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Synthesis of All Distinct α-Methyl-Substituted Isomers of Amino Bis(2,2′-Ethanoic Acid) Diethyl Ester and Ethylene Diamine Tetraacetic Acid Tetraethyl Ester Scaffolds

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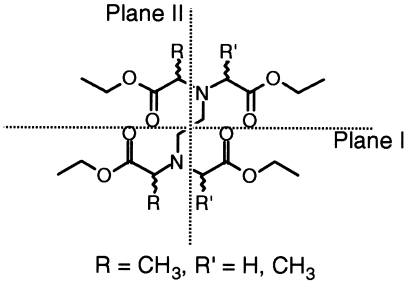
Abstract—The syntheses of three dialkylated and six tetraalkylated ethylene diamine tetraacetic acid tetraesters is described. The dialkylated derivatives were synthesized by a convergent non-racemizing route to yield three enantiomerically and diastereomerically pure tetraesters (*SS*)-**3a**, (*RR*)-**3b** and (R^*S^*)-**3c** in 55–57% yields from alanine ethyl ester **1**. Enantiomerically and diastereomerically pure tetraalkylated derivatives (*SSSS*)-**8a**, (*RRRR*)-**8b**, ($2R^*,2'S^*,2''R^*,2'''S^*$)-**8c**, ($2R^*,2'R^*,2''S^*,2'''S^*$)-**8d**, ($2R,2'R,2''R,2'''S$)-**8e** and ($2S,2'S,2''S,2'''R$)-**8f** were synthesized in two to five steps and 22–49% overall yields from alanine ethyl ester **1**.

Amino acid derivatives capable of mimicking peptide segments are becoming increasingly important in the design of enzyme-inhibitors. Enantiomerically pure scaffolds of amino bis(2,2′-ethanoic acid) constitute a part of many important drugs such as Enalapril, Enalkiren, Captopril, etc.[1] They are also useful synthetic intermediates in the formation of analeptics,[2] natural products,[3] anxiolytic agents,[4] antipsychotic agents,[5] and enantiomerically pure vicinal diamine scaffolds such as ethylene diamine tetraacetic acid tetraesters (EDTA tetraesters) described in this paper (Fig. 1). Vicinal diamino tetraester scaffolds are useful in medicinal chemistry,[6] polyazamacrocyclic and cryptate chemistry[7] and in the formation of heterocyclic rings.[8] EDTA derivatives, in particular, are important for studying metal chelation[9] and form synthetic intermediates for the preparation of bimolanes which prevent chlorosis in plants,[10] and topoisomerase II inhibitors which have anticancer properties.[11] A convenient synthesis for the enantiomerically pure derivatives possessing the EDTA scaffold is highly desirable, since their ultimate use in combinatorial solid phase syntheses could lead to the production of numerous biologically important libraries. This paper describes the synthetic design of nine EDTA tetraesters (Fig. 2) which have two or four methyl groups on the ethanoic acid branches of the molecules.

Upon examination, it is evident that some EDTA tetraesters with two or four chiral centers possess planes of symmetry. EDTA tetraesters (**3c**, **8c**, **8d**) are symmetric along plane I passing through the ethylene linker. Tetra(α-methyl) EDTA analog (**8c**; R′=Me) also exhibits symmetry along a second plane (plane II) perpendicular to plane I. This reduces the theoretically possible four (R′=H) and sixteen (R′=Me) isomers to three and six isomers, respectively. Thus, di(α-methyl) EDTA scaffolds (**3a**–**3c**, Fig. 2) exist in three stereoisomeric forms, whereas tetra(α-methyl) EDTA scaffolds (**8a**–**8f**) exist in six distinct stereoisomeric forms.



Synthetic Details

Di-alkylated amines **3a** and **3b** were synthesized (Scheme 1) in 57% overall yields from (*S*)- and (*R*)-alanine ethyl ester hydrochlorides (**1a** and **1b**), respectively. Intermediate diesters (*S*)-**2a** or (*R*)-**2b** were prepared as previously described.[12] No dialkylation was observed during the

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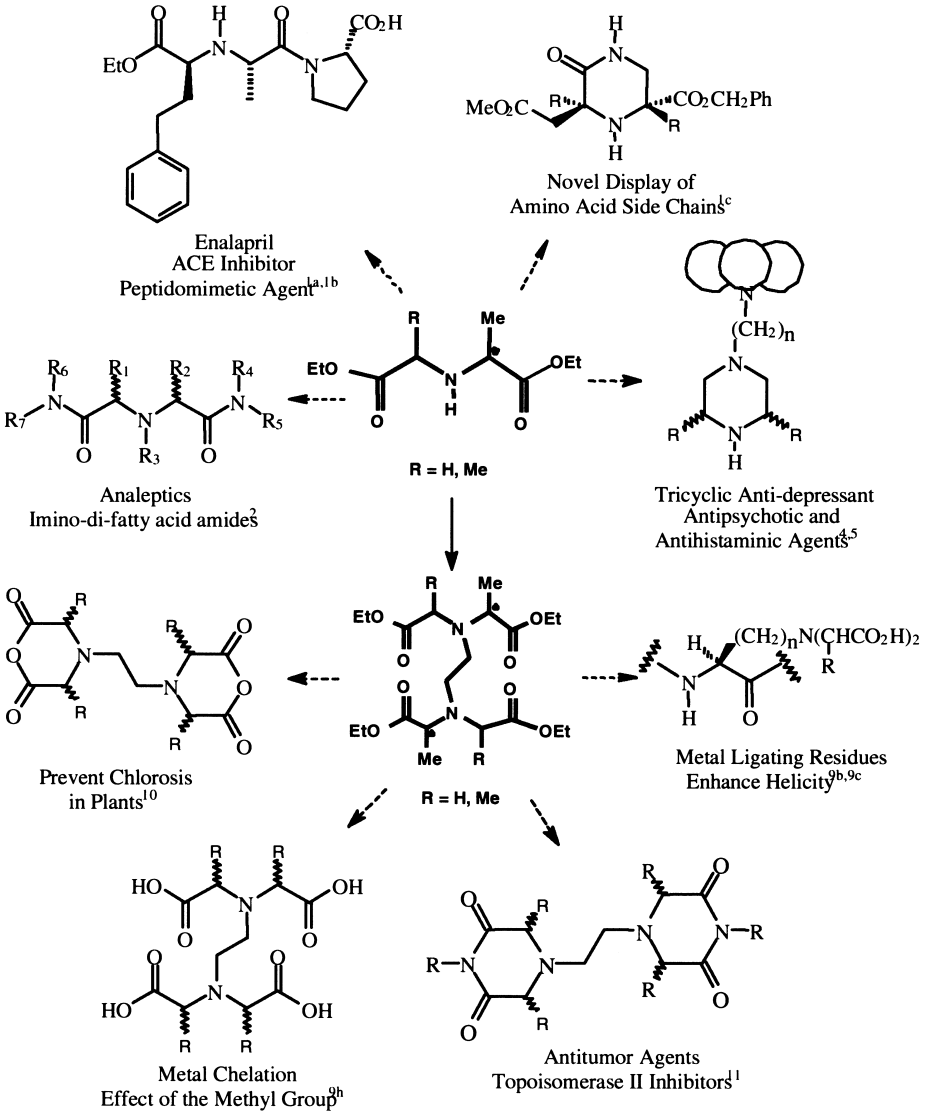


