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A NEW ROUTE TO IODINE-LABELED N-ISOPROPYL IODOAMPHETAMINE VIA ORGANOBORANES

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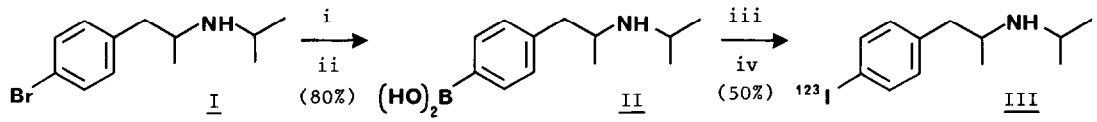
Abstract: N-Isopropyl amphetamineboronic acid was prepared via a new in-situ transmetallation reaction involving sonication. The boronic acid intermediate was radioiodinated via a novel iodination procedure.

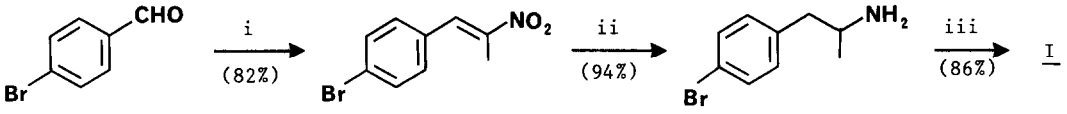
Amines are important chemical mediators of brain function. Because they are rapidly extracted from the blood, agents such as iodine-123 labeled, N-isopropyl p-iodoamphetamine, (III), have proven to be of great value in medical imaging[1]. Unless the aromatic ring is activated[2], radioiodination reactions are generally achieved via the decomposition of triazine precursors[3] or by direct halogen-halogen exchange reactions[4]. These methods can be somewhat difficult and may lead to dilution of the desired product with a chemically similar by-product. We have found that the organoboranes are effective precursors for a wide variety of labeled compounds[5]. The organoboranes are unique intermediates in that they tolerate a large number of functional groups and it is, often, these groups which impart the desired physiological response. To our knowledge, no syntheses have been reported in which an amino substituted boronic acid has been used as an intermediate in a synthesis of a labeled compound. This is a consequence of the fact that aminoboronic acids have been difficult to prepare and that the amine functionality can interfere in a number of synthetic transformations, including oxidative halogenations.

We wish to report that an arylboronic acid containing an amino group can be readily synthesized from the corresponding aryl halide (I) via a metallation-transmetallation sequence involving the sonication of the aryl halide in the presence of magnesium metal and a borane complex[6,7]; such sonic accelerated reactions are gaining importance in organoborane chemistry[8]. The resultant boronic acid (II) is then converted into the desired product (in 50% isolated yield) via a direct reaction with no-carrier-added iodine-123 labeled sodium iodide in the presence of a mild oxidant[9]. By carrying out the reaction at low pH, the amine functionality is protected, as the hydrochloride salt, from undesired oxidative side reactions; indeed, only trace quantities (< 4%) of other iodinated organic products are formed.



(i) BH_3, Mg,))); (ii) H_2O, Δ; (iii) $Na^{123}I$, HCl, Chloramine-T; (iv) NaOH

The required N-isopropyl p-bromoamphetamine is readily prepared via the reaction sequence outlined below.[10-12]



(i) $CH_3CH_2NO_2$, NH_4OAc; (ii) BH_3, $NaBH_4$, Δ; (iii) $NaBH_3CN$, CH_3COCH_3

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REFERENCES AND NOTES

1. B. L. Holman, T. C. Hill, J. F. Polak, R. G. L. Lee, and H. D. Royal, "Functional Brain Imaging with I-123 Labeled Amines", in "Radionuclide Imaging of the Brain", B. L. Holman, Ed. Churchill Livingston, New York, 1985.
2. C. A. Mathis, A. T. Shulgin, and T. Sargent, J. Labelled Compds. Radiopharm., 23, 115 (1986).
3. R. H. Seevers and R. E. Counsell, Chem. Rev., 82, 575 (1982).
4. K. M. Tramposch, H. F. Kung, and M. Blau, J. Med. Chem., 26, 121, 1983.
5. G. W. Kabalka, Acc. Chem. Res., 17, 215 (1984).
6. G. W. Kabalka, U. Sastry, K. A. R. Sastry, F. F. Knapp, Jr., and P. C. Srivastava, J. Organometal. Chem., 259, 269 (1983).
7. Excess BH_3•THF was added to an equimolar mixture of compound I and magnesium under an inert atmosphere. The mixture was subjected to ultrasonic agitation after stirring overnight [Branson Ultrasonic Cleaner, Model B-22-4, 117V 60Hz].
8. H. C. Brown and U. S. Racherla, J. Org. Chem., 51, 427 (1986).
9. G. W. Kabalka, E. E. Gooch, T. L. Smith, and M. A. Sells, Int. J. Appl. Radiat. Isot., 33, 223 (1982).
10. M. S. Mourad, R. S. Varma, and G. W. Kabalka, J. Org. Chem., 50, 133 (1985).
11. M. S. Mourad, R. S. Varma, and G. W. Kabalka, Synth. Commun., 14, 1099 (1984).
12. R. F. Borch, M. D. Bernstein, and H. D. Durst, J. Am. Chem. Soc., 93, 2897 (1971).

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