Journal of Labelled Compounds and Radiopharmaceuticals
J Label Compd Radiopharm 2007; **50**: 1234–1235.
Published online 10 September 2007 in Wiley InterScience
(www.interscience.wiley.com). DOI: 10.1002/jlcr.1406

JLCR

Short Research Article

Synthesis of a carbon-14 analogue of N-(3,5-dichlorobenzyl)-4-(fluoromethoxy) benzene carboximidamide-[carboxy-^{14}C] as NR2B-selective NMDA receptor†

GHOLAMHOSSEIN SHIRVANI*, NADER SAEMIAN and HOJATOLLAH MATLOUBI

Nuclear Research Center/AEOI, Chemical Division, P.O. Box 11365-3486, Tehran, Iran

Received 21 June 2006; Accepted 14 May 2007

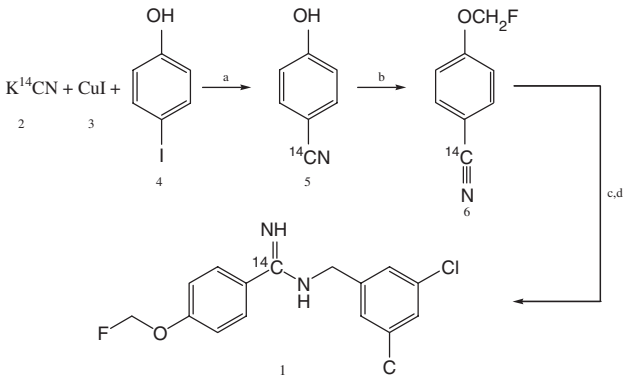
Keywords: carbon 14; benzamidine; NMDA receptor

Introduction

The NMDA receptor is highly expressed in the central nervous system (CNS) and is comprised of a minimum of two different subunits, NR1 and NR2. The NR1 subunit has at least eight isoforms (NR1a–h) and the NR2 subunit has four distinct subtypes (NR2A–D).[1] It has been suggested that NR2B-selective compounds may have a reduced side-effect profile when compared to NMDA receptor antagonists, and have been shown to be efficacious in preclinical pain models.[2] Among the known NR2B-selective compounds are ifenprodil, CP-101,606, Ro-25-6981 and a novel series of benzamidines.[3,4] Based on the benzamidine class of compounds, synthesis of flourine-18 and tritium-labelled N-(3,5-dichlorobenzyl)-4-(fluoromethoxy)benzene carboximidamide were reported by Hamill *et al.* for PET imaging and *vitro* studies, respectively.[5] In this report, the synthesis of N-(3,5-dichlorobenzyl)-4-(fluoromethoxy)-benzene carboximidamide-[carboxy-^{14}C] for metabolism studies is described.

Results and discussion

In this approach, according to the synthetic pathway shown in Scheme 1, the arylnitrile[cyano-^{14}C] 5 was derived from the addition of cuprous iodide 3 and potassium [^{14}C] cyanide 2 to aryl iodide 4 with good yield.[6]



Scheme 1

In the next step, after conversion of the arylnitrile-[cyano-^{14}C] 5 to the 4-(fluoro methoxy) benzonitrile [cyano-^{14}C] 6 by using chlorofluoromethane in DMF with cesium carbonate as the base,[7] the resulting nitrile [cyano-^{14}C] 6 was converted to N-(3,5-dichlorobenzyl)-4-(fluoromethoxy)benzenecarboximidamide-[carboxy-^{14}C] 1 via the Pinner synthesis.[8]

REFERENCES

1. Mori H, Mishina M. *Neuropharmacology* 1995; **34**: 1219.
2. Chizh BA, Headley PM, Tzchentke TM. *Trends Pharmacol Sci* 2001; **22**: 636.
3. Williams K. *Mol Pharmacol* 1993; **44**: 851.
4. Claiborne CF, McCauley JA, Libby BE, Curtis NR, Diggle HJ, Kulagowski JJ, Michelson SR, Anderson

*Correspondence to: Gholamhossein Shirvani, Nuclear Research Center/AEOI, Chemical Division, P.O. Box 11365-3486, Tehran, Iran. E-mail: gshirvani@aeoi.org.ir, basgh48@yahoo.com

†Proceedings of the Ninth International Symposium on the Synthesis and Applications of Isotopically Labelled Compounds, Edinburgh, 16–20 July 2006.

KD, Claremon DA, Freidinger RM, Bednar RA, Mosser SD, Gaul SL, Connolly TM, Condra CL, Bednar B, Stump GL, Lynch JJ, Macaulay A, Wafford KA, Koblan KS, Liverton NJ. *Bioorg Med Chem Lett* 2003; **13**: 697.
5. Hamill TG, McCauley JA, Burns HD. *J. Label Compd Radipharm* 2005; **48**: 1.
6. Saemian N, Shirvani G, Matloubi H. *Nukleonika* 2005; **50**: 139.
7. Taniguchi K, Shinjo K, Mizutani M *et al. Br J Pharmacol* 1997; **122**: 809.
8. Dox AW. *Org Synth* (*Coll.*) 1932; **1**: 5.

DOI: 10.1002.jlcr