Journal of Labelled Compounds and Radiopharmaceuticals
J Label Compd Radiopharm 2007; **50**: 888–894.
Published online in Wiley InterScience
(www.interscience.wiley.com). DOI: 10.1002/jlcr.1426

JLCR

Review Article

Isotope incorporation via organoboranes†

GEORGE W. KABALKA*

Departments of Chemistry and Radiology, The University of Tennessee, Room 612, Buehler Hall, Knoxville, TN 37996-1600, USA

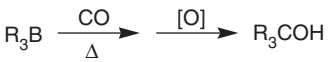
Received 2 March 2007; Accepted 7 June 2007

Abstract: Organoboranes can be used as precursors to a wide variety of functionally substituted, isotopically labeled compounds. Straightforward boron-based methods for incorporating short-lived and stable isotopes of carbon, nitrogen, oxygen, and the halogens have been developed over a period of 20 years. Application of these methods to biology, agriculture, and medicine has been slowed by the limited availability of boronated precursors containing functional groups appropriate to those fields. The situation has changed markedly with the advent of metal catalyzed boron-based reactions, which now produce a variety of important boronated materials readily available in the laboratory and from commercial sources. This is especially important in the medical and pharmaceutical communities where short-lived isotopes of carbon, nitrogen, and the halogens are demonstrating great value in positron and single photon emission tomographic procedures. Copyright © 2007 John Wiley & Sons, Ltd.

Keywords: organoborane; Suzuki; carbon-11; isotope; PET

Introduction

Although organoboranes were first reported in 1859, they were virtually ignored as synthetic organic intermediates until the discovery of the hydroboration reaction by Herbert C. Brown in 1956.[1,2] Notably, the first report of isotope incorporation (tritium) via borane intermediates appeared shortly after Brown's initial report of the hydroboration reaction.[3] The emphasis of the early tritiation study was on reaction mechanisms rather than the synthesis of radiolabeled organic molecules. My own introduction to the versatility of organoborane compounds in organic synthesis came about when I joined Professor Brown's group at Purdue in 1965. Even though he had 'written the book' on the use of organoborane reagents,[4] no organoborane-based routes to carbon–carbon bond formations were known until the high-temperature/pressure conversion of trialkylboranes to trialkylcarbinols was reported.[5] That situation changed rapidly in



Brown's Laboratory while I was at Purdue. It is interesting that my first publication was focused on the introduction of carbon into a molecule using carbon monoxide under relatively mild reaction conditions, a reaction that played a significant role in my initial isotope work.[6] What was clear in the 1960s was that organoboranes containing a large variety of functional groups could be prepared and that these functional groups tolerated a host of reactions in which the boron atom was replaced by other elements and functional groups. At that time, the preparative routes to functionalized organoborane reagents often involved the use of temporary protecting groups (including excess borane reagents), but the resulting organoboranes were unique amongst the reactive organometallic and

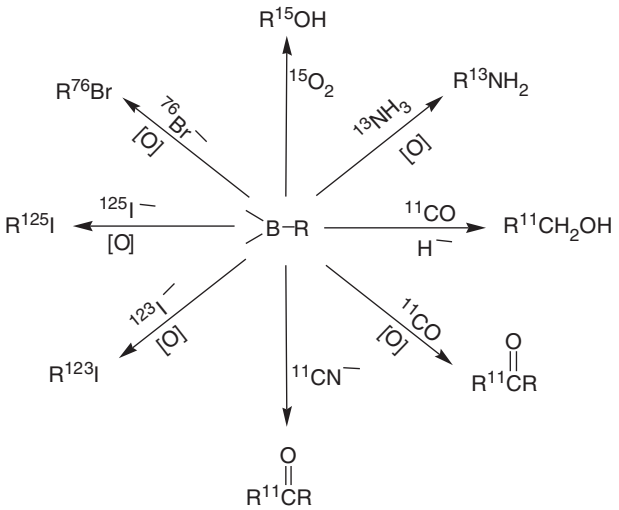
where X = OH, NH_2, CH_2OH, halogen, etc.
and R could contain $-CO_2H$, $-C\equiv N$,
$-$ SH, NH_2 halogen, etc.,

organometalloidal reagents available because they could contain a variety of functional groups while maintaining high reactivity.[7]

The realization that one could prepare reactive intermediates containing functional groups led me to investigate the use of organoboranes in isotope

*Correspondence to: George W. Kabalka, Departments of Chemistry and Radiology, The University of Tennessee, Room 612, Buehler Hall, Knoxville, TN 37996-1600, USA. E-mail: kabalka@utk.edu
Contract/grant sponsor: The U.S. Department of Energy; contract/grant number: DE-FG02-04ER63895
†Fiftieth Anniversary Special Issue, In memoriam John Jones.

