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ENANTIOSELECTIVE SYNTHESIS OF α-AMINO ACIDS FROM 10-SULFONAMIDO-ISOBORNYL ESTERS AND DI-*t*-BUTYL AZODICARBOXYLATE

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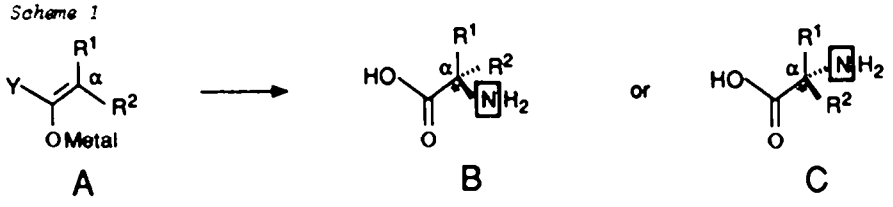
Abstract: Successive treatment of chiral esters 7 with LDA/Me_3SiCl and di-*t*-butyl azodicarboxylate/$TiCl_4$ and $Ti(OiPr)_4$ gave N,N-di-*t*-butoxycarbonylhydrazinoesters 11 which on deacylation, hydrogenolysis, transesterification and acidic hydrolysis furnished *(2S)*-α-amino acid hydrochlorides 13 in good overall yields, high enantiomeric purity and with efficient recovery of the alcohol auxiliary 4. Experimental evidence for the configuration and conformation of the intermediate O-silyl ketene acetals 1 is provided.

Introduction.

The synthesis of enantiomerically pure α-amino acids is an exciting issue [1] which has been addressed increasingly during the last few years.

Whereas previous efforts have successfully focussed on π-face-selective formations of the C(α),H- [2] and C(α),C- bonds [3] we first reported an indirect asymmetric formation of the C(α),N-bond: A → B or A → C (Scheme 1) [4].

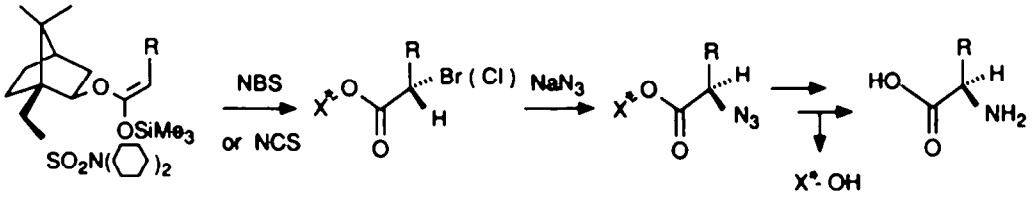
Scheme 1



A B C

Thus, simple π-face selective halogenation of esters via the O-silyl ketene acetals (prepared *in situ*) 1 → 2 [5] and subsequent S_N2-type halide substitution by azide 2 → 3, transesterification and hydrogenolysis 3 → 4 + 5 provided free amino acids 5 in 94 to 98% e.e. and in 42 to 57% overall yield (Scheme 2) [5,6,7]

Scheme 2



1 2 3 4 5

As an extension of this work and as a complement to a preliminary communication, [8] we present here a topologically reversed approach to α-amino acids 13 featuring a direct asymmetric formation of the C(α),N-bond *i.e.* A → C using di-*t*-butyl azodicarboxylate as a nitrogen electrophile [9]. Diethyl azodicarboxylate, known since 1922 to aminate enols and enolates [10] proved to be less suitable in our hands since mild N-deacylation of the N,N-diacylhydrazine products was required to permit smooth N,N-hydrogenolysis.

π-Face-Selective Conjugate Additions of Chiral Ester Enolate Derivatives to Di(tert-butyl) Azodicarboxylate (Scheme 3).

The crystalline starting esters 7 were obtained in 82 to 93% yield by reaction of acid chlorides 6 with the alcohol auxiliary 4 in the presence of AgCN [4,11].

Exploratory experiments involving additions of the lithium enolates 8 to azoesters proceeded with moderate stereodifferentiation from the predicted face. Thus, "kinetic" (1.1 mol-equiv of LDA, THF, -78°) deprotonation [12] of 7a (R = *n*Bu) followed by addition of di-*t*-butyl azodicarboxylate (1.25 mol-equiv, -78°, 2 min) furnished an 19:81-mixture of adducts 10a and 11a in 62 % yield.

Significantly higher selectivities were observed in the Lewis acid promoted 1,4-additions [13] 1 → 11 as depicted in Scheme 3 and in Table 1.

Scheme 3

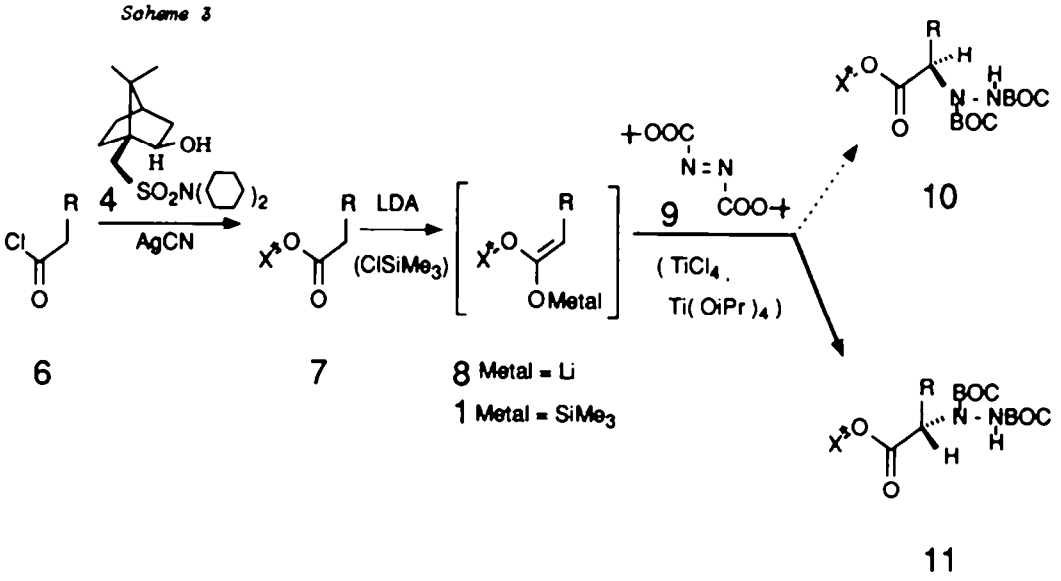


Table 1: *Preparation of Enantiomerically Pure N,N-Diacylhydrazinoesters* 11 *by Asymmetric 1,4-Addition*: 1 + 9 → 10 + 11.

Series	R	Ratio 10/11 Crude	Yield of 11 [a] after FC [%]	d.e. of 11 after FC [%]	C(2)-Config. of 11
a	CH_3	3.1 : 96.9	81	>99.5	*S*
b	C_2H_5	1.9 : 98.1	84	>99.5	*S*
c	C_3H_7	1.8 : 98.2	72 (88)	>99.5	*S*
d	$i\text{-}C_3H_7$	2.4 : 97.6	73 (95)	99	*S*
e	C_4H_9	3.7 : 96.3	85	>99.5	*S*
f	$i\text{-}C_4H_9$	3.4 : 96.6	71 (87)	>99.5	*S*
g	C_6H_{13}	2.0 : 98.0	69 (93)	>99.5	*S*
h	$PhCH_2$	1.8 : 98.2	76 (82)	>99.5	*S*
i	1-Adamantyl-CH_2	18.0 : 82.0	65 (81)	>99.5	*S*

[a] In parentheses, yield based on recovered starting ester 7.

Kinetically controlled deprotonation/silylation of esters 7 [14] followed by treatment of the resulting crude silyl ketene acetals 1 with $TiCl_4/Ti(OiPr)_4$ 2:1 and azoester 9 at -78° gave adducts 10 and 11 in good yields. Direct HPLC and 1H-NMR (360 MHz, 100°C) analyses of the crude product mixtures and full characterization of the separated isomers 10 and 11 showed the less

polar, major N,N-diacylhydrazinoesters 11 to be formed in diastereomeric excess (d.e.) of 91 to 96.4% (entries a to h). The lower π-face-differentiation (64% d.e.) observed in entry i may be attributed to the exceptional steric bulk of the adamantyl group. Flash chromatography (FC) or crystallization (11a) furnished without exception 11 in virtually 100% d.e.; their *(2S)*-configuration was assigned by transformation to *(2S)*-α-amino acids as described below.

Conversion of the Enantiomerically Pure N,N-Diacylhydrazine Products 11 to α-Amino Acids (Scheme 4, Table 2).

Scheme 4

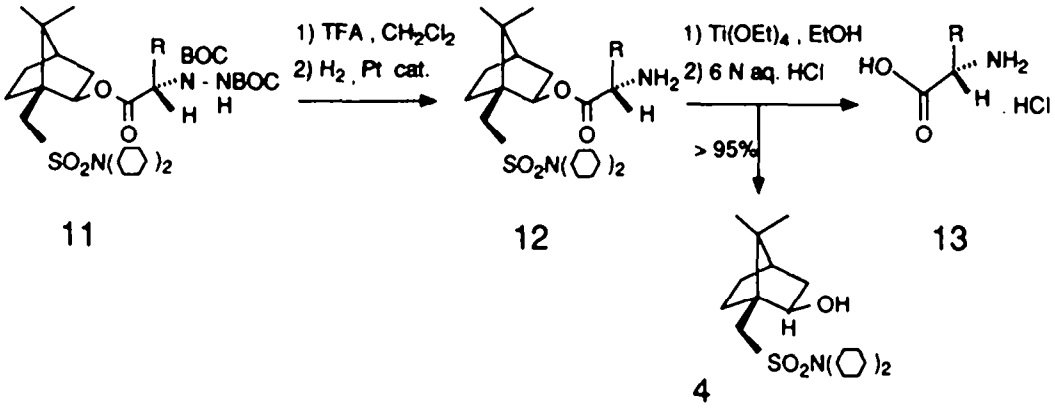


Table 2: *Conversion of N,N-Diacylhydrazinoesters 11 into (2S)-α-Amino Acid Hydrochlorides 13*

Series	R	Deacylation hydrogenolysis 11 → 12	Ester cleavage 12 → 4 + 13		
		Yield of 12 (cryst.) [%]	Yield of 4 [%]	Yield of 13 [%]	e.e. of 13 [%]
a	CH_3	83	94	83	95.0
b	C_2H_5	77	>99	91	99.7
c	C_3H_7	81	>99	86	99.2
d	$i\text{-}C_3H_7$	71	86	90	99.1
e	C_4H_9	80	>99	95	97.6
f	$i\text{-}C_4H_9$	70	>99	86	97.7
g	C_6H_{13}	55	95	89	96.9
h	$PhCH_2$	64[a]	>99	86[a]	98.4[a]
i	1-Adamantyl-CH_2	78	>99	65	95.2

[a] R = Cyclohexyl-CH_2

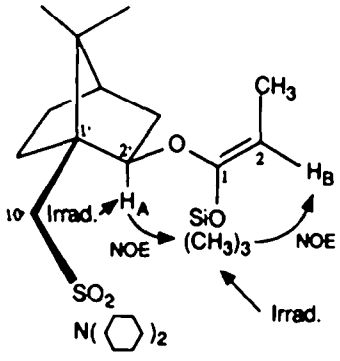
In order to achieve the required N,N-hydrogenolysis the *t*-butoxycarbonyl groups were first removed by stirring of 11 in trifluoroacetic acid/CH_2Cl_2 1:1 (0°, 3h). Evaporation of the solution and shaking of the residue with PtO_2 (catalytic amount, Ventron) in EtOH under H_2 (75 psi, r.t., 15h) smoothly afforded, after work-up, crystalline aminoesters 12 (55 to 83%) [15]. Entry h shows that hydrogenation of the phenyl ring occurs under these conditions to give cleanly the hexahydrophenylalanine ester 12, R = cyclohexyl-CH_2. Although acidic hydrolysis of esters 12 gave directly amino acid hydrochlorides 13 the auxiliary 4 was destroyed. More

advantageously, we regenerated the chiral alcohol 4 in >95% yield by non-destructive transesterification of 12 in the presence of $Ti(OEt)_4$. Heating of the resulting crude amino acid ethyl esters in 6N aq HCl at reflux and evaporation of the solution afforded the amino acid hydrochlorides 13 (49 to 77% yield from 11). The indicated absolute configuration and enantiomeric purities (97 to 99.7% e.e.) of the crude amino acids 13 were readily determined by GC comparison (chiral capillary column) [4,18] of their (N-trifluoroacetyl)-*n*-propyl esters with those of racemic and enantiomerically pure authentic samples and were further supported by chiroptic comparison [17].

