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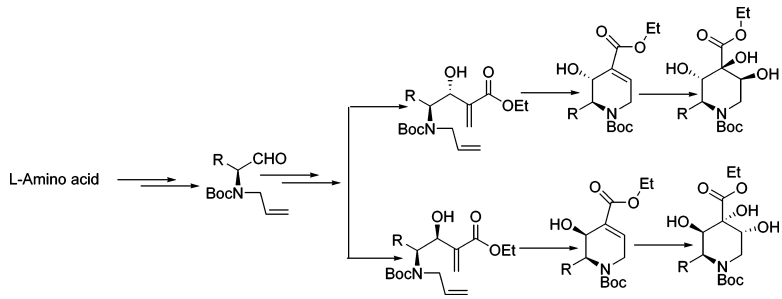

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"Diversity Oriented Synthesis" of Functionalized Chiral Tetrahydropyridines: Potential GABA Receptor Agonists and Azasugars from Natural Amino Acids via a Sequential Baylis−Hillman Reaction and RCM Protocol

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The preparation of chiral tetrahydropyridine-4-carboxylates as isoguvacine analogues and azasugars with a tertiary stereocenter from L-amino acids via diastereoselective a Baylis−Hillman reaction of *N*-allyl-Boc α-aminal, followed by ring-closing metathesis and dihydroxylation sequences, is reported.

Introduction

The Baylis−Hillman reaction is an effective method for the C−C bond formation reaction,[1] which results in highly functionalized products.[2] These products are useful in the synthesis of natural products such as polyketides and alkaloids.[3] In recent years, we were involved in expanding the horizon of the asymmetric Baylis−Hillman reaction[4] and also elaborating the ensuing adducts in the synthesis of bioactive natural products. One of the most useful methods for the construction of large- and medium-size heterocyclic rings is transition-metal-catalyzed ring-closing metathesis (RCM)[5] particularly notable because of functional group tolerance, operational simplicity, and ready availability of the catalyst, and equally useful is the catalytic dihydroxylation[6] reaction. Herein a Baylis−Hillman−RCM−cis-dihydroxylation protocol is used to first build the core tetrahydropyridine skeleton, which was later hydroxylated or hydrogenated to generate the additional chiral centers.

GABA is one of the major mammalin neurotransmitter inhibitors.[7] Many diseases such as schizophrenia, epilepsy, and Parkinson's have been linked to functions of GABA.[8] From in vitro studies, the tetrahydropyridine[9] moiety was identified as the pharmacophore for GABA inhibition. Some of the GABA analogues are *trans*-4-aminocrotonic acid,[10] muscimol,[11] isonipecotic acid, and 1,2,3,6-tetrahydropyridine-4-carboxylic acid.[12] Isoguvacine, a semirigid analogue of *trans*-4-aminocrotonic acid, THIP (Figure 1), acts as a GABA agonist with respect to some GABA receptors. These compounds and the analogues thereof interact with GABA postsynaptic receptors and the neuronal GABA transport system. Interestingly, some glycine antagonists are also structurally related to these analogues.[13]

As a part of our continued interest in the asymmetric Baylis−Hillman reaction and *C*-glycosides,[14] herein we report the synthesis of multifunctional products, having an

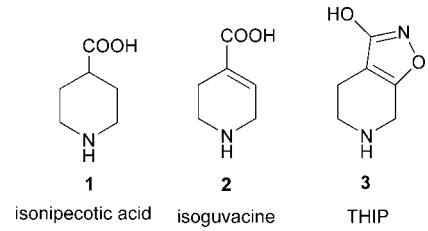

Figure 1. Specific GABA agonists.

α-methylene-β-hydroxy-γ-amino acid structure derived from chiral *N*-Boc allyl-α-aminoaldehydes with good diastereoselectivity. These adducts are transformed into 1,2,3,6-chiral tetrahydropyridine-4-carboxylates via RCM, which are related to isoguvacine. Finally, these adducts are further derivatized as azasugars.[15] Interestingly, all of these compounds closely resemble monosaccharides in terms of their shape and structure (Figure 2).

These glycosidase inhibitors are potentially useful in the treatment of cancer, viral infection including HIV, diabetes, lysosomal storage disorders such as Gaucher's, Fabry diseases, and non-insulin-dependent diabetes.[16]

Results and Discussion

During the course of our synthesis, amino acid **4** upon treatment with acetyl chloride in methanol gave the methyl ester hydrochloride **5** quantitatively, followed by Boc protection [$(Boc)_2$/Et_3N/THF)] giving **6** (95% overall yield for two steps). Then, reduction of the ester functionality (LAH/THF) followed by protection of the hydroxyl group of **7** as TBDMS ether (TBDMSCl/imidazole/CH_2Cl_2) gave **8** (70%). Compound **8** was allylated (allyl bromide/NaH/DMF) to afford tertiary amine **9** followed by deprotection (TBAF/THF/rt) of TBDMS ether affording a free primary alcohol, which was oxidized to an aldehyde under Swern oxidation conditions to the corresponding aldehyde **10** (Scheme 1).

With aldehyde in hand, our next task was to perform the Baylis−Hillman reaction under standard reaction conditions (DABCO/1,4-dioxane−water/rt) with ethyl acrylate. We also

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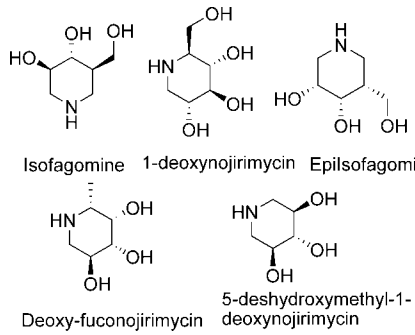
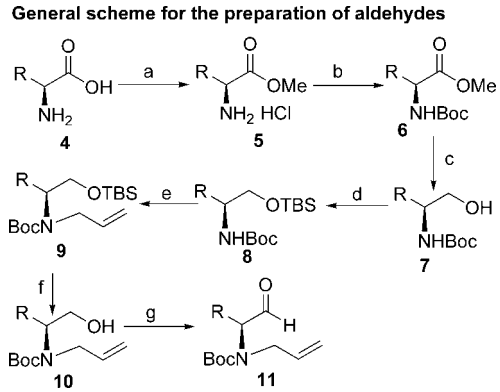


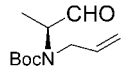
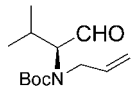
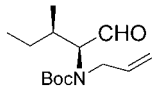
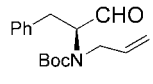
Figure 2. Natural and synthetic azasugars as glycosidase inhibitors.

Scheme 1[a]



[a] Reagents and conditions: (a) AcCl, MeOH, 0 °C to rt; (b) $(Boc)_2O$, Et_3N, THF, 0 °C to rt, 8 h (95% over two steps); (c) LAH (1.5 equiv), THF, 0 °C to rt, 2 h (74%); (d) TBDMSCI, imidazole, CH_2CI_2, 4 h (90%); (e) allyl bromide, NaH, DMF, 0 °C to rt, 6 h (79%); (f) TBAF, THF, rt; (g) $(COCI)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C, 1 h (80%).

