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Parallel synthesis of homochiral β-amino acids

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Abstract—The parallel asymmetric synthesis of an array of 30 β-amino acids of high enantiomeric purity using the conjugate addition of homochiral lithium *N*-benzyl-*N*-(α-methylbenzyl)amide as the key step is accomplished. The experimental simplicity and highly practical nature of the protocol is demonstrated by the efficient parallel conversion of 15 α,β-unsaturated esters to both enantiomeric series of the corresponding β-amino acids in high overall yields and selectivities with minimal purification involved in each step of the reaction protocol.

1. Introduction

Rapid progress has been made in recent years in the practice of a high throughput screening of compounds for biological testing. This procedure has ensured that synthetic chemists are constantly striving to develop new and efficient protocols for the production of arrays of compounds in a rapid and efficient way. Although the syntheses of numerous libraries of compounds using parallel synthesis have been reported, the vast majority of these arrays have been concerned with the preparation of achiral compounds, with limited characterisation data reported.[1]

The pharmacological activities of a variety of β-amino acids and their derivatives have been well documented.[2] For example, the α-hydroxy-β-phenylalanine component of Taxol®, a potent anti-cancer agent, was found to be essential to its anti-tumour activity[3] and (*S*)-β-tyrosine was found to be a key component of the antibiotic edeine A.[4] In addition, the pharmacological and conformational properties of synthetic peptides derived from β-amino acids have been receiving increasing attention.[5] The development of generally applicable, robust methodologies towards the asymmetric synthesis of β-amino acids and derivatives is of widespread interest to the synthetic community with numerous routes described in the literature.[6] These include Arndt-Eistert homologation of α-amino acids,[7] enzymatic resolutions,[8] stereoselective Mannich reactions,[9] the conjugate addition of amines to homochiral α,β-unsaturated esters,[10] the addition of *N*-benzylhydroxylamines to imides,[11] the catalytic reduction of β-amino crotonates[12] or β-acylamino acrylates[13] and the dipolar cycloaddition of homochiral nitrones[14] among others.[15] We have previously shown that the conjugate addition of homochiral lithium amides derived from α-methylbenzylamine to α,β-unsaturated esters may be used as a general route to allow the asymmetric synthesis of β-amino acid derivatives.[16,17]

Herein, the highly practical nature of this protocol is demonstrated by the parallel generation of an array of homochiral β-amino acids. These β-amino acids and the corresponding intermediate β-amino esters may be subsequently elaborated to generate libraries of β-amino acid derivatives and evaluated as organocatalysts in a variety of reaction manifolds.[18] To demonstrate both the experimental simplicity and synthetic versatility of this methodology, all reactions in this series were performed using a Radleys Carousel™ reaction station,[19] enabling the simultaneous completion of twelve reactions at once, with minimal purification involved in each step of the reaction protocol.

2. Results and discussion

2.1. Parallel synthesis of α,β-unsaturated esters; application of Horner–Wadsworth–Emmons methodology

In order to generate the desired array of β-amino acids from readily available starting materials, our synthetic strategy required a range of (*E*)-α,β-unsaturated ester substrates to undergo conjugate addition, which it was

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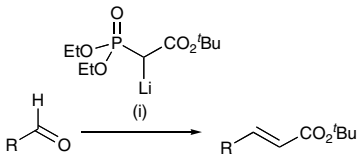


2-16

	R	Yield (%)	d.e.[20] (%)	Purity* (%)
2	Me	93	>95	>99
3	$(CH_3)_2CHCH_2$	89	>96	94.8
4	$CH_3(CH_2)_6$	93	>97	>99
5	4-(MeO)C_6H_4	89	>98	>99
6	3-(MeO)C_6H_4	93	>98	>99
7	2-(MeO)C_6H_4	88	>98	99.0
8	3,5-$(MeO)_2C_6H_3$	94	>98	>99
9	3,4-$(MeO)_2C_6H_3$	95	>98	99.3
10	2,4-$(MeO)_2C_6H_3$	78	>98	98.6
11	Ph	96	>98	>99
12	4-PhC_6H_4	87	>98	98.7
13	Piperon-3-yl	93	>98	>99
14	3-(BnO)C_6H_4	93	>98	>99
15	4-(BnO)C_6H_4	96	>98	98.8
16	3,4-$(BnO)_2C_6H_3$	93	>98	>99

Scheme 1. Reagents and conditions: (i) $(EtO)_2POCH(Li)CO_2{}^tBu$ **1**, THF, −78 °C to rt; *Purity determined by HPLC analysis.

envisaged could be readily prepared using Horner–Wadsworth–Emmons methodology from the corresponding aldehydes. In this manner, a range of commercially available alkyl and aryl aldehydes were treated with the lithium anion of *tert*-butyl diethylphosphonoacetate **1**, furnishing *tert*-butyl (*E*)-α,β-unsaturated esters **2**–**16** with a high diastereoselectivity (generally >98% de).[20] Purification of the desired α,β-unsaturated esters was carried out by chromatography on silica gel in an SPE tube on a Baker SPE manifold, which enabled simultaneous purification of all samples, giving the desired range of *tert*-butyl (*E*)-β-alkyl- and (*E*)-β-aryl-α,β-unsaturated esters **2**–**16** in high yields (78–96%) and in high de (>98% de) and in >94% purity as shown by HPLC analysis (Scheme 1).

2.2. Parallel synthesis of β-amino esters; conjugate addition of lithium (*R*)- or (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amide 17

With a range of α,β-unsaturated esters **2**–**16** in hand, conjugate addition of homochiral lithium (*R*)- and (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amide **17** (>98% ee) to each conjugate acceptor was followed. Following our standard protocol, addition of each of the α,β-unsaturated esters **2**–**16** to a THF solution of either lithium (*R*)- or (*S*)-amides **17** at −78 °C in THF proceeded to high conversion, giving each antipode of the β-amino esters **18**–**32** in uniformly high de (>95%). The absolute configuration at C(3) within β-amino esters **18**–**32** was assigned by analogy with previous models developed to explain the stereoselectivity observed during the addition of lithium amide **17** to α,β-unsaturated acceptors,[14] relative to the known configuration of the α-methylbenzyl stereocentre. Subsequent chromatographic purification using a BAKERBOND spe™ manifold[21] gave each antipode of β-amino esters **18**–**32** in excellent yield (79–98%) and in high de (>95%) in each case (Scheme 2).

2.3. Parallel synthesis of β-amino acids

With an array of β-amino esters **18**–**32** available in each enantiomeric series, deprotection to the corresponding β-amino acids was investigated. We have previously demonstrated that N-debenzylation of *N*-benzyl-*N*-α-methylbenzyl protected tertiary β-amino esters by catalytic hydrogenolysis is an efficient method for N-deprotection in these systems. Although this deprotection is typically achieved under 5 atm of hydrogen, this protocol is unsuitable for parallel synthesis using the Radleys Carousel™ reaction station, which necessitated the cleavage of the *N*-benzyl protecting groups of β-amino esters **18**–**32** under a hydrogen pressure of 1 atm. As the addition of acid is known to promote N-debenzylation,[16] the deprotection of β-amino esters **18**–**32** to their corresponding primary β-amino esters was carried out in a methanol/acetic acid/water mixture (40:4:1 v/v/v) using $Pd(OH)_2$ on C under a hydrogen balloon. After filtration through Celite to remove the heterogenous catalyst and concentration of the resulting reaction mixture, the crude product was subjected to chromatographic purification, giving the desired β-amino esters **33**–**47** in 73–93% yield (Scheme 3).

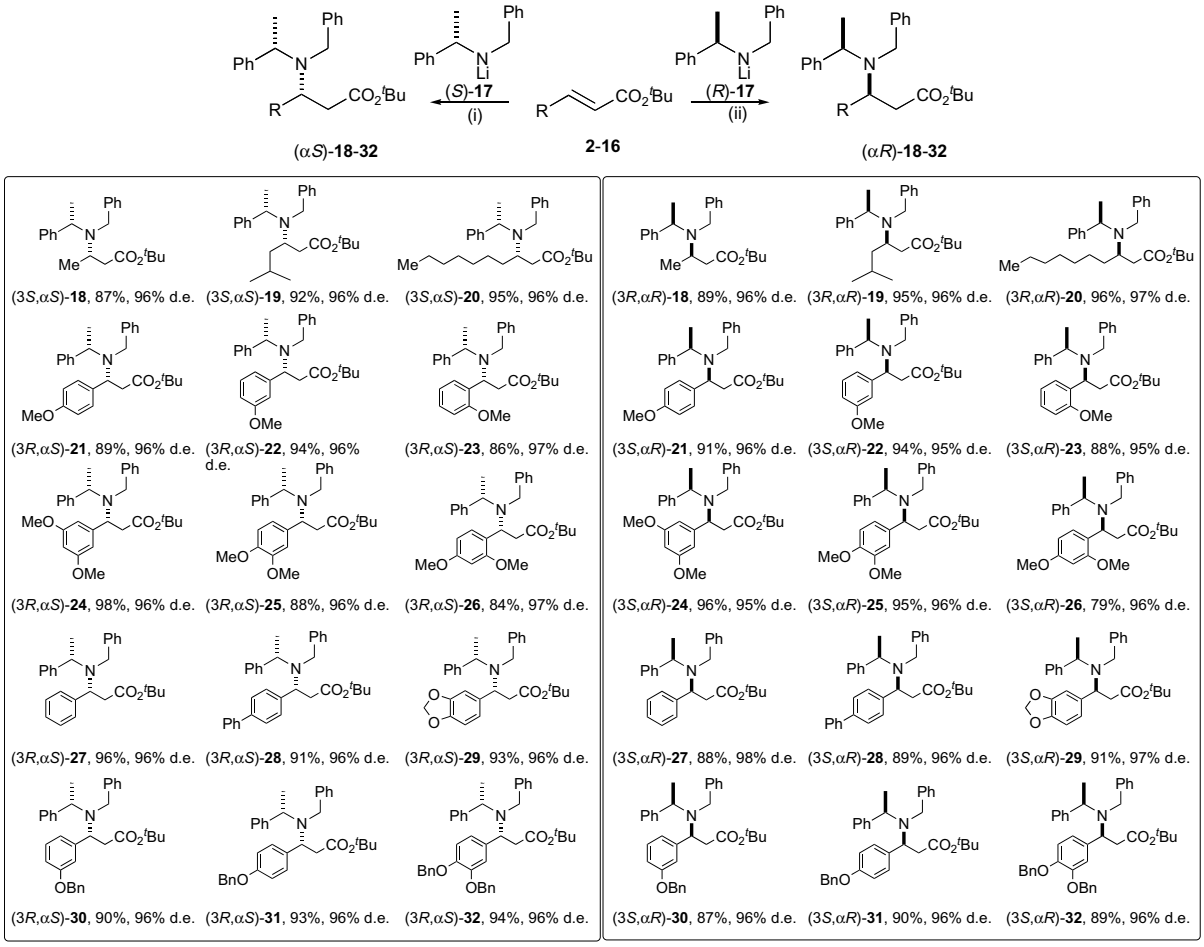
Subsequent ester hydrolysis of β-amino esters **33**–**47** by treatment with TFA, conversion to the corresponding hydrochloride salts and ion exchange chromatography yielded the free β-amino acids **48**–**61** in uniformly excellent yields (92–99%). The only exceptions to this protocol involved the isolation of (*R*)- and (*S*)-**58** as their hydrochloride salts due to the limited solubility of the free amino acids, and (*R*)- and (*S*)-**62** as their hydrochloride salts due to decomposition upon ion exchange chromatography (Scheme 4).

In conclusion, the generality and practicality of the highly diastereoselective conjugate addition reaction of homochiral lithium amides derived from α-methylbenzylamine with an array of β-alkyl and β-aryl α,β-unsaturated esters have been demonstrated. The resulting array of tertiary β-amino esters were readily deprotected by N-debenzylation via hydrogenolysis and subsequent ester hydrolysis afforded the corresponding β-amino acids in high yield and ee. The further functionalisation and elaboration of the intermediate β-amino esters to generate libraries of β-amino acid derivatives and the assessment of the corresponding β-amino acids as organocatalysts are currently underway in our laboratory.

