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UNUSUAL AMINO ACIDS
IV. ASYMMETRIC SYNTHESIS OF THIENYLALANINES

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Abstract: (Z)-2-N-Acylamino-3-thienyl-acrylic acids and their esters were prepared by known procedures and hydrogenated to the corresponding optically active 2-N-acetyl(or benzoyl)-3-(2- or 3-thienyl)-alanines with optical yields up to 90 % using the rhodium complexes of "PROPRAPHOS" **6a,b** and O,N-bis(diphenylphosphino)-2-exo-hydroxy,3-endo-methylamino-norbornane **6c** as chiral catalysts. Recrystallization and deacylation of the obtained amino acid derivatives yields the optically pure hydrochlorides of the thienylalanines and the free amino acids.

Introduction: Thiophene containing amino acids have received interest because of their potential pharmacological utility and their incorporation in synthetic peptides[1]. Racemic 2- and 3-thienyl derivatives have been prepared by several methods[2], whilst the optically active 2-thienyl compounds have mainly been obtained via classical or enzymatic procedures.[3]
(L)-3-Thienyl alanines were reported exclusively as components in oligopeptides[4]. In the field of asymmetric hydrogenation, the reaction of (Z)-thienyl-N-acyl-propenoic acids in presence of neutral or cationic Rh-DIOP complexes has been described by Cativiela et al.[5]

Results and Discussion: The substrates **(Z)-4** and **(Z)-5** used for the asymmetric hydrogenation were prepared as shown in Scheme 1.
Starting from the thienyl aldehydes **1**, the (Z)-2-methyl (or phenyl) oxazolones **(Z)-3** were available by the Erlenmeyer reaction. The ring opening leads to the dehydroamino acids **(Z)-4a-d** or their esters **(Z)-5a-d**, respectively[6]. The asymmetric hydrogenation of the substrates **4a-d** and **5a-d** was carried out using the catalysts **6a-c** and Rh-DIOP for comparison.
The results summarized in Tables 1 and 2 demonstrate that these chiral catalysts of the aminophosphine-phosphinite type are very efficient in both activity and enantioselectivity in the hydrogenation of thiophene derivatives. These systems are not poisoned by thiophen and have been shown to catalyze the asymmetric hydrogenation of normal[7] and unusual[8] dehydroamino acids with high rate and enantioselectivity.
Table 1 compiles the results for the hydrogenation of the thienyl acrylic acids. The efficiency of our catalytic systems with respect to DIOP is significant, especially in enantioselectivity, and the advantage of the PROPRAPHOS complex **6a** or **6b** is particularly clearly demonstrated (Table 2). The 2-thienyl derivatives **4a,b** give some higher rates and enantiomeric excesses with respect to the 3-thienyl compounds **4c,d**. The enantiomeric excess was not significantly enlarged in case of (Z)-2-acetamido-3-thienyl-propenoic acids

compared with their benzamido analogues which is in contrast to DIOP (table 1, entry 5, 8, 15 and results previously reported by Cativiela et al.[5]).

Table 1 Catalytic asymmetric hydrogenation of **4a-d**

Entry	Substr.	Cat.	Substr. Cat.	Product (config.)[a]	t/2[b] (min)	ee (%)	after Re-cryst.
1	**4a**	**6a**	100	**7a** (R)	2	90	> 99[d]
2	**4a**	**6b**	100	**7a** (S)	2	90	> 99
3	**4a**	**6a**	1000	**7a** (R)	26	89	> 99
4	**4a**	**6c**	100	**7a** (R)	3,5	78	
5	**4a**	DIOP[c]	100	**7a** (R)	2	77	
6	**4b**	**6b**	100	**7b** (S)	2,5	90	
7	**4b**	**6c**	100	**7b** (R)	4	80	
8	**4b**	DIOP[c]	100	**7b** (R)	2	31	
9	**4c**	**6a**	100	**7c** (R)	1	88	> 99[e]
10	**4c**	**6a**	1000	**7c** (R)	8	84	> 99
11	**4c**	**6c**	100	**7c** (R)	2,5	70	98
12	**4d**	**6a**	100	**7d** (R)	1	85	96[f]
13	**4d**	**6a**	500	**7d** (R)	3,5	84	95
14	**4d**	**6c**	100	**7d** (R)	2,5	65	
15	**4d**	DIOP[c]	100	**7d** (R)	2	42	

