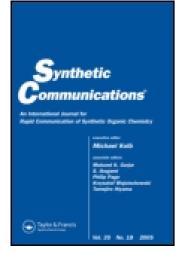
This article was downloaded by: [University of California, San Diego] On: 28 December 2014, At: 17:12 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



# Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: <u>http://www.tandfonline.com/loi/lsyc20</u>

# A CONVENIENT METHOD FOR THE SYNTHESIS OF β-AMINO ACIDS VIA THE ARNDT-EISTERT APPROACH USING p-TOLUENESULPHONYL CHLORIDE AS A CARBOXYLIC GROUP ACTIVATING AGENT

Ganga-Ramu Vasanthakumar <sup>a</sup> & Vommina V. Suresh Babu <sup>b</sup>

<sup>a</sup> Department of Studies in Chemistry, Bangalore University, Central College Campus, Bangalore, 560 001, India

<sup>b</sup> Department of Studies in Chemistry, Bangalore University, Central College Campus, Bangalore, 560 001, India

Published online: 16 Aug 2006.

To cite this article: Ganga-Ramu Vasanthakumar & Vommina V. Suresh Babu (2002) A CONVENIENT METHOD FOR THE SYNTHESIS OF β-AMINO ACIDS VIA THE ARNDT-EISTERT APPROACH USING p-TOLUENESULPHONYL CHLORIDE AS A CARBOXYLIC GROUP ACTIVATING AGENT, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 32:4, 651-657, DOI: <u>10.1081/SCC-120002414</u>

To link to this article: http://dx.doi.org/10.1081/SCC-120002414

# PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <a href="http://www.tandfonline.com/page/terms-and-conditions">http://www.tandfonline.com/page/terms-and-conditions</a>

#### SYNTHETIC COMMUNICATIONS, 32(4), 651-657 (2002)

# A CONVENIENT METHOD FOR THE SYNTHESIS OF β-AMINO ACIDS VIA THE ARNDT-EISTERT APPROACH USING *p*-TOLUENESULPHONYL CHLORIDE AS A CARBOXYLIC GROUP ACTIVATING AGENT

Ganga-Ramu Vasanthakumar and Vommina V. Suresh Babu\*

Department of Studies in Chemistry, Central College Campus, Bangalore University, Bangalore 560 001, India

## ABSTRACT

A simple method for the synthesis of Z-/Boc-/Fmoc-protected  $\beta$ -amino acids by the Arndt-Eistert approach employing *p*-toluenesulphonyl chloride for the activation of the carboxyl group of  $N^{\alpha}$ -protected amino acid is described. The method is rapid and gave good yields with optical purity.

 $\beta$ -Amino acids exhibit a wide spectrum of biological importance similar to natural  $\alpha$ -amino acids. They serve as building blocks for the synthesis of  $\beta$ -peptides,<sup>1</sup> and  $\beta$ -lactam antibiotics.<sup>2</sup> Seebach<sup>3</sup> and Gellman<sup>4,5</sup> groups reported that  $\beta$ -peptides also form stable secondary structures like their

651

Copyright © 2002 by Marcel Dekker, Inc.

www.dekker.com

<sup>\*</sup>Corresponding author.

ORDER		REPRINTS
-------	--	----------

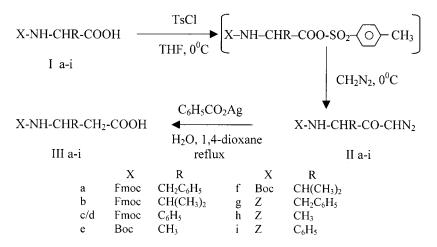
#### VASANTHAKUMAR AND SURESH BABU

α-peptide counterpart. β-Peptides shared by proteinaceous side chains of α-amino acids have been shown to be stable to common α-peptidases for few days.<sup>6</sup> The Arndt-Eistert method for the homologation of α-amino acids is one of the important routes for the synthesis of β-amino acids. This route involves the synthesis of commonly used α-aminoacyldiazomethanes from the  $N^{\alpha}$ -protected amino acids. For this, the activation of carboxylic group of α-amino acid employing the corresponding mixed anhydrides<sup>1,3,7</sup> (using isobutoxycarbonyl chloride or ethoxycarbonyl chloride) or acid chlorides<sup>8</sup> or acid fluorides<sup>9</sup> or activated esters<sup>10</sup> has been used.