Figure 1. Synthetic applications of α-methyl-substituted isomers of amino bis(2,2′-ethanoic acid) diethyl ester and ethylene diamine tetraacetic acid tetraethyl ester scaffolds.

preparation of (*S*)-**2a** or (*R*)-**2b**. Bis(coupling) of diesters (*S*)-**2a** or (*R*)-**2b** was expected to yield 1,2-ethanediyl bridged (*S*,*S*)-**3a** and (*RR*)-**3b**. There is little precedence for *N*-alkylations in electronically deactivated and hindered systems.[13] After numerous attempts, success was finally achieved by utilization of a combination of ethylene glycol di-*p*-tosylate and pentamethylpiperidine (PMP) in refluxing toluene. This non-racemizing reaction likely proceeds through the intermediacy of a highly reactive aziridinium ion.[14] The formation of such aziridinium salts from 2-haloethylamines and their high lability in the presence of nucleophiles is well precedented.[14] Both optically active compounds (*S*,*S*)-**3a** and (*RR*)-**3b** were found to be enantiomerically pure by proton and ^{13}C NMR spectroscopy; both rotated a plane of polarized light equally, but in opposite directions.

To synthesize the meso isomer R^*,S^*-**3c** (see Scheme 2), racemic alanine ethyl ester was alkylated with ethyl α-bromopropionate and coupled with 1,2-ethylene glycol di-*p*-tosylate to afford a mixture of meso and racemic alanyl tetraester derivatives *S*,*S*-**3a**, *R*,*R*-**3b** and (R^*S^*)-**3c**. This mixture of racemic and meso tetraesters was found to be inseparable by distillation, column chromatography or crystallization with chiral acids (mandelic acid) and thus was of no synthetic utility. Alternatively, alkylated *S*-alanine derivative **2a** was treated with a 3-fold excess of ethylene glycol di-*p*-tosylate in the hope of obtaining monotosylate **6**. However, the method only generated tetraester *S*,*S*-**3a** without detectable quantities of derivative **6**. This may be a function of a highly reactive aziridinium intermediate.[14] Thus, unsymmetrically 1,2-substituted-ethyl tetraester (R^*S^*)-**3c** is derived by stepwise coupling of constitutive monomeric units as depicted in Scheme 2.

The meso diastereomer (R^*S^*)-**3c** was prepared by N-alkylation of diester (*S*)-**2a** with benzyloxy ethylene monotosylate[15,16] to furnish intermediate (*S*)-**4** (92%) which was subsequently hydrogenated to produce diester-alcohol (*S*)-**5** in quantitative yields (Scheme 2). Alcohol (*S*)-**5** was prone to lactonization and was immediately taken to the next step. Tosylation generated an unstable ß-aminotosylate

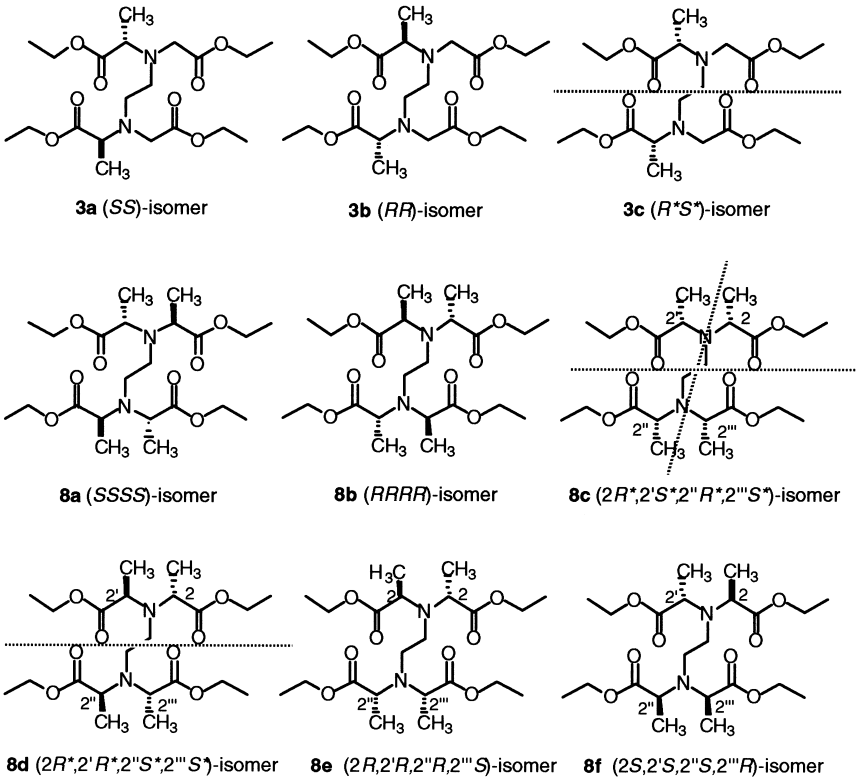
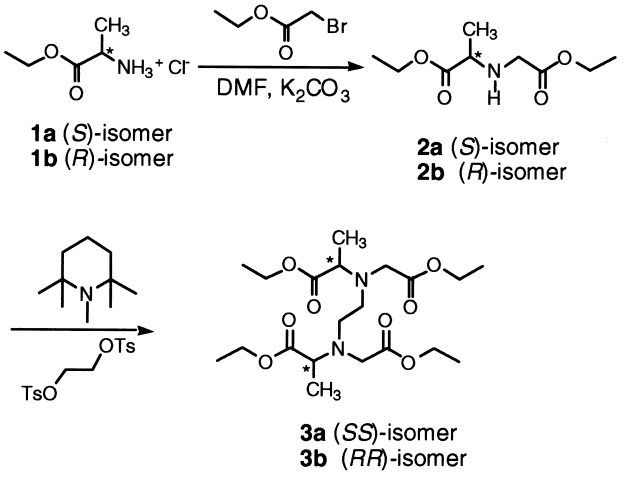


Figure 2. Ethylene diamine tetraacetic acid tetraethyl ester scaffolds showing the planes of symmetry.

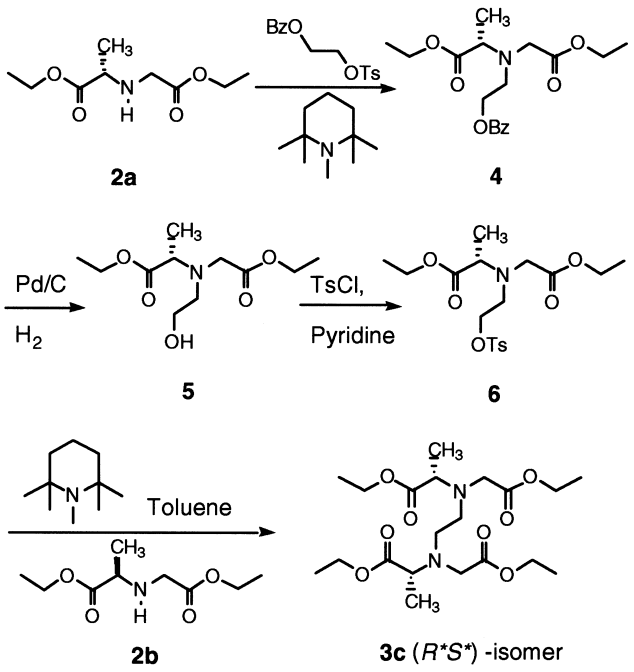
(*S*)-**6**, which decomposed on silica gel and proved difficult to purify by neutral alumina column chromatography. Use of potassium hydrogen sulphate as a milder substitute for aqueous HCl in the work up yielded 93% of tosylate not requiring further purification. Reaction of (*S*)-**6** with diester (*R*)-**2b** yielded the coupled tetraester (R^*S^*)-**3c** in 90% yield.

