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Unusual amino acids VIII. Asymmetric hydrogenation of some heteroaryl-N-CBZ and N-BOC aminocinnamic acid derivatives

Chr. Döbler, H.-J. Kreuzfeld, and **M. Michalik**

Institut für Organische Katalyseforschung an der Universität Rostock e.V., Rostock, Federal Republic of Germany

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Summary. (Z)-α-[(Benzyloxy)- or (tert.-butyloxy)carbonylamino]-β (thienyl)- or (furyl)-acrylic acids and their esters were prepared by known methods and hydrogenated to the corresponding optically active alanine derivatives with optical yields in the range of 58–93% ee using the cationic rhodium complex of "PROPRAPHOS".

Keywords: Amino acids – Non-proteinogenic optically active amino acids – Dehydroamino acids – Chiral rhodium catalysts – Asymmetric hydrogenation

Introduction

It is well known that among unnatural amino acids those bearing heterocyclic rings exhibit diverse pharmacological effects when introduced in biologically active systems.

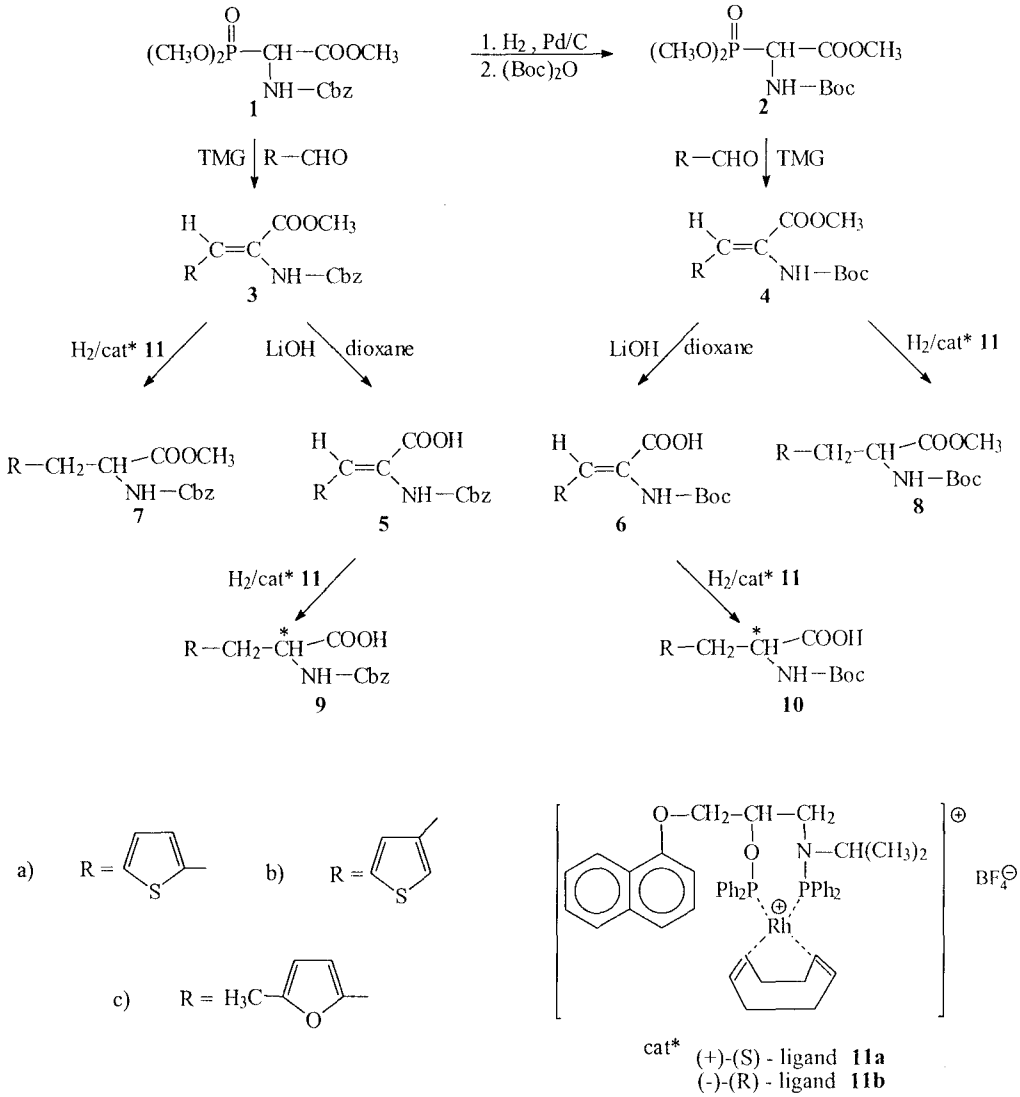
Some years ago we investigated the asymmetric synthesis of N-acetyl and N-benzoyl furyl- and thienylalanine derivatives by asymmetric hydrogenation using PROPRAPHOS-Ph as catalyst (Krause et al., 1992; Döbler et al., 1993). But the incorporation into peptides required orthogonal protecting groups. In early works we investigated the influence of t-butyl-oxycarbonyl(Boc) and benzyloxycarbonyl(Cbz) protective group on the rate and enantioselectivity of the hydrogenation (Kreuzfeld et al., 1993) and we synthesized numerous substituted arylamino acids directly by hydrogenation of the appropriate N-Boc and N-Cbz protected arylaminocinnamic acid derivatives (Krause et al., 1996). Now, to complete these investigations we want to report on the hydrogenation of thienyl- and furylamino-cinnamic acid derivatives bearing the mentioned protecting groups.

