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*Published in:*  
Tetrahedron: Asymmetry

*DOI:*  
[10.1016/S0957-4166\(01\)00071-4](https://doi.org/10.1016/S0957-4166(01)00071-4)

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*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2001

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Belokon, Y. N., Kochetkov, K. A., Ikonnikov, N. S., Strelkova, T. V., Harutyunyan, S. R., & Saghiyan, A. S. (2001). A new synthesis of enantiomerically pure syn-(S)- $\beta$ -hydroxy- $\alpha$ -amino acids via asymmetric aldol reactions of aldehydes with a homochiral Ni(II)-glycine/(S)-BPB Schiff base complex. *Tetrahedron: Asymmetry*, 12(3), 481-485. DOI: 10.1016/S0957-4166(01)00071-4

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# A new synthesis of enantiomerically pure *syn*-(*S*)- $\beta$ -hydroxy- $\alpha$ -amino acids via asymmetric aldol reactions of aldehydes with a homochiral Ni(II)-glycine/(*S*)-BPB Schiff base complex

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Received 12 January 2001; accepted 9 February 2001

**Abstract**—*syn*-(*S*)- $\beta$ -Hydroxy- $\alpha$ -amino acids were synthesised stereoselectively via elaboration of the asymmetric aldol reactions of aldehydes with a chiral Ni(II)-(*S*)-BPB/glycine Schiff base complex in the presence of equimolar NaH in THF. The stereoselectivity of the reaction was studied as a function of time, the reaction conditions, the nature of the carbonyl compounds and the base used. The synthetic potential of this asymmetric method was demonstrated in the preparation of *syn*-(*S*)- $\beta$ -hydroxy-leucine on a multi-gram scale. © 2001 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

$\alpha$ -Amino- $\beta$ -hydroxy acids of differing structures are important components of physiologically active peptides, cyclic peptides (Vancomycin, Cyclosporin, etc.) and enzyme inhibitors.<sup>1</sup> They are also useful intermediates in the synthesis of  $\beta$ -halo- $\alpha$ -amino acids,<sup>1–3</sup>  $\beta$ -lactams<sup>4a</sup> and other important compounds.<sup>4b</sup> In addition, there is growing interest in the design and synthesis of novel unnatural homochiral amino acids (including  $\beta$ -hydroxy- $\alpha$ -amino acids) to serve as substitutes for their natural analogues in peptides.<sup>5</sup>

A number of elegant approaches for the synthesis of enantiomerically pure  $\beta$ -hydroxy- $\alpha$ -amino acids, including the use of sugars,<sup>1,2</sup> electrophilic amination,<sup>6</sup>  $\beta$ -functionalisation of  $\alpha$ -amino acids<sup>7</sup> and diastereoselective aldol condensation protocols,<sup>8</sup> have been described. The most synthetically viable strategies developed to date for the stereocontrolled preparation of  $\beta$ -hydroxy- $\alpha$ -amino acids are based on the aldol reaction of homochiral glycine equivalents with carbonyl compounds.<sup>9,10</sup>

The aldol reaction between carbonyl compounds and

the Ni(II) complex **1**, which contains homochiral Schiff base ligands formed from glycine and (*S*)-*o*-[*N*-(*N'*-benzylpropyl)amino]benzophenone ((*S*)-BPB), is practically attractive<sup>10</sup> since the structure of complex **1** offers the advantage of relatively high C–H acidity of the glycine  $\alpha$ -protons,<sup>11</sup> allowing the use of a wide range of weak and strong bases under various conditions. In addition, the chiral auxiliary (*S*)-BPB is cheap, readily available<sup>12</sup> and recoverable, and can be used repeatedly without any loss of enantiomeric purity and chemical activity.<sup>10</sup> Unfortunately, (*S*)-**1** from commercially available (*S*)-BPB, according to the published procedures,<sup>10</sup> furnished *syn*-(*R*)- $\beta$ -hydroxy- $\alpha$ -amino acids under easily reproducible thermodynamically controlled conditions,<sup>10</sup> whereas for the synthesis of *syn*-(*S*)- $\beta$ -hydroxy- $\alpha$ -amino acids, the more expensive (*R*)-BPB had to be employed.<sup>10</sup>

Herein, we describe a new synthetic protocol for the synthesis of *syn*-(*S*)- $\beta$ -hydroxy- $\alpha$ -amino acids, employing (*S*)-BPB as a recoverable chiral auxiliary.