652

The use of *p*-toluenesulphonyl chloride (TsCl) in organic synthesis is widely known. It has been used for the activation of carboxylic group in the synthesis of amides and esters of simple carboxylic acids,<sup>11</sup> for the synthesis of peptides,<sup>12</sup>  $\beta$ -lactams<sup>13</sup> etc. This paper describes the use of TsCl for the activation of carboxylic group in the synthesis of  $N^{\alpha}$ -protected aminoacyldiazomethanes.

As shown in Scheme 1,  $N^{\alpha}$ -protected aminoacyldiazomethane was prepared by addition of TsCl and diazomethane (CH<sub>2</sub>N<sub>2</sub>) in dichloromethane (CH<sub>2</sub>Cl<sub>2</sub>) to  $N^{\alpha}$ -protected amino acid in THF at 0°C in presence of pyridine. The reaction proceeds through the formation of carboxylic– sulphonic mixed anhydride which was identified by IR spectra (1825– 1835 cm<sup>-1</sup>). The reaction was complete in about 30 min. All the resulting diazomethane derivatives were isolated as crystalline solids in good yield. They have been analysed by using IR by the presence of characteristic band at around 2105–2108 cm<sup>-1</sup> (-COCHN<sub>2</sub> group) and <sup>1</sup>H NMR. They were



Scheme 1. Synthesis of N-protected-β-homoamino acids.

Marcel Dekker, Inc.

270 Madison Avenue, New York, New York 10016



#### SYNTHESIS OF β-AMINO ACIDS

Downloaded by [University of California, San Diego] at 17:12 28 December 2014

then converted to their corresponding  $\beta$ -amino acids by the Wolff rearrangement using silver benzoate/1,4-dioxane/water by refluxing the mixture for 6 h at 70°C. All the *N*-protected  $\beta$ -amino acids were obtained as crystalline solids and were well characterised. The comparison of the determined optical rotations of the D- and L-isomers of Fmoc- $\alpha$ -Phg and that of  $\beta$ -Phg revealed that this method is completely free from racemisation.

Thus the present procedure is an efficient method for the synthesis of  $N^{\alpha}$ -protected aminoacyldiazomethane using TsCl for carboxylic group activation. The advantages of this method are (a) the mild reaction conditions (b) the use of cheaper reagent (c) the general applicability (d) the selectivity, and (e) the good yields.

#### **EXPERIMENTAL**

All the amino acids used, unless otherwise specified has L-configuration only. Melting points reported are uncorrected. Thin layer chromatography (TLC) was carried out using the solvent systems: (i) ethyl acetate:hexane (35:65), (ii) chloroform:methanol:acetic acid (45:2:1), (iii) chloroform:methanol (9:1) and the  $R_{\rm f}$  values are designated as  $R_{\rm f}A$ ,  $R_{\rm f}B$  and  $R_{\rm f}C$  respectively. <sup>1</sup>H NMR spectra were recorded on a Brucker AMX-400 MHz spectrometer. IR spectra were recorded on a Nicolet model impact 400 D FT-IR spectrometer. Elemental analyses were carried out by Perkin-Elmer Analyser and the samples were dried for 24h under vacuum before analysis. Diazomethane gas was generated by heating *N*-nitroso-*N*-methyl-*p*-toluene sulphonamide with alcoholic KOH.<sup>14</sup>

