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Stereoselective Reactions of α-Imide Substituted Radicals

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Abstract: The Barton esters **17** and **18**, synthesized from the corresponding amino acid derivatives **6** and **14**, were irradiated *in situ* with or without an external trap. Thus, thiopyridines **22** and **23**, phenylselenides **24** and **25**, esters **26** and **27** as well as deuterated products **34** and **35** were isolated when the radicals **20** and **21** were trapped with Barton esters **17** and **18** or with PhSeSePh, methyl acrylate or Bu_3SnD. In all cases the *anti* isomers were isolated as the major products in moderate to excellent selectivity. The stereochemical course of the radical reactions can be explained by the allylic strain model.

INTRODUCTION

Recently, Hart *et al.*[1] and Giese *et al.*[2] have shown that enolate radicals, substituted by a tertiary alkyl group, adopt preferred conformation **A** (Fig. 1), which minimizes allylic strain (A-strain) effects. According to this model, the different shielding by substituents R^1 and R^2 induces stereoselectivity in radical reactions.[3,4] In our first report[2] we predicted that not only ester but, besides others, also amine substituted radicals should adopt a preferred conformation because of the A-strain. Subsequent work of Renaud *et al.*[5] and Curran *et al.*[6] using saturated and unsaturated cyclic amines have verified this suggestion. This report describes our efforts in this area using a cyclic imide substituent at the radical center. According to the A-strain model, conformation **B** should be adopted by this radical and stereoselective trapping reactions should follow when R^1 and R^2 are different in size.

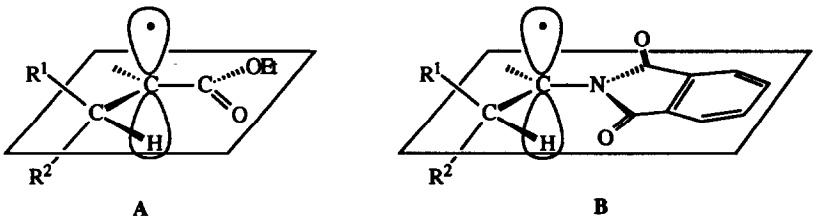
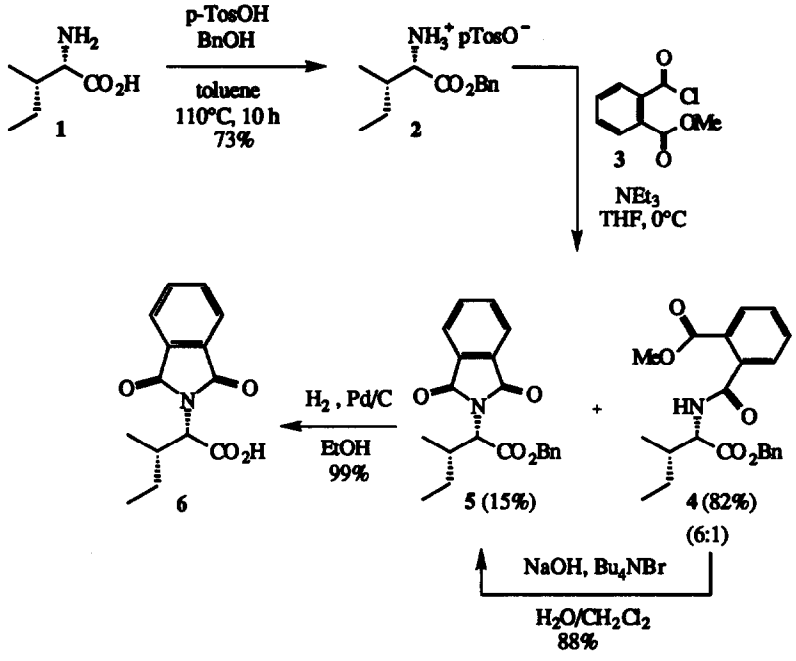


Fig. 1. A-strain conformations of α-ester (**A**) and α-imide substituted (**B**) radicals.

This article is dedicated to Professor Léon Ghosez on the occasion of his 60th birthday.

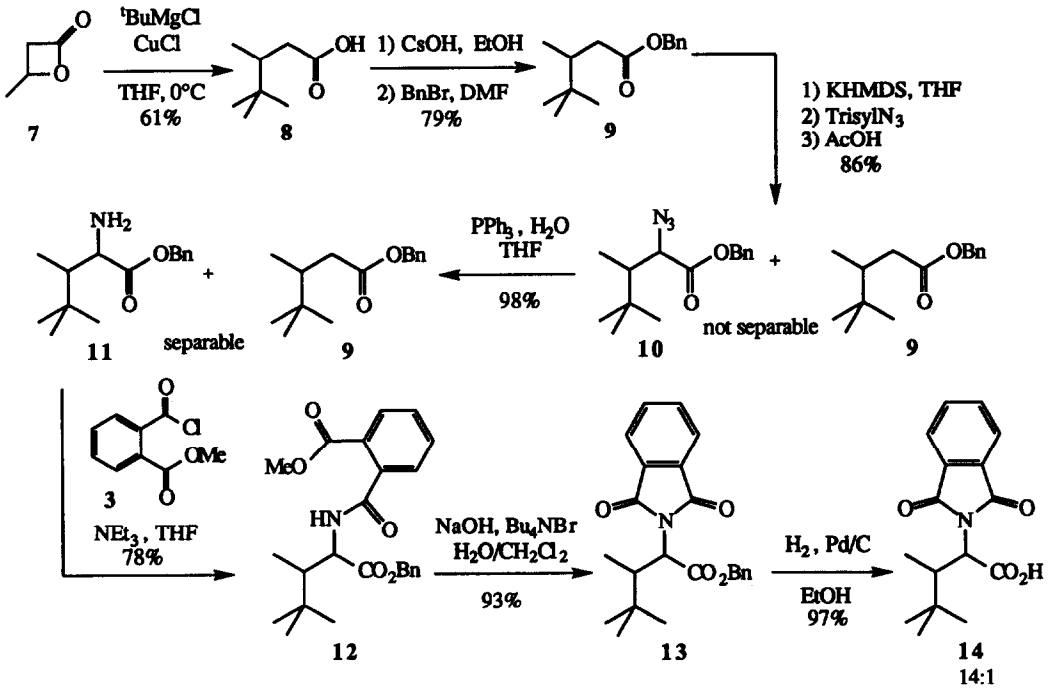
SYNTHESIS OF RADICAL PRECURSORS

Amino acid derivative **6** was synthesized in 4 steps starting from L-isoleucine (**1**). Isoleucine was converted to the benzyl ester **2** which was subsequently treated with phthalic acid monomethyl ester chloride (**3**) and triethylamine to give amide **4** and phthalimide **5**. The amide **4** could readily be cyclized to phthalimide **5**. Hydrogenation of ester **5** gave the desired isoleucine derivative **6** (Scheme 1).



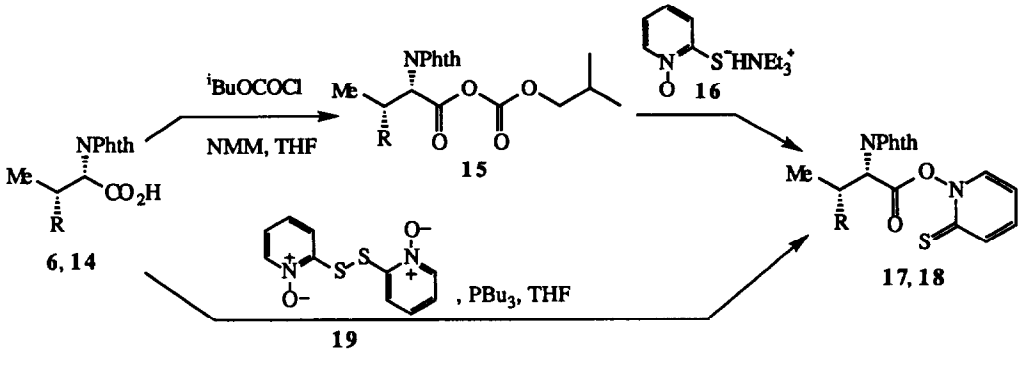
Scheme 1

Amino acid derivative **14** was synthesized as a racemate starting from β-butyrolactone (**7**). Opening of the lactone with ^{t}BuMgCl in the presence of CuCl and benzylation yielded ester **9**. The introduction of the amino group was achieved by azidation with trisyl azide. Following the work of Evans *et al.*[7], KHMDS was used as the base and acetic acid as the quenching reagent. Azide **10** was formed as a mixture of diastereomers. Since the ester and the azide were difficult to separate by flash chromatography, they were used as a mixture in the next step. The azide was reduced to amine **11** with Ph_3P and the unreacted ester **9** was removed by chromatography. The conversion of amine **11** to phthalimide **13** and deprotection to give **14** was achieved in the same way as described in the synthesis of **6** (Scheme 2).



Scheme 2

The amino acid derivatives **6** and **14** were converted into the corresponding Barton esters **17** and **18** either *via* the mixed anhydride **15** and subsequent treatment with the triethylammonium salt of thiohydroxamic acid (**16**)[8], or by treatment with disulfide **19** in the presence of PBu_3[9] (Scheme 3). The Barton esters were not isolated and the radical reactions were carried out immediately after complete formation of the Barton esters **17** and **18**.[10]

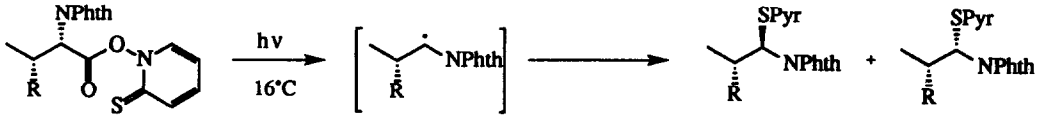


Scheme 3

TRAPPING OF THE RADICALS

Without external trap

When the Barton esters were irradiated with a 250 W sunlight lamp in the absence of an added radical trap, thiopyridines **22** and **23** were formed in moderate yields (Scheme 4).

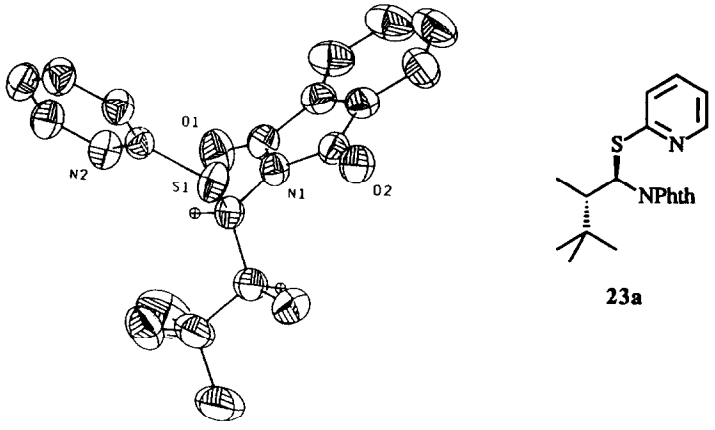


22a, 23a **22b, 23b**

17 **20** R = Et **22a/22b** = 1.7 : 1 (34%)
18 **21** R = ^{t}Bu **23a/23b** = 5.5 : 1 (53%)

Scheme 4

In the case of thiopyridines **23a,b** the major isomer **23a** could be separated by fractional crystallization and the configuration determined by X-ray analysis. An ORTEP-plot of the crystal structure of **23a** is shown in Fig. 2. By comparison of the NMR-spectroscopic signals of **23a,b** with those of **22a,b** it could be concluded that the reaction of **17** gave **22a** as the major isomer.