3. Experimental

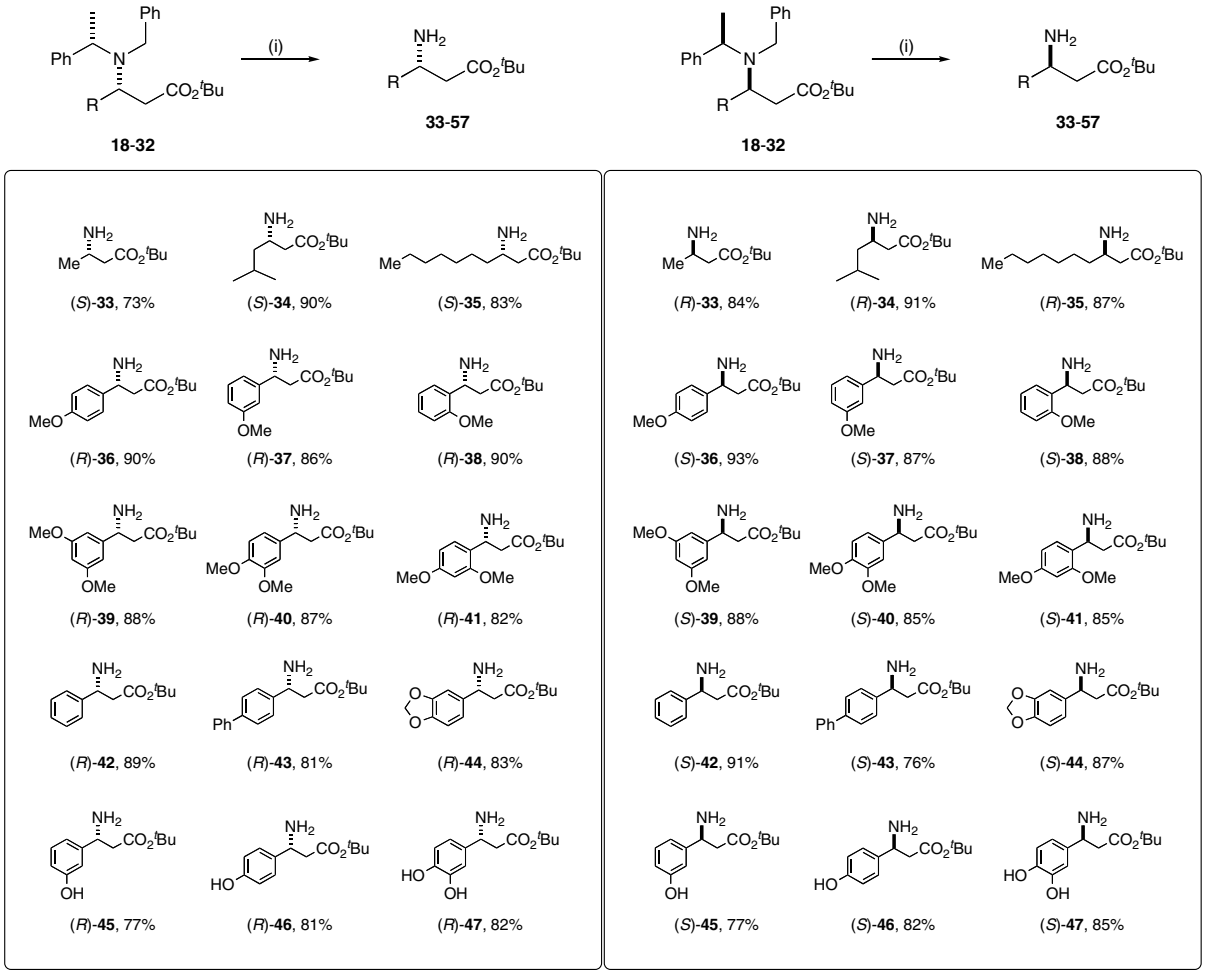
3.1. General experimental

All reactions involving organometallic or other moisture sensitive reagents were performed under an atmosphere



Scheme 2. Reagents and conditions: (i) (*S*)-**17**, THF, −78 °C, 2 h; (ii) (*R*)-**17**, THF, −78 °C, 2 h.

of nitrogen via standard vacuum line techniques. All glassware were flame-dried and allowed to cool under vacuum. THF was distilled under an atmosphere of dry nitrogen from sodium benzophenone ketyl. Water was distilled. *n*-Butyllithium was used as a solution in hexanes at the molarity stated. All other solvents and reagents were used as supplied (Analytical or HPLC grade), without prior purification. The reactions were dried with $MgSO_4$. Thin-layer chromatography (TLC) was performed on aluminium sheets coated with 60 F_{254} silica. Sheets were visualised using iodine, UV light or 1% aqueous $KMnO_4$ solution. Flash chromatography was performed on Kieselgel 60 silica. Nuclear magnetic resonance (NMR) spectra were recorded on Bruker DPX 400 (^{1}H: 400 MHz and ^{13}C: 100.6 MHz), AMX 500 (^{1}H: 500 MHz and ^{13}C: 125.3 MHz), Bruker W-H 300 (^{1}H: 300 MHz) or Varian 200 (^{1}H: 200 MHz) spectrometers in the deuterated solvent stated. All chemical shifts (δ) are quoted in parts per million and coupling constants (J) in hertz. Coupling constants are quoted twice, each being recorded as observed in the spectrum without averaging. Residual signals from the solvents were used as an internal reference. ^{13}C multiplicities were assigned using a DEPT sequence. In all cases, the reactions diastereoselectivity was assessed by peak integration of the ^{1}H NMR spectrum of the crude reaction mixture. Infrared spectra were recorded on a Perkin–Elmer 1750 IR Fourier Transform spectrophotometer using either thin films on NaCl plates (film) or KBr discs (KBr) as stated. Only the characteristic peaks are quoted. Low resolution mass spectra (m/z) were recorded on B.G. micromass ZAB 2F instrument, VG MassLab 20-250 or Micromass Platform 1 spectrometers and high resolution mass spectra (HRMS) on a Micromass Autospec 500 OAT spectrometer or on a Waters 2790 Micromass LCT Exact Mass Electrospray Ionisation Mass Spectrometer. The techniques used were chemical ionisation (CI, NH_3), atmospheric pressure chemical ionisation (APCI) or electrospray ionisation (ESI) using partial purification by HPLC with methanol/acetonitrile/water (40:40:20 v/v/v) as eluent. Optical rotations were recorded on a Perkin–Elmer 241 polarimeter with a water-jacketed 10 cm cell and specific rotations are given in units of 10^{-1} deg cm^2 g^{-1}. Concentrations are quoted in g/100 mL. Melting points were recorded on a Leica VMTG Galen III apparatus and are uncorrected. High-performance liquid chromatography (HPLC) was performed on a Gilson instrument equipped with Gilson 306 pumps, a Gilson 811C dynamic mixer, a Gilson 806 manometric module with an automated sample injection on a Gilson 215 Liquid Handler, configured with a Gilson 819 valve actuator. Separations were performed on a Varian Omnisphere 5 C18 (analytical) column (5 μm particle size, 150.0 mm × 4.6 mm). All experiments were performed under gradient elution with a flow rate of 1.0 mL/min: solvent A (H_2O containing 0.1% (v/v) TFA) and solvent B (CH_3CN), starting



Scheme 3. Reagents and conditions: (i) H_2 (1 atm), $Pd(OH)_2/C$, MeOH, H_2O, AcOH, rt, 15 h.

from 95% A, 5% B to 5% A, 95% B over 8 min then isocratic for 4 min. Absorption was measured at wavelengths of 220, 254 and 290 nm using a Gilson 170 Diode Array Detector.

3.2. Representative procedure 1

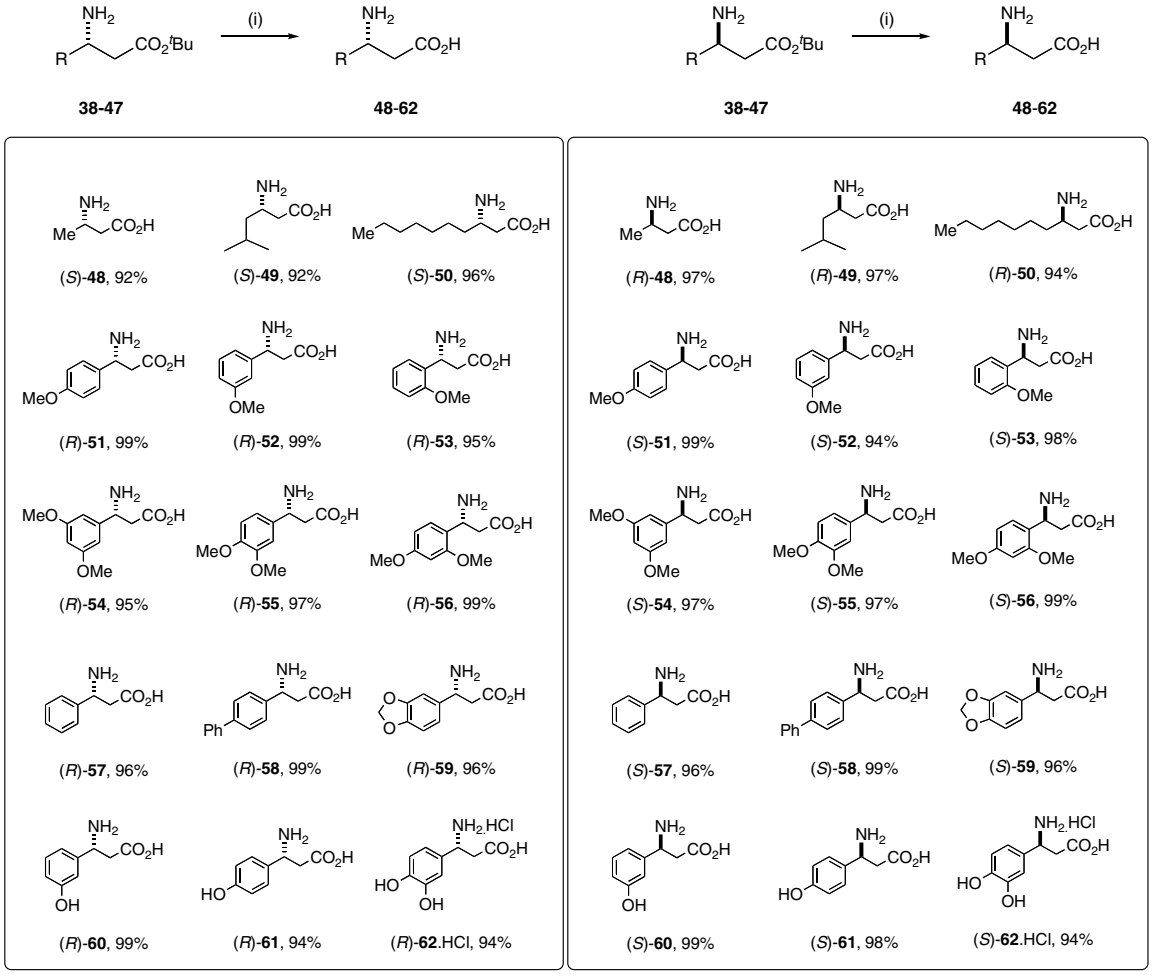
To a stirred solution of *tert*-butyl diethylphosphonoacetate (4.40 g, 17.4 mmol) in THF (15 mL) was slowly added *n*-BuLi (7.0 mL, 2.5 M in hexanes, 17.4 mmol) with cooling to −78 °C. After stirring for 30 min at −78 °C, a solution of the aldehyde (16.0 mmol) also cooled to −78 °C was transferred via a cannula. The resulting solution was stirred at −78 °C for 30 min before being allowed to warm to rt. The solution was subsequently cooled back to −78 °C and quenched with satd aq NH_4Cl (10 mL). The product was extracted with dichloromethane (3 × 20 mL) and the combined organic extracts were dried (Na_2SO_4), and the solvent was removed in vacuo to yield the crude product. The excess phosphonate was removed by passing through a plug of silica (DCM eluent) to yield the products which were used without further purification.