General Procedure for Preparation of  $N^{\alpha}$ -Protected Aminoacyldiazomethane Derivatives: TsCl (0.210 g, 1.1 mmol) and pyridine (0.08 mL, 1 mmol) were added to a solution of  $N^{\alpha}$ -protected amino acid (1 mmol) in THF (5 mL) and stirred at 0°C for 15 min. The reaction mixture was treated with a saturated solution of CH<sub>2</sub>N<sub>2</sub> in dry CH<sub>2</sub>Cl<sub>2</sub> (20 mL) and stirred for 1 h at 0°C. The progress of the reaction was monitored by TLC and IR. After completion of the reaction, the excess of CH<sub>2</sub>N<sub>2</sub> was decomposed by the dropwise addition of acetic acid. The mixture was washed with NaHCO<sub>3</sub> (25 mL × 3), 5% HCl (25 mL × 3) and brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and evaporated under reduced pressure. The resulting residue was recrystallized using CH<sub>2</sub>Cl<sub>2</sub>/hexane to yield the title compound as a crystalline solid.

 $N^{\alpha}$ -Fmoc-phenylalanyldiazomethane (IIa): Yield, 94%; m.p., 136°C;  $R_{\rm f}A$ , 0.62;  $R_{\rm f}B$ , 0.8;  $[\alpha]_{\rm D}^{25}$  + 16.5 (c = 1, CHCl<sub>3</sub>); Anal. Calc. for  $C_{25}H_{23}N_3O_3$ : C, 72.60; H, 5.60; N, 10.16; Found: C, 72.35; H, 5.57; N,

653

ORDER		REPRINTS
-------	--	----------

#### VASANTHAKUMAR AND SURESH BABU

9.78; IR ( $\gamma_{max}$ ): 2108 cm<sup>-1</sup> (-COCHN<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 3.1 (2H, d), 4.2 (2H, m), 4.5 (2H, d), 5.2 (1H, s), 5.4 (1H, br) and 7.2–7.7 (13H, m).

654

*N*<sup>α</sup>-Fmoc-valyldiazomethane (IIb): Yield, 85%; m.p., 124–125°C; *R*<sub>f</sub>A, 0.69; *R*<sub>f</sub>B, 0.81;  $[\alpha]_D^{25}$  – 23.40 (*c* = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>21</sub>H<sub>21</sub>N<sub>3</sub>O<sub>3</sub>: C, 69.4; H, 5.81; N, 11.56; Found: C, 69.28; H, 5.92; N, 11.46; IR (γ<sub>max</sub>): 2105 cm<sup>-1</sup> (-COCHN<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ): 0.90 (6H, d), 1.75 (1H, m), 4.10 (1H, m), 4.25 (1H, m), 4.45 (2H, m), 5.30 (1H, s), 5.4 (1H, d) and 7.3–7.9 (8H, m).

 $N^{\alpha}$ -Fmoc-phenylglycinyldiazomethane (IIc): Yield, 90%; m.p., 148–149°C;  $R_{\rm f}A$ , 0.66;  $R_{\rm f}B$ , 0.80;  $[\alpha]_D^{25} - 32.3$  (c = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>24</sub>H<sub>29</sub>N<sub>3</sub>O<sub>3</sub>: C, 72.50; H, 4.81; N, 10.57; Found: C, 72.68; H, 4.87; N, 10.6; IR ( $\gamma_{\rm max}$ ): 2107 cm<sup>-1</sup> (-COCHN<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 4.25 (2H, m), 4.4 (2H, d), 5.1 (1H, s), 6.05 (1H, br) and 7.2–7.8 (13H, m).

*N*<sup>α</sup>-Fmoc-D-phenylglycinyldiazomethane (IId): Yield, 92%; m.p., 153°C;  $R_{\rm f}A$ , 0.7;  $R_{\rm f}B$ , 0.83;  $[\alpha]_{\rm D}^{25}$  + 32.3 (*c* = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>24</sub>H<sub>29</sub>N<sub>3</sub>O<sub>3</sub>: C, 72.50; H, 4.81; N, 10.57; Found: C, 72.43; H, 4.90; N, 10.52; IR (γ<sub>max</sub>): 2106 cm<sup>-1</sup> (-COCHN<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 4.2 (2H, m), 4.5 (2H, d), 5.1 (1H, s), 6.05 (1H, br) and 7.2–7.8 (13H, m).

