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A synthesis of optically active α-quaternary α-amino acids and esters by assembling three components, ketones, (*R*)-chloromethyl *p*-tolyl sulfoxide, and sodium azide, via sulfinyloxiranes

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Abstract—Treatment of lithium α-sulfinyl carbanion of chloromethyl *p*-tolyl sulfoxides with ketones at low temperature afforded adducts in almost quantitative yields, which were exposed to *t*-BuOK to give sulfinyloxiranes in high yields. The sulfinyloxirane was reacted with benzylamine to give α-amino aldehyde, which was oxidized with iodine in methanol to afford α-amino carboxylic ester in moderate yield. The sulfinyloxiranes were treated with sodium azide to afford α-azido aldehydes in good yields. Oxidation with $NaClO_2$ followed by catalytic hydrogenation of the azido group of the α-azido aldehydes gave α-quaternary α-amino acids in good overall yields. The oxidation of the azido aldehydes with iodine in methanol in the presence of KOH followed by the catalytic hydrogenation resulted in α-quaternary α-amino acid methyl esters in good yields. When these reactions were carried out starting from unsymmetrical ketones and optically pure (*R*)-chloromethyl *p*-tolyl sulfoxide, a new method for a synthesis of optically active α-quaternary α-amino acids and esters in good overall yields was realized.

1. Introduction

Optically active α,α-disubstituted (α-quaternary) α-amino acids and their derivatives, including cyclic α-amino acids with the α-carbon embedded in the ring, have recently received considerable attention. α-Quaternary α-amino acids, in some case, are found as antibiotics, for example, lactacystin.[1] Very interestingly, α-methylisoleucine, α-methylalloisoleucine, and α-methylnorvaline have been found as meteoritic α-amino acids form the Murchison meteorite.[2]

Cyclic α-quaternary α-amino acids are also quite interesting compounds. For instance, 1-aminocyclopropane carboxylic acid is known to be the biosynthetic precursor of the plant hormone, ethylene.[3] 1-Aminocyclopentane-1,3-dicarboxylic acid acts as a metabotropic glutamate receptor (mGluR) agonist.[4] Recently, α-quaternary α-amino acids and cyclic α-amino acids are used in controlling peptide secondary structures.[5] Synthesis of α-quaternary α-amino acids[6] and cyclic α-amino acids[7] are actively investigated recently because of the importance of these compounds in molecular biology and synthetic organic chemistry as mentioned above.

We have also been interested in the synthesis of α-amino acids, including optically active α-quaternary α-amino acids and their derivatives, and cyclic α-amino acids.[8] In continuation of our investigation concerning the development of new synthetic methods for α-amino acids, we recently realized a new method for synthesis of α-quaternary α-amino acids and cyclic α-amino acids **5** from ketones **1**, chloromethyl *p*-tolyl sulfoxide **2**, and nitrogen nucleophiles (benzylamine or sodium azide). The key reaction is the nucleophilic opening of sulfinyloxiranes **3** with the nitrogen nucleophiles to afford aldehydes **4**. This method was developed into an asymmetric synthesis by using unsymmetrical ketones with optically active (*R*)-chloromethyl *p*-tolyl sulfoxide **2** (Scheme 1).[9]

2. Results and discussion

2.1. Synthesis of α-quaternary α-amino acid methyl ester from a sulfinyloxirane with benzylamine as a nitrogen nucleophile

We previously reported a method for synthesizing α-amino ketones and α-amino aldehydes by nucleophilic opening of sulfinyloxiranes with several amines.[10] Based on these experiences, at first, a synthesis of cyclic α-amino acid was investigated starting from cyclopentadecanone (Scheme 2).

Keywords: α-Amino acid; α-Quaternary α-amino acid; Cyclic α-amino acid; Sulfinyloxirane; Asymmetric synthesis.
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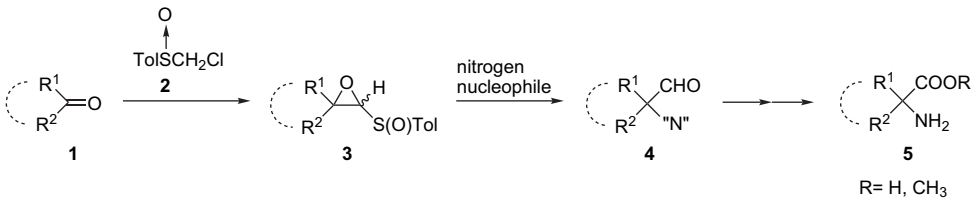
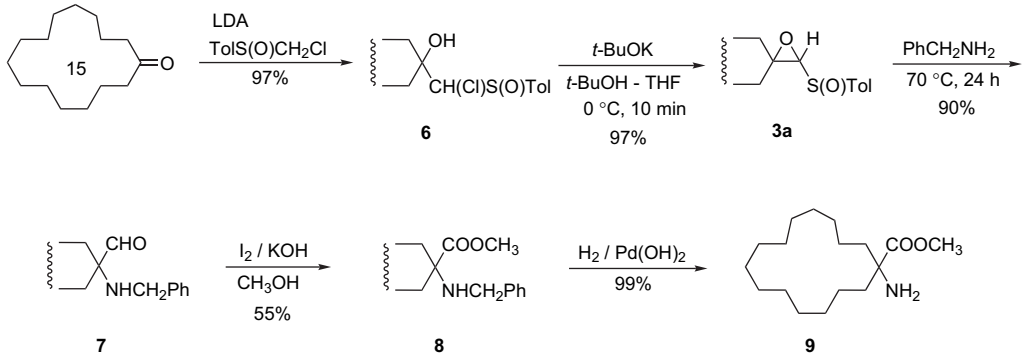


Scheme 1.



Scheme 2.

Lithium α-sulfinyl carbanion of chloromethyl *p*-tolyl sulfoxide at −78 °C was treated with cyclopentadecanone to give the adduct **6** in almost quantitative yield.[11] Treatment of **6** with 1.3 equiv of *t*-BuOK in a mixture of *t*-BuOH and THF at 0 °C resulted in the formation of sulfinyloxirane **3a** in 97% yield as crystals.[12] The sulfinyloxirane **3a** was warmed at 70 °C in 9 equiv of benzylamine without a solvent for 24 h to give cleanly the desired α-amino aldehyde **7** as crystals in 90% yield.

Next, we tried to oxidize the aldehyde group in **7** to a carboxylic acid or an ester group in the presence of amino group in the molecule, which is recognized to be rather difficult. After some examinations of the oxidation, a somewhat old-fashioned oxidation using iodine, reported by Inch,[13] was found to be successful. Thus, aldehyde **7** was treated with a solution of KOH and iodine in methanol at room temperature for 20 min to give the desired methyl ester **8** in 55% yield. However, the oxidation was found to be sensitive to the reaction conditions and the yield of **8** was variable and reproducibility was low. Finally, the benzyl group on the nitrogen of the ester **8** was removed under hydrogenolysis conditions using $Pd(OH)_2$ as a catalyst to afford cyclic α-amino acid methyl ester **9** in quantitative yield.

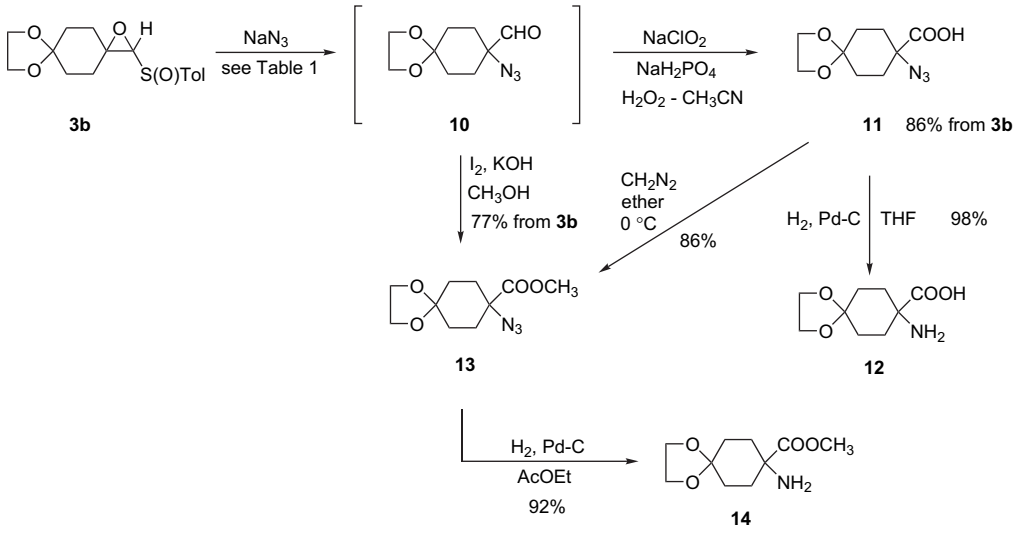
2.2. Synthesis of α-quaternary α-amino acids and methyl esters by the nucleophilic ring-opening of the sulfinyloxiranes with azido anion as a nitrogen nucleophile

As mentioned above, because of the oxidation of the aldehyde group in the presence of an amino group in the same molecule was found to be difficult, we next planned to use the azido anion as the nitrogen nucleophile expecting formation of azido aldehydes. We used sulfinyloxirane **3b**, synthesized from 1,4-cyclohexanedione mono ethylene ketal in the same way as described above, as a representative substrate of the investigation (Scheme 3).