3.3. Representative procedure 2

To a stirred solution of (*R*)- or (*S*)-*N*-benzyl-*N*-α-methylbenzylamine (1.86 g, 8.8 mmol) in THF (10 mL) was slowly added *n*-BuLi (3.5 mL, 2.5 M in hexanes, 8.8 mmol) with cooling to −78 °C. After 30 min, a solution of α,β-unsaturated ester (5.5 mmol) also at −78 °C was transferred via a cannula. The resulting solution was stirred at −78 °C for 3h before quenching with saturated aqueous NH_4Cl (5 mL). Upon warming to room temperature, the product was extracted with DCM. The organic fractions were combined, dried (Na_2SO_4) and the solvent was removed in vacuo. The residue was taken up in DCM and the excess auxiliary extracted with 10% aq citric acid. The organic layer was washed with saturated aqueous sodium bicarbonate, dried (Na_2SO_4) and the solvent removed in vacuo to yield the crude product, which was used without further purification.

3.4. Representative procedure 3

A stirred solution of lithium amide adduct (4.5 mmol) in methanol (20 mL), distilled water (2 mL) and acetic acid (0.5 mL) was degassed before palladium hydroxide on carbon (0.5 g) was added. A hydrogen balloon was attached and the resulting suspension stirred for 24 h under 1 atm of hydrogen. The reaction mixture was filtered through Celite® and the solvent removed in vacuo. The residue was partitioned between dichloromethane (20 mL) and saturated aqueous $NaHCO_3$ (10 mL). The organic phase was



Scheme 4. Reagents and conditions: (i) TFA, DCM, rt, 15 h.

separated and the aqueous phase was extracted with dichloromethane (2 × 20 mL). The combined organic layers were dried (Na_2SO_4) and the solvent removed in vacuo. The residue was purified by passing through a short plug of silica (doped 1% Et_3N; wash 1:1 Et_2O/pentane; elute 9:1 Et_2O/MeOH) to yield the product which was used without further purification.

3.5. Representative procedure 4

Trifluoroacetic acid (1 mL) was added dropwise to a stirred solution of β-amino ester (200 μmol) in dichloromethane (1 mL) under an atmosphere of argon, at room temperature. The solution was stirred for 15 h at room temperature. The solvents were removed in vacuo and co-evaporated with ethereal HCl. The residue was subjected to ion exchange chromatography (Dowex 80W-X8, elute 1 M NH_4OH) to yield the free amino acid.

3.6. *tert*-Butyl (*E*)-but-2-enoate 2

Yield: 2.11 g, 93%; HPLC (MeCN/H_2O) >99%; δ_H (400 MHz, $CDCl_3$) 1.46 (9H, s, C*Me*$_3$), 1.83 (3H, dd, *J* 6.9, 1.4, *Me*), 5.75 (1H, dq, *J* 15.5, 1.4, C*H*CO_2), 6.85 (1H, dq, *J* 15.5, 6.9, C*H*=CHCO_2).

3.6.1. *tert*-Butyl (*E*)-5-methyl-hex-2-enoate 3.

Yield: 2.62 g, 89%; HPLC (MeCN/H_2O) 94.8%; δ_H (400 MHz, $CDCl_3$) 0.92 (6H, d, *J* 6.7, CH*Me*$_2$), 1.48 (9H, s, C*Me*$_3$), 1.69–1.79 (1H, m, C*H*Me$_2$), 2.03–2.08 (2H, m, C*H*$_2$CHMe$_2$), 5.73 (1H, dt, *J* 15.6, 1.2, C*H*CO_2), 6.83 (1H, dt, *J* 15.6, 7.6, C*H*=CHCO_2).

3.6.2. *tert*-Butyl (*E*)-dec-2-enoate 4.

Yield: 3.36 g, 93%; HPLC (MeCN/H_2O) >99%; δ_H (400 MHz, $CDCl_3$) 0.87 (3H, t, *J* 6.8, *Me*), 1.21–1.35 (8H, m, C*H*$_2$), 1.40–1.47 (2H, m, C*H*$_2$CH$_2$CH=CH), 1.47 (9H, s, C*Me*$_3$), 2.11–2.19 (2H, m, C*H*$_2$CH=CH), 5.72 (1H, dt, *J* 15.6, 1.5, C*H*CO_2), 6.85 (1H, dt, *J* 15.6, 7.0, C*H*=CHCO_2).

3.6.3. *tert*-Butyl (*E*)-3-(4-methoxyphenyl)propenoate 5.

Yield: 3.33 g, 89%; mp 40–41 °C (lit.[22] mp 41–44 °C); HPLC (MeCN/H_2O) >99%; δ_H (400 MHz, $CDCl_3$) 1.53 (9H, s, C*Me*$_3$), 3.83 (3H, s, O*Me*), 6.25 (1H, d, *J* 15.6, C*H*CO_2), 6.89 (2H, d, *J* 9.2, *Ar*), 7.46 (2H, d, *J* 9.2, *Ar*), 7.55 (1H, d, *J* 15.6, C*H*=CHCO_2).

3.6.4. *tert*-Butyl (*E*)-3-(3-methoxyphenyl)propenoate 6. Yield: 3.48 g, 93%; HPLC (MeCN/H_2O) >99%; ν_{max}/cm^{-1} (film) 1707, 1638; δ_H (400 MHz, $CDCl_3$) 1.54 (9H, s, CMe_3), 3.82 (3H, s, O*Me*), 6.36 (1H, d, *J* 16.0, C*H*CO_2), 6.89–7.31 (4H, m, *Ar*), 7.56 (1H, d, *J* 16.0, C*H*=CHCO_2); δ_C (100 MHz, $CDCl_3$) 28.2, 55.2, 80.5, 112.7, 115.8, 120.4, 120.7, 129.8, 136.0, 143.4, 159.8, 166.2; *m*/*z* ($APCI^+$) 179 (100%), 161 (100); HRMS (CI^+) 235.1326 ($C_{14}H_{19}O_3$ requires 235.1334).

3.6.5. *tert*-Butyl (*E*)-3-(2-methoxyphenyl)propenoate 7. Yield: 3.60 g, 88%; HPLC (MeCN/H_2O) 99.0%; ν_{max}/cm^{-1} (film) 1706, 1631; δ_H (400 MHz, $CDCl_3$) 1.54 (9H, s, CMe_3), 3.89 (3H, s, O*Me*), 6.45 (1H, d, *J* 16.0, C*H*CO_2), 6.88–7.51 (4H, m, *Ar*), 7.92 (1H, d, *J* 16.0, C*H*=CHCO_2); δ_C (100 MHz, $CDCl_3$) 28.2, 55.4, 80.2, 111.0, 120.6, 120.6, 123.6, 128.7, 131.1, 138.9, 158.2, 166.8; *m*/*z* ($APCI^+$) 179 (100%), 161 (100); HRMS (ESI^+) 235.1339 ($C_{14}H_{19}O_3$ requires 235.1334).

3.6.6. *tert*-Butyl (*E*)-3-(3,5-dimethoxyphenyl)propenoate 8. Yield: 3.99 g, 94%; mp 45–46 °C; HPLC (MeCN/H_2O) >99%; ν_{max}/cm^{-1} ($CHCl_3$) 1702, 1640; δ_H (400 MHz, $CDCl_3$) 1.54 (9H, s, CMe_3), 3.80 (6H, s, O*Me*), 6.34 (1H, d, *J* 15.8, C*H*CO_2), 6.48 (1H, t, *J* 2.3, Ar(4)*H*), 6.65 (2H, d, *J* 2.3, Ar(4)*H* and Ar(6)*H*), 7.50 (1H, d, *J* 15.8, C*H*=CHCO_2); δ_C (100 MHz, $CDCl_3$) 28.6, 55.8, 81.0, 102.8, 106.3, 121.1, 137.0, 144.0, 161.4, 166.6; *m*/*z* ($APCI^+$) 209 (100%), 191 (83); HRMS (CI^+) 264.1261 ($C_{15}H_{20}O_4$ requires 264.1362).

3.6.7. *tert*-Butyl (*E*)-3-(3,4-dimethoxyphenyl)propenoate 9. Yield: 4.00 g, 95%; HPLC (MeCN, H_2O) 99.3%; δ_H (400 MHz, $CDCl_3$) 1.54 (9H, s, CMe_3), 3.90 (3H, s, O*Me*), 3.91 (3H, s, O*Me*), 6.25 (1H, d, *J* 15.8, C*H*CO_2), 6.83–7.10 (3H, m, *Ar*), 7.53 (1H, d, *J* 15.8, C*H*=CHCO_2).

3.6.8. *tert*-Butyl (*E*)-3-(2,4-dimethoxyphenyl)propenoate 10. Yield: 3.66 g, 78%; HPLC (MeCN/H_2O) 98.6%; ν_{max}/cm^{-1} ($CHCl_3$) 1701, 1626; δ_H (400 MHz, $CDCl_3$) 1.53 (9H, s, CMe_3), 3.83 (3H, s, O*Me*), 3.86 (3H, s, O*Me*), 6.36 (1H, d, *J* 16.0, C*H*CO_2), 6.42–6.53 (2H, m, *Ar*), 7.43 (1H, d, *J* 8.6, Ar(6)*H*), 7.83 (1H, d, *J* 16.0, C*H*=CHCO_2); δ_C (100 MHz, $CDCl_3$) 28.2, 55.4, 55.4, 79.9, 98.3, 105.1, 116.7, 118.0, 130.1, 138.8, 159.6, 162.4, 167.3; *m*/*z* ($APCI^+$) 209 (100%), 191 (100); HRMS (CI^+) 265.1443 ($C_{15}H_{21}O_4$ requires 265.1440).

3.6.9. *tert*-Butyl (*E*)-3-phenylpropenoate 11. Yield: 3.47 g, 96%; HPLC (MeCN/H_2O) >99%; δ_H (400 MHz, $CDCl_3$) 1.55 (9H, s, CMe_3), 6.38 (1H, d, *J* 16.2, C*H*CO_2), 7.35–7.56 (5H, m, *Ar*), 7.60 (1H, d, *J* 16.2, C*H*=CHCO_2).

3.6.10. *tert*-Butyl (*E*)-3-(4-biphenyl)propenoate 12. Yield: 3.90 g, 87%; mp 110–111 °C; HPLC (MeCN/H_2O) 98.7%; ν_{max}/cm^{-1} ($CHCl_3$) 1701, 1636; δ_H (400 MHz, $CDCl_3$) 1.58 (9H, s, CMe_3), 6.43 (1H, d, *J* 15.8, C*H*CO_2), 7.23–7.64 (9H, m, *Ar*), 7.65 (1H, d, *J* 15.8, C*H*=CHCO_2); δ_C (100 MHz, $CDCl_3$) 28.2, 80.5, 120.0, 127.0, 127.5, 127.8, 128.4, 128.9, 133.6, 140.2, 142.7, 143.1, 166.4; *m*/*z* ($APCI^+$) 225 (52%), 207 (100); HRMS (CI^+) 280.1469 ($C_{19}H_{20}O_2$ requires 280.1463).

3.6.11. *tert*-Butyl (*E*)-3-piperon-3-ylpropenoate 13. Yield: 3.70 g, 93%; mp 79–80 °C; HPLC (MeCN/H_2O) >99%; ν_{max}/cm^{-1} ($CHCl_3$) 1698, 1633; δ_H (400 MHz, $CDCl_3$) 1.53 (9H, s, CMe_3), 5.99 (2H, s, OCH_2O), 6.20 (1H, d, *J* 16.2, C*H*CO_2), 6.79 (1H, d, *J* 8.0, Ar(5)*H*), 6.97 (1H, dd, *J* 8.0, 1.6, Ar(6)*H*), 7.02 (1H, d, *J* 1.6, Ar(2)*H*), 7.49 (1H, d, *J* 16.2, C*H*=CHCO_2); δ_C (100 MHz, $CDCl_3$) 28.2 (CMe_3), 80.3, 101.4, 106.4, 108.5, 118.1, 124.1, 129.0, 143.2, 148.2, 149.3, 166.5; *m*/*z* ($APCI^+$) 193 (65%), 175 (100); HRMS (ESI^+) 249.1138 ($C_{14}H_{17}O_4$ requires 249.1127).

