

Short Research Article

Synthesis of isotope-labelled [1-¹³C]-amino acids from ¹³CO₂[†]

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

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Introduction

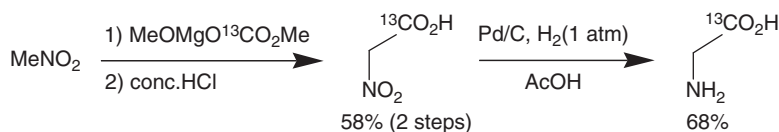
Much attention has been paid to the application of stable isotope-labelled ¹³C-amino acids to various biological studies, such as metabolism, the diagnosis of disease, and biosynthetic studies and the structural analysis of peptides and proteins, because ¹³C atom is analyzed in multiple ways as IR, NMR and mass spectroscopy.¹ We present here a convenient method for preparation of [1-¹³C]-amino acids by fixation of readily available ¹³CO₂ by means of methyl magnesium carbonate (MMC).

Results and discussion

¹³C-MMC was prepared from Mg(OMe)₂ and ¹³CO₂ in DMSO.² The reaction of nitromethane and ¹³C-MMC,

followed by hydroxylation gave [1-¹³C]-nitroacetic acid in 58% yield, which was subjected to hydrogenation with H₂ on Pd/C to afford [1-¹³C]-glycine in 68% yield. (Scheme 1)

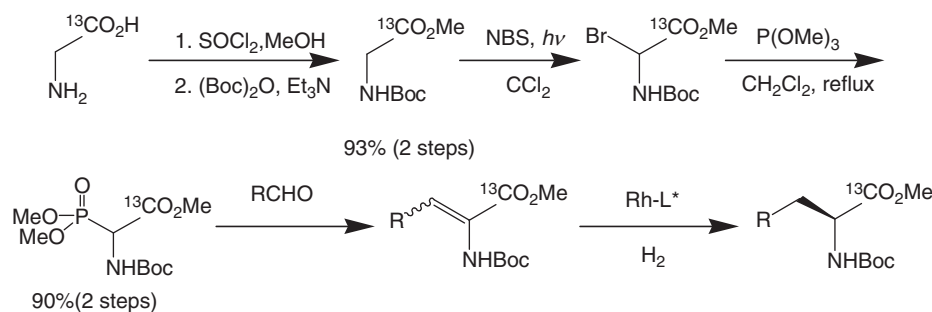
Synthesis of optically active amino acids from [1-¹³C]-glycine was also studied. Thus, [1-¹³C]-glycine was converted into 2-(methoxyphosphono)glycine derivative,³ which was subjected to the Horner–Wadsworth–Emmons reaction with several aldehydes to afford corresponding dehydroamino acid derivatives with high *Z* selectivity⁴ (Scheme 2). Rhodium catalyzed-asymmetric hydrogenation of dehydroamino acids gave [1-¹³C]-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

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**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

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