## 2. Results and discussion

A preliminary study of the mechanism of the condensation of aliphatic aldehydes with (*S*)-**1** in MeOH at high

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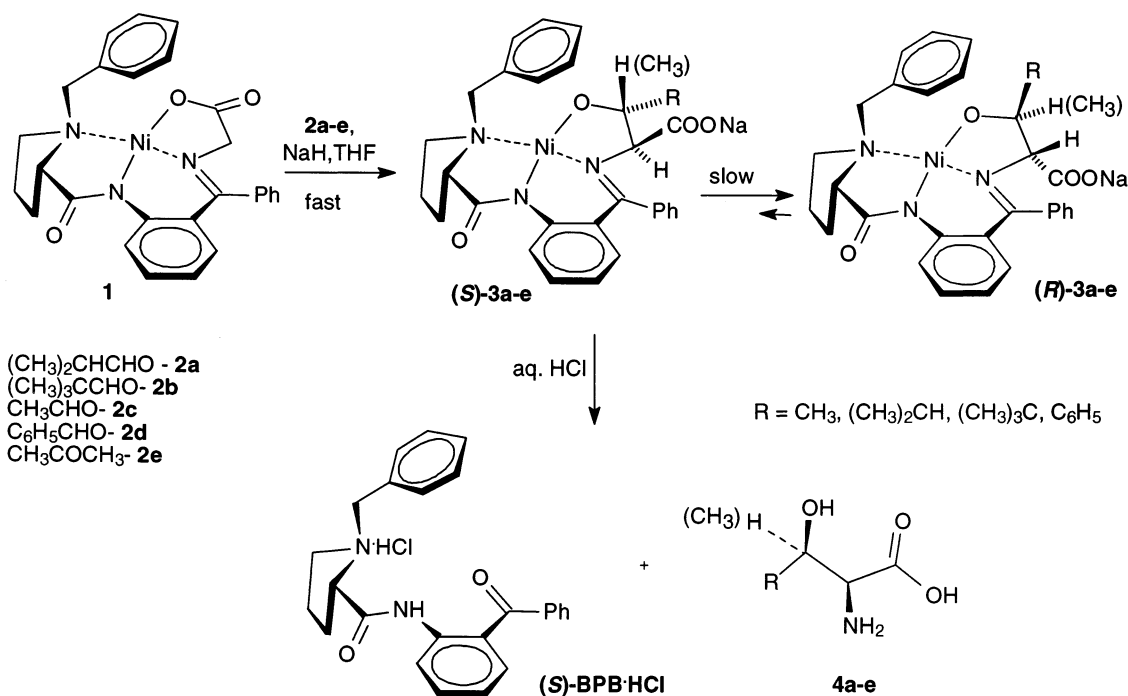
reaction  $\text{pH}^{10}$  indicated that the reaction had some unusual features. The most salient one was the rearrangement of the intermediate aldol condensation product, where the ionised hydroxyl group of the product substitutes for the ionised carboxyl group in the main coordination plane of the complex. This results in the formation of an ionised intermediate complex (see Scheme 1).<sup>10</sup> Kinetic and thermodynamic stereoselectivities were observed in the reaction with the latter favouring *syn*-(*R*)- $\beta$ -hydroxy- $\alpha$ -amino acids, whereas *syn*-(*S*)- $\beta$ -hydroxy- $\alpha$ -amino acids were initially formed.<sup>10c</sup> Unfortunately, under the experimental conditions it was difficult to stop the reaction at the kinetically controlled stage and within minutes the initial kinetic product was transformed into the thermodynamic product via a series of C–C bond breaking and forming reactions.<sup>10c</sup>

It was thought that by completing the reaction in aprotic solvents of relatively low dielectric constant the basicity of the intermediate ionised hydroxyl group of the aldol adduct would be increased and its O–Ni bond stabilised. Thus, the rate of equilibration between the diastereoisomeric complexes should decrease favouring the kinetic aldol product, *syn*-(*S*)- $\beta$ -hydroxy- $\alpha$ -amino acid.