At first, we started to find the reaction conditions concerning the ring-opening of sulfinyloxirane **3b** with sodium azide and the results of the investigation are summarized in Table 1. Initially, sulfinyloxirane **3b** was treated with NaN_3 (3 equiv) in DMSO at the concentration of 0.1 mol/L at 65 °C (entry 1). The starting material disappeared after 43 h and the desired azido aldehyde **10** was obtained; however, purification of **10** was found to be rather difficult and it appeared that **10** was somewhat unstable. The crude **10**, without further purification, was oxidized with $NaClO_2$ in the presence of H_2O_2 in acetonitrile[14] to afford the azido carboxylic acid **11** in 65% overall yield from **3b** (Table 1, entry 1).

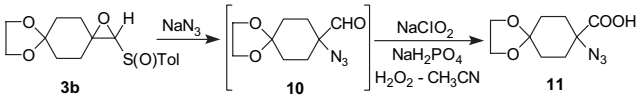
Improvement of the yield of **11** was studied (entries 2–6). The reaction time could be reduced by addition of 15-crown-5 in the reaction mixture; however, the yield was not improved (entry 2). Using higher concentration of the reaction mixture gave a worse result (entry 3). Using lower concentration of the reaction mixture showed no effect (entry 4). Finally, we changed the conditions of this reaction from an aprotic solvent to a protic solvent reported by Caron and Sharpless[15] and Crotti and co-workers[16] (entries 5 and 6). A solution of **3b** with NaN_3 (3 equiv) in methanol in the presence of water and ammonium chloride was refluxed for 16 h and the product **10** was oxidized to give **11** in much higher yield (82%). The best yield of **11** was obtained when 5 equiv of NaN_3 was used (entry 6).

Hydrogenation of the azido group in **11** was successfully carried out in THF with 10% Pd–C to give the desired cyclic quaternary α-amino acid **12** in quantitative yield (Scheme 3). In the case of a synthesis of α-amino acid ester directly from sulfinyloxirane **3b**, the crude azido aldehyde **10** was oxidized with iodine in methanol in the same way as described above for the synthesis of **8** (see Scheme 2). This reaction worked to afford the desired azido methyl ester **13** in 77% overall yield from **3b**. The same azido methyl ester **13** was



Scheme 3.

Table 1. Reaction of sulfinyloxirane **3b** with NaN_3 followed by oxidation of the resultant azido aldehyde **10** with $NaClO_2$



Entry	NaN_3/ equiv	Solvent	Concentration (mol/L)	Conditions	Yield of **11**[a]/%
1	3	DMSO	0.1	65 °C, 43 h	65
2	3[b]	DMSO	0.1	60 °C, 34 h	61
3	3	DMSO	0.5	65 °C, 36 h	24
4	3	DMSO	0.05	65 °C, 43 h	61
5	3	MeOH–H_2O (8:1)[c]	0.1	Reflux, 16 h	82
6	5	MeOH–H_2O (8:1)[c]	0.1	Reflux, 12 h	86

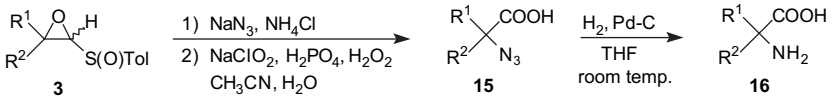
[a] Two-step overall yield from **3b**.
[b] 15-Crown-5 of 3.6 equiv was added.
[c] In the presence of NH_4Cl.

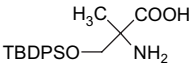
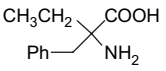
obtained from the azido carboxylic acid **11** by ester formation with diazomethane in 86% yield. Finally, the azido methyl ester **13** was catalytically reduced in ethyl acetate with Pd–C as a catalyst to give the desired cyclic quaternary α-amino acid methyl ester **14** in high yield.

In order to know the generality of this method for synthesis of α-quaternary α-amino acids and esters, we carried out the reactions using other ketones and the results are summarized in Tables 2 and 3. Table 2 shows the synthesis of α-quaternary α-amino acids, **16a** and **16b**, starting from *tert*-butyldiphenylsilyloxy-2-propanone and 1-phenyl-2-butanone, respectively. Sulfinyloxiranes **3c** and **3d** were synthesized from the ketones in quantitative yields. Ring-opening of the sulfinyloxiranes with NaN_3 followed by oxidation of the resultant aldehyde to azido carboxylic acids **15a** and **15b** proceeded quite smoothly. Finally, reduction of the azido group took place without any problem to afford the desired α-quaternary α-amino acids (**16a** and **16b**) in quantitative yields. It is worth noting that **16a** is an α-methylserine derivative and **16b** is an α-ethylphenylalanine. Asymmetric synthesis of these amino acids is discussed later (vide infra).

The results for the synthesis of α-quaternary α-amino acid methyl esters, including cyclic congeners, are summarized in Table 3. Starting from cyclobutanone, cyclodecanone, and cyclododecanone, the desired cyclic α-quaternary α-amino acid methyl esters were synthesized in good overall

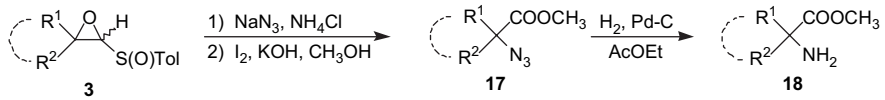
Table 2. Synthesis of α-quaternary α-amino acids **16** from sulfinyloxiranes **3** via α-azido carboxylic acids **15**

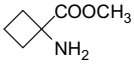
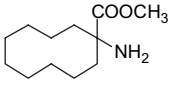
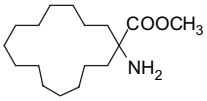
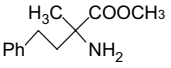
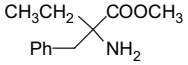


Entry	3				15		16	
		R^1	R^2	Yield/%[a]		Yield/%[b]		Yield/%
1	**3c**	CH_3	$TBDPSOCH_2$	98[c]	**15a**	94	**16a** 	99
2	**3d**	CH_3CH_2	$PhCH_2$	98[d]	**15b**	87	**16b** 	99

[a] Two-step overall yield from ketone.
[b] Two-step overall yield from **3**.
[c] A mixture of two diastereomers (70:30).
[d] A mixture of two diastereomers (65:35).

Table 3. Synthesis of α-quaternary α-amino acid methyl esters **18** from sulfinyloxiranes **3**



Entry	3				17		18	
		R^1	R^2	Yield/%[a]		Yield/%[b]		Yield/%
1	**3e**	$-(CH_2)_3-$		92	**17a**	55	**18a** 	98
2	**3f**	$-(CH_2)_9-$		80	**17b**	72	**18b** 	95
3	**3a**	$-(CH_2)_{14}-$		94	**17c**	75	**9** 	95
4	**3g**	CH_3	$PhCH_2CH_2$	90[c]	**17d**	67	**18c** 	99
5	**3d**	CH_3CH_2	$PhCH_2$	98[d]	**17e**	90	**18d** 	97

[a] Two-step overall yield from ketone.
[b] Two-step overall yield from **3**.
[c] A mixture of two diastereomers (59:41).
[d] A mixture of two diastereomers (65:35).

yield (entries 1–3). In the case of **3e**, the reaction of NaN_3 followed by oxidation with iodine gave moderate yield of azido ester **17a** (entry 1). The reactions starting from 4-phenyl-2-butanone and 1-phenyl-2-butanone gave **18c** and α-ethylphenylalanine methyl ester **18d**, respectively, in good overall yields (entries 4 and 5).

From the results described above, we concluded that the procedure mentioned above is highly applicable to many different kinds of ketones and a variety of α-quaternary α-amino acids and methyl esters could be synthesized.

2.3. Asymmetric synthesis of α-quaternary α-amino acids and methyl esters including cyclic congeners by using optically pure (*R*)-chloromethyl *p*-tolyl sulfoxide

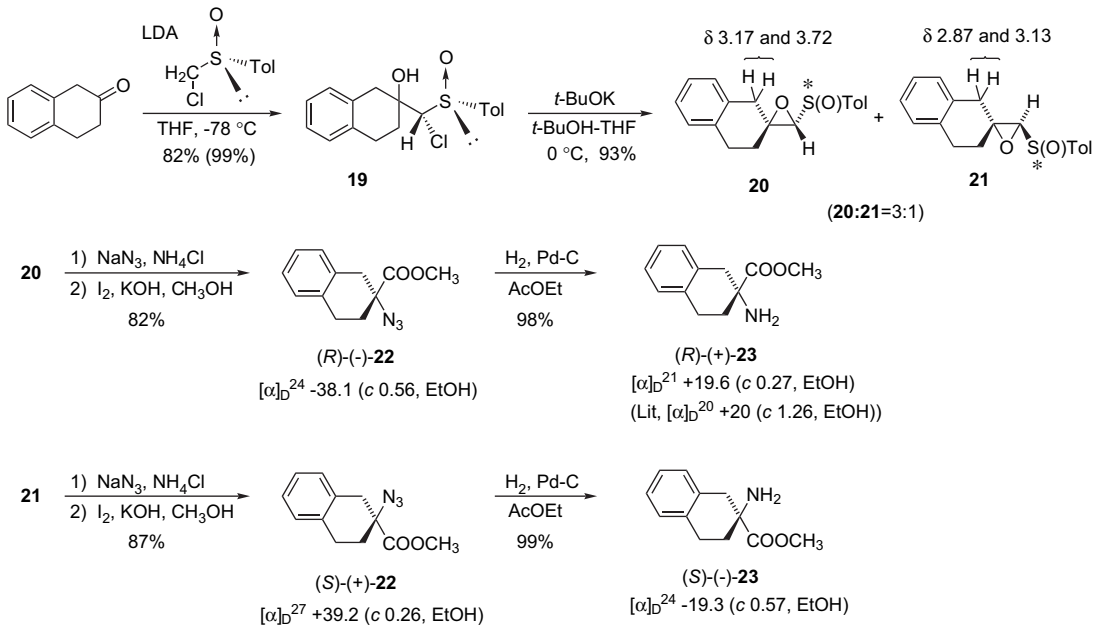
As a further development of this investigation, we next planned the asymmetric synthesis of α-quaternary α-amino acids and methyl esters including cyclic congeners by using optically pure (*R*)-chloromethyl *p*-tolyl sulfoxide. An asymmetric synthesis of methyl 2-aminotetraline-2-carboxylate, α-ethylphenylalanine and its methyl ester, and α-methylserine methyl ester is discussed below.