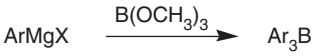
reactions. Over the years, we successfully developed methods for incorporating short and long-lived isotopes of carbon, nitrogen, oxygen, and the halogens.[8]



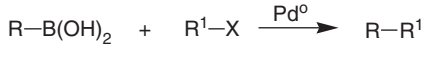
Our first isotope incorporation reactions were developed in 1973 as part of a mechanistic study focused on the hydroboration reaction (Scheme 1).[9] A few years later, we initiated a program focused on incorporation of carbon isotopes using organoboranes, the studies were catalyzed by a collaboration we initiated with Dr Clair Collins at the Oak Ridge National Laboratory in Oak Ridge, TN.[10] Clair and I had a mutual interest in preparing carbon-14-labeled reagents for use in the investigation of isotope effects in organic reactions. As part of this study I prepared carbon-14 labeled aldehydes and alcohols using the carbonylation reaction that I had investigated while working with H. C. Brown (Scheme 2).[11]

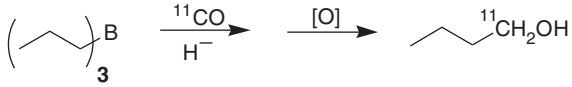
The carbonylation reaction can be moderated by heat, water, or hydride to generate alcohols, aldehydes, or ketones.[12–14] Thus, a large variety of carbon-14 and carbon-13[15,16] labeled molecules became readily attainable using carbonylation chemistry. We discovered that the carbonylation chemistry was not universally suitable for preparing complex carbon-11 labeled molecules because reactions leading to ketones and tertiary alcohols required reaction times that were too long for them to be applicable to the 20-min half-life of carbon-11. However, preparations of aldehydes, primary alcohols, and carboxylic acids were found to be quite rapid (~20 min) and we were able to prepare carbon-11-labeled alcohols (and aldehydes) in collaboration with Dr Ronald Finn and his coworkers (Scheme 3).[17]

We then discovered that carbon-11 ketones could also be prepared by utilizing a cyanide procedure developed by Andrew Pelter.[18,19] Of course, the cyanide incorporation route was also quite suitable for the preparation of carbon-13[20] and carbon-14-labeled molecules (Scheme 4).[21] Thus, it was well established by 1980 that organoboranes could be utilized to incorporate carbon isotopes. Carbon-11 labeling had been successfully achieved, yet essentially no applications were reported until the mid 1990s. The reason for the apparent lack of interest was that, in general, researchers found the preparation of the prerequisite organoborane reagents to be rather restrictive. Trialkylboranes were accessible via the hydroboration reaction only if the appropriate alkenes were available. The preparation of aromatic boron derivatives was even more problematic in that transmetallation reactions were generally required. The necessity of using reactive

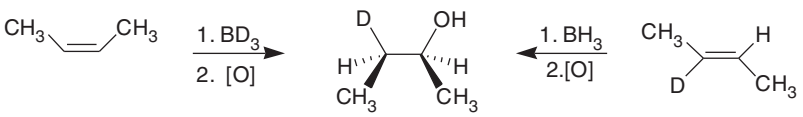


(and basic) Grignard and lithium reagents often precluded the presence of interesting and useful functionality in the target molecules.

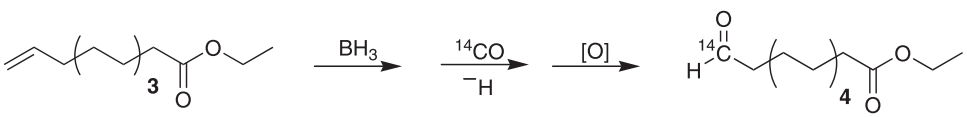




Scheme 3

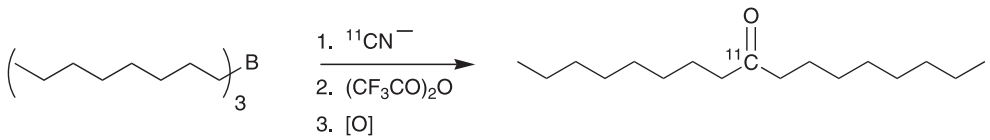


Scheme 1



Scheme 2

DOI: 10.1002.jlcr



Scheme 4

where: R, R^1 =
alkyl, vinyl, aryl and X = Cl, B, I, OTs, etc.

