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Chirality Transfer from Guanidinium Ylides to 3-Alkenyl (or 3-Alkynyl) Aziridine-2-carboxylates and Application to the Syntheses of (2*R*,3*S*)-3-Hydroxyleucinate and D-*erythro*-Sphingosine

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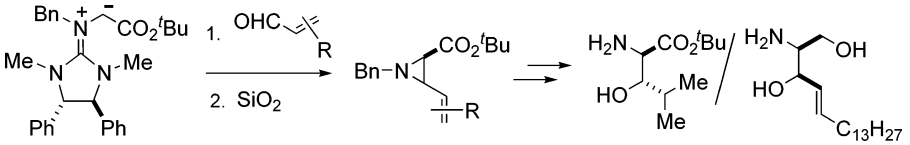

Reaction of chiral guanidinium ylides with α,β-unsaturated aldehydes gives 3-(α,β-unsaturated) aziridine-2-carboxylates in high diastereo- and enantioselectivities (up to 93% diastereomeric excess and 98% enantiomeric excess). 3-(1-Methylvinyl)- and 3-[(*E*)-pentadec-1-enyl]aziridine-2-carboxylates were successfully employed to prepare (2*R*,3*S*)-3-hydroxyleucinate and D-*erythro*-sphingosine, respectively.

Introduction

α-Amino-β-hydroxy acid is not only an important component of numerous peptide antibiotics or endogenous substances but also a key synthon in their synthesis. Thus, 3-hydroxyleucine appears in telomycin,[1] azinothricin,[2] and lysobacin,[3] and its (2*R*,3*S*)-derivative **1** has been used as a key compound in the enantioselective synthesis[4] of (+)-lactacystin[5] (**2**). D-*erythro*-Sphingosine [(2*S*,3*R*,4*E*)-2-aminooctadec-4-en-1,3-diol][6] (**3**) appears in ceramide (**4**). α-Amino-β-hydroxy acid units can be derived from the corresponding aziridine-2-carboxylates[7] by a stereoselective ring-opening reaction.[8] We recently reported new asymmetric synthesis of 3-arylaziridine-2-carboxylates from chiral guanidinium ylides and aryl (and heterocyclic) aldehydes.[9] Alkenyl (or alkynyl) aziridines have also been increasingly found as useful intermediates in organic synthesis;[10] however, there are not so many general methods for their enantioselective preparation.[11] We applied the guanidinium ylide chemistry to the reaction with α,β-unsaturated aldehydes and, then, examined the ring-opening reaction of aziridines formed, focusing on the preparation of α-amino-β-hydroxy acid derivatives. In this paper, we present the effective chirality transfer from guanidinium salts **5** (or **ent-5**) to 3-alkenyl (or 3-alkynyl) aziridine-2-carboxylates **7** (or **ent-7**) in the reactions with α,β-unsaturated aldehydes **6** and the syntheses of (2*R*,3*S*)-3-hydroxyleucinate **1** and D-*erythro*-sphingosine (**3**) from 3-(1-methylvinyl)- and

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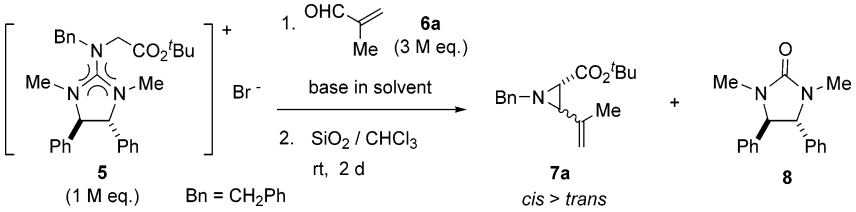
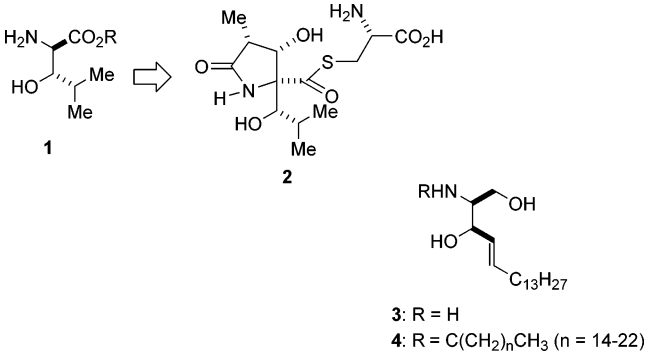
TABLE 1. Reaction of (*R,R*)-Guanidinium Bromide 5 with Methacrolein (6a) under Various Conditions Followed by Treatment with SiO_2



				yield (%) of 7[b]				
entry	base[a]/solvent	temp (°C)	time (d)	cis (ee)[c]	trans (ee)[c]	total	cis/trans	**8** (%)
1	TMG/none	25	1	62 (84)	9 (81)	71	87/13	100
2	TMG/THF	0	7	79 (87)	13	92	86/14	93
3	TMG/THF	25	3	76 (89)	14 (81)	90	84/16	93
4	TMG/THF	50	1.5	64 (89)	26 (82)	90	71/29	100
5	TMG/PhMe	0	7	80 (86)	12	92	87/13	100
6	TMG/PhMe	25	3	75 (88)	12 (83)	87	86/14	93
7	NaH/DMF	−10	2	39 (86)	25 (85)	64	61/39	78

[a] TMG = 1.5 Meq; NaH = 2.0 Meq. [b] Isolated yield. [c] Determined by a chiral HPLC and data without parenthesis means no measurement of ee.

[(*E*)-pentadec-1-enyl]aziridine-2-carboxylates, respectively, obtained in the asymmetric aziridinations.



Results and Discussion

Asymmetric Aziridination. According to our previous report,[9] reaction of (*R,R*)-guanidinium salt **5** with methacrolein (**6a**) was examined using either 1,1,3,3-tetramethylguanidine (TMG) or sodium hydride (NaH) as base under various conditions, followed by treatment with silica gel (SiO_2). As shown in Table 1, desired vinylaziridines **7a** were obtained as a diastereomeric mixture in 64−92% combined yields with a range of 81−89% enantiomeric excess (ee) together with a chiral urea **8**, recyclable to the starting guanidinum salt **5**. Inspection of coupling constant (J = 7.1 Hz) between 2-H (δ 2.35) and 3-H (δ 2.31) in the ^{1}H NMR spectrum of the major diastereoisomer indicated that *cis*-aziridine was preferentially formed (22−74% diastereomeric excess (de)). We already observed, in the aziridination using aryl aldehydes, that the diastereoselectivity of aziridine products is dependent upon the electronic character of substituent on aryl aldehydes used. In general, major isomers are trans derivatives in the cases of aldehydes carrying an electron-donating group, whereas cis ones mainly observed with aldehydes either carrying an electron-withdrawing group or without substituent.[12] Thus, cis-rich diastereoselectivity in the reaction of **5** and **6a** can be reasonably accepted as an example of the latter cases. As expected from the previous results,[9] TMG was found to be a more effective base than NaH not only for conversion but also for selectivity (entries 1−6 vs entry 7). Although the solvent-free reaction was operative (entry 1), the copresence of a limited amount of tetrahydrofuran (THF) or toluene as solvent led to better isolated yield (entries 2−6).

On the basis of our previous works,[9] the stereogenic center of the major enantiomers in *cis*-aziridines was expected to be of the (2*S*,3*S*) configuration when (*R,R*)-guanidinium bromide **5** is used as a chiral source. The expected absolute stereochemistry could be confirmed by chemical correlation of the *cis*-aziridine ***c*-7a** to *tert*-butyl *N*-Boc-(−)-leucinate (**9**), which was independently derived from (*S*)-(+)-leucine (**10**) {$[\alpha]^{24}_D$ −8.5 ($CHCl_3$) from ***c*-7a**; $[\alpha]^{24}_D$ −9.8 ($CHCl_3$) from **10**} (Scheme 1).