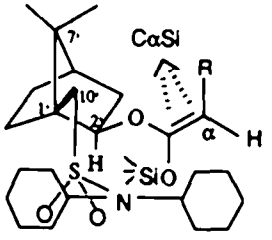
Rationalization of the π-Face Differentiation.

To understand the observed π-face discrimination on electrophilic amination of O-silyl ketene acetals 1 their *(E,Z)*-configuration and conformation had to be determined. In fact, NMR-Nuclear Overhauser Experiments on 1a showed that spin saturation of H_A caused a 2.1% enhancement of the Si-CH_3 signal which in turn, on irradiation, increased the H_B signal by 9.8% (Scheme 5).

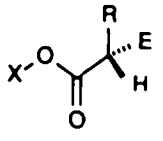
Scheme 5



1a



1



2 E = Br, Cl
11 E = N(BOC) - NHBOC
14 E = OAc
15 E = CH(OH)R

These results agree with the *(E)*-configuration of the O-silyl ketene acetal 1a and with a *syn*-periplanar disposition of the C(1),OSi- and C(2'),H_A- bonds. Based on X-ray-diffraction studies of esters of auxiliary 4 [18] we assume the C(10'),SO_2- and C(1'),C(7') bonds to be *anti*-periplanar and (as a result of sulfonamide conjugation) the lone pair on nitrogen to bisect the O-S-O- angle. Accordingly, one cyclohexane ring blocks the olefinic C(α)-*Re* (front) face and electrophiles $[E]^+$ such as Lewis acid coordinated azo ester 2 (→ 11) and aldehydes (→ 15) [19], as well as NBS, NCS (→ 2) [4] and $Pb(OAc)_4$ (→ 14) [20] attack 1 preferentially from the less hindered C(α)-*Si* (back) face [21].

Conclusion.

In summary, we have described a predictable enantioselective entry to *(2S)*-α-amino acids 13 (readily applicable to the syntheses of *(2R)*-α-amino acids, given the commercial availability of 4 and of its antipode) which is also complementary to the halogenation/azide displacement methodology [5]. Furthermore, the postulated general topicity of electrophilic attack to O-silyl ketene acetals 1 is supported by experimental evidence.

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EXPERIMENTAL

General:

All reactions were carried out under Ar with magnetic stirring, unless otherwise specified. Solvents were dried by distillation from drying agents as follows: Et_2O (Na), THF (Na), diisopropylamine (CaH_2). The *n*-butyllithium solutions were analyzed by *Gilman's* titration. Temperatures are expressed in degrees *Celsius*. 'Work-up' denotes extractions with an org. solvent, washing of the org. phase with sat. aq. NaCl soln., drying ($MgSO_4$), and evaporation (rotatory evaporator). Column flash chromatography (FC): SiO_2(*Merck* 60, 0.040 - 0.063 mm). HPLC: *Waters, ALC/GPP-244*, integrator *Mega, Serie Carlo Erba, LiChrosorb Si 60 (5 µm, Merck)*, refractometer *Waters R401*; retention time in min (areat). GC: *Hewlett-Packard 5790A*, integrator *HP 3390*, capillary column (fused silica, 0.25 i.d., 25 m) *Chirasil-Val* (Altech Associates Inc), 10 psi H_2, 2 min 100°, 5°/min→140°, unless otherwise specified; retention time in min (areat). Crystallizations were carried out in hexane, unless otherwise specified. M.p.: *Kofler* hot stage; uncorrected, [α]: *Perkin-Elmer-241* polarimeter; in $CHCl_3$, unless otherwise specified. IR: *Perkin-Elmer 257*, $CHCl_3$, unless otherwise specified. ^{1}H-NMR at 360 MHz ($CDCl_3$,10, 11 in $DMSOd_6$ at 100° to equilibrate rotamers), unless otherwise specified; ^{13}C-NMR at 50 MHz ($CDCl_3$), unless otherwise specified; standard tetramethylsilane (δ = 0 ppm); *J* in Hz. MS: *m/z* (rel.-%).

Preparation of 10-(*N*,*N*-Dicyclohexylaminosulfonyl)-2-bornyl Esters 7. General Procedure [11]:

AgCN (1.5 equiv.) was added to a mixture of auxiliary 4 (1 equiv.) and the acid chloride 6 (2 equiv.) in toluene (5 ml/mmole of 4). Heating of the mixture at 90 to 100° for 3 to 6 h, filtration through *Celite*, chromatography and crystallization afforded pure ester 7.

Amination of Esters 7 by Addition of O-Silyl Ketene Acetals 1 to Azo Ester 9. General Procedure:

Addition of Ester 7 (1 equiv.) in THF (2 ml/mmole of 7) to a mixture of freshly prepared $LiN(i\text{-}Pr)_2$ (1.1 equiv.) and $ClSiMe_3$ (1.75 equiv., -78°) in dry THF (4ml/mmole of LDA), stirring the mixture at -78° for 1h and, after removal of the cooling bath, stirring for 0.5 h, evaporation, extraction with pentane (for 11, CH_2Cl_2), filtration and evaporation of the pentane solution furnished crude O-silyl ketene acetal 1. $Ti(O\text{-}i\text{-}Pr)_4$ (0.5 mol-equiv.), followed by a solution of freshly recrystallized azo ester 9 (1.25 equiv.) in CH_2Cl_2(0.5 ml/ mmole) were added dropwise at -78° to a solution of $TiCl_4$ (1 equiv.) in CH_2Cl_2 (8 ml/mmole), and the resulting mixture was stirred for 5 min at -78°. Slow addition (over 10 min) of crude O-silyl ketene acetal 1 in CH_2Cl_2 (1.5ml/mmole) at -78°, stirring of the mixture at -78° for 1h, followed by addition of sat aq. $NaHCO_3$ (7ml/mmole 1), allowing the stirred mixture to warm to room temperature, filtration through *Celite* and work-up furnished crude mixtures of 1,4-adducts 10 and 11 which was analyzed by GC and separated by FC.

Conversion of *N*,*N*-Diacylhydrazinoesters 11 into α-Amino Esters 12. General Procedure:

CF_3COOH (10ml/mmole of 11) was added over 5 min to a solution of 11 in CH_2Cl_2 (10 ml/mmole) at 0°. The solution was stirred at 0° for 5 min, allowed to warm to room temperature, stirred for 3h, diluted with CCl_4 (5ml/mmole) and evaporated (2x). Drying the residue at 0.01 Torr for 3h, addition of EtOH (13 ml/mmole) and PtO_2(60 mg/mmole), shaking of the mixture in a *Parr* apparatus under H_2 (75 psi) at r.t. from 6 to 24h, filtration through *Celite*, evaporation , work-up, FC and recrystallization afforded pure α-aminoesters 12.

Cleavage of Amino Esters 12 to Auxiliary 4 and α-Amino Acid HCl 13. General Procedure:

A mixture of amino ester 12 (1 equiv) and $Ti(OEt)_4$ (1 equiv.) in dry EtOH (5 ml/mmole of 12) were heated at 70° for 3h (12a: r.t., 60h). Evaporation and chromatography afforded auxiliary 4 and the corresponding crude amino ethyl ester which was then heated under reflux in 6N aq. HCl (20 ml/mmole) for 1.5h. Washing of the solution with $CHCl_3$, evaporation and drying at 0.001 Torr for several h furnished amino acid hydrochloride 13 as a colorless solid.

Conversion of Amino Acid HCl 13 to their (*N*-trifluoracetyl)-*n*-propyl esters. General Procedure [18]: Acetyl chloride (0.3 ml) was added dropwise at 0° to *n*-propanol (1 ml) and the mixture was warmed to r.t. over 5 min. Addition of 13 (5 to 40 mg), heating of the solution at 100° for 40 min, evaporation and drying (0.01 Torr, 2h) gave a residue which was dissolved in CH_2Cl_2 (1 ml). To this solution trifluoracetic anhydride (0.2 ml) was added dropwise at 0°. Heating the mixture under reflux for 10 min, evaporation and drying (0.01 Torr, 2h) gave the corresponding (*N*-trifluoracetyl)-*n*-propionate (~100%) which was analyzed by GC, IR, ^{1}H-NMR and MS.

Synthesis of *(2S)*-Alanine hydrochloride (13a).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] Propionate (7a).- Using the general procedure, propionyl chloride (1.85 g, 20 mmol) was heated with auxiliary 4 (3.976g, 10 mmol) and AgCN (2.01 g, 15 mmol) at 95° for 3h to give after work-up, FC (hexane/Et_2O 3:1) and crystallization (hexane) 7a (4.277 g, 94%). M.p. 151-153°. IR: 2945, 2865, 1730, 1455, 1327, 1145, 1050, 980.^{1}H-NMR: 0.89 (*s*, 3 H); 0.99 (*s*, 3 H); 1.16 (*t*, *J* = 0.75, 3 H); 1.04-1.38 (7 H); 1.58-1.90 (18 H); 1.92-2.07 (2 H); 2.32 (*q*, *J* = 7.5, 2 H); 2.67 (*d*, *J* = 14, 1 H); 3.18-3.33 (*m*, 2 H); 3.27 (*d*, *J* = 14, 1 H); 4.96 (*dd*, *J* = 3, 8, 1 H). ^{13}C-NMR: 172.55 (*s*), 78.186 (*d*), 57.37 (*d*), 53.55(*t*), 49.27 (*s*), 49.02 (*s*), 44.40 (*d*), 39.57 (*t*), 32.78 (*t*), 32.65 (*t*), 30.07 (*t*), 27.83 (*t*), 26.97(*t*), 26.45 (*t*), 25.14 (*t*), 20.36 (*q*), 19.93 (*q*), 9.10 (*q*). MS: 453 (12, $C_{25}H_{43}NO_4S^+$), 298 (36); 244 (64), 228 (9), 181 (12), 135 (15), 107 (8), 93 (12), 83 (18), 67 (8), 57 (100), 55 (45).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2R)-2-(N,N'-di-tert-butoxycarbonyl)hydrazinopropionate (10a) *and [(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2S)-2-(N,N'-di-tert-butoxycarbonyl)hydrazinopropionate* (11a).- Using the general procedure, propionate 7a (1.59 g, 3.5 mmol) was converted to a crude mixture 10a/11a, HPLC (hexane/EtOAc 9:1, 2 ml/min.) 6.9 (95.9), 10.1 (3.1), which was chromatographed (hexane/EtOAc 10:1) to give after crystallization (hexane) the less polar, major product 11a (1.93 g, 81%). M.p. 168-170°, $[\alpha]_D$ = -22.4° (20°, c = 0.97). HPLC (hexane/EtOAc 9:1, 2 ml/min.): 7.0 (100). IR: 3390, 3320, 2940, 2860, 1740, 1720, 1480, 1455, 1395, 1370, 1325, 1165, 1145, 1110, 1050, 985. ^{1}H-NMR ($DMSOd_6$, 100°): 0.87 (*s*, 3 H); 0.98 (*s*, 3 H); 1.00-1.95 (27 H); 1.36 (*d*, *J* = 7, 3 H); 1.42 (18 H); 2.72 (*d*, *J* = 13.5, 1 H); 3.20-3.35 (2 H); 3.24 (*d*, *J* = 13.5, 1 H); 4.60 (*m*, 1 H); 4.75 (*m*, 1 H); 8.00-8.10 (*br*, 1 H). MS: no $C_{35}H_{61}N_3O_8S^+$, 683, 483 (19), 380 (20), 246 (15), 228