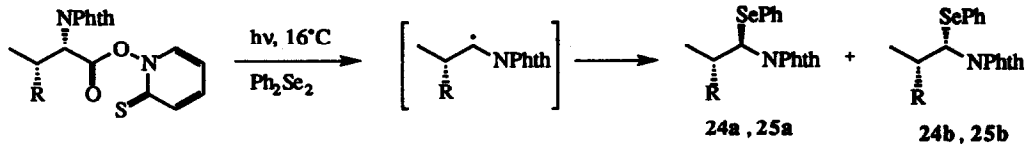


23a

Fig. 2. ORTEP-plot of the X-ray crystal structure of **23a**.

With PhSeSePh as external trap

Irradiation of the Barton esters **17** and **18** in the presence of 5 eq. of diphenyl diselenide gave the phenyl selenides **24a,b** and **25a,b** in good yields (Scheme 5). In both cases the *anti* isomers were the major products. The phenylselenides **24a,b** were stable, but **25a,b** decomposed slowly on standing at room temperature.

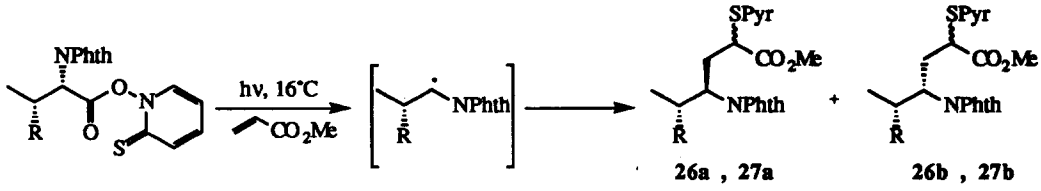


17	20	R = Et	24a / 24b = 1.9 : 1 (78%)
18	21	R = ^{t}Bu	25a / 25b = 15 : 1 (73%)

Scheme 5

With methyl acrylate as external trap

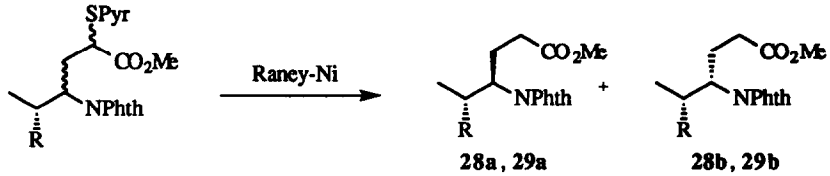
When the Barton esters **17** and **18** were irradiated in the presence of 2 eq. of methyl acrylate, addition products **26a,b** and **27a,b** were formed in small amounts (Scheme 6). The major products were thiopyridines **22a,b** and **23a,b**, respectively. When larger amounts of methyl acrylate were present, products containing two or more acrylate units were also formed and the yield of the desired products **26a,b** and **27a,b** was not improved.



17	20	R = Et	26a / 26b = 1.7 : 1 (19%)
18	21	R = ^{t}Bu	27a / 27b = 15 : 1 (9%)

Scheme 6

In order to assign the configurations of the addition products **26a,b** and **27a,b**, they were desulfurized with Raney-Ni to give the esters **28a,b** and **29a,b** without a change in the isomer ratio (Scheme 7).

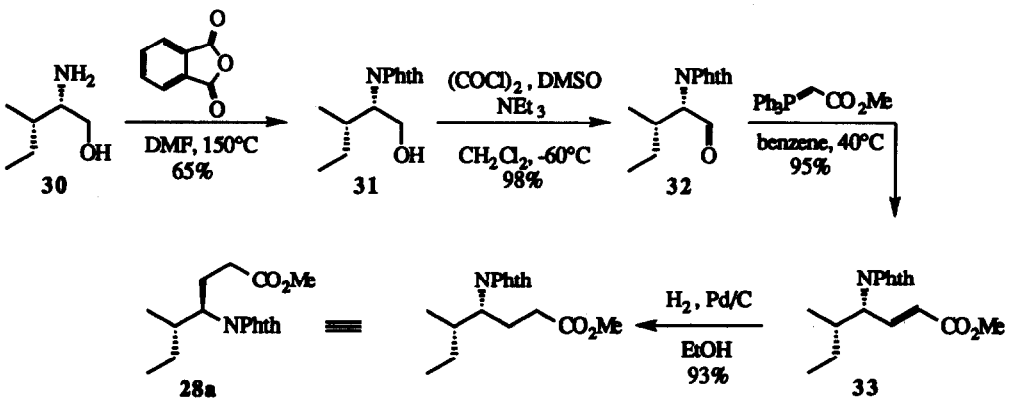


26	R = Et	28a , 28b (45%)
27	R = ^{t}Bu	29a , 29b (99%)

Scheme 7

The ester **28a** was synthesized by an independant route. L-isoleucinol (**30**) was heated with phthalic anhydride to give phthalimide **31**. Swern oxidation and subsequent Wittig reaction yielded alkene **33** as a single diastereomer. Reduction of the double bond gave the *anti* isomer **28a** which corresponded to the major

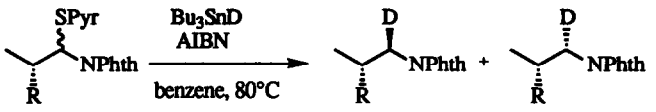
isomer from the radical reaction (Scheme 8). Again, by comparison of the NMR-spectroscopic data of **28a,b** with those of **29a,b** it was concluded that **29a** was the major isomer in the reaction of Barton ester **17**.



Scheme 8

With Bu_3SnD as external trap

Deuterated compounds **34a,b** and **35a,b** were formed in high yields when the thiopyridines **22a,b** and **23a,b** were heated to 80°C in the presence of Bu_3SnD and AIBN (Scheme 9).



22	R = Et	**34a / 34b** = 1.3 : 1 (79%)
23	R = ^{t}Bu	**35a / 35b** = 3.0 : 1 (81%)

Scheme 9

The major isomer **35a** has a small coupling constant of 4 Hz whereas the minor isomer **35b** exhibits a large coupling constant of 11.3 Hz (Fig. 3).

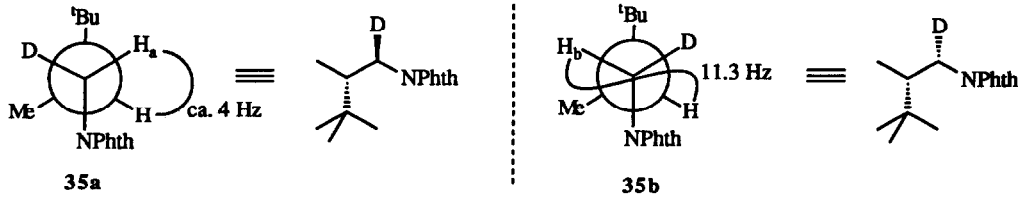
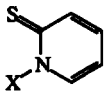


Fig. 3. Analysis of the coupling constants in the ^{1}H-NMR-spectra of **35** and assignment of the configurations.

DISCUSSION

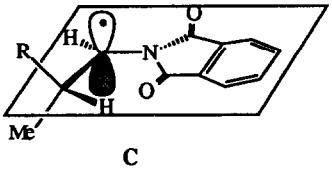
The data in Table 1 show that radical **21**, where the two alkyl groups at the stereogenic center are Me and ^{t}Bu, respectively, reacts stereoselectively. The extent of the selectivity depends upon the radical trap. The addition of radical **21** at the C,C π-bond is more selective than that at the C,S π-bond, and the PhSe-abstraction occurs with higher selectivity than the D-abstraction. This trend in stereoselectivity can be explained by the different steric demand of the radical traps.

Table 1. Stereoselectivity of the Reaction of Radicals **20** and **21** with Different Radical Traps at 16°C.

Substituent R at the radical (**20** or **21**)	Radical trap	Selectivity **a** : **b**
Et		1.7 : 1
^{t}Bu		5.5 : 1
Et	$H_2C{=}CHCO_2Me$	1.7 : 1
^{t}Bu		15 : 1
Et	Bu_3SnD	1.3 : 1[a]
^{t}Bu		3.0 : 1[a]
Et	PhSeSePh	1.9 : 1
^{t}Bu		15 : 1

a) Reaction temperature : 80°C.

Nitrogen-substituted radicals are stabilized by overlap of the unpaired electron with the nitrogen lone pair so that a partial double bond character of the C-N-bond results. To avoid 1,3-allylic strain effects, the ground state conformation with the lowest energy should be the one where the smallest substituent at the stereogenic center (the hydrogen) is directed towards the imide group as shown in conformation **C**. The two alkyl substituents at the stereogenic center shield both faces of the prochiral radical center with different efficiency so that the radical is attacked preferentially *anti* to the large substituent R.



C

Fig. 4. Preferred ground state conformation of radicals **20** and **21** according to the allylic strain model.

We also calculated the energies of the transition states for the hydrogen transfer to radical **21** using the AM1 method.[11,12]

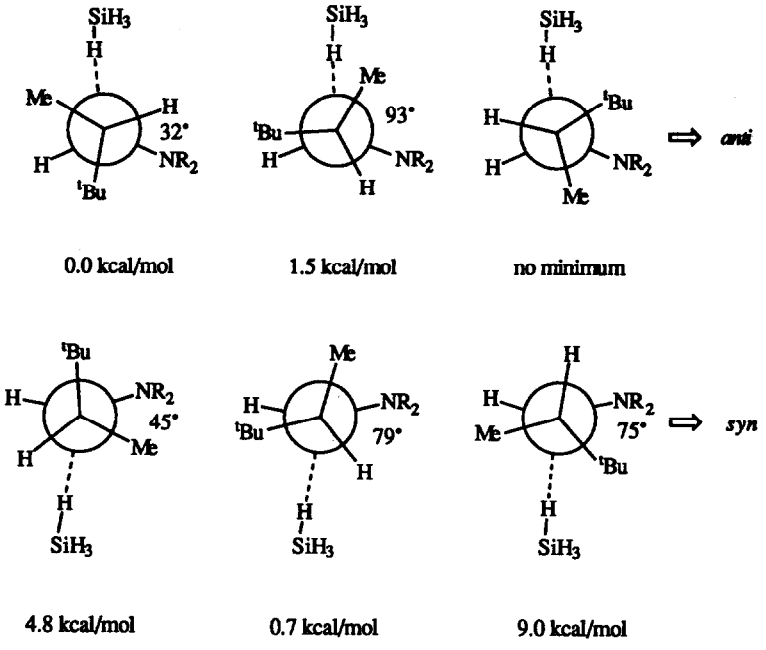


Fig. 5. Calculated energies for the transition states of hydrogen transfer to radical **21**.

To simplify the calculations, maleimide was used instead of phthalimide and silane was used as the hydrogen donor. The transition state with the lowest energy (0.0 kcal/mol) is the one that is predicted by the allylic strain model. The hydrogen at the stereocenter is directed towards the imide group and the hydrogen donor attacks the radical *anti* to the largest substituent leading to the major isomer **21a**. In the next lowest transition state (0.7 kcal/mol) the bulky ^{t}Bu group is close to the hydrogen atom at the radical center. This transition state leads to the minor isomer **21b**.

If the two alkyl substituents at the stereogenic center are similar in size, then the stereoselectivity should decrease. Thus radical **20**, with Me and Et substituents at the stereogenic center shows nearly no selectivity.

ACKNOWLEDGEMENTS

This work was supported by the Swiss National Science Foundation. U.H. thanks the Fonds der Chemischen Industie for a grant.