Scope and limitations of this asymmetric aziridination were investigated by varying the substituents on the α and β positions of unsaturated aldehydes, using enan-

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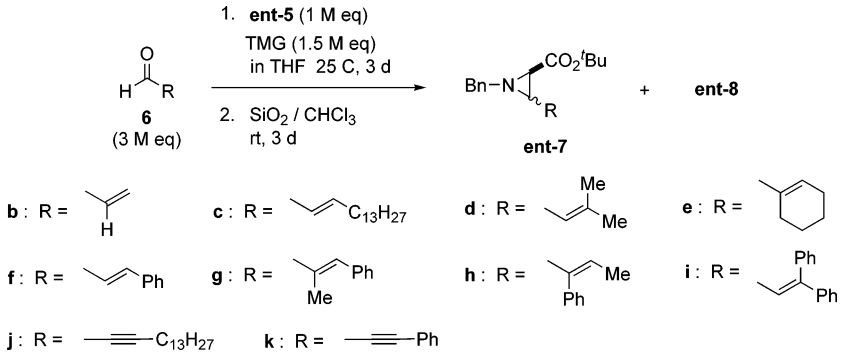
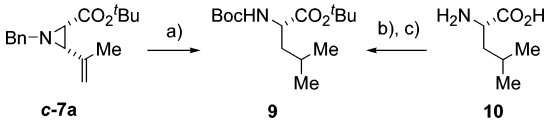
TABLE 2. Asymmetric Aziridination Using (*S,S*)-Guanidinium Bromide ent-5 and Various α,β-Unsaturated Aldehydes 6 in the Presence of TMG



		yield (%) of **ent-7**[a]				
entry	**6**	cis (ee)[b]	trans (ee)[b]	total	cis/trans	**ent-8** (%)
1	**6a**	80 (89)	12 (82)	92	87/13	92
2	**6b**	31 (58)	31	62	50/50	94
3	**6c**	46 (95)	41 (97)	87	53/47	quant.
4	**6d**	4	<1	<5	>80/20	89
5	**6e**	33 (99)	18	51	65/35	94
6	**6f**	22 (75)	60 (65)	82	27/73	91
7	**6g**	9 (93)	42 (92)	51	18/82	91
8	**6h**	28 (98)	2	30	93 /7	90
9	**6i**	32 (91)	10 (87)	42	76/24	94
10	**6j**	18	26	44	41/59	94
11[c]	**6k**	22 (91)	48 (98)	70	31/69	63

[a] Isolated yield. [b] Determined by chiral HPLC and data without parenthesis means no measurement of ee. [c] Ac_2O was used in the second step, instead of SiO_2.[12]

SCHEME 1. Chemical Correlation between *tert*-Butyl *cis*-1-Benzyl-3-isopropenylaziridine-2-carboxylate (*c*-7a) and (*S*)-(+)-Leucine (10)[a]



[a] Reagents and conditions: (a) H_2, 5% $Pd(OH)_2$/C, Boc_2O, MeOH, room temperature (rt), 12 h (94%); (b) Boc_2O, 1 N NaOH, ^{t}BuOH, rt, 15 h; (c) *N,N*-dimethylformamide di-*tert*-butyl acetal, benzene, rt, 21 h followed by 50 °C, 6 h (52% in 2 steps).

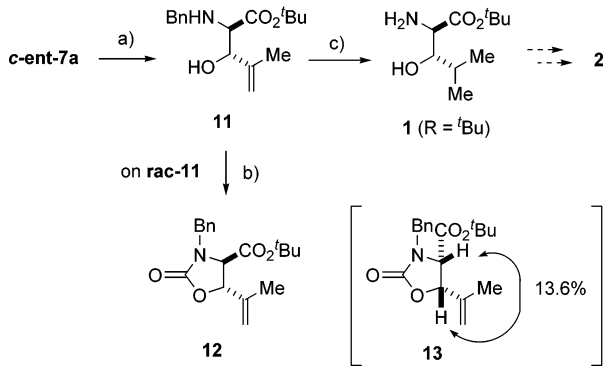
tiomeric (*S,S*)-guanidinium salt **ent-5** as a chiral source for the asymmetric induction of (2*R*)-aziridines **ent-7** (Table 2). The conditions of entry 3 in Table 1 were chosen as a standard condition for further aziridination reactions. Aziridines were generally formed in good to moderate yields with high ee; however, conversion and selectivity were strongly influenced by the substituent introduced.[13] Thus, no diastereoselectivity was observed in the cases of vinyl and β-alkylvinyl aldehydes (entries 2 and 3). Interestingly, *cis*- and *trans*-3-[(*E*)-pentadec-1-enyl]aziridines **7c**, possible synthetic precursors for D-*erythro*-sphingosine (**3**), were smoothly produced from (*E*)-hexadec-2-enal (**6c**) not only in high combined yield but also with high ee (entry 3). The reaction was greatly retarded when α,β-dialkylvinyl aldehyde was used (entry 4). Introduction of a substituent at the position like methacrolein (**6a**) led to the preferential production of cis isomers (entries 1, 5, and 8), whereas in the cinnamaldehyde series *trans*-aziridines were obtained as major isomers (entries 6 and 7), as expected from the result in the previous achiral version.[9] It was found that this aziridination was applicable to alkynyl aldehydes (entries 10 and 11). High ee was also observed in 3-phenylprop-2-ynal (**6k**).

Preparation of *t*-Butyl (2*R*,3*S*)-3-Hydroxyleucinate (1: R = ^{t}Bu). For the formal synthesis of (+)-lactacystin (**2**) conversion of *tert*-butyl *cis*-(2*R*,3*R*)-3-(1-methylvinyl)aziridine-2-carboxylate (***c*-ent-7a**, 89% ee, entry 1 in Table 2) to (2*R*,3*S*)-3-hydroxyleucinate **1** (R = ^{t}Bu) was examined (Scheme 2). Treatment of ***c*-ent-7a** with *p*-toluenesulfonic acid monohydrate ($TsOH\cdot H_2O$) smoothly afforded α-amino-β-hydroxy ester **11** in 93% yield as a single product. The stereochemistry was determined after conversion to the corresponding oxazolidinone **12** by reaction with carbonyldiimidazole (Im_2CO), in which a racemic ring-opened product **rac-11** was used as a starting material. In general, the coupling constant between 4-H and 5-H is ~9−10 Hz in *cis*-oxazolidinone systems, whereas ~4−6 Hz in trans systems.[14] The small coupling constant ($J_{4,5}$ = 5.2 Hz) observed in **12** indicates that the hydroxyl-inserted product **11** has threo stereochemistry. This deduction was supported by nuclear overhauser effect (NOE) enhancement (13.6%) between these protons observed in the corresponding *cis*-oxazolidinone derivative **13** ($J_{4,5}$ = 8.6 Hz) derived from the *trans*-aziridines. Thus, the ring-

(13) Low yields in some cases may be caused by dimerization of starting aldehydes. See: Laitalainen, T.; Kuronen, P.; Hesso, A. *Org. Pre. Pro. Int.* **1993**, *25*, 597−599.

(14) For the basic discussion on the coupling constant, see: Foglia, T. A.; Swern, D. *J. Org. Chem.* **1969**, *34*, 1680−1684. Williams, T. M.; Crumbie, R.; Mosher, H. S. *J. Org. Chem.* **1985**, *50*, 91−97. Cardillo, G.; Orena, M.; Sandri, S. *J. Org. Chem.* **1986**, *51*, 713−717.