The starting material (*S*)-**1** was prepared by a previously described procedure.<sup>12</sup> Condensation of **1** with aliphatic aldehydes **2a–2c**, and benzaldehyde **2d** was carried out in THF at different temperatures. In these reactions, to arrest equilibration between diastereoisomers, the reaction mixture was poured into cold aqueous acetic acid. Reversing the order of addition

invariably resulted in the formation of much greater amounts of the (*R*)-diastereoisomer. The complexes precipitated from the solution and were therefore easily isolated. Diastereoisomeric ratios were estimated either by <sup>1</sup>H NMR or by chiral GLC analysis of the amino acids recovered from the complexes after decomposition with aqueous HCl. In addition, CD spectra of the complexes served to assign the absolute configuration of the  $\alpha$ -carbon of the amino acid moiety.<sup>10</sup> In all cases the diastereoisomeric complex **3**, containing *syn*-(*S*)-amino acids, was predominantly formed in the reaction and could be separated from the reaction mixture (Table 1). Sodium hydride was found to be the base of choice as it gave better results than both *t*-BuOK and *t*-BuLi (with the ratio of *syn*-(*S*)-**3a**/*syn*-(*R*)-**3a** falling from 60/1 to 7/1 with *t*-BuOK and 5/1 when *t*-BuLi was used); additionally, *anti*-diastereoisomers formed in the mixture when sodium hydride was not used (Table 1, runs 1, 4 and 5). The effect of temperature on the diastereoisomeric ratio was not straightforward, with a seemingly negative influence on the reactions of **3a–3c** (Table 1, runs 1, 2, 3, 8 and 9), but a positive effect in the formation of the benzaldehyde adduct **3d**.

The acetone condensation was the most time-sensitive reaction, as extending the reaction by 7 min resulted in the ratio of (*S*)-**3d**/*(R)*-**3d** decreasing from 30/1 to 2/1 (Table 1, runs 12 and 13). The reaction of acetaldehyde gave the condensation product with a satisfactory ratio of *syn*-(*S*)/*syn*-(*R*) at 20°C after 3 minutes, whereas lowering the temperature and prolonging the reaction to 15 min resulted in a marked drop in selectivity (Table 1, runs 8 and 9).



Scheme 1.

**Table 1.** The aldol reaction of carbonyl compounds **2** with chiral Ni(II)–glycine complex **1**, using NaH in THF<sup>a</sup>

Run	Carbonyl compound <b>2</b>	<i>T</i> (°C)	Time (min)	Ratio of <i>syn</i> -(2 <i>S</i> )- <b>3</b> / <i>syn</i> -(2 <i>R</i> )- <b>3</b> <sup>b</sup>	Yield of <i>syn</i> -(2 <i>S</i> )- <b>3</b> (%)	( <i>S</i> )-Amino acid <b>4</b> , e.e. (%) <sup>c</sup> (yield from <b>1</b> (%) <sup>d</sup> )
1	(CH <sub>3</sub> ) <sub>2</sub> CHCHO ( <b>2a</b> )	16	10	60/1	96	95.5 (87)
2	(CH <sub>3</sub> ) <sub>2</sub> CHCHO ( <b>2a</b> )	–5	35	7/1	75 <sup>e</sup>	
3	(CH <sub>3</sub> ) <sub>2</sub> CHCHO ( <b>2a</b> )	–20	180	10/1	80 <sup>e</sup>	
4	(CH <sub>3</sub> ) <sub>2</sub> CHCHO ( <b>2a</b> )	20	5	7/1/4 <sup>f</sup>	60 <sup>g</sup>	
5	(CH <sub>3</sub> ) <sub>2</sub> CHCHO ( <b>2a</b> )	20	10	5/1/1 <sup>f</sup>	70 <sup>h</sup>	
6	(CH <sub>3</sub> ) <sub>3</sub> CCHO ( <b>2b</b> )	20	13	10/1	80	81 (62)
7	(CH <sub>3</sub> ) <sub>3</sub> CCHO ( <b>2b</b> )	–12	75	5/1	78	
8	CH <sub>3</sub> CHO ( <b>2c</b> )	20	3	60/1	80	95 (66)
9	CH <sub>3</sub> CHO ( <b>2c</b> )	0	15	6/1	80	
10	C <sub>6</sub> H <sub>5</sub> CHO ( <b>2d</b> )	–7	30	20/1	75 <sup>i</sup>	94 (55)
11	C <sub>6</sub> H <sub>5</sub> CHO ( <b>2d</b> )	20	4	3/2	55	
12	CH <sub>3</sub> COCH <sub>3</sub> ( <b>2e</b> )	20	7	30/1	85	99 (80)
13	CH <sub>3</sub> COCH <sub>3</sub> ( <b>2e</b> )	20	14	2/1	70	