3.6.12. *tert*-Butyl (*E*)-3-(3-benzyloxyphenyl)propenoate 14. Yield: 4.60 g, 93%; mp 66–67 °C; HPLC (MeCN/H_2O) >99%; ν_{max}/cm^{-1} ($CHCl_3$) 1702, 1638; δ_H (400 MHz, $CDCl_3$) 1.56 (9H, s, CMe_3), 5.09 (2H, s, PhCH_2O), 6.37 (1H, d, *J* 16.0, C*H*CO_2), 6.98–7.48 (10H, m, *Ar*), 7.57 (1H, d, *J* 16.0, C*H*=CHCO_2); δ_C (100 MHz, $CDCl_3$) 28.2, 70.0, 80.5, 113.8, 116.7, 120.5, 120.9, 127.5, 128.1, 128.6, 129.8, 136.1, 136.7, 143.4 (*C*(3)H), 159.0, 166.2; *m*/*z* ($APCI^+$) 255 (100%); HRMS (CI^+) 310.1570 ($C_{20}H_{22}O_3$ requires 310.1569).

3.6.13. *tert*-Butyl (*E*)-3-(4-benzyloxyphenyl)propenoate 15. Yield: 4.72 g, 96%; mp 74–75 °C; HPLC (MeCN/H_2O) 98.8%; ν_{max}/cm^{-1} ($CHCl_3$) 1698, 1634; δ_H (400 MHz, $CDCl_3$) 1.56 (9H, s, CMe_3), 5.10 (2H, s, PhCH_2O), 6.26 (1H, d, *J* 15.8, C*H*CO_2), 6.98 (2H, d, *J* 8.8, Ar(3)*H* and Ar(5)*H*), 7.33–7.50 (7H, m, *Ar*), 7.57 (1H, d, *J* 15.8, C*H*=CHCO_2); δ_C (100 MHz, $CDCl_3$) 28.2, 70.0, 80.2, 115.1, 117.8, 127.5, 127.6, 128.1, 128.6, 129.6, 136.5, 143.1, 160.3, 166.7; *m*/*z* ($APCI^+$) 255 (100%), 237 (45); HRMS (CI^+) 310.1559 ($C_{20}H_{22}O_3$ requires 310.1569).

3.6.14. *tert*-Butyl (*E*)-3-(3,4-dibenzyloxyphenyl)propenoate 16. Yield: 6.18 g, 93%; mp 85–87 °C; HPLC (MeCN/H_2O) >99%; ν_{max}/cm^{-1} ($CHCl_3$) 1698, 1634; δ_H (400 MHz, $CDCl_3$) 1.54 (9H, s, CMe_3), 5.18 (2H, s, PhCH_2O), 5.20 (2H, s, PhCH_2O), 6.20 (1H, d, *J* 15.8, C*H*CO_2), 6.92 (1H, d, *J* 8.3, Ar(2)*H*), 7.04–7.52 (12H, m, *Ar*), 7.49 (1H, d, *J* 15.8, C*H*=CHCO_2); δ_C (100 MHz, $CDCl_3$) 28.2, 70.9, 71.3, 80.3, 113.6, 114.2, 118.1, 122.7, 127.2, 127.3, 127.9, 128.1, 128.5, 136.8, 136.9, 143.3, 148.9, 150.7, 166.5; *m*/*z* ($APCI^+$) 361 (100%), 343 (38); HRMS (CI^+) 416.1994 ($C_{27}H_{28}O_4$ requires 416.1988).

3.6.15. *tert*-Butyl (3*S*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)butanoate (3*S*,α*S*)-18. Yield: 1.69 g, 87%; 96% de; $[\alpha]_D^{25} = +5.1$ (*c* 1.1, $CHCl_3$) {lit.[16] for (3*R*,α*R*)-**18** $[\alpha]_D^{20} = -3.4$ (*c* 1.2, CH_2Cl_2)}; δ_H (500 MHz, $CDCl_3$) 1.12 (3H, d, *J* 7.0, *Me*), 1.34 (3H, d, *J* 7.0, C(α)*Me*), 1.39 (9H, s, CMe_3), 2.02 (1H, dd, *J* 14.3, 9.3, C(2)H_2), 2.26 (1H, dd, *J* 14.3, 4.8, C(2)H_2), 3.40–3.48 (1H, m, C(3)*H*), 3.61 (1H, d, *J* 15.0, PhCH_2), 3.76 (1H, d, *J* 15.0, PhCH_2), 3.90 (1H, q, *J* 7.0, C(α)*H*), 7.20–7.46 (10H, m, *Ar*).

3.6.16. *tert*-Butyl (3*R*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-butanoate (3*R*,α*R*)-18. Yield: 1.73 g, 89%; 96% de; $[\alpha]_D^{25} = -5.2$ (*c* 1.1, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.17. *tert*-Butyl (3*S*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-5-methylhexanoate (3*S*,α*S*)-19. Yield: 2.02 g, 92%; 96% de; $[\alpha]_D^{25} = -3.0$ (*c* 1.4, $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 1712; δ_H (400 MHz, $CDCl_3$) 0.77 (3H, d, *J* 6.5, C(5)*Me*$_2$), 0.89 (3H, d, *J* 6.7, C(5)*Me*$_2$), 0.95–1.03 (1H, m, C(4)H_2), 1.34 (3H, d, *J* 6.9, C(α)*Me*), 1.43 (9H, s, C*Me*$_3$), 1.43–1.50 (1H, m, C(4)H_2), 1.88 (1H, dd, *J* 14.1, 9.9, C(2)H_2), 1.93–2.02 (1H, m, C(5)*H*), 2.08 (1H, dd, *J* 14.1, 3.0, C(2)H_2), 3.32–3.40 (1H, m, C(3)*H*), 3.50 (1H, d, *J* 15.2, PhCH_2), 3.80–3.86 (2H, m, C(α)*H* and PhCH_2), 7.23–7.47 (10H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 21.0, 21.9, 23.8, 24.4, 28.1, 37.6, 43.1, 50.1, 52.3, 58.9, 79.9, 126.5, 126.9, 128.0, 128.0, 128.1, 128.2, 142.4, 143.4, 172.2; *m*/*z* (ESI^+) 396 (100%); HRMS (ESI^+) 396.2895 ($C_{26}H_{38}NO_2$ requires 396.2903).

3.6.18. *tert*-Butyl (3*R*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-5-methylhexanoate (3*R*,α*R*)-19. Yield: 2.08 g, 95%; 96% de; $[\alpha]_D^{25} = +3.2$ (*c* 1.6, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.19. *tert*-Butyl (3*S*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)decanoate (3*S*,α*S*)-20. Yield: 2.29 g, 95%; 96% de; $[\alpha]_D^{25} = -6.4$ (*c* 2.9, $CHCl_3$) {lit.[23] for (3*R*,α*R*)-**20**, $[\alpha]_D^{22} = +5.3$ (*c* 1.03, $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.8, *Me*), 1.19–1.35 (10H, m, CH_2), 1.33 (3H, d, *J* 7.1, C(α)*Me*), 1.41 (9H, s, C*Me*$_3$), 1.42–1.65 (2H, m, C(4)H_2), 1.87 (1H, dd, *J* 14.6, 9.4, C(2)H_2), 1.96 (1H, dd, *J* 14.6, 3.4, C(2)H_2), 3.25–3.34 (1H, m, C(3)*H*), 3.49 (1H, d, *J* 15.2, PhCH_2), 3.66 (1H, d, *J* 15.2, PhCH_2), 3.82 (1H, q, *J* 7.1, C(α)*H*), 7.22–7.47 (10H, m, *Ar*).

3.6.20. *tert*-Butyl (3*R*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)decanoate (3*R*,α*R*)-20. Yield: 2.30 g, 96%; 97% de; $[\alpha]_D^{25} = +6.4$ (*c* 2.1, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.21. *tert*-Butyl (3*R*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(4-methoxyphenyl)propanoate (3*R*,α*S*)-21. Yield: 2.19 g, 89%; 96% de; $[\alpha]_D^{25} = -1.8$ (*c* 3.2, $CHCl_3$) {lit.[16] for (3*S*,α*R*)-**21**, $[\alpha]_D^{20} = +2.2$ (*c* 1.0, $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.24 (9H, s, C*Me*$_3$), 1.27 (3H, d, *J* 6.8, C(α)*Me*), 2.47 (1H, dd, *J* 14.5, 10.1, C(2)H_2), 2.55 (1H, dd, *J* 14.5, 5.2, C(2)H_2), 3.67 (2H, s, PhCH_2), 3.81 (3H, s, O*Me*), 4.01 (1H, *J* 6.8, C(α)*H*), 4.36 (1H, dd, *J* 10.1, 5.2, C(3)*H*), 6.88 (2H, *J* 8.7, Ar(3)*H* and Ar(5)*H*), 7.13–7.43 (13H, m, *Ar*).

3.6.22. *tert*-Butyl (3*S*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(4-methoxyphenyl)propanoate (3*S*,α*R*)-21. Yield: 2.22 g, 91%; 96% de; $[\alpha]_D^{25} = +2.0$ (*c* 2.1, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.23. *tert*-Butyl (3*R*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(3-methoxyphenyl)propanoate (3*R*,α*S*)-22. Yield: 2.31 g, 94%; 96% de; $[\alpha]_D^{25} = -3.2$ (*c* 2.8, $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 1716; δ_H (400 MHz, $CDCl_3$) 1.27 (9H, s, C*Me*$_3$), 1.29 (3H, d, *J* 6.8, C(α)*Me*), 2.49 (1H, dd, *J* 14.5, 9.9, C(2)H_2), 2.55 (1H, dd, *J* 14.5, 5.4, C(2)H_2), 3.70 (2H, s, PhCH_2), 3.83 (3H, s, O*Me*), 4.02 (1H, q, *J* 6.8, C(α)*H*), 4.40 (1H, dd, *J* 9.9, 5.4, C(3)*H*), 6.77–4.48 (14H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 16.7, 27.9, 38.6, 51.0, 55.2, 57.3, 59.7, 80.2, 112.5, 114.3, 120.6, 126.6, 126.9, 127.9, 128.1, 128.1, 128.2, 129.1, 141.8, 143.7, 144.3, 159.6, 171.2; *m*/*z* ($APCI^+$) 446 (100%); HRMS (ESI^+) 446.2696 ($C_{29}H_{36}NO_3$ requires 446.2695).

3.6.24. *tert*-Butyl (3*S*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(3-methoxyphenyl)propanoate (3*S*,α*R*)-22. Yield: 2.30 g, 94%; 95% de; $[\alpha]_D^{25} = +3.3$ (*c* 1.4, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.25. *tert*-Butyl (3*R*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(2-methoxyphenyl)propanoate (3*R*,α*S*)-23. Yield: 2.16 g, 86%; 97% de; $[\alpha]_D^{25} = -13.7$ (*c* 2.0, $CHCl_3$) {lit.[16] for (3*S*,α*R*)-**23**, $[\alpha]_D^{20} = +15.0$ (*c* 0.9, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 1.18 (9H, s, C*Me*$_3$), 1.25 (3H, d, *J* 6.4, C(α)*Me*), 2.59 (1H, dd, *J* 13.5, 9.8, C(2)H_2), 2.63 (1H, dd, *J* 13.5, 6.3, C(2)H_2), 3.73 (2H, AB q, *J* 15.0, PhCH_2), 3.85 (3H, s, O*Me*), 4.08 (1H, q, *J* 6.4, C(α)*H*), 4.86 (1H, dd, *J* 9.8, 6.3, C(3)*H*), 6.85–7.44 (14H, m, *Ar*).

3.6.26. *tert*-Butyl (3*S*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(2-methoxyphenyl)propanoate (3*S*,α*R*)-23. Yield: 2.16 g, 88%; 95% de; $[\alpha]_D^{25} = +13.6$ (*c* 2.6, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.27. *tert*-Butyl (3*R*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(3,5-dimethoxyphenyl)propanoate (3*R*,α*S*)-24. Yield: 2.57 g, 98%; 96% de; $[\alpha]_D^{25} = -1.6$ (*c* 1.1, $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 1717; δ_H (500 MHz, $CDCl_3$) 1.29 (9H, s, C*Me*$_3$), 1.30 (3H, d, *J* 6.5 Hz, C(α)*Me*), 2.46 (1H, dd, *J* 14.6, 10.0, C(2)H_2), 2.53 (1H, dd, *J* 14.6, 5.1, C(2)H_2), 3.70 (2H, AB doublet, *J* 15.0, PhCH_2), 3.80 (6H, s, O*Me*), 4.03 (1H, q, *J* 6.5, C(α)*H*), 4.36 (1H, dd, *J* 10.0, 5.1, C(3)*H*), 6.35–6.37 (1H, m, Ar(4)*H*), 6.60 (2H, d, *J* 2.0, Ar(2)*H* and Ar(6)*H*), 7.20–7.49 (10H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 16.8, 28.0, 38.5, 51.0, 55.3, 57.4, 59.7, 80.3, 99.0, 106.5, 126.6, 126.9, 127.9, 128.1, 128.2, 128.2, 141.7, 144.3, 144.6, 160.6, 171.2; *m*/*z* ($APCI^+$) 476 (100%); HRMS (ESI^+) 476.2804 ($C_{30}H_{38}NO_4$ requires 476.2801).