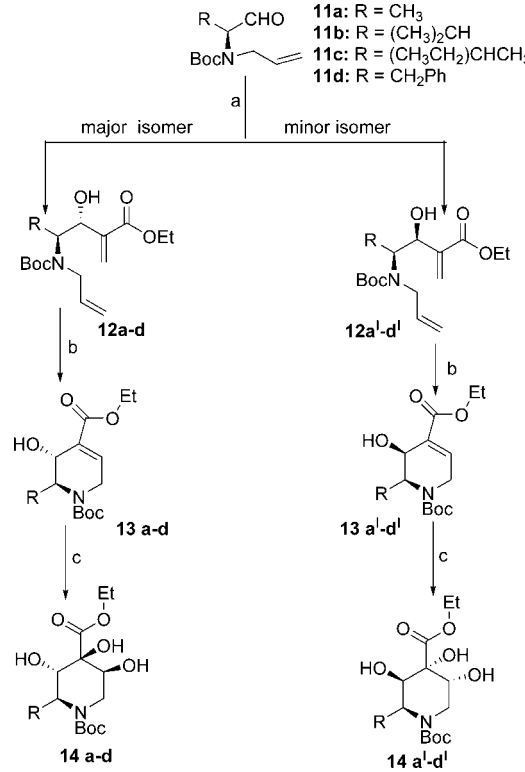
Table 1. Series of Aminoaldehyde-Derived Baylis−Hillman Products

Entry	Aldehyde	Products (*anti*/*syn*)	Time (h)	Yield(%)
1		**12a:12a^{I}** (78:24)	50	75
2		**12b:12b^{I}** (85:15)	48	80
3		**12c:12c^{I}** (82:18)	48	77
4		**12d:12d^{I}** (77:23)	50	74

tried the reaction in several solvents like CH_2Cl_2, DMSO, and sulfolane. Better results were obtained when sulfolane[17] was the solvent because the rate of the reaction was faster and afforded separable diastereomers (*de* 54–70%) as products **12a–d** and **12a′−d′** in good yields as well (Table 1).

If the aldehydes have an electron-withdrawing group in N substitution, the Baylis−Hillman reaction was faster than that when no electron-withdrawing group was present.[18a]

Scheme 2[a]



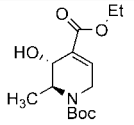
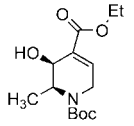
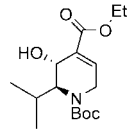
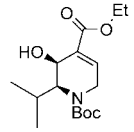
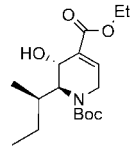
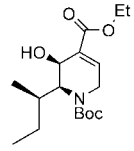
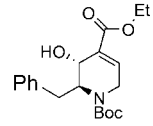
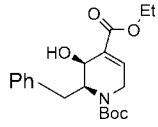
[a] Reagents and conditions: (a) Ethyl acrylate (1.5 eq), DABCO (1 eq), sulfolane, rt; (b) G-II catalyst (0.1 eq), toluene, reflux, (71-84%); (c) OsO_4, NMMO (50% aq. sol.), acetone–water (4:1), (81-86%).

Similarly, the stereoselectivity in the Baylis−Hillman reaction depends on the substitutions on the nitrogen atom in α-aminoaldehydes.[18b,c] For example, if the aminoaldehydes have N,N disubstitution, the adduct formed was an anti stereoisomer (major), which can be explained on the basis of the Felkin−Anh open-chain model. On the contrary, the syn stereoselectivity is observed for the NH-Boc-protected aminoaldehydes. This phenomenon could be rationalized by invoking the proton-bridged Cram cyclic model, due to the hydrogen bond between the aldehyde and NH group. Compound **12a** was identified from the ^{1}H NMR spectrum wherein the allylic proton appeared at δ 4.60 as a broad doublet downfield in the major isomer while the same proton appeared at δ 4.42 as a double–doublet in its diastereomer **12a′**. Our next task was the synthesis of substituted chiral tetrahydropyridines with RCM protocol. Among the commercially available ruthenium-based alkylidine Grubbs catalysts,[19] Grubbs' second-generation catalyst is stable to air and moisture and useful in an acidic environment, which was widely used for the synthesis of hindered substituted dienes, aminodienes, and large-size rings.

The Baylis−Hillman adducts **12a−d** and **12a′−d′** upon cyclization independently with (0.1 equiv) Grubbs' second-generation catalyst in toluene at reflux conditions furnished products **13a–d** and **13a′–d′**, respectively (Scheme 2 and Table 2) without racemization. By using this protocol, we prepared C_5-C_6-substituted tetrahydropyridine-4-carboxylates as isoguvacine analogues.

Further, these compounds upon exposure to catalytic dihydroxylation with OsO_4, with 4-methylmorphorine *N*-

Table 2. Series of Chiral Tetrahydropyridines[a]

Entry	Baylis-Hillman Product	Tetrahydropyridines	Time (h)	Yield[a] (%)
1	**13a**		20	83
2	**13a′**		22	80
3	**13b**		18	81
4	**13b′**		18	82
5	**13c**		22	82
6	**13c′**		22	79
7	**13d**		24	84
8	**13d′**		24	84

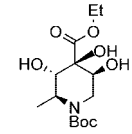
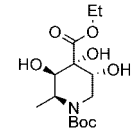
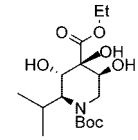
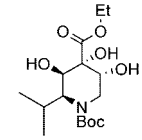
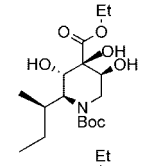
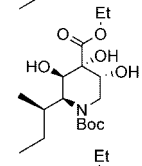
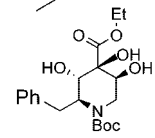
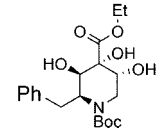
[a] Isolated yields for the final step.

oxide as a cooxidant in acetone−water (4:1), furnished dihydroxylated products **14a–d** and **14a′–d′** (Table 3), respectively, as single diastereomers interestingly with a tertiary stereogenic center. These substituted piperidinetriols are regarded as derivatives of their parent, naturally occurring and synthetic azasugars (Figures 2 and 3).

The stereochemistry of all of the triols **14a–d** and **14a′–d′** were assigned based on Kishi's analogy that the newly generated chiral centers are anti to the existing one.[20]

Earlier compound **13d** was dihydroxylated to afford stereochemically diverse entities possessing chiral tertiary stereocenters (**14d** and **14d′**; Scheme 2). Next, the latent diversity points of one of the products, **13d**, was demonstrated (Scheme 3) by subjecting it to hydrogenation in the presence of Pd−C at room temperature to give **13′a** and **13′b** in quantitative yields as a separable mixture. Both **13′a** and **13′b** form yet another class of interesting chiral piperidines as products.

Table 3. Series of Azasugars[a]

Entry	Tetrahydropyridine	Azasugars	Time (h)	Yield[a](%)	de (%)
1	**14a**		32	94	≥99:1
2	**14a′**		36	92	≥99:1
3	**14b**		38	95	≥99:1
4	**14b′**		38	90	≥99:1
5	**14c**		40	88	≥99:1
6	**14c′**		38	91	≥99:1
7	**14d**		43	97	≥99:1
8	**14d′**		40	92	≥99:1

[a] Isolated yields for the final step.

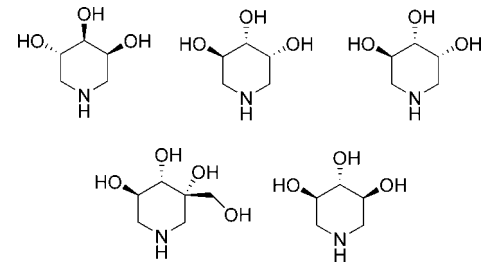
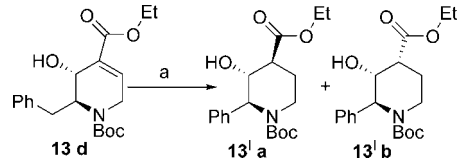


Figure 3. Some polyhydroxypiperidines.