Asymmetric synthesis of both enantiomers of methyl 2-aminotetraline-2-carboxylate from β-tetralone is shown in Scheme 4. Lithium α-sulfinyl carbanion generated from optically pure (*R*)-chloromethyl *p*-tolyl sulfoxide[10b] with LDA at −78 °C was treated with β-tetralone to give the adduct **19** as a mixture of two diastereomers in 82% yield (99% yield calculated from the consumed sulfoxide).[17] Without separation, the mixture was treated with *t*-BuOK in a mixture of *t*-BuOH–THF at 0 °C to afford a 3:1 mixture of sulfinyloxiranes **20** and **21**. These sulfinyloxiranes were easily separated by silica gel column chromatography. The enantiomeric excess of **20** and **21** was determined to be over 99% by HPLC using CHIRALPAK AD as a chiral stationary column.

The absolute configuration of sulfinyloxiranes **20** and **21** could easily be determined as shown in Scheme 4. Thus, as we already reported, the addition reaction of the lithium α-sulfinyl carbanion of (*R*)-chloromethyl *p*-tolyl sulfoxide to carbonyl carbon was proved to induce *R* configuration at the carbon bearing the chlorine atom.[10b] The whole stereochemistry of the sulfinyloxiranes **20** and **21** was easily determined from the ^1H NMR spectrum. As shown in Scheme 4, the chemical shift of the benzylic hydrogens of the main product **20** was markedly lowered compared with those of **21**, which indicates that the benzylic carbon and the sulfinyl group of **20** should be cis.[10b]

The main product **20** was treated with NaN_3 in the same way as described above and the resulting azido aldehyde was oxidized with I_2 in methanol to give the desired azido methyl ester (*R*)-(−)-**22** in 82% overall yield from **20**. The enantiomeric excess of (*R*)-(−)-**22** was determined to be over 99% by HPLC using CHIRALCEL OD as a chiral stationary column. Finally, the catalytic hydrogenation of (*R*)-(−)-**22** with Pd–C/H_2 in ethyl acetate gave the expected (*R*)-(+)-methyl 2-aminotetraline-2-carboxylate (*R*)-(+)-**23** in a quantitative yield. All the spectral data and the specific rotations were highly consistent with the reported value.[18] The minor sulfinyloxirane **21** was treated with NaN_3 followed by I_2 in methanol to give the enantiomer of the azido methyl ester (*S*)-(+)-**22** in 87% yield. Finally, the catalytic hydrogenation of (*S*)-(+)-**22** gave (*S*)-(−)-**23** in a quantitative yield.

In continuation of the asymmetric synthesis of α-quaternary α-amino acids and their derivatives, an asymmetric synthesis

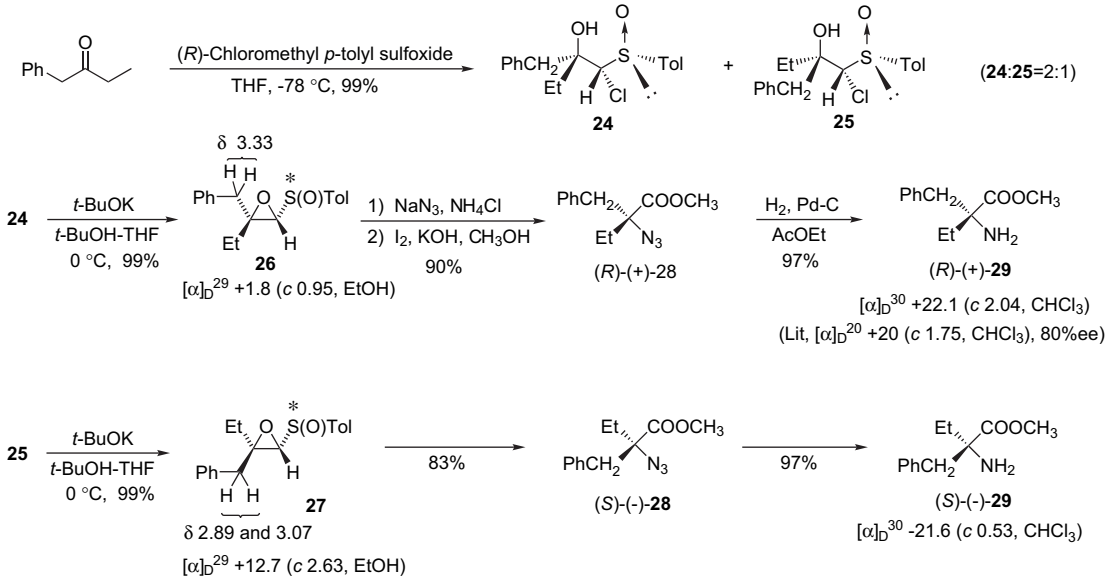


Scheme 4. Asymmetric synthesis of both enantiomers of methyl 2-aminotetraline-2-carboxylate **23** from β-tetralone and (*R*)-chloromethyl *p*-tolyl sulfoxide.

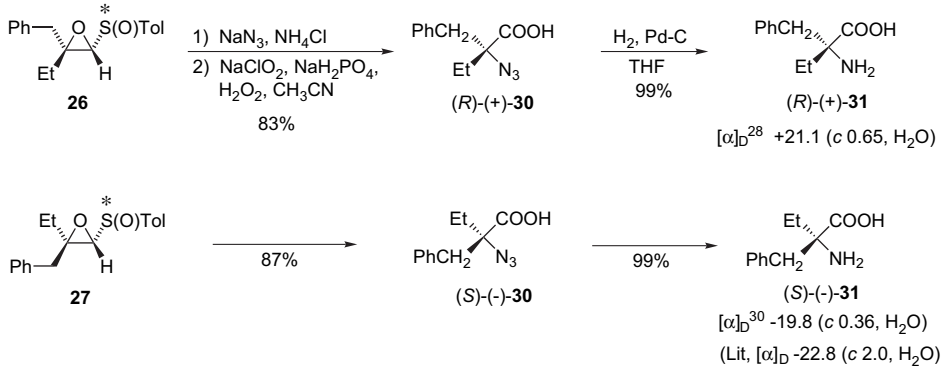
of both enantiomers of α-ethylphenylalanine methyl ester **29** and α-ethylphenylalanine **31** was investigated from 1-phenyl-2-butanone as shown in Schemes 5 and 6. At first, lithium α-carbanion of (*R*)-chloromethyl *p*-tolyl sulfoxide was reacted with 1-phenyl-2-butanone to give adducts **24** and **25** in quantitative yield. In this case, the ratio of the main product **24** and minor product **25** was 2:1. These adducts were separated by silica gel column chromatography and both were treated with *t*-BuOK to afford sulfinyloxiranes **26** and **27**, respectively, in quantitative yields.

The absolute structure of sulfinyloxiranes **26** and **27** was determined by the chemical shift of their ^{1}H NMR, as mentioned above, as shown in Scheme 5. The optical purity was determined to be over 99% by using HPLC with chiral column (CHIRALCEL OD). The main sulfinyloxirane **26** was treated with NaN_3 followed by iodine in methanol to give azido methyl ester (*R*)-**28** in 90% overall yield. Finally, the azido group in (*R*)-**28** was hydrogenated in ethyl acetate with Pd–C as a catalyst to give (*R*)-α-ethylphenylalanine methyl ester (*R*)-(+)-**29** in quantitative yield. All the spectral data and the specific rotations were highly consistent with the reported value.[19] In the same way, the minor sulfinyloxirane **27** gave (*S*)-α-ethylphenylalanine methyl ester (*S*)-(−)-**29** in good overall yield through azido methyl ester (*S*)-**28**.

Synthesis of α-amino acid itself, not its ester, is also quite important. We investigated the synthesis of both enantiomers of α-ethylphenylalanine **31** from the optically active



Scheme 5. Asymmetric synthesis of both enantiomers of α-ethylphenylalanine methyl ester **29** from 1-phenyl-2-butanone and (*R*)-chloromethyl *p*-tolyl sulfoxide.

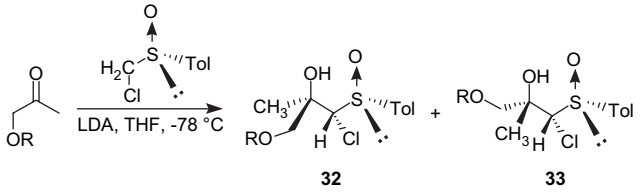


Scheme 6. Asymmetric synthesis of both enantiomers of α-ethylphenylalanine **31** from sulfinyloxiranes **26** and **27.**

sulfinyloxiranes **26** and **27** (Scheme 6). The main sulfinyloxirane **26** was treated with NaN_3 and the resultant azido aldehyde was oxidized with $NaClO_2$ to afford azido carboxylic acid (*R*)-(+)-**30** in 83% overall yield. The purified (*R*)-**30** was hydrogenated in THF with Pd–C as a catalyst to give the desired amino acid (*R*)-(+)-**31** in quantitative yield. Starting from the sulfinyloxirane **27** the enantiomer of α-ethylphenylalanine (*S*)-(−)-**31** was obtained in high overall yield and all the spectral data and the specific rotations were consistent with the reported value.[20] Purification of the α-amino acid **31** was performed as follows: After the hydrogenation, the catalyst was filtered off and the solvent was evaporated. The residue was dissolved in a small amount of water and the cloud was removed by passing the solution slowly through a pad of Celite. Water was evaporated and the residual crystals were recrystallized from methanol.