Catalysts **6a-c** as crystallized cationic complex, 0.01 mmol; 15 ml MeOH, 25 °C, 0.1 MPa H_2

[a] assumed configuration, comparison with DIOP[5], [b] t/2 time for uptake of 50 % of theoretical hydrogen volume. The value gives a rough indication since exact measurement of the rate and the diffusion control has not been performed. [c] cationic complex, in situ formed from (-)-DIOP [d] from ethylacetate/hexane, [e] from H_2O, [f] from acetonitrile, mother liquor product.

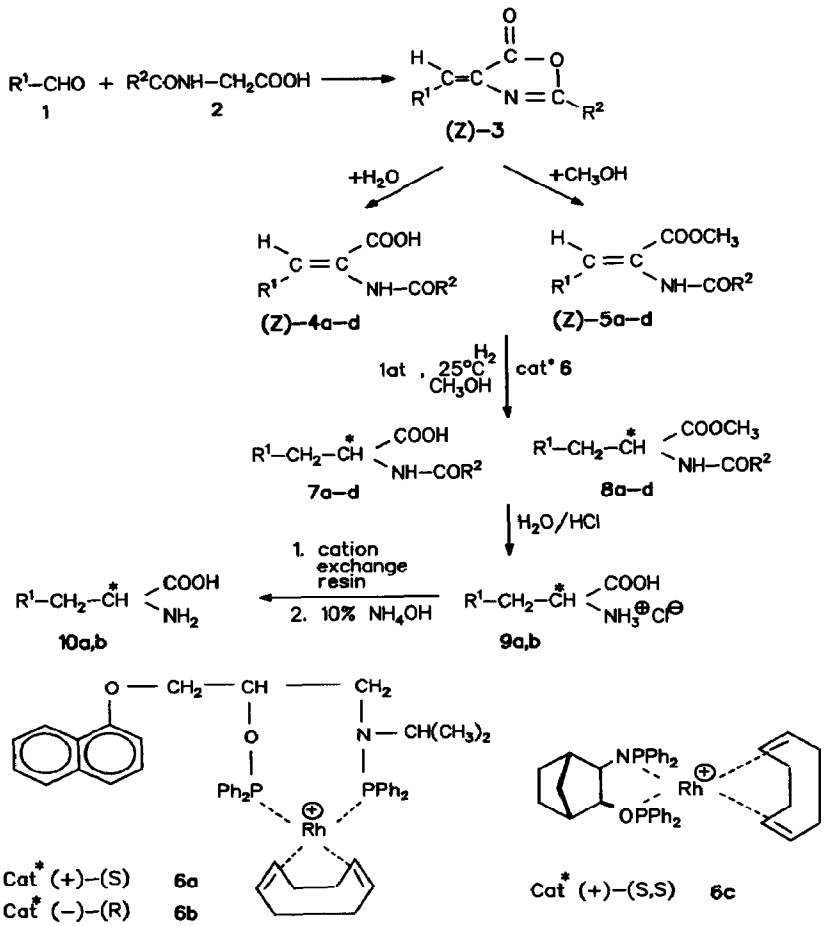
In some cases the enantiomeric purities can be raised by recrystallisation to become > 99 % ee (see last column in Table 1).

The (S)-configured catalyst **6a** induces (R)-configured thienylalanines, whilst catalyst **6b** shows the opposite behaviour. Catalyst **(+)-6c** gives (R)-product, and thus the (S,S)-configuration can be supposed from comparison.

Because of the high activity and enantioselectivity of the catalyst **6a** & **6b** the substrate : catalyst ratio was increased up to 1000 : 1 (Table 1, entry 3, 10).

The same holds for the methyl esters **5a-d** (Table 2) where rate and selectivity nearly correspond to the results in Table 1 which is in accordance with experiences formerly made. Indeed, already the increase of the substrate : catalyst ratio up to 500 : 1 leads to a significant rise of the hydrogenation time (see entry 2,7).

The deacylation using 6 N hydrochloric acid of the hydrogenated N-acetyl products, the acids **7a, c** (> 99 % ee) as well as the ester **8a** (> 99 % ee), yields amino acid hydrochlorides (> 99 % ee). Free amino acids **10a, b** resulted from the hydrochlorides **9a, b** via cation exchange resin (DOWEX 50) by elution with 10 % ammonia.