The diastereomeric mixture of (R^*S^*)-**7c** and (*S*,*S*)-**7a** (Scheme 3) is known.[12,17] Reaction of (*S*)- or (*R*)-alanine ethyl ester HCl with ethyl bromopropionate yielded a diastereomeric mixture of (R^*S^*)-**7c** with (*S*,*S*)-**7a** or (R^*S^*)-**7c** with (*R*,*R*)-**7b**, respectively. The diastereomers were successfully separated by simple column chromatographic techniques (1:4 ethyl acetate–hexanes) over silica gel. The pure diastereomers were coupled with ethylene glycol di-*p*-tosylate to yield tetraesters ($2R^*,2'S^*,2''R^*,2'''S^*$)-**8c**, (*S*,*S*,*S*,*S*)-**8a** and (*R*,*R*,*R*,*R*)-**8b**. Tetraesters (*S*,*S*,*S*,*S*)-**8a** and (*R*,*R*,*R*,*R*)-**8b** exhibited equal and opposite rotations of polarized light ($[\alpha]_D^{22}=-93.69$ (0.555, DMF) and $[\alpha]_D^{24}=+95.65$ (0.735, DMF), respectively), whereas ($2R^*,2'S^*,2''R^*,2'''S^*$)-**8c** did not rotate the plane of polarized light under the same conditions. Additionally, ^{1}H and ^{13}C NMR spectra were in accordance with the assigned structures. The tetraester ($2R^*,2'S^*,2''R^*,2'''S^*$)-**8c** shows a singlet at δ 2.87 for equivalent methylene protons of the linker, whereas both (*S*,*S*,*S*,*S*)-**8a** and (*R*,*R*,*R*,*R*)-**8b** show a multiplet δ (2.99–2.78) for the linker methylene protons which are magnetically non equivalent.



Scheme 1.

For tetraesters [(2*S*,2′*S*,2″*S*,2‴*R*)-**8f**, (2*R*,2′*R*,2″*R*,2‴*S*)-**8e** and ($2R^*,2'R^*,2''S^*,2'''S^*$)-**8d**], either ($R^*,S^*$)-**7c** or (*S*,*S*)-**7a** were treated with silyl protected ethylene glycol monotosylate or benzyl protected ethylene glycol monotosylate[15,16] to yield the corresponding protected ethoxy derivatives **9a**–**9d** (in 65–87% yields) as depicted in Scheme 4. TBDMS-protected compounds **9a** and **9c** racemized when deprotected with HF-pyridine or acetic acid and methanol. Therefore, hydroxyethyl compounds (R^*,S^*)-**10b** and (*S*,*S*)-**10a** were prepared by hydrogenation of benzyloxy derivatives (R^*,S^*)-**9d** and (*S*,*S*)-**9b**, respectively, in 99+% yields. Both (R^*,S^*)-**10b** and (*S*,*S*)-**10a** were prone to lactonization on standing and were immediately taken to the next step. Reaction of *p*-TsCl with alcohols (R^*,S^*)-**10b** and (*S*,*S*)-**10a** yielded the corresponding tosylates (R^*,S^*)-**11b** and (*S*,*S*)-**11a** in 93–95% yields. Reaction of ß-aminotosylates (R^*,S^*)-**11b** and (*S*,*S*)-**11a** with diesters (*S*,*S*)-**7a** and (*R*,*R*)-**7b** yielded the



Scheme 2.

unsymmetrically substituted tetraesters **8d**–**8f** in 64–77% yields. (2*S*,2′*S*,2″*S*,2‴*R*)-**8f** and (2*R*,2′*R*,2″*R*,2‴*S*)-**8e** are enantiomers and yielded similar spectral data but opposite rotations. The methylene protons of the central linker chain are magnetically non-equivalent, yielding a complex multiplet. (2R^*,2′R^*,2″S^*,2‴S^*)-**8d** did not rotate the plane of polarized light and showed a distinctly different spectrum when compared to (2*S*,2′*S*,2″*S*,2‴*R*)-**8f** and (2*R*,2′*R*,2″*R*,2‴*S*)-**8e**. The central linker protons appear as a singlet at δ 2.91.

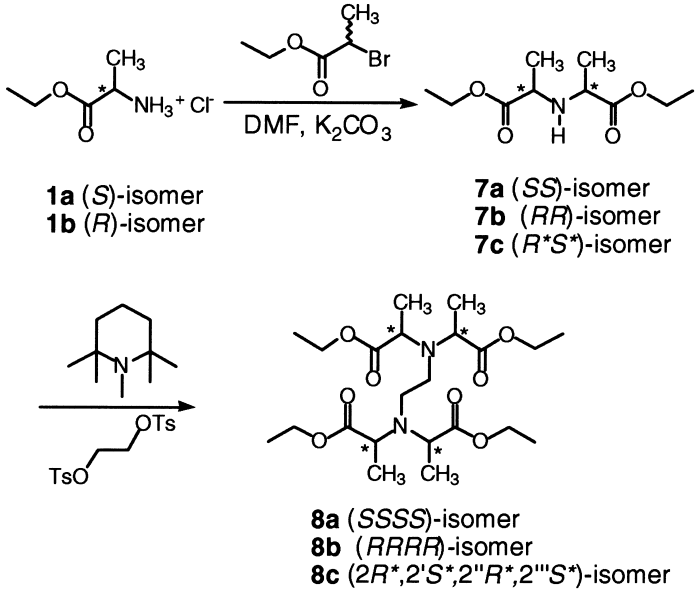
Thus, the syntheses of the three enantiomerically and diastereomerically pure dialkylated tetraesters (*S*,*S*)-**3a**, (*RR*)-**3b** and (R^*S^*)-**3c** was achieved in 55–57% overall yields from alanine ethyl ester **1**. Enantiomerically and diastereomerically pure tetraalkylated derivatives (*SSSS*)-**8a**, (*RRRR*)-**8b**, (2R^*,2′S^*,2″R^*,2‴S^*)-**8c**, (2R^*,2′R^*,2″S^*,2‴S^*)-**8d**, (2*R*,2′*R*,2″*R*,2‴*S*)-**8e** and (2*S*,2′*S*,2″*S*,2‴*R*)-**8f** were synthesized in two to five steps and 22–49% overall yields from alanine ethyl ester **1**.