EXPERIMENTAL SECTION

General methods

THF was distilled over K/benzophenone. Flash chromatography (FC): silica gel C-560KV, 35-70 mm, Chemische Fabrik Uetikon. M.p.: Büchi apparatus 530, uncorrected. ^{1}H- and ^{13}C-NMR-spectra: Varian Gemini 300 (300 MHz); δ in ppm rel. to TMS as internal standard, J in Hz; $CDCl_3$ as solvent. MS: VG 70-250; CI, NH_3 for chemical ionization; FAB = fast atom bombardment; EI = electronic ionization; m/z relative intensities (in %) in parentheses. IR: Perkin-Elmer 781 or Perkin-Elmer FT-IR 1600, in cm^{-1}.

Computational methods

All calculations were done on IBM/RS6000 workstations. In the semiempirical calculations the AM1 method was used with UHF wavefunctions as implemented in the MOPAC 6.0[11] program package. The transition states were located using the eigenvector following routine and were tested *via* frequency calculations. A spin contamination with an expectation value S^2 below 0.8 was observed in all transition states. The *ab initio* single point calculations were performed with the Gaussian 92[12] program package using the UHF/6-31G* method, where a spin contamination with an expectation value S^2 lower than 0.8 was observed.

Synthesis of the amino acid derivatives

Ammonium tosylate of benzyl (2*S*,3*S*)-2-amino-3-methyl-pentanoate (2). A mixture of 13.1 g (0.10 mol) L-isoleucine (**1**), 20.9 g (0.11 mol) *p*-toluenesulfonic acid-monohydrate and 40 ml (0.39 mol) benzyl alcohol was refluxed in 100 ml of toluene and the water was collected in a Dean-Stark trap. After 10 h, toluene and excess benzyl alcohol were distilled off *in vacuo*. The colourless solid was suspended in toluene/ether, filtered and washed with ether. Recrystallization from methanol/ether gave 18.4 g of benzyl ester-*p*-toluenesulfonate **2** as colourless crystals. Concentration of the mother liquid and recrystallization of the residue from methanol/ether gave another 4.02 g of **2**. The toluene/ether-mixture from above was concentrated and the obtained residue was recrystallized from methanol/ether to give 6.40 g **2**. Altogether, 28.8 g (73%) of pure **2** were obtained. M.p. 147°C. IR (KBr). 3020, 2860, 1740, 1605, 1525, 1455, 1190, 1035, 1010, 815, 675. ^{1}H-NMR: 0.73 (*t*, *J*=7.4, 3 H, C*H*$_3$-CH$_2$-), 0.83 (*d*, *J*=6.7, 3 H, C*H*$_3$-CH-), 1.21 and 1.32 (2*m*, 2 H, CH$_3$-C*H*$_2$-), 1.92 (*m*, 1 H, CH$_3$-C*H*-), 2.31 (*s*, 3 H, Tos-CH$_3$), 3.97 (*d*, *J*=3.9, 1 H, NH_3^+-C*H*-), 5.01 and 5.13 (2*d*, *J*=12.3, 12.2, 2 H, -CO$_2$-C*H*$_2$-Ph), 7.08 (*d*, *J*=8.0, 2 H, Tos-m-H), 7.27 (*m*, 5 H, Ph), 7.75 (*d*, *J*=8.2, 2 H, Tos-o-H), 8.20 (*b*, 3 H, -NH_3^+). ^{13}C-NMR: 11.55 (*C*H$_3$-CH$_2$-), 14.26 (*C*H$_3$-CH-), 21.35 (Tos-CH$_3$), 25.59 (CH$_3$-*C*H$_2$-), 36.40 (CH$_3$-*C*H-), 57.30 (CO$_2$-*C*H$_2$-Ph), 67.62 (NH_3^+-*C*H), 126.10, 128.30, 128.35, 128.40, 128.69 (*o*,*m*,*p*-Ph and *o*,*m*-Tos), 134.78 (*p*-Tos), 140.07 (*i*-Ph), 141.48 (*i*-Tos), 168.48 (-CO$_2$-). MS (FAB): 394 (1, $[M+1]^+$), 222 (100), 91 (42). Anal. calc. for $C_{13}H_{19}NO_2 + C_7H_7SO_3H$ (393.50, free base: 221.30): C 61.05, H 6.92, N 3.56; found: C 60.95, H 7.14, N 3.68

Benzyl (2*S*,3*S*)-3-methyl-2-phthalimido-pentanoate (5) and Benzyl (2*S*,3*S*)-N-[2-(methoxycarbonyl)-benzoyl]-2-amino-3-methyl-pentanoate (4). A solution of 3.60 g (20.0 mmol) phthalic acid-monomethyl ester, 16.4 g (10 ml, 137 mmol) thionyl chloride and 2 drops DMF was heated under reflux for 1 h. Excess thionyl chloride was removed *in vacuo*. The residue was dissolved in 5 ml of benzene

and concentrated *in vacuo* to remove all thionylchloride. The oily residue was dissolved in 10 ml of THF and added *via* syringe pump during 30 min to a suspension of 6.69 g (17.0 mmol) of benzylester-*p*-toluenesulfonate **2** and 4.05 g (5.58 ml, 40.0 mmol) of triethylamine in 40 ml of THF at 0°C. After 2 h, the reaction mixture was poured onto ice/water, left standing overnight and extracted with ethyl acetate (3x). The combined organic phases were dried over $MgSO_4$ and concentrated. After FC (hexane/ethyl acetate 5:1→2:1), 5.36 g (82%) of amide **4** (6:1 mixture of 2 isomers) and 913 mg (15%) of phthalimide **5** were obtained as colourless oils. (**5**): IR (neat): 3040, 2970, 1775, 1745, 1720, 1460, 1385, 1195, 1075, 910, 735, 720. ^{1}H-NMR: 0.87 (*t*, *J*=7.3, 3 H, C*H*$_3$-CH$_2$-), 1.09 (*m*, 1 H, CH$_3$-C*H*H'), 1.11 (*d*, *J*=6.7, 3 H, C*H*$_3$-CH-), 1.52 (*m*, 1 H, CH$_3$-CH*H*'-), 2.59 (*m*, 1 H, -C*H*-CO$_2$-), 5.13 and 5.20 (2*d*, *J*=12.4, 12.4, -CO$_2$-C*H*$_2$-Ph), 7.28 (*s*, 5 H, Ph), 7.74 and 7.85 (2*m*, 4 H, Phth). ^{13}C-NMR: 10.85 (*C*H$_3$-CH$_2$-), 16.73 (*C*H$_3$-CH-), 25.70 (CH$_3$-*C*H$_2$-), 34.44 (CH$_3$-*C*H-), 57.12 (-*C*H-CO$_2$-), 66.99 (-CO$_2$-*C*H$_2$-Ph), 123.36 (*m*-Phth), 127.95, 128.08, 128.32 (*o*,*m*,*p*-Ph), 131.53 (*i*-Phth), 134.05 (*o*-Phth), 135.23 (*i*-Ph), 167.63 (N(CO)), 168.67 (-CO$_2$-). MS (EI): 351 (0.2, M$^+$), 245 (27), 216 (69), 160 (100), 91 (80). Anal. Calc. for $C_{21}H_{21}NO_4$ (351.40): C 71.78, H 6.02, N 3.99; found: C 71.64, H 5.90, N 4.14. (**4**): IR (Film): 3357, 2963, 2877, 1731, 1660, 1531, 1455, 1295, 1272, 1191, 1158, 1230, 746, 699. ^{1}H-NMR (minor isomer with *): 0.92 (*t*, *J*=7.4, 3 H, C*H*$_3$-CH$_2$-), 0.99 (*d*, *J*=6.8, 3 H, C*H*$_3$-CH-), 1.24 (*m*, 1 H, CH$_3$-C*H*H'-), 1.46 (*m*, 1 H, CH$_3$-CH*H*'-), 2.05 (*m*, 1 H, CH$_3$-C*H*-), 3.82 (*s*, 3 H, -CO$_2$C*H*$_3$), 4.87 and 4.97* (2 *dd*, *J*=4.7, 8.7; *J*=3.9, 9.1, 1 H, -C*H*-CO$_2$-), 5.18 (*d*, J=12.2, 1 H, -CO$_2$-C*H*H'-Ph), 5.25 (*d*, *J*=12.2, 1 H, -CO$_2$-CH*H*'-Ph), 6.31* and 6.37 (2 *d*, *J*=9.7; J=8.6, 1 H, -NH), 7.37 (*m*, 5 H, Ph), 7.51 and 7.88 (*m* and *d*, *J*=7.5, 4 H, Phth). ^{13}C-NMR (minor isomer with *): 11.58 and 11.75* (*C*H$_3$-CH$_2$-), 14.58* and 15.42 (*C*H$_3$-CH-), 25.11 and 26.15* (CH$_3$-*C*H$_2$-), 37.83* and 38.03 (CH$_3$-*C*H-), 52.39 and 53.37 (-CO$_2$-*C*H$_3$), 55.77* and 56.86 (-*C*H-CO$_2$-), 67.02 (-CO$_2$-*C*H$_2$-Ph), 127.57, 129.71, 130.07 and 131.82 (*o*,*m*,Phth), 128.34, 128.40 and 128.54 (*o*,*m*,*p*-Ph), 129.31 (*i*-Phth), 135.27 (*i*-Ph), 137.74 (*i*-Phth), 166.93 (-N(CO)), 168.80 and 169.01* (-*C*O$_2$-CH$_2$-Ph), 171.65 and 172.02* (-*C*O$_2$-CH$_3$). MS (CI): 384 (100, [M+1]$^+$), 352 (44), 163 (68), 91 (30). Anal. calc. for $C_{22}H_{25}NO_5$ (383.45): C 68.91, H 6.57, N 3.65; found: C 68.70, N 6.32, N 3.46

Benzyl (2*S*,3*S*)-N-phthalimido-2-amino-3-methyl-pentanoate (5). A mixture of 5.20 g (13.6 mmol) amide **4**, 45 mg (0.14 mmol) Bu_4NBr, 11.9 g of a NaOH solution (5%), and 12 ml of CH_2Cl_2 was stirred vigorously for 70 min. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2x). The combined organic phases were dried over $MgSO_4$ and concentrated. After FC (hexane/ethyl acetate 10:1→7:1) 4.21 g (88%) of pure phthalimide **5** were obtained as a colourless oil.

(2*S*,3*S*)-3-Methyl-2-phthalimido-pentanoic acid (6). To a solution of 900 mg (2.56 mmol) benzyl ester **5** in 140 ml of ethanol was added 90 mg Pd/C (10%) and the reaction mixture was stirred under hydrogen overnight. After filtration through Celite and concentration, 666 mg (99%) of acid **6** were obtained as a beige solid. M.p. 114-120°C. IR (KBr): 3260, 2980, 2950, 1765, 1695, 1405, 1195, 1105, 915, 735. ^{1}H-NMR: 0.86 (*t*, *J*=7.2, 3 H, C*H*$_3$-CH$_2$-), 1.08 (*m*, 1 H, CH$_3$-C*H*H'-), 1.12 (*d*, *J*=6.6, 3 H, C*H*$_3$-CH-), 1.51 (*m*, 1 H, CH$_3$-CH*H*'-), 2.53 (*m*, 1 H, CH$_3$-C*H*-), 4.70 (*d*, *J*=8.2, 1 H, -C*H*-CO$_2$H), 7.74 (*m*, 2 H, Phth) 7.86 (*m*, 2 H, Phth), 10.97 (*b*, 1 H, -CO$_2$H). ^{13}C-NMR: 10.86 (*C*H$_3$-CH$_2$-), 16.76 (*C*H$_3$-CH-), 25.80 (CH$_3$-*C*H$_2$-), 34.33 (CH$_3$-*C*H-), 57.03 (-*C*H-CO$_2$H), 123.59 (*o*-Phth), 131.57 (*i*-Phth), 134.22 (*m*-Phth), 167.76

(N(CO)), 174.56 (-CO_2H). MS (EI): 261 (10, M^+), 216 (58), 187 (91), 160 (100). Anal. calc. for $C_{14}H_{15}NO_4$ (261.28): C 64.36, H 5.79, N 5.36; found: C 64.28, H 5.60, N 5.49.