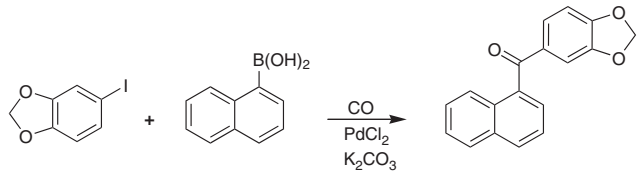
The situation changed dramatically in the 1980s when Akira Suzuki and Norio Miyaura discovered a new palladium-catalyzed carbon–carbon bond forming reaction. The reaction involves the insertion of palladium into the carbon–halogen bond via an oxidative addition, transfer of the organic group from boron to palladium to form a disubstituted palladium, and then reductive elimination of the palladium to generate the new carbon–carbon bond.[22,23] [Suzuki also spent time in Brown's laboratory in the 1960s[24] and was an early collaborator in one of my studies.[25]]

The coupling reactions generally occur at, or near, room temperature and require the presence of very mild organic and inorganic bases. One only needs to examine a current organic chemistry journal to realize the impact of the palladium-catalyzed, boron-based, Suzuki-Miyaura reaction.

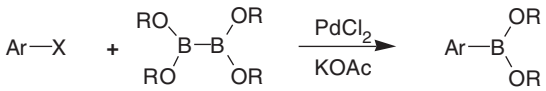
The reaction can also be utilized to insert carbon oxides by simply adding carbon monoxide or carbon dioxide (Scheme 5).[26,27]

As significant as Suzuki chemistry has become, the true catalyst for its use was a derivative reaction first reported by Miyaura, which provided a straightforward route to the requisite arylboronic ester (and thus acid) starting materials (Scheme 6).[28]

The new boronic acid chemistry was soon extended to include the coupling of a variety of aryl halides triflates with pinacol diboron and related reagents.[29] These developments have changed the face of organic synthesis by making a wide variety of boronic acids and esters readily available in the laboratory and from commercial sources. The availability of functionalized boronic acid (and ester) starting materials and the nontoxic nature of boron (except to roaches and termites!) has served to make boron chemistry attractive to the radiolabeling community. This is especially true in the positron emission tomography (PET) arena where carbon-11 is a very important isotope because of



Scheme 5

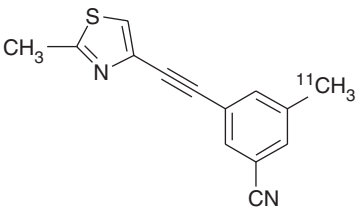


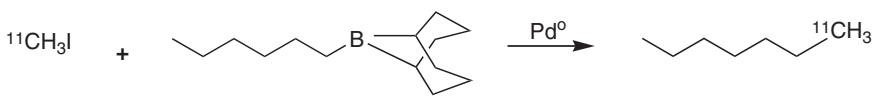
Scheme 6

regulatory concerns in the medical field. Since the chemical properties of a substance are not dependent on the carbon isotope ratio, toxicity data for carbon-11 analogues of stable molecules are readily available. This makes the preparation of new drug applications for PET studies more straightforward. Langstrom and his coworkers were amongst the first to re-examine organoboron chemistry for carbon-11 incorporation using Suzuki methodology. Their initial focus was on coupling carbon-11 labeled methyl iodide to an alkylboron reagent (Scheme 7).[30]

The method has been utilized to prepare carbon-11-labeled palmitic acid with carbon-11 at the terminal position[31] and a diaryl alkyne, glutamate receptor agent.[32]

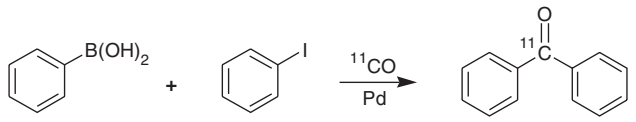
The methylation of aromatic groups has also been found to provide carbon-11-labeled products in high yields with high radiochemical purity.[33]