*N*<sup>α</sup>**-Boc-alanyldiazomethane (IIe):** Yield, 93%; m.p., 82°C; *R*<sub>f</sub>A, 0.72; *R*<sub>f</sub>B, 0.82;  $[\alpha]_D^{25} - 21.7$  (*c* = 1, CHCl<sub>3</sub>); Anal. Calc. for C, 50.69; H, 7.08; N, 19.70; Found: C, 50.80; H, 7.20; N, 19.47; IR (γ<sub>max</sub>): 2106 cm<sup>-1</sup> (-COCHN<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ): 1.05 (3H, d), 1.32 (9H, s), 4.21 (1H, m), 5.25 (1H, s) and 5.5 (1H, br).

*N*<sup>α</sup>**-Boc-valyldiazomethane (IIf):** Yield, 90%; m.p., 64°C; *R*<sub>f</sub>A, 0.72; *R*<sub>f</sub>B, 0.83;  $[\alpha]_D^{25} - 30.4$  (*c* = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>11</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub>: C, 54.75; H, 7.93; N, 17.41; Found: C, 54.62; H, 7.78; N, 17.42; IR ( $\gamma_{max}$ ): 2107 cm<sup>-1</sup> (-COCHN<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 0.92 (6H, d), 1.32 (9H, s), 1.75 (1H, m), 4.21 (1H, br), 5.20 (1H, s) and 5.42 (1H, br).

 $N^{\alpha}$ -Z-phenylalanyldiazomethane (IIg): Yield, 92%; m.p., 82–83°C;  $R_{\rm f}A$ , 0.68;  $R_{\rm f}B$ , 0.78;  $[\alpha]_{\rm D}^{25}$  + 48.2 (c = 1, CHCl<sub>3</sub>); Anal. Calc. for  $C_{18}H_{17}N_3O_3$ : C, 66.86; H, 5.29; N, 12.99; Found: C, 66.72; H, 5.35; N, 12.86; IR ( $\gamma_{\rm max}$ ): 2107 cm<sup>-1</sup> (-COCHN<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 2.9 (2H, d), 4.45 (1H, m), 5.0 (2H, s), 5.22 (1H, s), 5.46 (1H, br) and 7.2–7.3 (10H, m).

*N*<sup>α</sup>-*Z*-alanyldiazomethane (IIh): Yield, 88%; m.p., 93–94°C; *R*<sub>f</sub>A, 0.70; *R*<sub>f</sub>B, 0.81; [α]<sup>25</sup><sub>D</sub> − 50.3 (*c* = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>12</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub>: C, 58.29; H, 5.29; N, 16.99; Found: C, 57.95; H, 5.13; N, 16.78; IR ( $\gamma_{max}$ ): 2107 cm<sup>-1</sup> (-COCHN<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ): 1.2 (3H, d), 4.26 (1H, m), 5.1 (2H, s), 5.25 (1H, s), 5.5 (1H, br) and 7.32 (5H, s).

 $N^{\alpha}$ -**Z**-phenylglycyldiazomethane (IIi): Yield, 86%; m.p., 83–84°C;  $R_{\rm f}$ A, 0.69;  $R_{\rm f}$ B, 0.79;  $[\alpha]_{\rm D}^{25}$  – 36.4 (c = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>17</sub>H<sub>15</sub>N<sub>3</sub>O<sub>3</sub>: C, 66.01; H, 4.88; N, 13.58; Found: C, 65.72; H, 4.76; N, 13.72; IR

Downloaded by [University of California, San Diego] at 17:12 28 December 2014

ORDER		REPRINTS
-------	--	----------

## SYNTHESIS OF β-AMINO ACIDS

 $(\gamma_{max})$ : 2108 cm<sup>-1</sup> (-COCHN<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 4.5 (1H, br), 5.02 (2H, s), 5.22 (1H, s), 5.40 (1H, br) and 7.25 (10H, s).