3, 7, 4, 8, 5	R^1	R^2
a		CH_3
b		C_6H_5
c		CH_3
d		C_6H_5

9, 10	R^1	R^2
a		—
b		—

SCHEME 1

Table 2 Catalytic asymmetric hydrogenation of **5a-d**

Entry	Substr.	Cat.	Substr. Cat.	Product (config.)	t/2 (min)	ee (%)	after Re-cryst.
1	**5a**	**6a**	100	**8a** (R)	3	88	> 99[a]
2	**5a**	**6a**	500	**8a** (R)	20	86	> 99
3	**5a**	**6c**	100	**8a** (R)	4	77	
4	**5b**	**6b**	100	**8b** (S)	4	90	
5	**5b**	**6c**	100	**8b** (R)	5	75	
6	**5c**	**6a**	100	**8c** (R)	1	86	98[a]
7	**5c**	**6a**	500	**8c** (R)	15	83	98
8	**5c**	**6c**	100	**8c** (R)	2	72	
9	**5d**	**6a**	100	**8d** (R)	1,5	85	93[a]
10	**5d**	**6c**	100	**8d** (R)	2,5	70	
11	**5d**	DIOP	100	**8d** (R)	2	20	

Cat. 0.01 mmol; 15 ml MeOH, 25 °C, 0.1 MPa H_2, [a] ethylacetate/hexane

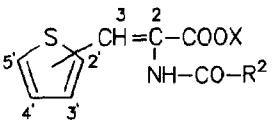
For structure elucidation and characterization of the compounds **4**, **5**, **7** and **8**, the ^1H and ^{13}C NMR spectra have been recorded.

Table 3 ^1H-Chemical shifts and coupling constants (in parentheses) of compounds **4** and **5** (in DMSO-d_6)

	4a	**4b**	**4c**	**4d**	**5a**	**5b**	**5c**	**5d**
H-2'	-	-	7.92 dd (3.0; 0.7)	7.96 dd (3.0; 0.8)	-	-	7.95 dd (3.0; 0.7)	8.02 dd (2.9; 0.9)
H-3'	7.51 d (3.8)	7.58[a]	-	-	7.55 d (3.5)	7.60[a]	-	-
H-4'	7.14 dd (5.0; 3.8)	7.13 dd (5.0; 3.8)	7.43 dd (5.0; 0.7)	7.45 dd (5.1; 0.8)	7.15 dd (5.3; 3.5)	7.16 dd (5.1; 3.7)	7.43 dd (5.0; 0.7)	7.45 dd (5.1; 0.9)
H-5'	7.74 d (5.0)	7.71 d (5.0)	7.60 dd (5.0; 3.0)	7.58[a]	7.79 d (5.3)	7.75 d (5.1)	7.62 dd (5.0; 3.0)	7.60[a]
H-3	7.72 s	7.90 s	7.36 s	7.62 s	7.75 s	7.93 s	7.33 s	7.61 s
COOX	12.50	12.62	12.62	12.71	3.73	3.77	3.70	3.75
NH	9.22	9.78	9.42	9.95	9.36	9.90	9.44	10.10
$COCH_3$	2.05	-	2.03	-	2.05	-	2.04	-
o-Ph	-	8.05 m	-	8.06 m	-	8.06 m	-	8.06 m
m, p-Ph	-	7.65-7.50 m	-	7.65-7.50 m	-	7.68-7.52 m	-	7.68-7.52 m

[a] overlapped with the phenyl protons

The ^{1}H-chemical shifts and ^{1}H-^{1}H coupling constants are summarized in the Tables 3 and 4 and the ^{13}C chemical shifts are given in Tables 5 and 6.