Scheme 7

DOI: 10.1002.jlcr



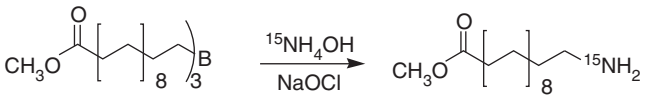
Scheme 8

Applications of the Suzuki technology are not limited to alkylation chemistry.[34] Kojima and his coworkers discovered that the palladium-catalyzed reactions could be utilized for carbonyl insertion and a number of modifications have since been developed.[26,35] Our early carbon-11 carbonylation reactions were limited by the paucity of organoborane preparative routes. Suzuki and Miyaura solved the availability problem and the new palladium-catalyzed carbonylation chemistry holds great promise. For example, Zeisler and his coworkers demonstrated that carbon-11 labeled benzophenone could be prepared from phenylboronic acid[36] in yields that were equivalent to those we obtained earlier using trialkylboranes (Scheme 8).[37]

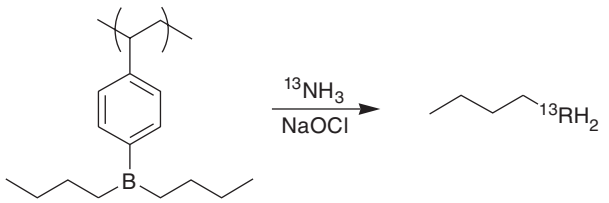
In an illustration of the reaction's functional group tolerance, the reaction was used to prepare carbon-11 labeled 2-(2-benzoylphenoxy)-*N*-phenylacetamide from phenylboronic acid (Scheme 9).[38]

More recently, Langstrom and his collaborators have investigated the effect of various bases[39] and leaving groups on the carbonylation reaction and its application to the preparation of carbon-11 labeled molecules.[40] These studies provide the groundwork for the ready application of the Suzuki chemistry to routine radiopharmaceutical production.[41] There is reason to believe that advances will appear at an increasing rate as PET researchers become aware of the versatility of organoboranes in synthesis. Interestingly, borane itself has been utilized to efficiently capture carbon-11 carbon monoxide.[42]

Our studies were not limited to incorporation of carbon isotopes. Nitrogen isotopes, for example, are of value in biology, agriculture, and medicine. H. C. Brown laid the foundation for our later studies when he found that chloramines and hydroxylamine-*O*-sulfonic acid would react with organoboranes to yield amines.[43,44] Unfortunately, these reagents are not readily amenable for incorporating isotopes of nitrogen either due to stability (chloramines) or availability of appropriately isotopically labeled starting materials.



Scheme 10



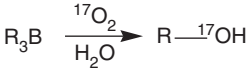
Scheme 11

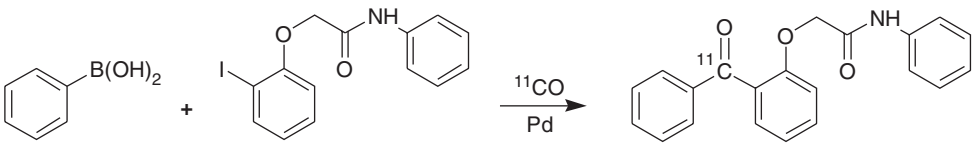
The situation, of course, is especially problematic for nitrogen-13 with its 10-min half-life.

We initiated a study focused on the rapid and convenient incorporation of nitrogen and found that ammonium hydroxide would react instantaneously with organoboranes in the presence of sodium hypochlorite (Scheme 10).[45]

We then utilized the new chemistry to prepare a series of nitrogen-13 labeled amines in collaboration with Dr Ronald Finn (Scheme 11).[46] The use of polystyrene-based materials was developed for potential application in nuclear medicine facilities. We also prepared nitrogen-13-labeled γ-aminobutyric acid and putrescine using the new chemistry.[47]