3,4,4-Trimethyl-pentanoic acid (8). To a suspension of 19.8 mg (0.20 mmol) CuCl in 30 ml of THF at 0°C were slowly added 6 ml (12.0 mmol) of ^{t}BuMgCl (2.00M in ether) and then dropwise 861 mg (815 µl, 10.0 mmol) of β-butyrolactone (7) in 10 ml of THF. After 40 min, the reaction mixture was quenched with 5 ml of 3N HCl and the organic phase was extracted with 3N NaOH-sol. (3x). The combined aqueous phases were acidified with conc. HCl and extracted with ether (3x). The combined organic phases were dried over $MgSO_4$ and concentrated to obtain 890 mg (61%) of crude acid **8**, a colourless oil which was used in the next step without purification. A pure sample could be obtained by FC (CH_2Cl_2/MeOH/AcOH 100:10:1). IR (Film): 2964, 2686, 1704, 1469, 1304, 942. ^{1}H-NMR: 0.88 (*s*, 9 H, -C(C*H*$_3$)$_3$), 0.93 (*d*, *J*=6.8, 3 H, -CH(C*H*$_3$)), 1.80 (*qdd*, *J*=6.8, 3.2, 10.7, 1 H, -C*H*(CH$_3$)), 1.99 (*dd*, *J*=14.8, 10.7, 1 H, -C*H*H'-CO_2H), 2.55 (*dd*, *J*=3.2, 14.8, 1 H, -CH*H*'-CO_2H). ^{13}C-NMR: 15.05 (-CH-*C*H$_3$), 27.15 (-C(*C*H$_3$)$_3$), 32.75 (-*C*(CH$_3$)$_3$), 37.46 (-*C*H$_2$-CO_2H), 39.84 (-*C*H-CH$_3$), 181.01 (-CO_2H). MS (EI): 129 (6, $[M-CH_3]^+$), 57 (100). $C_8H_{16}O_2$ (144.21)

Benzyl 3,4,4-trimethyl-pentanoate (9). In 56 ml of ethanol, 8.08 g (56.0 mmol) of acid **8** were dissolved, the solution was cooled to 0°C and slowly neutralized with 9.40 g (56.0 mmol) CsOH (1M in H_2O). The reaction mixture was concentrated and the residue was co-evaporated twice with toluene. The oily residue was dissolved in 56 ml of DMF and treated with 9.58 g (6.63 ml, 56.0 mmol) of benzyl bromide. After 3 h, the mixture was concentrated *in vacuo*, the residue taken up in 500 ml of H_2O and extracted with ethyl acetate (3x). The combined organic phases were washed with sat. aq. $NaHCO_3$-sol. (2x) and H_2O (2x), dried over $MgSO_4$ and concentrated. After FC (hexane/ethyl acetate 30:1), 10.3 g (79%) of benzyl ester **9** were obtained as a colourless oil. IR (Film): 2962, 1737, 1380, 1295, 1155, 698. ^{1}H-NMR: 0.86 (*s*, 9 H, -C(C*H*$_3$)$_3$), 0.87 (*d*, *J*=7.5, 3 H, -CH-C*H*$_3$), 1.82 (*m*, 1 H, -C*H*-CH$_3$), 2.01 (*dd*, *J*=10.8, 14.6, 1 H, -C*H*H'-CO_2-), 2.53 (*dd*, *J*=3.4, 14.8, 1 H, -CH*H*'-CO_2-), 5.11 (*s*, 2 H, -CO_2-C*H*$_2$Ph), 7.34 (*m*, 5 H, Ph). ^{13}C-NMR: 14.98 (-CH-*C*H$_3$), 27.10 (-C(*C*H$_3$)$_3$), 32.69 (-*C*(CH$_3$)$_3$), 37.48 (-*C*H$_2$-CO_2-), 39.93 (-*C*H-CH$_3$), 66.06 (-CO_2-*C*H$_2$Ph), 128.04, 128.11, 128.42 (*o*,*m*,*p*-Ph), 136.05 (*i*-Ph), 173.88 (-*C*O$_2$-CH$_2$Ph). MS (EI): 234 (3, M^+), 118 (28), 91 (100). Anal. calc. for $C_{15}H_{22}O_2$ (234.34) C 76.88, H 9.46; found: C 77.10, H 9.67

Benzyl 2-azido-3,4,4-trimethyl-pentanoate (10). To a solution of 44.4 ml (22.2 mmol) KHMDS (0.5M in toluene) in 60 ml of THF at -78°C were added under argon 4.00 g (17.1 mmol) of benzylester **9** in 60 ml of THF. This enolate solution was added quickly to a solution of 6.59 g (21.3 mmol) trisyl azide in 60 ml of THF at -78°C and the reaction mixture was quenched after 1 min with 1.13 g (1.08 ml, 18.8 mmol) acetic acid and stirred another 2 h in a warm water bath. The reaction mixture was divided between 300 ml of dilute NaCl-sol. and 300 ml of CH_2Cl_2 and the aqueous phase was extracted with CH_2Cl_2 (3x). The combined organic phases were washed with H_2O, dried over $MgSO_4$ and concentrated. After FC (hexane/ether 50:1), 3.95 g (86%) of a mixture of azide **10** and starting material **9** were obtained in a ratio of 6.3:1. It was very difficult to separate these two compounds and they were therefore used as a mixture in the next step. For characterization purposes, a sample was purified by FC (hexane/CH_2Cl_2 1:1). The obtained azide **10** was a mixture of

diastereomers in a ratio of 8:1. IR (Film): 2964, 2106, 1742, 1456, 1268, 1188, 697. ^{1}H-NMR (The signals of the minor isomer were hidden under those of the major isomer. Therefore, only the signals of the major isomer are given): 0.86 (*d*, *J*=7.1, 3 H, -CH-C*H*$_3$), 0.96 (*s*, 9 H, -C(C*H*$_3$)$_3$), 1.91 (*qd*, *J*=7.1, 2.5, 1 H, -C*H*-CH$_3$), 4.26 (*d*, *J*=2.5, 1 H, -C*H*-N$_3$), 5.23 (*s*, 2 H, -CO$_2$-C*H*$_2$Ph), 7.37 (*m*, 5 H, Ph). ^{13}C-NMR (minor isomer with *): 9.97 and 12.84* (-CH-*C*H$_3$), 27.90* and 28.00 (-C(*C*H$_3$)$_3$), 33.12 (-*C*(CH$_3$)$_3$), 44.57* and 44.83 (-*C*H-CH$_3$), 63.91 and 64.57* (-*C*H-N$_3$), 67.26* and 67.43 (-CO$_2$-*C*H$_2$Ph), 128.25, 128.40 and 128.52 (*o*,*m*,*p*-Ph), 135.09 (*i*-Ph), 170.79 (-*C*O$_2$Ph). MS (CI, NH$_3$): 293 (24, [M+1+NH$_3$]$^+$), 248 (100), 108 (42), 91 (60). Anal. calc. for C$_{14}$H$_{21}$N$_3$O$_2$ (275.35): C 65.43, H 7.69, N 15.26; found:C 65.65, H 7.73, N 15.34

Benzyl 2-amino-3,4,4-trimethyl-pentanoate (11). A solution of 3.50 g (12.7 mmol) azide **10** (contaminated with benzyl ester **9**), 5.01 g (19.1 mmol) PPh$_3$ and 460 mg (460 µl, 25.4 mmol) H$_2$O in 120 ml of THF were stirred at room temperature for 4 d and 2 h at 50°C. After concentration, the residue was stirred with hexane and the liquid was decanted (8x). The hexane phases were combined and concentrated to give 5.72 g crude amine **11**. Purification with FC (CH$_2$Cl$_2$/MeOH 40:1→20:1) yielded 3.52 g amine **11**, which still contained a little Ph$_3$PO. The compound was taken up in hexane and undissolved material was separated. Concentration of the hexane solution yielded 2.98 g (98%) of pure amine **11** as a colourless oil. The product was a mixture of 2 diastereomers in a ratio of 5:1 and was used as such in the next step. The diastereomers could be separated by FC (CH$_2$Cl$_2$/MeOH 50:1). Major isomer **11a**: IR (Film): 3387, 2960, 1732, 1456, 1365, 1193, 1166, 967, 735, 697. ^{1}H-NMR: 0.80 (*d*, *J*=7.2, 3 H, -CH-C*H*$_3$), 0.98 (*s*, 9 H, -C(C*H*$_3$)$_3$), 1.35 (*b*, 2 H, -NH$_2$), 1.80 (*qd*, *J*=7.2, 2.2, 1 H, -C*H*-CH$_3$), 3.82 (*d*, *J*=2.2, 1 H, -C*H*-NH$_2$), 5.15 (*s*, 2 H, -CO$_2$-C*H*$_2$Ph), 7.35 (*m*, 5 H, Ph). ^{13}C-NMR: 8.65 (-CH-*C*H$_3$), 28.32 (-C(*C*H$_3$)$_3$), 33.32 (-*C*(CH$_3$)$_3$), 44.72 (-*C*H-CH$_3$), 55.44 (-C*H*-NH$_2$), 66.59 (-CO$_2$-*C*H$_2$Ph), 128.03, 128.16, 128.49 (*o*,*m*,*p*-Ph), 135.88 (*i*-Ph), 176.70 (-*C*O$_2$CH$_2$Ph). MS (EI): 164 (7), 114 (71), 91 (58), 58 (100). Minor isomer **11b**: IR (Film): 2961, 2872, 1731, 1159, 736, 697. ^{1}H-NMR: 0.92 (*s*, 9 H, -C(C*H*$_3$)$_3$), 0.93 (*d*, *J*=7.2, 3 H, -CH-C*H*$_3$), 1.56 (*b*, 2 H, -NH$_2$), 1.61 (*qd*, *J*=7.2, 3.9, 1 H, -C*H*-CH$_3$), 3.62 (*d*, *J*=3.9, 1 H, -C*H*-NH$_2$), 5.06 (*d*, *J*=12.2, 1 H, -CO$_2$-CH*H*'Ph), 5.17 (*d*, *J*=12.2, 1 H, -CO$_2$-CH*H*'Ph), 7.36 (*m*, 5 H, Ph). ^{13}C-NMR: 11.11 (-CH-*C*H$_3$), 28.15 (-C(*C*H$_3$)$_3$), 33.34 (-*C*(CH$_3$)$_3$), 49.14 (-*C*H-CH$_3$), 56.19 (-C*H*-NH$_2$), 66.41 (-CO$_2$-*C*H$_2$Ph), 128.17, 128.36, 128.41 (*o*,*m*,*p*-Ph), 135.40 (*i*-Ph), 175.64 (-*C*O$_2$CH$_2$Ph). MS (EI): 164 (10), 114 (79), 91 (89), 58 (100). Anal. calc. for C$_{14}$H$_{23}$NO$_2$ (237.34): C 70.85, H 9.77, N 5.90; found: C 71.05, H 9.55, N 6.00.