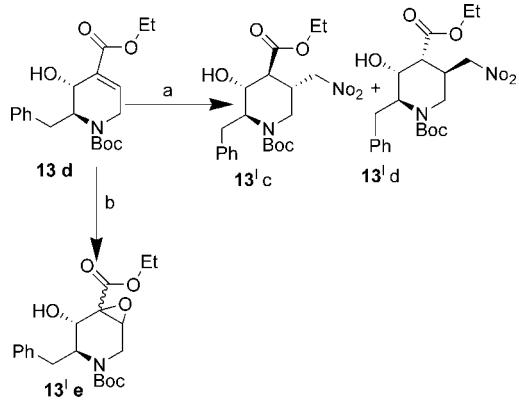
In an attempt to extend the utility, yet another protocol was conceived, wherein chiral dihydropiperidine **13d** (Scheme 4) was subjected to a Michael addition reaction[21] in the presence of CH_3NO_2, K_2CO_3, and TBAF at room temperature in THF to give a separable mixture of diastereomers **13′c** and **13′d**, and the same dihydropiperidine **13d** was converted to epoxide[21,22] (DBU, TBHP, DCE) to result in an inseparable mixture of diastereomeric product **13′e**. The high usefulness of the epoxide functionality need not be empha-

Scheme 3[a]



[a] (a) H_2, Pd/C, EtOAc, 8 h.

Scheme 4[a]



[a] (a) K_2CO_3, CH_3NO_2, TBAF, THF, 1 h. (b) DBU, TBHP, DCE, 5 h.

sized herein because it is prone to many ring-opening reactions with different nucleophiles to generate diverse libraries.

Conclusion

In conclusion, we have prepared a series of multifunctional adducts having an α-methylene-β-hydroxy-γ-amino acid structural motif by the Baylis−Hillman reaction of chiral *N*-Boc-α-aminoaldehydes with ethyl acrylate in good yields and diastereoselectivities. In order to attain maximum diversity, these adducts upon RCM reaction were converted into functionalized chiral tetrahydropyridines as potential analogues of isoguvacine; further, the same compounds upon cis-dihydroxylation resulted in stereochemically high diverse azasugars.

Experimental Section

Solvents were dried over standard drying agents and freshly distilled prior to use. ^{1}H NMR (200, 300, and 400 MHz) and ^{13}C NMR (50 and 75 MHz) spectra were measured with a Varian Gemini FT-200 MHz spectrometer, Bruker Avance 300 MHz, and Unity 400 MHz with tetramethylsilane (TMS) as the internal standard for solutions in deuteriochloroform. *J* values are given in hertz. IR spectra were recorded on a Perkin-Elmer IR-683 spectrophotometer with NaCl optics. Optical rotations were measured with a Jasco DIP 300 digital polarimeter at 25 °C. Mass spectra were recorded on CEC-21-11013 or Fannigan Mat 1210 double-focusing mass spectrometers operating at a direct inlet system. Organic solutions were dried over anhydrous Na_2SO_4 and concentrated below 40 °C in vacuo.

***tert*-Butyl *N*-Allyl-*N*-[(1*S*)-2-hydroxy-1-methylethyl]carbamate (10a).** A solution of compound *tert*-butyl *N*-allyl-*N*-((1*S*)-2-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-1-methylethyl)carbamate (**9a**; 1.0 g, 3.04 mmol) was treated with TBAF (4.56 mL, 1 M solution in THF) in THF at room temperature for 10 h. Then the solvent was removed under reduced pressure, and the residue was subjected to column chromatography (silica gel 60–120 mesh, *n*-hexane−EtOAc, 8.2:1.8) to afford the primary alcohol **10a** (0.60 g, 92%) as a thick yellow syrup. $[\alpha]_D = -44.05$ (*c* 0.8, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$, TMS): δ 5.78–5.71 (m, 1H), 5.16–5.04 (m, 2H), 3.96–3.92 (m, 1H), 3.78–3.70 (m, 2H), 3.51–3.59 (m, 2H), 1.43 (s, 9H), 1.14 (d, 3H, $J = 6.96$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 156.3, 137.7, 116.1, 79.9, 64.0, 63,0, 27.4, 17.0. IR (neat): 3456, 2973, 1677, 1447, 1170 cm^{-1}. ESIMS: *m*/*z* 316 $(M + H)^+$, 338 $(M + Na)^+$. Anal. Calcd for $C_{11}H_{21}NO_3$: C, 61.37; H, 9.83. Found: C, 61.30; H, 9.88.

***tert*-Butyl *N*-Allyl-*N*-[(1*S*)-2-hydroxy-1-methylethyl]carbamate (10b).** A solution of compound *tert*-butyl *N*-allyl-*N*-[(1*S*)-1-([1-(*tert*-butyl)-1,1-dimethylsilyl]oxymethyl)-2-methylpropyl]carbamate (**9b**; 1.0 g, 2.80 mmol) was treated with TBAF (4.20 mL, 1 M solution in THF) in THF at room temperature for 10 h. Then the reaction mixture was worked up and purified as described for **10a** to afford the product (silica gel 60–120 mesh, *n*-hexane−EtOAc, 8.4:1.6) **10b** (0.65 g, 95%) as a white syrup. $[\alpha]_D = -16.75$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$, TMS): δ 5.9–5.8 (m, 1H), 5.16–5.08 (m, 2H), 3.8–3.6 (m, 4H), 3.2–3.1 (m, 1H), 2.7 (br s, OH), 2.15–2.11 (m, 1H), 1.46 (s, 9H), 0.97 (d, 3H, $J = 7.03$ Hz), 0.89 (d, 3H, $J = 7.03$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 156.7, 135.1, 80.0, 65.6, 62.7, 49.5, 28.0, 26.0, 20.0, 19.2. IR (neat): 3447, 2970, 1689, 1455, 1365, 1171 cm^{-1}. ESIMS: *m*/*z* 244 $(M + H)^+$, 266 $(M + Na)^+$. Anal. Calcd for $C_{13}H_{25}NO_3$: C, 64.16; H, 10.36. Found: C, 64.18; H, 10.42.

***tert*-Butyl *N*-Allyl-*N*-[(1*S*,2*R*)-1-(hydroxymethyl)-2-methylbutyl]carbamate (10c).** A solution of compound *tert*-butyl *N*-allyl-*N*-[(1*S*,2*R*)-1-([1-(*tert*-butyl)-1,1-dimethylsilyl]-oxymethyl)-2-methylbutyl]carbamate (**9c**; 1.0 g, 2.70 mmol) was treated with TBAF (4.04 mL, 1 M solution in THF) in THF at room temperature for 12 h. Then the reaction mixture was worked up and purified as described for **10a** to afford the product (silica gel 60–120 mesh, *n*-hexane−EtOAc, 8.5:1.5) **10c** (0.64 g, 93%) as a pale-yellow syrup. $[\alpha]_D = -20.66$ (*c* 1.1, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$, TMS): δ 5.92–5.76 (m, 1H), 5.13 (dd, 2H, $J = 8.31$ and 15.10 Hz), 3.87–3.57(m, 3H), 3.17 (q, 1H, $J = 6.80$ Hz), 2.20–2.14 (m, 1H), 1.90–1.80 (m, 1H), 1.76–1.68 (m, 1H), 1.46 (s, 9H), 0.97 (t, 3H, $J = 6.80$ Hz), 0.89 (d, 3H, $J = 6.8$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 156.7, 135.3, 116.1, 79.9, 65.8, 63.5, 62.7, 57.7, 49.4, 28.2, 26.8, 20.1, 19.4, 18.4. IR (neat): 3449, 2970, 2932, 1670, 1456, 1365, 1173 cm^{-1}. ESIMS: *m*/*z* 280 $(M + Na)^+$. Anal. Calcd for $C_{14}H_{27}NO_3$: C, 65.33; H, 10.57. Found: C, 65.46; H, 10.61.