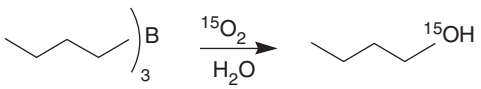
Oxygen isotopes are also of value in biology and medicine. It is well known to scientists in the organoborane field that low molecular weight organoboranes are pyrophoric, a property noted by Franklin in his initial report.[1] In fact the bright green flame that is generated when a pyrophoric organoborane is exposed to air is rather diagnostic of borane reagents. The preliminary study of the reaction of organoboranes with oxygen gas was actually carried out early in my career when, during the course of my thesis work, I discovered that molecular oxygen could be used to quantitatively generate alcohols.[48] Later, we applied the reaction to the synthesis of oxygen-17-labeled alcohols.[49]





Scheme 9

DOI: 10.1002.jlcr

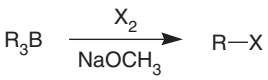


Scheme 12

Biodistribution studies of oxygen-15 labeled butanol revealed that it might be superior to oxygen-15 labeled water for use in PET blood flow studies.[50] In a subsequent study carried out with Drs Fowler and Lambrecht at Brookhaven National Laboratory, we developed a simple organoborane oxidation route that could be used to generate oxygen-15 butanol (Scheme 12).[51]

Berridge and his collaborators then modified the reaction by adsorbing the tributylborane on alumina in an effort to develop a system amenable to the clinical environment.[52,53] It is heartening to note that the tributylborane method for preparing oxygen-15 labeled butanol has found use in the PET community.[54–57]

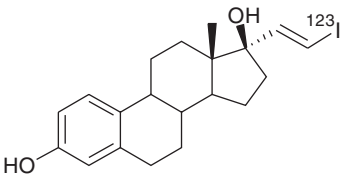
Radiohalogens have played a long and important role in nuclear medicine and biology. In earlier work, Brown and his collaborators discovered that organoboranes could be used as precursors for a variety of organic halides.[58,59] The reactions were not utilized extensively in organic synthesis because the strong base required for the reaction could lead to destruction of sensitive functional groups and due to potential side reactions such as dehydrohalogenation and ether formation.



Because of our interest in the use of isotopes for pharmaceutical development, we embarked on a systematic mechanistic study of organoborane halogenation reactions and discovered that the reactions proceed via an electrophilic attack by a electron-deficient halogen species on an electron-rich boron complex.[60] This was significant because it meant that strong bases could be avoided by simply oxidizing a halide ion in the presence of a mild boron complexing agent. We used reagents such as chloramine-T and *N*-chloro-succinimide to successfully radioiodinate organoboranes in less that a minute![61]

The reactions proceed readily at the no-carrier-added level and tolerate a variety of functional groups. For instance, the reaction can be used to prepare ω-substituted fatty acids (Scheme 13).[62]

The method works equally well for preparing radiobrominated reagents.[63] We utilized the new radiolohalogenation chemistry to synthesize a variety of molecules of interest in nuclear medicine. Our preparation of 17-α-iodovinylestradiol proved to be the first use of a terminal iodovinyl group as a method for increasing the *in vivo* retention time of a radioiodine.[64,65]

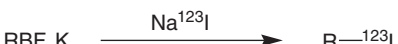


In collaboration with F. F. Knapp and his colleagues we used the new chemistry to prepare a series of radioiodinated tellurium-substituted fatty acids.[66,67] The boron-iodination technique was used to prepare a variety of physiologically active agents.[68–72]

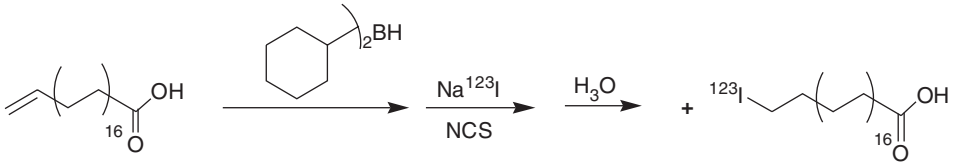
The most effective method for stabilizing radiohalogens *in vivo* involves the preparation of arylhalide derivatives. Until recently, it has been very difficult to prepare arylboronic acids containing functional groups of interest in medicine because of the necessity of using transmetallation reactions to generate the necessary boron precursor. Thus, it is not surprising that other metal–halogen exchange reactions have proven more popular for preparing radiohalogenated pharmaceuticals in recent years. However, the advent of Suzuki–Miyaura chemistry has changed the situation dramatically.