Benzyl *N*-[2-(methoxycarbonyl)-benzoyl]-2-amino-3,4,4-trimethyl-pentanoate (12) and **Benzyl 2-phthalimido-3,4,4-trimethyl-pentanoate (13).** A solution of 2.81 g (15.6 mmol) phthalic acid monomethyl ester, 12.6 g (7.71 ml, 106 mmol) thionyl chloride and 2 drops DMF were heated under reflux for 1 h and the reaction mixture was concentrated. The residue was dissolved in 3 ml benzene and concentrated to remove all remaining thionyl chloride. The acid chloride was dissolved in 9 ml of THF and was added *via* syringe pump during 30 min to a solution of 3.30 g (13.2 mmol) amino acid-benzyl ester **11** and 3.22 g (4.43 ml, 31.8 mmol) NEt$_3$ in 30 ml of THF. After 2 h, the reaction mixture was poured on ice and left standing overnight. The phases were separated and the aqueous phase was extracted with ethyl acetate (3x). The combined organic phases were dried over MgSO$_4$ and concentrated. After FC (hexane/ethyl acetate 4:1→3:1), 520 mg (10%) of phthalimide **13** and 4.21 g (78%) amide **12** were obtained as colourless oils. The 2

compounds were obtained each as a mixture of diastereomers in a ratio of 16:1 (amide **12**) and 2:1 (phthalimide **13**). (**12**): IR (Film): 3361, 2955, 1731, 1666, 1519, 1295, 1271, 1193, 1128, 967, 738, 699. ^{1}H-NMR (The signals of the minor isomer are hidden by those of the major isomer. Therefore, only the signals of the major isomer are given.): 0.88 (*d*, *J*=7.1, 3 H, C*H*$_3$-CH-), 1.02 (*s*, 9 H, -C(C*H*$_3$)$_3$), 1.97 (*dq*, *J*=2.0, 7.2, 1 H, CH$_3$-C*H*-), 3.78 (*s*, 3 H, -CO$_2$C*H*$_3$), 5.20 (*s*, 2 H, -CO$_2$-C*H*$_2$Ph), 5.23 (*dd*, *J*=1.9, 9.6, 1 H, -C*H*-NH-), 6.24 (*d*, *J*=9.6, 1 H, -NH), 7.36 (*m*, 5 H, Ph), 7.47 (*m*, 2 H, Phth), 7.86 (*m*, 2 H, Phth). ^{13}C-NMR (minor isomer with *): 9.57 and 11.65* (*C*H$_3$-CH-), 27.77 and 28.08* (-C(*C*H$_3$)$_3$), 33.39 (-*C*(CH$_3$)$_3$), 44.14 and 46.77* (CH$_3$-*C*H-), 52.43 (-CO$_2$*C*H$_3$), 53.27 and 54.55* (-*C*H-NH-), 66.99* and 67.11 (-CO$_2$*C*H$_2$Ph), 127.37 (Phth), 128.13, 128.29 and 128.54 (*o*,*m*,*p*-Ph), 129.66, 129.78, 130.15 and 131.72 (Phth), 135.50 (*i*-Ph), 137.64 (Phth), 167.10 (-*C*O$_2$CH$_2$Ph), 168.63 (-*C*O$_2$CH$_3$), 172.88 (-NH-*C*O-). MS (EI): 396 (0.1), 380 (0.1), 276 (21), 163 (100), 91 (17). Anal. calc. for C$_{24}$H$_{29}$NO$_5$ (411.50): C 70.05, H 7.10, N 3.40; found: C 69.80, H 6.89, N 3.52. (**13**): IR (Film): 2962, 1776, 1748, 1719, 1468, 1384, 1197, 1065, 902, 728. ^{1}H-NMR (The signals of the minor isomer are hidden under those of the major isomer. Therefore, only the signals of the major isomer are given): 0.94 (*d*, *J*=6.1, 3 H, C*H*$_3$-CH), 0.95 (*s*, 9 H, -C(C*H*$_3$)$_3$), 2.67 (*qd*, *J*=4.7, 7.2, 1 H, CH$_3$-C*H*-), 5.08 (*d*, *J*=4.4, 1 H, -C*H*-N-), 5.10 (*d*, *J*=12.4, 1 H, -CO$_2$-C*H*H'-Ph), 5.18 (*d*, *J*=12.4, 1 H, -CO$_2$-CH*H*'-Ph), 7.24 (*m*, 5 H, Ph), 7.73 (*m*, 2 H, Phth), 7.84 (*m*, 2 H, Phth). ^{13}C-NMR (minor isomer with *): 11.90 and 13.00* (*C*H$_3$-CH-), 27.33* and 27.56 (-C(*C*H$_3$)$_3$), 33.43 and 34.02* (-*C*(CH$_3$)$_3$), 42.16 and 45.16* (CH$_3$-*C*H-), 53.14 and 54.30* (-*C*H-N-), 67.12* and 67.39 (-CO$_2$-*C*H$_2$Ph), 123.29* and 123.35 (*o*-Phth), 127.99, 128.03, 128.13*, 128.25 and 128.36* (*o*,*m*,*p*-Ph), 131.62 (*i*-Phth), 133.95* and 134.02 (*m*-Phth), 135.20 (*i*-Ph), 167.88 (N(*C*O)$_2$), 169.33 (-*C*O$_2$-CH$_2$Ph). MS (CI, NH$_3$): =380 (100, [M+1]$^+$), 244 (25), 188 (23), 91 (51). Anal. calc. for C$_{23}$H$_{25}$NO$_4$ (379.46): C 72.80, H 6.64, N 3.69; found: C 72.60, H 6.50, N 3.70

Benzyl 2-phthalimido-3,4,4-trimethyl-pentanoate (13). A mixture of 4.17 g (10.1 mmol) amide **12**, 444 mg (11.1 mmol) NaOH (5% in H$_2$O), and 32.2 mg (0.10 mmol) Bu$_4$NBr in 20 ml of CH$_2$Cl$_2$ was stirred vigorously for 6 h. The phases were separated and the aqueous phase was extracted with CH$_2$Cl$_2$ (3x). The combined organic phases were dried over MgSO$_4$ and concentrated. After FC (hexane/ethyl acetate 3:1), 3.56 g (93%) of phthalimide **13** were obtained as a colourless oil as a mixture of diastereomers in a ratio of 13:1. Also, 154 mg of starting material **12** were recovered.

2-Phthalimido-3,4,4-trimethyl-pentanoic acid (14). A solution of 3.50 g (9.22 mmol) benzyl ester **13** in 250 ml of ethanol was treated with 350 mg Pd/C (10%) and stirred under hydrogen for 3.5 h. The reaction mixture was filtered through Celite and concentrated. After FC (CH$_2$Cl$_2$/MeOH/AcOH 100:5:1), 2.60 g (97%) of amino acid **14** were obtained as colourless crystals as a mixture of diastereomers in a ratio of 14:1. M.p.: 146-147°C. IR (KBr): 2972, 2909, 1780, 1731, 1382, 1292, 1262, 1120, 1067, 1056, 900, 722. ^{1}H-NMR (minor isomer with *): 0.95 (*s*, 9 H, -C(C*H*$_3$)$_3$), 0.96 and 1.28* (2*d*, *J*=7.0 and 7.2, 3 H, C*H*$_3$-CH), 2.24* and 2.56 (*m* and *qd*, *J*=7.3, 4.4, 1 H, CH$_3$-C*H*-), 5.04* and 5.12 (2*d*, *J*=3.2 and 4.3, 1 H, -C*H*-N-), 7.74 (*m*, 2 H, Phth), 7.87 (*m*, 2 H, Phth), 11.2 (*b*, 1H, -CO$_2$*H*). ^{13}C-NMR (minor isomer with *): 11.97 and 13.11* (*C*H$_3$-CH-), 27.26* and 27.59 (-C(*C*H$_3$)$_3$), 33.46 (-*C*(CH$_3$)$_3$), 42.31 and 45.18* (CH$_3$-*C*H-), 52.88 and 54.01* (-*C*H-N-), 123.48* and 123.52 (*o*-Phth), 131.60 (*i*-Phth), 134.12* and 134.14 (*m*-Phth), 167.87

($N(CO)_2$), 175.40 ($-CO_2H$). MS (CI,NH_3): 307 (32, $[M+1+NH_3]^+$), 290 (100, $[M+1]^+$), 244 (24), 188 (12). Anal. calc. for $C_{16}H_{19}NO_4$ (289.33): C 66.42, H 6.62, N 4.84; found:C 66.45, H 6.60, N 4.75.

Radical reactions

(1*SR*,2*S*)-2-Methyl-1-phthalimido-1-thio-pyridyl-butane (22). To a solution of 131 mg (0.50 mmol) acid **6** in 2.5 ml of THF at -20°C was added under argon 55.6 mg (61 µl, 0.55 mmol) of N-methylmorpholine and 75.1 mg (72 µl, 0.55 mmol) of ^{i}butyl chloroformate. After 10 min, the flask was protected from light and a solution of 76.3 mg (0.60 mmol) thiohydroxamic acid and 60.7 mg (84 µl, 0.60 mmol) NEt_3 in 2 ml THF was added followed by a trace of DMAP. After 30 min, the yellow suspension was filtered into a water-jacketed flask with maximum protection from light. The original flask was rinsed with 5 ml of THF. After stirring under argon for 30 min, the reaction mixture was irradiated with a 250W-daylight lamp for 5 min and then concentrated. After 2 FC (hexane/ethyl acetate 8:1 and CH_2Cl_2/ether 20:1), 55.4 mg (34%) thiopyridine **22** were obtained as a colourless solid as a mixture of 2 diastereomers in a ratio of 1.7:1. IR (neat): 3060, 2970, 1780, 1715, 1575, 1380, 1125, 1075, 885, 760, 720. ^{1}H-NMR (minor isomer with *): 0.90 and 0.96* (2*t*, *J*=7.4, 7.4, 3 H, C*H*$_3$-CH$_2$-), 0.95* and 1.20 (2*d*, *J*=6.9, 6.9, 3 H, C*H*$_3$-CH-), 1.19, 1.39*, 1.51 and 1.94* (4*m*, 2 H, CH$_3$-C*H*$_2$-), 2.49 (*m*, 1 H, CH$_3$-C*H*-), 6.38* and 6.39 (2*d*, *J*=10.4, 10.4, 1 H, -CH-SPyr), 6.96 (*m*, 1 H, SPyr), 7.17 (*d*, *J*=8.0, 1 H, SPyr), 7.44 (*t*, *J*=9.9, 1 H, SPyr), 7.70 (*m*, 2 H, Phth), 7.83 (*m*, 2 H, Phth), 8.42 (*m*, 1 H, SPyr). ^{13}C-NMR (minor isomer with *): 10.93, 11.04* (*C*H$_3$-CH$_2$-), 15.92*, 16.56 (*C*H$_3$-CH-), 26.04, 26.45* (CH$_3$-*C*H$_2$-), 38.08, 38.24* (CH$_3$-*C*H-), 58.47*, 58.88 (-*C*H-SPyr), 119.94 (5'-SPyr), 122.44*, 122.52 (3'-SPyr), 123.19*, 123.35 (*o*-Phth), 131.76 (*i*-Phth), 133.96 (*m*-Phth), 136.14 (4'-SPyr), 149.41 (6'-SPyr). 157.25*, 157.28 (2'-SPyr), 167.41 (N(CO)). MS (EI): 326 (0.4, M^+), 216 (51.7), 160 (100). Anal. calc. for $C_{18}H_{18}N_2O_2S$ (326.41): C 66.24, H 5.56, N 8.58; found: C 66.05, H 5.41, N 8.80.