3.6.28. *tert*-Butyl (3*S*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(3,5-dimethoxyphenyl)propanoate (3*S*,α*R*)-24. Yield: 2.51 g, 96%; 95% de; $[\alpha]_D^{25} = +1.8$ (*c* 1.0, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.29. *tert*-Butyl (3*R*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(3,4-dimethoxyphenyl)propanoate (3*R*,α*S*)-25. Yield: 2.29 g, 88%; 96% de; $[\alpha]_D^{25} = -1.0$ (*c* 1.0, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 1.26 (9H, s, C*Me*$_3$), 1.28 (3H, d, *J* 7.0, C(α)*Me*), 2.48 (1H, dd, *J* 14.6, 10.0, C(2)H_2), 2.55 (1H, dd, *J* 14.6, 5.0, C(2)H_2), 3.68 (2H, AB q, *J* 14.8, PhCH_2), 3.87 (3H, s, O*Me*), 3.91 (3H, s, O*Me*), 3.99 (1H, q, *J* 7.0, C(α)*H*), 4.36 (1H, dd, *J* 10.0, 5.0, C(3)*H*), 6.79–7.48 (13H, m, *Ar*).

3.6.30. *tert*-Butyl (3*S*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(3,4-dimethoxyphenyl)propanoate (3*S*,α*R*)-25. Yield: 2.48 g, 95%; 96% de; $[\alpha]_D^{25} = +1.0$ (*c* 1.1, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.31. *tert*-Butyl (3*R*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(2,4-dimethoxyphenyl)propanoate (3*R*,α*S*)-26. Yield: 2.20 g, 84%; 97% de; $[\alpha]_D^{25} = -8.4$ (*c* 0.8, $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 1718; δ_H (500 MHz, $CDCl_3$) 1.19 (9H, s, C*Me*$_3$), 1.24 (3H, d, *J* 6.5, C(α)*Me*), 2.57 (1H, dd, *J* 14.0, 9.8, C(2)H_2), 2.61 (1H, dd, *J* 14.0, 6.3, C(2)H_2), 3.70 (2H, AB q, *J* 14.8, PhCH_2), 3.81 (6H, s, O*Me*, O*Me*), 4.06 (1H, q, *J* 6.5, C(α)*H*), 4.60 (1H, dd, *J* 9.8, 6.3, C(3)*H*), 6.46 (1H, s, Ar(3)*H*), 7.14–7.47 (12H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 14.6, 27.7, 40.0, 50.8, 53.7, 55.1, 55.3, 56.5, 79.7, 98.4, 103.8, 122.2, 126.2, 126.4, 127.7, 127.9, 128.0, 128.0, 129.7, 142.3, 144.7, 158.9, 159.8, 171.1; *m*/*z* (APCI$^+$) 265 (100%); HRMS (ESI$^+$) 476.2800 ($C_{30}H_{38}NO_4$ requires 476.2801).

3.6.32. *tert*-Butyl (3*S*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(2,4-dimethoxyphenyl)propanoate (3*S*,α*R*)-26. Yield: 2.07 g, 79%; 96% de; $[\alpha]_D^{25} = +8.6$ (*c* 1.0, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.33. *tert*-Butyl (3*R*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-phenylpropanoate (3*R*,α*S*)-27. Yield: 3.47 g, 96%; 96% de; $[\alpha]_D^{25} = -7.2$ (*c* 1.0, $CHCl_3$) {lit.[16] for (3*S*,α*R*)-**27**, $[\alpha]_D^{20} = +3.9$ (*c* 0.7, $CHCl_3$)}; δ_H (500 MHz, $CDCl_3$) 1.24 (9H, s, C*Me*$_3$), 1.28 (3H, d, *J* 6.8, C(α)*Me*), 2.51 (1H, dd, *J* 13.4, 9.8, C(2)H_2), 2.57 (1H, dd, *J* 13.4, 5.3, C(2)H_2), 3.69 (2H, AB doublet, *J* 14.3, PhCH_2), 4.01 (1H, q, *J* 6.8, C(α)*H*), 4.42 (1H, dd, *J* 9.8, 5.3, C(3)*H*), 7.12–7.45 (15H, m, *Ar*).

3.6.34. *tert*-Butyl (3*S*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-phenylpropanoate (3*S*,α*R*)-27. Yield: 3.60 g, 88%; 98% de; $[\alpha]_D^{25} = +7.3$ (*c* 0.8, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.35. *tert*-Butyl (3*R*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(4-biphenyl)propanoate (3*R*,α*S*)-28. Yield: 2.47 g, 91%; 96% de; $[\alpha]_D^{25} = +1.7$ (*c* 1.2, $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 1717; δ_H (500 MHz, $CDCl_3$) 1.26 (9H, s, C*Me*$_3$), 1.32 (3H, d, *J* 6.8, C(α)*Me*), 2.54 (1H, dd, *J* 15.0, 9.7, C(2)H_2), 2.58 (1H, dd, *J* 15.0, 5.0, C(2)H_2), 3.73 (2H, s, PhCH_2), 4.05 (1H, q, *J* 6.8, C(α)*H*), 4.46 (1H, dd, *J* 9.7, 5.0, C(3)*H*), 7.22–7.71 (19H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 16.6, 27.9, 38.6, 51.1, 57.3, 59.5, 80.3, 126.7, 126.9, 127.0, 127.1, 127.3, 128.0, 128.1, 128.3, 128.8, 128.8, 139.9, 141.0, 141.1, 141.8, 144.2, 171.3; *m*/*z* (APCI$^+$) 492 (100%); HRMS (ESI$^+$) 492.2917 ($C_{34}H_{38}NO_2$ requires 492.2903).

3.6.36. *tert*-Butyl (3*S*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(4-biphenyl)propanoate (3*S*,α*R*)-28. Yield: 2.40 g, 89%; 96% de; $[\alpha]_D^{25} = -1.6$ (*c* 1.1, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.37. *tert*-Butyl (3*R*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(piperon-3-yl)propanoate (3*R*,α*S*)-29. Yield: 2.34 g, 93%; 96% de; $[\alpha]_D^{25} = -6.3$ (*c* 1.5, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 1.27 (9H, s, C*Me*$_3$), 1.29 (3H, d, *J* 6.9, C(α)*Me*), 2.41 (1H, dd, *J* 14.5, 10.4, C(2)H_2), 2.51 (1H, dd, *J* 14.5, 4.5, C(2)H_2), 3.67 (2H, s, PhCH_2), 4.00 (1H, q, *J* 6.9, C(α)*H*), 4.31 (1H, dd, *J* 10.4, 4.5, C(3)*H*), 5.96 (2H, s, OCH_2O), 6.76 (1H, d, *J* 8.0, Ar(5)*H*), 6.84 (1H, dd, *J* 8.0, 1.5, Ar(6)*H*), 7.97 (1H, d, *J* 1.5, Ar(2)*H*), 7.16–7.46 (10H, m, *Ar*).

3.6.38. *tert*-Butyl (3*S*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(piperon-3-yl)propanoate (3*S*,α*R*)-29. Yield: 2.29 g, 91%; 97% de; $[\alpha]_D^{25} = +5.9$ (*c* 1.2, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.39. *tert*-Butyl (3*R*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(3-benzyloxyphenyl)propanoate (3*R*,α*S*)-30. Yield: 2.58 g, 90%; 96% de; $[\alpha]_D^{25} = -2.5$ (*c* 1.5, $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 1717; δ_H (500 MHz, $CDCl_3$) 1.26 (3H, d, *J* 6.8, C(α)*Me*), 1.27 (9H, s, C*Me*$_3$), 2.49 (1H, dd, *J* 12.7, 9.7, C(2)H_2), 2.55 (1H, dd, *J* 12.7, *J* 5.3, C(2)H_2), 3.68 (2H, s, PhCH_2N), 4.00 (1H, q, *J* 6.8, C(α)*H*), 4.39 (1H, dd, *J* 9.7, 5.3, C(3)*H*), 5.10 (2H, s, PhCH_2O), 6.90–7.54 (19H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 16.6, 28.0, 38.6, 51.0, 57.2, 59.7, 70.0, 80.3, 113.7, 115.1, 120.9, 126.6, 126.9, 127.5, 128.0, 128.1, 128.2, 128.7, 129.2, 137.3, 141.8, 143.7, 144.2, 158.8, 171.2; *m*/*z* (APCI$^+$) 522 (100%); HRMS (ESI$^+$) 522.3002 ($C_{35}H_{40}NO_3$ requires 522.3008).

3.6.40. *tert*-Butyl (3*S*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(3-benzyloxyphenyl)propanoate (3*S*,α*R*)-30. Yield: 2.50 g, 87%; 96% de; $[\alpha]_D^{25} = +2.7$ (*c* 1.1, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.41. *tert*-Butyl (3*R*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(4-benzyloxyphenyl)propanoate (3*R*,α*S*)-31. Yield: 2.66 g, 93%; 96% de; $[\alpha]_D^{25} = -2.1$ (*c* 1.4, $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 1714; δ_H (500 MHz, $CDCl_3$) 1.23 (9H, s, C*Me*$_3$), 1.27 (3H, d, *J* 7.0, C(α)*Me*), 2.46 (1H, dd, *J* 14.5, 10.4, C(2)H_2), 2.54 (1H, dd, *J* 14.5, 4.5, C(2)H_2), 3.67 (2H, s, PhCH_2N), 4.00 (1H, q, *J* 7.0, C(α)*H*), 4.36 (1H, dd, *J* 10.4, 4.5, C(3)*H*), 5.07 (2H, s, PhCH_2O), 6.95 (2H, d, *J* 8.5, Ar(3)*H* and Ar(5)*H*), 7.22–7.52 (17H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 16.5, 27.9, 38.8, 50.9, 57.2, 59.3, 70.0, 80.2, 114.5, 126.6, 126.9, 127.6, 127.9, 128.0, 128.2, 128.6, 129.4, 134.3, 137.2, 142.0, 144.4, 157.9, 171.3; *m*/*z* (APCI$^+$) 522 (21%), 311 (100); HRMS (ESI$^+$) 522.3007 ($C_{35}H_{40}NO_3$ requires 522.3008).

3.6.42. *tert*-Butyl (3*S*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(4-benzyloxyphenyl)propanoate (3*S*,α*R*)-31. Yield: 2.61 g, 90%; 96% de; $[\alpha]_D^{25} = +2.0$ (*c* 1.0, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.43. *tert*-Butyl (3*R*,α*S*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(3,4-dibenzyloxyphenyl)propanoate (3*R*,α*S*)-32. Yield: 3.24 g, 94%; 96% de; $[\alpha]_D^{25} = +2.2$ (*c* 2.3,

$CHCl_3$) {lit.[16] for (3*S*,α*R*)-**32**, $[\alpha]_D^{22} = -2.0$ (*c* 1.4, $CHCl_3$)}; δ_H (500 MHz, $CDCl_3$) 1.18 (3H, d, *J* 6.8, C(α)*Me*), 1.24 (9H, s, C*Me*$_3$), 2.43 (1H, dd, *J* 14.5, 10.1, C(2)*H*$_2$), 2.51 (1H, dd, *J* 14.5, 5.0, C(2)*H*$_2$), 3.62 (2H, s, PhC*H*$_2$*N*), 3.93 (1H, q, *J* 6.8, C(α)*H*), 4.29 (1H, dd, *J* 10.1, 5.0, C(3)*H*), 5.18 (2H, s, PhC*H*$_2$O), 5.21 (2H, s, PhC*H*$_2$O), 6.97–7.61 (23H, m, *Ar*).