General Procedure for Preparation of *N*-Protected β-Amino Acid: Silver benzoate (5.7 mg,  $2.5 \times 10^{-2}$  mmol) was added to a solution of  $N^{\alpha}$ -protected aminoacyldiazomethane (1 mmol) in 1,4-dioxane (10 mL) and water (5 mL) and refluxed at 70°C for 6 h. It was filtered and the solvent was evaporated under reduced pressure. The residue was dissolved in saturated aqueous Na<sub>2</sub>CO<sub>3</sub> (20 mL) and stirred for 20 min. The mixture was washed with ether (20 mL × 3). The aqueous layer was acidified to pH 2 and extracted with ethyl acetate (20 mL × 3). The extracts were pooled, washed with water (20 mL × 2), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and evaporated under reduced pressure. The residue was precipitated using CH<sub>2</sub>Cl<sub>2</sub>/hexane to get the title compound as a crystalline solid.

*N*-Fmoc-β-homophenylalanine (IIIa): Yield, 85%; m.p., 110–112°C  $R_{\rm f}B$ , 0.63;  $R_{\rm f}C$ , 0.75;  $[\alpha]_{\rm D}^{25}$  – 26.2 (c = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>25</sub>H<sub>23</sub>NO<sub>4</sub>: C, 75.05; H, 5.58; N, 3.70; Found: C, 75.21; H, 5.46; N, 3.80; IR ( $\gamma_{\rm max}$ ): 1703 cm<sup>-1</sup> (CO of urethane); <sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 2.43 (1H, d), 2.52 (2H, m), 2.71 (1H, d), 3.6 (1H, m), 4.1 (1H, m), 4.2 (2H, m) and 7.3–7.8 (14H, m).

*N*-Fmoc-β-homovaline (IIIb): Yield, 80%; m.p., 153–154°C;  $R_{\rm f}$ B, 0.60;  $R_{\rm f}$ C, 0.78;  $[\alpha]_{\rm D}^{25}$  – 36.4 (*c* = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>21</sub>H<sub>23</sub>NO<sub>4</sub>: C, 70.14; H, 5.89; N, 4.20; Found: C, 70.06; H, 5.67; N, 4.35; IR ( $\gamma_{\rm max}$ ): 1705 cm<sup>-1</sup> (CO of urethane); <sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 0.85 (6H, d), 1.75 (1H, m), 2.30 (1H, d), 2.45 (1H, d), 3.75 (1H, m), 4.30 (3H, m) and 7.3–7.8 (9H, m).

*N*-Fmoc-β-homophenylglycine (IIIc): Yield, 82%; m.p., 96–98°C;  $R_{\rm f}$ B, 0.61;  $R_{\rm f}$ C, 0.78; [α]<sub>D</sub><sup>25</sup> – 22.2 (c = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>24</sub>H<sub>21</sub>NO<sub>4</sub>: C, 74.40; H, 5.45; N, 3.61; Found: C, 74.26; H, 5.23; N, 3.80; IR ( $\gamma_{\rm max}$ ): 1705 cm<sup>-1</sup> (CO of urethane); <sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 2.5 (2H, d), 4.25 (2H, m), 4.4 (2H, d), 5.85 (1H, br) and 7.2–7.8 (13H, m).

*N*-Fmoc-β-D-homophenylglycine (IIId): Yield, 84%; m.p., 102°C;  $R_{\rm f}B$ , 0.62;  $R_{\rm f}C$ , 0.79;  $[\alpha]_{\rm D}^{25}$  + 21.8 (c = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>24</sub>H<sub>21</sub>NO<sub>4</sub>: C, 74.40; H, 5.45; N, 3.61; Found: C, 74.34; H, 5.16; N, 3.76; IR ( $\gamma_{\rm max}$ ): 1705 cm<sup>-1</sup> (CO of urethane); <sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 2.4 (2H, d), 4.25 (2H, m), 4.3 (2H, d), 5.80 (1H, br), 7.2–7.8 (13H, m) and 8.3 (1H, br).