Masquelin (Masquelin et al., 1994) described the synthesis of ß-(2- and 3-furyl-)-alanines and ß-(2- and 3-thienyl-)-alanines by asymmetric hydrogenation of N-Cbz protected (Z)-α,β-didehydro esters. They obtained ee values close to 100% using rhodium complexes of 1.2-ethanediylbis(2-

methoxyphenyl)phenylphosphine (DIPAMP) and bis(phospholano)benzene (DUPHOS) at 40°C and 60 bar H_2 pressure.

Results and discussion

The enamides used for the asymmetric hydrogenation were prepared as shown in Scheme 1. Starting from methyl-2-[(benzyloxy)carbonylamino]-2-(dimethoxyphosphinyl)-acetate **1** the esters **3a–c** and **4a–c** are available, the use of a strong base such as N,N,N',N'-tetramethyl-guanidine (TMG) in CH_2Cl_2 favours the formation of Z-**3** and **4** (Schmidt et al., 1992). The desired pure methyl esters were obtained after chromatography. Hydrolysis with LiOH in dioxane/water gives the acid derivatives **5a–c** and **6a–c**. The hydro-



Scheme 1

Table 1. Catalytic asymmetric hydrogenation of the substrates **3a,b,c–6a,b,c**

Entry	Substrate	cat* (ligand)	product (config.)	$t/_2$[a] (min)	ee (%)
1.	**3a**	**11a**	**7a** (R)	190	79
2.	**3a**	(S, S)-BPPM	**7a** (R)	30	78
3.	**3a**	(R, R)-DIOP	**7a** (R)	20	35
4.	**5a**	**11b**	**9a** (S)	170	61
5.	**5a**	(S, S)-BPPM	**9a** (R)	140	58
6.	**4a**	**11a**	**8a** (R)	60	86
7.	**4a**	(S, S)-BPPM	**8a** (R)	50	80
8.	**4a**	(R, R)-DIOP	**8a** (R)	15	13
9.	**6a**	**11a**	**10a** (R)	40	79
10.	**6a**	(S, S)-BPPM	**10a** (R)	35	75
11.	**3b**	**11b**	**7b** (S)	20	88
12.	**3b**	(S, S)-BPPM	**7b** (R)	8	86
13.	**3b**	(R, R)-DIOP	**7b** (R)	7	37
14.	**5b**	**11a**	**9b** (R)	18	90
15.	**5b**	(S, S)-BPPM	**9b** (R)	13	85
16.	**4b**	**11a**	**8b** (R)	13	92
17.	**4b**	(S, S)-BPPM	**8b** (R)	8	84
18.	**4b**	(R, R)-DIOP	**8b** (R)	5	14
19.	**6b**	**11a**	**10b** (R)	7	93
20.	**6b**	(S, S)-BPPM	**10b** (R)	6	89
21.	**3c**	**11a**	**7c** (R)	80	84
22.	**5c**	**11a**	**9c** (R)	180	60
23.	**4c**	**11a**	**8c** (R)	60	89
24.	**6c**	**11b**	**10c** (S)	50	82