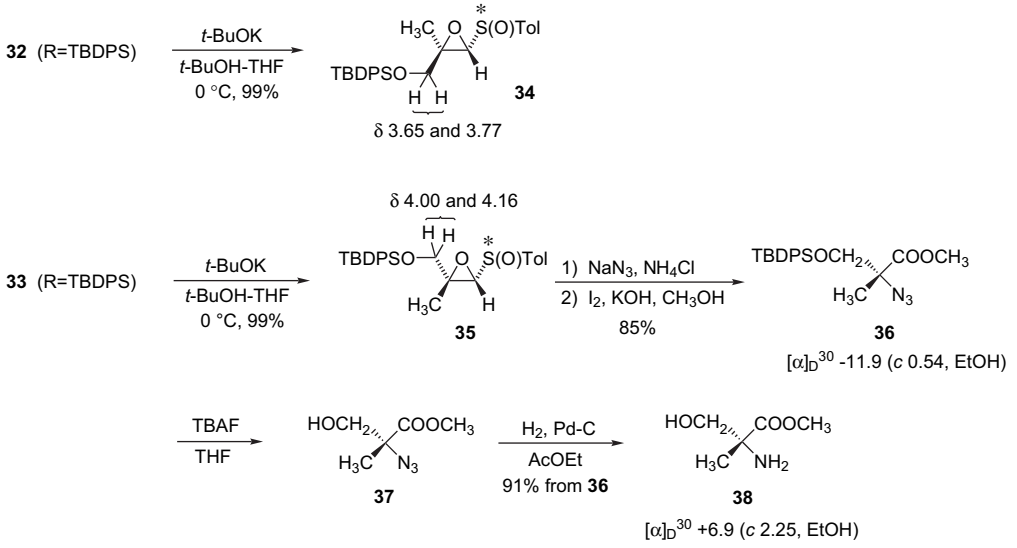
Finally, asymmetric synthesis of the serine derivative, (*R*)-α-methylserine methyl ester **38**, was investigated starting from hydroxyacetone (Scheme 7 and Table 4). First, diastereoselectivity of the addition reaction of lithium carbanion of chloromethyl *p*-tolyl sulfoxide with hydroxyacetone and its derivatives was studied and the results are summarized in Table 4.

Table 4. Diastereoselective addition of chloromethyl *p*-tolyl sulfoxide to *O*-protected acetols



Entry	R	LDA (equiv)	**32**:**33**	Yield/%
1	H	2.5	1:1	82
2	THP	1.2	1:1.5	99
3	TBDMS	1.5	1:2.0	94
4	TBDPS	1.5	1:2.3	99

The addition reaction of lithium α-sulfinyl carbanion of chloromethyl *p*-tolyl sulfoxide with hydroxyacetone itself gave adducts **32** and **33** in good yields; however, no diastereoselectivity was observed (entry 1). We synthesized *O*-protected hydroxyacetones and performed the addition reaction and found that the most bulky protecting group (TBDPS) showed the highest diastereoselectivity (entry 4).



Scheme 7. Asymmetric synthesis of (*R*)-α-methylserine methyl ester **38** from the main adduct of TBDPS-protected acetol and (*R*)-chloromethyl *p*-tolyl sulfoxide.

A synthesis of methylserine methyl ester **38** was investigated starting from this main adduct (R=TBDPS).

First, the minor adduct **32** and the main adduct **33** were converted to sulfinyloxiranes **34** and **35**, respectively, and the stereochemistry of these compounds was determined from ^{1}H NMR as mentioned above. Sulfinyloxirane **35** was treated with NaN_3 followed by iodine to give azido methyl ester **36** in good yield. The silyl protecting group of **36** was removed with TBAF to give the alcohol **37**, which was reduced with Pd–C as a catalyst in ethyl acetate to afford the desired α-methylserine methyl ester **38** in 91% overall yield from **36**.

In conclusion, a new method for the synthesis of α-quaternary α-amino acids and their methyl esters was realized starting from unsymmetrical ketones and chloromethyl *p*-tolyl sulfoxides through sulfinyloxiranes in good overall yields in relatively short steps. Asymmetric synthesis of α-quaternary α-amino acids and their methyl esters was also developed by using optically active chloromethyl *p*-tolyl sulfoxide. The absolute stereochemistry of the sulfinyloxiranes, at the same time absolute configuration of the amino acids or their esters, was easily determined from ^{1}H NMR of the optically active sulfinyloxiranes, which is one of the most striking characteristics of this method.

3. Experimental

3.1. General

All melting points are uncorrected. ^{1}H NMR spectra were measured in a $CDCl_3$ solution with JEOL JNM-LA 500 spectrometer. Electron-impact mass spectra (MS) were obtained at 70 eV by direct insertion. Silica gel 60 (Merck) containing 0.5% fluorescence reagent 254 and a quartz column were used for column chromatography and the products having UV absorption were detected by UV irradiation. In experiments requiring a dry solvent and reagent, benzylamine, DMSO, DMF, and acetonitrile were distilled from CaH_2 and THF was distilled from diphenylketyl. Methanol, *t*-BuOH, and ethyl acetate were distilled before use.

3.1.1. 2′-(*p*-Tolylsulfinyl)spiro[cyclopentadecane-1,1′-oxirane] (3a). This sulfinyloxirane was synthesized from cyclopendadecanone and chloromethyl *p*-tolyl sulfoxide through the adduct **6**[10] in almost quantitative yield in a similar way as described before.[11] Colorless crystals; mp 71–72 °C (AcOEt–hexane). IR (KBr) 2928, 2848, 1464, 1444, 1086, 1049 (SO), 810, 756 cm^{-1}; ^{1}H NMR δ 1.33–1.74 (26H, m), 1.87–1.93 (1H, m), 2.02–2.08 (1H, m), 2.42 (3H, s), 3.62 (1H, s), 7.35, 7.58 (each 2H, d, *J*=8.0 Hz). MS *m*/*z* (%) 236 (M$^+$, 32), 140 (100), 139 (24), 91 (45), 81 (33). Calcd for $C_{23}H_{36}O_2S$: M, 376.2436. Found: *m*/*z* 376.2432. Anal. Calcd for $C_{23}H_{36}O_2S$: C, 73.35; H, 9.64; S, 8.51. Found: C, 73.35; H, 9.59; S, 8.54.

3.1.2. 1-(Benzylamino)cyclopentadecanecarbaldehyde (7). A solution of **3a** (414 mg; 1.1 mmol) in dry benzylamine (1.08 mL; 9.9 mmol) was warmed at 70 °C for 24 h. The benzylamine was evaporated under vacuum to give a residue, which was purified by silica gel column chromatography to give **7** (340 mg; 90%) as colorless crystals; mp 56.5–58 °C (EtOH–H_2O). IR (KBr) 3322 (NH), 2923, 2857, 2787, 2696, 1709 (CO), 1455, 694 cm^{-1}; ^{1}H NMR δ 1.21–1.63 (29H, m), 3.55 (2H, s), 7.24–7.34 (5H, m), 9.39 (1H, s). MS *m*/*z* (%) 343 (M$^+$, 1), 272 (15), 202 (11), 146 (50), 133 (8), 91 (100). Calcd for $C_{23}H_{37}NO$: M, 343.2873. Found: *m*/*z* 343.2878. Anal. Calcd for $C_{23}H_{37}NO$: C, 80.41; H, 10.86; N, 4.08. Found: C, 80.42; H, 10.80; N, 4.23.

3.1.3. Methyl 1-(benzylamino)cyclopentadecanecarboxylate (8). A solution of KOH (80 mg; 1.43 mmol) in methanol (2 mL) was added to a solution of iodine (155 mg; 0.61 mmol) in 2 mL of methanol at room temperature with stirring. After 10 min, the solution was added dropwise to a solution of the aldehyde **7** (30 mg; 0.087 mmol) in methanol. The reaction mixture was stirred at room temperature for 20 min. The reaction was quenched by adding satd aq $Na_2S_2O_3$ and the whole was extracted with $CHCl_3$. The extract was washed with satd aq NH_4Cl and dried over $MgSO_4$. The product was purified by silica gel column chromatography to give **8** (17.8 mg; 55%) as colorless needles; mp 106–107.5 °C (EtOH–hexane). IR (KBr) 3338 (NH), 2928, 2855, 1716 (CO), 1459, 1218, 701 cm^{-1}; ^{1}H NMR δ 1.20–1.40 (25H, m), 1.57–1.65 (2H, m), 1.73–1.79 (2H, m), 3.51 (2H, s), 3.73 (3H, s), 7.22–7.32 (5H, m). MS *m*/*z* (%) 373 (M$^+$, 0.5), 315 (23), 314 (100), 91 (27). Calcd for $C_{24}H_{39}NO_2$: M, 373.2981. Found: *m*/*z* 373.2964. Anal. Calcd for $C_{24}H_{39}NO_2$: C, 77.16; H, 10.52; N, 3.75. Found: C, 77.32; H, 10.52; N, 3.94.