3.6.44. *tert*-Butyl (3*S*,α*R*)-3-(*N*-benzyl-*N*-α-methylbenzylamino)-3-(3,4-dibenzyloxyphenyl)propanoate (3*S*,α*R*)-32. Yield: 3.08 g, 89%; 96% de; $[\alpha]_D^{25} = -2.0$ (*c* 2.2, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.45. *tert*-Butyl (*S*)-3-aminobutanoate (*S*)-33. Yield: 0.52 g, 73%; $[\alpha]_D^{25} = +21.4$ (*c* 0.6, $CHCl_3$); δ_H (200 MHz, $CDCl_3$) 1.12 (3H, d, *J* 6.5, *Me*), 1.42 (9H, s, C*Me*$_3$), 2.28 (1H, dd, *J* 15.7, 8.0, C(2)*H*$_2$), 2.32 (1H, dd, *J* 15.7, 5.4, C(2)*H*$_2$), 3.21–3.39 (1H, m, C(3)*H*).

3.6.46. *tert*-Butyl (*R*)-3-aminobutanoate (*R*)-33. Yield: 0.60 g, 84%; $[\alpha]_D^{25} = -22.2$ (*c* 0.5, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.47. *tert*-Butyl (*S*)-3-amino-5-methylhexanoate (*S*)-34. Yield: 0.81 g, 90%; $[\alpha]_D^{25} = +21.2$ (*c* 2.9, $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$) 3385, 1726; δ_H (200 MHz, $CDCl_3$) 0.83 (3H, d, *J* 6.6, C(5)*Me*$_2$), 0.85 (3H, d, *J* 6.6, C(5)*Me*$_2$), 1.22–1.42 (2H, m, C(4)*H*$_2$), 1.43 (9H, s, C*Me*$_3$), 1.55–1.77 (1H, m, C(5)*H*), 2.34–2.55 (2H, m, C(2)*H*$_2$), 3.28–3.41 (1H, m, C(3)*H*); δ_C (100 MHz, $CDCl_3$) 22.0, 22.2, 24.6, 28.1, 44.3, 46.2, 46.7, 80.4, 172.0; *m*/*z* (ESI^+) 202 (100%); HRMS (ESI^+) 202.1813 ($C_{11}H_{24}NO_2$ requires 202.1807).

3.6.48. *tert*-Butyl (*R*)-3-amino-5-methylhexanoate (*R*)-34. Yield: 0.82 g, 91%; $[\alpha]_D^{25} = -21.1$ (*c* 2.5, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.49. *tert*-Butyl (*S*)-3-aminodecanoate (*S*)-35. Yield: 0.91 g, 83%; $[\alpha]_D^{25} = +11.2$ (*c* 1.4, $CHCl_3$) {lit.[23] for (*R*)-**35**, $[\alpha]_D^{25} = -6.5$ (*c* 0.8, $CHCl_3$)}; δ_H (200 MHz, $CDCl_3$) 0.82 (3H, t. *J* 6.1, *Me*), 1.18–1.37 (12H, m, C*H*$_2$), 1.40 (9H, s, C*Me*$_3$), 1.55 (2H, br s, N*H*$_2$), 2.10 (1H, dd, *J* 16.0, 8.8, C(2)*H*$_2$), 2.30 (1H, dd, *J* 16.0, 4.1, C(2)*H*$_2$), 3.04–3.18 (1H, m, C(3)*H*).

3.6.50. *tert*-Butyl (*R*)-3-aminodecanoate (*R*)-35. Yield: 0.95 g, 87%; $[\alpha]_D^{25} = -11.3$ (*c* 1.3, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.51. *tert*-Butyl (*R*)-3-amino-3-(4-methoxyphenyl)propanoate (*R*)-36. Yield: 1.02 g, 90%; $[\alpha]_D^{25} = -16.4$ (*c* 1.5, $CHCl_3$) {lit.[16] $[\alpha]_D^{20} = -14.1$ (*c* 0.8, $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.42 (9H, s, C*Me*$_3$), 1.73 (2H, br s, N*H*$_2$), 2.50–2.60 (2H, m, C(2)*H*$_2$), 3.80 (3H, s, O*Me*), 4.34 (1H, dd, *J* 7.8, 6.0, C(3)*H*), 6.87 (2H, d, *J* 8.7, Ar(3)*H*, Ar(5)*H*), 7.28 (2H, d, *J* 8.7, Ar(2)*H*, Ar(6)*H*).

3.6.52. *tert*-Butyl (*S*)-3-amino-3-(4-methoxyphenyl)propanoate (*S*)-36. Yield: 1.05 g, 93%; $[\alpha]_D^{25} = +16.5$ (*c* 1.4, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.53. *tert*-Butyl (*R*)-3-amino-3-(3-methoxyphenyl)propanoate (*R*)-37. Yield: 0.97 g, 86%; $[\alpha]_D^{25} = +15.4$ (*c* 1.5, $CHCl_3$); ν_{max}/cm^{-1} (film) 3381, 1724; δ_H (400 MHz, $CDCl_3$) 1.43 (9H, s, C*Me*$_3$), 1.75 (2H, br s, N*H*$_2$), 2.52–2.62 (2H, m, C(2)*H*$_2$), 3.80 (3H, s, O*Me*), 4.35 (1H, app t, *J* 6.8, C(3)*H*), 6.78–6.82 (1H, m, Ar(4)*H*), 6.90–6.95 (1H, m, Ar(6)*H*), 6.93 (1H, s, Ar(2)*H*), 7.21–7.26 (1H, m, Ar(5)*H*); δ_C (100 MHz, $CDCl_3$) 28.1, 45.3, 52.7, 55.2, 80.7, 111.7, 112.8, 118.6, 129.5, 146.5, 159.8, 171.3; *m*/*z* ($APCI^+$) 252 (8%), 196 (100); HRMS (ESI^+) 252.1594 ($C_{14}H_{22}NO_3$ requires 252.1600).

3.6.54. *tert*-Butyl (*S*)-3-amino-3-(3-methoxyphenyl)propanoate (*S*)-37. Yield: 0.98 g, 87%; $[\alpha]_D^{25} = -15.5$ (*c* 1.4, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.55. *tert*-Butyl (*R*)-3-amino-3-(2-methoxyphenyl)propanoate (*R*)-38. Yield: 1.02 g, 90%; $[\alpha]_D^{25} = +22.4$ (*c* 2.4, $CHCl_3$) {lit.[16] for (*S*)-**38**, $[\alpha]_D^{20} = -20.0$ (*c* 0.7, $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.42 (9H, s, C*Me*$_3$), 1.82 (2H, br s, N*H*$_2$), 2.61 (1H, dd, *J* 15.6, 9.0, C(2)*H*$_2$), 2.71 (1H, dd, *J* 15.6, 4.9, C(2)*H*$_2$), 3.86 (3H, s, O*Me*), 4.58 (1H, dd, *J* 9.0, 4.9, C(3)*H*), 6.85–6.96 (2H, m, *Ar*), 7.20–7.34 (2H, m, *Ar*).

3.6.56. *tert*-Butyl (*S*)-3-amino-3-(2-methoxyphenyl)propanoate (*S*)-38. Yield: 1.00 g, 88%; $[\alpha]_D^{25} = -22.0$ (*c* 2.4, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.57. *tert*-Butyl (*R*)-3-amino-3-(3,5-dimethoxyphenyl)propanoate (*R*)-39. Yield: 1.11 g, 88%; $[\alpha]_D^{25} = +12.3$ (*c* 2.2, $CHCl_3$); ν_{max}/cm^{-1} (film) 3377, 1723; δ_H (400 MHz, $CDCl_3$) 1.42 (9H, s, C*Me*$_3$), 1.71 (2H, br s, N*H*$_2$), 2.48–2.57 (2H, m, C(2)*H*$_2$), 3.76 (6H, s, O*Me*), 4.29 (1H, dd, *J* 7.9, 5.8, C(3)*H*), 6.34 (1H, t, *J* 2.3, Ar(4)*H*), 6.51 (2H, d, *J* 2.3, Ar(2)*H* and Ar(6)*H*); δ_C (100 MHz, $CDCl_3$) 28.1, 45.3, 52.9, 55.3, 80.7, 99.3, 104.2, 147.4, 160.9, 171.3; *m*/*z* ($APCI^+$) 282 (19%), 226 (81), 209 (100); HRMS (ESI^+) 282.1715 ($C_{15}H_{24}NO_4$ requires 282.1705).

3.6.58. *tert*-Butyl (*S*)-3-amino-3-(3,5-dimethoxyphenyl)-propanoate (*S*)-39. Yield: 1.12 g, 88%; $[\alpha]_D^{25} = -11.7$ (*c* 2.7, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.59. *tert*-Butyl (*R*)-3-amino-3-(3,4-dimethoxyphenyl)propanoate (*R*)-40. Yield: 1.10 g, 87%; $[\alpha]_D^{25} = +11.1$ (*c* 2.5, $CHCl_3$); ν_{max}/cm^{-1} (film) 3374, 1723; δ_H (400 MHz, $CDCl_3$) 1.41 (9H, s, C*Me*$_3$), 1.73 (2H, br s, N*H*$_2$), 2.49–2.59 (2H, m, C(2)*H*$_2$), 3.84 (3H, s, O*Me*), 3.87 (3H, s, O*Me*), 4.32 (1H, app t, *J* 6.8, C(3)*H*), 6.80 (1H, d, *J* 8.3, Ar(6)*H*), 6.87 (1H, dd, *J* 8.3, 2.0, Ar(5)*H*), 6.91 (1H, d, *J* 2.0, Ar(2)*H*); δ_C (100 MHz, $CDCl_3$) 28.0, 45.5, 52.4, 55.8, 55.9, 80.7, 109.4, 111.0, 118.3, 137.4, 148.1, 149.0, 171.4;

m/*z* (APCI$^+$) 265 (86%), 209 (100); HRMS (ESI$^+$) 282.1711 ($C_{15}H_{24}NO_4$ requires 282.1705).

3.6.60. *tert*-Butyl (*S*)-3-amino-3-(3,4-dimethoxyphenyl)propanoate (*S*)-40. Yield: 1.07 g, 85%; $[\alpha]_D^{25} = -11.0$ (*c* 2.5, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.61. *tert*-Butyl (*R*)-3-amino-3-(2,4-dimethoxyphenyl)propanoate (*R*)-41. Yield: 1.04 g, 82%; mp 83–84 °C; $[\alpha]_D^{25} = +17.0$ (*c* 2.2, $CHCl_3$); ν_{max}/cm^{-1} (KBr) 2981, 1732; δ_H (400 MHz, $CDCl_3$) 1.41 (9H, s, C*Me*$_3$), 1.88 (2H, br s, N*H*$_2$), 2.58 (1H, dd, *J* 15.5, 8.7, C(2)*H*$_2$), 2.66 (1H, dd, *J* 15.5, 5.0, C(2)*H*$_2$), 3.78 (3H, s, O*Me*), 3.81 (3H, s, O*Me*), 4.49 (1H, dd, *J* 8.7, 5.0, C(3)*H*), 6.40–6.46 (2H, m, *Ar*), 7.18–7.22 (1H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 28.1, 43.4, 48.0, 55.2, 55.3, 80.3, 98.7, 103.8, 125.3, 127.5, 157.8, 159.8, 171.8; *m*/*z* (APCI$^+$) 282 (22%), 265 (100); HRMS (ESI$^+$) 282.1702 ($C_{15}H_{24}NO_4$ requires 282.1705).

3.6.62. *tert*-Butyl (*S*)-3-amino-3-(2,4-dimethoxyphenyl)propanoate (*S*)-41. Yield: 1.07 g, 85%; $[\alpha]_D^{25} = -16.9$ (*c* 1.6, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.63. *tert*-Butyl (*R*)-3-amino-3-phenylpropanoate (*R*)-42. Yield: 0.89 g, 89%; $[\alpha]_D^{25} = +18.3$ (*c* 2.5, $CHCl_3$) {lit.[16] for (*S*)-**42** $[\alpha]_D^{20} = -21.0$ (*c* 1.0, $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.42 (9H, s, C*Me*$_3$), 1.74 (2H, br s, N*H*$_2$), 2.58 (2H, app d, *J* 6.9, C(2)*H*$_2$), 4.37 (1H, app t, *J* 6.9, C(3)*H*), 7.21–7.37 (5H, m, *Ar*).