SCHEME 2. Synthesis of (2*R*,3*S*)-3-Hydroxyleucinate 1 from *tert*-Butyl *cis*-(2*R*,3*R*)-3-(1-Methylvinyl)aziridine-2-carboxylate (*c*-ent-7a)[a]



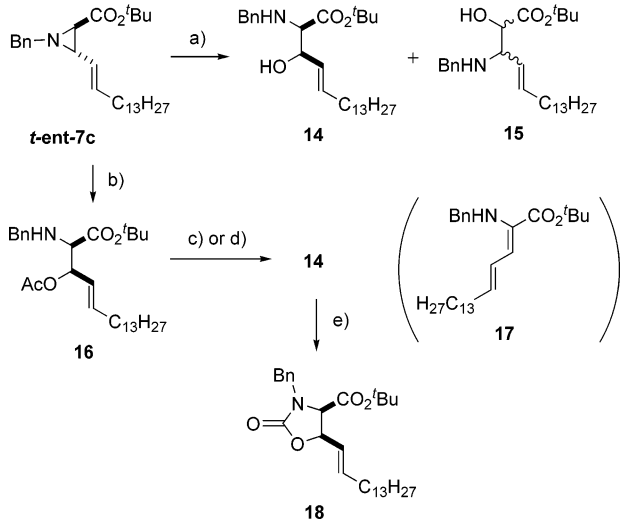
[a] Reagents and conditions: (a) TsOH·H_2O, THF/H_2O, 25 °C, 30 min then 50 °C, 20 h (93%); (b) Im_2CO, 35 °C, 2 days (90%); (c) H_2, 10% Pd/C, 25 °C, 9.5 h (91%).

opening reaction should be controlled by S_N2 type substitution leading to inversion at the C3 position.[15] Catalytic hydrogenation of **11** in the presence of 10% palladium on carbon (Pd/C) smoothly gave (2*R*,3*S*)-3-hydroxyleucinate **1**.[16] High retention of chirality in **1** (87% ee) supported the stereoselective ring-opening reaction of ***c*-ent-7a** with TsOH.

In literatures (2*R*,3*S*)-3-hydroxyleucine derivatives **1** had been prepared in 48−65% overall yields using aldol-type reaction (92% ee),[17] epoxidation (97% ee),[4a] dihydroxylation (87% ee),[4b] and aminohydroxylation (70% ee)[4c] as key step under asymmetric conditions. In our synthetic method **1** can be prepared in 68% overall yield with 87% ee from the guanidinium salt **5**.

Synthesis of D-*erythro*-Sphingosine (3). (a) From the *trans*-aziridine *t*-ent-7c. Next, we examined the enantioselective synthesis[18] of D-*erythro*-sphingosine (**3**) from both *trans*-(2*R*,3*S*)- ***t*-ent-7c** and *cis*-(2*R*,3*R*)-3-[(*E*)-pentadec-1-enyl]aziridine-2-carboxylates ***c*-ent-7c** obtained in entry 3 in Table 2. At first the ring-opening reactions of the former ***t*-ent-7c** (97% ee) were examined (Scheme 3). To directly introduce a hydroxyl function into the aziridine skeleton, reaction with TsOH was tried under the same condition as in Scheme 2. Although a desired α-amino-β-hydroxy ester **14** was obtained in 71% yield with good de, a regioisomerically ring-opened product, β-amino-α-hydroxy ester **15**, was also produced in 16% yield without diastereoselectivity. Therefore, acetic acid (AcOH) was used as an alternative nucleophile

SCHEME 3. Ring-opening Reaction of the *trans*-Aziridine *t*-ent-7c[a]



[a] Reagents and conditions: (a) TsOH·H_2O, THF/H_2O, 25 °C, 35 h [**14**, 71%; **15**, 16% (cis:trans = ca. 1:1)]; (b) AcOH, 25 °C, 2.5 h (quant); (c) KOH, THF/MeOH, 0 °C, 15 min (**14**: 99%); (d) KOH, EtOH/H_2O, 2 °C, 0.5 h (**14**, 18%; **17**, 52%); (e) Im_2CO, CH_2Cl_2, 25 °C, 12 h (99%).

for the ring-opening reaction, and an acetoxy-inserted product **16** was quantitatively afforded as a single diastereoisomer. α-Amino-β-hydroxy ester **14** was obtained in 99% yield when **16** was subjected to methanolysis (KOH, THF/MeOH), whereas conventional alkaline hydrolysis (KOH, EtOH/H_2O) afforded **14** only in low yield (18%); instead, a conjugated dehydration product **17** was mainly produced (52%). The erythro stereochemistry of the ring-opened α-amino-β-hydroxy ester **14** was determined by NOE enhancement (15%) and coupling constant (J = 9.2 Hz) between 4-H (δ 3.95) and 5-H (δ 4.93) of the corresponding 2-oxazolidinone **18**.[14]

Johnson et al.[19] reported the total synthesis of L-*erythro*-sphingosine from the corresponding enantiomeric methyl ester of **18** derived from enzymatically prepared cyanohydrin derivative. Although this means that the synthesis of natural D-*erythro*-sphingosine could be formally achieved in this stage, we independently developed our own route. After protection of the hydroxyl group of α-amino-β-hydroxy ester **14** with triisopropylsilyl (TIPS) function the silyl ether **19** was treated with lithium aluminum hydride. An intended reduced product **20** was obtained in 82% yield, but concomitant removal of the TIPS function was also observed as diol **21** was formed in 18% yield. After conversion of **20** to oxazolidinone **22**, selective debenzylation was carried out under Birch reduction conditions[19] to give an *N*-deprotected oxazolidinone **23** in high yields. Successively, removal of the TIPS function of **23** with fluoride ion followed by alkaline hydrolysis quantitatively afforded D-*erythro*-sphingosine (**3**), which was fully characterized as a crystalline triacetate **24**, melting point (mp) 100−102 °C, $[\alpha]_D^{24}$ −13.0 ($CHCl_3$).[20] Thus, **3** was synthesized in 62% overall yield

(15) We have observed that the ring-opening reaction of 3-arylaziridine-2-carboxylates is greatly dependent upon the nature of substituent on the aryl group. These results will be reported elsewhere in the near future.

(16) The threo stereochemistry of **1** was further confirmed by ^1H NMR examination ($J_{4,5}$ = 6.0 Hz) after cyclization to an oxazolidinthione using diimidazolethiocarbonyl (Im_2CS).

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(18) For reviews of the synthesis of sphingosine, see: Byun, H.-S.; Bittman, R. In *Phospholipids Handbook*; Cevc, G., Ed.; Dekker: New York, 1993; pp 97−140. Koskinen, P. M.; Koskinen, A. M. P. *Synthesis* **1998**, 1075−1091. Curfman, C.; Liotta, D. *Methods Enzymol.* **1999**, *311*, 391−440. Koskinen, P. M.; Koskinen, A. M. P. *Methods Enzymol.* **1999**, *311*, 458−479. Jung, K.-H.; Schmidt, R. R. In *Lipid Synthesis and Manufacture*; Gunstone, F. D., Ed.; Sheffield Academic: Schefield UK, 1999; pp 208−249.

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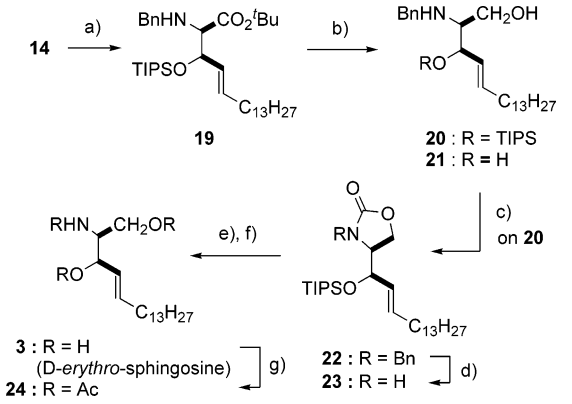
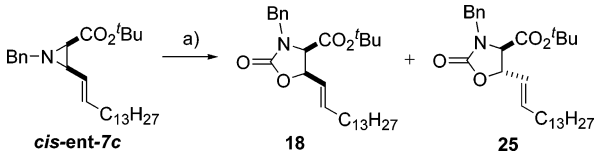
(20) Data of triacetate derived from sphingosine, see: Findeis, M. A.; Whitesides, G. M. *J. Org. Chem.* **1987**, *52*, 2838−2848.