3.1.4. Methyl 1-aminocyclopentadecanecarboxylate (9). Palladium hydroxide (20 wt % Pd on carbon; 18 mg) was added to a solution of **8** (17.5 mg) in ethyl acetate (0.5 mL) and the reaction mixture was stirred at room temperature under hydrogen atmosphere for 12 h. The catalyst was filtered off and the solvent was evaporated to give a residue, which was purified by short silica gel column to afford **9** (13.1 mg; 99%) as a colorless oil; IR (neat) 3381(NH), 3314 (NH), 2929, 2857, 1732 (CO), 1460, 1222 cm^{-1}; ^{1}H NMR δ 1.25–1.37 (26H, m), 1.53–1.59 (2H, m), 1.69–1.75 (2H, m), 3.71 (3H, s). MS *m*/*z* (%) 283 (M$^+$, trace), 268 (2), 225 (16), 224 (100). Calcd for $C_{17}H_{33}NO_2$: M, 283.2511. Found: *m*/*z* 283.2504.

3.1.5. 2″-(*p*-Tolylsulfinyl)dispiro[1,3-dioxolane-2,1′-cyclohexane-4′,1″-oxirane] (3b). Colorless crystals; mp 88–89 °C (AcOEt–hexane). IR (KBr) 2964, 2891, 1092, 1031 (SO), 931 cm^{-1}; ^{1}H NMR δ 1.56–1.64 (1H, m), 1.79–2.12 (6H, m), 2.31–2.37 (1H, m), 2.43 (3H, s), 3.73 (1H, s), 3.96–4.02 (4H, m), 7.37, 7.60 (each 2H, d, *J*=8.0 Hz). MS *m*/*z* (%) 308 (M$^+$, 0.8), 169 (100), 140 (36), 125 (26), 99 (76), 86 (50). Calcd for $C_{16}H_{20}O_4S$: M, 308.1082. Found: *m*/*z* 308.1084. Anal. Calcd for $C_{16}H_{20}O_4S$: C, 62.31; H, 6.54; S, 10.40. Found: C, 62.32; H, 6.52; S, 10.40.

3.1.6. 2-(*tert*-Butyldiphenylsilanyloxy)methyl-2-methyl-3-(*p*-tolylsulfinyl)oxirane (3c). Less polar isomer (*Z*)-**3c**: Colorless crystals; mp 122.0–123.0 °C (AcOEt–hexane). IR (KBr) 3050, 2932, 2858, 1493, 1472, 1428, 1112, 1048 (SO), 811, 743, 702 cm^{-1}; ^{1}H NMR δ 1.12 (9H, s), 1.53 (3H, s), 2.40 (3H, s), 3.71 (1H, s), 4.00 (1H, d, *J*=11.6 Hz), 4.16 (1H, d, *J*=11.6 Hz), 7.32 (2H, d, *J*=7.9 Hz), 7.40–7.49 (8H, m), 7.71–7.75 (4H, m). MS *m*/*z* (%) 464

(M^+, trace), 407 (20), 268 (24), 267 (100), 243 (18), 239 (20), 199 (61), 197 (33), 140 (37), 135 (64), 129 (28), 91 (20). Calcd for $C_{27}H_{32}O_3SSi$: M, 464.1841. Found: *m/z* 464.1844. Anal. Calcd for $C_{27}H_{32}O_3SSi$: C, 69.79; H, 6.94; S, 6.90. Found: C, 69.54; H, 6.93; S, 7.15.

More polar isomer (*E*)-**3c**: Colorless oil; IR (neat) 2931, 2859, 1493, 1472, 1428, 1113, 1088, 1048 (SO), 703 cm^{-1}; ^1H NMR δ 1.01 (9H, s), 1.72 (3H, s), 2.43 (3H, s), 3.65 (1H, d, *J*=11.9 Hz), 3.77 (1H, d, *J*=11.9 Hz), 3.90 (1H, s), 7.35–7.38 (6H, m), 7.40–7.43 (2H, m), 7.59–7.64 (6H, m). MS *m/z* (%) 464 (M^+, trace), 268 (24), 267 (100), 239 (20), 199 (57), 197 (32), 183 (22), 139 (38), 135 (66), 129 (31), 91 (22). Calcd for $C_{27}H_{32}O_3SSi$: M, 464.1841. Found: *m/z* 464.1836.

3.1.7. 2-Benzyl-2-ethyl-3-(*p*-tolylsulfinyl)oxirane (3d). Less polar isomer (*Z*)-**3d**: Colorless oil; IR (neat) 3029, 2973, 2939, 1598, 1495, 1455, 1401, 1085, 1045 (SO), 1016, 704 cm^{-1}; ^1H NMR δ 0.87 (3H, t, *J*=7.9 Hz), 1.53 (1H, sextet, *J*=7.4 Hz), 1.61 (1H, sextet, *J*=7.4 Hz), 2.45 (3H, s), 3.33 (2H, s), 3.78 (1H, s), 7.25–7.31 (1H, m), 7.34–7.41 (6H, m), 7.64 (2H, d, *J*=8.3 Hz). MS *m/z* (%) 300 (M^+, trace), 161 (25), 140 (34), 139 (15), 92 (20), 91 (100). Calcd for $C_{18}H_{20}O_2S$: M, 300.1184. Found: *m/z* 300.1186.

More polar isomer (*E*)-**3d**: Colorless crystals; mp 77.5–78.5 °C (AcOEt–hexane). IR (KBr) 3029, 2972, 2925, 1598, 1495, 1454, 1085, 1049 (SO), 703 cm^{-1}; ^1H NMR δ 1.23 (3H, t, *J*=7.6 Hz), 1.86 (1H, sextet, *J*=7.1 Hz), 2.01 (1H, sextet, *J*=7.1 Hz), 2.42 (3H, s), 2.89 (1H, d, *J*=14.7 Hz), 3.07 (1H, d, *J*=14.7 Hz), 3.67 (1H, s), 7.18–7.31 (5H, m), 7.35 (2H, d, *J*=8.3 Hz), 7.57 (2H, d, *J*=8.3 Hz). Anal. Calcd for $C_{18}H_{20}O_2S$: C, 71.97; H, 6.71; S, 10.67. Found: C, 72.02; H, 6.69; S, 10.68.

3.1.8. 2′-(*p*-Tolylsulfinyl)spiro[cyclobutane-1,1′-oxirane] (3e). Colorless oil; IR (neat) 2942, 1493, 1416, 1086, 1051 (SO), 815 cm^{-1}; ^1H NMR δ 1.97–2.04 (2H, m), 2.41–2.47 (1H, m), 2.43 (3H, s), 2.55–2.62 (1H, m), 2.66–2.72 (1H, m), 2.84–2.90 (1H, m), 3.77 (1H, s), 7.36, 7.59 (each 2H, d, *J*=8.2 Hz). MS *m/z* (%) 222 (M^+, 0.3), 206 (2), 140 (43), 139 (45), 123 (16), 92 (57), 91 (42), 83 (100). Calcd for $C_{12}H_{14}O_2S$: M, 222.0714. Found: *m/z* 222.0712.

3.1.9. 2′-(*p*-Tolylsulfinyl)spiro[cyclodecane-1,1′-oxirane] (3f). Colorless crystals; mp 61.5–62.5 °C (AcOEt–hexane). IR (KBr) 2936, 2906, 1483, 1085, 1045 (SO), 809 cm^{-1}; ^1H NMR δ 1.55–1.93 (16H, m), 2.00–2.10 (1H, m), 2.17–2.31 (1H, m), 2.42 (3H, s), 3.63 (1H, s), 7.35, 7.58 (each 2H, d, *J*=8.1 Hz). MS (FAB) *m/z* (%) 307 ($[M+H]^+$, 55), 289 (10), 167 (100), 154 (51), 149 (52), 141 (63), 140 (51), 81 (39). Calcd for $C_{18}H_{27}O_2S$: [M+H] 307.1732. Found: *m/z* 307.1737. Anal. Calcd for $C_{18}H_{27}O_2S$: C, 70.55; H, 8.55; S, 10.46. Found: C, 70.54; H, 8.57; S, 10.45.

3.1.10. 2-Methyl-2-(2-phenylethyl)-3-(*p*-tolylsulfinyl)-oxirane (3g). Less polar isomer (*Z*)-**3g**: Colorless oil; IR (neat) 3005, 1599, 1494, 1455, 1381, 1218, 1086, 1040 (SO), 1016, 771 cm^{-1}; ^1H NMR δ 1.46 (3H, s), 2.21–2.35 (2H, m), 2.42 (3H, s), 2.85–2.91 (1H, m), 2.98–3.04 (1H, m), 3.70 (1H, s), 7.21–7.28 (3H, m), 7.32 (2H, d, *J*=7.3 Hz), 7.36 (2H, d, *J*=8.0 Hz), 7.58 (2H, d, *J*=8.0 Hz). MS *m/z* (%) 300 (M^+, trace), 140 (20), 92 (19), 91 (100). Calcd for $C_{18}H_{20}O_2S$: M, 300.1184. Found: *m/z* 300.1185.

More polar isomer (*E*)-**3g**: Colorless oil; IR (neat) 3027, 2927, 1599, 1495, 1455, 1395, 1208, 1087, 1047 (SO), 1016, 701 cm^{-1}; ^1H NMR δ 1.76 (3H, s), 1.94 (2H, t, *J*=8.3 Hz), 2.42 (3H, s), 2.68–2.72 (2H, m), 3.71 (1H, s), 7.12–7.15 (2H, m), 7.17–7.20 (1H, m), 7.24–7.29 (2H, m), 7.36 (2H, d, *J*=8.0 Hz), 7.60 (2H, d, *J*=8.0 Hz). MS *m/z* (%) 300 (M^+, trace), 140 (28), 92 (18), 91 (100). Calcd for $C_{18}H_{20}O_2S$: M, 300.1184. Found: *m/z* 300.1192.