We re-examined the boron–halogen exchange reaction to validate the use of the newly available aryl- and vinylboron esters and found them to be ideal precursors (Scheme 14).[73,74]

Even more significant was our recent discovery that organotrifluoroborates can be used as radiohalogenation precursors. The trifluoroborates[75] are crystalline, air-stable solids that can be stored indefinitely.[76,77]

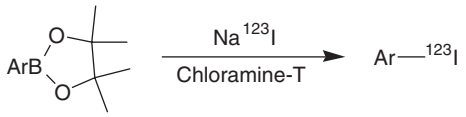


We have applied the new chemistry to a number of useful agents including our recent synthesis of an *iodine*-123 labeled rofecoxib agent (Scheme 15).[78]

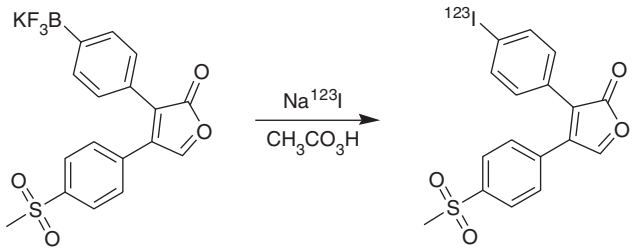


Scheme 13

DOI: 10.1002.jlcr



Scheme 14



Scheme 15

The method can be used to prepare numerous radioiodinated aryl, vinyl, and alkynyl iodides[79] and is suitable for preparing bromine-76 derivatives.[80]

When we initiated our studies, we focused on the use of organoborane chemistry for isotope incorporation. We were convinced that they would become the precursors of choice. Our optimism was based on their tolerance to many of the functional groups important in biology, agriculture, and medicine, as well as their minimal environmental and toxicological load. Our optimism proved to be a bit premature due to the paucity of preparative methods. Suzuki and others have solved essentially all of the preparative problems and have provided improved chemical pathways. Once again, the role of the organoboranes in the isotope field appears quite bright.

Acknowledgement

Financial support from the Robert H. Cole Foundation is gratefully acknowledged.

REFERENCES

1. Franklin E, Duppa B. *Proc Royal Soc* London 1859; **10**: 568.
2. Brown HC, Rao BCS. *J Am Chem Soc* 1956; **78**: 5694–5695.
3. Nam NH, Russo AJ, Nystrom RF. *Chem Ind* (*London*) 1963; 1876–1877.
4. Brown HC. *Hydroboration*. W. A. Benjamin Inc: New York, NY, 1962.
5. Hillman MED. *J Am Chem Soc* 1962; **84**: 4715–4720.
6. Brown HC, Kabalka GW, Rathke MW. *J Am Chem Soc* 1967; **89**: 4530–4531.
7. Brown HC. *Boranes in Organic Chemistry*. Cornell University Press: Ithaca, NY, 1972.
8. Kabalka GW. *Acc Chem Res* 1984; **17**: 215–221.
9. Kabalka GW, Bowman NS. *J Org Chem* 1973; **38**: 1607.
10. Brewster JH. *Aspects of Mechanism and Organometallic Chemistry*. Plenum Press: New York, NY, 1978.
11. Kabalka GW, Gooch EE, Collins CJ, Raaen VF. *J Chem Soc, Chem Commun* 1979; 607–608.
12. Brown HC, Rathke MW. *J Am Chem Soc* 1967; **89**: 2737.
13. Brown HC, Rathke MW. *J Am Chem Soc* 1967; **89**: 2738–2740.
14. Brown HC, Coleman RA, Rathke MW. *J Am Chem Soc* 1968; **90**: 495–501.
15. Kabalka GW, Delgado MC, Sastry U, Sastry KAR. *J Chem Soc, Chem Commun* 1982; 1273–1274.
16. Kabalka GW, Delgado MC, Sastry U, Sastry KAR. *J Org Chem* 1984; **49**: 174–176.
17. Kothari PJ, Finn RD, Vora MM, Boothe TE, Emran AM, Kabalka GW. *Int J Appl Radiat Isot* 1985; **36**: 412–413.
18. Pelter A, Hutchings MG, Rowe K, Smith K. *J Chem Soc, Perkins Trans I* 1975; 138–142.
19. Kothari PJ, Finn RD, Kabalka GW, Vora MM, Boothe TE, Emran AM. *Int J Appl Radiat Isot* 1986; **37**: 469–470.
20. Mohammad M, Kabalka GW, Sastry A, Finn RD. *Org Prep Proced Int* 1985; **17**: 17–22.
21. Kabalka GW. *Synth Commun* 1980; **10**: 93–97.
22. Miyaura N, Suzuki A, Yanagi T. *Synth Commun* 1981; **11**: 513–519.
23. Miyaura N, Suzuki A. *Chem Rev* 1995; **95:** 2457–2583.
24. Brown HC, Suzuki A. *J Am Chem Soc* 1967; **69**: 1933–1941.
25. Kabalka GW, Brown HC, Suzuki A. *J Am Chem Soc* 1970; **92**: 710–712.
26. Wakita Y, Yasunaga T, Akita M, Kojima M. *J Organomet Chem* 1986; **301**: C17–C20.
27. Suzuki A, Brown HC. *Organic Synthesis via Boranes Vol. 3 Suzuki Coupling*. Aldrich Chemical Company; Wisconsin, WI, 2003.
28. Ishiyama T, Murata M, Miyaura N. *J Org Chem* 1995; **60**: 7508–7510.
29. Murata M, Oyama T, Watanabe S, Masuda Y. *J Org Chem* 2000; **65**: 164–168.
30. Andersson Y, Cheng A, Langstrom B. *Acta Chem Sand* 1995; **49**: 683–688.
31. Hostettler ED, Fallis S, McCarthy TJ, Welch MJ, Katzendlenbogan JA. *J Org Chem* 1998; **63**: 1348–1351.
32. Hamill TG, Krause S, Ryan C, Bonnefous C, Govek S, Seiders TJ, Cosford NDP, Roppe J, Kamenecka T, Patel S, Gibson RE, Sanabria S, Riffel K, Eng W, King C, Yang X, Green MD, O'Malley SS,