(1*SR*,2*S*)-2-Methyl-1-phenylseleno-1-phthalimido-butane (24) To a suspension of 131 mg (0.50 mmol) of amino acid **6** and 139 mg (0.55 mmol) disulfide **19** in 16.5 ml THF in a water-jacketed flask was added under argon and protection from light 111 mg (135 µl, 0.55 mmol) of Bu_3P and, after 35 min 780 mg (2.50 mmol) of diphenyldiselenide. The reaction mixture was irradiated with a 250W-daylight lamp for 5 min and concentrated. After 2 FC (hexane/ethyl acetate 6:1 and CH_2Cl_2/ether 80:1) 145 mg (78%) of **24** were obtained as a slightly yellow oil as a mixture of 2 diastereomers in a ratio of 1.9:1. IR (neat): 2965, 2931, 1774, 1716, 1467, 1380, 1357, 1323, 1069, 1022, 880, 740, 727, 692. ^{1}H-NMR (minor isomer with *): δ=0.83 and 0.96* (2*t*, *J*=7.4, 3 H, -C*H*$_3$-CH$_2$-), 0.87* and 1.20 (2*d*, *J*=6.6; *J*=6.7, 3 H, C*H*$_3$-CH-), 1.09, 1.32, 1.44* and 1.98* (4*qdd*, *J*=7.0, 1.3, 15.4; *J*=6.3, 1.6, 15.3; *J*=7.5, 3.5, 15.2 and *J*=7.4, 3.2, 15.1, 2 H, CH$_3$-C*H*$_2$-), 2.68 (*m*, 1 H, -C*H*-CH$_3$), 5.37* and 5.39 (2*d*, *J*=10.9, 1 H, -C*H*-SePh), 7.13 (*m*, 3 H, *m*,*p*-Ph), 7.52 (*m*, 2 H, *o*-Ph), 7.69 (*m*, 2 H, Phth), 7.77 (*m*, 2 H, Phth). ^{13}C-NMR (minor isomer with *): 10.40 and 10.69 (*C*H$_3$-CH-), 16.15* and 17.57 (*C*H$_3$-CH-), 26.22 and 27.29* (CH$_3$-*C*H$_2$-), 38.00 and 38.27* (CH$_3$-*C*H), 58.17* and 58.47 (-*C*H-SePh), 123.23 (*o*-Phth), 128.05*, 128.08 and 128.93 (Ph), 131.51 (*i*-Phth), 134.01 (*m*-Phth), 135.50* and 135.70 (*i*-Ph), 167.12 (N(CO)). MS (CI): 389 (1), 372 (0.4, M^+), 233 (41), 216 (100), 86 (92). Anal. calc. for $C_{19}H_{19}NO_2Se$ (372.33): C 61.30, H 5.14, N 3.67; found: C 61.46, H 5.20, N 3.80.

Methyl (2*SR*,4*SR*,5*S*)-5-methyl-4-phthalimido-2-thio-pyridyl-heptanoate (26) and (1*SR*,2*S*)-2-Methyl-1-phthalimido-1-thio-pyridyl-butane (22). To a solution of 131 mg (0.50 mmol) amino acid **6** in 3.5 ml of THF were added under argon at -20°C 55.6 mg (61 µl, 0.55 mmol) of N-methylmorpholine and 75.1 mg (72 µl, 0.55 mmol) of ^{i}butyl-chloroformate. After 40 min, the reaction mixture was protected from light and a solution of 76.3 mg (0.60 mmol) thiohydroxamic acid and 60.7 mg (84 µl, 0.60 mmol) NEt_3 in 2 ml THF and a trace of DMAP were added. After 20 min, the yellow suspension was filtered into a water-jacketed flask with maximum protection from light, and 5 ml of THF were used to rinse the original flask. The reaction mixture was stirred for 30 min under an argon atmosphere. Then, 86.1 mg (90 µl, 1.00 mmol) of methylacrylate and 10 ml of THF were added and the reaction mixture was photolyzed for 5 min with a 250W-daylight lamp. After concentration and FC of the residue (hexane/ethyl acetate 8:1→5:1), 51.1 mg (31%) thiopyridine **22** and 114 mg crude ester **26** were obtained. Another 2 FC (CH_2Cl_2/ether 20:1 and hexane/ether 6:1) yielded 38.8 mg (19%) ester **26** as a colourless oil as a mixture of 4 isomers. (**26**): IR (Film): 3465, 3048, 2965, 2877, 1771, 1732, 1713, 1579, 1388, 1366, 1122, 874, 760, 723. ^{1}H-NMR (minor isomer with *): 0.81*, 0.83*, 0.93 and 0.94 (4*t*, all *J*=7.4, 3 H, C*H*$_3$-CH$_2$-), 0.82*, 1.02 and 1.04 (3*d*, *J*=6.8, 7.1 and 6.9, 3 H, C*H*$_3$-CH-), 1.05*, 1.25, 1.35 and 1.65* (4*m*, 2 H, CH$_3$-C*H*$_2$-), 2.11, 2.21*, 2.33, 2.64 and 2.58 (5*m*, 3 H, CH$_3$-C*H*- u. -C*H*$_2$-CH-CO$_2$CH$_3$), 3.61 and 3.71* (2*s*, 3 H, -CO$_2$CH$_3$), 4.00* and 4.34 (2*m*, 1 H, -CH-N-), 4.61* and 4.75 (2*m*, 1 H, -C*H*-CO$_2$CH$_3$), 6.83 (*m*, 1 H, SPyr), 7.09 (*m*, 1 H, SPyr), 7.41 (m, 1 H, SPyr), 7.73 and 7.85 (2*m*, 5 H, SPyr and Phth). ^{13}C-NMR (minor isomer with *): 10.51*, 10.55, 10.68*, 10.91 (*C*H$_3$-CH$_2$-), 15.79*, 15.82*, 16.08, 16.21 (*C*H$_3$-CH-), 25.83, 25.97, 26.13*, 26.23* (CH$_3$-*C*H$_2$-), 30.67, 30.93*, 32.79*, 32.84 (-*C*H$_2$-CH-CO$_2$CH$_3$), 36.04, 36.24*, 37.17 (CH$_3$-*C*H-), 42.67, 42.75*, 42.78, 42.83* (-*C*H-CO$_2$CH$_3$), 52.49, 52.58* (-CO$_2$*C*H$_3$), 53.65*, 53.92, 54.77*, 55.05 (-*C*H-N-), 119.70, 119.84* (5'-SPyr), 122.16*, 122.33 (3'-SPyr), 122.99, 123.11* (*o*-Phth), 131.86 (*i*-Phth), 133.60, 133.81* (*m*-Phth), 136.02*, 136.06 (4'-SPyr), 148.72, 149.06* (6'-SPyr), 156.12 (2'-SPyr), 168.53*, 168.60 (N(CO)), 172.27, 172.88*, 172.92 (-*C*O$_2$CH$_3$). MS (EI): 412 (2, M$^+$), 244 (14), 196 (100). $C_{22}H_{24}N_2O_4S$ (412.51).

Methyl (4*SR*,5*S*)-5-methyl-4-phthalimido-heptanoate (28). Approximately 500 mg Raney-Nickel (suspension in water) were stirred with 1 ml of methanol and the solvent was decanted (3x). The water-free Raney-Nickel was suspended in 1.5 ml of MeOH and 82.1 mg (0.20 mmol) of ester **26** in 1 ml of methanol were added. After 45 min, the reaction mixture was filtered and concentrated. FC (hexane/ethyl acetate 10:1) yielded 27.3 mg (45%) methyl ester **28** as a colourless oil as a mixture of 2 diastereomers in a ratio of 1.9:1. IR (neat): 2970, 2875, 1773, 1740, 1720, 1390, 1378, 1172, 1070, 722. ^{1}H-NMR (minor isomer with *): 0.82 and 0.95* (2*t*, *J*=7.4, 7.4, 3 H, C*H*$_3$-CH$_2$-), 0.80* and 1.04 (2*d*, *J*=6.7, 6.7, 3 H, C*H*$_3$-CH-), 1.05, 1.29, 1.68, 2.23 and 2.41 (5*m*, 7 H, CH$_3$-C*H*$_2$-C*H*- and -C*H*$_2$-C*H*$_2$-CO$_2$CH$_3$). 3.58 and 3.59* (2*s*, 3 H, -CO$_2$CH$_3$), 3.95 (*m*, 1 H, -C*H*-N-), 7.73 (*m*, 2 H, Phth), 7.84 (*m*, 2 H, Phth). ^{13}C-NMR (minor isomer with *): 10.63, 10.71* (*C*H$_3$-CH$_2$-), 15.96*, 16.30 (*C*H$_3$-CH-), 24.76*, 24.80 (-*C*H$_2$-CH$_2$-CO$_2$CH$_3$), 26.08, 26.31* (CH$_3$-*C*H$_2$-), 31.39 (-*C*H$_2$-CO$_2$CH$_3$), 36.19, 36.46* (CH$_3$-*C*H-), 51.63 (-CO$_2$*C*H$_3$), 56.16*, 56.31 (-*C*H-N), 123.26 (*o*-Phth), 131.65 (*i*-Phth), 134.02 (*m*-Phth), 168.77*, 168.84 (N(CO)), 173.24 (-*C*O$_2$CH$_3$). MS (EI): 303 (1, M$^+$), 246 (50), 214 (34), 186 (100). Anal. calc. for $C_{17}H_{21}NO_4$ (303.36): C 67.31, H 6.98, N 4.62; found: C 67.45, H 6.70, N 4.54.

(1*SR*,2*S*)-1-Deutero-2-methyl-1-phthalimido-butane (34). To a solution of 65.3 mg (0.20 mmol) thiopyridine **22** in 2 ml of benzene at 80°C was added under argon a solution of 93.5 mg (0.32 mmol) Bu_3SnD and 6.6 mg (0.04 mmol) AIBN in 2 ml of benzene during 30 min *via* syringe pump. After 2 h, 2 ml of CCl_4 were added and the reaction mixture was refluxed for 1 h. After concentration, the residue was stirred vigorously overnight in a mixture of 4 ml sat. I_2/CH_2Cl_2-sol. and 4 ml sat. KF/H_2O solution. The reaction mixture was filtered through Celite and washed several times with CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2 (3x). The combined organic phases were washed with $Na_2S_2O_3$-sol., H_2O and brine, dried over $MgSO_4$ and concentrated. After FC (hexane/ethyl acetate 6:1), 34.7 mg (79%) of deuterated phthalimide **34** were obtained as a colourless oil as a mixture of 2 isomers in a ratio of 1.3:1. IR (neat): 2962, 1771, 1715, 1467, 1397, 721. ^{1}H-NMR (minor isomer with *): 0.90 and 0.91* (2*d*, *J*=6.8, 3 H, C*H*$_3$-CH-), 0.93 and 0.94* (2*t*, *J*=7.5, 3 H, C*H*$_3$-CH$_2$-), 1.20 and 1.44* (2*m*, 2 H, CH$_3$-C*H*$_2$-), 1.91 (*m*, 1 H, CH$_3$-C*H*-), 3.49* and 3.57 (2*d*, *J*=8.0, 6.8, 1 H, -C*H*D), 7.70 (*m*, 2 H, Phth), 7.85 (*m*, 2 H, Phth). ^{13}C-NMR: 11.11 (*C*H$_3$-CH$_2$-), 16.83 (*C*H$_3$-CH-), 26.96 (CH$_3$-*C*H$_2$-), 33.99 (CH$_3$-*C*H-), 43.67 (*t*, *J*=21.2, -*C*HD), 123.10 (*o*-Phth), 132.04 (*i*-Phth), 133.78 (*m*-Phth), 168.63 (N(CO)). MS (EI): 218 (31, M$^+$), 161 (100). Anal. calc. for $C_{13}H_{14}DNO_2$ (218.27): C 71.54, H 6.47, N 6.42; found: C 71.70, H 6.35, N 6.54