Experimental

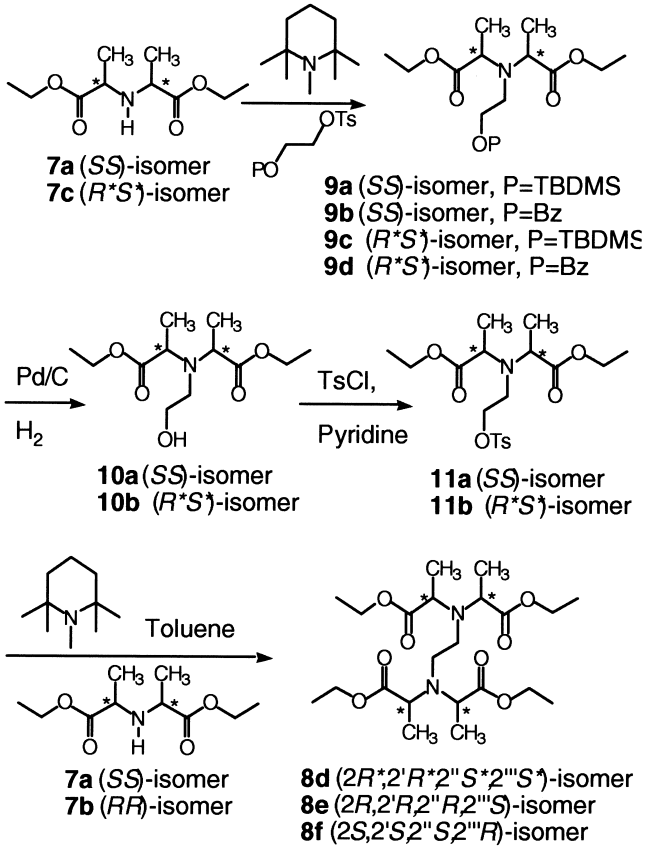
(*S*)-*N*-(Carboxymethyl)alanine, diethyl ester[12] (2a). L-Alanine ethyl ester hydrochloride (1.54 g, 10 mmol), K_2CO_3 (4.15 g, 30 mmol) and ethyl bromoacetate (1.67 g, 10 mmol) in 10 mL of dry dimethylformamide were refluxed under Ar for 16 h. After cooling the suspended solids were filtered and washed with ethanol. The filtrate was concentrated in vacuo and the residue chromatographed (3:2 hexanes–ethyl acetate) to yield 1.42 g (72%) of a colorless liquid. $[\alpha]_D^{23}=-25.92$ (2.014, CH_3OH); IR (Neat) 3368, 3000, 2956, 2928, 2896, 1748, 1457, 1380, 1205, 1165, 1030 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.15 (q, J=7.1 Hz, 4 H), 3.41 (d AB pattern, J=17.2 Hz, 1 H), 3.33 (d AB pattern, J=17.2 Hz, 1 H), 3.36 (q, J=7.0 Hz, 1 H), 2.01 (s, 1 H), 1.30 (d, J=7.0 Hz, 3 H), 1.24 (t, J=7.1 Hz, 3 H), 1.23 (t, J=7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.7 (C), 171.7 (C), 60.9 (CH_2), 55.9 (CH), 48.9 (CH_2), 18.7 (CH_3), 14.2 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_9H_{17}NO_4$: C, 53.17; H, 8.44; N, 6.89. Found: C, 52.92; H, 8.38; N, 6.80.

(*R*)-*N*-(Carboxymethyl)alanine, diethyl ester[12] (2b). *R*-**2b** was prepared from D-Alanine ethyl ester hydrochloride (Indofine Chemicals) in similar yield as for *S*-**2a**. $[\alpha]_D^{23}=+25.12$ (1.27, CH_3OH).

(*S*,*S*)-*N*,*N*′-Ethylenebis[*N*-(carboxymethyl)alanine], tetraethyl ester (3a). A mixture of diester **2a** (1.02 g, 5 mmol), ethylene glycol di-*p*-tosylate (0.93 g 2.5 mmol) and 1,2,2,6,6-pentamethylpiperidine (0.78 g, 5 mmol) in 2 mL of dry toluene was refluxed under Ar for 2 days. After



Scheme 3.



Scheme 4.

cooling to room temperature, the mixture was diluted with ether and filtered. The filtrate was evaporated and the residue chromatographed (3:2 hexanes–ethyl acetate) to yield 798 mg (79%) of a light yellow liquid. $[\alpha]_D^{27}=-47.82$ (1.125, DMF); IR (Neat) 3000, 2960, 2928, 2890, 1740, 1470, 1455, 1380, 1190, 1160, 1035 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.15 (q, J=7.2 Hz, 8 H), 3.67 (q, J=7.2 Hz, 2 H), 3.58 (d, J_{AB}=17.6 Hz, 2 H), 3.48 (d, J_{AB}=17.6 Hz, 2 H), 2.81 (s, 4 H), 1.30 (d, J=7.2 Hz, 6 H), 1.27 (t, J=7.1 Hz, 6 H), 1.26 (t, J=7.1 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.8 (C), 172.1 (C), 60.4 (CH_2), 60.3 (CH_2), 59.6 (CH), 52.8 (CH_2), 51.8 (CH_2), 16.1 (CH_3), 14.3 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{20}H_{36}N_2O_8$: C, 55.52; H, 8.39; N, 6.48. Found: C, 55.28; H, 8.67; N, 6.34.

(*R,R*)-*N,N'*-Ethylenebis[*N*-(carboxymethyl)alanine], tetraethyl ester (3b). *RR*-**3b** was prepared from *R*-**2b** in similar yield as for *SS*-**3a**. $[\alpha]_D^{23}=+50.2$ (1.02, DMF).

(*S*)-*N*-[2-(Benzyloxy)ethyl]-*N*-(carboxymethyl)alanine, diethyl ester (4). A mixture of tetraester **2a** (7.11 g, 35 mmol), 1-*O*-benzyl-2-*O*-*p*-toluenesulfonyl glycol (10.72 g, 35 mmol) and 1,2,2,6,6-pentamethylpiperidine (5.44 g, 35 mmol) in 28 mL of dry toluene was refluxed under Ar for 4 days. After cooling to room temperature, the mixture was diluted with ether and filtered. The filtrate was evaporated and the residue chromatographed (1:4 ethyl acetate–hexanes) to yield 10.86 g (92%) of a light yellow liquid. $[\alpha]_D^{24}=-28.33$ (1.08, DMF); IR (Neat) 3110, 3086, 3052, 3000, 2960, 2923, 2880, 1760, 1745, 1507, 1462, 1380, 1255, 1180, 1100, 1036, 930, 865, 742, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.23 (m, 5 H), 4.49 (s, 2 H), 4.13 (q, J=7.1 Hz, 2 H), 4.11 (q, J=7.1 Hz, 2 H), 3.68 (q, J=7.2 Hz, 2 H), 3.60 (t, J=5.8 Hz, 2 H), 3.57 (d AB pattern, J=17.7 Hz, 1 H), 3.53 (d AB pattern, J=17.7 Hz, 1 H), 2.97 (t, J=5.7 Hz, 1 H), 2.96 (t, J=5.9 Hz, 1 H), 1.33 (d, J=7.2 Hz, 3 H), 1.25 (t, J=7.1 Hz, 3 H), 1.22 (t, J=7.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.0 (C), 172.2 (C), 138.4 (C), 128.3 (CH), 127.5 (CH), 127.5 (CH), 73.0 (CH_2), 70.0 (CH_2), 60.4 (CH), 53.0 (CH_2), 52.4 (CH_2), 16.4 (CH_3), 14.3 (CH_3), 14.2 (CH_3). Anal. Calcd for $C_{18}H_{27}NO_5$: C, 64.06; H, 8.07; N, 4.15. Found: C, 63.79; H, 8.21; N, 3.73.