(20), 181 (53), 135 (100), 107 (25), 98 (14), 93 (31), 83 (46), 79 (16), 67 (10), 59. (88), 57 (35), 55 (48). Further elution furnished the minor, more polar epimer 10a (containing 23% of 11a): HPLC (hexane/EtOAc 9:1, 2 ml/min.): 7.4 (22.8), 9.6 (77.2). IR: 3390, 2940, 2860, 1745, 1720, 1480, 1455, 1395, 1370, 1325, 1165, 1145, 1110, 1050, 985. ^{1}H-NMR (DMSOd$_6$, 100°): 0.87 (*s*, 3 H); 0.99 (*s*, 3 H); 1.00-1.98 (27 H); 1.30 (*d*, *J* = 7,3 H); 1.39 (*s*, 9 H); 1.41 (*s*, 9 H); 2.67 (*d*, *J* = 13.5, 1 H); 3.20-3.35 (2 H); 3.31 (*d*, *J* = 13.5, 1 H); 4.45-4.55 (*m*, 1 H); 4.75-4.82 (*m*, 1 H); 8.35-8.55 (1 H).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] (2R)-2-aminopropionate (12a).- Using the general procedure, hydrazinoester 11a (342 mg, 0.5 mmol) gave after N,N-deacylation and hydrogenolysis (12h), FC (hexane/EtOAc 1:1, then EtOAc) and crystallization aminoester 12a (187 mg, 80%). M.p. 173-175°, $[\alpha]_D$ = -36.6°(20°,c = 1.02). IR: 3380, 2945, 2860, 1735, 1600, 1455, 1395, 1375, 1325, 1170, 1145, 1110, 1050, 985. ^{1}H-NMR: -0.90 (*s*, 3 H); 1.00 (*s*, 3 H); 1.05-1.90 (25 H); 1.37 (*d*, *J* = 7, 3 H); 1.90-2.06 (2 H); 2.68 (*d*, *J* = 13.5, 1 H); 3.20-3.30 (2 H); 3.24 (*d*, *J* = 13.5, 1 H); 3.50 (*q*, *J* = 7, 1 H); 4.98 (*dd*, *J* = 3.5, 8, 1 H). ^{13}C-NMR: 175.20 (*s*), 78.89 (*d*), 57.48 (*d*), 53.83 (*t*), 49.91 (*d*), 49.43 (*s*), 49.10 (*s*), 44.38 (*d*), 39.52 (*t*), 32.82 (*t*), 32.66 (*t*), 30.26 (*t*), 26.92 (*t*), 26.44 (*t*), 25.15 (*t*), 20.35 (*q*), 19.94 (*q*), 19.90 (*q*). MS: no $C_{25}H_{44}N_2O_4S^{+\cdot}$-468, 381 (20), 181 (100), 135 (32), 107 (21), 93 (37), 83 (42), 55 (55).

(2S)-Alanine Hydrochloride (13a).- Using the general procedure, transesterification of aminoester 12a (610 mg, 1.3 mmol, r.t., 60h) and FC (hexane/EtOAc 7:1, then EtOH) furnished auxiliary 4 (487 mg, 94%) to give, after acidic hydrolysis of the crude ethyl ester, 13a as a colorless solid (136 mg, 83%). $[\alpha]_D$ = +6.3° (20°, H_2O, c = 1.20). ^{1}H-NMR (D_2O): 1.41 (*d*, *J* = 7.5, 3 H); 3.96 (*t*, *J* = 7.5, 1 H).

n-Propyl (2S)-2-Trifluoroacetamidopropionate.- Using the general procedure crude 13a (10 mg 0.08 mmol) gave the corresponding (N-trifluoracetyl)-*n*-propyl ester (20 mg, ~100%). GC (Chirasil-Val, 100°): 3.15 (2.5), 3.69 (96.5). IR: 3410, 2980, 2940, 2880, 1785, 1730, 1535, 1455, 1400, 1290. ^{1}H-NMR: 0.96 (*t*, *J* = 7.5, 3 H); 1.52 (*d*, *J* = 7, 3 H); 1.6 (*s*, *br.*, 1 H); 1.72 (*m*, 2 H); 4.20 (*m*, 2 H); 4.63 (*m*, 1 H). The (N-trifluoracetyl)-*n*-propyl ester prepared from commercial *(2S)*-alanine shows identical IR, ^{1}H-NMR and MS spectra. GC (Chirasil-Val, 100°) of (N-trifluoracetyl)-*n*-propyl esters prepared from commercial *(2S)*-alanine: 3.68 (100); coinjection of the latter with the sample derived from 13a: 3.70 (major); from commercial *(2RS)*-alanine: 3.25 (49.0), 3.78 (49.9).

Synthesis of *(2S)*-2-Aminobutanoic Acid Hydrochloride (13b).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] Butanoate (7b).- Using the general procedure, auxiliary 4 (1.99 g, 5 mmol) was heated with butanoyl chloride and AgCN at 90° for 3h to give after work-up, FC (hexane/EtOAc 4:1) and crystallization 7b (2.18 g, 93%). M.p. 142-143°. IR: 2950, 2870, 1735, 1460, 1395, 1325, 1170, 1150, 1110, 975. ^{1}H-NMR: 0.89 (*s*, 3 H); 0.97 (*t*, *J* = 7.5, 3 H); 0.99 (*s*, 3 H); 1.05-1.90 (27 H); 1.94-2.07 (2 H); 2.28 (*t*, *J* = 7.5, 2 H); 2.66 (*d*, *J* = 13.5, 1 H); 3.22-3.32 (2 H); 3.26 (*d*, *J* = 13.5, 1 H); 4.95 (*dd*, *J* = 3.5, 8, 1 H). ^{13}C-NMR (50 MHz): 171.88 (*s*), 78.26 (*d*), 57.40 (*d*), 53.65 (*t*), 49.28 (*s*), 49.05 (*s*), 4.43 (*d*), 39.64 (*t*), 36.57 (*t*), 32.77 (*t*), 32.67 (*t*), 30.09 (*t*), 26.96 (*t*), 26.46 (*t*), 25.15 (*t*), 20.42 (*q*), 19.94 (*q*), 18.38 (*t*), 13.70 (*q*). MS: 467 (1, $C_{26}H_{45}NO_4S^{+\cdot}$-), 298 (3), 244 (8), 181 (14), 135 (18), 107 (11), 93 (13), 83 (20), 71 (100), 55 (46). HR-MS: 467.3091, ($C_{26}H_{45}NO_4S^{+\cdot}$ calc.: 467.3069).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2R)-2-(N,N'-di-tert-butoxycarbonyl)hydrazinobutyrate (10b) *and [(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2S)-2-(N,N'-di-tert-butoxycarbonyl)hydrazinobutyrate* (11b).- Using the general procedure, butyrate 7b (2.34 g, 5 mmol) was converted to a crude mixture 10b/11b, HPLC (hexane/EtOAc 9:1, 1 ml/min.) 8.5 (88.1), 12.3 (1.7), which was chromatographed (hexane/EtOAc 11:1) to give the less polar major product 11b (2.93 g, 84%) as an amorphous solid. $[\alpha]_D$ = -31.4° (20°, c = 1.24), HPLC (hexane/EtOAc 9:1, 1 ml/min.): 8.6 (100). IR: 3390, 3300, 2940, 2860, 1730, 1470, 1450, 1395, 1370, 1325, 1170, 1150, 1110, 1050, 985. ^{1}H-NMR (DMSOd$_6$, 100°): 0.86 (*s*, 3 H); 0.98 (*s*, 3 H); 1.00 (*t*, *J* = 7, 3 H); 1.05-2.00 (29 H); 1.40 (*s*, 18 H); 2.72 (*d*, *J* = 13.5, 1 H) ;3.20-3.35 (2 H); 3.25 (*d*, *J* = 13.5, 1 H); 4.42 (*m*, 1 H); 4.76 (*m*, 1 H); 7.75-7.90 (*br.* 1 H). MS: 697 (<1, $C_{36}H_{63}N_3O_8S^{+\cdot}$), 497 (50), 380 (40), 298 (12), 246 (22), 228 (33), 181 (50), 164 (10), 135 (100), 117 (30), 93 (25), 83 (40), 73 (55), 57 (60). Further elution furnished the more polar, minor isomer 10b: HPLC (hexane/EtOAc 9:1, 1 ml/min.): 12.2 (100). IR: 3380, 2940, 2860, 1745, 1715, 1480, 1455, 1395, 1370, 1325, 1170, 1145, 1110, 1050, 985. ^{1}H-NMR (DMSOd$_6$, 100°): 0.86 (*s*, 3 H); 0.92 (*t*, *J* = 7,3 H); 0.98 (*s*, 3 H); 1.00-2.05 (29 H); 1.40 (*s*, 9 H); 1.43 (*s*, 9 H); 2.68 (*d*, *J* = 13.5, 1 H); 3.20-3.35 (2 H); 3.29 (*d*, *J* = 13.5, 1 H); 4.44 (*m*, 1 H); 4.77 (*m*, 1 H); 8.15-8.35 (*br.* 1 H). MS: 697 (<1, $C_{36}H_{63}N_3O_8S^{+\cdot}$), 497 (40), 380 (37), 298 (9), 246 (21), 228 (29), 181 (45), 164 (10), 135 (100), 117 (30), 93 (23), 83 (36), 73 (53), 57 (68).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] (2R)-2-aminobutyrate (12b).- Using the general procedure, hydrazinoester 11b (2.20 g, 3.15 mmol) gave after N,N-deacylation and hydrogenolysis (22h), FC (hexane/EtOAc 2:1, then EtOAc) and crystallization aminoester 12b (1.18 g, 77%). M.p. 158-160°. $[\alpha]_D$ = -32.9° (20°, c = 1.27). IR: 3380, 3320, 2940, 2860, 1735, 1600, 1455, 1395, 1375, 1325, 1170, 1145, 1110, 1050, 985. ^{1}H-NMR: 0.86 (*s*, 3 H); 0.94 (*t*, *J* = 7.5, 3 H); 0.96 (*s*, 3 H); 1.00-1.34 (8 H); 1.54-1.86 (19 H); 1.90-2.06 (2 H); 2.66 (*d*, *J* = 13.5, 1 H); 3.18-3.30 (2 H); 3.24 (*d*, *J* = 13.5, 1 H); 3.36 (*dd*, *J* = 5.5, 7, 1 H); 4.98 (*dd*, *J* = 3.5, 8, 1 H). ^{13}C-NMR: 174.81 (*s*), 78.86 (*d*), 57.50 (*d*) 55.35 (*d*), 53.80 (*t*), 49.40 (*s*), 49.08 (*s*), 44.40 (*d*), 39.54 (*t*), 32.81 (*t*), 32.68 (*t*), 30.31 (*t*), 27.07 (*t*), 26.92 (*t*), 26.45 (*t*), 25.16 (*t*), 20.35 (*q*), 19.90 (*q*), 9.74 (*q*). MS: no $C_{26}H_{46}N_2O_4S^{+\cdot}$-482, 181 (34), 180 (28), 138 (13), 135 (11), 104 (10), 98 (11), 93 (18), 83 (19), 58 (100), 57 (77), 55 (24).

(2S)-Aminobutyric Acid Hydrochloride (13b).- Using the general procedure, transesterification of aminoester 12b (920 mg, 1.9 mmol) and FC (hexane/EtOAc 7:1, then EtOH) furnished auxiliary 4 (760 mg, 100%) to give, after acidic hydrolysis of the crude ethyl ester, 13b as a colorless solid (240 mg, 91%). $[\alpha]_D$ = +10.1° (20°, H_2O, c = 1.11). ^{1}H-NMR (D_2O): 0.87 (*t*, *J* = 7.5, 3 H); 1.77-1.91 (2 H); 3.86 (*t*, *J* = 6,1 H).

n-Propyl (2S)-2-Trifluoracetamidobutyrate.- Using the general procedure crude 13b (10 mg 0.07 mmol) gave the corresponding (N-trifluoracetyl)-*n*-propyl ester (20 mg, ~100%). GC (Chirasil-Val): 3.90 (0.15), 4.38 (99.7). IR: 3420, 2980, 2940, 2180, 1730, 1840, 1460, 1175. ^{1}H-NMR (200 MHz): 0.95 (*t*, *J* = 7.5, 3 H); 0.98 (*t*, *J* = 7.5, 3 H); 1.60-2.10 (4 H); 4.15 (*m*, 2 H); 4.60 (*q*, *J* = 7, 1 H); 6.92 (*s*, *br*, 1 H). MS: no $C_9H_{14}F_3NO_3^{+\cdot}$-241, 154 (100), 126 (8), 69 (10). The (N-trifluoracetyl)-*n*-propyl ester prepared from commercial *(2S)*-2-aminobutyric acid shows identical IR, ^{1}H-NMR and MS spectra. GC (Chirasil-Val) of (N-trifluoracetyl)-*n*-propyl esters prepared from commercial *(2S)*-2-butyric acid: 4.38 (100); coinjection of the latter with the sample derived from 13b: 4.40 (major); from commercial *(2RS)*-2-aminobutyric acid): 3.94 (49.4), 4.40 (49.4).