3.6.64. *tert*-Butyl (*S*)-3-amino-3-phenylpropanoate (*S*)-42. Yield: 0.91 g, 91%; $[\alpha]_D^{25} = -17.9$ (*c* 1.4, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.65. *tert*-Butyl (*R*)-3-amino-3-(4-biphenyl)propanoate (*R*)-43. Yield: 1.09 g, 81%; mp 59–60 °C; $[\alpha]_D^{25} = +11.8$ (*c* 1.4, $CHCl_3$); ν_{max}/cm^{-1} (KBr) 3326, 1723; δ_H (400 MHz, $CDCl_3$) 1.44 (9H, s, C*Me*$_3$), 1.77 (2H, br s, N*H*$_2$), 2.64 (2H, app d, *J* 6.9, C(2)*H*$_2$), 4.44 (1H, app t, *J* 6.9, C(3)*H*), 7.31–7.52 (9H, m, *Ar*); δ_C (100 MHz, $CDCl_3$) 28.1, 45.3, 52.5, 80.8, 126.8, 127.2, 127.3, 127.3, 128.8, 140.2, 140.8, 143.8, 171.3; *m*/*z* (APCI$^+$) 298 (3%), 281 (6), 225 (100); HRMS (ESI$^+$) 298.1822 ($C_{19}H_{24}NO_2$ requires 298.1807).

3.6.66. *tert*-Butyl (*S*)-3-amino-3-(4-biphenyl)propanoate (*S*)-43. Yield: 1.02 g, 76%; $[\alpha]_D^{25} = -11.3$ (*c* 1.1, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.67. *tert*-Butyl (*R*)-3-amino-3-(piperon-3-yl)propanoate (*R*)-44. Yield: 0.99 g, 83%; $[\alpha]_D^{25} = +13.2$ (*c* 2.2, $CHCl_3$); ν_{max}/cm^{-1} (film) 3379, 1724; δ_H (400 MHz, $CDCl_3$) 1.41 (9H, s, C*Me*$_3$), 1.68 (2H, br s, N*H*$_2$), 2.51 (2H, app d, *J* 6.9, C(2)*H*$_2$), 4.28 (1H, app t, *J* 6.9, C(3)*H*), 5.92 (2H, s, OC*H*$_2$O), 6.73 (1H, d, *J* 8.0, Ar(5)*H*), 6.79 (1H, dd, *J* 8.0, 1.7, Ar(6)*H*), 6.86 (1H, d, *J* 1.7, Ar(2)*H*); δ_C (100 MHz, $CDCl_3$) 28.1, 45.5, 52.6, 80.8, 101.0, 106.8, 108.1, 119.5, 138.9, 146.6, 147.7, 171.3; *m*/*z* (APCI$^+$) 266 (4%), 249 (28), 193 (100); HRMS (ESI$^+$) 266.1395 ($C_{14}H_{20}NO_4$ requires 266.1392).

3.6.68. *tert*-Butyl (*S*)-3-amino-3-(piperon-3-yl)propanoate (*S*)-44. Yield: 1.04 g, 87%; $[\alpha]_D^{25} = -13.0$ (*c* 2.2, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.69. *tert*-Butyl (*R*)-3-amino-3-(3-hydroxyphenyl)propanoate (*R*)-45. Yield: 0.82 g, 77%; mp 111–113 °C; $[\alpha]_D^{25} = +7.8$ (*c* 1.2, $CHCl_3$); ν_{max}/cm^{-1} (KBr) 3278, 2973, 1726; δ_H (400 MHz, $CDCl_3$) 1.42 (9H, s, C*Me*$_3$), 2.54–2.66 (2H, m, C(2)*H*$_2$), 4.29 (1H, dd, *J* 8.3, 5.5, C(3)*H*), 6.68–6.81 (3H, m, *Ar*), 7.15 (1H, app t, *J* 7.8, Ar(5)*H*); δ_C (100 MHz, $CDCl_3$) 28.0, 44.2, 52.5, 81.1, 113.5, 115.1, 118.0, 129.8, 144.9, 157.1, 171.4; *m*/*z* (APCI$^+$) 238 (4%), 182 (100); HRMS (ESI$^+$) 238.1445 ($C_{13}H_{20}NO_3$ requires 238.1443).

3.6.70. *tert*-Butyl (*S*)-3-amino-3-(3-hydroxyphenyl)propanoate (*S*)-45. Yield: 0.82 g, 77%; $[\alpha]_D^{25} = -7.8$ (*c* 1.3, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.71. *tert*-Butyl (*R*)-3-amino-3-(4-hydroxyphenyl)propanoate (*R*)-46. Yield: 0.87 g, 81%; mp 91–92 °C; $[\alpha]_D^{25} = +9.0$ (*c* 1.1, $CHCl_3$); ν_{max}/cm^{-1} (KBr) 3300, 2980, 1715; δ_H (400 MHz, $CDCl_3$) 1.42 (9H, s, C*Me*$_3$), 2.58 (1H, dd, *J* 15.9, 5.0, C(2)*H*$_2$), 2.65 (1H, dd, *J* 15.9, 8.9, C(2)*H*$_2$), 4.25 (1H, br s, O*H*), 4.31 (1H, dd, *J* 8.9, 5.0, C(3)*H*), 6.70 (2H, d, *J* 8.5, Ar(3)*H* and Ar(5)*H*), 7.16 (2H, d, *J* 8.5, Ar(2)*H* and Ar(6)*H*); δ_C (100 MHz, $CDCl_3$) 28.0, 44.5, 52.1, 81.1, 115.8, 127.6, 134.6, 156.1, 171.6; *m*/*z* (APCI$^+$) 221 (14%), 165 (100); HRMS (ESI$^+$) 238.1450 ($C_{13}H_{20}NO_3$ requires 238.1443).

3.6.72. *tert*-Butyl (*S*)-3-amino-3-(4-hydroxyphenyl)propanoate (*S*)-46. Yield: 0.88 g, 82%; $[\alpha]_D^{25} = -8.5$ (*c* 1.1, $CHCl_3$); other physical and spectroscopic properties identical with those described above.

3.6.73. *tert*-Butyl (*R*)-3-amino-3-(3,4-dihydroxyphenyl)propanoate (*R*)-47. Yield: 0.93 g, 82%; $[\alpha]_D^{25} = -7.9$ (*c* 0.3, MeOH); δ_H (400 MHz, CD_3OD) 1.38 (9H, s, C*Me*$_3$), 1.32 (4H, br s, N*H*$_2$, O*H*), 2.80 (1H, dd, *J* 16.0, 7.7, C(2)*H*$_2$), 2.93 (1H, dd, *J* 16.0, 7.1, C(2)*H*$_2$), 4.36–4.43 (1H, m, C(3)*H*), 6.76 (1H, dd, *J* 8.2, 2.0, Ar(6)*H*), 6.81 (1H, dd, *J* 8.2, Ar(5)*H*), 6.88 (1H, d, *J* 2.0, Ar(2)*H*).

3.6.74. *tert*-Butyl (*S*)-3-amino-3-(3,4-dihydroxyphenyl)propanoate (*S*)-47. Yield: 0.97 g, 85%; $[\alpha]_D^{25} = +8.0$ (*c* 0.4, MeOH); other physical and spectroscopic properties identical with those described above.

3.6.75. (*S*)-3-Aminobutanoic acid (*S*)-48. Yield: 19 mg, 92%; mp 207–208 °C (lit.[24] mp 210 °C); $[\alpha]_D^{25} = +32.0$ (*c* 0.6, H_2O) {lit.[24] $[\alpha]_D^{20} = +34$ (*c* 0.6, H_2O)}; δ_H (400 MHz, D_2O) 1.18 (3H, d, *J* 6.5, *Me*), 2.25–2.40 (2H, m, C(2)*H*$_2$), 3.39–3.50 (1H, m, C(3)*H*).

3.6.76. (*R*)-3-Aminobutanoic acid (*R*)-48. Yield: 20 mg, 97%; $[\alpha]_D^{25} = -32.4$ (*c* 0.6, H_2O); other physical and spectroscopic properties identical with those described above.

3.6.77. (*S*)-3-Amino-5-methylhexanoic acid (*S*)-49. Yield: 19 mg, 92%; mp 222–224 °C (lit.[25] mp 227 °C); $[\alpha]_D^{25} = +27.8$ (*c* 0.6, H_2O) {lit.[25] $[\alpha]_D^{24} + 27$ (*c* 1, H_2O)}; δ_H (400 MHz, D_2O) 0.78 (3H, d, *J* 6.4, C(5)Me_2), 0.80 (3H, d, *J* 6.4, C(5)Me_2), 1.32–1.47 (2H, m, C(4)H_2), 1.50–1.64 (1H, m, C(5)*H*), 2.28 (1H, dd, *J* 16.6, 8.1, C(2)H_2), 2.44 (1H, dd, *J* 16.6, 4.8, C(2)H_2), 3.40–3.48 (1H, m, C(3)*H*).

3.6.78. (*R*)-3-Amino-5-methylhexanoic acid (*R*)-49. Yield: 20 mg, 97%; $[\alpha]_D^{25} = -27.9$ (*c* 0.7, H_2O); other physical and spectroscopic properties identical with those described above.

3.6.79. (*S*)-3-Aminodecanoic acid (*S*)-50. Yield: 37 mg, 96%; mp 215–216 °C (lit.[23] mp 202–204 °C); $[\alpha]_D^{25} = +2.5$ (*c* 0.1, H_2O); δ_H (400 MHz, D_2O) 0.73 (3H, t, *J* 7.0, *Me*), 1.08–1.29 (10H, m, CH_2), 1.46–1.53 (2H, m, C(4)H_2), 2.30 (1H, dd, *J* 16.7, 8.3, C(2)H_2), 2.44 (1H, dd, *J* 16.7, 4.9, C(2)H_2), 3.30–3.39 (1H, m, C(3)*H*).

3.6.80. (*R*)-3-Aminodecanoic acid (*R*)-50. Yield: 36 mg, 94%; $[\alpha]_D^{25} = -2.4$ (*c* 0.2, H_2O); other physical and spectroscopic properties identical with those described above.

3.6.81. (*R*)-3-Amino-3-(4-methoxyphenyl)propanoic acid (*R*)-51. Yield: 41 mg, 99%; mp 229–230 °C (lit.[8] 238–340 °C); $[\alpha]_D^{25} = +0.6$ (*c* 0.1, H_2O) {lit.[16] for (*S*)-**51**, $[\alpha]_D^{20} = -1.4$ (*c* 0.2, H_2O); δ_H (400 MHz, D_2O) 2.71 (1H, dd, *J* 16.2, 6.8, C(2)H_2), 2.82 (1H, dd, *J* 16.2, 8.0, C(2)H_2), 3.75 (3H, s, O*Me*), 4.53 (1H, dd, *J* 8.0, 6.8, C(3)*H*), 6.97 (2H, d, *J* 8.8, Ar(3)*H*, Ar(5)*H*), 7.32 (2H, d, *J* 8.8, Ar(2)*H*, Ar(6)*H*).

3.6.82. (*S*)-3-Amino-3-(4-methoxyphenyl)propanoic acid (*S*)-51. Yield: 41 mg, 99%; $[\alpha]_D^{25} = -0.8$ (*c* 0.2, H_2O); other physical and spectroscopic properties identical with those described above.

3.6.83. (*R*)-3-Amino-3-(3-methoxyphenyl)propanoic acid (*R*)-52. Yield: 41 mg, 99%; mp 215–216 °C; $[\alpha]_D^{25} = +3.8$ (*c* 0.9, H_2O); ν_{max}/cm^{-1} (KBr) 2981, 1606; δ_H (400 MHz, D_2O) 2.70 (1H, dd, *J* 16.3. 6.4, C(2)H_2), 2.80 (1H, dd, *J* 16.3, 8.2, C(2)H_2), 3.75 (3H, s, O*Me*), 4.53 (1H, dd, *J* 8.2, 6.4, C(3)*H*), 6.92–7.00 (3H, m, *Ar*), 7.29–7.37 (1H, m, Ar(5)*H*); δ_C (100 MHz, D_2O) 53.0, 55.8, 55.8, 113.0, 115.1, 119.8, 131.0, 138.1, 159.7, 177.5; *m*/*z* (ESI^-) 194 (100%); HRMS (ESI^-) 194.0814 ($C_{10}H_{12}NO_3$ requires 194.0817).