SCHEME 4. Synthesis of D-*erythro*-Sphingosine (3) from the Ring-Opened Product 14[a]



[a] Reagents and conditions: (a) TIPSOTf, NEt_3, CH_2Cl_2, 2 °C, 30 min (95%); (b) $LiAlH_4$, THF, 25 °C, 10 min (**20**, 82%; **21**, 18%); (c) Im_2CO, CH_2Cl_2, 25 °C, 12 h (97%); (d) Li, liq NH_3, Et_2O, −70 °C, 5 min (89%); (e) TBAF, THF, rt, 1.5 h; (f) 2 N NaOH aq, EtOH, 80 °C, 2.5 h; (g) Ac_2O, pyridine, DMAP, CH_2Cl_2, rt, 3 h (**24**, 93% from **23**)

SCHEME 5. Trial for Direct Conversion of the *cis*-Aziridine *c*-ent-7c to *cis*-Oxazolidinone 18[a]



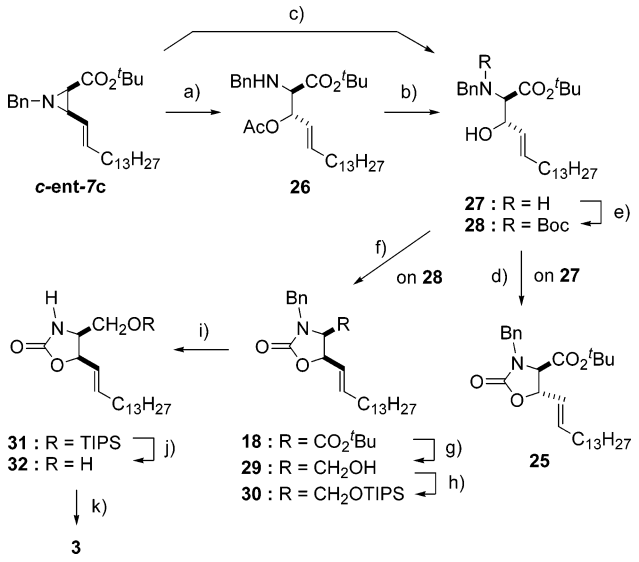
[a] Reagents and conditions: (a) $ClCO_2Me$, MeCN, 80 °C, 7 h (**18**, 25%; **25**, 8%)

with high optical purity (~97% ee), starting from the *trans*-aziridine ***t*-ent-7c** through eight steps.

(b) From the *cis*-aziridine *c*-ent-7c. Application of the above reaction scheme to the synthesis of D-*erythro*-sphingosine (**3**) from the corresponding *cis*-aziridine ***c*-ent-7c** requests stereochemical inversion at the C3 position of a ring-opened product because of the undesired production of *threo*-(2*R*,3*S*)-amino alcohol by S_N2-type ring-opening reaction of the *cis*-aziridine. As mentioned above, *cis*-oxazolidinone **18** can be a possible precursor for D-*erythro*-sphingosine (**3**) according to the synthetic method by Johnson et al.[19] Therefore, we follow their route for comparison with our modified route shown in Scheme 4. Recently Lee et al.[21] reported direct conversion of a *cis*-aziridine system to a *cis*-oxazolidinone. Thus, reaction of ***c*-ent-7c** with methyl chloroformate, in which double inversion processes should occur as a main reaction path, was attempted (Scheme 5); however, a 3:1 mixture of *cis*-**18** and *trans*-oxazolidinones **25** was formed in low yields (33%). These situations made us examine a stepwise procedure as an alternative approach (see, Scheme 6).

Although treatment of ***c*-ent-7c** (95% ee) with TsOH·H_2O gave a desired α-amino-β-hydroxy ester **27** and a regioisomeric β-amino-α-hydroxy ester (not shown) in 77 and 11% yields, respectively, similar to the trans isomer (see Scheme 3), a ring-opened product **26** was unexpectedly produced in low yield (<50%) on exposure of ***c*-ent-7c** to AcOH without solvent at room temperature. The acetoxy-inserted product **26** was obtained when the reaction was carried out in dichloromethane, even in moderate yield (62%), and subsequent methanolysis afforded the α-amino-β-hydroxy ester **27** (58% in two steps). A small coupling constant (J = 5.6 Hz) between 4-H and 5-H of the corresponding oxazolidine derivative **25** indicates that the ring-opened product **27** with a *threo* stereochemistry is, as expected, formed by inversion at the C3 position of an aziridine skeleton.[14] After introduction of *t*-butoxycarbonyl (Boc) group to the nitrogen atom of **27**, treatment with methanesulfonyl choloride led to an intramolecular cyclization[22] with stereochemical inversion at the C3 position, resulting in the production of *cis*-oxazolidinone **18** in high yield, which was identical with the sample obtained in Scheme 3.

SCHEME 6. Synthesis of D-*erythro*-Sphingosine (3) from the *cis*-Aziridine *c*-ent-7c[a]



[a] Reagents and conditions: (a) AcOH, CH_2Cl_2, 0 °C, 3 d (62%); (b) KOH, THF/MeOH, 0 °C, 15 min (93%); (c) TsOH·H_2O, THF/H_2O (1:1), 25 °C, 35 h (77%); (d) Im_2CO, CH_2Cl_2, rt, 12 h (93%); (e) Boc_2O, 45 °C, 4 h (95%); (f) MsCl, NEt_3, CH_2Cl_2, 0 °C, 30 min (96%); (g) $LiBH_4$, THF, 50 °C, 2 d (73%); (h) TIPSOTf, NEt_3, CH_2Cl_2, 2 °C, 30 min (97%); (i) Li, liq NH_3, Et_2O, −72 °C, 5 min (78%); (j) TBAF, THF, rt, 1.5 h (70%); (k) 2 N NaOH aq, EtOH, 80 °C, 2.5 h (quant)

According to the method of Johnson,[19] the ester function was reduced with lithium borohydride to afford the corresponding alcohol **29** in 73% yield with partial recovery of the starting **18** (20%). After protection of the alcoholic function of **29** with TIPSOTf, selective removal of the benzyl group of **30** was effected under Birch reduction conditions to give an *N*-deprotected oxazolidinone **31**. Treatment of **31** with fluoride anion followed by alkaline hydrolysis completed the alternative synthesis of D-*erythro*-sphingosine (**3**) from the *cis*-aziridine ***c*-ent-7c** (95% ee) in 27% overall yield without loss of enantiopurity through eight steps. Thus, it was found that the modified route (Schemes 3 and 4) is practically superior to the reported route.

Key strategies for the construction of a chiral amino alcohol unit in the reported syntheses of D-*erythro*-

(21) Shim, T. B.; Kang, S. H.; Lee, K. S.; Lee, W. K. *J. Org. Chem.* **2003**, *68*, 104−108.

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sphingosine (**3**) can be classified into five-types of reactions except the ring-opening of aziridines:[23] C−C bond formation,[19,24] the ring-opening of epoxides with a nitrogen nucleophile,[25] displacement of alcohols or halides with a nitrogen nucleophile,[20,26] reduction of aminoketone,[27] and modification of natural chiral sources including phytosphingosine.[28] Among those major accesses are the C−C bond formation and the displacement methods. As for aziridine-participating synthesis only one approach had been reported, in which *cis*-(2*R*,3*R*)-*N*-toluenesulfinylaziridine derivative, an activated aziridine,[29] prepared by aldol-type reaction of the sulfinylimine derived from (+)-menthyl-(*R*)-*p*-toluenesulfinate with bromoacetate,[30] was used. Thus, our approach offers the second report of this kind and the unique example of the use of unactivated aziridine[29] as well as the first access from *trans*-aziridine with high effectivity (62%).[31]

Conclusions

In conclusion, reaction of chiral guanidinium ylides with α,β-unsaturated aldehydes successfully gave a variety of α,β-unsaturated aziridine-2-carboxylates in good to moderate yields and chirality of the guanidinium ylides was effectively transferred to the 2 and 3 positions of aziridine products (up to 93% de and 98% ee). The formed α,β-unsaturated aziridines are easily converted into α-amino-β-hydroxy esters synthetic precursors. Thus, (2*R*,3*S*)-3-hydroxyleucinate was enantioselectively prepared from (2*R*,3*R*)-3-isopropenylaziridine-2-carboxylate obtained using methacrolein as aldehyde substrate. In addition, D-*erythro*-sphingosine was synthesized in good overall yield with high optical purity starting from both *trans*-(2*R*,3*S*)- and *cis*-(2*R*,3*R*)-3-[(*E*)-pentadec-1-enyl]-aziridine-2-carboxylates.