Synthesis of *(2S)*-Norvaline Hydrochloride (13c).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] Valerate (7c).- Using the general procedure, auxiliary 4 (2.39 g, 6 mmol) was heated with valeroyl chloride and AgCN at 90° for 3h to give after work-up, FC (hexane/EtOAc 4:1) and crystallization 7c (2.37 g, 82%). M.p. 158-160°. IR: 2950, 2870, 1735, 1460, 1395, 1330, 1170, 1150, 1105, 975. ^{1}H-NMR: 0.89 (*s*, 3 H); 0.93 (*t*, *J* = 7.5, 3 H); 1.00 (*s*, 3 H); 1.03-1.90 (29 H); 1.93-2.06 (2 H); 2.30 (*t*, *J* =7.5, 2 H); 2.67 (*d*, *J* = 13.5, 1 H); 3.20-3.32 (2 H); 3.27 (*d*, *J* = 13.5, 1 H); 4.95 (*dd*, *J* = 3.5, 8, 1 H). ^{13}C-NMR (50 MHz): 172.05 (*s*), 78.27 (*d*), 57.41 (*d*), 53.65 (*t*), 49.28 (*s*), 49.06 (*s*), 44.43 (*d*), 39.64 (*t*), 34.35 (*t*), 32.76 (*t*), 32.70 (*t*), 30.08 (*t*), 26.96 (*t*) 26.87 (*t*), 26.45 (*t*), 25.14 (*t*), 22.31 (*t*), 20.42 (*q*), 19.96 (*q*), 13.66 (*q*). MS: 481 (12 $C_{27}H_{47}NO_4S^{+\cdot}$), 298 (27), 244 (35), 181 (41), 135 (47), 85 (100), 57 (50), 55 (44). HR-MS: 481.3230, $C_{27}H_{47}NO_4S^{+\cdot}$, calc.: 481.3226.)

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2R)-2-(N,N'-di-tert-butoxycarbonyl)hydrazinovalerate (10c) *and [(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2S)-2-(N,N'-di-tert-butoxycarbonyl)hydrazinovalerate* (11c).- Using the general procedure, valerate 7c (1.98 g, 4.1 mmol) was converted to a crude mixture 10c/11c, HPLC (hexane/EtOAc 9:1, 1 ml/min.) 8.4 (98.2), 11.0 (1.8), which was chromatographed (hexane/EtOAc 12:1) to give recovered ester 7c (316 mg, 16%) followed by the less polar major product 11c (2.1 g, 72%, amorphous solid). $[\alpha]_D$ = -29.7° (20°, c = 0.98). HPLC (hexane/EtOAc 9:1, 1 ml/min.): 8.4 (100). IR: 3390, 3320, 2940, 2860, 1730, 1480, 1460, 1395, 1370, 1325, 1170, 1150, 1110, 1050, 985. ^{1}H-NMR (DMSOd$_6$, 100°): 0.87 (*s*, 3 H); 0.89 (*t*, *J* = 7, 3 H); 0.98 (*s*, 3 H); 1.00-1.95 (31 H); 1.44 (*s*, 18 H); 2.74 (*d*, *J* = 13.5, 1 H); 3.20-3.35 (2 H); 3.24 (*d*, *J* = 13.5, 1 H); 4.52 (*m*, 1 H); 4.76 (*m*, 1 H); 7.65-7.80 (*br*. 1 H). MS: 712 (<1, $C_{37}H_{65}N_3O_8S^{+\cdot}$), 511 (40), 481 (20), 467 (12), 380 (30), 298 (15), 246 (20), 228 (22), 181 (50), 164 (10), 135 (100), 107 (30), 87 (80), 69 (15), 57 (97), 55 (55), 44 (55). Further elution afforded the more polar, minor isomer 10c (containing 18% of 11c). HPLC (hexane/EtOAc 9:1, 1 ml/min.): 8.4 (18.1), 11.0 (74.6). IR: 3390, 2940, 2860, 1740, 1715, 1610, 1480, 1455, 1395, 1370, 1325, 1170, 1145, 1110, 1050, 980. ^{1}H-NMR (DMSOd$_6$, 100°): 0.84 (*s* 3 H); 0.88 (*t*, *J* = 7, 3 H); 0.99 (*s*, 3 H); 1.00-2.10 (31 H); 1.40 (*s* 9 H); 1.43 (*s* 9 H); 2.68 (*d*, *J* = 13.5, 1 H); 3.20-3.35 (2 H); 3.30 (*d*, *J* = 13.5, 1 H); 4.78 (*m*, 1 H); 4.78 (*m*, 1 H); 8.20-8.40 (*br*. 1 H). MS: no $C_{37}H_{65}N_3O_8S^{+\cdot}$-712, 511 (36), 380 (32), 298 (12), 246 (18), 228 (25), 181 (54), 135 (100), 107 (23), 87 (79), 69 (11), 57 (70), 55 (38), 44 (22).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] (2R)-2-aminovalerate (12c).- Using the general procedure, hydrazinoester 11c (2.10 g, 2.95 mmol) gave after N,N-deacylation and hydrogenolysis (22h), FC (hexane/EtOAc 2:1, then EtOAc) and crystallization aminoester 12c (1.20 g, 81%). M.p. 133-135°. $[\alpha]_D$ = -32.2° (20°, $CHCl_3$, c = 1.04). IR: 3380, 2945, 2860, 1735, 1600, 1470, 1455, 1395, 1375, 1325, 1170, 1150, 1110, 1050, 980. ^{1}H-NMR: 0.85 (*s*, 3 H); 0.89 (*t*, *J* = 7.5, 3 H); 0.96 (*s*, 3 H); 1.00-1.85 (29 H); 1.90-2.05 (2 H); 2.66 (*d*, *J* = 13.5, 1 H); 3.18-3.32 (2 H); 3.24 (*d*, *J* = 13.5, 1 H); 3.41 (*dd*, *J* = 5.5, 7, 1 H); 4.98 (*dd*, *J* = 3.5, 8, 1 H). ^{13}C-NMR: 175.10 (*s*), 78.83 (*d*), 57.47 (*d*), 53.95 (*d*), 53.81 (*t*), 49.39 (*s*), 49.06 (*s*), 44.39 (*d*), 39.48 (*t*), 36.19 (*t*), 32.78 (*t*), 32.67 (*t*), 30.32 (*t*), 26.93 (*t*), 26.44 (*t*), 25.14 (*t*), 20.33 (*q*), 19.86 (*q*), 18.62 (*t*), 13.83 (*q*). MS: no $C_{27}H_{48}N_2O_4S^{+\cdot}$-496, 181 (28), 180 (21), 138 (10), 83 (11), 72 (100), 55 (12).

(2S)-Norvaline Hydrochloride (13c).- Using the general procedure, transesterification of aminoester 12c (1.04 g, 2.09 mmol) and FC (hexane/EtOAc 7:1, then EtOAc/EtOH 1:1) furnished auxiliary 4 (837 mg, ~100%) to give, after acidic hydrolysis of the crude ethyl ester, 13c as a colorless solid (276 mg, 86%). $[\alpha]_D$ = +7.9° (20°, H_2O, c = 2.02). ^{1}H-NMR (D_2O): 0.79 (*t*, *J* = 7.5, 3 H); 1.19-1.37 (2 H); 1.66-1.87 (2 H); 3.90 (*t*, *J* = 6,1 H).

n-Propyl (2S)-2-Trifluoracetamidovalerate.- Using the general procedure crude 13c (15 mg, 0.1 mmol) gave the corresponding (N-trifluoracetyl)-*n*-propyl ester (25 mg, ~100%). GC (Chirasil-Val): 5.35 (0.4), 6.02 (98.5). IR: 3420, 2980, 2940, 2880, 1730, 1535, 1478, 1175. ^{1}H-NMR: 0.96 (*t*, *J* = 7.5, 3 H), 0.97 (*t*, *J* = 7.5, 3 H), 1.26 - 2.48 (2 H), 1.72 (*sext*. *J* = 7, 2 H), 1.70 - 1.82 (1 H), 1.93 (*m*, 1 H), 4.17 (2 H), 4.63 (*q*, *J* = 7, 1 H), 6.8 - 7.1 (1 H). MS: no $C_{10}H_{16}F_3NO_3$+ -255, 168 (100), 126 (43), 114 (15), 69 (13). The (N-trifluoracetyl)-*n*-propyl ester prepared from commercial *(2S)*-2-aminovaleric acid shows identical IR, ^{1}H-NMR and MS spectra. GC (Chirasil-Val) of (N-trifluoracetyl)-*n*-propyl esters prepared from commercial *(2S)*-2-aminovaleric acid: 6.02 (100); coinjection of the latter with the sample derived from 13c: 6.03 (major); from commercial *(2RS)*-2-aminovaleric acid: 5.43 (50.0), 6,02 (50.0).

Synthesis of *(2S)*-Valine Hydrochloride (13d).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] Isovalerate (7d).- Using the general procedure, auxiliary 4 (2.39 g, 6 mmol) was heated with isovaleroyl chloride and AgCN at 90° for 4.5h to give after work-up, FC (hexane/EtOAc 4:1) and crystallization 7d (2.52 g, 87%). M.p. 168-170°. IR: 2950, 2870, 1735, 1470, 1460, 1395, 1375, 1330, 1170, 1150, 1110, 1050, 985. ^{1}H-NMR: 0.89 (*s*, 3 H); 0.97 (*d*, *J* = 6.5, 3 H); 0.98 (*d*, *J* = 6.5, 3 H); 0.99 (*s* 3 H); 1.02-1.90 (25 H); 1.94-2.20 (5 H); 2.66 (*d*, *J* = 13.5, 1 H); 3.20-3.30 (2 H); 3.26 (*d*, *J* = 13.5, 1 H); 4.94 (*dd*, *J* = 13.5, 1 H). ^{13}C-NMR: 171.41 (*s*), 78.33 (*d*), 57.40 (*d*), 53.64 (*t*), 49.23 (*s*), 49.05 (*s*), 44.43 (*d*), 43.75 (*t*), 39.70 (*t*), 32.75 (*t*), 32.70 (*t*), 30.11 (*t*), 26.97 (*t*), 25.53 (*d*), 25.15 (*t*), 22.44 (*q*), 20.42 (*q*), 19.93 (*q*),. MS: 481 (21 $C_{27}H_{47}NO_4S^{+\cdot}$), 298 (40), 244 (46), 181 (46), 135 (42), 85 (100), 57 (43). HR-MS: 481.3233, ($C_{27}H_{47}NO_4S^{+\cdot}$, calc.: 481.3226.)

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2S)-2-(N,N'-di-tert-butoxycarbonyl)hydrazinoisovalerate (10d) *and [(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2S)-2-(N,N'-di-tert-butoxycarbonyl)hydrazinoisovalerate* (11d).- Using the general procedure, isovalerate 7d (2.44 g, 5.06 mmol) was converted to a crude mixture 10d/11d, HPLC (hexane/EtOAc 9:1, 1.5 ml/min.) 4.8 (97.6), 6.1 (2.4), which was chromatographed (hexane/EtOAc 10:1) to give recovered 7d (540 mg, 22%) followed by the major product 11d (2.63 g, 73%, amorphous solid). $[\alpha]_D$ = -27.8° (20°, c = 0.18). HPLC (hexane/EtOAc 9:1, 1.5 ml/min.): 4.8 (99.0), 6.1 (1.0). IR: 3400, 3310, 2940, 2860, 1740, 1720, 1480, 1455, 1395, 1370, 1325, 1165, 1145, 1110, 1050, 980. ^{1}H-NMR (DMSOd$_6$, 100): 0.88 (*s*, 3 H); 0.99 (*s*, 3 H); 1.01 (*d*, *J* = 7, 3 H); 1.03 (*d*, *J* = 7, 3 H); 1.00-2.00 (27 H); 1.44 (*s*, 9 H); 1.45 (*s*, 9 H); 2.27 (*m*, 1 H); 2.70 (*d*, *J* = 13.5, 1 H); 3.20-3.35 (2 H), 3.22 (*d*, *J* = 13.5, 1 H); 4.39 (*m*, 1 H); 4.76 (*m*, 1 H). MS: no $C_{37}H_{65}N_3O_8S^{+\cdot}$-711, 511 (56), 380 (37), 246 (19), 228 (28), 181 (41), 135 (100), 107 (20), 98 (14), 93 (24). The minor product 10d was not isolated.