***tert*-Butyl *N*-Allyl-*N*-[(1*S*)-1-benzyl-2-hydroxyethyl]carbonate (10d).** A solution of compound *tert*-butyl *N*-allyl-*N*-((1*S*)-1-benzyl-2-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxyethyl)carbamate (**9d**; 1.0 g, 2.47 mmol) was treated with TBAF (4.04 mL, 1 M solution in THF) in THF at room temperature for 12 h. Then the reaction mixture was worked up and purified as described for **10a** to afford the product (silica gel 60–120 mesh, *n*-hexane−EtOAc, 8.0:20) **10c** (0.64 g,

90%) as a yellow syrup. $[\alpha]_D = -155.54$ (*c* 0.95, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$, TMS): δ 7.29–7.09 (m, 5H), 5.74–5.70 (m, 1H), 5.13–4.99 (m, 2H), 3.76–3.61 (m, 4H), 3.40 (br s, 1H), 3.05–2.87 (m, 1H), 1.43 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 156.1, 138.0, 135.0, 129.0, 128.0, 126.0, 116.0, 79.7, 63.6, 50.3, 28.0. IR (neat): 3441, 2975, 2927, 1688, 1454, 1365, 1169, 700 cm^{-1}. ESIMS: *m/z* 314 $(M + Na)^+$. Anal. Calcd for $C_{17}H_{25}NO_3$: C, 70.07; H, 8.65. Found: C, 70.01; H, 8.66.

General Procedure for Compounds 12a and 12a′. A solution of *tert*-butyl *N*-allyl-*N*-[(1*S*)-1-methyl-2-oxoethyl]-carbamate (**11a**; 1.0 g, 4.7 mmol) was treated with ethyl acrylate (1.02 mL, 9.39 mmol) and DABCO (0.63 g, 5.63 mmol) in sulfolane at room temperature for 50 h. Then the reaction reaction mixture was diluted with water (2 × 20 mL) and extracted with ether (2 × 30 mL). The combined organic layers were washed with brine (25 mL), dried (Na_2SO_4), and concentrated under reduced pressure to get a residue, which was purified by column chromatography (silica gel 60–120 mesh, *n*-hexane−EtOAc, 9.4:0.6) to afford the acrylates **12a** (0.86 g, 58.5%) and **12a′** (0.24 g, 16.5%) as thick yellow syrups.

Ethyl 2-{(1*R*,2*S*)-2-[Allyl(*tert*-butoxycarbonyl)amino]-1-hydroxypropyl}acrylate (12a). $[\alpha]_D = +1.82$ (*c* 1.86, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 6.26 (s, 1H), 5.96 (s, 1H), 5.84–5.71 (m, 1H), 5.14–5.05 (m, 2H), 4.60 (br d, 1H), 4.20 (q, 2H, J = 6.80 and 14.35 Hz), 3.86 (dd, 1H, J = 3.77 and 15.86 Hz), 3.66 (dd, 1H, J = 6.80 and 15.86 Hz), 3.52–3.48 (m, 1H), 1.43 (s, 9H), 1.31 (t, 3H, J = 6.80 Hz), 1.18 (d, 3H, J = 6.80 Hz). ^{13}C NMR (50 MHz, $CDCl_3$, TMS): δ 165.8, 155.7, 139.9, 134.4, 126.0, 115.7, 79.6, 73.6, 60.1, 57.3, 50.6, 29.1, 27.8, 13.6, 11.1. IR (neat): 3446, 2978, 2932, 1711, 1693, 1666, 1456, 1403, 1365, 1253, 1171, 1094, 1030, 914, 817, 773 cm^{-1}. ESIMS: *m/z* 314 $(M + H)^+$, 336 $(M + Na)^+$. Anal. Calcd for $C_{16}H_{27}NO_5$: C, 61.32; H, 8.68. Found: C, 61.28; H, 8.70.

Ethyl 2-{(1*S*,2*S*)-2-[Allyl(*tert*-butoxycarbonyl)amino]-1-hydroxypropyl}acrylate (12a′). $[\alpha]_D = -2.46$ (*c* 1.06, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 6.28 (s, 1H), 5.93 (s, 1H), 5.77–5.62 (m, 1H), 5.45 (br d, 1H, OH), 5.11–5.02 (m, 2H), 4.42 (q, 2H, J = 5.66 and 8.68 Hz), 4.20 (q, 2H, J = 6.80 and 13.98 Hz), 3.84–3.74 (m, 2H), 3.39 (dd, 1H, J = 7.17 and 15.29 Hz), 1.42 (s, 9H), 1.33 (t, 3H, J = 7.17 Hz), 1.24 (d, J = 7.17 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 166.0, 156.7, 141.6, 134.4, 125.2, 116.3, 80.1, 73.6, 60.3, 57.7, 51.9, 29.4, 28.1, 14.9, 13.9. IR (neat): 3439, 2980, 2936, 1714, 1698, 1657, 1467 1396, 1371, 1253, 1169, 1101, 1021, 894, 810 cm^{-1}. ESIMS: *m/z* 314 $(M + H)^+$, 336 $(M + Na)^+$. Anal. Calcd for $C_{16}H_{27}NO_5$: C, 61.32; H, 8.68. Found: C, 61.29; H, 8.60.

General Procedure for Compounds 12b and 12b′. A solution of *tert*-butyl *N*-allyl-*N*-[(1*S*)-1-formyl-2-methylpropyl]carbamate (**11b**; 1.0 g, 4.15 mmol) was treated with ethyl acrylate (0.90 mL, 8.30 mmol) and DABCO (0.56 g, 4.98 mmol) in sulfolane at room temperature for 48 h. Then the reaction mixture was worked up and purified as described for **12a** and **12a′** to afford the acrylates (silica gel 60–120 mesh, *n*-hexane−EtOAc, 9.5:0.5) **12b** (0.96 g, 68%) and **12b′** (0.17 g, 12%) as syrups.

Ethyl 2-(1*R*,2*S*)-2-[Allyl(*tert*-butoxycarbonyl)amino]-1-hydroxy-3-methylbutylacrylate (12b). $[\alpha]_D = +16.17$ (*c* 0.21, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$, TMS): δ 6.33 (s, 1H), 6.23 (d, 1H, J = 9.55 Hz), 5.96 (s, 1H), 5.60 (m, 1H), 5.00 (m, 2H), 4.71 (br dd, 1H, J = 1.47 and 8.81 Hz), 4.16 (m, 2H), 3.50 (dd, 2H, J = 7.35 and 10.29 Hz), 2.98 (dd, 1H, J = 2.94 and 10.29 Hz), 2.8–2.6 (m, 1H), 1.42 (s, 9H), 1.32 (t, 3H, J = 7.35 and 13.96 Hz), 1.10 (d, 3H, J = 6.61 Hz), 0.89 (d, 3H, J = 6.61 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 166.1, 142.4, 134.3, 125.5, 116.7, 80.6, 71.7, 70.5, 60.3, 56.6, 29.5, 26.5, 21.0, 20.1, 14.0. IR (neat): 3451, 3001, 1713, 1697, 1679, 1460, 1419, 1367, 1248, 1134, 1106, 917, 823, 767 cm^{-1}. ESIMS: *m/z* 342 $(M + H)^+$, 364 $(M + Na)^+$. Anal. Calcd for $C_{18}H_{31}NO_5$: C, 63.32; H, 9.15. Found: C, 63.26; H, 9.18.

Ethyl 2-(1*S*,2*S*)-2-[Allyl(*tert*-butoxycarbonyl)amino]-1-hydroxy-3-methylbutylacrylate (12b′). $[\alpha]_D = -6.93$ (*c* 0.39, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$, TMS): δ 6.15 (s, 1H), 5.94–5.71 (m, 1H), 5.58 (s, 1H), 5.11 (dd, 2H, J = 10.15, 17.96, and 1.56 Hz), 4.20 (q, 2H, J = 7.03 and 14.06 Hz), 3.73 (t, 1H, J = 6.25 and 10.94 Hz), 2.61 (dd, 2H, J = 2.34 and 9.37 Hz), 1.44 (s, 9H), 1.25 (d, 3H, J = 7.03 Hz), 1.31 (t, 3H, J = 7.03 Hz), 0.90 (d, 3H, J = 7.03 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 168.3, 147.9, 135.2, 120.0, 114.6, 80.6, 71.3, 68.2, 62.8, 54.9, 29.0, 24.3, 21.0, 20.9, 11.6. IR (neat): 3450, 3136, 2987, 1720, 1699, 1689, 1467, 1410, 1376, 1260, 1100, 813, 793 cm^{-1}. ESIMS: *m/z* 342 $(M + H)^+$, 364 $(M + Na)^+$. Anal. Calcd for $C_{18}H_{31}NO_5$: C, 63.32; H, 9.15. Found: C, 63.23; H, 9.31.

