Journal of Labelled Compounds and Radiopharmaceuticals
J Label Compd Radiopharm 2007; **50**: 622–623.
Published online in Wiley InterScience
(www.interscience.wiley.com). DOI: 10.1002/jlcr.1379

JLCR

Short Research Article

Synthesis of isotope-labelled [1-^{13}C]-amino acids from $^{13}CO_2$†

TAKAYUKI NAKAJIMA, KAZUKI NAKAYAMA and ISAO SHIMIZU*

Department of Applied Chemistry, School of Science and Engineering, Waseda University, Ohkubo 3-4-1, Shinjuku-ku, Tokyo 169-8555, Japan

Received 8 July 2006; Revised 2 March 2007; Accepted 30 March 2007

Keywords: isotope-labelled [1-^{13}C]-amino acids; $^{13}CO_2$; asymmetric hydrogenation

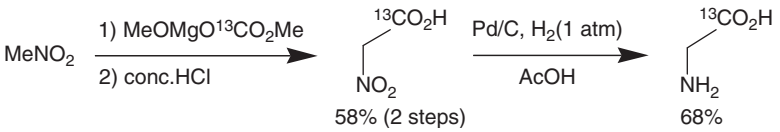
Introduction

Much attention has been paid to the application of stable isotope-labelled ^{13}C-amino acids to various biological studies, such as metabolism, the diagnosis of disease, and biosynthetic studies and the structural analysis of peptides and proteins, because ^{13}C atom is analyzed in multiple ways as IR, NMR and mass spectroscopy.[1] We present here a convenient method for preparation of [1-^{13}C]-amino acids by fixation of readily available $^{13}CO_2$ by means of methyl magnesium carbonate (MMC).

Results and discussion

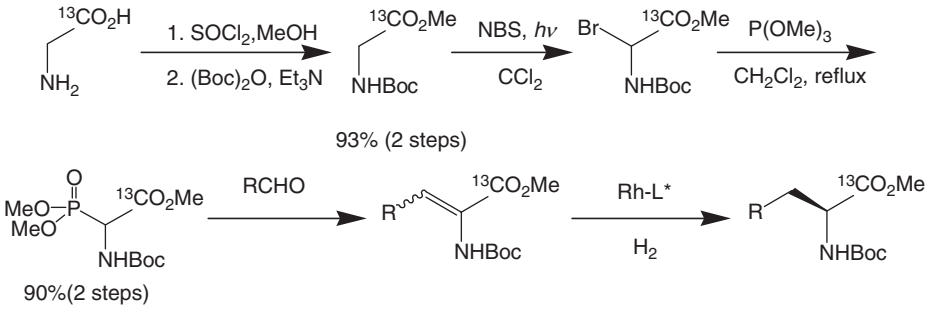
^{13}C-MMC was prepared from $Mg(OMe)_2$ and $^{13}CO_2$ in DMSO.[2] The reaction of nitromethane and ^{13}C-MMC, followed by hydroxylation gave [1-^{13}C]-nitroacetic acid in 58% yield, which was subjected to hydrogenation with H_2 on Pd/C to afford [1-^{13}C]-glycine in 68% yield. (Scheme 1)

Synthesis of optically active amino acids from [1-^{13}C]-glycine was also studied. Thus, [1-^{13}C]-glycine was converted into 2-(methoxyphosphono)glycine derivative,[3] which was subjected to the Horner–Wadsworth–Emmons reaction with several aldehydes to afford corresponding dehydroamino acid derivatives with high *Z* selectivity[4] (Scheme 2). Rhodium catalyzed-asymmetric hydrogenation of dehydroamino acids gave [1-^{13}C]-amino acids with high ee (Table 1).[5]



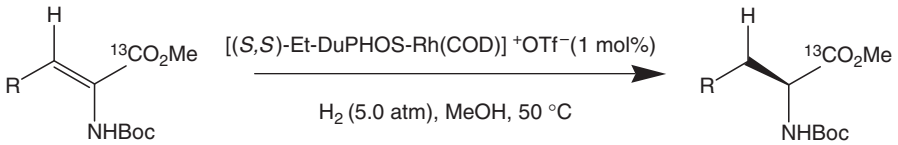
Scheme 1

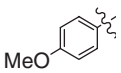
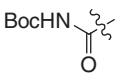
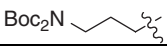
*Correspondence to: Isao Shimizu, Department of Applied Chemistry, School of Science and Engineering, Waseda University, Ohkubo 3-4-1, Shinjuku-ku, Tokyo 169-8555, Japan. E-mail: shimizui@waseda.jp
†Proceedings of the Ninth International Symposium on the Synthesis and Applications of Isotopically Labelled Compounds, Edinburgh, 16–20 July 2006.



Scheme 2

Table 1 Asymmetric hydrogenation of dehydroamino acids



Entry	R	Time (h)	Yield (%)	ee (%)
1		22	99	92
2		16	98	94
3		22	99	94
4	H	26	98	96
5		22	99	93
6		19	98	94
7		19	97	93
8		18	99	92

REFERENCES

1. (a) Mason AJ, Siarheyeva A, Haase W, Lorch M, Veen H, Glaubitz C. *FEBS Lett* 2004; **568**: 117; (b) Löhr F, Rogov VV, Shi M, Bernhard F, Dötsch V. *J Biomol NMR* 2002; **23**: 333; (c) Persson J, Näsholm T. *Physiol Plant* 2001; **113**: 352; (d) Torizawa T, Ono AM, Terauchi T, Kainosho M. *J Am Chem Soc* 2005; **127**: 12620.
2. Finkbeiner HM, Stiles M. *J Am Chem Soc* 1963; **85**: 616.
3. Kober R, Steglich W. *Liebigs Ann Chem* 1983; 599.
4. Schmidt U, Griesser H, Leitenberger V, Lieberknecht A, Mangold R, Meyer R, Riedl B. *Synthesis* 1992; 487.
5. Burk MJ, Feaster JE, Nugent A, Harlow RL. *J Am Chem Soc* 1993; **115**: 10125.

DOI: 10.1002.jlcr