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] (2R)-2-aminoisovalerate (12d).- Using the general procedure, hydrazinoester 11d (2.60 g, 3.65 mmol) gave after N,N-deacylation and hydrogenolysis (22h), FC (hexane/EtOAc 2:1→1:2) and crystallization aminoester 12d (1.29 g, 71%). M.p. 154-156°. $[\alpha]_D$ = -30.5° (20°, $CHCl_3$, c = 1.02). IR: 3380, 3320, 2940, 2860, 1735, 1600, 1455, 1395, 1375, 1325, 1165, 1145, 1110, 1050, 980. ^{1}H-NMR: 0.89 (*s*, 3 H); 0.90 (*d*, *J* = 7, 3 H); 0.99 (*s*, 3 H); 1.02 (*d*, *J* = 7, 3 H); 1.05-2.12 (28 H); 2.67 (*d*, *J* = 13.5, 1 H); 3.18-3.30 (4 H); 4.98 (*dd*, *J* = 3.5, 8, 1 H). ^{13}C-NMR: 174.63 (*s*), 78.95 (*d*), 59.65 (*d*), 57.52 (*d*), 53.86 (*t*), 49.46 (*s*), 49.10.(*s*), 44.44 (*d*), 39.54 (*t*), 32.84 (*t*), 32.76 (*t*), 31.36 (*d*), 30.39 (*t*), 26.97 (*t*), 26.50 (*t*), 25.21 (*t*), 20.38 (*q*), 19.94 (*q*), 19.71 (*q*), 16.78 (*q*). MS: no $C_{27}H_{48}N_2O_4S^{+\cdot}$-496, 181 (22), 180 (19), 135 (10), 83 (11), 72 (100), 55 (14).

(2S)-Valine Hydrochloride (13d).- Using the general procedure, transesterification of aminoester 12d (800 mg, 1.61 mmol) and FC (hexane/EtOAc 7:1, then EtOAc/EtOH 1:1) furnished auxiliary 4 (550 mg, 86%) to give, after acidic hydrolysis of the crude ethyl ester, 13d as a colorless solid (223 mg, 90%). $[\alpha]_D$ = +13.1° (20°, H_2O, c = 1.62). ^{1}H-NMR (D_2O): 0.93 (*d*, *J* = 7, 3 H); 0.96 (*d*, *J* = 7, 3 H); 2.23 (*m*, 1 H); 3.73 (*d*, *J* = 4.5, 1 H).

n-Propyl (2S)-2-Trifluoracetamidoisovalerate.- Using the general procedure crude 13d (15 mg 0.1 mmol) gave the corresponding (N-trifluoracetyl)-*n*-propyl ester (25 mg, ~100%). GC (Chirasil-Val): 4.00 (0.4), 4.36 (92.6). IR: 3420, 2980, 2940, 2880, 1730, 1535, 1470, 1395, 1375, 1175. ^{1}H-NMR: 0.93 (*d*, *J* = 7, 3 H); 0.94 (*t*, *J* = 7, 3 H); 0.95 (*d*, *J* = 7, 3 H); 1.68 (*sextet*, *J* = 7, 2 H); 2.25 (*m*, 1 H); 4.15 (2 H); 4.57 (*dd*, *J* = 5, 9, 1 H); 6.75-6.90 (*br*. 1 H). MS: no $C_{10}H_{16}F_3NO_3^{+\cdot}$-255, 168 (100), 163 (28), 153 (31), 114 (10), 55 (52). The (N-trifluoracetyl)-*n*-propyl ester prepared from commercial *(2S)*-valine shows identical IR, ^{1}H-NMR and MS spectra. GC (Chirasil-Val) of (N-trifluoracetyl)-*n*-propyl esters prepared from commercial *(2S)*-valine: 4.32 (100); coinjection of the latter with the sample derived from 13d: 4.34 (major); from commercial *(2RS)*-valine: 4.02 (48.3), 4.33 (49.1).

Synthesis of *(2S)*-Norlaucine, Hydrochloride (13e).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] Hexanoate (7e).- Using the general procedure, auxiliary 4 (2.39 g, 6 mmol) was heated with hexanoyl chloride and AgCN at 100° for 3.5h to give after work-up, FC (hexane/EtOAc 4:1) and crystallization 7e (2.86 g, 96%). M.p. 148-150°. IR: 2950, 2860, 1735, 1470, 1455, 1390, 1375, 1325, 1165, 1145, 1110, 1050, 980. ^{1}H-NMR: 0.88 (*s*, 3 H); 0.89 (*t*, *J* = 7.5, 3 H); 0.98 (*s*, 3 H); 1.05-1.90 (31 H); 1.90-2.04 (2 H); 2.28 (*t*, *J* = 7.5, 2 H); 2.66 (*d*, *J* = 13.5, 1 H); 3.20-3.32 (2 H); 3.26 (*d*, *J* = 13.5, 1 H); 4.94 (*dd*, *J* = 3.5, 8, 1 H). ^{13}C-NMR (50 MHz): 172.03 (*s*), 78.25 (*d*), 57.45 (*d*), 53.69 (*t*), 49.29 (*s*), 49.05 (*s*), 44.45 (*d*), 39.66 (*t*), 34.58 (*t*), 32.76 (*t*), 32.72 (*t*) 31.34 (*t*), 30.10 (*t*), 26.99 (*t*), 26.47 (*t*), 25.16 (*d*), 24.51 (*t*), 22.31 (*t*), 20.41 (*q*), 19.96 (*q*), 13.89 (*q*). MS: 495 (1 $C_{28}H_{49}NO_4S^{+\cdot}$), 298 (12), 244 (23), 181 (50), 151 (11), 135 (60), 107 (30), 99 (100), 83 (60), 71 (64), 55 (85). HR-MS: 495.3373, ($C_{28}H_{49}NO_4S^{+\cdot}$,calc. 495.3383.)

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2R)-2-(N,N'-di-tert-butoxycarbonyl)hydrazinohexanoate (10e) *and [(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2S)-2-(N,N'-di-tert-butoxycarbonyl)hydrazinohexanoate* (11e).- Using the general procedure, hexanoate 7e (1.72 g, 3.47 mmol) was converted to a crude mixture 10e/11e, HPLC (hexane/EtOAc 9:1, 1.5 ml/min.) 5.3 (95.5), 7.2 (3.7), which was chromatographed (hexane/EtOAc 12:1) to give the less polar major product 11e (2.14 g, 85%, amorphous solid). $[\alpha]_D$ = -29.2° (20°, c = 0.96). HPLC (hexane/EtOAc 9:1, 1.5 ml/min.): 5.1 (100). IR: 3390, 3320, 2950, 2870, 1730, 1480, 1455, 1395, 1370, 1330, 1170, 1150, 1110, 1050, 985. ^{1}H-NMR (DMSOd$_6$, 100°): 0.87 (*s*, 3 H); 0.87 (*t*, *J*, = 7, 3 H); 0.98 (*s*, 3 H); 1.00-1.95 (33 H); 1.41 (*s*, 18 H); 2.72 (*d*, *J* = 13.5, 1 H);3.20-3.35 (2 H); 3.22 (*d*, *J* = 13.5, 1 H); 4.49 (*m*, 1 H); 4.75 (*m*, 1 H); 7.65-7.90 (*br*. 1 H). MS: no $C_{38}H_{67}N_3O_8S^{+\cdot}$-725, 525 (85), 380 (82), 298 (29), 181 (15), 135 (34), 101 (55), 83 (33), 57 (100). Further elution furnished the minor isomer 10e. HPLC (hexane/EtOAc 9:1, 1.5 ml/min.): 5.1 (2.1), 6.8 (97.8). IR: 3400, 2940, 2860, 1745, 1720, 1480, 1460, 1395, 1370, 1330, 1170, 1150, 1110, 1050, 985. ^{1}H-NMR (DMSOd$_6$, 100°): 0.84 (*s*, 3 H); 0.87 (*t*, *J* = 7, 3 H); 0.98 (*s*, 3 H);

[redacted]

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] (2R)-2-aminohexanoate (12e).- Using the general procedure, hydrazinoester 11e (790 mg, 1.09 mmol) gave after N,N-deacylation and hydrogenolysis (15h), FC (hexane/EtOAc 1:1, then EtOAc) and crystallization aminoester 12e (445 mg, 80%). M.p. 124-126°. $[\alpha]_D$ = -33.2°(20°, c = 0.22). IR: 3540, 3380, 3320, 2940, 2860, 1735, 1600, 1455, 1395, 1375, 1330, 1170, 1145, 1110, 1050, 985. ^{1}H-NMR (360 MHz): 0.85 (*s*, 3 H); 0.86 (*t*, *J* = 7, 3 H), 0.96 (*s*, 3 H); 1.00-1.86 (31 H); 1.90-2.06 (2 H); 2.65 (*d*, *J* = 13.5, 1 H); 3.20-3.30 (2 H); 3.23 (*d*, *J* = 13.5, 1 H); 3.39 (*dd*, *J* = 5.5, 7, 1 H); 4.97 (*dd*, *J* = 3.5, 8, 1 H). ^{13}C-NMR: 175.12 (*s*), 78.84 (*d*), 57.50 (*d*), 54.09 (*d*), 53.82 (*t*), 49.43 (*s*), 49.05 (*s*), 44.04. (*d*), 39.50 (*t*), 33.78 (*t*), 32.78 (*t*), 32.68 (*t*), 30.29 (*t*), 27.48 (*t*), 26.91 (*t*), 26.42 (*t*), 25.16 (*t*), 22.43 (*t*), 20.31 (*q*), 19.87 (*q*), 13.79 (*q*). MS: no $C_{28}H_{50}N_2O_4S^{+\cdot}$-510, 181 (17), 180 (16), 86 (100), 85 (47), 83 (11), 55 (15).

(2S)-Norleucine. Hydrochloride (13a).- Using the general procedure, transesterification of aminoester 12a (185 mg, 0.36 mmol) and FC (hexane/EtOAc 7:1, then EtOH) furnished auxiliary 4 (145 mg, ~100%) to give, after acidic hydrolysis of the crude ethyl ester, 13a as a colorless solid (57 mg, 95%). $[\alpha]_D$ = +10.3° (20°, H_2O, c = 1.05). ^{1}H-NMR (D_2O): 0.76 (*t*, *J* = 7.5, 3 H); 1.13-1.33 (4 H); 1.71-1.89 (2 H); 3.88 (*t*, *J* = 6, 1 H).

n-Propyl (2S)-2-Trifluoroacetamidohexanoate.- Using the general procedure crude 13a (10 mg 0.06 mmol) gave the corresponding (N-trifluoracetyl)-*n*-propyl ester (18 mg, ~100%). GC (Chirasil-Val): 6.91 (1.2), 7.62 (97.8). IR: 3420, 2970, 2940, 2880, 1730, 1535, 1470, 1175. ^{1}H-NMR: 0.92 (*t*, *J* = 7, 3 H), 0.98 (*t*, *J* = 7, 3 H), 1.20 - 1.48 (4 H), 1.72 (*sext.*, *J* = 7, 2 H), 1.70 - 1.85 (1 H), 1.90 - 2.02 (1 H), 4.18 (2 H), 4.62 (*q*, *J* = 7, 1 H), 6.89 (*s*, *br*, 1 H). MS: no $C_{11}H_{18}F_3NO_3^{+\cdot}$-269, 182 (85), 153 (14), 140 (12), 126 (49), 114 (30), 69 (100), 55 (16). The (N-trifluoracetyl)-*n*-propyl ester prepared from commercial *(2S)*-norleucine shows identical IR, ^{1}H-NMR and MS spectra. GC (Chirasil-Val) of (N-trifluoracetyl)-*n*-propyl esters prepared from commercial *(2S)*-norleucine: 7.62 (100); coinjection of the latter with the sample derived from 13a: 7.62 (major); from commercial *(2RS)*-norleucine: 6.94 (49.7), 7.60 (49.7).