General Procedure for Compounds 12c and 12c′. A solution of *tert*-butyl *N*-allyl-*N*-[(1*S*,2*R*)-1-formyl-2-methylbutyl]carbamate (**11c**; 1.0 g, 3.92 mmol) was treated with ethyl acrylate (0.85 mL, 7.84 mmol) and DABCO (0.53 g, 4.70 mmol) in sulfolane at room temperature for 48 h. Then the reaction mixture was worked up and purified as described for **12a** and **12a′** to afford the acrylates (silica gel 60–120 mesh, *n*-hexane−EtOAc, 9.6:0.4) **12c** (0.88 g, 63.14%) and **12c′** (0.19 g, 13.86%) as light-yellow syrups.

Ethyl 2-(1*R*,2*S*,3*R*)-2-[Allyl(*tert*-butoxycarbonyl)amino]-1-hydroxy-3-methylpentylacrylate (12c). $[\alpha]_D = -48.92$ (*c* 4.00, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 6.34 (s,1H), 6.31 (d, 1H, J = 9.82 Hz), 5.96 (s, 1H), 5.60 (m, 1H), 4.99 (dd, 2H, J = 6.61, 10.57 Hz), 4.74 (d, 1H, J = 10.01 Hz), 4.19 (q, 2H, J = 7.17, 14.16 Hz), 3.57 (dd, 1H, J = 6.61, 15.48 Hz), 3.44 (dd, 1H, J = 6.04, 15.29 Hz), 3.10 (dd, 1H, J = 3.39, 10.95 Hz) 2.5 (m, 1H), 1.54 (m, 1H), 1.42 (s, 9H), 1.36–1.25 (m, 4H), 0.971 (dt, 3H, J = 1.13, 7.36 Hz), 0.88 (dd, 3H, J = 1.32, 6.80 Hz);^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 166.1, 157.3, 142.5, 134.3, 125.5, 116.6, 80.6, 70.6, 60.3, 50.6, 32.7, 28.1, 26.4, 15.8, 14.0, 11.2; IR (neat): 3445, 2972, 2931, 1711, 1692, 1664, 1459, 1403, 1367, 1254, 1163, 1074, 1029, 917, 818, 776 cm^{-1}; ESIMS: *m/z* 356 $(M+H)^+$, 378 $(M+Na)^+$; Anal. Calcd for $C_{19}H_{33}NO_5$: C, 64.20; H, 9.36. Found: C, 64.60; H, 9.44.

Ethyl 2-(1*S*,2*S*,3*R*)-2-[Allyl(*tert*-butoxycarbonyl)amino]-1-hydroxy-3-methylpentylacrylate (12c′). $[\alpha]_D = +95.00$ (*c* 5.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 6.33 (s, 1H), 6.26 (d, 1H, J = 9.82 Hz), 5.96 (s, 1H), 5.68–5.54 (m, 1H), 4.98–4.93 (m, 2H), 4.75 (dd, 1H, J = 2.26 and

9.06 Hz), 4.16 (q, 2H, J = 3.77 and 10.575 Hz), 3.58 (dd, 1H, J = 6.80 and 15.10 Hz), 3.38 (dd, 1H, J = 6.80 and 15.10 Hz), 3.06 (dd, 1H, J = 3.02 and 10.57 Hz), 2.45–2.43 (m, 1H), 1.46–1.44 (d, 2H, J = 4.53 Hz), 1.41 (s, 9H), 1.31 (t, 3H, J = 7.55 Hz), 1.06 (d, 3H, J = 6.80 Hz), 0.92 (t, 3H, J = 6.80 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 166.4, 157.8, 142.8, 135.6, 127.0, 119.9, 80.0, 72.1, 64.3, 51.5, 32.1, 28.6, 26.4, 13.1, 12.9, 10.7. IR (neat): 3444, 2969, 2929, 1691, 1660, 1457, 1400, 1367, 1258, 1161, 1074, 1028, 916, 800, 762 cm^{-1}. ESIMS: m/z 356 $(M + H)^+$, 378 $(M + Na)^+$. Anal. Calcd for $C_{19}H_{33}NO_5$: C, 64.20; H, 9.36. Found: C, 64.16; H, 9.38.

General Procedure for Compounds 12d and 12d′. A solution of *tert*-butyl *N*-allyl-*N*-[(1*S*)-1-formyl-3-phenylpropyl]carbamate (**11d**; 1.0 g, 3.46 mmol) was treated with ethyl acrylate (0.75 mL, 6.92 mmol) and DABCO (0.46 g, 4.15 mmol) in sulfolane at room temperature for 50 h. Then the reaction mixture was worked up and purified as described for **12a** and **12a′** to afford the acrylates (silica gel 60–120 mesh, *n*-hexane−EtOAc, 9.3:0.7) **12d** (0.767 g, 57%) and **12d′** (0.23 g, 17%) as thick yellow syrups.

Ethyl 2-(1*R*,2*S*)-2-[Allyl(*tert*-butoxycarbonyl)amino]-1-hydroxy-4-phenylbutylacrylate (12d). $[\alpha]_D$ = −3.30 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.21–7.10 (dd, 3H, J = 6.80 and 13.60 Hz), 7.02 (d, 2H, J = 6.80 Hz), 6.36 (s, 1H), 6.12 (s, 1H), 5.50 (br d, 1H), 5.22–5.09 (m, 1H), 4.87–4.76 (dd, 2H, J = 15.86 and 21.90 Hz), 4.24 (q, 2H, J = 7.55 and 14.35 Hz), 3.44 (dd, 2H, J = 7.55 and 15.86 Hz), 3.24 (dd, 1H, J = 12.84 and 24.17 Hz), 3.17 (d, 1H, J = 5.29 Hz), 2.72 (d, 1H, J = 10.57 Hz), 1.47 (s, 9H), 1.34 (t, 3H, J = 6.80 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 166.1, 156.4, 139.8, 139.1, 133.8, 129.1, 127.8, 126.6, 125.7, 115.9, 72.9, 73.9, 66.2, 60.3, 53.6, 30.6, 27.9, 13.6. IR (neat): 3447, 2978, 2929, 2400, 1710, 1662, 1457, 1168, 1081, 751, 700 cm^{-1}. ESIMS: m/z 390 $(M + H)^+$, 412 $(M + Na)^+$. Anal. Calcd for $C_{22}H_{31}NO_5$: C, 67.84; H, 8.02. Found: C, 67.89; H, 8.13.