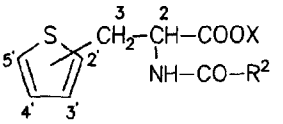


Table 4 ^{1}H-Chemical shifts and coupling constants (in parentheses) of compounds 7 and 8 (7 in DMSO-d_6; 8 in $CDCl_3$)

	7a	7b	7c	7d	8a	8b	8c	8d
H-2'	-	-	7.21 dd	7.30 dd	-	-	6.93 dd	6.99 dd
			(3.0; 1.2)	(3.0; 0.9)			(3.0; 1.2)	(3.0; 1.2)
H-3'	6.89 dd	6.98 dd	-	-	6.74 dd	6.80 dd	-	-
	(3.5; 1.1)	(3.5;1.1)			(3.4; 1.0)	(3.5;1.1)		
H-4'	6.94 dd	6.94 dd	7.01 dd	7.10 dd	6.89 dd	6.94 dd	6.80 dd	6.87 dd
	(5.0; 3.5)	(5.0;3.5)	(4.9; 1.2)	(4.9; 0.9)	(5.2; 3.4)	(5.1;3.5)	(4.9; 1.2)	(4.9; 1.2)
H-5'	7.34 dd	7.33 dd	7.43 dd	7.43 dd	7.16 dd	7.17 dd	7.20 dd	7.25 dd
	(5.0; 1.1)	(5.0;1.1)	(4.9; 3.0)	(4.9; 3.0)	(5.2; 1.0)	(5.2;1.1)	(4.9; 3.0)	(4.9; 3.0)
H-3	3.27; 3.09[a]	3.45;3.35[a]	3.09; 2.87[a]	3.23; 3.15[a]	3.35; 3.29[a]	3.53;3.50[a]	3.11; 3.05[a]	3.31; 3.25[a]
H-2	4.41 ddd[b]	4.62 ddd[b]	4.40ddd[b]	4.64 ddd[b]	4.83 ddd[b]	5.09 ddd[b]	4.79 dd[b]	5.04 ddd[b]
	(8.8;8.0;4.8)	(8.2;10.0;4.3)	(8.5;9.5;5.0)	(8.2;9.9;4.8)	(7.7;4.9;4.9)	(7.4;4.8;4.8)	(7.8;6.0;5.5)	(7.6;5.6;5.6
COOX	12.68	12.82	12.69	12.80	3.65	3.80	3.65	3.77
NH	8.20 d	8.76 d	8.21 d	8.76 d	6.32 d	6.74 d	6.40 d	6.72 d
	(8.0)	(8.2)	(8.5)	(8.2)	(7.7)	(7.4)	(7.8)	(7.6)
$COCH_3$	1.85	-	1.81	-	1.99	-	1.92	-
o-Ph	-	7.87 m	-	7.85 m	-	7.78 m	-	7.72 m
m, p-Ph	-	7.58-7.45 m	-	7.57-7.42m	-	7.55-7.40 m	-	7.50-7.35

[a] AB-part of an ABX-spectrum (**7a**: $J_{3a\text{-}3b}$=14.9, $J_{3a\text{-}2}$=8.8, $J_{3b\text{-}2}$=4.8; **7b**:$J_{3a\text{-}3b}$=14.8, $J_{3a\text{-}2}$=10.0, $J_{3b\text{-}2}$=4.3; **7c**: $J_{3a\text{-}3b}$=14.5, $J_{3a\text{-}2}$=9.5, $J_{3b\text{-}2}$=5.0; **7d**: $J_{3a\text{-}3b}$=14.4, $J_{3a\text{-}2}$=9.9, $J_{3b\text{-}2}$=4.8; **8a**: $J_{3a\text{-}3b}$=14.5, $J_{3a\text{-}2}$=$J_{3b\text{-}2}$=4.9; **8b**: $J_{3a\text{-}3b}$=15.0, $J_{3a\text{-}2}$=$J_{3b\text{-}2}$=5.0; **8c**: $J_{3a\text{-}3b}$=14.5, $J_{3a\text{-}2}$=6.0, $J_{3b\text{-}2}$=5.5; **8d**: $J_{3a\text{-}3b}$=14.4, $J_{3a\text{-}2}$=$J_{3b\text{-}2}$=5.6) [b] dd after addition of D_2O

The assignment of the proton signals of the thiophene ring was performed based on splitting patterns, the magnitude of coupling constants and the chemical shifts, which can be expected for substituted thiophenes[9]. The assignment of the ^{13}C signals could be ensured by recording the DEPT-spectra[10], and additionally in the case of compounds **5a, 5c, 5d, 8a** and **8d,** respectively, ^{13}C/^{1}H-correlation spectra[10] have been recorded. In this way an unambiguous identification of the thiophene signals, and in the case of compounds **4** and **5** also for C-6 and C-7, which are overlapped with thiophene signals, could be reached.