Synthesis of *(2S)*-Leucine, Hydrochloride (13f).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] 4-Methylvalerate (7f).- Using the general procedure, auxiliary 4 (2.39 g, 6 mmol) was heated with 4-methylvaleroyol chloride and AgCN at 90° for 5h to give after work-up, FC (hexane/EtOAc 4:1) and crystallization 7f (2.50 g, 84%). M.p. 193-194°. IR: 2950, 2870, 1735, 1460, 1395, 1375, 1325, 1170, 1150, 1110, 1050, 985. ^{1}H-NMR: 0.90 (*s*, 3 H); 0.91 (*d*, *J* = 6.5, 6 H); 1.00 (*s*, 3 H); 1.05-1.90 (28 H); 1.90-2.05 (2 H); 2.30 (*t*, *J* = 7.5, 2 H); 2.68 (*d*, *J* = 13.5, 1 H); 3.20-3.30 (2 H); 3.26 (*d*, *J* = 13.5, 1 H); 4.95 (*dd*, *J* = 3.5, 8, 1 H). ^{13}C-NMR: 172.24 (*s*), 78.29 (*d*), 57.45 (*d*), 53.65 (*t*), 49.27 (*s*), 49.05 (*s*), 44.45 (*d*), 39.62 (*t*), 33.52 (*t*), 32.72 (*t*), 32.57 (*t*), 30.09 (*t*), 27.70 (*d*), 26.96 (*t*), 26.46 (*t*), 25.14 (*t*), 22.19 (*q*), 22.15 (*q*), 20.41 (*q*), 19.98 (*q*). MS:495 (20 $C_{28}H_{49}NO_4S^{+\cdot}$), 298 (47), 244 (56), 181 (62), 135 (83), 99 (100), 81 (54), 55 (77). HR-MS: 495.3383, ($C_{28}H_{49}NO_4S^{+\cdot}$ calc.: 495.3382.)

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2R)-2-(N,N'-di-tert-butoxycarbonyl)hydrazinopropionate (10f) *and [(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2S)-2-(N,N'-di-tert-butoxycarbonyl)hydrazinopropionate* (11f).- Using the general procedure, 4-methylvalerate 7f (2.38 g, 4.8 mmol) was converted to a crude mixture 10f/11f. HPLC (hexane/EtOAc 9:1, 1 ml/min.): 6.5 (77.3), 9.8 (2.7), which was chromatographed (hexane/EtOAc 13:1) to give recovered 7f (382 mg, 16%) followed by the less polar major product 11f (2.46 g, 71%). $[\alpha]_D$ = -28.6° (20°, c = 0.99). HPLC (hexane/EtOAc 9:1, 1 ml/min.): 6.8 (100). IR: 3500, 3420, 2940, 2860, 1725, 1610, 1480, 1460, 1395, 1370, 1325, 1170, 1145, 1110, 1050, 985. ^{1}H-NMR ($DMSOd_6$, 100°): 0.87 (*s*, 3 H); 0.89 (*d*, *J* = 7, 3 H); 0.91 (*d*, *J* = 7, 3 H); 0.98 (*s*, 3 H); 1.00-1.98 (30 H); 1.40 (*s*, 18 H); 2.75 (*d*, *J* = 13.5, 1 H); 3.20-3.35 (2 H); 3.22 (*d*, *J* = 13.5, 1 H); 4.59-4.68 (*m*, 1 H), 4.74-4.81 (*m*, 1 H). MS: no $C_{38}H_{67}N_3O_8S^{+\cdot}$-725, 525 (50), 380 (37), 298 (15), 228 (27), 181 (63), 135 (100), 101 (88), 83 (45), 57 (77). Further elution furnished the more polar product 10f. HPLC (hexane/EtOAc 9:1, 1 ml/min.): 6.9 (0.3), 9.1 (99.7). IR: 3390, 2940, 2860, 1745, 1720, 1480, 1455, 1395, 1370, 1325, 1170, 1145, 1110, 1050, 985. ^{1}H-NMR ($DMSOd_6$, 100°): 0.86 (*s*, 3 H); 0.90 (*d*, *J* = 7, 6 H); 1.00 (*s*, 3 H); 1.00-2.02 (30 H); 1.44 (*s*, 9 H); 1.47 (*s* 9 H); 2.67 (*d*, *J* = 13.5, 1 H); 3.20-3.35 (2 H); 3.24 (*d*, *J* = 13.5, 1 H); 4.62 (*m*, 1 H); 4.79 (*m*, 1 H).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] (2R)-2-amino-4-methylvalerate (12f).- Using the general procedure, hydrazinoester 11f (697 mg, 0.96 mmol) gave after N,N-deacylation and hydrogenolysis (6h), FC (hexane/EtOAc 1:1, then EtOAc) and crystallization aminoester 12f (341 mg, 70%). M.p. 97-99°. $[\alpha]_D$ = -33.4° (20°, c = 0.99). IR: 3380, 2950, 2860, 1735, 1600, 1455, 1395, 1375, 1325, 1165, 1145, 1110, 1050, 985. ^{1}H-NMR: 0.86 (*s*, 3 H); 0.89 (*d*, *J* = 6.5, 3 H); 0.91 (*d*, *J* = 6.5, 3 H); 0.97 (*s*, 3 H); 1.00-2.02 (30 H); 2.66 (*d*, *J* =13.5, 1 H); 3.20-3.30 (2 H); 3.24 (*d*, *J* = 13.5, 1 H); 3.40 (*dd*, *J* = 5.5, 7, 1 H); 4.98 (*dd*, *J* = 3.5, 8, 1 H). ^{13}C-NMR: 175.73 (*s*), 78.69 (*d*), 57.54 (*d*), 53.90 (*t*), 52.68 (*d*), 49.45 (*s*), 49.09 (*s*), 44.40 (*d*), 43.60 (*t*), 39.41 (*t*), 32.79 (*t*), 32.73 (*t*), 30.43 (*t*), 26.95 (*t*), 26.45 (*t*), 25.15 (*t*), 24.80 (*d*), 22.82 (*q*), 21.96 (*q*), 20.32 (*q*), 19.91 (*q*). MS: no $C_{28}H_{50}N_2O_4S^{+\cdot}$-510, 380 (11), 181 (21), 135 (10), 86 (100), 55 (11).

(2S)-Leucine Hydrochloride (13f).- Using the general procedure, transesterification of aminoester 12f (280 mg, 0.56 mmol) and FC (hexane/EtOAc 7:1, then EtOAc, then EtOH) furnished auxiliary 4 (225 mg, ~100%) to give after acidic hydrolysis of the crude ethyl ester 13f as a colorless solid (80 mg, 86%). $[\alpha]_D$ = +2.8° (20°, H_2O, c = 0.61). ^{1}H-NMR (D_2O): 0.91 (*d*, *J* = 7, 3 H); 0.93 (*d*, *J* = 7, 3 H); 1.55-1.75 (3 H); 3.87 (*m*, 1 H).

n-Propyl (2S)-2-Trifluoroacetamido-4-methylvalerate.- Using the general procedure crude 13f (12 mg 0.07 mmol) gave the corresponding (N-trifluoracetyl)-*n*-propyl ester (20 mg, ~100%). GC (Chirasil-Val): 6.41 (1.1), 7.21 (95.2). IR: 3420, 2988, 2940, 2880, 1735, 1535, 1470, 1380, 1150. ^{1}H-NMR: 0.94 (*t*, *J* = 7, 3H), 0.96 (*d*, *J* = 6, 6 H), 1.5 - 1.8 (5 H), 4.14 (*t*, *J* = 7, 2 H), 4.65 (*m*, 1 H), 6.7 - 6.8 (1 H). MS: no $C_{11}H_{18}F_3NO_3^{+\cdot}$-269, 213 (84), 183 (73), 171 (51), 166 (71), 153 (68), 139 (52), 126 (88), 114 (100), 99 (42), 70 (93), 57 (83), 55 (82). The (N-trifluoracetyl)-*n*-propyl ester prepared from commercial *(2S)*-4-methylvaleric acid shows identical IR, ^{1}H-NMR and MS spectra. GC (Chirasil-Val) of (N-trifluoracetyl)-*n*-propyl esters prepared from commercial *(2S)*-4-methylvaleric acid: 7.21 (100); coinjection of the latter with the sample derived from 13f: 7.22 (major); from commercial *(2RS)*-4-methylvaleric acid: 6.56 (49.9), 7.31 (49.8).

Synthesis of *(2S)*-2-Aminooctanoic Acid Hydrochloride (13g).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] Octanoate (7g).- Using the general procedure, auxiliary 4 (2.39 g, 6 mmol) was heated with octanoyl chloride and AgCN at 90° for 4.5h to give after work-up, FC (hexane/EtOAc 4:1) and crystallization 7g (2.80 g, 89%). M.p. 163-165°. IR: 2950, 2870, 1735, 1470, 1405, 1375, 1340, 1180, 1155. 1120, 1065, 995. ^{1}H-NMR: 0.88 (*t*, *J* = 7.5, 3 H); 0.89 (*s*, 3 H); 0.99 (*s*, 3 H); 1.05-1.90 (*m*, 35 H); 1.92-2.07 (*m*, 2 H); 2.29 (*t*, *J* = 7.5, 2 H); 2.66 (*d*, *J* = 13.5, 1 H); 3.20-3.32 (*m*, 2 H); 3.27 (*d*, *J* = 13.5, 1 H);

4.95 (*dd*, *J* = 3.5, 8, 1 H). ^{13}C-NMR (50 MHz): 172.05 (*s*), 78.26 (*d*), 57.41 (*d*), 53.66 (*t*), 49.26 (*s*), 49.09 (*s*), 44.43 (*d*), 39.62 (*t*), 34.61 (*t*), 32.73 (*t*), 32.70 (*t*), 31.64 (*t*), 30.08 (*t*), 29.17 (*t*), 28.91 (*t*), 27.00 (*t*), 26.45 (*t*), 25.14 (*t*), 24.83 (*t*), 22.52 (*t*), 20.41 (*q*), 19.94 (*q*), 14.00 (*q*). MS: 523 (1 $C_{30}H_{53}NO_4S^{+\cdot}$), 298 (7), 244 (16), 181 (32), 135 (37), 127 (64), 93 (23), 83 (38), 57 (100), 55 (70). HR-MS: 523.3702, ($C_{36}H_{53}NO_4S^{+\cdot}$ calc.: 523.3695.)

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2R)-2-(N,N'-di-tert-butoxycarbonyl)hydrazinooctanoate (10g) *and [(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2S)-2-(N,N'-di-tert-butoxycarbonyl)hydrazinooctanoate* (11g).- Using the general procedure, octanoate 7f (524 mg, 1 mmol) was converted to a crude mixture 10g/11g, HPLC (hexane/EtOAc 9:1, 1 ml/min.) 7.1 (70.1), 8.9 (1.4), which was chromatographed (hexane/EtOAc 13:1) to give recovered 7g (125 mg, 24%) followed by the less polar major product 11g (519 mg, 69%, amorphous solid). $[\alpha]_D$ = -30.5° (20°, c = 0.97). HPLC (hexane/EtOAc 9:1, 1 ml/min.): 6.9 (100). IR: 3400, 3320, 2940, 2860, 1730, 1480, 1460, 1395, 1370, 1330, 1170, 1145, 1110, 1050, 985. ^{1}H-NMR (DMSOd$_6$, 100°): 0.88 (*t*, *J* = 7, 3 H); 0.89 (*s*, 3 H); 0.96 (*s*, 3 H); 1.00-1.95 (37 H); 1.43 (*s*, 18 H); 2.74 (*d*, *J* = 13.5, 1 H); 3.20-3.35 (2 H); 3.23 (*d*, *J* = 13.5, 1 H); 4.51 (*m*, 1 H); 4.76 (*m*, 1 H). MS: no $C_{40}H_{71}N_3O_8S^{+\cdot}$-754, 350 (10), 275 (10), 225 (11), 210 (13), 167 (45), 124 (90), 119 (100), 99 (31), 86 (34), 76 (48), 51 (68). Further elution furnished the more polar, minor product 10g. HPLC (hexane/EtOAc 9:1, 1 ml/min.): 8.9 (100). IR: 3400, 2940, 2860, 1745, 1720, 1480, 1460, 1395, 1370, 1330, 1170, 1145, 1110, 1050, 985. ^{1}H-NMR (DMSOd$_6$, 100°): 0.86 (*s*, 3 H); 0.87 (*t*, *J* = 7.3 H), 0.99 (*s*, 3 H). 1.00-2.05 (37 H); 1.41 (*s*, 9 H); 1.43 (*s*, 9 H); 2.68 (*d*, *J* = 13.5, 1 H); 3.20-3.35 (2 H); 3.25 (*d*, *J* = 13.5, 1 H); 4.53 (*m*, 1 H); 4.78 (*m*, 1 H). MS: no $C_{40}H_{71}N_3O_8S^{+\cdot}$-754, 350 (11), 275 (10), 225 (11), 210 (13), 167 (45), 124 (90), 119 (100), 99 (32), 86 (34), 76 (48), 51 (67).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] (2S)-2-aminooctanoate (12g).- Using the general procedure, hydrazinoester 11g (730 mg, 0.98 mmol) gave after N,N-deacylation and hydrogenolysis (24h), FC (hexane/EtOAc 2:1, then EtOAc) and crystallization aminoester 12g (290 mg, 55%). M.p. 124-126°, $[\alpha]_D$ = -31.6° (20°, c = 1.00). IR: 3380, 2940, 2860, 1735, 1615, 1455, 1395, 1375, 1330, 1170, 1145, 1110, 1050, 985. ^{1}H-NMR: 0.85 (*t*, *J* = 7.5, 3 H); 0.86 (*s*, 3 H); 0.96 (*s*, 3 H) 1.00-2.05 (37 H); 2.66 (*d*, *J* = 13.5, 1 H); 3.20-3.30 (2 H); 3.24 (*d*, *J* = 13.5, 1 H); 3.40 (*dd*, *J* = 5.5, 7, 1 H); 4.97 (*dd*, *J* = 3.5, 8, 1 H). ^{13}C-NMR: 175.14 (*s*), 78.86 (*d*), 57.51 (*d*), 54.15 (*d*), 53.86 (*t*), 49.43 (*s*), 49.06 (*s*), 44.42 (*d*), 39.49 (*t*), 34.12 (*t*), 32.81 (*t*), 32.72 (*t*), 31.59 (*t*), 30.31 (*t*), 29.07 (*t*), 26.95 (*t*), 26.45 (*t*), 25.37 (*t*), 25.16 (*t*), 22.48 (*t*), 20.32 (*q*), 19.88 (*q*), 13.96 (*q*). MS: no $C_{30}H_{54}N_2O_4S^{+\cdot}$-538, 181 (23), 180 (21), 114 (100), 113 (35), 83 (15), 55 (20).