Hargreaves R, Burns HD. *Synapse* 2005; **56**: 206–216.
33. Hostettler ED, Terry GE, Burns HD. *J Label Compd Radiopharm* 2005; **48**: 629–634.
34. Miyaura N, Suzuki A. *Chem Rev* 1995; **95**: 2457–2483.
35. Suzuki A. *Organoboranes in Organic Synthesis*. Hokkaidi University Press: Hokkado, Japan, 2004.
36. Zeisler SK, Nader M, Theobald A, Oberdorfer F. *Appl Radiat Isot* 1997; **48**: 1091–1095.
37. Kothari PJ, Finn RD, Kabalka GW, Vora MM, Boothe TE, Emran M, Mohammadi M. *Appl Radiat Isot* 1986; **37**: 471–473.
38. Nader MW, Oberdorfer F. *Appl Radiat Isot* 2002; **57**: 681–685.
39. Rahman O, Llop J, Langstrom B. *Eur J Org Chem* 2004; 2674–2678.
40. Rahman O, Kihlberg T, Langstrom B. *Eur J Org Chem* 2004; 474–478.
41. Rahman O, Langstrom B, Kihlberg T, Llop J. *PCT Int Appl*, WO 2005/066100A1, 2005; 36.
42. Audrain H, Martearello L, Gee A, Bender D. *J Chem Soc Chem Commun* 2004; 558–559.
43. Brown HC, Heydkamp WR, Breuer E, Murphy WS. *J Am Chem Soc* 1964; **86**: 3565–3566.
44. Rathke MW, Inoue N, Varma KR, Brown HC. *J Am Chem Soc* 1966; **88**: 2870–2871.
45. Kabalka GW, Sastry KAR, McCollum GW, Lane CA. *J Chem Soc Chem Commun* 1982; 62.
46. Kothari PJ, Finn RD, Kabalka GW, Vora MM, Boothe TE, Emran AM. *Appl Radiat Isot* 1986; **37**: 469–470.
47. Kabalka GW, Wang Z, Green JF, Goodman MM. *Appl Radiat Isot* 1992; **43**: 389–391.
48. Brown HC, Midland M, Kabalka GW. *J Am Chem Soc* 1971; **93**: 1024–1025.
49. Kabalka GW, Reed TJ, Kunda SA. *Synth Commun* 1983; **13**: 737–740.
50. Dischino DD, Welch MJ, Kilbourn MR, Raichle ME. *J Nucl Med* 1985; **24**: 1030–1038.
51. Kabalka GW, Lambrecht RM, Sajjad M, Fowler JS, Kunda SA, McCollum GW, MacGregor R. *Int J Appl Radiat Isot* 1985; **36**: 853–855.
52. Berridge MS, Franceschini MP, Tweson TJ, Gould KL. *J Nucl Med* 1986; **27**: 834 –837.
53. Berridge MS, Cassidy EH, Terris AH. *J Nucl Med* 1990; **31**: 1727–1731.
54. Moerlin SM, Gaehle GG, Lechner KR, Bera RK, Welch MJ. *Appl Radiat Isot* 1993; **44**: 213–218.
55. Herzog H, Seitz RJ, Tellmann L, Schlang G, Kleinschmidt A, Nebeling B, Stoecklin G, Muehller-Gaertner HW. *Eur J Nucl Med* 1994; **21**: 138–143.