[a] $t/_2$ time for uptake of 50% of the theoretical volume of hydrogen.

genation reaction was catalysed by the cationic rhodium complexes with (+)-(S)- or (−)-(R)-ligand **11a** or **11b** (see Scheme 1). The results are given in Table 1. These measurements demonstrate that the PROPRAPHOS-ligand is efficient in the hydrogenation of Boc and Cbz protected heteroaryl derivatives under normal conditions (atmospheric pressure, room temperature), but activity and enantioselectivity are generally lower in comparison with the acetyl and benzoyl derivatives (Krause et al., 1992; Döbler et al., 1993). The 3-substituted derivatives give significantly higher rates and enantiomeric excesses compared to the 2-heteroaryl derivatives. We found that the use of Boc protected substrates leads to a reduced hydrogenation time and some higher ee values.

In our comparative investigation we found similar results for the BPPM-ligand but a strong loss of selectivity using DIOP. This effect is increased, if the Boc derivatives were used. The same results we found in the asymmetric hydrogenation of the phenylalanine precursor (Kreuzfeld et al., 1993).

Material and methods

General: All reactions with air- or moisture-sensitive reactants and solvents were carried out in oven dried glassware under a positive pressure of dry argon. ^1H and ^{13}C NMR

measurements were recorded on a 300 MHz spectrometer (Bruker ARX 300). The calibration of spectra was carried out be means of solvent peaks (δ ^{1}H = 7.25; δ ^{13}C = 77.0). The assignment of the signals of the thiophene ring has been reviewed (Döbler et al., 1993). The spectra of the Cbz derivatives agree with the literature data (Masquelin et al., 1994). Optical rotation was measured on a GYROMAT-HP polarimeter (FA. Dr. Kernchen, Seelze). The enantiomeric excesses (% ee) were determined by HPLC on a Hewlett-Packard 1090 chromatograph series II, fitted with a 250 × 4.6 mm CHIRACEL OD-H column (eluent: n-hexane/isopropanol), for the amino acid derivatives **9** and **10** after esterification with diazomethane. Melting points are uncorrected and were determined on a Boetius microscope.

Hydrogenation: The hydrogenation experiments were performed in a standard apparatus. 1 mmol of substrate, 15 ml methanol, 25°C and 0.1 Mpa H_2, substrate:catalyst = 100:1. The complexes [Rh(COD)(ligand)]BF_4 for the ligands DIOP and BPPM were prepared *in situ*, the PROPRAPHOS-complexes **11** are crystalline compounds.

Methyl esters **3**: The substrates **3a–c** were prepared following Schmidt's procedure by reaction of methyl 2-[(benzyloxy)carbonylamino]-2-(dimethoxyphosphoryl)-acetate **1** with the appropriate aldehydes (−30°C, CH_2Cl_2) in presence of TMG, the final product was chromatographed (SiO_2, AcOEt/hexane) to give pure (Z)-**3**.

Methyl esters **4**: Methyl 2-[(tert.-butyloxy)carbonylamino]-2-(dimethoxyphosphoryl)-acetate **2** was prepared from **1** and reacts according **1** to the substrates (Z)-**4a–c** (see Scheme 1).

Acrylic acids **5 and 6**: To a solution of **3** or **4** (5 mmol) in dioxane (18 ml) a solution of LiOH × H_2O (11 mmol) in 8 ml H_2O was added at room temperature. After a reaction time of 2 h the mixture was evaporated, the aqueous solution acidified with 1N HCl and extracted with AcOEt. The combined organic layer was washed with water, dried (Na_2SO_4) and evaporated, the residue was recrystallized.

N-Cbz- and N-Boc-thienylalanine methylesters **7 and 8**: After the hydrogenation reaction was finished the solvent was evaporated. The residue was dissolved in benzene and filtered on a small column of silica (Kieselgel 60, Merck) to remove the catalyst. After evaporation of the solvent oily compounds were isolated. The compounds **8a** and **8b** became partially crystalline. A small amount of hexane was added, the insoluble crystals were removed by filtration (preferable racemate), and a nearly optically pure proudct was obtained after evaporation.