<sup>a</sup> The concentration of complex **1** in THF was 0.18 M; the molar ratio of complex **1**:**2**:NaH=1:2:1; for details see Section 4.

<sup>b</sup> Determined by <sup>1</sup>H NMR analysis of crude reaction mixture.

<sup>c</sup> See Section 4 for details of chiral GLC analysis of amino acids **4**.

<sup>d</sup> Before crystallisation of the amino acids **4**.

<sup>e</sup> The yield was determined by weighing the preparatively isolated **3** after precipitation with hexane.

<sup>f</sup> The configuration of the third diastereomer **3** was not determined.

<sup>g</sup> *tert*-BuOK was used as a base.

<sup>h</sup> *tert*-BuLi was used as a base.

<sup>i</sup> The yield was determined after separating **1** from the reaction mixture (ratio **3**/**1**=6/1).

### 3. Conclusion

A very simple and efficient procedure for the synthesis of *syn*-(*S*)-β-hydroxy-α-amino acids via the aldol condensation of aldehydes with the Ni(II)-(*S*)-BPB/glycine Schiff base complex in THF has been elaborated. The procedure is amenable to scale-up and there seems to be no limit to the possible increase in the volume of the procedure.

## 4. Experimental

### 4.1. Methods, materials and chemicals

<sup>1</sup>H NMR spectra were recorded on Bruker WP-200 and 400 instruments (200 and 400 MHz) using C<sub>6</sub>D<sub>6</sub> as an external standard. NMR data are reported in δ units. The optical rotation measurements were obtained on a Perkin–Elmer 241 polarimeter. Electronic absorption spectra were recorded on a Specord M-40 instrument. CD-spectra were recorded on a JASCO-J-700 spectropolarimeter. The reactions were monitored by TLC on Silufol plates; for the preparative TLC silica gel 60 F254 (Merck) was employed. GLC enantiomeric analyses<sup>13</sup> of the amino acids **4a–4e** were performed on a Characid-L-Val type phase, by using their *N*-trifluoroacetyl *n*-propyl esters. Fused silica capillary column 40 m×0.23 mm ID. Film 0.12 μm. Col. temp.: 160°C for **2a**, **2b**, 140°C for **2c** and **2e**, 170°C for **2d**. Carrier-gas He: 1.80 bar. All aldehydes and THF (from LiAlH<sub>4</sub>) were distilled prior to use. Synthesis of **1** was performed as described earlier.<sup>12</sup> All reactions were performed under an anhydrous argon atmosphere.

### 4.2. Aldol reactions of complex **1** with carbonyl compounds

**4.2.1. Reaction with 2-methylpropan-1-al **2a**.** A 1 L flask was flame dried in vacuo and filled with Ar, then charged sequentially with a solution of **1** (40 g, 0.08 mol) in THF (450 mL) and NaH (60% in oil, 3.2 g, 0.08 mmol). The stirred mixture was cooled (solid CO<sub>2</sub>–Me<sub>2</sub>CO bath) and degassed by the freeze/thaw technique under Ar. The temperature was raised to 16°C and aldehyde **2a** (14.58 mL, 11.56 g, 0.16 mmol) was added. The reaction was monitored by TLC (EtOAc:CHCl<sub>3</sub>=3:1). After 10 min the reaction was quenched by pouring the mixture into 10% AcOH (3 L). The red crystals formed were filtered, washed with water and air-dried to afford near pure **3a** (44.26 g, 0.077 mol, 96%, (*S*)-**3a**/*R*-**3a**=60:1). An analytically pure sample of **3a** was obtained by further purification by TLC (EtOAc:CHCl<sub>3</sub>=3:1).