(*S*)-*N*-(Carboxymethyl)-*N*-[2-hydroxyethyl]alanine, diethyl ester (5). Diester **4** (1.01 g, 3 mmol), 0.45 g of $Pd(OH)_2$ (20% on C, 50% H_2O) in 20 mL of ethyl acetate was hydrogenated at 1 atm of H_2 for 3 h. The catalyst was filtered, thoroughly washed, and the solution evaporated to yield 739 mg (100%) of a light yellow liquid. $[\alpha]_D^{27}=-32.81$ (0.82, DMF); IR (Neat) 3500, 3000, 2960, 2923, 2896, 1742, 1470, 1460, 1382, 1304, 1100, 1070, 1035, 865 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.19 (q, J=7.0 Hz, 2 H), 4.17 (q, J=7.0 Hz, 2 H), 3.71 (br s, 1 H), 3.59 (q, J=7.6 Hz, 1 H), 3.59–3.46 (m, 2 H), 3.58 (d AB pattern, J=18.3 Hz, 1 H), 3.44 (d AB pattern, J=18.3 Hz, 1 H), 2.87 (t, J=5.0 Hz, 2 H), 1.34 (d, J=7.3 Hz, 3 H), 1.28 (t, J=7.1 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.8 (C), 173.4 (C), 61.0 (CH_2), 60.6 (CH_2), 60.2 (CH), 59.2 (CH_2), 56.0 (CH_2), 52.3 (CH_2), 16.2 (CH_3), 14.3 (CH_3), 14.1 (CH_3); Anal. Calcd for $C_{11}H_{21}NO_5$: C, 53.43; H, 8.56; N, 5.66. Found: C, 53.84; H, 8.64; N, 5.27.

(*S*)-*N*-(Carboxymethyl)-*N*-(2-hydroxyethyl)alanine, diethyl ester, *p*-toluenesulfonate (6). To a solution of *p*-toluenesulfonyl chloride (458 mg, 2.4 mmol) in 0.5 mL of pyridine at −5°C was added a solution of **5** (494 mg, 2 mmol) in 2 mL of pyridine in a dropwise manner. The resulting mixture was stirred at −5°C for 3 h and refrigerated for 16–18 h. Subsequently, 2 mL of H_2O was added and the aqueous mixture was extracted with ether (20 mL). The ether layer was washed with 1 M $KHSO_4$ solution (3×20 mL) and brine (1×20 mL), dried over Na_2SO_4 and concentrated in vacuo to yield 750 mg (93%)of a pale yellow liquid. $[\alpha]_D^{27}=-19.9$ (1.00, DMF); IR (Neat) 3000, 2960, 2922, 2892, 1747, 1610, 1505, 1455, 1370, 1300, 1260, 1182, 1106, 1035, 970, 915, 823, 776, 670, 557 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, *J*=8.3 Hz, 2 H), 7.34 (d, *J*=8.0 Hz, 2 H), 4.25–4.08 (m, 2 H), 4.10 (q, *J*=6.2 Hz, 4 H), 3.54 (q, *J*=7.2 Hz, 1 H), 3.48 (s, 2 H), 3.13–3.01 (m, 2 H), 2.45 (s, 3 H), 1.27 (d, *J*=7.6 Hz, 3 H), 1.25 (t, *J*=7.2 Hz, 3 H), 1.24 (t, *J*=7.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5 (C), 171.6 (C), 144.7 (C), 133.1 (C), 129.8 (CH), 127.9 (CH), 69.3 (CH_2), 60.6 (CH_2), 60.3 (CH), 53.3 (CH_2), 51.2 (CH_2), 21.6 (CH_3), 16.4 (CH_3), 14.3 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{18}H_{27}NO_7S$: C, 53.85; H, 6.78; N, 3.49. Found: C, 53.68; H, 6.57; N, 3.28.

(*R,*S**)-*N*,*N*′-ethylenebis[*N*-(carboxymethyl)alanine], tetraethyl ester (3c).** A mixture of **2b** (244 mg, 1.2 mmol), **6** (402 mg, 1 mmol) and 1,2,2,6,6-pentamethylpiperidine (160 mg, 1 mmol) in 2 mL of dry toluene was heated at reflux under Ar for 2 days. After cooling to room temperature, the mixture was diluted with ether and filtered. The filtrate was evaporated and the residue chromatographed (4:1 dichloromethane–ether) to yield 389 mg (90%) of a yellow liquid. $[\alpha]_D^{27}=-0.00$ (0.81, DMF); IR (Neat) 3000, 2960, 2928, 2896, 1740, 1470, 1455, 1380, 1190, 1160, 1035 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.14 (q, *J*=7.1 Hz, 8 H), 3.65 (q, *J*=7.2 Hz, 2 H), 3.56 (d AB pattern, *J*=17.59 Hz, 2 H), 3.51 (d AB pattern, *J*=17.58 Hz, 2 H), 2.81 (qd, *J*=10.4, 2.4 Hz, 4 H), 1.30 (d, *J*=7.2 Hz, 6 H), 1.27 (t, *J*=7.1 Hz, 6 H), 1.26 (t, *J*=7.2 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.8 (C), 172.1 (C), 60.2 (CH_2), 60.3 (CH_2), 59.7 (CH), 52.9 (CH_2), 51.8 (CH_2), 16.1 (CH_3), 14.3 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{20}H_{36}N_2O_8$: C, 55.52; H, 8.39; N, 6.48. Found: C, 55.44; H, 8.02; N, 6.17.

(2*S*,2′*S*)-Diethyl 2,2′-iminodipropionate (7a) and (2S*,2′R*)-diethyl 2,2′-iminodipropionate (7c). A mixture of L-alanine ethyl ester hydrochloride (1.54 g, 10 mmol), potassium carbonate (4.15 g, 30 mmol) and ethyl bromopropionate (1.67 g, 10 mmol) in 10 mL of dry dimethylformamide was heated at refluxed under Ar for 12 h. After cooling the suspended solids were filtered and washed with ethanol. The filtrate was concentrated in vacuo and the residue chromatographed (4:1 hexane–ethyl acetate) to first elute 0.75 g (35%) of a yellow liquid (**7c**) followed by 0.6 g (28%) of **7a** as a light yellow liquid.**7c** $[\alpha]_D^{21}=-0.07$ (1.462, CH_3OH); IR (Neat) 3358, 3000, 2958, 2912, 2892, 1830, 1747, 1456, 1420, 1384, 1308, 1260, 1210, 1165, 1105, 1060, 1027, 864, 758 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ(4.17 (q, *J*=7.0 Hz, 4 H), 3.38 (q, *J*=6.9 Hz, 2 H), 1.31 (d, *J*=7.0 Hz, 6 H), 1.28 (t, *J*=7.1 Hz, 3 H), 1.27 (t, *J*=7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.8 (C), 60.8 (CH_2), 54.3 (CH),18.8 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{10}H_{19}NO_4$: C, 55.27; H, 8.82; N, 6.45. Found: C, 55.56; H, 8.54; N, 6.24. **7a** $[\alpha]_D^{21}=-59.54$ (1.295, CH_3OH); $[\alpha]_D^{24}=-63.07$ (1.205, DMF); IR (Neat) 3360, 3000, 2960, 2912, 2894, 1740, 1460, 1380, 1305, 1265, 1175, 1100 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.19 (q, *J*=7.2 Hz, 2 H), 4.18 (q, *J*=7.1 Hz, 2 H), 3.38 (q, *J*=7.0 Hz, 2 H), 1.33 (d, *J*=7.0 Hz, 6 H), 1.28 (t, *J*=7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.3 (C), 60.8 (CH_2), 55.2 (CH), 19.4 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{10}H_{19}NO_4$: C, 55.27; H, 8.82; N, 6.45. Found: C, 54.92; H, 8.89; N, 6.35.