N-Cbz- and N-Boc-thienylalanines **9 and 10**: The hydrogenation products were dissolved in diluted aqueous Na_2CO_3, treated with charcoal and filtered to remove the catalyst. The solution was acidified with 1N HCl and extracted with AcOEt. In the case of the Cbz-derivatives a nearly optically pure compound could be isolated by recrystallisation from AcOEt/hexane (mother liquor product).

Methyl (Z)-2-[(benzylox)carbonylamino]-3-(2-thienyl)prop-2-enoate **3a**: From **1** and thiophene-2-carbaldehyde (Fluka). 77%, m.p. 112–113°C (AcOEt/hexane) [lit.: 113.5°C (Masquelin et al., 1994)]. Anal. calcd. for $C_{16}H_{15}NO_4S$ (317.4): C 60.55 H 4.76 N 4.41 S 10.11; found: C 60.61 H 4.72 N 4.25 S 10.04.

Methyl (Z)-2-[(benzyloxy)carbonylamino]-3-(3-thienyl)prop-2-enoate **3b**: From **1** and thiophene-3-carbaldehyde (Fluka). Yield 88%, m.p. 88°C (AcOEt/hexane), [lit.: 90°C (Masquelin et al., 1994)]. Anal. calcd. for $C_{16}H_{15}NO_4S$ (317.4): C 60.55 H 4.76 N 4.41 S 10.11; found: C 60.62 H 4.79 N 4.60 S 10.17.

Methyl (Z)-2-[(benzyloxy)carbonylamino]-3-(5-methyl-2-furyl)prop-2-enoate **3c**: From **1** and 5-methylfuran-2-carbaldehyde. Yield 86%, m.p. 70°C. Anal. calcd. for $C_{17}H_{17}NO_5$ (315.3): C 64.75 H 5.43 N 4.44; found: C 64.88 H 5.48 N 4.56.

Methyl (Z)-2-[(tert.-butylox)carbonylamino]-3-(2-thienyl)prop-2-enoate **4a**: From **2** and thiophene-2-carbaldehyde. Yield 71%, m.p. 87°C (Ether/pentane). Anal. calcd. for $C_{13}H_{17}NO_4S$ (283.4): C 55.10 H 6.05 N 4.94 S 11.32; found: C 55.05 H 6.15 N 5.01 S 11.49.

Methyl (Z)-2-[(tert.-butyloxy)carbonylamino]-3-(3-thienyl)prop-2-enoate **4b**: From **2** and thiophene-3-carbaldehyde. Yield 73%, m.p. 79°C (Ether/pentane). Anal. calcd. for $C_{13}H_{17}NO_4S$ (283.4): C 55.10 H 6.05 N 4.94 S 11.32; found: C 55.12 H 6.07 N 5.10 S 11.42.

Methyl (Z)-2-[(tert.-butyloxy)carbonylamino]-3-(5-methyl-2-furyl)prop-2-enoate **4c**: From **2** and 5-methylfuran-2-carbaldehyde. Yield: 68%, m.p. 114°C. Anal. calcd. for $C_{14}H_{19}NO_5$ (281.3): C 59.77 H 6.81 N 4.98; found: C 59.91 H 6.92 N 4.97.

(Z)-2-[(Benzyloxy)carbonylamino]-3-(2-thienyl)propenoic acid **5a**: From **3a**. Yield 71%, m.p. 132–133°C (AcOEt/hexane). Anal. calcd. for $C_{15}H_{13}NO_4S$ (303.35): C 59.39 H 4.32 N 4.62 S 10.57; found: C 59.40 H 4.47 N 4.51 S 10.75.

(Z)-2-[(Benzyloxy)carbonylamino]-3-(3-thienyl)propenoic acid **5b**: From **3b**. Yield 68%, m.p. 145–146°C (AcOEt/hexane). Anal. calcd. for $C_{15}H_{13}NO_4S$ (303.35): C 59.39 H 4.32 N 4.62 S 10.57; found: C 59.49 H 4.44 N 4.68 S 10.68.

(Z)-2-[(Benzyloxy)carbonylamino]-3-(5-methyl-2-furyl)propenoic acid **5c**: From **3c**. Yield 81%, m.p. 140°C. Anal. calcd. for $C_{16}H_{15}NO_5$ (301.3): C 63.78 H 5.02 N 4.65; found: C 63.69 H 5.08 N 4.75.