Ni(II)-(*S*)-BPB/(2*S*,3*R*)-2-amino-3-hydroxy-4-methylpentanoic acid Schiff base complex **3a**. Mp=157°C. [α]<sub>D</sub><sup>25</sup>=+3100 (0.04, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>): 0.83 (3H, d, *J*=6.5 Hz), 1.16 (3H, d, *J*=6.9 Hz), 1.65–2.84 (8H, m, Pro-H, γ-CH), 3.86 (1H, m, β-CH), 3.59, 4.43 (2H, AB, *J*=12.7 Hz, CH<sub>2</sub>Ph), 4.13 (1H, d, *J*=6.9 Hz, α-CH), 6.67–7.56 (11H, m, ArH), 8.07–8.09 (2H, m, ArH), 8.23–8.25 (1H, m, ArH). Anal. calcd for C<sub>31</sub>H<sub>33</sub>N<sub>3</sub>NiO<sub>4</sub>: C, 65.29; H, 5.83; N, 7.36. Found: C, 64.9; H, 5.8; N, 7.11%.

**4.2.2. Reaction with 2,2-dimethylpropan-1-al (trimethylacetaldehyde) **2b**.** The reaction was conducted as above starting from complex **1** (3 g, 6 mmol). Reaction time

was 13 min. Yield of crude product **3b** was 80% ((*S*)-**3b**/*R*)-**3b**=10:1). The crude complex was dissolved in the minimum  $\text{CHCl}_3$  and crystallised under stirring by addition of a small amount of hexane. After several hours the crystals were filtered to afford **3b** in 70% chemical yield, ((*S*)-**3b**/*R*)-**3b**=50:1). Complex **3b** was further purified by TLC ( $\text{EtOAc}:\text{CHCl}_3=3:1$ ).

Ni(II)-(*S*)-BPB/(2*S*,3*R*)-2-amino-3-hydroxy-4,4-dimethylpentanoic acid Schiff base complex **3b**. Mp=161°C.  $[\alpha]_{\text{D}}^{25}=+3020$  (0.04,  $\text{CHCl}_3$ ). Lit.,<sup>10c</sup> mp=157–159°C.  $[\alpha]_{\text{D}}^{25}=+3215$  (0.04,  $\text{CHCl}_3$ ).

**4.2.3. Reaction with ethanal 2c.** The reaction was conducted as described above, starting from complex **1** (2 g, 4 mmol) at 20°C. The reaction was complete within 3 min. The reaction was monitored by TLC ( $\text{CHCl}_3$ ;  $\text{CH}_3\text{COCH}_3=6:1$ ). The yield of crude product **3c** was 80% ((*S*)-**3c**/*R*)-**3c**=60:1). An analytically pure sample of complex **3c** was obtained by preparative LC ( $\text{EtOAc}:\text{CHCl}_3=3:1$ ).

Ni(II)-(*S*)-BPB/(2*S*,3*R*)-2-amino-3-hydroxybutanoic acid [(2*S*,3*R*)-threonine] Schiff base complex **3c**. Mp=210°C.  $[\alpha]_{\text{D}}^{25}=+3540$  (0.04,  $\text{CHCl}_3$ ). Lit.,<sup>10c</sup>  $[\alpha]_{\text{D}}^{25}=+3244$  (0.00127,  $\text{CH}_3\text{CN}$ ).

**4.2.4. Reaction with benzaldehyde 2d.** The reaction was conducted as above starting from 2 g (4 mmol) of complex **1** at –7°C. Reaction time was 30 min. Yield of the crude product **3d** was 75% ((*S*)-**3d**/*R*)-**3d**=20:1).