Experimental Section

General Procedure for Aziridine Formation (Tables 1 and 2). (A) TMG/SiO_2 (or Ac_2O) System. To a solution of **5** (or **ent-5**) (100 mg) and **6** (3 equiv) in an appropriate solvent (0.1 mL) was added TMG (1.5 equiv) at 25 °C under argon, and the whole was stirred at the same temperature for 3 days. After dilution with $CHCl_3$ (2 mL) either the mixture was added into a suspension of SiO_2 (3 g) in $CHCl_3$ (10 mL) and stirred for 2 days or the mixture was stirred with Ac_2O (3 equiv) for 30 min. In the former case after removal of the SiO_2 through a Celite pad, the filtrate was concentrated, whereas the reaction mixture was directly concentrated in the latter case. The residue obtained was purified by column chromatography to give **7** and **8**.

(B) NaH/SiO_2 System. A suspension of **5** (or **ent-5**) (100 mg) and NaH (2.0 equiv) in DMF (0.5 mL) was stirred at −10 °C for 30 min (the mixture turned yellow) under argon. To the mixture was added **6** (3.0 equiv) and the whole was stirred at the same temperature for 2 days. The same workup as above gave **7** and **8**.

***t*-Butyl 1-Benzyl-3-isopropenylaziridine-2-carboxylate (Entry 1 in Table 2). (2*R*,3*R*)-*cis*-Derivative *c*-ent-7a.** A colorless needles, mp 65−66 °C; chiral high-performance liquid chromatography (HPLC) [CHIRALCEL OD-H, *n*-hexane/2-propanol = 800:1, flow rate = 0.5 mL/min, detection wavelength = 215 nm, t_R (major) = 36.7 min, t_R (minor) = 46.3 min], 89% ee; $[\alpha]^{20}_D$ +51.1 (*c* 2.0, $CHCl_3$); IR (ATR) ν_{max} 1732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.43 (s, 9H), 1.70 (s, 3H), 2.31 (d, *J* = 7.1 Hz, 1H), 2.35 (d, *J* = 7.1 Hz, 1H), 3.38 (d, *J* = 13.7 Hz, 1H), 3.88 (d, *J* = 13.7 Hz, 1H), 4.92 (br s, 1H), 5.10 (br s, 1H), 7.23−7.27 (m, 1H), 7.32 (dif. dd, *J* = 7.6, 7.1 Hz, 2H), 7.40 (dif. d, *J* = 7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 28.0, 45.4, 48.8, 63.4, 80.9, 113.4, 127.0, 127.9, 128.2, 138.1, 138.3, 167.4; high-resolution fast-atom bombardment mass spectroscopy (HRFABMS) *m/z* 274.1792 (calcd for $C_{17}H_{24}NO_2$: 274.1807). **(2*R*,3*S*)-*trans*-Derivative *t*-ent-7a.** A pale-yellow oil; chiral HPLC [CHIRALCEL OD-H, *n*-hexane/2-propanol = 800:1, flow rate = 0.5 mL/min, detection wavelength = 215 nm, t_R (minor) = 15.7 min, t_R (major) = 23.8 min], 82% ee; $[\alpha]^{22}_D$ +59.4 (*c* 0.8, $CHCl_3$); IR (ATR) ν_{max} 1720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (invertomer ratio = ca. 10:1) δ_{major} 1.39 (s, 9H), 1.64 (s, 3H), 2.65 (d, *J* = 2.3 Hz, 1H), 2.77 (d, *J* = 2.3 Hz, 1H), 3.96 (d, *J* = 14.1 Hz, 1H), 4.09 (d, *J* = 14.1 Hz,

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1H), 4.91 (br s, 1H), 5.05 (br s, 1H), 7.23 (t, J = 7.1 Hz, 1H), 7.30 (dd, J = 7.7, 7.1 Hz, 2H), 7.35 (dif. d, J = 7.0 Hz, 2H); δ_{minor} 2.33 (br s, 1H), 3.01 (br s, 1H), 3.45 (br d, J = 13.6 Hz, 1H), 3.79 (br d, J = 13.6 Hz, 1H), 4.97 (br s, 1H), 5.21 (br s, 1H), 7.23−7.35 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_{major} 18.2, 28.0, 41.4, 50.5, 54.6, 81.5, 113.1, 126.7, 127.9, 128.1, 139.5, 142.2), 168.2; HRFABMS *m/z* 274.1816 (calcd for $C_{17}H_{24}NO_2$: 274.1807).

***t*-Butyl 1-Benzyl-3-(pentadec-1-enyl)aziridine-2-carboxylate (Entry 3 in Table 2). (2*R*,3*R*)-*cis*-Derivative *c*-ent-7c.** Colorless needles, mp 45−46 °C; chiral HPLC [CHIRALCEL OD-H, *n*-hexane/2-propanol = 1000:1, flow rate = 0.5 mL/ min, detection wavelength = 215 nm, t_R (major) = 33.8 min, t_R (minor) = 40.3 min], 95% ee; $[\alpha]^{23}_D$ −5.3 (*c* 1.5, $CHCl_3$); IR (KBr) υ_{max} 1728 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.25−1.35 (br, 22H), 1.46 (s, 9H), 2.03 (br dt, J = 7.0, 7.0 Hz, 2H), 2.29 (d, J = 6.7 Hz, 1H), 2.36 (dd, J = 8.2, 6.7 Hz, 1H), 3.63 (d, J = 14.7 Hz, 1H), 3.66 (d, J = 14.7 Hz, 1H), 5.46 (dd, J = 15.6, 8.2 Hz, 1H), 5.80 (dt, J = 15.6, 7.0 Hz, 1H), 7.22−7.25 (m, 1H), 7.31 (t, J = 7.6 Hz, 2H), 7.35 (d, J = 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.7, 28.2, 29.1, 29.3, 29.5, 29.59, 29.64, 29.7, 31.9, 32.4, 45.1, 47.4, 63.1, 81.2, 124.9, 126.9, 127.6, 128.2, 136.0, 138.1, 168.2; HRFABMS *m/z* 442.3663 (calcd for $C_{29}H_{48}NO_2$: 442.3685).

(2*R*,3*S*)-*trans*-Derivative *t*-ent-7c. A pale-yellow oil; chiral HPLC [CHIRALCEL OD-H, *n*-hexane/2-propanol = 250:1, flow rate = 0.5 mL/min; detection wavelength = 215 nm, t_R (major) = 13.4 min, t_R (minor) = 18.0 min], 97% ee; $[\alpha]^{23}_D$ −6.6 (*c* 2.7, $CHCl_3$); IR (film) υ_{max} 1720 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) (invertomer ratio = ca. 10:9) δ_{major} 0.88 (t, J = 7.0 Hz, 3H), 1.22−1.34 (br, 22H), 1.38 (s, 9H), 2.02 (dt, J = 7.0, 7.0 Hz, 2H), 2.56 (d, J = 2.6 Hz, 1H), 2.72 (dd, J = 7.3, 2.6 Hz, 1H), 3.94 (d, J = 13.9 Hz, 1H), 4.13 (d, J = 13.9 Hz, 1H), 5.20 (dd, J = 15.4, 7.3 Hz, 1H), 5.80 (dt, J = 15.4, 7.0 Hz, 1H), 7.20−7.36 (m, 5H); δ_{minor} 0.88 (t, J = 7.0 Hz, 3H), 1.22−1.34 (br, 22H), 1.46 (s, 9H), 2.07 (dt, J = 7.0, 7.0 Hz, 2H), 2.20 (d, J = 2.8 Hz, 1H), 3.00 (dd, J = 8.8, 2.8 Hz, 1H), 3.65 (d, J = 14.3 Hz, 1H), 3.84 (d, J = 14.3 Hz, 1H), 5.41 (dd, J = 15.6, 8.8 Hz, 1H), 5.92 (dt, J = 15.6, 7.0 Hz, 1H), 7.20−7.36 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) (a mixture of invertomers) δ 14.0, 22.6, 27.8, 27.9, 28.86, 28.90, 28.96, 29.01, 29.2, 29.35, 29.36, 29.46, 29.53, 29.54, 29.6, 31.8, 32.2, 32.5, 42.7, 45.38, 45.40, 47.7, 54.3, 55.5, 80.9, 81.1, 122.00, 122.01, 126.5, 126.6, 127.4, 127.8, 127.9, 128.0, 134.5, 138.9, 139.0, 139.3, 167.9, 169.5; HRFABMS *m/z* 442.3663 (calcd for $C_{29}H_{48}NO_2$: 442.3685).