Table 5 ^{13}C-Chemical shifts of compounds **4** and **5** (in DMSO-d_6)

	4a	**4b**	**4c**	**4d**	**5a**	**5b**	**5c**	**5d**
C-2'	136.6	136.7	129.6	130.2	136.2	136.2	129.8	130.7
C-3'	133.3	133.6	135.5	135.7	133.7	133.7	135.0	135.3
C-4'	127.3	127.3	128.4	128.0	127.3	127.3	128.2	127.9
C-5'	131.3	131.5	126.8	128.6	131.6	131.9	126.8	128.8
C-3	129.0	129.7	126.9	127.2	129.1	130.0	126.8	127.3
C-2	124.1	124.2	125.7	125.7	123.0	123.1	124.8	124.7
COOX	166.2	166.1	166.7	166.8	165.2	165.1	165.7	166.0
NHCO	169.9	166.5	169.5	166.3	169.8	166.4	169.4	166.2
OCH_3	-	-	-	-	52.1	52.2	52.1	52.4
$COCH_3$	23.1	-	22.9	-	22.9	-	22.6	-
C-1"	-	134.0	-	133.9	-	134.0	-	133.5
C-2"	-	127.9	-	128.0	-	127.8	-	127.9
C-3"	-	128.6	-	128.8	-	128.6	-	128.8
C-4"	-	131.9	-	132.1	-	132.0	-	132.2

Table 6 ^{13}C-Chemical shifts of compounds **7** and **8** (**7** in DMSO-d_6; **8** in $CDCl_3$)

	7a	**7b**	**7c**	**7d**	**8a**	**8b**	**8c**	**8d**
C-2'	139.6	140.1	122.6	122.4	137.2	139.6	122.5	122.7
C-3'	126.3	126.3	138.2	138.7	126.6	126.4	135.9	135.9
C-4'	126.9	126.8	129.0	129.0	126.9	126.9	128.0	128.2
C-5'	124.7	124.7	126.0	126.1	124.7	124.9	125.7	126.0
C-3	31.3	30.8	31.7	32.2	31.8	30.6	32.0	32.2
C-2	53.6	54.3	53.3	54.0	52.9	54.4	52.5	53.0
COOX	172.6	172.7	173.5	173.5	171.4	171.7	172.0	171.9
NHCO	169.4	166.6	169.6	166.8	169.7	166.6	169.7	166.8
OCH_3	-	-	-	-	52.4	52.2	52.2	52.4
$COCH_3$	22.5	-	22.7	-	23.0	-	22.8	-
C-1"	-	134.1	-	134.2	-	133.8	-	133.7
C-2"	-	127.5	-	127.7	-	127.5	-	126.9
C-3"	-	128.5	-	128.6	-	128.4	-	128.5
C-4"	-	131.5	-	131.7	-	131.6	-	131.7

Conclusions: The catalyst PROPRAPHOS in previous investigations applied for the asymmetric hydrogenation of unusual dehydro amino acid derivatives, proved to be also useful in the asymmetric hydrogenation of thienylalanine precursors without loss of activity and stereoselectivity. The procedure may be scaled up. After recrystallisation and acidic hydrolysis, which runs in this case without appreciable racemization, optically pure thienylalanines are easily accessable to be used in oligo peptide synthesis.

Experimental: ^{1}H NMR and ^{13}C NMR spectra were recorded on a 250 MHz spectrometer (Bruker, AC 250). The calibration of the spectra was carried out by means of solvent peaks ($CDCl_3$: δ ^{1}H=7.25, δ ^{13}C=77,0; DMSO-d_6: δ ^{1}H=2.50; δ ^{13}C=39.7). Optical rotation was measured on a Polamat A polarimeter (Carl Zeiss, Jena). The enantiomeric excesses (% ee) were determined by GLC on a Hewlett-Packard chromatograph 5880A fitted with a 4.3 m capillary column XE-60 (N-L-valine-tert.butylamide, FID, split 1:60, 175 °C) for the acylated amino acid derivatives **8a-d**, for **7a-d** after esterification with diazomethane. HPLC measurements were carried out on a KNAUER chromatograph (pump 64) equipped with a CHIRALPAK WH column (J. T. Baker B. V.) and connected with an EPSON PC AX 2e. Melting points are uncorrected and were determined on a Boetius microscope.