1-Phthalimido-1-thio-pyridyl-2,3,3-trimethyl-butane (23). To a solution of 145 mg (0.50 mmol) amino acid **14** and 139 mg (0.55 mmol) disulfide **19** in 2.5 ml THF were added 111 mg (135 µl, 0.55 mmol) of Bu_3P under argon at 0°C with protection from light. The reaction mixture was stirred for 1 h at room temperature and then transferred into a water-jacketed flask. After addition of a further 7 ml THF, the solution was irradiated with a 250 W-daylight lamp for 5 min and concentrated. After 2 FC (hexane/ethyl acetate 5:1 and CH_2Cl_2/Ether 80:1), 93.9 mg (53%) of thiopyridine **23** were obtained as a colourless solid as a mixture of 2 diastereomers in a ratio of 5.5:1. IR (KBr): 2961, 1763, 1716, 1578, 1456, 1418, 1385, 1348, 1326, 1122, 888, 775, 717. ^{1}H-NMR (minor isomer with *): 1.02 and 1.05* (2*s*, 9 H, -C(C*H*$_3$)$_3$), 1.10* and 1.37 (2*d*, *J*=7.3 and 7.1, 3 H, -CH-C*H*$_3$), 2.07 and 2.20* (2*dq*, *J*=7.1, 4.1 and *J*=7.2, 5.6, 1 H, -C*H*-CH$_3$), 6.78* and 6.89 (2*d*, *J*=5.6 and 4.1, 1 H, -C*H*-SPyr), 6.94 (*m*, 1 H, SPyr), 7.12 (*m*, 1 H, SPyr), 7.42 (*m*, 1 H, SPyr), 7.67 (*m*, 2 H, Phth), 7.80 (*m*, 2 H, Phth), 8.40 (*m*, 1 H, SPyr). ^{13}C-NMR (minor isomer with*): 12.78* and 13.66 (-CH-*C*H$_3$), 27.89 and 28.07* (-C(*C*H$_3$)$_3$), 34.38 (-*C*(CH$_3$)$_3$), 48.78 (-*C*H-CH$_3$), 55.04* and 56.87 (-*C*H-SPyr), 119.66* and 119.92 (5'-SPyr), 121.99* and 122.68 (3'-SPyr), 123.10 and 123.17* (*o*-Phth), 131.83 (*i*-Phth), 133.74 and 133.80* (*m*-Phth), 136.00 (4'-SPyr), 149.29 (6'-SPyr), 156.75 (2'-SPyr), 167.13 (N(CO)). MS (CI, NH$_3$): 355 (92, [M+1]$^+$), 244 (72), 188 (58), 112 (100). Anal. calc. for $C_{20}H_{22}N_2O_2S$ (354.47): C 67.77, H 6.26, N 7.90; found: C 67.59, H 6.14, N 7.73.

Crystal data of **23a**: Molecular formula $C_{20}H_{22}N_2O_2S$. Spacegroup C_C. Unit cell dimensions a=16.433, b=12.712, c=9.579 Å, α=90°, β=111.824°, γ=90°, V=1857.7 Å^3, Z=4, F(000)=752. Temperature=298 K, Θmax=74.33°, radiation Cu*K*α, λ=1.54178 Å. scan mode ω/2Θ. Collected intensities ±h, -k, -l. Absorption 16.2392 cm^{-1}. No. of ind. reflections 2006. No. of refl. used in ref. 1922. No. of variables 227. Max and min Δρ [e* Å^{-3}] 0.44, -0.20. Final R 3.43. Final R$_W$ 4.13. Weighting scheme wght* [1-(ΔF/6*σF)^2]^2.

1-Phthalimido-1-phenylseleno-2,3,3-trimethyl-heptane (25). To a suspension of 145 mg (0.50 mmol) amino acid **14** and 139 mg (0.55 mmol) disulfide **19** in 16.5 ml THF in a water-jacketed flask

were added 111 mg (135 µl, 0.55 mmol) of Bu_3P under argon and protection from light. After 15 min, 780 mg (2.50 mmol) of diphenyldiselenide were added to the mixture. The reaction mixture was irradiated with a 250W-daylight lamp for 5 min and concentrated. After FC (hexane/ether 4:1→2:1), 173 mg of crude selenide **25** and 70.7 of mg crude thiopyridine **23** were obtained. Selenide **25** could be purified by 2 FC (CH_2Cl_2/ether 80:1 and hexane/ether 5:1) and yielded 110 mg (55%) of **25** as a colourless oil as a mixture of 2 diastereomers in a ratio of 15:1. The compound decomposes relatively fast at room temperature. IR (neat): 2963, 1774, 1715, 1468, 1380, 1351, 1329, 1058, 883, 740, 723. ^{1}H-NMR (minor isomer with *): δ=0.93 and 0.95* (2*s*, 9 H, -C(CH_3)$_3$), 1.17* and 1.34 (2*d*, all *J*=7.1, 3 H, -CH-CH_3), 2.26* and 2.36 (2*m*, 1 H, -CH-CH_3), 5.85 and 5.91* (2*d*, *J*=6.5 and 4.8, 1 H, -CH-SePh), 7.06 (*dd*, *J*=7.5, 7.1, 2 H, *m*-Ph), 7.15 (*t*, *J*=7.4, 1 H, *p*-Ph), 7.47 (*d*, *J*=6.9, 2 H, *o*-Ph), 7.66 (*m*, 2 H, Phth), 7.70 (*m*, 2 H, Phth). ^{13}C-NMR (minor isomer with *): 13.15* and 15.07 (-CH-CH_3), 27.71 and 28.07* (-C(CH_3)$_3$), 34.46 and 34.55* (-C(CH_3)$_3$), 46.78 and 49.94* (-CH-CH_3), 54.04* and 56.08 (-CH-SePh), 123.12 and 123.26* (*o*-Phth), 128.23*, 128.43, 128.87 and 129.04* (Ph), 131.92 (*i*-Phth), 133.96 (*m*-Phth), 136.63 (*i*-Ph), 166.90 (N(CO)). MS (EI): 244 (14), 188 (100), 57 (30). Anal. calc. for $C_{21}H_{23}NO_2Se$ (400.38): C 63.00, H 5.79, N 3.50; found: C 62.90, H 5.53, N 3.40.

Methyl 4-phthalimido-2-thio-pyridyl-5,6,6-trimethyl-heptanoate (27) and 1-Phthalimido-1-thio-pyridyl-2,3,3-trimethyl-butane (23). To a suspension of 145 mg (0.50 mmol) aminoacid **14** and 139 mg (0.55 mmol) disulfide **19** in 16.5 ml THF in a water-jacketed flask and protection from light were added under argon 111 mg (135 µl, 0.55 mmol) of Bu_3P and 172 mg (180 µl, 2.00 mmol) of methyl acrylate. After 1 h, the clear yellow solution was irradiated with a 250W-daylight lamp for 5 min. After FC (hexane/ethyl acetate 5:1), 66.0 mg of crude thiopyridine **23** and 87.9 mg of crude ester **27** were obtained. Compounds **27** und **23** were each purified by FC (CH_2Cl_2/ether 80:1) to give 56.0 mg of thiopyridine **23** (31%) as colourless crystals as a mixture of 2 diastereomers in a ratio of 5.0:1 and 27.9 mg (13%) of ester **27** as a colourless oil as a mixture of 4 diastereomers. (**27**): IR (neat): 2954, 1771, 1736, 1710, 1578, 1454, 1416, 1367, 1121, 160, 720. ^{1}H-NMR (minor isomers with *): δ=0.93, 0.95* and 0.96 (3*s*, 9 H, -C(CH_3)$_3$), 1.15, 1.16, 1.37* and 1.42* (4*d*, all *J*=7.3, 3 H, -CH-CH_3), 1.67* and 1.79 (2*m*, 1 H, -CH-CH_3), 2.09, 2.24*, 2.35, 2.50*, 2.76, 3.03*, 3.27 and 3.39* (8*m*, 2 H, -CH_2-CHSPyr), 3.59, 3.62*, 3.69* and 3.73 (4*s*, 3 H, -CO_2CH_3), 4.59 and 4.68 (2*m*, 1 H, -CH-CH_3), 4.49 and 4.83 (2*m*, 1 H, -CH-N-), 6.84 (*m*, 1 H, SPyr), 7.06 and 7.15 (2*d*, all *J*=8.1, 1 H, SPyr), 7.41 (*m*, 1 H, SPyr), 7.69-7.86 (*m*, 5 H, SPyr and Phth). ^{13}C-NMR (only the signals of the major isomers are given): 11.41 and 11.57 (-CH-CH_3), 27.56 and 28.04 (-C(CH_3)$_3$), 29.66 and 32.41 (-CH_2-CHSPyr), 33.84 and 34.09 (-C(CH_3)$_3$), 42.68 and 43.38 (-CH-SPyr), 47.31 and 48.14 (-CH-CH_3), 50.50 (-CH-N-), 52.50 and 52.60 (-CO_2CH_3), 119.74 and 119.83 (5'-SPyr), 122.5 and 122.38 (3'-SPyr), 122.94 (*o*-Phth), 132.21 (*i*-Phth), 133.60 and 133.75 (*m*-Phth), 136.03 and 136.09 (4'-SPyr), 148.83 and 149.03 (6'-SPyr), 156.13 and 156.25 (2'-SPyr), 168.44 (b, N(CO)), 172.30 and 172.83 (-CO_2CH_3). MS (CI, NH_3): 441 (100, $[M+1]^+$). Anal. calc. for $C_{24}H_{28}N_2O_4S$ (440.56): C 65.43, H 6.41, N 6.36; found: C 65.20, H 6.18, N 6.38.

4-Phthalimido-5,6,6-trimethyl-heptanoic acid (29). Approximately 600 mg of Raney-Nickel (suspension in H_2O) were treated with 2 ml of methanol and the solvent was decanted (3x). The water-free

Raney Nickel was suspended in 2 ml of methanol and 27.9 mg (0.06 mmol) of ester **27** in 2 ml of methanol were added. After 45 min, the reaction mixture was filtered through Celite and concentrated. FC of the residue yielded 19.8 mg (99%) ester **29** as a colourless oil as a mixture of 2 diastereomers in a ratio of 13:1. IR (neat): 2955, 1772, 1737, 1710, 1468, 1366, 1329, 1199, 1173, 1112, 1048, 720. ^{1}H-NMR (minor isomer with *): 0.93 and 0.97* (2*s*, 9 H, -C(C*H*$_3$)$_3$), 1.16 (*d*, *J*=7.2, 3 H, -CH-C*H*$_3$), 1.83 (*qd*, *J*=3.9, 7.3, 1 H, -C*H*-CH$_3$), 1.94 (*m*, 1 H, -C*H*H-CH$_2$-CO$_2$CH$_3$), 2.21 (*dd*, *J*=7.7, 6.9, 2 H, -CH$_2$-C*H*$_2$-CO$_2$CH$_3$), 2.53.and 2.76* (2*m*, 1 H, -CH*H*-CH$_2$-CO$_2$CH$_3$), 3.58 and 3.59* (2*s*, 3 H, -CH$_2$-CO$_2$C*H*$_3$), 4.37 (*ddd*, *J*=12.4, 3.6, 3.7, 1 H, -C*H*-N-), 7.71 (*m*, 2 H, Phth), 7.82 (*m*, 2 H, Phth). ^{13}C-NMR (minor isomer with *): 11.69 and 11.94* (-CH-*C*H$_3$), 24.23 (-*C*H$_2$-CH$_2$-CO$_2$CH$_3$), 27.66 and 28.00* (-C(*C*H$_3$)$_3$), 31.35 and 31.55* (-CH$_2$-*C*H$_2$-CO$_2$CH$_3$), 33.96 (-*C*(CH$_3$)$_3$), 46.85 and 47.26* (-*C*H-CH$_3$), 51.58, 51.87 and 52.25* (-*C*H-N- and -CO$_2$*C*H$_3$), 123.12 (*o*-Phth), 131.77 (*i*-Phth), 133.89 (*m*-Phth), 168.60 (N(CO)), 173.20 (-*C*O$_2$CH$_3$). MS (CI, NH$_3$): 349 (32, [M+1+NH$_3$]$^+$), 332 (100, [M+1]$^+$), 300 (8), 246 (7), 186 (7). Anal. calc. for C$_{19}$H$_{25}$NO$_4$ (331.41): C 68.86, H 7.60, N 4.23; found: C 68.70, H 7.35, N 4.45.