3.1.11. 8-Azido-1,4-dioxaspiro[4,5]decane-8-carboxylic acid (11). A solution of **3b** (20.1 mg; 0.065 mmol) in methanol (0.56 mL) and water (0.07 mL) was heated with NaN_3 (21.2 mg; 0.33 mmol) in the presence of NH_4Cl (7.7 mg; 0.15 mmol) for 12 h under reflux. The reaction mixture was diluted with water, and the whole was extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and the solvent was evaporated under vacuum to afford the azido aldehyde **10**. Without further purification, $NaClO_2$ (74.3 mg; 0.82 mmol) was added to a solution of azido aldehyde **10** in acetonitrile (0.13 mL), NaH_2PO_4 (95.3 mg) in water and 35% H_2O_2 (71 mg; 0.65 mmol). The reaction mixture was stirred at room temperature for 16 h. A small amount of Na_2SO_3 was added to destroy the unreacted $NaClO_2$ and H_2O_2 at 0 °C. Acidification with 10% aqueous HCl afforded **11** (12.7 mg; 86% from **3b**) as colorless prisms; mp 60–62 °C (AcOEt–hexane). IR (KBr) 2935, 2890, 2111 (N_3), 1719 (CO), 1265, 1152, 1106, 954 cm^{-1}; ^1H NMR δ 1.70–1.73 (2H, m), 1.83 (2H, ddd, *J*=13.0, 12.8, 4.0 Hz), 1.96 (2H, d, *J*=13.8 Hz), 2.17 (2H, ddd, *J*=13.3, 13.1, 4.0 Hz), 3.94–4.00 (4H, m). MS *m/z* (%) 227 (M^+, trace), 185 (2), 155 (3), 126 (46), 99 (100), 82 (25). Anal. Calcd for $C_9H_{13}N_3O_4$: C, 47.57; H, 5.77; N, 18.49. Found: C, 47.62; H, 5.79; N, 18.04.

3.1.12. 8-Amino-1,4-dioxaspiro[4,5]decane-8-carboxylic acid (12). Palladium carbon 10% (54 mg) was added to a solution of **11** (54 mg; 0.24 mmol) in THF (2.4 mL). The reaction mixture was stirred at room temperature for 13 h under hydrogen atmosphere. The catalyst was filtered off and the solvent was evaporated under vacuum to afford **12** (47 mg; 98%) as colorless crystals; dec 193 °C. IR (KBr) 2954, 2931, 2883, 2598, 1616 (CO), 1560, 1400, 1333, 1273, 1129, 1095, 880 cm^{-1}; ^1H NMR (D_2O) δ 1.61 (2H, t, *J*=11.0 Hz), 1.69–1.81 (4H, m), 2.05–2.10 (2H, m), 3.89 (4H, s). MS (FAB) *m/z* (%) 202 ($[M+H]^+$, 43), 185 (92), 154 (49), 138 (23), 137 (52), 136 (31), 93 (100). Calcd for $C_9H_{16}NO_4$: M, 202.1079. Found: *m/z* 202.1081.

3.1.13. Methyl 8-Azido-1,4-dioxaspiro[4,5]decane-8-carboxylate (13). CH_2N_2 in Et_2O was added dropwise to a solution of **11** (37.5 mg; 0.17 mmol) in Et_2O at 0 °C until the light yellow color of excess CH_2N_2 appeared. The reaction mixture was stirred for 10 min. After concentration, the residue was purified by silica gel flash chromatography to give **13** (34.1 mg; 86%) as a colorless oil. IR (neat) 2959, 2935, 2884, 2109 (N_3), 1739 (CO), 1440, 1277, 1249, 1151, 1105, 938 cm^{-1}; ^1H NMR δ 1.66–1.70 (2H, m), 1.82 (2H, ddd, *J*=12.9, 12.7, 4.0 Hz), 1.89–1.95 (2H, m), 2.13 (2H,

ddd, J=13.2, 13.0, 4.0 Hz), 3.80 (3H, s), 3.92–3.99 (4H, m). MS m/z (%) 241 (M^+, trace), 126 (61), 99 (100), 82 (25).

3.1.14. Direct oxidation of 3b to 13 using iodine in methanol. A solution of **3b** (20 mg; 0.065 mmol) in methanol (0.58 mL) and water (0.072 mL) was heated under reflux with NaN_3 (21.1 mg; 0.33 mmol) in the presence of NH_4Cl (7.6 mg; 0.14 mmol) for 11 h. The reaction mixture was diluted with water, and the whole was extracted with $CHCl_3$. The solution was dried over $MgSO_4$ and the solvent was evaporated under vacuum to afford the azido aldehyde **10**. A solution of iodine (115 mg; 0.45 mmol) and a 4% (w/w) solution of potassium hydroxide (59.2 mg; 0.91 mmol) in methanol (1.4 g) was stirred at room temperature for 10 min. This solution was added dropwise to a solution of the azido aldehyde **10** in methanol (1 mL). The reaction mixture was stirred at room temperature for 20 min. The reaction was quenched by satd aq $Na_2S_2O_3$. The whole was extracted with $CHCl_3$ and the organic layer was washed with brine, and dried over $MgSO_4$. After concentration, the residue was purified by silica gel flash chromatography to give **13** (12.1 mg; 77% from **3b**) as a colorless oil.

3.1.15. Methyl 8-amino-1,4-dioxaspiro[4,5]decane-8-carboxylate (14). Colorless oil; IR (neat) 3376 (NH), 3310 (NH), 2953, 2885, 1729 (CO), 1440, 1241, 1108 cm^{-1}; ^1H NMR δ 1.55–1.69 (6H, m), 1.83–1.95 (2H, m), 2.05–2.16 (2H, m), 3.72 (3H, s), 3.95 (4H, s). MS m/z (%) 215 (M^+, 3), 187 (8), 168 (12), 156 (100), 99 (31), 94 (45), 86 (33). Calcd for $C_{10}H_{17}NO_4$: M, 215.1158. Found: m/z 215.1156.

3.1.16. 2-Azido-3-(*tert*-butyldiphenylsilanyloxy)-2-methylpropionic acid (15a). Colorless amorphous; IR (KBr) 3072, 2933, 2860, 2651, 2103 (N_3), 1719 (CO), 1428, 1259, 1113, 824, 702 cm^{-1}; ^1H NMR δ 1.05 (9H, s), 1.36 (1H, s), 3.80 (1H, d, J=10.4 Hz), 3.98 (1H, d, J=10.4 Hz), 7.39–7.44 (6H, m), 7.66–7.70 (4H, m). MS (FAB) m/z (%) 429 ($[M+H+Na_2]^+$, 30), 428 (100), 406 ($[M+H+Na]^+$, 30), 301 (30), 199 (21), 197 (20), 135 (43), 123 (68). Calcd for $C_{20}H_{25}N_3O_3SiNa$: M, 406.1563. Found: m/z 406.1559.

3.1.17. 2-Azido-2-benzylbutyric acid (15b). Yellow amorphous; IR (neat) 2977, 2109 (N_3), 1714 (CO), 1454, 1260, 701 cm^{-1}; ^1H NMR δ 1.03 (3H, t, J=7.5 Hz), 1.76–1.85 (1H, m), 1.97–2.05 (1H, m), 3.04 (1H, d, J=14.0 Hz), 3.22 (1H, d, J=14.0 Hz), 7.24–7.34 (5H, m). MS m/z (%) 219 (M^+, 1), 147 (12), 92 (50), 91 (100). Calcd for $C_{11}H_{13}N_3O_2$: M, 219.1007. Found: m/z 219.1009.

3.1.18. 2-Amino-3-(*tert*-butyldiphenylsilanyloxy)-2-methylpropionic acid (16a). Colorless crystals; dec 195 °C (MeOH). IR (KBr) 3049, 2931, 2857, 1645 (CO), 1589, 1509, 1428, 1400, 1362, 1113, 1088, 701 cm^{-1}; ^1H NMR (CD_3OD) δ 1.08 (9H, s), 1.39 (3H, s), 3.68 (1H, d, J=10.7 Hz), 4.00, (1H, d, J=10.7 Hz), 7.34–7.47 (6H, m), 7.65–7.72 (4H, m). MS (FAB) m/z (%) 358 ($[M+H]^+$, 100), 234 (36), 199 (20), 174 (37), 135 (30). Calcd for $C_{20}H_{28}NO_3Si$: 358.1838. Found: m/z 358.1834.

3.1.19. 2-Amino-2-benzylbutyric acid (16b). Colorless crystals; dec 218 °C (MeOH). IR (KBr) 3411, 2970, 1619 (CO), 1522, 1497, 1397, 703 cm^{-1}; ^1H NMR (CD_3OD) δ 1.00 (3H, t, J=7.6 Hz), 1.68–1.72 (1H, m), 2.01–2.05 (1H, m), 2.95 (1H, d, J=14.1 Hz), 3.27 (1H, d, J=14.1 Hz), 7.24–7.35 (5H, m). MS (FAB) m/z (%) 194 ($[M+H]^+$, 100), 154 (22), 148 (31), 137 (18), 93 (18). Calcd for $C_{11}H_{16}NO_2$: 194.1181. Found: m/z 194.1181.

3.1.20. Methyl 1-azidocyclobutanecarboxylate (17a). Colorless oil; IR (neat) 2957, 2108 (N_3), 1739 (CO), 1250, 1138 cm^{-1}; ^1H NMR δ 1.96–2.11 (2H, m), 2.25–2.31 (2H, m), 2.58–2.64 (2H, m), 3.82 (3H, s).