Hydrogenation, general procedure:

Hydrogenations were performed under normal pressure and 25 °C as described principally by Kagan[11]. 1 ml of the hydrogenated solution was esterified by a freshly prepared solution of diazomethane (**7a-d**) in order to determine the ee by GLC. The other part was freed from the solvent and recrystallized.

Deacylation, general procedure:

The recrystallized optically active thienyl compounds were refluxed in 6 N hydrochloric acids for 6 hours. The solution was extracted with ether, the acidic aqueous solution treated with charcoal and concentrated under reduced pressure at 30-35 °C. The crystals were washed several times with absolute acetone and dried over phosphorous pentoxide under vacuo.

Chemicals:

All solvents were purified and dried by usual methods and stored, if necessary, under argon.

Catalysts were prepared according to published methods[7].

(R)-N-Acetyl-3-(2-thienyl)-alanine (7a):

m. p. 164-165 °C (ethylacetate), Lit.[3d] 169 °C, $[\alpha]_D^{25}$ -42.8 (c 1, EtOH), > 99 % ee (GLC)

Lit.[3d,12] -43.15; Lit.[5b] -39.0 (72 % ee)

$C_9H_{11}NO_3S$ (213.3), calcd. C 50.69 H 5.20 N 6.57 S 15.04

found C 50.45 H 5.33 N 6.67 S 14.93

(S)-N-Benzoyl-3-(2-thienyl)-alanine (7b):

m. p. 100-102 °C (ethylacetate), $[\alpha]_D^{25}$ - 13.3 (c 1, EtOH)

91 % ee (GLC), Lit. [5b] $[\alpha]_D^{25}$ - 1.9 (12 % ee)

$C_{14}H_{13}NO_3S$ (275.3), calcd. C 61.07 H 4.76 N 5.09 S 11.65

found C 60.87 H 4.78 N 5.18 S 11.46

(R)-N-Acetyl-3-(3-thienyl)-alanine (7c):
m. p. 176-178 °C (H_2O), $[\alpha]_D^{25}$ -46.2 (c 1, EtOH), > 99 % ee (GLC)
$C_9H_{11}NO_3S$ (213.3), calcd. C 50.69 H 5.20 N 6.57 S 15.04
found C 50.89 H 5.21 N 6.74 S 15.19

(R)-N-Benzoyl-3-(3-thienyl)-alanine (7d):
m. p. 135 °C (acetonitril, mother liquor) $[\alpha]_D^{25}$ + 4.1 (c 1, EtOH), 96 % ee (GLC)
$C_{14}H_{13}NO_3S$ (275.3), calcd. C 61.07 H 4.76 N 5.09 S 11.65
found C 60.98 H 4.87 N 5.29 S 11.60

(R)-N-Acetyl-3-(2-thienyl)-alanine-methyl ester (8a):
m. p. 112-114 °C (ethylacetate/hexane), $[\alpha]_D^{25}$ -16.7 (c 1, EtOH), > 99 % ee (GLC)
$C_{10}H_{13}NO_3S$ (227.3), calcd. C 52.84 H 5.76 N 6.16 S 14.11
found C 52.72 H 5.91 N 6.26 S 13.96

(S)-N-Benzoyl-3-(2-thienyl)-alanine-methyl ester (8b):
m. p. 72-74 °C (ethylacetate/hexane), $[\alpha]_D^{25}$ - 39.7 (c 1, EtOH), 90 % ee (GLC)
$C_{15}H_{15}NO_3S$ (289.4), calcd. C 62.26 H 5.22 N 4.84 S 11.08
found C 62.47 H 5.28 N 5.02 S 11.19

(R)-N-Acetyl-3-(3-thienyl)-alanine-methyl ester (8c):
m. p. 106-108 °C (ethylacetate/hexane), $[\alpha]_D^{25}$ -14.6 (c 1, EtOH), 98 % ee (GLC)
$C_{10}H_{13}NO_3S$ (227.3), calcd. C 52.84 H 5.76 N 6.16 S 14.11
found C 52.72 H 5.70 N 6.23 S 14.21