(2*R*,2′*R*)-diethyl 2,2′-iminodipropionate (7b). *RR*-**7b** was prepared from D-alanine ethyl ester hydrochloride (Indofine Chemicals) in similar yield as for *SS*-**7a**. $[\alpha]_D^{27}=+59.89$ (0.915, DMF).

(2*S*,2′*S*,2″*S*,2‴*S*)-Tetraethyl 2,2′,2″,2‴-(ethylene-dinitrilo)-tetra-propionate (8a). A mixture of **7a** (1.09 g, 5 mmol), ethylene glycol di-*p*-tosylate (0.93 g 2.5 mmol) and 1,2,2,6,6-pentamethylpiperidine (0.78 g, 5 mmol) in 4 mL of dry toluene was heated at reflux under Ar for 7 days. After cooling to room temperature, the mixture was diluted with ether and filtered. The filtrate was evaporated and the residue chromatographed (6:1 hexanes–ethyl acetate) to yield 550 mg (48%) of a pale yellow liquid. $[\alpha]_D^{22}=-93.69$ (0.555, DMF); IR (Neat) 3000, 2958, 2915, 2892, 1744, 1455, 1380, 1337, 1305, 1260, 1185, 1160, 1110, 1060, 1030, 960, 864, 795, 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.10 (q, *J*=7.1 Hz, 8 H), 3.64 (q, *J*=7.2 Hz, 4 H), 2.99–2.78 (m, 4 H), 1.28 (d, *J*=7.2 Hz, 12 H), 1.26 (t, *J*=7.1 Hz, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.0 (C), 60.1 (CH_2), 56.4 (CH), 47.7 (CH_2), 17.4 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{22}H_{40}N_2O_8$: C, 57.36; H, 8.76; N, 6.08. Found: C, 57.06; H, 8.81; N, 6.42.

(2*R*,2′*R*,2″*R*,2‴*R*)-Tetraethyl 2,2′,2″,2‴-(ethylene-dinitrilo)-tetra-propionate (8b). *RRRR*-**8a** was prepared from *RR*-**7b** in similar yield as for *SSSS*-**8a**. $[\alpha]_D^{24}=+95.65$ (0.735, DMF).

(2*R,2′*S**,2″*R**,2‴*S**)-Tetraethyl 2,2′,2″,2‴-(ethylene-dinitrilo)tetra-propionate (8c).** A mixture of **7c** (1.085 g, 5 mmol), ethylene glycol di-*p*-tosylate (0.93 g, 2.5 mmol) and 1,2,2,6,6-pentamethylpiperidine (0.78 g, 5 mmol) in 4 mL of dry toluene was heated at reflux under Ar for 7 days. After cooling to room temperature, the mixture was diluted with ether and filtered. The filtrate was evaporated and the residue chromatographed (6:1 hexanes–ethyl acetate) to yield 327 mg (28%) of a white crystalline solid. $[\alpha]_D^{27}=-0.27$ (0.73, DMF); ^1H NMR (300 MHz, $CDCl_3$) δ 4.12 (q, *J*=7.1 Hz, 8 H), 3.64 (q, *J*=7.1 Hz, 4 H), 2.87 (s, 4 H), 1.28 (d, *J*=7.1 Hz, 12 H), 1.26 (t, *J*=7.1 Hz, 12 H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 174.6 (C), 60.2 (CH_2), 57.6 (CH), 48.1 (CH_2), 16.2 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{22}H_{40}N_2O_8$: C, 57.36; H, 8.76; N, 6.08. Found: C, 57.24; H, 8.54; N, 5.98.

(2*S*,2′*S*)-Diethyl 2,2′-[*tert*-butyldimethylsiloxy ethylimino]-dipropionate (9a). A mixture of **7a** (217 mg, 1 mmol), *tert*-butyldimethylsilyl protected ethylene glycol

mono-*p*-tosylate (330 mg, 1 mmol) and 1,2,2,6,6-pentamethylpiperidine (160 mg, 1 mmol) in 1 mL of dry toluene was heated at reflux under Ar for 2 days. After cooling to room temperature, the mixture was diluted with ether and filtered. The filtrate was evaporated and the residue chromatographed (2% ethanol in 1:5:4 ether–hexanes–dichloromethane) to yield 321 mg (86%) of a light yellow liquid. $[\alpha]_D^{23}=-49.4$ (0.50, DMF); IR (Neat) 3000, 2972, 2948, 2911, 2872, 1747, 1472, 1395, 1380, 1264, 1162, 1107, 1030, 930, 842, 782 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.04 (q, J=7.2 Hz, 4 H), 3.62 (q, J=7.2 Hz, 2 H), 3.51 (t, J=6.7 Hz, 2 H), 2.97 (t, J=6.7 Hz, 2 H), 1.23 (d, J=7.2 Hz, 6 H), 1.20 (t, J=7.2 Hz, 6 H), 0.84 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1 (C), 63.9 (CH_2), 60.1 (CH_2), 58.9 (CH), 49.5 (CH_2), 25.9 (CH_3), 18.3 (C), 17.4 (CH_3), 14.2 (CH_3).

(2*S*,2′*S*)-Diethyl 2,2′-[2-(benzyloxy)ethylimino]-dipropionate (9b). A mixture of **7a** (4.34 g, 20 mmol), 1-*O*-benzyl-2-*O*-*p*-toluenesulfonyl glycol (6.13 g, 20 mmol) and 1,2,2,6,6-pentamethylpiperidine (3.11 g, 20 mmol) in 15 mL of dry toluene was heated at reflux under Ar for 7 days. After cooling to room temperature, the mixture was diluted with ether and filtered. The filtrate was evaporated and the residue chromatographed (1:6 ethyl acetate–hexanes) to yield 4.53 g (65%) of a light yellow liquid. $[\alpha]_D^{27}=-53.67$ (0.885, DMF); IR (Neat) 3040, 3025, 3000, 2960, 2920, 2880, 1745, 1505, 1462, 1380, 1340, 1308, 1255, 1162, 1110, 1030, 865, 740, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38–7.23 (m, 5 H), 4.52 (s, 2 H), 4.09 (q, J=7.1 Hz, 4 H), 3.70 (q, J=7.2 Hz, 2 H), 3.48 (t, J=6.1 Hz, 2 H), 3.15 (t, J=6.2 Hz, 2 H) 1.29 (d, J=7.2 Hz, 6 H), 1.24 (t, J=7.1 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1 (C), 138.6 (C), 128.3 (CH), 127.5 (CH), 73.0 (CH_2), 71.1 (CH_2), 60.2 (CH_2), 56.9 (CH), 46.8 (CH_2), 17.3 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{19}H_{29}NO_5$: C, 64.92; H, 8.32; N, 3.99. Found: C, 65.15; H, 8.26; N, 3.74.