(2S)-2-Aminooctanoic Acid Hydrochloride (13g).- Using the general procedure, transesterification of aminoester 12g (250 mg, 0.46 mmol) and FC (hexane/EtOAc 7:1, then EtOAc, then EtOH) furnished auxiliary 4 (175 mg, 95%) to give, after acidic hydrolysis of the crude ethyl ester, 13g as a colorless solid (81 mg, 89%). $[\alpha]_D$ = +8.8° (20°, H_2O, c = 0.40). ^{1}H-NMR (D_2O): 0.72 (*t*, *J* = 7.5, 3 H); 1.10-1.35 (8 H); 1.70-1.85 (2 H); 3.79 (*t*, *J* = 6, 1 H).

n-Propyl (2S)-2-Trifluoracetamidooctanoate.- Using the general procedure crude 13g (16 mg 0.08 mmol) gave the corresponding (N-trifluoracetyl)-*n*-propyl ester (25 mg, ~100%). GC (Chirasil-Val) 10.50 (1.5), 11.17 (95.5). IR: 3420, 2970, 2940, 2870, 1730, 1535, 1470, 1395, 1175. ^{1}H-NMR: 0.88 (*t*, *J* = 7, 3 H), 0.96 (*t*, *J* = 7, 3 H); 1.17 - 1.45 (8 H), 1.55 - 1.85 (3 H), 1.92 (*m*, 1 H), 4.17 (2 H), 4.62 (*q*, *J* = 7, 1 H), 6.89 (*s*, *br*, 1 H). MS: 198 (7), 297 (2, $C_{13}H_{22}F_3NO_3^{+\cdot}$), 210 (77), 171 (16), 153 (32), 140 (15), 126 (49), 114 (28), 97 (99), 82 (15), 69 (67), 57 (42), 55 (100). The (N-trifluoracetyl)-*n*-propyl ester prepared from commercial *(2RS)*-2-aminooctanoic acid shows identical IR, ^{1}H-NMR and MS spectra. GC (Chirasil-Val) of (N-trifluoracetyl)-*n*-propyl esters prepared from commercial *(2RS)*-aminooctanoic acid: 10.68 (49.9), 11.24 (49.9); coinjection of the latter sample with the sample derived from 13g: 11.11 (major).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] 3-phenylpropionate (7h).- Using the general procedure, auxiliary 4 (1.79 g, 4.5 mmol) was heated with 3-phenylpropanoyl chloride and AgCN at 100° for 5h to give after work-up, FC (hexane/EtOAc 5:1) and crystallization (EtOH, 2x) 7h (2.20 g, 92%). M.p. 152-154°. IR: 3020, 2950, 2870, 1730, 1600, 1465, 1450, 1390, 1370, 1325, 1165, 1140, 1105, 1045, 980. ^{1}H-NMR: 0.88 (*s*, 3 H); 0.92 (*s*, 3 H); 1.00-1.85 (25 H); 1.90-2.05 (2 H); 2.54-2.71 (2 H); 2.67 (*d*, *J* = 13.5, 1 H); 2.99 (*t*, *J* = 8, 2 H); 3.20-3.32 (2 H); 3.25 (*d*, *J* = 13.5 1 H); 4.97 (*dd*, *J* = 3.5, 8, 1 H); 7.17-7.33 (5 H). ^{13}C-NMR (50 MHz): 171.23 (*s*), 140.42 (*s*), 128.41 (*d*), 120.9 (*d*), 126.17 (*d*), 78.55 (*d*), 57.45 (*d*), 53.71 (*t*), 49.32 (*s*), 49.06 (*s*), 44.44 (*d*), 39.50 (*t*), 36.07 (*t*), 32.72 (*t*), 30.80 (*t*), 30.12 (*t*), 26.98 (*t*), 26.45 (*t*), 25.13 (*t*), 20.40 (*q*), 19.91 (*q*),. MS: 529 (6, $C_{31}H_{47}NO_4S^{+\cdot}$), 380 (48), 298 (40), 244 (46), 228 (17), 181 (47), 135 (96), 105 (92), 91 (100), 83 (48), 67 (17), 55 (65). HR-MS: 529.3214, ($C_{31}H_{47}NO_4S^{+\cdot}$ calc.: 529.3226.)

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2R)-2-(N,N'-di-tert-butoxycarbonyl)hydrazino-3-phenylpropionate (10h) *and [(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2S)-2-(N,N'-di-tert-butoxycarbonyl)hydrazino-3-phenylpropionate* (11h).- Using the general procedure, 3-phenylpropionate 7h (2.12 g, 4 mmol) was converted to a crude mixture 10h/11h, HPLC (hexane/EtOAc 9:1, 1 ml/min.) 7.3 (91.6), 11.3 (1.7), which was chromatographed (hexane/EtOAc 13:1) to give recovered 7h (127 mg, 6%) followed by the less polar major product 11h (2.36 g, 76%, amorphous solid). $[\alpha]_D$ = -35.2°(20°, c = 0.59). HPLC (hexane/EtOAc 9:1, 1 ml/min.): 7.6 (100). IR: 3380, 3310, 2940, 2860, 1735, 1605, 1500, 1480, 1455, 1395, 1370, 1325, 1170, 1145, 1110, 1050, 985. ^{1}H-NMR (DMSOd$_6$, 100°): 0.89 (*s*, 3 H); 0.96 (*s*, 3 H); 1.00-1.95 (29 H); 1.37 (*s*, 9 H); 1.40 (*s*, 9 H); 2.76 (*d*, *J* = 13.5, 1 H); 3.25-3.40 (2 H); 3.30 (*d*, *J* = 13.5, 1 H); 4.76-4.88 (2 H); 7.20-7.40 (5 H). MS: no $C_{41}H_{65}N_3O_8S^{+\cdot}$ -760, 380 (42), 298 (13), 228 (18), 181 (23), 163 (33), 135 (100), 83 (50), 56 (65), 55 (62). The minor product 10h was not isolated.

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] (2S)-2-amino-3-cyclohexylpropionate (12h).- Using the general procedure, hydrazinoester 11h (2.15 g, 2.83 mmol) gave after N,N-deacylation and hydrogenolysis (13h), FC (hexane/EtOAc 4:1, then EtOAc) and crystallization aminoester 12h (980 mg, 64%). M.p. = 95-97°, $[\alpha]_D$ = -28.4° (20°, c = 1.07). IR: 3380, 2940,

2860, 1730, 1600, 1450, 1390, 1370, 1325, 1165, 1145, 1110, 1050, 980. ^{1}H-NMR: 0.85 (*s*, 3 H); 0.96 (*s*, 3 H); 1.00-1.85 (38 H); 1.85-2.04 (2 H); 2.65 (*d*, *J* = 13.5, 1 H); 3.18-3.30 (2 H); 3.23 (*d*, *J* = 13.5, 1 H); 3.43 (*dd*, *J* = 6, 8, 1 H); 4.98 (*dd*, *J* = 3.5, 8, 1 H). ^{13}C-NMR: 175.90 (*s*), 78.64 (*d*), 57.51 (*d*), 53.90 (*t*), 51.95 (*d*), 49.46 (*s*), 49.08 (*s*), 44.42 (*d*), 42.26 (*t*), 39.41 (*t*), 34.10 (*d*), 33.56 (*t*), 32.78 (*t*), 32.74 (*t*), 30.42 (*t*), 26.93 (*t*), 26.42 (*t*), 26.06 (*t*), 25.97 (*t*), 25.16 (*t*), 20.31 (*q*), 19.94 (*q*). MS: no $C_{31}H_{54}N_2O_4S^{+\cdot}$, 409 (11), 380 (19), 315 (23), 298 (19), 272 (14), 259 (41), 244 (20), 181 (26), 126 (100), 107 (10), 93 (11), 83 (18), 55 (22).

(2S)-3-Cyclohexylalanine Hydrochloride (13h).- Using the general procedure, transesterification of aminoester 12h (551 mg, 1 mmol) and FC (hexane/EtOAc 7:1, then EtOAc, then EtOH) furnished auxiliary 4 (400 mg,~100%) to give, after acidic hydrolysis of the crude ethyl ester, 13h as a colorless solid (183 mg, 88%). $[\alpha]_D$ = +3.4°(20°, H_2O, c = 0.53). ^{1}H-NMR (D_2O,): 0.65-0.85 (2 H); 0.90-1.15 (3 H); 1.22 (*m*, 1 H); 1.38-1.60 (6 H); 1.65 (*m*, 1 H); 3.84 (*dd*, *J* = 5.5, 8.5, 1 H).

n-Propyl (2S)-2-Trifluoracetamido-3-cyclohexylpropionate.- Using the general procedure crude 13h (20 mg 0.1 mmol) gave the corresponding (N-trifluoracetyl)-*n*-propyl ester (30 mg, ~100%). GC (Chirasil-Val, 100→140°, 140°,10min): 15.69 (0.8), 17.16 (99.2). IR: 3420, 3020, 2980, 2930, 1730, 1535, 1450, 1170,. ^{1}H-NMR: 0.94 (*t*, *J* = 7, 3 H); 0.8 - 1.0 (2 H), 1.02-1.38 (4 H); 1.50-2.05 (9 H); 4.14 (2 H); 4.68 (*m*, 1 H); 6.68-6.84 (1 H). MS: no $C_{14}H_{22}F_3NO_3^{+\cdot}$-309, 306 (13), 270 (7), 240 (5), 212 (5), 170 (3), 149 (5) 140 (19), 126 (100), 109 (17), 97 (7), 83 (25), 69 (17), 57 (18), 55 (55). The (N-trifluoracetyl)-*n*-propyl ester prepared *via* hydrogenation from commercial *(2S)*-3-phenylalanine shows identical IR, ^{1}H-NMR and MS spectra. GC (Chirasil-Val) of (N-trifluoracetyl)-*n*-propyl esters prepared *via* hydrogenation from commercial *(2S)*-3-phenylalanine: 16.97 (100); *via* hydrogenation from commercial *(2RS)*-3-phenylalanine: 16.12 (49.7), 17.27 (49.8). *(2S)*-Phenylalanine (190 mg, 1.15 mmol) and PtO_2 (50 mg) in 2N aq HCl (22 ml) were shaken under H_2 (75 psi, *Parr*) at r.t. for 16h to give after filtration through *Celite* evaporation of the filtrate and drying of the residue a comparison sample of 13h (240 mg, ~100%).