(R)-N-Benzoyl-3-(3-thienyl)-alanine-methyl ester (8d):
m. p. 85-86 °C (ethylacetate/hexane), $[\alpha]_D^{25}$ + 35.2 (c 1, EtOH), 93 % ee (GLC)
$C_{15}H_{15}NO_3S$ (289.4), calcd. C 62.26 H 5.22 N 4.84 S 11.08
found C 62.15 H 5.25 N 4.95 S 11.20

(R)-3-(2-Thienyl)-alanine-hydrochloride (9a):
m. p. 228-232 °C (H_2O), $[\alpha]_D^{25}$ + 15.0 (c 1, H_2O), > 99 % ee (HPLC)
^1H NMR (DMSO-d_6): 3.46, 3.40 (dq, 2H, CH_2-3, $J_{3a\text{-}3b}$=15.4 Hz, $J_{3a\text{-}2}$=6.0 Hz, $J_{3b\text{-}2}$=5.6 Hz); 4.09 (dd, 1H, H-2, J=6.0 Hz, J=5.6 Hz); 6.97 (dd, 1H, H-4', J=5.1 Hz, J=3.0 Hz); 7.03 (d, 1H, H-3', J=3.0 Hz); 7.40 (d, 1H, H-5', J=5.1); 8.70 (b, 3H, NH_3Cl); 13.50 (b, 1H, COOH).
^{13}C NMR (DMSO-d_6): 29.9 (C-3); 53.3 (C-2); 125.8 (C-5'); 127.4 (C-3'); 128.1 (C-4'); 136.2 (C-2'); 170.0 (COOH).
$C_7H_{10}ClNO_2S$ (207.7), calcd. C 40.48 H 4.85 Cl 17.08 N 6.75 S 15.44
found C 40.53 H 4.90 Cl 17.23 N 6.70 S 15.60

(R)-3-(3-Thienyl)-alanine-hydrochloride (9b):

m. p. 226-229 °C (H_2O), $[\alpha]_D^{25}$ + 23.2 (c 1, H_2O), 99,6 % ee (HPLC)

^1H NMR (DMSO-d_6): 3.23, 3.20 (dq, 2H, CH_2-3, $J_{3a\text{-}3b}$=15.0 Hz, $J_{3a\text{-}2}$=$J_{3b\text{-}2}$=6.2 Hz); 4.10 (dd, 1H, H-2, J=6.2 Hz, J=6.2 Hz); 7.04 (dd, 1H, H-4', J=4.8 Hz, J=1.0); 7.35 (dd, 1H, H-2', J=2.9 Hz, J=1.0 Hz); 7.48 (dd, 1H, H-5', J=4.9, J=2.9); 8.60 (b, 3H, NH_3Cl); 13.50 (b, 1H, COOH).

^{13}C NMR (DMSO-d_6): 30.4 (C-3); 52.8 (C-2); 124.1 (C-2'); 126.5 (C-5'); 128.9 (C-4'); 135.2 (C-3'); 170.3 (COOH).

$C_7H_{10}ClNO_2S$ (207.7), calcd. C 40.48 H 4.85 Cl 17.08 N 6.75 S 15.44
found C 40.42 H 4.65 Cl 16.89 N 6.84 S 15.54

(R)-3-(2-Thienyl)-alanine (10a):

m. p. 246-258 °C (H_2O), Lit.[3d] 265-266 °C, Lit.[3a] 239-244 °C

$[\alpha]_D^{25}$ + 31.8 (c 1, H_2O), > 99 % ee (HPLC)

Lit. [3d] + 31.4, Lit. [3a] + 31.7

$C_7H_9NO_2S$ (171.2), calcd. C 49.10 H 5.30 N 8.18 S 18.73
found C 49.02 H 5.34 N 8.30 S 18.59

(R)-3-(3-Thienyl)-alanine (10b):

m. p. 239-242 °C (H_2O), $[\alpha]_D^{25}$ + 42.6 (c 1, H_2O), > 99 % ee (HPLC)

$C_7H_9NO_2S$ (171.2), calcd. C 49.10 H 5.30 N 8.18 S 18.73
found C 49.20 H 5.23 N 8.32 S 19.03

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