6 with 1,3-dibromo-5,5-dimethylhydantoin (DBMH) and trifluoromethanesulfonic acid (triflic acid)<sup>1</sup> was purified by distillation and converted to 1-phenyl-13C6-ethanol by Grignard Reaction with acetaldehyde.<sup>2</sup> Subsequent dehydration of the alcohol with potassium bisulfite yielded phenyl-13C6-ethene.<sup>3</sup> The overall yield of phenyl-13C6-ethene starting from benzene-13C6 was approximately 50%. Unreacted benzene-13C6 was recovered via distillation of bromobenzene-13C6.

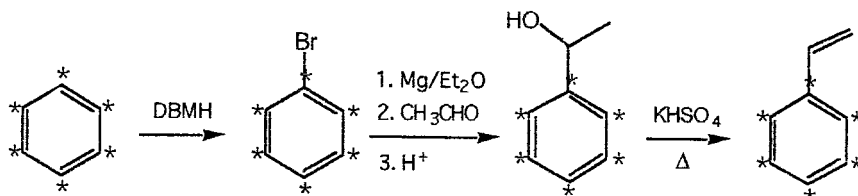
## Experimental

### General

When required, glassware and cannula were flame-dried prior to use. NMR spectra were recorded on a Bruker AC 250 MHz FT-NMR spectrometer. GC analyses were performed on a Gow-Mac Gas Chromatograph Series 350 equipped with a Thermal Conductivity Detector using a 20% DC 200 on Chrom.-P 80/100 mesh column. All yields reported were determined by GC and corrected for purity.

### Bromobenzene-13C6(1)

To a 250-ml pear-shaped flask equipped with magnetic stirrer and condenser with drying tube attached, were added benzene-13C6 (4.9409 g, 58.8 mmol), freshly distilled dichloromethane (70 ml), triflic acid (99<sup>+</sup>%, 5.0265 g, 33.5 mmol) and DBMH (9.7299 g, 34.0 mmol). During the addition of the DBMH, the flask was covered with aluminum foil. The cloudy, yellow mixture was allowed to reflux in



Scheme 1.

the dark for 2 h. A saturated solution of sodium bisulfite (35 ml) was then added to the product mixture until the amber organic layer was decolorized. The mixture was neutralized with 2 M sodium carbonate (60 ml). The organic layer was separated and the aqueous layer extracted with dichloromethane. The combined organic extracts were dried over magnesium sulfate and distilled to afford 7.47 g of bromobenzene-13C6 (77% yield, 96.7% GC purity);  $^1\text{H NMR}$ :  $\delta$  7.50 (m, 2H, *ortho* H's), 7.25 (m, 3H, *meta* and *para* H's).

### *1-Phenyl-13C6-ethanol (2)*

Magnesium turnings (3.3 g, 135.7 mmol), a crystal of iodine and a magnetic stirbar were placed in a flame-dried 100-ml three-necked round-bottomed flask equipped with thermometer, reflux condenser and addition funnel. The apparatus was then carefully flame-dried again and kept under an argon atmosphere. Ether (21 ml) was introduced into the flask through the addition funnel by cannula. Bromobenzene-13C6 (4.45 ml of mixture, 4.30 ml, 40.8 mmol) was then transferred to the funnel via cannula and carefully added to the mixture at room temperature. The beginning of the reaction was evidenced by the disappearance of the iodine color which changed from light yellow to gray, then finally to dark brown. The flask was placed in a warm water bath to induce reflux. After 30 min of continuous reflux, the mixture was placed in an ice bath and allowed to cool to 0°C. To the addition funnel was added a mixture of ether (7 ml) and acetaldehyde (5.0 ml, 89.2 mmol) by cannula. The acetaldehyde solution was slowly added to the stirring Grignard reagent over a 63 min period with the temperature held below 15°C. The reaction mixture became milky yellow and viscous after the addition. Ice water was added to quench the reaction and magnesium salts were dissolved with the addition of 15% sulfuric acid. The organic layer was separated and the aqueous layer extracted with diethyl ether. The combined organic layers were dried over magnesium sulfate, and concentrated *in vacuo* to yield 4.31 g of 1-phenyl-13C6-ethanol (83% yield, 89.8% GC purity);  $^1\text{H NMR}$ :  $\delta$  7.30 (m, 5H, Ar H's), 4.85 (q, 1H, methine H), 2.10 (s, 1H, OH), 1.40 (d, 3H, CH<sub>3</sub>).

### *Phenyl-13C6-ethene (3)*

1-Phenyl-13C6-ethanol (4.55 g mixture, 4.08 g, 31.9 mmol), potassium bisulfate (0.28 g), copper metal (0.08 g) and hydroquinone (spatula tip)

were added to a 15-ml pear-shaped flask equipped with short-path distillation apparatus with thermometer and magnetic stirbar. The flask was wrapped with aluminum foil and placed in an oil bath. With a vapor temperature  $<150^{\circ}\text{C}$  and oil bath temperature  $>200^{\circ}\text{C}$ , the distillate was collected. The organic layer was separated and the aqueous layer extracted with diethyl ether. The combined organic phases were dried over magnesium sulfate and concentrated to give 2.54 g of phenyl- $^{13}\text{C}_6$ -ethene (72% yield, 81.7% GC purity);  $^1\text{H}$  NMR:  $\delta$  7.69 (m, 2H, *ortho* H's), 7.53 (m, 3H, *meta* and *para* H's), 6.99 (dd, 1H, CH), 6.03 (dd, 1H, H *cis* to ring), 5.15 (dd, 1H, H *trans* to ring).

## Conclusion

Phenyl- $^{13}\text{C}_6$ -ethene, while commercially available, is prohibitively expensive. Benzene- $^{13}\text{C}_6$ , purchased for a moderate price, can be converted to phenyl- $^{13}\text{C}_6$ -ethene in three synthetic steps in about 50% yield. This yield is somewhat higher than previously reported, where phenyl- $^{14}\text{C}_6$ -ethene was prepared from benzene- $^{14}\text{C}_6$  in 28% yield.<sup>2</sup> It should be noted that during optimization of the reactions, when using freshly opened reagents, yields were slightly higher for the Grignard reaction (91%) and the dehydration (80%). Phenyl- $^{13}\text{C}_6$ -ethene will be polymerized, sulfonated and pyrolyzed in a way similar to that previously reported using naturally abundant carbon-12 reagents<sup>6-8</sup> to yield a porous carbon-13 matrix which will be evaluated as a potential PET target material for the accelerator production of ammonia- $^{13}\text{N}$ .

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