Ethyl 2-(1*S*,2*S*)-2-[Allyl(*tert*-butoxycarbonyl)amino]-1-hydroxy-4-phenylbutylacrylate (12d′). $[\alpha]_D$ = +0.18 (c 0.95, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$, TMS): δ 7.25–7.13 (m, 5H), 6.31 (s, 1H), 5.97 (s, 1H), 5.22–5.05 (m, 1H), 4.87–4.80 (m, 2H), 4.52 (dd, 2H, J = 7.34 and 14.69 Hz), 4.22–4.05 (q, 2H, J = 7.34 and 14.69 Hz), 3.75–3.63 (m, 1H), 3.35–3.05 (m, 4H), 1.44 (s, 9H), 1.28 (t, 3H, J = 7.34 Hz). ^{13}C NMR (50 MHz, $CDCl_3$, TMS): δ 166.0, 157.0, 141.7, 138.7, 133.5, 129.1, 128.0, 126.0, 125.2, 116.5, 80.4, 71.9, 61.0, 60.1, 55.0, 35.1, 28.0, 13.8. IR (neat): 3447, 2978, 2929, 2400, 1710, 1662, 1457, 1168, 1081, 751, 700 cm^{-1}. ESIMS: m/z 390 $(M + H)^+$, 412 $(M + Na)^+$. Anal. Calcd for $C_{22}H_{31}NO_5$: C, 67.84; H, 8.02. Found: C, 67.81; H, 8.29.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*R*)-3-Hydroxy-2-methyl-1,2,3,6-tetrahydro-1,4-pyridinedicarboxylate (13a). A solution of **12a** (0.1 g, 0.32 mmol) and Grubbs' second-generation catalyst (0.027 g, 0.032 mmol) in dry toluene (60 mL) was stirred at reflux temperature for 20 h. Then the solvent was removed under reduced pressure, and the residue was subjected to chromatography (silica gel 60–120 mesh, *n*-hexane−EtOAc, 8.8:1.2) to afford **13a** (0.075 g, 83%) as a yellow syrup. $[\alpha]_D$ = −58.00 (c 0.15, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 6.98 (m, 1H), 4.57–4.46 (m, 2H), 4.32 (d, 1H, J = 4.34 Hz), 4.22 (q, 2H, J = 6.94 and 13.89 Hz), 3.66 (dd, 1H, J = 2.60 and 21.70 Hz), 2.31 (br d, OH), 1.48 (s, 9H), 1.33 (t, 3H, J = 6.94 and 13.89 Hz), 1.02 (d, 3H, J = 6.94 Hz). ^{13}C NMR (50 MHz, $CDCl_3$, TMS): δ 166.0, 155.2, 137.7, 132.1, 128.7, 80.5, 66.6, 0.95, 51.5, 40.2, 29.7, 28.3, 17.9, 15.19, 14.4. IR (neat): 3392, 2978, 2929, 1695, 1663, 1454, 1365, 1254, 1170, 1088, 961, 751, 701 cm^{-1}. ESIMS: m/z 284 $(M - H)^+$. Anal. Calcd for $C_{14}H_{23}NO_5$: C, 58.93; H, 8.12. Found: C, 59.01; H, 8.15.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*S*)-3-Hydroxy-2-methyl-1,2,3,6-tetrahydro-1,4-pyridinedicarboxylate (13a′). A solution of **12a′** (0.1 g, 0.32 mmol) and Grubbs' second-generation catalyst (0.027 g, 0.032 mmol) in dry toluene (60 mL) was stirred at reflux temperature for 22 h. Then the solvent was removed under reduced pressure, and the residue was purified by chromatography (silica gel 60–120 mesh, *n*-hexane−EtOAc, 8.7:1.3) to afford **13a** (0.073 g, 80%) as a yellow syrup. $[\alpha]_D$ = −4.24 (c 0.9, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$, TMS): δ 6.84 (m, 1H), 4.82–4.68 (m, 1H), 4.30–4.26 (m, 1H), 4.23 (q, 2H, J = 7.81 and 14.84 Hz), 4.16 (dd, 1H, J = 6.25 and 7.81 Hz), 3.60 (dd, 1H, J = 3.12 and 9.37 Hz), 1.46 (s, 1H), 1.33 (t, 1H, J = 7.03 Hz), 1.12 (d, 3H, J = 6.25 Hz). ^{13}C NMR (50 MHz, $CDCl_3$, TMS): δ 166.8, 155.1, 136.5, 131.0, 100.2, 96.1, 80.4, 68.2, 61.1, 57.8, 42.5, 32.0, 29.9, 28.3, 27.6, 22.9, 22.0, 20.1, 14.2. IR (neat): 3492, 2934, 2903, 1718, 1514, 1389, 1370, 1253, 1198, 983, 873, 786 cm^{-1}. ESIMS: m/z 308 $(M + Na)^+$. Anal. Calcd for $C_{14}H_{23}NO_5$: C, 58.93; H, 8.12. Found: C, 58.84; H, 8.23.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*S*)-3-Hydroxy-2-isopropyl-1,2,3,6-tetrahydro-1,4-pyridinedicarboxylate (13b′). A solution of **12b′** (0.1 g, 0.29 mmol) and Grubbs' second-generation catalyst (0.024 g, 0.029 mmol) in dry toluene (60 mL) was stirred at reflux temperature for 18 h. Then the solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel 60–120 mesh, *n*-hexane−EtOAc, 8.8:1.2) to afford **13b′** (0.075 g, 82%) as a yellow syrup. $[\alpha]_D$ = −54.20 (c 0.09, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$, TMS): δ 6.83 (m, 1H), 4.80–4.73 (m, 1H), 4.20 (q, 2H, J = 6.94 and 13.88 Hz), 4.16–4.10 (m, 2H), 3.69 (dd, 1H, J = 2.98 and 6.03 Hz), 1.45 (s, 9H), 1.32 (t, 3H, J = 7.34 Hz), 1.09 (d, 3H, J = 6.36 Hz), 0.83 (d, 3H, J = 6.36 Hz). IR (neat): 3449, 2976, 2930, 1692, 1699, 1457, 1366, 1297, 1250, 1078, 1051, 876, 761 cm^{-1}. ESIMS: m/z 314 $(M + H)^+$. Anal. Calcd for $C_{16}H_{27}NO_5$: C, 61.32; H, 8.65. Found: C, 61.27; H, 8.68.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*R*)-3-Hydroxy-2-isopropyl-1,2,3,6-tetrahydro-1,4-pyridinedicarboxylate (13b). A solution of **12b** (0.1 g, 0.28 mmol) and Grubbs' second-generation catalyst (0.024 g, 0.029 mmol) in dry toluene (60 mL) was stirred at reflux temperature for 18 h. Then the solvent was removed under reduced pressure, and the residue was purified by chromatography (silica gel 60–120 mesh, *n*-hexane−EtOAc, 9:1) to afford **13b** (0.074 g, 81%) as a yellow syrup. $[\alpha]_D$ = −0.53 (c 0.006, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$, TMS): δ 6.84 (m, 1H), 4.81–4.70 (m, 1H), 4.22 (q, 2H, J = 6.59 and 13.91 Hz), 4.18–4.11 (m, 2H), 3.7 (td, 1H, J = 2.93 and 5.86 Hz), 1.46 (s, 9H), 1.33 (t, 3H, J = 7.32 Hz), 1.12 (d, 3H, J = 6.59 Hz), 0.846 (d, 3H,