Ni(II)-(*S*)-BPB/(2*S*,3*R*)-2-amino-3-hydroxy-3-phenylpropanoic acid Schiff base complex **3d**. Mp=214–215°C.  $[\alpha]_{\text{D}}^{25}=+1900$  (0.04,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ ): 1.52–3.30 (8H, m, Pro-H,  $\beta$ -CH), 3.40, 4.16 (2H, AB,  $J=12.7$  Hz,  $\text{CH}_2\text{Ph}$ ), 4.46 (1H, s, OH), 4.60 (1H, m,  $\alpha$ -CH), 6.68–7.62 (16H, m, ArH), 7.98–8.00 (2H, m, ArH), 8.27–8.29 (1H, m, ArH). Anal. calcd for  $\text{C}_{34}\text{H}_{31}\text{N}_3\text{NiO}_4$ : C, 67.5; H, 5.13; N, 6.95. Found: C, 66.84; H, 5.47; N, 7.20%.

**4.2.5. Reaction with acetone 2e.** The reaction was conducted as above starting from 0.5 g (1 mmol) of complex **1** at 20°C. Reaction time was 7 min. The reaction was monitored by TLC ( $\text{CHCl}_3$ ;  $\text{CH}_3\text{COCH}_3=6:1$ ). The yield of crude product **3e** was 85% ((*S*)-**3e**/*R*)-**3e**=30:1).

Ni(II)-(*S*)-BPB/(2*S*)-2-amino-3-hydroxy-3-methylbutanoic acid Schiff base complex **3e**. Mp=218–221°C.  $[\alpha]_{\text{D}}^{25}=+2707$  (0.04,  $\text{CHCl}_3$ ). Anal. calcd for  $\text{C}_{30}\text{H}_{31}\text{N}_3\text{NiO}_4$ : C, 64.75; H, 5.57; N, 7.55. Found: C, 65.3; H, 5.34; N, 7.02.  $^1\text{H NMR}$ ( $\text{CDCl}_3$ ): 1.55 (3H, s, Me), 1.59 (3H, s, Me), 2.03–3.48 (7H, m, Pro-H), 3.46, 4.35 (2H, AB,  $J=12.4$  Hz,  $\text{CH}_2\text{Ph}$ ), 3.96 (1H, s,  $\alpha$ -CH), 6.65–7.57 (11H, m, ArH), 8.07–8.08 (2H, m, ArH), 8.37–8.39 (1H, m, ArH).

The reactions at low temperatures and with other bases such as *tert*-BuOK and *tert*-BuLi were conducted as above.

### 4.3. General procedure for the isolation of amino acids from the Ni(II)-complexes and recovery of chiral auxiliary (*S*)-BPB

The crude complex **3** was decomposed by refluxing with methanolic solution of 6N HCl as described earlier,<sup>10</sup> then the solution was evaporated to dryness. Water was added to the residue and the insoluble material was filtered, washed with water and dried to afford (*S*)-BPB·HCl. To the aqueous layer a solution of aq.  $\text{NH}_3$  was added to pH 8 and the solution was extracted with  $\text{CHCl}_3$  several times. Amino acid **4** was recovered from the solution by the ion-exchange technique (DOWEX-50,  $\text{H}^+$  form). The yield was determined using  $^1\text{H NMR}$  analysis of the reaction mixture with (*S*)-leucine as an internal standard, and the e.e. (>99%) was determined by chiral GLC.

**4.3.1. (2*S*,3*R*)-2-Amino-3-hydroxy-4-methylpentanoic acid 4a [*syn*-(2*S*)- $\beta$ -hydroxyvaline].** From complex **3a** (44.0 g), **4a** (10.2 g, 87%, e.e. 95.5%) was prepared. The crude product was recrystallised from an  $\text{EtOH-H}_2\text{O}$  mixture to give the enantiomerically pure compound (9.4 g, 80%, e.e. >99%). Mp=210°C.  $[\alpha]_{\text{D}}^{25}=+19$  (1.0, 5N HCl). Lit.,<sup>10c</sup>  $[\alpha]_{\text{D}}^{25}=+18.5$  (1.0, 5N HCl).

**4.3.2. (2*S*)-2-Amino-3-hydroxy-3-methylbutanoic acid 4e [(2*S*)- $\beta$ -hydroxyvaline].** Yield before crystallisation 80% (e.e. 99%), after crystallisation 65% (e.e. 99.9%). Mp=202–203°C.  $[\alpha]_{\text{D}}^{25}=+13.5$  (0.64, 6N HCl). Lit.<sup>10b</sup> for -(2*R*)- $\beta$ -hydroxyvaline. Mp=200–201°C.  $[\alpha]_{\text{D}}^{25}=-11.2$  (2.0, 5N HCl).