3.1.21. Methyl 1-azidocyclodecanecarboxylate (17b). Colorless oil; IR (neat) 2927, 2106 (N_3), 1743 (CO), 1251, 1202 cm^{-1}; ^1H NMR δ 1.45–1.66 (14H, m), 1.84–2.04 (4H, m), 3.81 (3H, s).

3.1.22. Methyl 1-azidocyclopentadecanecarboxylate (17c). Colorless oil; IR (neat) 2930, 2858, 2107 (N_3), 1743 (CO), 1460, 1255 cm^{-1}; ^1H NMR δ 1.24–1.42 (24H, m), 1.66–1.73 (2H, m), 1.82–1.88 (2H, m), 3.79 (3H, s).

3.1.23. Methyl 2-azido-2-methyl-4-phenylbutyrate (17d). Colorless oil; IR (neat) 3028, 2955, 2105 (N_3), 1741 (CO), 1604, 1498, 1457, 1380, 1251, 1174, 1113, 1068, 700 cm^{-1}; ^1H NMR δ 1.55 (3H, s), 1.93–1.99 (1H, m), 2.10–2.16 (1H, m), 2.53–2.59 (1H, m), 2.69–2.75 (1H, m), 3.76 (3H, m), 7.16–7.21 (3H, m), 7.26–7.30 (2H, m). MS (FAB) m/z (%) 234 ($[M+H]^+$, 3), 197 (54), 149 (30), 135 (100), 105 (40), 91 (51). Calcd for $C_{12}H_{16}N_3O_2$: 234.1243. Found: m/z 234.1243.

3.1.24. Methyl 2-azido-2-benzylbutyrate (17e). Colorless oil; IR (neat) 3032, 2976, 2954, 2106 (N_3), 1739 (CO), 1497, 1456, 1243, 1199, 1122, 1003, 701 cm^{-1}; ^1H NMR δ 0.97 (3H, t, J=7.3 Hz), 1.75 (1H, sextet, J=7.0 Hz), 1.92 (1H, sextet, J=7.0 Hz), 3.01 (1H, d, J=14.1 Hz), 3.16 (1H, d, J=14.1 Hz), 3.76 (3H, s), 7.20 (2H, d, J=7.6 Hz), 7.24–7.32 (3H, m). MS m/z (%) 233 (M^+, trace), 145 (10), 91 (100). Calcd for $C_{12}H_{15}N_3O_2$: M, 233.1164. Found: m/z 233.1166.

3.1.25. Methyl 1-aminocyclobutanecarboxylate (18a). Colorless oil; IR (neat) 3370 (NH), 2927, 2856, 1733 (CO), 1275, 1122 cm^{-1}; ^1H NMR δ 1.91–2.04 (4H, m), 2.53–2.58 (2H, m), 3.76 (3H, s). MS (FAB) m/z (%) 130 ($[M+H]^+$, 13), 93 (100), 75 (52). Calcd for $C_6H_{12}NO_2$: 130.0868. Found: m/z 130.0865.

3.1.26. Methyl 1-aminocyclodecanecarboxylate (18b). Colorless oil; IR (neat) 3377 (NH), 2925, 1732 (CO), 1196 cm^{-1}; ^1H NMR δ 1.47–1.75 (18H, m), 1.85–1.91 (2H, m), 3.70 (3H, s). MS (FAB) m/z (%) 214 ($[M+H]^+$, 34), 185 (25), 154 (100), 137 (83), 136 (86), 107 (29), 93 (53), 89 (23). Calcd for $C_{12}H_{24}NO_2$: 214.1808. Found: m/z 214.1814.

3.1.27. Methyl 2-amino-2-methyl-4-phenylbutyrate (18c). Colorless oil; IR (neat) 3377 (NH), 3311 (NH), 3027, 2926, 2856, 1731 (CO), 1603, 1497, 1454, 1199, 1117, 700 cm^{-1}; ^1H NMR δ 1.38 (3H, s), 1.77 (2H, s), 1.86–1.92 (1H, m), 2.01–2.07 (1H, m), 2.49–2.55 (1H, m), 2.63–2.69 (1H, m), 3.71 (3H, s), 7.16–7.20 (3H, m), 7.27 (2H, d, J=6.7 Hz). MS m/z (%) 207 (M^+, 3), 149 (11), 148

(100), 102 (21), 91 (67). Calcd for $C_{12}H_{17}NO_2$: M, 207.1260. Found: *m/z* 207.1262.

3.1.28. Methyl 2-amino-2-benzylbutyrate (18d). Colorless oil; IR (neat) 3379 (NH), 3316 (NH), 3030, 2967, 1732 (CO), 1604, 1495, 1455, 1196, 1117, 997, 757, 703 cm^{-1}; ^1H NMR δ 0.89 (3H, t, J=7.7 Hz), 1.59–1.66 (3H, m), 1.95 (1H, sextet, J=7.7 Hz), 2.76 (1H, d, J=13.1 Hz), 3.17 (1H, d, J=13.1 Hz), 3.70 (3H, s), 7.13 (2H, d, J=6.7 Hz), 7.20–7.30 (3H, m). MS (FAB) *m/z* (%) 208 ($[M+H]^+$, 100), 149 (18), 148 (60), 116 (26), 91 (38). Calcd for $C_{12}H_{18}NO_2$: 208.1337. Found: *m/z* 208.1337.

3.1.29. (2*S*,3*R*,*R*s)-(+)-2-Tetralin-2-yl-3-(*p*-tolylsulfinyl)oxirane (20). Colorless crystals; mp 78–79.5 °C (AcOEt–hexane). IR (KBr) 2925, 1495, 1086, 1046 (SO), 750 cm^{-1}; ^1H NMR δ 1.69–1.74 (1H, m), 2.18 (1H, ddd, J=13.5, 10.6, 5.5 Hz), 2.43 (3H, s), 2.87–2.95 (1H, m), 2.96–3.05 (1H, m), 3.17 (1H, d, J=18.0 Hz), 3.72 (1H, d, J=18.0 Hz), 3.86 (1H, s), 7.13–7.21 (4H, m), 7.37 (2H, d, J=8.0 Hz), 7.62 (2H, d, J=8.0 Hz). $[\alpha]_D^{24}$ +61.8 (*c* 0.40, $CHCl_3$). Racemic-**20**: Colorless prisms; mp 104–105 °C (AcOEt–hexane). MS *m/z* (%) 298 (M^+, trace), 154 (48), 129 (100), 128 (47), 91 (39). Calcd for $C_{18}H_{18}O_2S$: M, 298.1028. Found: *m/z* 298.1034. Anal. Calcd for $C_{18}H_{18}O_2S$: C, 72.45; H, 6.08; S, 10.75. Found: C, 72.35; H, 6.00; S, 10.67.

3.1.30. (2*R*,3*R*,*R*s)-(−)-2-Tetralin-2-yl-3-(*p*-tolylsulfinyl)oxirane (21). Colorless crystals; mp 81.5–83.5 °C (AcOEt–hexane). IR (KBr) 2925, 1495, 1455, 1086, 1048 (SO), 754 cm^{-1}; ^1H NMR δ 2.28–2.33 (1H, m), 2.39–2.47 (1H, m), 2.44 (3H, s), 2.87 (1H, d, J=17.4 Hz), 3.07–3.17 (2H, m), 3.13 (1H, d, J=17.4 Hz), 3.88 (1H, s), 7.02 (1H, d, J=6.7 Hz), 7.12–7.20 (3H, m), 7.38, 7.62 (each 2H, d, J=8.6 Hz). $[\alpha]_D^{23}$ −60.7 (*c* 0.47, $CHCl_3$). Racemic-**21**: Colorless crystals; mp 133–135 °C (AcOEt–hexane). MS *m/z* (%) 298 (M^+, trace), 158 (48), 140 (23), 129 (100), 91 (41). Calcd for $C_{18}H_{18}O_2S$: M, 298.1027. Found: *m/z* 298.1027. Anal. Calcd for $C_{18}H_{18}O_2S$: C, 72.45; H, 6.08; S, 10.75. Found: C, 72.45; H, 6.09; S, 10.79.

3.1.31. (*R*)-(−)-Methyl 2-azidotetraline-2-carboxylate (22). Colorless oil; $[\alpha]_D^{24}$ −38.1 (*c* 0.56, EtOH). IR (neat) 3022, 2954, 2108 (N_3), 1743 (CO), 1455, 1435, 1282, 1256 cm^{-1}; ^1H NMR δ 2.17–2.20 (2H, m), 2.87 (1H, dt, J=17.4, 4.9 Hz), 2.95–3.04 (1H, m), 3.00 (1H, d, J=16.8 Hz), 3.31 (1H, d, J=16.8 Hz), 3.84 (3H, s), 7.08–7.17 (4H, m). MS *m/z* (%) 231 (M^+, trace), 188 (25), 144 (100), 129 (31), 117 (73), 115 (25). Calcd for $C_{12}H_{13}N_3O_2$: M, 231.1008. Found: *m/z* 231.1008. (*S*)-(+)-**22**: Colorless oil; $[\alpha]_D^{26}$ +39.2 (*c* 0.26, EtOH).

3.1.32. (*R*)-(+)-Methyl 2-aminotetraline-2-carboxylate (23). Colorless oil; $[\alpha]_D^{21}$ +19.6 (*c* 0.27, EtOH). IR (neat) 3375 (NH), 3302 (NH), 2950, 2848, 1731 (CO), 1215 cm^{-1}; ^1H NMR δ 1.87–1.94 (1H, m), 2.13–2.20 (1H, m), 2.75 (1H, d, J=16.5 Hz), 2.83 (1H, dt, J=17.1, 5.5 Hz), 3.00 (1H, ddd, J=17.1, 10.1, 6.1 Hz), 3.30 (1H, d, J=16.5 Hz), 3.74 (3H, s), 7.06–7.14 (4H, m). MS *m/z* (%) 205 (M^+, 12), 146 (100), 129 (43), 128 (12), 104 (15). Calcd for $C_{12}H_{15}NO_2$: M, 205.1103. Found: *m/z* 205.1103. (*S*)-(−)-**23**: Colorless oil; $[\alpha]_D^{24}$ −19.3 (*c* 0.57, EtOH).

