

Research Article

A facile synthesis of radioiodinated alkynyl iodides using potassium alkynyltrifluoroborates

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Summary

Radioiodinated alkynyl iodides have been synthesized for the first time from the corresponding potassium alkynyltrifluoroborates. High yields of radiochemically pure products are obtained. Copyright © 2005 John Wiley & Sons, Ltd.

Key Words: organotrifluoroborates; alkynyl iodide; radioiodination; peracetic acid

Introduction

We introduced the concept of using the terminal iodovinyl group as a method for stabilizing radioiodine *in vivo* over 20 years ago when we prepared 17α [^{123}I]iodovinyloestradiol.^{1,2} The radioiodine was introduced via an iododeboration reaction using a vinylboronic acid precursor.^{2,3} Over the years, many radiolabeled compounds have been synthesized utilizing organoborane as well as a variety of organometallic precursors. Recently, potassium organotrifluoroborates have proven to be versatile intermediates in organic synthesis because of their remarkable chemical stability.^{4–7} They are crystalline solids that are stable to both air and water.^{8,9} Organotrifluoroborates have also proven to be useful precursors for the synthesis of aryl and vinyl iodides.¹⁰ We now wish to report a rapid, direct and high yield synthesis of high specific activity, iodine-123 labeled, alkynyl iodides from alkynyltrifluoroborates.

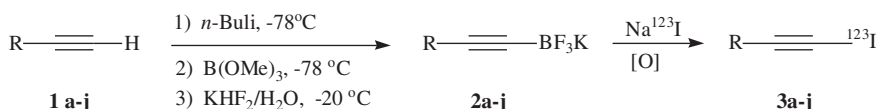
Results and discussion

Potassium alkynyltrifluoroborate precursors **2a–j** were prepared from the corresponding alkynes **1a–j** (Scheme 1). Deprotonation of the corresponding

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R- Alkyl and Aryl

Scheme 1. Synthesis of Iodine-123 Labeled Iodoalkynes

Table 1. The synthesis of no-carrier-added iodine-123 labeled alkynyl iodides

Starting material	R	Product	Radiochemical yields (%) ^{a,b}
2a	Phenyl	3a	92
2b	4-Methylphenyl	3b	94
2c	1-Cyclohexenyl	3c	90
2d	1-Chloropropyl	3d	91
2e	Hexyl	3e	88
2f	<i>tert</i> -Butyl	3f	85
2g	4-Methoxyphenyl	3g	91
2h	4-Cyanophenyl	3h	89
2i	1-Hydroxybutyl	3i	86
2j	<i>tert</i> -Butyldimethylsilyloxybutyl	3j	92

^a Isolated yields.

^b Products exhibited *R*_f values identical to authentic samples.

terminal alkyne with *n*-BuLi at -78°C in THF was followed by reaction of the lithium salt with trimethylborate. The transmetallation was performed at -78°C for 1 h and then at -20°C for an additional hour. The resulting organoborate complex was allowed to react with KHF_2 at -20°C for 1 h and then at ambient temperature for 1 h to yield the desired potassium alkynyltrifluoroborate.^{4,7} A variety of iodine-123 labeled alkynyl iodides were prepared from the corresponding alkynyltrifluoroborates. The results of this study are summarized in Table 1. Alkynyltrifluoroborate **2a-j** were subjected to radioiodination using no-carrier-added Na^{123}I and peracetic acid in 50% aqueous THF to yield **3a-j**. A representative radio TLC spectrum is presented in Figure 1. The radiochemical purity of the products was typically $>98\%$ and the overall radiochemical yields generally exceed 85%.