(2*S,2′*R**)-Diethyl 2,2′-[*tert*-butyldimethylsiloxy ethylimino]di-propionate (9c).** A mixture of **7c** (217 mg, 1 mmol), *tert*-butyldimethylsilyl protected ethylene glycol mono-*p*-tosylate (330 mg, 1 mmol) and 1,2,2,6,6-pentamethylpiperidine (160 mg, 1 mmol) in 1 mL of dry toluene was heated at reflux under Ar for 2 days. After cooling to room temperature, the mixture was diluted with ether and filtered. The filtrate was evaporated and the residue chromatographed (95:5 dichloromethane–ether) to yield 324 mg (87%) of a light yellow liquid. $[\alpha]_D^{27}=+0.00$ (0.625, DMF); IR (Neat) 3000, 2980, 2953, 2920, 2880, 1750, 1475, 1422, 1400, 1265, 1185, 1170, 1110, 1030, 845, 785 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ(4.08 (q, J=7.1 Hz, 4 H), 3.63 (q, J=7.2 Hz, 2 H), 3.54 (t, J=6.9 Hz, 2 H), 2.92 (t, J=6.9 Hz, 2 H), 1.24 (d, J=7.1 Hz, 6 H), 1.22 (t, J=7.1 Hz, 6 H), 0.84 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.7 (C), 64.0 (CH_2), 60.2 (CH_2), 58.0 (CH), 49.7 (CH_2), 25.9 (CH_3), 18.3 (C), 16.4 (CH_3), 14.2 (CH_3).

(2*S,2′*R**)-Diethyl 2,2′-[2-(benzyloxy)ethyl imino]-dipropionate (9d).** A mixture of **7c** (1.09 g, 5 mmol), 1-*O*-benzyl-2-*O*-*p*-toluenesulfonyl glycol (1.53 g, 5 mmol) and 1,2,2,6,6-pentamethylpiperidine (777 mg, 5 mmol) in 4 mL of dry toluene was heated at reflux under Ar for 7 days. After cooling to room temperature, the mixture was diluted with ether and filtered. The filtrate was evaporated and the residue chromatographed (1:6 ethyl acetate–hexanes) to yield 1.5 g (85%) of a light yellow liquid. $[\alpha]_D^{27}=-0.00$ (0.51, DMF); IR (Neat) 3040, 3026, 3000, 2960, 2920, 2880, 1744, 1505, 1460, 1392, 1375, 1308, 1260, 1210, 1172, 1105, 1030, 865, 742, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.24 (m, 5 H), 4.51 (s, 2 H), 4.10 (q, J=7.1 Hz, 4 H), 3.70 (q, J=7.2 Hz, 2 H), 3.50 (t, J=6.6 Hz, 2 H), 3.10 (t, J=6.5 Hz, 2 H) 1.29 (d, J=7.2 Hz, 6 H), 1.24 (t, J=7.1 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8 (C), 138.6 (C), 128.3 (CH), 127.5 (CH), 127.5 (CH), 73.1 (CH_2), 71.3 (CH_2), 60.3 (CH_2), 57.9 (CH), 47.1 (CH_2), 16.3 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{19}H_{29}NO_5$: C, 64.92; H, 8.32; N, 3.99. Found: C, 65.48; H, 8.44; N, 3.93.

(2*S*,2′*S*)-Diethyl 2,2′-[2-hydroxyethylimino]dipropionate (10a). Dipropionate **9b** (351 mg, 1 mmol) and 20% $Pd(OH_2)$ on carbon (150 mg) in 10 mL of ethyl acetate was hydrogenated under 1 atm of H_2 at ambient temperature for 24 h. The solution was filtered over celite to yield 260 mg (100%) of a light yellow liquid. $[\alpha]_D^{26}=-61.35$ (1.115, DMF); IR (Neat) 3478, 3000, 2960, 2926, 2895, 1740, 1464, 1385, 1338, 1305, 1650, 1105, 1030, 864 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.14 (q, J=7.1 Hz, 4 H), 3.67 (q, J=7.2 Hz, 2 H), 3.60–3.45 (m, 2 H), 3.18–2.88 (m, 2 H), 1.33 (d, J=7.2 Hz, 6 H), 1.27 (t, J=7.1 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2 (C), 60.7 (CH_2), 59.6 (CH_2), 57.1 (CH), 48.4 (CH_2), 16.1 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{12}H_{23}NO_5$: C, 55.14; H, 8.88; N, 5.36. Found: C, 55.46; H, 8.96; N, 5.01.

(2*S,2′*R**)-Diethyl 2,2′-[2-hydroxyethyl imino]dipropionate (10b).** Dipropionate **9d** (1.05 g, 3 mmol) and 20% $Pd(OH_2)$ on carbon (450 mg) in 20 mL of ethyl acetate was hydrogenated under 1 atm of H_2 at room temperature for 3 h. The solution was filtered through celite, and the filtrate evaporated to yield 782 mg (100%) of a colorless liquid. $[\alpha]_D^{26}=-0.17$ (0.66, DMF); IR (Neat) 3480, 3000, 2958, 2920, 2892, 1740, 1470, 1456, 1385, 1305, 1140, 1100, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.16 (q, J=7.1 Hz, 4 H), 3.67 (q, J=7.2 Hz, 2 H), 3.53 (t, J=5.2 Hz, 2 H), 3.00 (t, J=5.2 Hz, 2 H), 1.32 (d, J=7.2 Hz, 6 H), 1.28 (t, J=7.2 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.2 (C), 60.8 (CH_2), 59.3 (CH_2), 56.4 (CH), 49.7 (CH_2), 15.6 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{12}H_{23}NO_5$: C, 55.14; H, 8.88; N, 5.36. Found: C, 55.11; H, 8.65; N, 5.05.

(2*S*,2′*S*)-Diethyl 2,2′-[2-hydroxyethyl imino]-dipropionate *p*-toluene-sulfonate (11a). To a solution of *p*-toluenesulfonyl chloride (458 mg, 2.4 mmol) in 0.5 mL of pyridine at −5°C was added a solution of **10a** (522 mg, 2 mmol) in 2 mL of pyridine in a dropwise manner. The resulting mixture was stirred at −5°C for 3 h and refrigerated for 16–18 h. Subsequently, 2 mL of H_2O was added and the aqueous mixture was extracted with ether (20 mL). The ether layer was washed with 1 M $KHSO_4$ solution (3×20 mL) and brine (1×20 mL), dried over Na_2SO_4 and concentrated in vacuo to yield 786 mg (95%) of a pale yellow liquid. $[\alpha]_D^{27}=-40.87$ (0.925, DMF); IR (Neat) 3000, 2957, 2920, 2890, 1745, 1608, 1465, 1370, 1197, 1184, 1104, 1026, 1010, 960, 910, 820 cm^{-1}; ^1H NMR

(300 MHz, $CDCl_3$) δ 7.79 (d, J=8.3 Hz, 2 H), 7.34 (d, J=8.2 Hz, 2 H), 4.07 (q, J=7.2 Hz, 4 H), 4.01–3.90 (m, 2 H), 3.57 (q, J=7.2 Hz, 2 H), 3.31–3.14 (m, 2 H), 2.45 (s, 3 H), 1.23 (t, J=7.0 Hz, 6 H), 1.22 (d, J=7.1 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.7 (C), 144.7 (C), 133.3 (C), 129.8 (CH), 127.9 (CH), 69.2 (CH_2), 60.3 (CH_2), 56.6 (CH), 46.0 (CH_2), 21.6 (CH_3), 17.3 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{19}H_{29}NO_7S$: C, 54.92; H, 7.04; N, 3.37. Found: C, 54.85; H, 6.89; N, 3.23.