(Z)-2-[(tert.-Butyloxy)carbonylamino]-3-(2-thienyl)propenoic acid **6a**: From **4a**. Yield 83%, m.p. 172–173°C (toluene). Anal. calcd. for $C_{12}H_{15}NO_4S$ (269.33): C 53.51 H 5.61 N 5.20 S 11.91; found: C 53.75 H 5.72 N 5.27 S 11.67.

(Z)-2-[(tert.-Butyloxy)carbonylamino]-3-(3-thienyl)propenoic acid **6b**: From **4b**. Yield 89%, m.p. 185°C (toluene). Anal. calcd. for $C_{12}H_{15}NO_4S$ (269.33): C 53.51 H 5.61 N 5.20 S 11.91; found: C 53.31 H 5.49 N 5.31 S 11.80.

(Z)-2-[(tert.-Butyloxy)carbonylamino]-3-(5-methyl-2-furyl)propenoic acid **6c**: From **4c**. Yield 72%, m.p. 175°C. Anal. calcd. for $C_{13}H_{17}NO_5S$ (267.3): C 58.42 H 6.41 N 5.24; found: C 58.37 H 6.24 N 5.32.

Methyl (R)-2-[(benzyloxy)carbonylamino]-3-(2-thienyl)propanoate **7a**: From **3a**. Oil, $[\alpha]_D^{25}$ −44.7 (c 1, $CHCl_3$), ee 78% (HPLC), [lit.: $[\alpha]_D^{25}$ −55.4 (c 0.5, $CHCl_3$), ee 98.0% (Masquelin et al., 1994)]. Anal. calcd. for $C_{16}H_{17}NO_4S$ (319.4): C 60.17 H 5.37 N 4.39 S 10.04; found: C 60.24 H 5.19 N 4.50 S 10.00.

Methyl (R)-2-[(benzyloxy)carbonylamino]-3-(3-thienyl)propanoate **7b**: From **3b**. Oil, $[\alpha]_D^{25}$ −41.8 (c 1, $CHCl_3$), ee 88% (HPLC), [lit.: $[\alpha]_D^{25}$ −45.0 (c 0.5, $CHCl_3$), ee 96.5% (Masquelin et al., 1994)]. Anal. calcd. for $C_{16}H_{17}NO_4S$ (319.4): C 60.17 H 5.37 N 4.39 S 10.04; found: C 60.27 H 5.48 N 4.60 S 10.02.

Methyl (R)-2-[(tert.-butyloxy)carbonylamino]-3-(2-thienyl)propanoate **8a**: From **4a**. Oil, $[\alpha]_D^{25}$ −57.9 (c 1, $CHCl_3$), ee >99% (HPLC). Anal. calcd. for $C_{13}H_{19}NO_4S$ (285.4): C 54.71 H 6.71 N 4.91 S 11.24; found: C 54.93 H 6.83 N 4.88 S 11.19.
^{1}H NMR ($CDCl_3$): δ 7.15 (dd, 1H, $J_{4,5} \sim 5.0$ Hz, $J_{3,5} \sim 1.2$ Hz, thienyl H-5); 6.92 (dd, 1H, $J_{4,5} \sim 5.0$ Hz, $J_{3,4} \sim 3.5$ Hz, thienyl H-4); 6.79 (ddt, 1H, $J_{3,4} \sim 3.5$ Hz, $J_{3,5} \sim 1.2$ Hz, $J_{3,CH_2} \sim 0.8$ Hz, thienyl H-3); 5.10 (b, 1H, NH); 4.58 (m, 1H, CH); 3.73 (s, 3H, OCH_3); 3.33 (m, 2H, CH_2); 1.43 (s, 9H, $C(CH_3)_3$).
^{13}C NMR ($CDCl_3$): δ 171.6 (COO); 155.0 (NHCO); 137.5 (thienyl C-2); 126.9 (thienyl C-4); 126.6 (thienyl C-3); 124.7 (thienyl C-5); 80.0 ($\underline{C}(CH_3)_3$); 54.3 (CH); 52.3 (OCH_3); 32.4 (CH_2); 28.8 ($C(\underline{C}H_3)_3$).