56. Herzog H, Seitz RJ, Gellmann L, Kops ER, Juelicher F, Schlaug G, Kleinschmidt A, Mueller-Gaertner HW. *J Cereb Blood Flow Metab* 1996; **16**: 645–664.
57. Jonsson C, Pagani M, Ingvar M, Thurfjell L, Kimiaei S, Jacobsson H, Larsson SA. *Eur J Nucl Med* 1998; **25**: 157–165.
58. Brown HC, Rathke MW, Rogic MM. *J Am Chem Soc* 1968; **90**: 5038–5050.
59. Brown HC, Lane CF. *J Am Chem Soc* 1970; **92**: 6660–6661.
60. Brown HC, DeLue NR, Kabalka GW, Hedgecock HC. *J Am Chem Soc* 1976; **98**: 1290–1291.
61. Kabalka GW, Gooch EE. *J Chem Soc, Chem Commun* 1981; 1011.
62. Kabalka GW, Gooch EE, Otto CA. *J Radioanal Chem* 1981; **65**: 115–121.
63. Kabalka GW, Sastry KAR, Pagni PG. *J Radioanal Chem* 1982; **74**: 315–321.
64. Kabalka GW, Gooch EE, Sastry KAR. *J Nucl Med* 1981; **22**: 908–912.
65. Kabalka GW. *Radiohalogenation Method*. U.S. Patent 4,45, 149, 1984.
66. Knapp FF, Goodman MM, Kabalka GW, Sastry KAR. *J Med Chem* 1984; **27**: 94–97.
67. Srivastava PC, Callahan FF, Owen AP, Kabalka GW, Sastry KAR. *J Med Chem* 1985; **28**: 408–413.
68. Kabalka GW, Varma RS, Jineraj UK, Huang L, Painter SK. *J Label Compd Radiopharm* 1985; **22**: 333–338.
69. Srivastava PC, Callahan AP, Cunningham EG, Knapp FF. *J Med Chem* 1983; **26**: 742–746.
70. Goodman MM, Kabalka GW, Marks RC, Knapp FF, Lee J, Liang Y. *J Med Chem* 1992; **35**: 280–285.
71. Kabalka GW, Shoup TM, Daniel GB, Goodman MM. *Nucl Med Biol* 2000; **27**: 279–287.
72. Srivastava PC, Knapp FF. *J Med Chem* 1984*;* **27***:* 978–981.
73. Kabalka GW, Akula MR, Zhang J. *Nucl Med Biol* 2002; **29**: 841–843.
74. Kabalka GW, Akula MR, Zhang J. *Nucl Med Biol* 2003; **39**: 369–372.
75. Vedejs E, Chapman RW, Fields SC, Schrimpf LS. *J Org Chem* 1995; **60**: 3020–3027.
76. Kabalka GW, Mereddy AR, *Nucl Med Biol* 2004; **31**: 935–938.
77. Kabalka GW. *Method for Halogenations or Radiohalogenating a Chemical Compound*. U.S. Patent 7041859, 2006.
78. Schuller HM, Kabalka GW. *Diagnosis of Diseases Associated with Cox-2 Expression*. U.S. Patent Appl Pub. US 2006067879, 2006.
79. Kabalka GW, Mereddy AR. *J Label Compd Radiopharm* 2005; **48**: 359–362.
80. Kabalka GW, Mereddy AR, Green JF. *J Label Compd Radiopharm* 2006; **49**: 11–15.

DOI: 10.1002.jlcr