1-Deutero-1-phthalimido-2,3,3-trimethyl-butane (35). To a solution of 69.4 mg (0.20 mmol) thiopyridine **23** in 2.5 ml benzene at 80°C were added under argon a solution of 90.5 mg (0.31 mmol) Bu$_3$SnD and 6.57 mg (0.04 mmol) AIBN during 1.5 h *via* syringe pump. After 1 h, 2 ml CCl$_4$ were added and the solution was refluxed for 2 h. After concentration, the residue was stirred vigorously in mixture of 4 ml sat. KF/H$_2$O-sol. and 4 ml sat. I$_2$/CH$_2$Cl$_2$-sol. overnight. The reaction mixture was filtered through Celite and diluted with H$_2$O. The aqueous phase was extracted with CH$_2$Cl$_2$ (3x). The combined organic phases were washed with Na$_2$S$_2$O$_3$-sol, H$_2$O and brine, dried over MgSO$_4$ and concentrated. After FC (hexane/ethyl acetate 6:1→3:1), 39.8 mg (81%) deuterated phthalimide **35** were obtained as colourless crystals as a mixture of 2 diastereomers in a ratio of 3:1. M.p.: 73°C. IR (KBr): 2959, 1764, 1720, 1466, 1396, 1190, 1089, 925, 907, 745, 718. ^{1}H-NMR (minor isomer with *): 0.81 (*d*, *J*=6.9, 3 H, -CH-C*H*$_3$), 0.99 (*s*, 9 H, -C(C*H*$_3$)$_3$), 1.81 (*m*, 1 H, -C*H*-CH$_3$), 3.50* and 3.72 (*d* and *b*, *J*=11.3 and ca. 4, 1 H, -N-C*H*D-), 7.71 (*m*, 2 H, Phth), 7.83 (*m*, 2 H, Phth). ^{13}C-NMR: 12.80 (-CH-*C*H$_3$), 27.30 (-C(*C*H$_3$)$_3$), 32.55 (-*C*(CH$_3$)$_3$), 40.50 (*t*, *J*=20.7, -N-*C*HD), 41.73 (-*C*H-CH$_3$), 122.99 (*o*-Phth), 132.03 (*i*-Phth), 133.67 (*m*-Phth), 168.55 (N(CO)). MS (EI): 246 (14, M$^+$), 190 (68), 161 (100), 57 (50). Anal. calc. for C$_{15}$H$_{18}$DNO$_2$ (246.33): C 73.14, H 7.37, N 5.69; found: C 72.98, H 7.63, N 5.58.

Independent synthesis

(2*R*,3*S*)-3-Methyl-2-phthalimido-pentanol (31). A solution of 626 mg (5.34 mmol) isoleucinol (**30**) and 871 mg (5.88 mmol) phthalic anhydride in 8 ml DMF were stirred at 150°C under argon for 1 h. After cooling to room temperature, the reaction mixture was poured onto 60 ml of water and the aqueous phase was extracted with CH$_2$Cl$_2$ (3x). The combined organic phases were dried over MgSO$_4$ and concentrated. FC (hexane/ethyl acetate 3:1) yielded 859 mg (65%) of phthalimide **31** as a colourless oil. IR (neat): 3461, 2966, 1772, 1704, 1467, 1393, 1370, 1070, 1022, 723. ^{1}H-NMR: 0.84 (*t*, *J*=7.3, 3 H, C*H*$_3$-CH$_2$-), 1.06 (*d*, *J*=6.7, 3 H, C*H*$_3$-CH-), 1.10 and 1.31 (2*m*, 2 H, CH$_3$-C*H*$_2$-), 2.31 (*m*, 1 H, CH$_3$-C*H*-), 2.74 (*b*, 1 H, O*H*), 3.91 (*dd*, *J*=2.0, 11.3, 1 H, HO-C*H*H'-), 4.10 (*ddd*, *J*=2.4, 7.3, 9.7,1 H, -N-C*H*-), 4.15 (*dd*, *J*=7.4, 11.3, 1 H, HO-CH*H*'-), 7.85 (*m*, 2 H, Phth), 7.73 (*m*, 2 H, Phth). ^{13}C-NMR: 10.38 (*C*H$_3$-CH$_2$-), 15.70 (*C*H$_3$-CH-

), 25.74 (CH_3-CH_2-), 32.78 (CH_3-C*H*-), 58.29 (-N-CH-), 61.75 (-CH_2-OH), 123.17 (*p*-Phth), 131.50 (*i*-Phth), 133.91 (*m*-Phth), 169.23 (N(CO)). MS (EI): 247 (1, M^+), 216 (96), 160 (100). Anal. calc. for $C_{14}H_{17}NO_3$ (247.29): C 68.00, H 6.93, N 5.66; found: C 67.90, H 6.82, N 5.62.

(2*S*,3*S*)-3-Methyl-2-phthalimido-pentanal (32). To 60 ml of CH_2Cl_2 at -60°C were added under argon 495 mg (335 µl, 3.90 mmol) of oxalyl chloride and 507 mg (461 µl, 6.49 mmol) of DMSO. After 3 min, 803 mg (3.25 mmol) of alcohol **31** in 11 ml of CH_2Cl_2 were added dropwise and, after 1 h, 1.32 g (1.81 ml, 13.0 mmol) of NEt_3 were added. The reaction mixture was stirred for 5 min, quenched with water and warmed to room temperature. The aqueous phase was extracted with CH_2Cl_2 (2x). The organic phase was washed successively with 1% aq. HCl, water, 5% aq. Na_2CO_3-sol. and brine, dried over $MgSO_4$ and concentrated to give 783 mg (98%) of crude aldehyde **32**. This was used immediately in the next step to prevent epimerization. The aldehyde **32** could be purified by FC (hexane/ethyl acetate 4:1). IR (neat): 2967, 2877, 1776, 1715, 1467, 1384, 877, 720. ^{1}H-NMR: 0.89 (*t*, *J*=7.4, 3 H, C*H*$_3$-CH_2-), 1.13 (*m*, 1 H, CH_3-C*H*H'-), 1.22 (*d*, *J*=6.6, 3 H, C*H*$_3$-CH-), 1.47 (*m*, 1 H, CH_3-CH*H*'-), 2.57 (*m*, 1 H, CH_3-C*H*-), 4.46 (*d*, *J*=9.3, 1 H, -C*H*-CHO), 7.89 (*m*, 2 H, Phth), 7.76 (*m*, 2 H, Phth), 9.85 (*s*, 1 H, -CHO). ^{13}C-NMR: 10.31 (*C*H_3-CH_2-), 16.30 (*C*H_3-CH-), 25.70 (CH_3-*C*H_2-), 33.23 (CH_3-*C*H-), 63.19 (-*C*H-CHO), 123.44 (*o*-Phth), 131.47 (*i*-Phth), 134.19 (*m*-Phth), 167.78 (-N(CO)-), 196.40 (CHO-). MS (EI): 216 (41), 160 (100). Anal. calc. for $C_{14}H_{15}NO_3$ (245.28): C 68.56, H 6.16, N 5.71; found: C 68.40, H 6.30, N 5.81.

Methyl *E*-(4*S*,5*S*)-5-methyl-4-phthalimido-hept-2-enoate (33). A suspension of 680 mg (2.77 mmol) aldehyde **32** and 1.11 g (3.33 mmol) methoxycarbonyl methylene-triphenylphosphorane in 4 ml of benzene was stirred under argon at 40°C for 2 h. The reaction mixture was quenched with water and extracted with CH_2Cl_2 (3x). The combined organic phases were dried over $MgSO_4$ and concentrated. After FC (hexane/ethyl acetate 4:1) 792 mg (95%) of alkene **33** were obtained as a colourless oil. IR (neat): 2966, 1772, 1706, 1467, 1385, 1234, 1179, 1073, 721. ^{1}H-NMR: 0.85 (*t*, *J*=7.5, 3 H, C*H*$_3$-CH_2-), 0.98 (*d*, *J*=6.8, 3 H, C*H*$_3$-CH-), 1.07 and 1.40 (2*m*, 2 H, CH_3-C*H*$_2$-), 2.45 (*m*, 1 H, CH_3-C*H*-), 3.72 (*s*, 3 H, -CO_2CH_3), 4.52 (*ddd*, *J*=0.8, 9.7, 10.5, 1 H, =CH-C*H*-), 5.97 (*dd*, *J*=1.0, 15.6, 1 H, =C*H*-CO_2CH_3), 7.29 (*dd*, *J*=8.8, 15.7, 1 H, =C*H*-CH-), 7.73 (*m*, 2 H, Phth), 7.85 (*m*, 2 H, Phth). ^{13}C-NMR: 10.35 (*C*H_3-CH_2-), 16.21 (*C*H_3-CH-), 25.51 (CH_3-*C*H_2-), 34.80 (CH_3-*C*H-), 51.61 (-CO_2*C*H_3), 57.30 (=CH-*C*H-), 123.32 (*o*-Phth), 124.20 (=*C*H-CH-), 131.60 (*i*-Phth), 134.06 (*m*-Phth), 143.59 (=*C*H-CO_2CH_3), 166.15 (-*C*O_2CH_3), 167.74 (N(CO)). MS (EI): 270 (10), 244 (100), 213 (74), 184 (68). Anal. calc. for $C_{17}H_{19}NO_4$ (301.34): C 67.76, H 6.36, N 4.65; found: C 67.80, H 6.49, N 4.50.

Methyl (4*R*,5*S*)-5-methyl-4-phthalimido-heptanoate (28a). A solution of 666 mg (2.21 mmol) alkene **33** in 12 ml ethanol was treated with 66 mg of Pd/C (10%) and stirred under hydrogen for 6 h. The reaction mixture was filtered through Celite and concentrated. After FC (hexane/ethyl acetate 5:1), 623 mg (93%) of ester **28a** were obtained as a colourless oil. IR (neat): 2967, 2878, 1773, 1738, 1712, 1467, 1389, 1367, 1174, 723. ^{1}H-NMR: 0.82 (*t*, *J*=7.4, 3 H, C*H*$_3$-CH_2-), 1.03 (*m*, 1 H, CH_3-C*H*H'-), 1.04 (*d*, *J*=6.7, 3 H, C*H*$_3$-CH-), 1.34 (*m*, 1 H, CH_3-CH*H*'-), 2.41 and 2.22 (2*m*, 5 H, CH_3-C*H*- and -C*H*$_2$-C*H*$_2$-CO_2CH_3), 3.58 (*s*, 3 H, -CO_2C*H*$_3$), 3.94 (*ddd*, *J*=3.5, 10.0, 11.5, 1 H, -N-CH-), 7.72 (*m*, 2 H, Phth), 7.83 Hz (*m*, 2

H, Phth). ^{13}C-NMR: 10.56 (CH_3-CH_2-), 16.23 (CH_3-CH-), 24.73 (-CH_2-CH_2-CO_2CH_3), 26.00 (CH_3-CH_2-), 31.31 (-CH_2-CO_2CH_3), 36.11 (CH_3-CH-), 51.54 (-CO_2CH_3), 56.22 (-N-CH-), 123.16 (*o*-Phth), 131.56 (*i*-Phth), 133.91 (*m*-Phth), 168.66 (N(CO)), 173.12 (-CO_2CH_3).

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