Methyl (R)-2-[(tert.-butyloxy)carbonylamino]-3-(3-thienyl)propanoate **8b**: From **4b**. Oil, $[\alpha]_D^{25}$ −48.8 (c 1, $CHCl_3$), ee >99% (HPLC). Anal. calcd. for $C_{13}H_{19}NO_4S$ (285.4): C 54.71 H 6.71 N 4.91 S 11.24; found: C 54.66 H 6.80 N 5.15 S 11.08.
^{1}H NMR ($CDCl_3$): δ 7.25 (dd, 1H, $J_{4,5}$ ~ 5.0 Hz, $J_{2,5}$ ~ 3.0 Hz, thienyl H-5); 6.99 (dd, 1H, $J_{2,5}$ ~ 3.0 Hz, $J_{2,4}$ ~ 1.3 Hz; J_{2,CH_2} ~ 0.8 Hz, thienyl H-2); 4.98 (b, 1H, NH); 4.56 (m, 1H, CH); 3.71 (s, 3H, OCH_3); 3.12 (m, 2H, CH_2); 1.42 (s, 9H, $C(CH_3)_3$).
^{13}C NMR ($CDCl_3$): δ 172.3 (COO); 155.1 (NHCO); 136.1 (thienyl C-3); 128.3 (thienyl C-4); 125.8 (thienyl C-5); 122.7 (thienyl C-2); 80.0 ($\underline{C}(CH_3)_3$); 53.9 (CH); 32.9 (CH_2); 28.3 ($C(\underline{C}H_3)_3$).

(R)-2-[(Benzyloxy)carbonylamino]-3-(2-thienyl)propanoic acid **9a**: From **5a**. White powder, m.p. 85–86°C, [lit.: 86.5°C (Masquelin et al., 1994)]. $[\alpha]_D^{25}$ −51.8 (c 1, $CHCl_3$), ee 97.0% (HPLC), [lit.: $[\alpha]_D^{25}$ −49.3 (c 1, $CHCl_3$), ee 98.9 (Masquelin et al., 1994)]. Anal. calcd. for $C_{15}H_{15}NO_4S$ (305.4): C 59.00 H 4.95 N 4.59 S 10.50; found: C 59.07 H 4.93 N 4.67 S 10.36.

(R)-2-[(Benzyloxy)carbonylamino]-3-(3-thienyl)propanoic acid **9b**: From **5b**. White powder, m.p. 91°C, [lit.: 90°C (Masquelin et al., 1994)]. $[\alpha]_D^{25}$ −52.5 (c 1, $CHCl_3$), ee 99% (HPLC), [lit.: $[\alpha]_D^{25}$ −51.3° (c 1, $CHCl_3$), ee 99.8% (Masquelin et al., 1994)]. Anal. calcd. for $C_{15}H_{15}NO_4S$ (305.4): C 59.00 H 4.95 N 4.59 S 10.50; found: C 58.83 H 4.77 N 4.56 S 10.36.

(R)-2-[(tert.-Butyloxy)carbonylamino]-3-(2-thienyl)propanoic acid **10a**: From **6a**. Oil, $[\alpha]_D^{25}$ −36.9 (c 1, $CHCl_3$), $[\alpha]_D^{25}$ −19.4 (c 2, 95% EtOH), ee 79% (HPLC) [lit.: $[\alpha]_D^{25}$ −25.2 (c 2, 95% EtOH) optically pure, (Lipkowski et al., 1980)]. Anal. calcd. for $C_{12}H_{17}NO_4S$ (271.4): C 53.12 H 6.32 N 5.16 S 11.82; found: C 53.28 H 6.25 N 4.94 S 11.59.
^{1}H NMR ($CDCl_3$): δ 7.17 (dd, 1H, $J_{4,5}$ ~ 5.0 Hz, $J_{3,5}$ ~ 1.0 Hz, thienyl H-5); 6.94 (dd, 1H, $J_{4,5}$ ~ 5.0 Hz; $J_{3,4}$ ~ 3.5 Hz, thienyl H-4); 6.84 (dd, 1H, $J_{3,4}$ ~ 3.5 Hz, $J_{3,5}$ ~ 1.0 Hz, thienyl H-3); 6.33 (b, 1H, COOH); 5.10 (d, 1H, $J_{NH,CH}$ ~ 6.5 Hz, NH); 4.59 (b, 1H, CH); 3.38 (m, 2H, CH_2); 1.43 (s, 9H, $C(CH_3)_3$).
^{13}C NMR ($CDCl_3$): δ 175.5 (COO); 155.4 (NHCO); 137.4 (thienyl C-2); 127.0 (thienyl C-4); 126.8 (thienyl C-3); 124.8 (thienyl C-5); 80.4 ($\underline{C}(CH_3)_3$); 54.3 (CH); 32.1 (CH_2); 28.3 ($C(\underline{C}H_3)_3$).