J = 6.59 Hz). ^{13}C NMR (50 MHz, $CDCl_3$, TMS): δ 166.5, 155.1, 136.1, 80.2, 67.0, 60.9, 57.5, 42.6, 31.8, 29.6, 28.2, 27.5, 22.5, 21.5, 20.1, 13.9. IR (neat): 3454, 2968, 2929, 1692, 1465, 1368,1299, 1241, 1170, 1133, 1086, 1049, 863, 770 cm^{-1}. ESIMS: m/z 314 $(M + H)^+$. Anal. Calcd for $C_{16}H_{27}NO_5$: C, 61.32; H, 8.65. Found: C, 61.29; H, 8.72.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*R*)-3-Hydroxy-2-[(1*R*)-1-methylpropyl]-1,2,3,6-tetrahydro-1,4-pyridinedicarboxylate (13c). A solution of **12c** (0.1 g, 0.28 mmol) and Grubbs' second-generation catalyst (0.024 g, 0.028 mmol) in dry toluene (60 mL) was stirred at reflux temperature for 22 h. Then the solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel 60–120 mesh, *n*-hexane−EtOAc, 9.2:1.8) to afford **13c** (0.075 g, 82%) as a yellow syrup. $[\alpha]_D = -7.22$ (c 0.815, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$, TMS): δ 6.84 (m, 1H), 4.819–4.687 (m, 1H), 4.32–4.08 (m, 4H), 3.71 (dd, 1H, J = 2.94 and 21.30 Hz), 1.91–1.71 (m, 1H), 1.46 (s, 9H), 1.41–1.25 (m, 4H), 1.05 (d, 2H, J = 6.61 Hz), 0.94– 0.82 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 166.0, 155.0, 136.2, 128.9, 127.1, 105.2, 84.6, 80.2, 71.5, 69.3, 66.7, 60.9, 60.1, 57.1, 55.7, 53.7, 41.4, 34.2, 28.2, 27.3, 16.8, 15.8, 14.2, 11.2, 0.9. IR (neat): 3469, 2987, 2938, 2645, 1696, 1660, 1471, 1414, 1368, 1277, 1163, 1079, 1029, 920, 807, 780 cm^{-1}. ESIMS: m/z 356 $(M + H)^+$, 378 $(M + Na)^+$. Anal. Calcd for $C_{17}H_{29}NO_5$: C, 62.36; H, 8.93. Found: C, 62.31; H, 8.80.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*S*)-3-Hydroxy-2-[(1*R*)-1-methylpropyl]-1,2,3,6-tetrahydro-1,4-pyridinedicarboxylate (13c′). A solution of **12c′** (0.1 g, 0.28 mmol) and Grubbs' second-generation catalyst (0.02 g, 0.028 mmol) in dry toluene (60 mL) was stirred at reflux temperature for 22 h. Then the solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel 60–120 mesh, *n*-hexane−EtOAc, 9:1) to afford **13c′** (0.072 g, 79%) as a yellow syrup. $[\alpha]_D = -17.06$ (c 5.6, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 6.83 (m, 1H), 4.80–4.74 (m, 1H), 4.29–4.19 (m, 3H), 4.14 (dd, 1H, J = 2.26 and 6.04 Hz), 3.70 (dd, 1H, J = 3.02 and 21.90 Hz), 1.87–1.80 (m, 1H), 1.46 (s, 9H), 1.43–1.41 (m, 1H), 1.33 (t, 3H, J = 7.55 Hz), 1.04 (d, 3H, J = 6.80 Hz), 0.90–0.84 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 166.3, 154.8, 136.1, 130.4, 80.0, 66.8, 60.8, 56.9, 42.7, 33.7, 28.1, 25.6, 16.6, 14.1, 11.0. IR (neat): 3482, 2971, 2932, 2876, 1693, 1456, 1401, 1368, 1296, 1245, 1169, 1087, 1023, 889, 864, 765 cm^{-1}. ESIMS: m/z 356 $(M + H)^+$, 378 $(M + Na)^+$. Anal. Calcd for $C_{17}H_{29}NO_5$: C, 62.36; H, 8.93. Found: C, 62.40; H, 8.91.

1-(*tert*-Butyl)4-Ethyl(2*S*,3*R*)-2-Benzyl-3-hydroxy-1,2,3,6-tetrahydro-1,4-pyridinedicarboxylate (13d). A solution of **12d** (0.1 g, 0.26 mmol) and Grubbs' second-generation catalyst (0.026 g, 0.022 mmol) in dry toluene (60 mL) was stirred at reflux temperature for 24 h. Then the solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel 60–120 mesh, *n*-hexane−EtOAc, 9:1) to afford **13d** (0.078 g, 84%) as a yellow crystalline solid. Mp: 135 °C. $[\alpha]_D = -0.54$ (c 3.34, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.27–7.08 (m, 5H), 6.98 (m, 1H), 4.75–4.39 (m, 3H), 4.23 (q, 2H,J = 7.55 and 14.35 Hz), 3.70 (d, 1H, J = 21.90 Hz), 2.57 (dd, 1H, J = 5.29 and 13.60 Hz), 2.47 (dd, 1H, J = 9.82 and 13.60 Hz), 1.33 (t, 3H, J = 6.80 Hz), 1.21 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 165.6, 155.1, 137.9, 136.4, 131.7, 128.9, 128.3, 80.0, 64.8, 60.9, 58.2, 56.2, 40.3, 29.5, 27.8, 14.0. IR (KBr): 3448, 2975, 2926, 1716, 1680, 1404, 1255, 1106, 758 cm^{-1}. ESIMS: m/z 384 $(M + Na)^+$. Anal. Calcd for $C_{20}H_{27}NO_5$: C, 66.46; H, 7.83. Found: C, 66.39; H, 7.88.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*S*)-2-Benzyl-3-hydroxy-1,2,3,6-tetrahydro-1,4-pyridinedicarboxylate (13d′). A solution of **12d′** (0.1 g, 0.26 mmol) and Grubbs' second-generation catalyst (0.026 g, 0.022 mmol) in dry toluene (60 mL) was stirred at reflux temperature for 24 h. Then the solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel 60–120 mesh, *n*-hexane−EtOAc, 7.5:2.5) to afford **13d′** (0.078 g, 84%) as a yellow syrup. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.27–7.13 (m, 5H), 6.95–6.90 (m, 1H), 4.74–4.69 (m, 2H), 4.49–4.34 (m, 1H), 4.25 (q, 2H, J = 6.99 and 13.97 Hz), 3.76 (dd, 1H, J = 3.88 and 20.96 Hz), 3.11 (m, 1H), 2.35 (dd, 1H, J = 11.46 and 13.97 Hz), 1.36 (t, 3H, J = 6.99 Hz), 1.10 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 166.4, 154.0, 138.7, 136.1, 129.2, 128.1, 125.9, 79.8, 65.6, 61.0, 54.4, 40.4, 30.6, 29.5, 27.7, 14.0. IR (neat): 3467, 2986, 2929, 1709, 1683, 1439, 746 cm^{-1}. ESIMS: m/z 384 $(M + Na)^+$. Anal. Calcd for $C_{20}H_{27}NO_5$: C, 66.46; H, 7.83. Found: C, 66.48; H, 7.81.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*S*,4*S*,5*S*)-3,4,5-Trihydroxy-2-methylhexahydro-1,4-pyridinedicarboxylate (14a). To a solution of **13a** (0.1 g, 0.35 mmol) in acetone−water (1.6:1) was added a 5% OsO_4 solution in toluene (0.18 mL, 0.035 mmol). After 15 min, an aqueous 50% NMMO solution (0.178 mL, 0.035) was added, and the mixture was stirred for 32 h. To the solution were added Na_2SO_3 and Na_2SO_4, and then the mixture was filtered through a Celite pad and the filterate was evaporated and extracted with ethyl acetate (2 × 15 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure to get a residue, which was subjected to chromatography (silica gel 60–120 mesh, *n*-hexane−EtOAc, 6.5:3.5) to afford the **14a** (0.106 g, 94%) single diastereomer as a thick yellow syrup. $[\alpha]_D = -1.76$ (c 1.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 4.27 (q, 2H, J = 7.41 and 14.82 Hz), 4.06 (dd, 1H, J = 3.02 and 6.04 Hz), 3.70–3.63 (m, 2H), 3.60–3.53 (m, 2H), 3.45 (t, 1H, J = 6.04 Hz), 1.25 (s, 9H), 0.93 (t, 3H, J = 7.55 Hz), 0.86 (d, 3H, J = 6.80 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 173.9, 157.6, 82.3, 77.5, 74.9, 66.7, 60.4, 53.3, 46.1, 28.3, 12.9, 11.9. IR (neat): 3423, 2919, 2854, 1726, 1696 1367,1247, 1679, 1100, 1077, 869, 778 cm^{-1}. ESIMS: m/z 318 $(M - H)^+$, 342 $(M + Na)^+$. Anal. Calcd for $C_{14}H_{25}NO_7$: C, 52.65; H, 7.89. Found: C, 52.68; H, 7.83.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*R*,4*R*,5*R*)-3,4,5-Trihydroxy-2-methylhexahydro-1,4-pyridinedicarboxylate (14a′). To a solution of **13a′** (0.1 g, 0.35 mmol) in acetone−water (1.6:1) was added a 5% OsO_4 solution in toluene (0.18 mL, 0.035 mmol). After 15 min, an aqueous 50% NMMO solution (0.164 mL, 0.035) was added and the mixture was stirred for 36 h. Then the reaction mixture was worked up