### Acknowledgements

The work was supported by ISTC Project A-356.

### References

1. *Amino Acids, Peptides and Proteins; Special Periodical Reports*; Chem. Soc.: London, 1968–1995; Vols. 1–28. See a very useful set of references cited in: Blaskovich, M.; Evindear, G.; Rose, N. G. W.; Wilkinson, S.; Luo, Y.; Lajoire, G. A. *J. Org. Chem.* **1998**, *63*, 3631.
2. Pansare, S. V.; Veredas, J. C. *J. Org. Chem.* **1987**, *52*, 4804.
3. Badorrey, R.; Cativiela, C.; Diaz-de-Villegas, M. D.; Galvez, J. A. *Tetrahedron: Asymmetry* **2000**, *11*, 1015.
4. (a) Lotz, B. T.; Miller, M. J. *J. Org. Chem.* **1993**, *58*, 618; (b) Coppola, G. M.; Shuster, H. F. *Asymmetric Synthesis. Construction of Chiral Chiral Molecules Using Amino Acids*; John Wiley & Sons: Toronto, 1987.
5. (a) Gante, J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1699; (b) Giannis, J. A.; Kolter, T. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1244; (c) Hruby, V. J.; Al-Obeidi, F.; Kazmierski, W. *Biochem. J.* **1990**, *268*, 249; (d) Gibson, S. E.; Guillo, N.; Tozer, M. J. *Tetrahedron* **1999**, *55*, 585.
6. Sting, A. R.; Seebach, D. *Tetrahedron* **1996**, *52*, 279.
7. Coulon, E.; Cano de Andrade, M. D.; Ratovelomanadavidal, V.; Genet, J.-P. *Tetrahedron Lett.* **1998**, *39*, 6467.

8. (a) Solladie-Cavallo, A.; Nsenda, T. *Tetrahedron Lett.* **1998**, 38, 2191; (b) Harwood, L. M.; Robertson, S. M. *Chem. Commun.* **1998**, 2641; (c) Horikawa, M.; Busch-Petersen, J.; Corey, E. *Tetrahedron Lett.* **1999**, 40, 3843.
9. (a) Duthaler, R. P. *Tetrahedron* **1994**, 40, 1539; (b) Evans, D. A.; Sjogren, E. B.; Weber, A. E.; Conn, R. E. *Tetrahedron Lett.* **1987**, 28, 39; (c) Soloshonok, V. A.; Hajashi, T. *Tetrahedron: Asymmetry* **1994**, 5, 1091.
10. (a) Belokon, Y. N. *Janssen Chim. Acta* **1992**, 10, 4; (b) Belokon, Y. N.; Bulychev, A. G.; Vitt, S. V.; Struchkov, Y. T.; Batsanov, A. S.; Timofeeva, T. V.; Tsyryapkin, V. A.; Ryzhov, M. G.; Lysova, L. A.; Bakhmutov, V. I.; Belikov, V. M. *J. Am. Chem. Soc.* **1985**, 107, 4252; (c) Soloshonok, V. A.; Avilov, D. V.; Kuchar, V. P.; Tararov, V. I.; Saveleva, T. F.; Churkina, T. D.; Ikonnikov, N. S.; Kochetkov, K. A.; Orlova, S. A.; Pysarevsky, A. P.; Struchkov, Y. T.; Raevski, N. I.; Belokon, Y. N. *Tetrahedron: Asymmetry* **1995**, 6, 1741.
11. Terehova, M. I.; Belokon, Y. N.; Maleev, V. I.; Chernoglazova, N. I.; Kochetkov, K. A.; Belikov, V. M.; Petrov, E. S. *Izv. Akad. Nauk, Ser. Khim. SSSR* **1986**, 905 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1986**, 35, 824).
12. Belokon, Y. N.; Tararov, V. I.; Maleev, V. I.; Savel'eva, T. F.; Ryzhov, M. G. *Tetrahedron: Asymmetry* **1998**, 9, 4249.
13. Makaparskin, S.; Birrel, P.; Gil-av, E.; Oro, I. *J. Chromatogr. Sci.* **1970**, 8, 177.