***t*-Butyl (2*R*,3*S*)-2-Benzylamino-3-hydroxy-4-methylpent-4-enoate (11).** A solution of ***c*-ent-7a** (145 mg, 0.529 mmol) in THF (2 mL) containing TsOH H_2O (107 mg, 0.563 mmol) was stirred at 25 °C for 30 min and then at 50 °C for 20 h. After being cooled to 0 °C and made alkaline, conventional workup afforded **11** as a pale-yellow oil (143 mg, 93%), which was used in the next step without purification: $[\alpha]^{21}_D$ +45.0 (*c* 1.2, $CHCl_3$); IR (film) ν_{max} 3448, 3307, 1726 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (s, 9H), 1.76 (s, 3H), 3.18 (d, J = 8.1 Hz, 1H), 3.71 (d, J = 13.0 Hz, 1H), 3.83 (d, J = 13.0 Hz, 1H), 3.93 (d, J = 8.1 Hz, 1H), 4.93 (m, 1H), 4.99 (m, 1H), 7.26−7.34 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.8, 28.0, 52.6, 64.6, 76.5, 82.0, 114.7, 127.3, 128.3, 128.5, 139.2, 143.5, 172.2; HRFABMS *m/z* 292.1934 (calcd for $C_{17}H_{26}NO_3$: 292.1913).

(*dl*)-*tert*-Butyl *trans*-3-Benzyl-5-isopropenyl-2-oxo-1,3-oxazolidine-4-carboxylate (rac-12). A mixture of **rac-11** (32 mg, 0.108 mmol) and Im_2CO (22 mg, 95% purity, 0.129 mmol) in CH_2Cl_2 (1 mL) was stirred at 35 °C for 3 days under argon. After evaporation the residue was purified by column chromatography (SiO_2, *n*-hexane/AcOEt = from 10:1 to 4:1) to afford the oxazolidinone **rac-12** as a colorless oil (31 mg, 90%); IR (film) ν_{max} 1763, 1743 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48 (s, 9H), 1.61 (br s, 3H), 3.62 (d, J = 5.1 Hz, 1H), 4.18 (d, J = 14.8 Hz, 1H), 4.78 (d, J = 5.3 Hz, 1H), 4.95 (d, J = 14.8 Hz, 1H), 4.96 (br s, 1H), 5.09 (br s, 1H), 7.23−7.37 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5, 27.9, 47.1, 60.6, 78.7, 83.4, 114.4, 128.1, 128.4, 128.9, 135.0, 140.5, 157.2, 168.4; HRFABMS *m/z* 318.1701 (calcd for $C_{18}H_{24}NO_4$: 318.1705).

***t*-Butyl (2*R*,3*S*)-3-Hydroxyleucinate (1).** A mixture of **11** (124 mg, 0.424 mmol) and 10% Pd/C (93 mg) in EtOH (10 mL) was stirred at 25 °C for 9.5 h under hydrogen. Conventional workup followed by column chromatography (SiO_2, AcOEt) afforded **1** as a pale-yellow oil (78 mg, 91%): $[\alpha]^{23}_D$ −11.2 (*c* 1.4, $CHCl_3$); IR (film) ν_{max} 3371, 1728 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (d, J = 6.8 Hz, 3H), 1.01 (d, J = 6.8 Hz, 3H), 1.48 (s, 9H), 1.68−1.79 (m, 1H), 2.06 (br s, 3H), 3.39−3.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6, 19.5, 28.0, 30.8, 56.4, 77.1, 81.5, 173.8; FABMS *m/z*: 204 (48), 148 (100).

***t*-Butyl (2*R*,3*R*,4*E*)-2-Benzylamino-3-acetoxyoctadec-4-enoate (16).** A mixture of ***t*-ent-7c** (222 mg, 0.50 mmol) and AcOH (0.6 mL, 10.5 mmol) was stirred at 25 °C for 2.5 h and concentrated. The residue was purified by column chromatography (SiO_2, *n*-hexane/AcOEt = from 20:1 to 10:1) to afford **16** as a pale-yellow oil (252 mg, quant)**;** $[\alpha]^{23}_D$ −6.2 (*c* 2.5, $CHCl_3$); IR (film) υ_{max} 3332, 1735 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.25−1.36 (br, 22H), 1.46 (s, 9H), 2.00−2.05 (m, 2H), 2.03 (s, 3H), 3.35 (d, J = 5.1 Hz, 1H), 3.70 (d, J = 13.4 Hz, 1H), 3.88 (d, J = 13.4 Hz, 1H), 5.40 (dd, J = 7.7, 5.1 Hz, 1H), 5.46 (br dd, J = 15.0, 7.7 Hz, 1H), 5.76 (dt, J = 15.0, 7.0 Hz, 1H), 7.22−7.35 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 21.2, 22.7, 28.1, 28.8, 29.1, 29.3, 29.4, 29.55, 29.62, 29.635, 29.643, 29.7, 31.9, 32.3, 52.2, 64.1, 75.4, 81.6, 124.3, 127.0, 128.2, 128.3, 136.7, 139.7, 169.7, 171.0; HRFABMS *m/z* 502.3897 (calcd for $C_{31}H_{52}NO_4$: 502.3896).

***t*-Butyl (2*R*,3*R*,4*E*)-2-Benzylamino-3-hydroxyoctadec-4-enoate (14).** A solution of **16** (388 mg, 0.77 mmol) in THF (29 mL) was stirred with a solution of KOH in MeOH (prepared from KOH 1.023 g in MeOH 2.1 mL) (0.86 mL, 6.29 mmol) at 0 °C for 15 min. Conventional workup followed by column chromatography (NH−SiO_2, *n*-hexane/AcOEt = from 10:1 to 5:1) afforded **14** as a pale-yellow oil (351 mg, 99%); $[\alpha]^{23}_D$ +21.1 (*c* 3.0, $CHCl_3$); IR (film) υ_{max} 3448, 3317, 1728 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.24−1.32 (m, 22H), 1.46 (s, 9H), 1.99 (br dt, J = 7.0, 7.0 Hz, 2H), 3.29 (br s, 1H), 3.37 (d, J = 4.8 Hz, 1H), 3.63 (d, J = 12.6 Hz, 1H), 3.90 (d, J = 12.6 Hz, 1H), 4.30 (br dd, J = 6.4, 4.8 Hz, 1H), 5.30 (ddt, J = 15.4, 6.4, 1.1 Hz, 1H), 5.71 (dtd, J = 15.4, 7.0, 1.1 Hz, 1H), 7.24−7.33 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 28.1, 29.0, 29.1, 29.3, 29.4, 29.5, 29.59, 29.60, 29.62, 31.9, 32.2, 52.7, 65.3, 71.5, 81.6, 127.2, 127.3, 128.3, 128.4, 133.7, 139.5, 171.5; HRFABMS *m/z* 460.3785 (calcd for $C_{29}H_{50}NO_3$: 460.3791).