*N*-Boc-β-homoalanine (IIIe): Yield, 88%; m.p., 98–99°C;  $R_{\rm f}$ B, 0.62;  $R_{\rm f}$ C, 0.72;  $[\alpha]_{\rm D}^{25}$  – 18.1 (*c* = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>9</sub>H<sub>17</sub>NO<sub>4</sub>: C, 53.45; H, 8.47; N, 6.92; Found: C, 53.28; H, 8.56; N, 6.56; IR ( $\gamma_{\rm max}$ ): 1690 cm<sup>-1</sup> (CO of urethane); <sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 1.2 (3H, d), 1.33 (9H, s), 2.4 (2H, d), 4.01 (1H, m), 5.25 (1H, br) and 8.4 (1H, br).

*N*-Boc-β-homovaline (IIIf): Yield, 86%; m.p., 65–66°C;  $R_{\rm f}B$ , 0.61;  $R_{\rm f}C$ , 0.70;  $[\alpha]_{\rm D}^{25} - 20.2$  (c = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>11</sub>H<sub>21</sub>NO<sub>4</sub>: C, 57.37; H, 9.19; N, 6.08; Found: C, 56.90; H, 9.34; N, 5.82; IR ( $\gamma_{\rm max}$ ): 1690 cm<sup>-1</sup>

Marcel Dekker, Inc.

270 Madison Avenue, New York, New York 10016

655

ORDER		REPRINTS
-------	--	----------

### VASANTHAKUMAR AND SURESH BABU

(CO of urethane); <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ): 0.94 (6H, d), 1.32 (9H, s), 1.72 (1H, m), 2.5 (2H, d), 4.20 (1H, br), 5.4 (1H, br) and 8.3 (1H, br).

656

*N-Z*-β-homophenylalanine (IIIg): Yield, 88%; m.p., 84–85°C;  $R_{\rm f}B$ , 0.60;  $R_{\rm f}C$ , 0.68;  $[\alpha]_{\rm D}^{25}$  – 36.2 (c = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>18</sub>H<sub>19</sub>NO<sub>4</sub>: C, 69.21; H, 6.13; N, 4.48; Found: C, 69.63; H, 6.47; N, 4.32; IR ( $\gamma_{\rm max}$ .): 1698 cm<sup>-1</sup> (CO of urethane): <sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 2.36 (2H, d), 2.71 (2H, d), 3.8 (1H, m), 5.01 (2H, s), 5.3 (1H, m), 7.07 (5H, s), 7.28 (5H, s) and 9.4 (1H, br).

*N-Z*-β-homoalanine (IIIh): Yield, 84%; m.p., 122°C; *R*<sub>f</sub>B, 0.60; *R*<sub>f</sub>C, 0.69;  $[\alpha]_D^{25}$  – 19.8 (*c* = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>12</sub>H<sub>15</sub>NO<sub>4</sub>: C, 61.00; H, 6.39; N, 5.92; Found: C, 61.27; H, 6.23; N, 5.87; IR (γ<sub>max</sub>): 1700 cm<sup>-1</sup> (CO of urethane); <sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 1.2 (3H, d), 2.4 (2H, d), 3.6 (1H, m), 5.1 (2H, s), 5.4 (1H, br), 7.31 (5H, s) and 8.4 (1H, br).

*N*-*Z*-β-homophenylglycine (IIIi): Yield, 82%; m.p., 86–88°C; *R*<sub>f</sub>B, 0.63; *R*<sub>f</sub>C, 0.74; [α]<sub>D</sub><sup>25</sup> – 18.5 (*c* = 1, CHCl<sub>3</sub>); Anal. Calc. for C<sub>17</sub>H<sub>17</sub>NO<sub>4</sub>: C, 68.44; H, 5.74; N, 4.95; Found: C, 68.23; H, 5.68; N, 4.67; IR (max): 1702 cm<sup>-1</sup> (CO of urethane); <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ): 2.5 (2H, d), 4.2 (1H, m), 5.01 (2H, s), 5.46 (1H, br), 7.25 (10H, s) and 8.6 (1H, br).

