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Short Research Article

No-carrier-added radiohalogenations utilizing organoborates†

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Introduction

The preparation of high specific activity, no-carrier-added radiohalogenated agents is important in nuclear medicine imaging. The use of organoboranes as precursors to radiohalogenated pharmaceuticals has been of interest to us for many years.[1,2] Although boron reagents can be prepared containing a wide variety of functional groups and are easy to use, their preparation can be problematic. The discovery of the Suzuki coupling reaction has markedly changed this situation, making boronic acids readily available.

Trifluoroborate derivatives have also proven to be versatile intermediates in organic synthesis because of their remarkable chemical reactivity. Interestingly, they are crystalline ionic solids that are stable to both air and water for extended periods, and they are readily prepared from the corresponding boronic acids.[3,4] Trifluoroborate salts are as versatile as boronic acids in organic synthesis[5,6,7] and are far simpler to remove from reaction mixtures due to their ionic nature. We have developed a rapid and high yield syntheses of high specific activity iodine-123 and bromine-76 labeled molecules from the corresponding organotrifluoroborates.[8,9] The fact that only the products are lipophilic makes the new reaction ideal for kit applications since a simple Sep-Pak filtration results in a radiochemically pure product.

$$RB(OH)_2 \xrightarrow[MeOH]{KHF_2} RBF_3K \xrightarrow[\text{peracetic acid}]{Na^*X} R^*X$$

where R=alkenyl, alkynyl or aryl; $^*X=^{123}I$ or ^{76}Br.

Results and discussion

A variety of iodine-123 and bromine-76 labeled aryl, vinyl and alkynyl iodides were prepared from the corresponding aryl-, vinyl-, and alkynyltrifluoroborate salts. The organotrifluoroborates were subjected to radiohalogenations using $Na^{123}I$ or NH_4 ^{76}Br in the presence of peracetic acid. Radiohalogenations of aryltrifluoroborates containing electron-donating substituents are rapid and efficient, while those containing electron-withdrawing groups require longer reaction times. The presence of a nitro group effectively inhibits the reaction. Halogenations of vinyltrifluoroborates were found to proceed with retention of stereochemistry providing access to a variety of (*E*) and (*Z*) vinyl halides. The radiochemical purity of the products are typically >98% and the overall radiochemical yields generally exceed 75%.

Interestingly, aryl halogenation reactions are less facile than the corresponding halogenation of vinyl-and alkynyltrifluoroborates. No-carrier-added radiohalogenations are generally complete in 10 min or less. However, no-carrier-added radioiodinations of aryltrifluoroborates require up to 5 h, depending on the

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substituent. No-carrier-added radiobrominations of aryl derivatives are so slow that only carrier-added data reactions are synthetically useful.

Conclusion

A convenient, high yield radiohalogenation procedure for preparing no-carrier-added radiohalogenated aryl-, vinyl- and alkynyl iodides has been developed. The organotrifluoroborate precursors are extremely stable, readily handled, and easily prepared. The reaction is also suitable for the preparation of aryl-, vinyl- and alkynyl bromine-76 labelled analogues. The reactions are readily adaptable to kit applications for the preparation of a wide variety of and no-carrier-added radiohalogenated reagents.

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REFERENCES

1. Kabalka GW, Akula MR, Zhang J. *Nucl Med Biol* 2003a; **30**: 369–372.
2. Kabalka GW, Varma RS. *Tetrahedron* 1989; **45**: 6601–6621.
3. Vedejs E, Chapman RW, Fields SC, Lin, S, Schrimpf MR. *J Org Chem* 1995; **60**: 3020–3027.
4. Darses S, Genet J-P, Brayer J-L, Demoute J-P. *Tetrahedron Lett* 1997; **38**: 4393–4396.
5. Molander GA, Ravero MR. *Org Lett* 2002; **4**: 107–109.
6. Kabalka GW, Venkataiah B, Dong G. *Org Lett* 2003b; **5**: 3803–3805.
7. Kabalka GW, Mereddy MA. *Nucl Med Biol* 2004; **31**: 935–938.
8. Kabalka GW, Mereddy MA. *J Label Compd Radiopharm* 2005; **48**: 359–362.
9. Kabalka GW, Mereddy MA, Green JF. *J Label Compd Radiopharm* 2006; **49**: 11–15.

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