***t*-Butyl (1′*E*,4*R*,5*R*)-*cis*-3-Benzyl-2-oxo-5-(pentadec-1-enyl)-1,3-oxazolidine-4-carboxylate (18).** A mixture of **14** (301 mg, 0.66 mmol) and Im_2CO (116 mg, 95% purity, 0.68 mmol) in CH_2Cl_2 (1.5 mL) was stirred at 25 °C for 12 h under argon. After evaporation, the residue was purified by column chromatography (SiO_2, *n*-hexane/AcOEt = from 10:1 to 5:1) to afford **18** as colorless prisms, which were recrystallized from *n*-hexane (315 mg, 99%); mp 52−53 °C; chiral HPLC [CHIRALCEL OD-H; *n*-hexane/2-propanol = 100: 1; flow rate = 1.0 mL/ min; detection wavelength = 254 nm; t_R (minor) = 18.6 min, t_R (major) = 26.1 min], 92% ee; $[\alpha]^{25}_D$ +34.3 (*c* 3.3, $CHCl_3$); IR (film) υ_{max} 1754, 1718 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.25−1.38 (br m, 22H), 1.44 (s, 9H), 2.04 (br dt, J = 7.2, 7.2 Hz, 2H), 3.95 (d, J = 9.2 Hz, 1H), 4.00 (d, J = 14.7 Hz, 1H), 4.93 (dd, J = 9.2, 7.9 Hz, 1H), 4.94 (d, J = 14.7 Hz, 1H), 5.42 (ddt, J = 15.6, 7.9, 1.5 Hz, 1H), 5.89 (dt, J = 15.6, 7.0 Hz, 1H), 7.24, 7.24 (each br d, J = 8.2 Hz, 1H), 7.30−7.37 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.7, 28.0, 28.5, 29.1, 29.3, 29.4, 29.5, 29.605, 29.612, 29.63, 29.64, 31.9, 32.2, 47.3, 61.3, 76.0, 83.0, 122.0, 128.1, 128.6, 128.9, 135.2, 138.9, 157.6, 166.7; FABMS *m/z* 486 (MH^+), 91 (100). Anal. Calcd for $C_{30}H_{47}NO_4$: C, 74.19; H, 9.75; N, 2.88. Found: C, 74.25; H, 9.72; N, 2.91.

***t*-Butyl (2*R*,3*R*,4*E*)-2-Benzylamino-3-triisopropylsilanyloxyoctadec-4-enoate (19).** A solution of **14** (436 mg, 0.95 mmol), TIPSOTf (0.26 mL, 0.97 mmol, 1.02 equiv), and

NEt_3 (0.14 mL, 1.0 mmol) in CH_2Cl_2 (4.4 mL) was stirred at 2 °C for 30 min. Conventional workup followed by column chromatography (SiO_2, *n*-hexane/AcOEt = from 10:1 to 4:1) afforded **19** as a colorless oil (557 mg, 95%); $[\alpha]^{24}_D$ −1.5 (*c* 3.1, $CHCl_3$); IR (film) υ_{max} 3333, 1736, 1725 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 0.88 (t, J = 7.0 Hz, 3H), 1.00−1.06 (m, 21H), 1.25−1.34 (m, 22H), 1.47 (s, 9H), 2.01 (br dt, J = 6.7, 6.1 Hz, 2H), 3.29 (d, J = 4.0 Hz, 1H), 3.69 (d, J = 13.4 Hz, 1H), 3.91 (d, J = 13.4 Hz, 1H), 4.50 (dd, J = 7.3, 4.0 Hz, 1H), 5.52 (dd, J = 15.3, 7.3 Hz, 1H), 5.59 (dt, J = 15.3, 6.1 Hz, 1H), 7.21−7.24 (dd, J = 7.0, 6.7 Hz, 1H), 7.28−7.33 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.1, 18.0, 18.1, 22.7, 28.1, 29.0, 29.2, 29.3, 29.5), 29.58, 29.62, 29.64, 29.7, 31.9, 32.2, 52.2, 67.4, 76.0, 80.7, 126.7, 128.16, 128.20, 129.6, 133.1, 140.2, 171.3; HRFABMS *m/z* 616.5150 (calcd for $C_{38}H_{70}NO_3Si$: 616.5125).

Reduction of 19: (2*S*,3*R*,4*E*)-2-Benzylamino-3-triisopropylsilanyloxyoctadec-4-en-1-ol (20) and (2*S*,3*R*,4*E*)-2-Benzylaminooctadec-4-en-1,3-diol (21). A mixture of **19** (325 mg, 0.53 mmol) and $LiAlH_4$ (52 mg, 80% purity, 1.10 mmol) in THF (7 mL) was stirred at 25 °C for 10 min under argon. Conventional workup followed by column chromatography (NH−SiO_2, *n*-hexane/AcOEt = from 10:1 to 5:1) afforded **20** as a colorless oil (235 mg, 82%) and **21** as colorless plates (37 mg, 18%), respectively. **20**: $[\alpha]^{25}_D$ −12.7 (*c* 2.1, $CHCl_3$); IR (film) υ_{max} 3448, 3324 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.00−1.11 (m, 21H), 1.26−1.35 (m, 22H), 2.03 (br dt, J = 7.3, 7.0 Hz, 2H), 2.63 (ddd, J = 5.5, 4.6, 4.6 Hz, 1H), 3.06 (br s, 1H), 3.61 (dd, J = 10.7, 5.5 Hz, 1H), 3.66 (dd, J = 10.7, 4.6 Hz, 1H), 3.81 (d, J = 13.1 Hz, 1H), 3.88 (d, J = 13.1 Hz, 1H), 4.36 (dd, J = 7.9, 4.6 Hz, 1H), 5.43 (br dd, J = 15.6, 7.9 Hz, 1H), 5.63 (dt, J = 15.6, 7.0 Hz, 1H), 7.23−7.32 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.5, 14.1, 18.06, 18.12, 22.7, 29.0, 29.2, 29.3, 29.5, 29.58, 29.64, 29.66, 29.67, 31.9, 32.2, 51.6, 59.9, 63.4, 74.9, 127.0, 128.1, 128.4, 130.4, 133.7, 140.3; HRFABMS *m/z* 546.4704 (calcd for $C_{34}H_{64}NO_2Si$: 546.4706). **21**: mp 45−47 °C; $[\alpha]^{22}_D$ −7.0 (*c* 0.5, $CHCl_3$); IR (KBr) υ_{max} 3341 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.25−1.38 (m, 22H), 1.97 (br s, 3H), 2.04 (dt, J = 7.0, 7.0 Hz, 2H), 2.67 (dt, J = 4.8, 4.8 Hz, 1H), 3.70 (d, J = 4.8 Hz, 2H), 3.83 (d, J = 13.2 Hz, 1H), 3.87 (d, J = 13.2 Hz, 1H), 4.24 (dd, J = 6.8, 4.8 Hz, 1H), 5.44 (ddt, J = 15.4, 6.8, 1.5 Hz, 1H), 5.75 (dtd, J = 15.4, 7.0, 0.9 Hz, 1H); 7.24−7.36 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.7, 29.1, 29.2, 29.3, 29.5, 29.57, 29.62, 29.65, 29.66, 31.9, 32.3, 51.4, 60.5, 61.6, 72.5, 127.1, 128.1, 128.5, 129.3, 134.0, 139.9; HRFABMS *m/z* 390.3373 (calcd for $C_{25}H_{44}NO_2$: 390.3372).