Experimental

Elemental analyses were performed by Atlantic Micro Labs, Inc., Norcross Georgia. Melting points were recorded on an electro thermal Digital Melting Point Apparatus and are uncorrected. ^1H and ^{13}C spectra were recorded on a Bruker AC 250 MHz NMR spectrometer. The chemical shift values are expressed in parts per million (δ) relative to tetramethylsilane. Radio thin layer

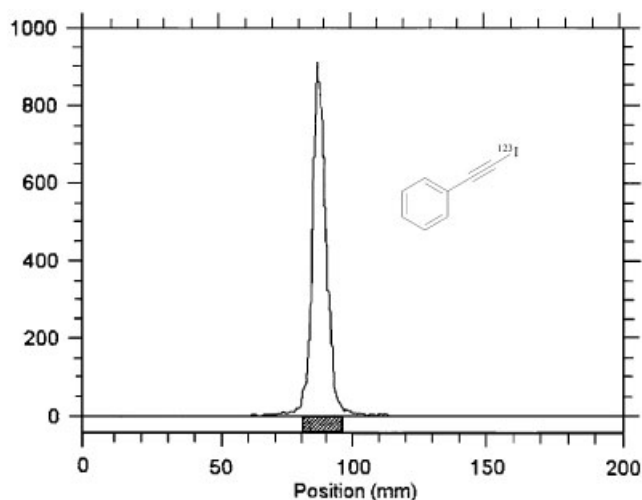


Figure 1. Radio-TLC of 1- ^{123}I iodo-2-phenylethyne

chromatography was carried out using a Bioscan, AR-2000 imaging scanner. All precursor alkynes, *n*-BuLi and $\text{B}(\text{OMe})_3$ were purchased from Aldrich Chemical Company. Na^{123}I was obtained from Nordion Inc., Vancouver, Canada. All reactions were carried out using dry solvents under an inert atmosphere.

Synthesis of potassium (2-phenylethynyl)trifluoroborate, 2a. (Representative procedure for preparing potassium alkynyltrifluoroborates)

A solution of phenylacetylene (1.02 g, 10.0 mmol) in 20 ml of dry THF was cooled to -78°C under argon. *n*-Butyllithium (6.25 ml, 1.60 M in hexane, 10 mmol) was added dropwise and the solution stirred for 1 h. Trimethylborate (1.58 g, 15.0 mmol, 1.5 equiv) was then added dropwise at -78°C and the solution stirred for 1 h. The reaction mixture was then allowed to warm to -20°C and stirred for an additional hour. A saturated aqueous solution of potassium hydrogen difluoride (4.70 g, 60.0 mmol, 6 equivalents) was added to the vigorously stirred solution. The resulting mixture was allowed to stir for 1 h at -20°C , after which it was allowed to warm to room temperature. The solvent was removed under reduced pressure and the resulting white solid was dried under high vacuum for two hours to remove all water. The solid was then washed with acetone (20 ml) and then with hot acetone (20 ml). The resulting organic solution was filtered and the solvent removed to afford a white solid. The solid was recrystallized from hot acetonitrile to produce the desired product (1.41 g, 68%) whose physical and spectral properties were identical to those reported in the literature.⁷

Radiosynthesis of 1-[¹²³I]iodo-2-phenylethyne (Representative procedure)

Alkynyltrifluoroborate **2a** (100 μ l of 5.2×10^{-2} in 50% aqueous tetrahydrofuran) was placed in a 2 ml Wheaton vial containing no-carrier-added Na¹²³I (37 MBq in 0.1% aqueous NaOH). To this was added peracetic acid (100 μ l, 0.3% solution in methanol). The reaction vial was sealed, covered with aluminum foil, and the mixture stirred for 15 min at room temperature. A drop of 10% aqueous sodium thiosulfate was added to decompose the excess iodine and the radiiodinated product was isolated by passing it through a silica gel Sep-Pak using petroleum ether as eluent. The radiochemical purity of the 1-[¹²³I]iodo-2-phenylethyne, **3a**, was determined by radio-TLC (aluminum backed silica gel plate, hexane); $R_f = 0.68$ (Figure 1). The decay corrected radiochemical yield was determined to be 92% and radiochemical purity was 98%. The total synthesis time was 20 min.

Conclusion

A novel high yield approach for preparing radioiodinated alkynyl iodides from the corresponding alkynyltrifluoroborates was developed. The reaction provides a versatile route to a variety of new radioiodinated reagents.

Acknowledgements

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