Synthesis of *(2S)*-3-(Adamant-1-yl)alanine (13i).

3-(Tricyclo[3.3.1.1^{3,7}]decan-1-yl)propionic Acid.- Dry DMSO (1.76 g, 22.5 mmol) was added dropwise at -60° to a solution of oxalyl chloride (1.43 g, 12.25 mmol) in CH_2Cl_2 (40 ml). Stirring of the mixture at -60° for 10 min, addition (over 15 min) of 1-adamantylmethanol (1.50 g, 9 mmol) in CH_2Cl_2 (15 ml), stirring for 15 min, slow addition of NEt_3 (5.16 g, 51 mmol), warming of the reaction mixture to 0°, quenching with water (30 ml), work-up (CH_2Cl_2), and FC (toluene/EtOAc 60:1) gave 1-adamantylcarboxaldehyde (1.5g, ~100%) which was directly subjected to the following transformations. A 1.64 N solution of *n*-butyllithium in hexane (5.5 ml, 9 mmol) was added dropwise at 10° to a solution of dimethyl trimethylsilyloxycarbonylmethanephosphonate [21] (2.16 g, 9 mmol) in THF (75 ml). Stirring the mixture for 40 min, addition of 1-adamantylcarboxaldehyde (1.38 g, 8 mmol) in THF (9 ml), stirring for 1h, pouring the reaction mixture into 5% aq. NaOH (150 ml), washing with Et_2O (2x100 ml), acidification of the aq. phase to pH = 1 with 37% aq. HCl, extraction with CH_2Cl_2 drying ($MgSO_4$) and evaporation of the organic extracts afforded crude 3-(1-adamantyl)-2-propenoic acid (1.47 g, 88%) which was stirred in EtOH (25 ml) with 10% Pd/C (210 mg) under H_2 (1 atm) for 16h. Filtration through *Celite* and evaporation of the filtrate furnished crude 3-(1-adamantyl)propionic acid IR: 3520, 3500-2400, 2910, 2850, 1715, 1450,. ^{1}H-NMR: 1.45 (*t*, *J* = 7, 2 H); 1.47 (*s*, *br*., 6 H); 1.67 (6 H); 1.98 (*s*, *br*. 3 H); 2.32 (*t*, *J* = 7, 2 H), which was transformed into the ester 7i as described below.

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] 3-(1-adamantyl)propionate (7i).- Heating of crude 3-(1-adamantyl)propionic acid (1.43 g, 6.84 mmol) with oxalyl chloride (excess) in benzene at reflux for 1.5h, evaporation and heating of the residue with auxiliary 4 (2.16 g, 5.44 mmol) and AgCN (1.10 g, 8.16 mmol) in toluene at 90° for 18h gave after work-up, FC (hexane/EtOAc 40:1) and crystallization 7i (3.06 g, 96% from 4). M.p. 175-176°. IR: 2940, 2915, 2870, 1730, 1450, 1330, 1170, 1145, 1110, 1050, 985. ^{1}H-NMR: 0.89 (*s*, 3 H); 1.00 (*s*, 3 H); 1.00-1.90 (39 H); 1.92-2.04 (5 H); 2.21-2.30 (2 H); 2.67 (*d*, *J* = 13.5, 1 H); 3.20-3.30 (2 H); 3.27 (*d*, *J* = 13.5, 1 H); 4.93 (*dd*, *J* = 3.5, 8, 1 H). ^{13}C-NMR (50 MHz): 172.81 (*s*), 78.29 (*d*), 57.46 (*d*), 53.61 (*t*), 49.25 (*s*), 49.06 (*s*), 44.43 (*d*), 42.04 (*t*), 39.55 (*t*), 38.62 (*t*), 37.00 (*t*), 32.72 (*t*), 31.74 (*t*), 30.10 (*t*), 28.51 (*d*), 28.17 (*s*), 26.97 (*t*), 26.47 (*t*), 25.14 (*t*), 20.41 (*q*), 20.01 (*q*). MS: 587 (16, $C_{35}H_{57}NO_4S^{+\cdot}$), 380 (11), 298 (40), 244 (47), 191 (85), 179 (60), 135 (100), 121 (10), 107 (24), 93 (14), 83 (35), 67 (16), 55 (35). HR-MS: 587.3993, ($C_{35}H_{57}NO_4S^{+\cdot}$ -calc.: 587.4008.

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2R)-2-(N,N'-di-tert-butoxycarbonyl)hydrazino 3-(1-adamantyl)-propionate (10i) *and [(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] [(2S)-2-(N,N'-di-tert-butoxycarbonyl)hydrazino 3-(1-adamantyl)propionate* (11i).- Using the general procedure, 3-(1-adamantyl)propionate 7i (1.67 g, 2.77 mmol) was converted to a crude mixture 10i/11i. HPLC (hexane/EtOAc 9:1, 1 ml/min.) 6.6 (68.2), 8.8 (15.0), which was chromatographed (hexane/EtOAc 13:1→5:1) to give recovered 7i (260 mg, 16%) followed by the the less polar major product 11i (1.47 g, 65%). HPLC (Hexane/-EtOAc 9:1, 1 ml/min.) 6.6 (100). IR: 3400, 3300, 2930, 2850, 1740, 1715, 1480, 1455, 1392, 1370, 1325, 1165, 1143, 1048, 980. ^{1}H-NMR (DMSOd_6, 100°) 0.87 (*s*, 3 H), 1.00 (*s*, 3 H), 1.45 (*s*, 18 H), 1.03 - 2 (45 H), 2.77 (*d*, *J* = 13.5, 1 H), 3.20 (*d*, *J* = 13.5, 1 H), 3.25 - 3.37 (2 H), 4.70 - 4.84 (2 H). MS: no $C_{45}H_{75}N_3O_8S^{+\cdot}$, - 817, 717 (<1), 617 (3) 587 (5.5), 380 (5.5), 298 (15), 244 (19), 191 (32), 181 (35), 135 (100), 107 (30), 93 (36), 83 (41), 56 (91). HPCL (hexane/EtOAc 1:1, 1 ml/min.) : 6.74 (0.95) 8.47 (98.3). IR : 3390, 2930, 2850, 1745, 1710, 1480, 1455, 1393, 1370, 1325, 1165, 1145, 1048, 980. ^{1}H-NMR (DMSOd_6, 100°) 0.84 (*S*, 3 H), 1.00 (*S*, 3 H), 1.40 (*S*, 9 H), 1.43 (*s*, 9 H), 1.06 - 2.06 (*m*, 45 H), 2.60 - 2.70 (*m*, 1 H), 3.25 - 3.45 (*m*, 3 H), 4.6 - 4.75 (*m*, 2 H). MS: no $C_{45}H_{75}N_3O_8S^{+\cdot}$- 817, 717 (5), 617 (40), 587 (19), 380 (6), 298 (8), 221 (18), 193 (48), 135 (100), 107 (26), 93 (33), 83 (40), 67 (14), 55 (47).

[(1S,2R)-10-(N,N-Dicyclohexylaminosulfonyl)born-2-yl] (2R)-2-amino- 3-(1-adamantyl)propionate (12i).- Using the general procedure, hydrazinoester 11i (1.39 g, 1.7 mmol)

gave after N,N-deacylation and hydrogenolysis (20h), FC (hexane/EtOAc 6:1, then EtOAc) and crystallization aminoester 12i (797 mg, 78%). M.p. 161 - 163°, $[\alpha]_D$ = - 25.7° (20°, c = 1.33). IR : 2935, 2910, 2865, 1735, 1455, 1325, 1185, 1165, 1145, 1110, 1049, 980 ^{1}H-NMR: 0.85 (*s*, 3 H), 0.98 (*s*, 3 H), 1.00 - 2.02 (46 H), 2.66 (*d*, *J* = 13.5, 1 H), 3.25 (*d*, *J* = 13.5, 1 H), 3.18 - 3.32 (2 H), 3,43 (*dd*, *J* = 5,7, 1 H), 4.95 (*dd*, *J* = 3, 8, 1 H). ^{13}C-NMR: 176.27 (*s*), 78.60 (*d*), 57.54 (*d*), 54.00 (*t*), 50.18 (*d*), 49.49 (*s*), 49.28 (*s*), 49.12 (*s*), 44,40 (*s*), 42.65 (*t*), 39.07 (*t*), 36.87 (*t*), 32.82 (*t*), 32.73 (*t*), 32.30 (*t*), 30.49 (*t*), 28.55 (*d*), 26.95 (*t*), 26.46 (*t*), 26.42 (*t*), 25.16 (*t*), 20.33 (*q*), 20.04 (*q*). MS: no $C_{35}H_{58}N_2O_4S^{+\cdot}$ - 602, 531 (<1), 430 (<1) 379 (<3), 315 (12), 259 (22), 178 (47), 135 (100), 83 (68), 55 (96).

(2S)-3-(1-Adamantyl)alanine Hydrochloride (13i).- Using the general procedure, transesterification of aminoester 12i (440 mg, 0.73 mmol, 4h) and FC (hexane/EtOAc 6:1, then EtOAc/EtOH) furnished auxiliary 4 (288 mg, 99%) to give, after acidic hydrolysis of the crude ethyl ester, 13i as a colorless solid (122 mg, 65%). $[\alpha]_D$ = +16.1° (21°, MeOH, c=0.85); lit [17b] $[\alpha]_D$ = +16.2° (20°, aq MeOH c=1). IR (KBr): 3450, 2910, 2850, 1740, 1575, 1490, 1455, 1409, 1350. ^{1}H-NMR: (CD_3OD): 1.55 - 2.1 (17 H), 3.52 - 3.68 (1 H). MS: no $C_{13}H_{22}ClNO_2^{+\cdot}$-259, 178 (74), 135 (100), 120 (7), 107 (12), 93 (28), 81 (14), 79 (30), 74 (14), 67 (18), 57 (12), 55 (19).

n-Propyl (2S)-2-Trifluoracetamido-3-(1-adamantyl)propionate.- Using the general procedure crude 13i gave the corresponding (N-trifluoracetyl)-*n*-propyl ester. GC (Chirasil-Val, 150°, 5°/min-180°, 10 min): 16.92 (2.4), 18.43 (97.6). IR: 3440, 3025, 2970, 2910, 2860, 1735, 1540, 1455, 1175. ^{1}-NMR: 0.98 (*t*, *J* = 7.5, 3 H), 1.4 - 1.8 (13 H), 2.0 (3 H), 2.2 (2 H), 4.12 (*dt*, *J* = 7, <1, 2 H), 4.7 (*dt J* = 8.5, 3.5, 1 H), 6.52 - 6.62, (1 H). MS: no $C_{18}H_{26}F_3NO_3^{+\cdot}$-361, 343 (<1), 301 (13), 274 (29), 135 (100), 107 (6), 93 (16), 79 (18), 67 (9), 55 (6)

Preparation and NOE of O-Trimethylsilyl Ketene Acetal 1a.

1.6N *n*-butyllithium in hexane (0.7 ml, 1.1 mmol) was added at -20° to a solution of diisoproylamine (0.16 ml, 1.1 mmol) in THF (3 ml). Slow addition of propionate 7a (443 mg, 1 mmol) in THF (0.8 ml) at -78°, then rapid addition of chlorotrimethylsilane (0.22 ml 1.1 mmol), warming to r.t. over a period of 3h, evaporation, trituration of the residue with pentane, and evaporation gave O-silyl ketene acetal 1a (422 mg, 82%, colorless oil). IR: 2995, 2888, 2400, 2360, 1685, 1463, 1331, 1256, 1150, 1112, 981, 856, 737, 575. ^{1}H-NMR: 0.25 (*s*, 9 H); 0.88 (*s*, 3 H); 1.03 (*s*, 3 H); 1.08-1.44 (10 H); 1.47 (*d*, *J* = 6, 3 H); 1.44-1.92 (16 H); 2.05 (*m*, 1 H); 2.68 (*d*, *J* = 14, 1 H); 3.2-3.36 (2 H); 3.49 (*d*, *J* = 14, 1 H); 3.53 (*q*, *J* = 6, 1 H); 4.50 (*dd*, *J* = 3, 8, 1 H). Spin saturation of H-C(2') → NOE (2.1%) of H_3C-Si; spin saturation of H-C-Si → NOE (9.8%) of olefinic H-C(2); spin saturation of H_3C-C(2') → NOE (7.2%) of olefinic H-C(2).

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