(1′*R*,2′*E*,4*S*)-3-Benzyl-4-(1-triisopropylsilanyloxyhexadec-2-enyl)-1,3-oxazolidin-2-one (22). A mixture of **20** (233 mg, 0.43 mmol) and Im_2CO (73 mg, 95% purity, 0.43 mmol) in CH_2Cl_2 (1 mL) was stirred at 25 °C for 12 h. After concentration the residue was purified by column chromatography (SiO_2, *n*-hexane/AcOEt = from 10:1 to 5:1) to afford **22** as a colorless oil (237 mg, 97%): chiral HPLC [CHIRALCEL OD-H, *n*-hexane/2-propanol = 100: 1; flow rate = 1.0 mL/ min; detection wavelength = 254 nm; t_R (minor) = 10.6 min, t_R (major) = 13.0 min], 92% ee; $[\alpha]^{25}_D$ −11.4 (*c* 2.4, $CHCl_3$); IR (film) υ_{max} 1757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.02−1.13 (m, 21H), 1.22−1.36 (m, 22H), 2.01 (br dt, J = 6.8, 6.8 Hz, 2H), 3.60 (ddd, J = 9.0, 5.3, 2.8 Hz, 1H), 4.15 (d, J = 15.2 Hz, 1H), 4.18 (dd, J = 9.0, 8.8 Hz, 1H), 4.27 (dd, J = 8.8, 5.3 Hz, 1H), 4.34 (dd, J = 7.7, 2.6 Hz, 1H), 4.96 (d, J = 15.2 Hz, 1H), 5.32 (br dd, J = 15.6, 7.7 Hz, 1H), 5.66 (dt, J = 15.6, 6.8 Hz, 1H), 7.28−7.37 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.5, 14.1, 18.02, 18.03, 22.7, 28.8, 29.2, 29.3, 29.4, 29.57, 29.62, 29.64, 29.65, 31.9, 32.2, 46.3, 59.1, 63.2, 73.1, 127.8, 127.9, 128.0, 128.7, 135.4, 136.0, 158.9; HRFABMS *m/z*: 572.4515 (calcd for $C_{35}H_{62}NO_3Si$: 572.4499).

(1′*R*,2′*E*,4*S*)-4-(1-Triisopropylsilanyloxyhexadec-2-enyl)-1,3-oxazolidin-2-one (23). A solution of **22** (118 mg, 0.21 mmol) in Et_2O (3.2 mL) was slowly added to a solution of Li (60 mg, 8.7 mmol) in liquid ammonia (12 mL) at −70 °C under argon and the whole was stirred at same temperature for 5 min. After quickly quenched with phosphate buffer (prepared from 0.5 M KH_2PO_4 and 0.5 M K_2HPO_4 in water, pH 6.8) (5 mL) the mixture was diluted with water (30 mL) and extracted with AcOEt (50 mL). Conventional workup followed by column chromatography (SiO_2, *n*-hexane/AcOEt = 3:1) afforded **23** as a colorless oil (88 mg, 89%): $[\alpha]^{20}_D$ −13.3 (*c* 1.1, MeOH); IR (film) υ_{max} 3260, 1761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.03−1.07 (m, 21H), 1.26−1.37 (m, 22H), 2.05 (br dt, J = 6.8, 6.8 Hz, 2H), 3.79 (dt, J = 8.6, 5.3 Hz, 1H), 4.08 (dd, J = 7.9, 4.9 Hz, 1H), 4.30 (dd, J = 8.8, 4.9 Hz, 1H), 4.43 (t, J = 8.8 Hz, 1H), 4.95 (br s, 1H), 5.36 (br dd, J = 15.6, 8.1 Hz, 1H), 5.73 (dt, J = 15.6, 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.3, 14.1, 17.96, 18.02, 22.7, 28.9, 29.2, 29.3, 29.4, 29.57, 29.62, 29.64, 29.65, 31.9, 32.2, 57.2, 66.9, 75.8, 127.9, 136.2, 159.5; HRFABMS *m/z* 482.4045 (calcd for $C_{28}H_{56}NO_3Si$: 482.4029).

D-*erythro*-Sphingosine [(2*S*,3*R*,4*E*)-2-Aminooctadec-4-ene-1,3-diol] (3). A mixture of **23** (127 mg, 0.26 mmol) and a 1.0 M solution of TBAF in THF, (0.3 mL, 0.30 mmol) was stirred 25 °C for 1.5 h and concentrated. The residue was dissolved in EtOH (2.1 mL) and then stirred with 2 N NaOH aq (2.1 mL) at 80 °C for 2.5 h. Conventional workup afforded **3** (103 mg) as colorless solids, which was subjected to acetylation without further purification; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.26−1.47 (m, 22H), 2.01 (dt, J = 6.8, 6.8 Hz, 2H), 2.86 (br dt, J = 5.8, 4.7 Hz, 1H), 3.62 (dd, J = 10.7, 5.8 Hz, 1H), 3.70 (dd, J = 10.7, 4.7 Hz, 1H), 4.04 (dd, J = 6.6, 6.6 Hz, 1H), 5.48 (ddt, J = 15.4, 7.1, 1.5 Hz, 1H), 5.72 (dtd, J = 15.4, 7.0, 0.7 Hz, 1H). [ref 20: ^1H NMR ($CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.15−1.4 (m, 22H), 2.06 (q, J = 7.0 Hz, 2H), 2.89 (m, 1H), 3.67 (m, 2H), 4.04 (t, J = 6.3 Hz, 1H), 5.48 (dd, J = 15.3, 7.1 Hz, 1H), 5.76 (dt, J = 15.3, 6.7 Hz, 1H)].

D-*erythro*-Sphingosine Triacetate 24. A mixture of crude **3** (103 mg, 0.26 mmol), Ac_2O (0.16 mL, 1.70 mmol), DMAP (6.4 mg, 0.05 mmol), and pyridine (0.35 mL, 4.33 mmol) in CH_2Cl_2 (3.5 mL) was stirred at 25 °C for 3 h. Conventional workup followed by recrystallization from *n*-hexane/AcOEt afforded **24** as a colorless solid (105 mg, 93%); mp 100−102 °C; $[\alpha]^{24}_D$ −13.0 (*c* 1.6, $CHCl_3$); IR (KBr) υ_{max} 3288, 1736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.25−1.36 (m, 22H), 1.99 (s, 3H), 2.07 (s, 3H), 2.07 (s, 3H), 2.01−2.06 (m, 2H), 4.04 (dd, J = 11.6, 3.8, Hz, 1H), 4.31 (dd, J = 11.6, 6.0 Hz, 1H), 4.43 (dddd, J = 9.0, 6.0, 6.0, 3.8 Hz, 1H), 5.28 (dd, J = 7.5, 6.0 Hz, 1H), 5.39 (ddt, J = 15.3, 7.5, 1.1 Hz, 1H), 5.66 (d, J = 9.0 Hz 1H), 5.79 (dt, J = 15.3, 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 20.7, 21.0, 22.6, 23.2, 28.8, 29.0, 29.2, 29.3, 29.46, 29.52, 29.536, 29.543, 29.6, 31.8, 32.2, 50.6, 62.5, 73.7, 124.1, 137.2, 169.7, 169.9, 170.8; HRFABMS *m/z* 426.3208 (calcd for $C_{24}H_{44}NO_5$: 426.3219). Anal. Calcd for $C_{24}H_{43}NO_5$: C, 67.73; H, 10.18; N, 3.29. Found: C, 67.99; H, 10.37; N, 3.31. [ref 20 mp 101−102 °C; $[\alpha]^{25}_D$ −13.3 (*c* 1.4, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.15−1.4 (m, 22H), 1.95−2.1 (m, 11H; Me peaks at 1.98, 2.06, 2.07), 4.04 (dd, J = 11.5, 3.8, Hz, 1H), 4.30 (dd, J = 11.5, 6.0 Hz, 1H), 4.38−4.48 (m, 1H), 5.28 (t, J = 7.0 Hz, 1H), 5.38 (dd, J = 15.0, 7.4, 1.1 Hz, 1H), 5.68 (d, J = 9.0 Hz 1H; NH), 5.79 (dt, J = 15.0, 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1, 20.8, 21.1, 22.7, 23.3, 28.9, 29.1, 29.3, 29.4, 29.6, 31.9, 32.3, 50.6, 62.5, 73.7, 124.0, 137.2, 169.6, 169.8, 170.7].

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Supporting Information Available: The spectral data of aziridines in Tables 1 and 2 except entries 1 and 3 in Table 2 and Experimental procedures except for the preparation of the leucinate (Scheme 2) and the synthesis of D-*erythro*-sphingosine from *trans*-aziridine (Schemes 3 and 4). This material is available free of charge via the Internet at http://pubs.acs.org.

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