3.6.84. (*S*)-3-Amino-3-(3-methoxyphenyl)propanoic acid (*S*)-52. Yield: 38 mg, 94%; $[\alpha]_D^{25} = -3.9$ (*c* 1.0, H_2O); other physical and spectroscopic properties identical with those described above.

3.6.85. (*R*)-3-Amino-3-(2-methoxyphenyl)propanoic acid (*R*)-53. Yield: 37 mg, 95%; mp 208–210 °C (lit.[16] mp 208–210 °C); $[\alpha]_D^{25} = -18.5$ (*c* 0.5, H_2O) {lit.[16] for (*S*)-**53**, $[\alpha]_D^{20} = +15.5$ (*c* 1.0, H_2O)}; δ_H (400 MHz, D_2O) 2.66 (1H, dd, *J* 16.2, 6.5, C(2)H_2), 2.82 (1H, dd, *J* 16.2, 8.5, C(2)H_2), 3.78 (3H, s, O*Me*), 4.62 (1H, dd, *J* 8.5, 6.5, C(3)*H*), 6.88–6.99 (2H, m, *Ar*), 7.15–7.32 (2H, m, *Ar*).

3.6.86. (*S*)-3-Amino-3-(2-methoxyphenyl)propanoic acid (*S*)-53. Yield: 38 mg, 98%; $[\alpha]_D^{25} = +18.8$ (*c* 0.6, H_2O); other physical and spectroscopic properties identical with those described above.

3.6.87. (*R*)-3-Amino-3-(3,5-dimethoxyphenyl)propanoic acid (*R*)-54. Yield: 38 mg, 95%; mp 202–203 °C; $[\alpha]_D^{25} = -0.8$ (*c* 0.7, H_2O); ν_{max}/cm^{-1} (KBr) 3129br, 1638; δ_H (400 MHz, D_2O) 2.62 (1H, dd, *J* 16.4, 6.1, C(2)H_2), 2.72 (1H, dd, *J* 16.4, 8.4, C(2)H_2), 3.67 (6H, s, O*Me*), 4.42 (1H, dd, *J* 8.4, 6.1, C(3)*H*), 6.42 (1H, t, *J* 2.2, Ar(4)*H*), 6.51 (1H, d, *J* 2.2, Ar(2)*H* and Ar(6)*H*); δ_C (100 MHz, D_2O) 40.6, 53.0, 55.8, 101.1, 105.7, 139.0, 161.0, 177.3; *m*/*z* ($APCI^+$) 226 (5%), 209 (100); HRMS (ESI^-) 224.0917 ($C_{11}H_{14}NO_4$ requires 224.0923).

3.6.88. (*S*)-3-Amino-3-(3,5-dimethoxyphenyl)propanoic acid (*S*)-54. Yield: 39 mg, 97%; $[\alpha]_D^{25} = +0.7$ (*c* 0.8, H_2O); other physical and spectroscopic properties identical with those described above.

3.6.89. (*R*)-3-Amino-3-(3,4-dimethoxyphenyl)propanoic acid (*R*)-55. Yield: 39 mg, 97%; mp 216–218 °C; $[\alpha]_D^{25} = -0.9$ (*c* 0.7, H_2O); δ_H (400 MHz, D_2O) 2.64 (1H, dd, *J* 16.3, 6.5, C(2)H_2), 2.76 (1H, dd, *J* 16.3, 8.2, C(2)H_2), 3.68 (3H, s, O*Me*), 3.72 (3H, s, O*Me*), 4.44 (1H, dd, *J* 8.2, 6.5, C(3)*H*), 6.87–9.97 (3H, m, *Ar*).

3.6.90. (*S*)-3-Amino-3-(3,4-dimethoxyphenyl)propanoic acid (*S*)-55. Yield: 39 mg, 97%; $[\alpha]_D^{25} = +0.9$ (*c* 0.7, H_2O); other physical and spectroscopic properties identical with those described above.

3.6.91. (*R*)-3-Amino-3-(2,4-dimethoxyphenyl)propanoic acid (*R*)-56. Yield: 40 mg, 99%; mp 215–217 °C; $[\alpha]_D^{25} = -5.1$ (*c* 0.8, H_2O); ν_{max}/cm^{-1} (KBr) 2947, 1616; δ_H (400 MHz, D_2O) 2.66 (1H, dd, *J* 16.3, 6.4, C(2)H_2), 2.84 (1H, dd, *J* 16.3, 8.5, C(2)H_2), 3.71 (3H, s, O*Me*), 3.77 (3H, s, O*Me*), 4.59 (1H, dd, *J* 8.5, 6.4, C(3)*H*), 6.49 (1H, dd, *J* 8.5, 2.4, Ar(5)*H*), 6.54 (1H, d, *J* 2.4, Ar(2)*H*), 7.13 (1H, d, *J* 8.5, Ar(6)*H*); δ_C (100 MHz, D_2O) 38.9, 49.7, 55.8, 99.2, 105.6, 116.4, 129.7, 158.6, 161.4, 178.0; *m*/*z* (ESI^-) 224 (100%); HRMS (ESI^-) 224.0922 ($C_{11}H_{14}NO_4$ requires 224.0923).

3.6.92. (*S*)-3-Amino-3-(2,4-dimethoxyphenyl)propanoic acid (*S*)-56. Yield: 41 mg, 99%; $[\alpha]_D^{25} = +5.3$ (*c* 0.6, H_2O); other physical and spectroscopic properties identical with those described above.

3.6.93. (*R*)-3-Amino-3-phenylpropanoic acid (*R*)-57. Yield: 36 mg, 96%; mp 227–229 °C (lit.[16] mp 227–229 °C); $[\alpha]_D^{25} = +6.8$ (*c* 0.9, H_2O) {lit.[26] for (*S*)-**57**, $[\alpha]_D^{22} = -6.3$ (*c* 0.8, H_2O)}; δ_H (200 MHz, D_2O) 2.70 (1H, dd, *J* 15.9, 7.0, C(2)H_2), 2.86 (1H, dd, *J* 15.9, 7.5, C(2)H_2), 4.48–4.57 (1H, m, C(3)*H*), 7.28–7.43 (5H, m, *Ar*).

3.6.94. (*S*)-3-Amino-3-phenylpropanoic acid (*S*)-57. Yield: 36 mg, 96%; $[\alpha]_D^{25} = -6.3$ (*c* 0.6, H_2O); other physical and spectroscopic properties identical with those described above.

3.6.95. (*R*)-3-Amino-3-(4-biphenyl)propanoic acid hydrochloride (*R*)-58·HCl. Yield: 41 mg, 99%; mp 239–240 °C; $[\alpha]_D^{25} = -3.3$ (*c* 0.8, MeOH); ν_{max}/cm^{-1} (KBr) 3011 br, 1728; δ_H (400 MHz, CD_3OD) 3.05 (1H, dd, *J* 17.1, 6.4, C(2)H_2), 3.17 (1H, dd, *J* 17.1, 7.6, C(2)H_2), 4.77 (1H, dd, *J* 7.6, 6.4, C(3)*H*), 7.34–7.75 (9H, m, *Ar*); δ_C (100 MHz, CD_3OD) 38.1, 51.9, 127.0, 127.8, 127.9, 127.9, 129.0, 135.4, 140.3, 142.6, 177.5; *m*/*z* (ESI^-) 240 (100%); HRMS (ESI^-) 240.1020 ($C_{15}H_{14}NO_2$ requires 240.1025).

3.6.96. (*S*)-3-Amino-3-(4-biphenyl)propanoic acid hydrochloride (*S*)-58·HCl. Yield: 41 mg, 99%; $[\alpha]_D^{25} = +3.3$ (*c* 0.8, MeOH); other physical and spectroscopic properties identical with those described above.

3.6.97. (*R*)-3-Amino-3-(piperon-3-yl)propanoic acid (*R*)-59. Yield: 38 mg, 96%; mp 219–220 °C; $[\alpha]_D^{25} = -42.0$ (*c* 0.3, H_2O); ν_{max}/cm^{-1} (KBr) 2890 br, 1653; δ_H (400 MHz, D_2O) 2.65 (1H, dd, *J* 16.2, 6.9, C(2)H_2), 2.76 (1H, dd, *J* 16.2, 8.2, C(2)H_2), 4.44 (1H, dd, *J* 8.2, 6.9, C(3)*H*), 5.86 (2H, s, OCH_2O), 6.78–6.89 (3H, m, *Ar*); δ_C (100 MHz, D_2O) 40.7, 52.9, 101.8, 107.6, 109.2, 121.5, 130.0, 148.1, 148.1, 177.4; *m*/*z* (ESI^+) 208 (100%); HRMS (ESI^-) 208.0613 ($C_{10}H_{10}NO_4$ requires 208.0610).

3.6.98. (*S*)-3-Amino-3-(piperon-3-yl)propanoic acid (*S*)-59. Yield: 38 mg, 96%; $[\alpha]_D^{25} = +42.4$ (*c* 0.3, H_2O); other physical and spectroscopic properties identical with those described above.

3.6.99. (*R*)-3-Amino-3-(3-hydroxyphenyl)propanoic acid (*R*)-60. Yield: 38 mg, 99%; 233–234 °C; $[\alpha]_D^{25} = +7.2$ (*c* 0.5, H_2O); ν_{max}/cm^{-1} (KBr) 3021, 1568; δ_H (200 MHz, D_2O) 2.68 (1H, dd, *J* 16.3, 6.5, C(2)H_2), 2.77 (1H, dd, *J* 16.3, 8.1, C(2)H_2), 4.47 (1H, dd, *J* 8.1, 6.5, C(3)*H*), 6.81–6.98 (3H, m, *Ar*), 7.21–7.34 (1H, m, Ar(5)*H*); δ_C (100 MHz, D_2O) 40.7, 52.9, 114.2, 116.5, 119.2, 131.1, 138.2, 156.3, 177.5; *m*/*z* (ESI^-) 180 (100%); HRMS (ESI^-) 180.0658 ($C_9H_{10}NO_3$ requires 180.0661).

3.6.100. (*S*)-3-Amino-3-(3-hydroxyphenyl)propanoic acid (*S*)-60. Yield: 39 mg, 99%; $[\alpha]_D^{25} = -7.2$ (*c* 0.3, H_2O); other physical and spectroscopic properties identical with those described above.

3.6.101. (*R*)-3-Amino-3-(4-hydroxyphenyl)propanoic acid (*R*)-61. Yield: 36 mg, 94%; mp 220–221 °C; $[\alpha]_D^{25} = -6.0$ (*c* 0.6, H_2O); δ_H (400 MHz, D_2O) 2.66 (1H, dd, *J* 16.2, 6.6, C(2)H_2), 2.78 (1H, dd, *J* 16.2, 8.2, C(2)H_2), 4.41–4.48 (1H, m, C(3)*H*), 6.81 (2H, d, *J* 8.7, Ar(3)*H* and Ar(5)*H*), 7.22 (2H, d, *J* 8.7, Ar(2)*H* and Ar(6)*H*).

3.6.102. (*S*)-3-Amino-3-(4-hydroxyphenyl)propanoic acid (*S*)-61. Yield: 37 mg, 98%; $[\alpha]_D^{25} = +5.9$ (*c* 0.5, H_2O); other physical and spectroscopic properties identical with those described above.

3.6.103. (*R*)-3-Amino-3-(3,4-hydroxyphenyl)propanoic acid hydrochloride (*R*)-62·HCl. Yield: 37 mg, 94%; $[\alpha]_D^{25} = -4.6$ (*c* 0.5, MeOH); δ_H (400 MHz, CD_3OD) 2.93 (1H, dd, *J* 17.1, 6.2, C(2)H_2), 3.02 (1H, dd, *J* 17.1, 8.9, C(2)H_2), 4.43–4.52 (1H, m, C(3)*H*), 6.76–6.92 (3H, m, *Ar*).

3.6.104. (*S*)-3-Amino-3-(3,4-hydroxyphenyl)propanoic acid hydrochloride (*S*)-62·HCl. Yield: 37 mg, 94%; $[\alpha]_D^{25} = +4.8$ (*c* 0.2, MeOH); other physical and spectroscopic properties identical with those described above.

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