(2*S,2′*R**)-Diethyl 2,2′-[2-hydroxyethyl imino]dipropionate *p*-toluene-sulfonate (11b).** To a solution of *p*-toluenesulfonyl chloride (458 mg, 2.4 mmol) in 0.5 mL of pyridine at −5°C was added a solution of **10b** (522 mg, 2 mmol) in 2 mL of pyridine in a dropwise manner. The resulting mixture was stirred at −5°C for 3 h and refrigerated for 16–18 h. Subsequently, 2 mL of H_2O was added and the aqueous mixture was extracted with ether (20 mL). The ether layer was washed with 1 M $KHSO_4$ solution (3×20 mL) and brine (1×20 mL), dried over Na_2SO_4 and concentrated in vacuo to yield 774 mg (93%) of a pale yellow liquid. $[\alpha]_D^{27}$=−0.24 (0.785, DMF); IR (Neat) 3000, 2960, 2922, 2892, 1744, 1609, 1460, 1370, 1182, 1104, 1058, 1027, 962, 913 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J=8.3 Hz, 2 H), 7.34 (d, J=8.0 Hz, 2 H), 4.09 (q, J=7.1 Hz, 4 H), 3.98 (t, J=7.0 Hz, 2 H), 3.57 (q, J=7.2 Hz, 2 H), 3.17 (t, J=6.7 Hz, 2 H), 2.45 (s, 3 H), 1.24 (t, J=7.1 Hz, 6 H), 1.24 (d, J=7.2 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2 (C), 144.7 (C), 133.2 (C), 129.8 (CH), 127.9 (CH), 70.0 (CH_2), 60.5 (CH_2), 58.2 (CH), 46.1 (CH_2), 21.6 (CH_3), 16.5 (CH_3), 14.1 (CH_3); Anal. Calcd for $C_{19}H_{29}NO_7S$: C, 54.92; H, 7.04; N, 3.37. Found: C, 54.92; H, 7.00; N, 3.32.

(2*R,2′*R**,2″*S**,2‴*S**)-Tetraethyl 2,2′,2″,2‴-(ethylenedinitrilo)tetra-propionate (8d).** A mixture of **11a** (208 mg, 0.5 mmol), **7b** (132 mg, 0.6 mmol) and 1,2,2,6,6-pentamethylpiperidine (80 mg, 0.5 mmol) in 1 mL of dry toluene was heated at reflux under Ar for 2 days. After cooling to room temperature, the mixture was diluted with ether and filtered. The filtrate was evaporated and the residue chromatographed (9:1 dichloromethane–ether) to yield 163 mg (71%) of a light yellow liquid. $[\alpha]_D^{27}$=−0.12 (0.755, DMF); IR (Neat) 3000, 2960, 2920, 2895, 1745, 1470, 1455, 1370, 1335, 1160, 1110, 1030, 860 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.10 (q, J=7.2 Hz, 4 H), 3.67 (q, J=7.2 Hz, 2 H), 2.91 (s, 4 H), 1.29 (d, J=7.2 Hz, 6 H), 1.25 (t, J=7.1 Hz, 6 H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 174.0 (C), 60.1 (CH_2), 56.5 (CH), 47.8 (CH_2), 17.3 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{22}H_{40}N_2O_8$: C, 57.36; H, 8.76; N, 6.08. Found: C, 57.61; H, 8.65; N, 5.84.

(2*R*,2′*R*,2″*R*,2‴*S*)-Tetraethyl 2,2′,2″,2‴-(ethylene-dinitrilo)tetra-propionate (8e). A mixture of **11b** (208 mg, 0.5 mmol), **7b** (132 mg, 0.6 mmol) and 1,2,2,6,6-pentamethylpiperidine (80 mg, 0.5 mmol) in 1 mL of dry toluene was heated at reflux under Ar for 2 days. After cooling to room temperature, the mixture was diluted with ether and filtered. The filtrate was evaporated and the residue chromatographed (9:1 dichloromethane–ether) to yield 178 mg (77%) of a light yellow liquid. $[\alpha]_D^{27}$=+41.05 (0.86, DMF); IR (Neat) 3000, 2960, 2920, 2890, 1740, 1470, 1380, 1160, 1110, 1060, 1030, 865 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.12 (q, J=7.3 Hz, 4 H), 4.09 (q, J=7.3 Hz, 4 H), 3.64 (q, J=7.1 Hz, 4 H), 2.99–2.75 (m, 4 H), 1.33–1.21 (m, 24 H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 174.6 (C), 174.0 (C), 60.2 (CH_2), 60.0 (CH_2), 57.6 (CH), 57.5 (CH), 56.5 (CH), 48.0 (CH_2), 47.8 (CH_2), 17.3 (CH_3), 16.2 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{22}H_{40}N_2O_8$: C, 57.36; H, 8.76; N, 6.08. Found: C, 57.66; H, 8.69; N, 5.93.

(2*S*,2′*S*,2″*S*,2‴*R*)-Tetraethyl 2,2′,2″,2‴-(ethylene-dinitrilo)tetra-propionate (8f). A mixture of **11b** (208 mg, 0.5 mmol), **7a** (132 mg, 0.6 mmol) and 1,2,2,6,6-pentamethylpiperidine (80 mg, 0.5 mmol) in 1 mL of dry toluene was heated at reflux under Ar for 2 days. After cooling to room temperature, the mixture was diluted with ether and filtered. The filtrate was evaporated and the residue chromatographed (9:1 dichloromethane–ether) to yield 146 mg (64%) of a light yellow liquid. $[\alpha]_D^{27}$=−34.85 (0.835, DMF); IR (Neat) 3000, 2960, 2920, 2900, 1745, 1455, 1420, 1380, 1160, 1110, 1060, 1030, 865 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.12 (q, J=7.2 Hz, 4 H), 4.09 (q, J=7.2 Hz, 4 H), 3.64 (q, J=7.1 Hz, 4 H), 2.98–2.75 (m, 4 H), 1.33–1.21 (m, 24 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.6 (C), 174.0 (C), 60.2 (CH_2), 60.1 (CH_2), 57.6 (CH), 57.5 (CH), 56.5 (CH), 48.0 (CH_2), 47.8 (CH_2), 17.3 (CH_3), 16.2 (CH_3), 14.2 (CH_3); Anal. Calcd for $C_{22}H_{40}N_2O_8$: C, 57.36; H, 8.76; N, 6.08. Found: C, 57.06; H, 8.46; N, 5.89.

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