(R)-2-[(tert.-Butyloxy)carbonylamino]-3-(3-thienyl)propanoic acid **10b**: From **6b**. Oil, $[\alpha]_D^{25}$ −43.9 (c 1, $CHCl_3$), ee 93%. Anal. calcd. for $C_{12}H_{17}NO_4S$ (271.4): C 53.12 H 6.32 N 5.16 S 11.82; found: C 53.38 H 6.48 N 4.98 S 11.62.
^{1}H NMR ($CDCl_3$): δ 7.95 (b, 1H, COOH); 7.27 (dd, 1H, $J_{4,5}$ ~ 5.0 Hz), $J_{2,5}$ ~ 3.0 Hz, thienyl H-5); 7.04 (dd, 1H, $J_{2,5}$ ~ 3.0 Hz, $J_{2,4}$ ~ 1.3 Hz, thienyl H-2); 6.93 (dd, 1H, $J_{4,5}$ ~ 5.0 Hz, $J_{2,4}$ ~ 1.3 Hz, thienyl H-4); 4.98 (d, 1H, $J_{NH,CH}$ ~ 6.5 Hz, NH); 4.58 (b, 1H, CH); 3.18 (m, 2H, CH_2); 1.42 (s, 9H, $C(CH_3)_3$).
^{13}C NMR ($CDCl_3$): δ 176.1 (COO); 155.4 (NHCO); 136.0 (thienyl C-3); 128.4 (thienyl C-4); 125.9 (thienyl C-5); 122.9 (thienyl C-2); 80.3 ($\underline{C}(CH_3)_3$); 53.8 (CH); 32.4 (CH_2); 28.3 ($C(\underline{C}H_3)_3$).

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References

Döbler Chr, Kreuzfeld HJ, Krause HW, Michalik M (1993) Unusual amino acids IV. Asymmetric synthesis of thienylalanines. Tetrahedron: Asymmetry 4: 1833–1842

Krause HW, Kreuzfeld HJ, Döbler Chr (1992) Unusual amino acids I. Asymmetric synthesis of furylalanine derivatives. Chirality 4: 110–115

Krause HW, Kreuzfeld HJ, Schmidt U, Döbler Chr, Michalik M, Taudien S, Fischer Chr (1996) Unusual amino-acids VI. Substituted arylamino acids by asymmetric hydrogenation of N-Cbz and N-Boc protected dehydroamino acid derivatives. Chirality 8: 173–188

Kreuzfeld HJ, Döbler Chr, Krause HW, Facklam Chr (1993) Unusual amino acids V. Asymmetric hydrogenation of (Z)-N-acylamidocinnamic acid derivatives bearing different protective groups. Tetrahedron: Asymmetry 4: 2047–2051

Masquelin T, Broger E, Müller K, Schmid R, Obrecht D (1994) 124. Synthesis of enantiomerically pure D- and L-(heteroaryl)alanines by asymmetric hydrogenation of (Z)-α-amino-α,β-didehydroesters. Helv Chim Acta 77(5): 1395–1411

Lipkowski AW, Flouret G (1980) Resolution of β-2-thienylalanine enantiomers by a convenient method. Pol J Chem 54: 2225–2228

Schmidt U, Griesser H, Leitenberger V, Lieberknecht A, Mangold R, Meyer R, Riedl B (1992) Diastereoselective formation of (Z)-didehydroamino acid esters. Synthesis: 487–490

Authors' address: Dr. Christian Döbler, Institut für Organische Katalyseforschung an der Universität Rostock e.V., Buchbinderstraße 5–6, D-18055 Rostock, Federal Republic of Germany, E-mail: cdoebl@chemiel.uni-rostock.de

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