### ACKNOWLEDGMENTS

We are grateful to Prof. K. M. Sivanandaiah and B. S. Sheshadri for usefull discussions, to Department of Science and Technology, Government of India for financial support. GRVK thanks KSVN Trust for their kind help.

### REFERENCES

- 1. Banerjee, A.; Balaram, P. Current Science 1997, 12, 1067.
- 2. Kim, S.; Lee, P.H.; Lee, T.A. J. Chem. Soc. Chem. Comm. 1988, 1242.
- 3. Seebach, D.; Matthews, J.L. Chem. Commun. 1997, 2015.
- 4. Apella, D.H.; Christianson, L.A.; Klein, D.A.; Powell, D.R.; Huang, X.; Barchi Jr., J.J.; Gellman, S.H. Nature **1997**, *387*, 381.
- 5. Gellman, S.H. Acc. Chem. Res. 1998, 31, 173.
- 6. Hintermann, T.; Seebach, D. Chimia 1997, 50, 244.
- 7. Ellmerer-Muller, E.P.; Brossner, D.; Naslonh, N.; Tako, A. Helv. Chim. Acta **1998**, *81*, 59.
- Leggio, A.; Liguori, A.; Procopio, A.; Sindona, G. J. Chem. Soc. Perkin Trans. 1 1997, 1969.

Marcel Dekker, Inc.

270 Madison Avenue, New York, New York 10016

ORDER		REPRINTS
-------	--	----------

## SYNTHESIS OF β-AMINO ACIDS

- 9. Ananda, K.; Gopi, H.N.; Suresh Babu, V.V. J. Peptide Research 2000, 55, 289.
- (a) Suresh Babu, V.V.; Gopi, H.N.; Ananda, K. J. Peptide Research 1999, 53, 308; (b) Ananda, K.; Suresh Babu, V.V. Indian J. Chemistry 1999, 38B, 418.
- 11. Brewster, J.H.; Ciotti Jr., C.J. J. Am. Chem. Soc. 1955, 77, 6214.
- 12. Theodoropoulos, D.; Gazopoulos, J. J. Org. Chem. 1962, 27, 2091.
- 13. Wasserman, H.H.; Glazer, E.A.; Hearn, M.J. Tetrahedron Lett. **1973**, *49*, 4855.
- Furniss, B.S.; Hannaford, A.J.; Smith, P.W.G.; Tatchell, A.R. Vogel's Textbook of Practical Organic Chemistry, Educational Low-Priced Books Scheme, ELBS, Longman UK. Fifth Edition, 1989, pp. 430–433.

Received in the Netherlands April 4, 2001



# **Request Permission or Order Reprints Instantly!**

Interested in copying and sharing this article? In most cases, U.S. Copyright Law requires that you get permission from the article's rightsholder before using copyrighted content.

All information and materials found in this article, including but not limited to text, trademarks, patents, logos, graphics and images (the "Materials"), are the copyrighted works and other forms of intellectual property of Marcel Dekker, Inc., or its licensors. All rights not expressly granted are reserved.

Get permission to lawfully reproduce and distribute the Materials or order reprints quickly and painlessly. Simply click on the "Request Permission/Reprints Here" link below and follow the instructions. Visit the <u>U.S. Copyright Office</u> for information on Fair Use limitations of U.S. copyright law. Please refer to The Association of American Publishers' (AAP) website for guidelines on <u>Fair Use in the Classroom</u>.

The Materials are for your personal use only and cannot be reformatted, reposted, resold or distributed by electronic means or otherwise without permission from Marcel Dekker, Inc. Marcel Dekker, Inc. grants you the limited right to display the Materials only on your personal computer or personal wireless device, and to copy and download single copies of such Materials provided that any copyright, trademark or other notice appearing on such Materials is also retained by, displayed, copied or downloaded as part of the Materials and is not removed or obscured, and provided you do not edit, modify, alter or enhance the Materials. Please refer to our <u>Website</u> User Agreement for more details.

# **Order now!**

Reprints of this article can also be ordered at http://www.dekker.com/servlet/product/DOI/101081SCC120002414