SYNTHESIS OF IODINE-125 LABELLED ARYL AND VINYL IODIDES

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SUMMARY

Iodine-125 labelled vinyl and aryl iodides are formed via the reaction of sodium iodide-125 with vinyl- and arylboronic acids. Good yields of isomerically pure products are obtained.

Keywords: Iodine-125, Organoborane, Vinyl Iodide, Aryl Iodide

INTRODUCTION

Radioiodine has been used extensively for labelling organic molecules due to the variety of readily available, medically useful iodine isotopes.[1] Iodine has become increasingly important in recent years because of its ideal physical properties and because of the development of convenient cyclotron production techniques.[2]

We recently reported that iodine can be readily incorporated into organic molecules via the reaction of organoboranes with sodium iodide in the presence of chloramine-T.[3] The reaction is rapid, stereospecific, and proceeds in the presence of a variety of functional groups.

$$R_3B \xrightarrow[\text{Chloramine-T}]{\text{NaI}} R\text{-}I$$

The organoboranes are stable (except to oxygen) and readily prepared via hydroboration[4] or transmetallation reactions. We demonstrated that the reaction could be used to synthesize a variety of radioiodine labelled alkyl iodides.[5,6]

We wish to report that the reaction is a convenient route to a series of

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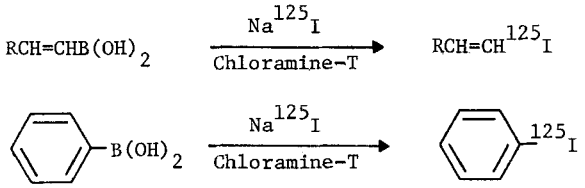
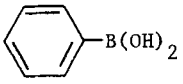
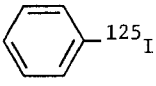
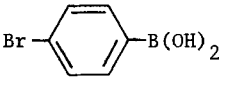
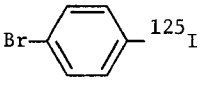
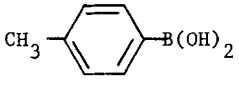
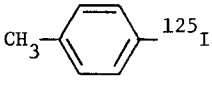
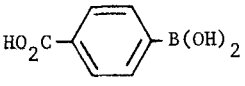
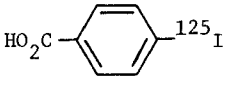
radiolabelled aryl and vinyl iodides via reaction of the corresponding aryl and vinylboronic acids.



The reactions provide good yields of pure products (as opposed to the isomeric mixtures generally obtained via standard aromatic substitution reactions) and should prove a valuable addition to the repertoire of scientists involved in radioiodine labelling. Our results are summarized in Tables I and II.

TABLE I

Iodine-125 Labelled Aryl Iodides

Arylboronic Acid[a]	Product[b]	R_f[c]	Radiochemical[d] Yield (%)
		0.93	91
		0.93	78
		0.91	86
		0.79[e]	74

[a] Prepared via transmetallation reactions via procedures published in references 9 and 10. (The first two compounds are commercially available.)

[b] All products exhibited physical and spectral characteristics in accord with authentic samples.

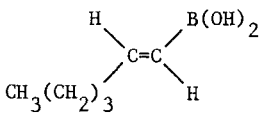
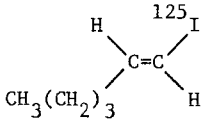
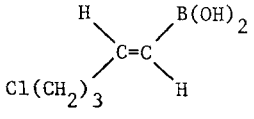
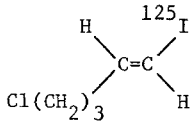
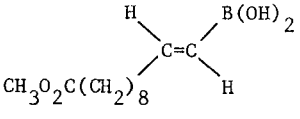
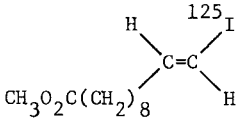
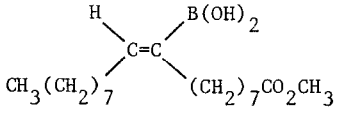
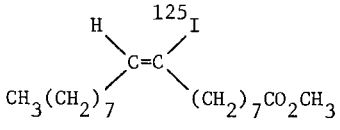
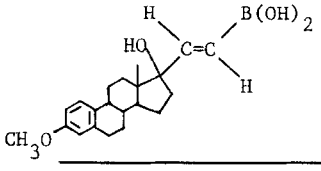
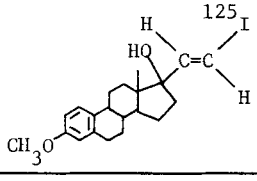
[c] R_f values determined via TLC on Silica Gel GF (250 nm); solvent: petroleum ether (30-60°C).

[d] Isolated yields.

[e] TLC solvent was ethyl acetate:methanol (75:25).

TABLE II

Iodine-125 Labelled Vinyl Iodides

Vinylboronic Acid[a]	Product[b]	R_f[c]	Radiochemical[d] Yield (%)
		0.97	77
		0.66	87
		0.84[e]	56
		0.88[e,f]	41
		0.5[g]	55

[a] Prepared via the hydroboration of the corresponding alkynes with catecholborane. The preparation of these agents is detailed in references 7 and 8.

[b] All products exhibited physical and spectral characteristics in accord with authentic samples and values are presented in references 7 and 8.

[c] R_f values determined via TLC on Silica Gel GF (250 nm); solvent: petroleum ether (30-60°C).

[d] Isolated Yields.

[e] TLC solvent was petroleum ether (30-60°C):ethyl acetate (90:10).

[f] A 50:50 mixture of the 9- and 10-iodo isomers due to the fact that the boron was attached to both the 9 and 10 positions; determined by control experiments.

[g] TLC solvent was petroleum ether (30-60°C):methanol:ethyl acetate (200:35:35).

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EXPERIMENTAL

Reagents

Sodium iodide-125 (New England Nuclear) was diluted to 4 mCi/mole with aqueous sodium iodide (1M). The vinyl- and arylboronic acids were prepared via published procedures.[7-10] Phenylboronic and p-Bromophenylboronic acids were used as received (Aldrich Chemical Co.)

Chemical and Radiochemical Purity

The chemical and radiochemical purity of the products were determined by thin layer chromatography using silica gel plates (250 μ with fluorescent indicator). Authentic samples of the unlabelled products[7,8] were applied adjacent to the reaction mixtures. In all systems, the radioactivity was associated with a spot having an R_f value identical to that of the unlabelled material.

Iodination - General Procedures

The vinylboronic acid (2 mmol) was dissolved in 8 mL of 50% aqueous tetrahydrofuran in a round bottomed flask which was shielded from light. Aqueous sodium iodide-125 (2.0 mmol, 2.0 mL of a 1.0M solution, 4 mCi/mole) was added, followed by chloramine-T (4.0 mmol, 0.9 g) dissolved in 8 mL of 50% aqueous tetrahydrofuran. The reaction mixture was stirred at room temperature until the color faded (∿15 min.) and then diluted with 20 mL of water. The product was extracted into ether, the solution dried over anhydrous $MgSO_4$, and the solvent removed. The products were purified by chromotography on silica gel using 90:10 petroleum ether: ethyl acetate as eluent. [The aryl iodides are prepared in an analogous fashion using 50% aqueous methanol as the solvent system.]

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