3.1.33. (1*R*,2*S*,*R*s)-(−)-2-Benzyl-1-chloro-1-(*p*-tolylsulfinyl)-2-butanol (24). Colorless oil; $[\alpha]_D^{30}$ −131.9 (*c* 0.53, EtOH). Racemic-**24**: Colorless crystals; mp 161–162 °C (AcOEt–hexane). IR (KBr) 3368, 2964, 1495, 1454, 1086, 1045 (SO), 1032, 701 cm^{-1}; ^1H NMR δ 1.06 (3H, t, J=7.3 Hz), 1.78 (1H, sextet, J=7.4 Hz), 2.02 (1H, sextet, J=7.4 Hz), 2.41 (3H, s), 2.52 (1H, s), 3.19 (1H, d, J=14.1 Hz), 3.26 (1H, d, J=14.1 Hz), 4.31 (1H, s), 7.27–7.37 (9H, m). Anal. Calcd for $C_{18}H_{21}ClO_2S$: C, 64.18; H, 6.28; Cl, 10.52; S, 9.52. Found: C, 64.18; H, 6.23; Cl, 10.45; S, 9.50.

3.1.34. (1*R*,2*R*,*R*s)-(−)-2-Benzyl-1-chloro-1-(*p*-tolylsulfinyl)-2-butanol (25). Colorless crystals; $[\alpha]_D^{30}$ −50.8 (*c* 0.53, EtOH). Racemic-**25**: Colorless crystals; mp 120.5–121.5 °C (AcOEt–hexane); IR (KBr) 3324, 2970, 1456, 1084, 1042 (SO), 1017, 703 cm^{-1}; ^1H NMR δ 1.06 (3H, t, J=7.6 Hz), 1.90 (1H, sextet, J=7.3 Hz), 1.99 (1H, sextet, J=7.3 Hz), 2.41 (3H, s), 2.61 (1H, s), 3.09 (1H, d, J=14.0 Hz), 3.26 (1H, d, J=14.0 Hz), 4.22 (1H, s), 7.24–7.34 (7H, m), 7.40 (2H, d, J=8.0 Hz). Anal. Calcd for $C_{18}H_{21}ClO_2S$: C, 64.18; H, 6.28; Cl, 10.52; S, 9.52. Found: C, 63.89; H, 6.24; Cl, 10.36; S, 9.42.

3.1.35. (2*S*,3*R*,*R*s)-(+)-2-Benzyl-2-ethyl-3-(*p*-tolylsulfinyl)oxirane (26). Colorless oil; $[\alpha]_D^{29}$ +1.8 (*c* 0.95, EtOH). Spectral data see (*Z*)-**3d**.

3.1.36. (2*R*,3*R*,*R*)-(+)-2-Benzyl-2-ethyl-3-(*p*-tolylsulfinyl)oxirane (27). Colorless crystals; mp 82–83 °C (AcOEt–hexane); $[\alpha]_D^{29}$ +12.7 (*c* 2.63, EtOH). Spectral data see (*E*)-**3d**.

3.1.37. (*R*)-(+)-Methyl 2-azido-2-benzylbutyrate (28). Colorless oil; $[\alpha]_D^{30}$ +41.8 (*c* 1.52, EtOH). Spectral data see **17e**.

3.1.38. (*S*)-(−)-Methyl 2-azido-2-benzylbutyrate (28). Colorless oil; $[\alpha]_D^{29}$ −40.8 (*c* 1.03, EtOH). Spectral data see **17e**.

3.1.39. (*R*)-(+)-Methyl 2-amino-2-benzylbutyrate (29). Colorless oil; $[\alpha]_D^{30}$ +22.1 (*c* 2.04, $CHCl_3$). Spectral data see **18d**.

3.1.40. (*S*)-(−)-Methyl 2-amino-2-benzylbutyrate (29). Colorless oil; $[\alpha]_D^{30}$ −21.6 (*c* 0.53, $CHCl_3$). Spectral data see **18d**.

3.1.41. (*R*)-(+)-2-Azido-2-benzylbutyric acid (30). Colorless oil; $[\alpha]_D^{29}$ +38.9 (*c* 0.99, EtOH). Spectral data see **15b**.

3.1.42. (*S*)-(−)-2-Azido-2-benzylbutyric acid (30). Colorless oil; $[\alpha]_D^{27}$ −43.4 (*c* 0.43, EtOH). Spectral data see **15b**.

3.1.43. (*R*)-(+)-2-Amino-2-benzylbutyric acid (31). Colorless oil; $[\alpha]_D^{30}$ +21.1 (*c* 0.65, H_2O). Spectral data see **16b**.

3.1.44. (*S*)-(−)-2-Amino-2-benzylbutyric acid (31). Colorless oil; $[\alpha]_D^{30}$ −19.8 (*c* 0.36, H_2O). Spectral data see **16b**.

3.1.45. (1*R*,2*R*,*R*s)-(−)-3-(*tert*-Butyldiphenylsilanyloxy)-1-chloro-2-methyl-1-(*p*-tolylsulfinyl)-2-propanol (32). Colorless oil; $[\alpha]_D^{31}$ −124.2 (*c* 0.66, EtOH). IR (neat) 3369,

3072, 2932, 2859, 1494, 1472, 1392, 1217, 1087 (SO) cm^{-1}; ^1H NMR δ 1.07 (9H, s), 1.42 (3H, s), 2.44 (3H, s), 3.30 (1H, s), 3.70 (1H, d, J=10.4 Hz), 3.86 (1H, d, J=10.4 Hz), 4.60 (1H, s), 7.34–7.50 (10H, m), 7.59–7.65 (4H, m). MS m/z (%) 499 (M^+, trace), 445 (33), 444 (23), 443 (75), 199 (75), 198 (28), 139 (100), 135 (47), 91 (21). Calcd for $C_{27}H_{32}O_3ClSSi$: M, 499.1530. Found: m/z 499.1535.

3.1.46. (1*R*,2*S*,*R*s)-(−)-3-(*tert*-Butyldiphenylsilanyloxy)-1-chloro-2-methyl-1-(*p*-tolylsulfinyl)-2-propanol (33). Colorless oil; $[\alpha]_D^{31}$ −91.5 (c 1.29, EtOH). IR (neat) 3401, 3011, 2932, 2859, 1494, 1472, 1463, 1428, 1217, 1088 (SO), 760 cm^{-1}; ^1H NMR δ 1.10 (9H, s), 1.57 (3H, s), 2.44 (3H, s), 3.15 (1H, s), 3.80 (1H, d, J=10.4 Hz), 3.92 (1H, d, J=10.4 Hz), 4.68 (1H, s), 7.34 (2H, d, J=8.0 Hz), 7.36–7.49 (8H, m), 7.65–7.71 (4H, m). MS m/z (%) 499 (M^+, trace), 445 (32), 444 (22), 443 (74), 199 (75), 197 (27), 139 (100), 135 (47), 91 (20). Calcd for $C_{27}H_{32}O_3ClSSi$: M, 499.1530. Found: m/z 499.1521.

3.1.47. (2*R*,3*R*,*R*s)-(−)-34. Colorless oil; $[\alpha]_D^{30}$ −22.8 (c 1.16, EtOH). Spectral data see (*E*)-**3c**.

3.1.48. (2*S*,3*R*,*R*s)-(+)-35. Colorless crystals, mp 80–81 °C (AcOEt–hexane); $[\alpha]_D^{30}$ +30.3 (c 2.51, EtOH). Spectral data see (*Z*)-**3c**.

3.1.49. (*R*)-(−)-Methyl 2-azido-3-(*tert*-butyldiphenylsilanyloxy)-2-methylpropionate (36). Colorless oil; $[\alpha]_D^{27}$ −11.9 (c 0.54, EtOH). IR (neat) 2933, 2859, 2106 (N_3), 1745 (CO), 1473, 1460, 1428, 1299, 1236, 1113, 825, 702 cm^{-1}; ^1H NMR δ 1.04 (9H, s), 1.32 (3H, s), 3.76 (1H, d, J=10.0 Hz), 3.79 (3H, s), 3.94 (1H, d, J=10.0 Hz), 7.38–7.47 (6H, m), 7.64–7.68 (4H, m). MS (FAB) m/z (%) 398 ([M+H]$^+$, 1), 340 (100), 320 (59), 213 (75), 197 (24), 135 (42). Calcd for $C_{21}H_{28}O_3N_3Si$: M, 398.1900. Found: m/z 398.1894.

3.1.50. (*R*)-(+)-Methyl 2-amino-3-hydroxy-2-methylpropionate (38). Colorless oil; $[\alpha]_D^{30}$ +6.9 (c 2.25, EtOH); IR (neat) 3366 (NH), 2957, 1732 (CO), 1651, 1460, 1235, 1139, 1054 cm^{-1}; ^1H NMR δ 1.29 (3H, s), 2.45 (3H, s, NH_2, OH), 3.46 (1H, d, J=10.7 Hz), 3.75 (3H, s), 3.78 (1H, d, J=10.7 Hz). MS (FAB) m/z (%) 134 ([M+H]$^+$, 100), 74 (25), 57 (14), 55 (12). Calcd for $C_5H_{12}O_3N$: M, 134.0818. Found: m/z 134.0818.

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