and purified as described for **14a** to afford the **14a′** (silica gel 60–120 mesh, *n*-hexane−EtOAc, 6:4) single diastereomer (0.104 g, 92%) as a thick yellow syrup. $[\alpha]_D = -1.76$ (*c* 1.5, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$, TMS): δ 4.27 (q, 2H, $J = 7.45$ and 14.15 Hz), 4.14–4.06 (m, 2H), 3.93 (d, 1H, $J = 4.47$ Hz), 3.62–3.61 (m, 2H), 1.45 (s, 9H), 1.35 (t, 3H, $J = 7.45$ Hz), 1.23 (d, 3H, $J = 7.45$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 173.4, 156.5, 80.3, 75.5, 72.9, 67.4, 62.4, 51.0, 44.7, 28.3, 13.8, 13.0. IR (neat): 3395, 2925, 2854, 1729, 1691, 1367, 1250, 1168, 1098, 1066, 1026, 863, 768 cm^{-1}. ESIMS: *m*/*z* 318 $(M - H)^+$, 342 $(M + Na)^+$. Anal. Calcd for $C_{14}H_{25}NO_7$: C, 52.65; H, 7.89. Found: C, 52.71; H, 7.92.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*S*,4*S*,5*S*)-3,4,5-Trihydroxy-2-isopropylhexahydro-1,4-pyridinedicarboxylate (14b). To a solution of **13b** (0.1 g, 0.32 mmol) in acetone−water (1.6:1) was added a 5% OsO_4 solution in toluene (0.162 mL, 0.032 mmol). After 15 min, an aqueous 50% NMMO solution (0.149 mL, 0.64) was added and the mixture was stirred for 40 h. Then the reaction mixture was worked up and purified as described for **14a** to afford the **14b**(silica gel 60–120 mesh, *n*-hexane−EtOAc, 6:4) single diastereomer (0.104 g, 95%) as a thick yellow syrup. $[\alpha]_D = -10.19$ (*c* 1.91, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$, TMS): δ 4.28 (q, 2H, $J = 7.34$ and 13.96 Hz), 4.15 (m, 1H), 4.02 (m, 1H), 3.71 (dd, 1H, $J = 5.14$ and 14.69 Hz), 3.50 (m, 2H), 3.35 (br d, OH), 3.31 (br d, OH), 2.35 (br d, OH), 1.46 (s, 9H), 1.36 (t, 3H, $J = 7.34$ Hz), 0.97–0.94 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$, TMS): δ 174.6, 158.9, 80.6, 75.6, 70.7, 67.9, 62.6, 47.3, 28.2, 26.4, 20.4, 20.0, 14.0. IR (neat): 3434, 2987, 1721, 1653, 1460, 1412, 1368, 1098, 878, 799 cm^{-1}. ESIMS: *m*/*z* 370 $(M + Na)^+$. Anal. Calcd for $C_{16}H_{29}NO_7$: C, 55.32; H, 8.41. Found: C, 55.27; H, 8.42.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*R*,4*R*,5*R*)-3,4,5-Trihydroxy-2-isopropylhexahydro-1,4-pyridinedicarboxylate (14b′). To a solution of **13b′** (0.1 g, 0.32 mmol) in acetone−water (1.6:1) was added a 5% OsO_4 solution in toluene (0.162 mL, 0.032 mmol). After 15 min, an aqueous 50% NMMO solution (0.149 mL, 0.64) was added and the mixture was stirred for 38 h. Then the reaction mixture was worked up and purified as described for **14a** to afford the **14b′** (silica gel 60–120 mesh, *n*-hexane−EtOAc, 5.8:4.2) single diastereomer (0.099 g, 90%) as a thick yellow syrup. $[\alpha]_D = +32.18$ (*c* 0.07, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$, TMS): δ 4.30 (q, 2H, $J = 6.98$ and 13.97 Hz), 4.14 (br s, 1H), 4.03 (t, 1H, $J = 5.26$ Hz), 3.72 (dd, 1H, $J = 5.20$ and 13.89 Hz), 3.47 (m, 2H), 3.42 (br d, OH), 3.29 (br d, OH), 2.35 (br d, OH), 1.46 (s, 9H), 1.36 (t, 3H, $J = 6.98$ Hz), 0.98–0.93 (m, 6H). IR (neat): 3434, 2967, 1721, 1664, 1458, 1423, 1336, 942, 812 cm^{-1}. ESIMS: *m*/*z* 370 $(M + Na)^+$. Anal. Calcd for $C_{16}H_{29}NO_7$: C, 55.32; H, 8.41. Found: C, 55.34; H, 8.46.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*S*,4*S*,5*S*)-3,4,5-Trihydroxy-2-[(1*R*)-1-methylpropyl]hexahydro-1,4-pyridinedicarboxylate (14c). To a solution of **13c** (0.1 g, 0.306 mmol) in acetone−water (1.6:1) was added a 5% OsO_4 solution in toluene (0.15 mL, 0.030 mmol). After 15 min, an aqueous 50% NMMO solution (0.142 mL, 0.61) was added and the mixture was stirred for 40 h. Then the reaction mixture was worked up and purified as described for **14a** to afford the **14c** (silica gel 60–120 mesh, *n*-hexane−EtOAc, 5.5:4.5) single diastereomer (0.097 g, 88%) as a white solid. Mp: 120 °C. $[\alpha]_D = -29.35$ (*c* 0.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 4.31 (q, 2H, $J = 6.80$ and 14.35 Hz), 4.17 (br s, 1H), 4.04 (br s, 1H), 3.73 (td, 1H, $J = 4.52$ and 9.05 Hz), 3.51 (br s, 2H), 3.41 (br s, OH), 3.378 (br s, OH), 2.29–2.15 (m, 1H), 1.46 (s, 9H), 1.36 (t, 3H, $J = 6.80$ Hz), 1.18–1.06 (m, 1H), 0.96–0.88 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 174.6, 159.1, 81.0, 68.3, 62.8, 61.3, 47.5, 32.3, 28.5, 26.1, 16.1, 14.2, 10.7. IR (KBr): 3460, 2923, 2924, 1726, 1688, 1423, 1364, 1251, 1171, 1066, 1026, 854, 802 cm^{-1}. ESIMS: *m*/*z* 362 $(M + H)^+$, 384 $(M + Na)^+$. Anal. Calcd for $C_{17}H_{31}NO_7$: C, 56.49; H, 8.65. Found: C, 56.44; H, 8.67.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*R*,4*R*,5*R*)-3,4,5-Trihydroxy-2-[(1*R*)-1-methylpropyl]hexahydro-1,4-pyridinedicarboxylate (14c′). To a solution of **13c′** (0.1 g, 0.306 mmol) in acetone−water (1.6:1) was added a 5% OsO_4 solution in toluene (0.15 mL, 0.030 mmol). After 15 min, an aqueous 50% NMMO solution (0.142 mL, 0.61) was added and the mixture was stirred for 38 h. Then the reaction mixture was worked up and purified as described for **14a** to afford the **14c′** (silica gel 60–120 mesh, *n*-hexane−EtOAc, 5.2:4.8) single diastereomer (0.1 g, 91%) as a thick yellow syrup. $[\alpha]_D = +47.38$ (*c* 1.7, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 4.31 (q, 2H, $J = 6.94$ and 13.89 Hz), 4.15 (d, 1H, $J = 3.47$ Hz), 4.06 (t, 1H, $J = 5.20$ Hz), 3.75 (dd, 1H, $J = 5.20$ and 13.89 Hz), 3.36 (dd, 2H, $J = 5.20$ and 13.89 Hz), 2.25–2.10 (m, 1H), 1.59–1.46 (m, 1H), 1.15–1.00 (m, 1H), 1.46 (s, 9H), 1.36 (t, 3H, $J = 6.94$ Hz), 0.94 (t, 6H, $J = 6.94$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 174.7, 158.9, 80.6, 75.7, 71.1, 67.9, 62.6, 61.3, 47.6, 32.3, 28.5, 25.9, 16.2, 14.0, 11.2. IR (neat): 3442, 2968, 2929, 1721, 1663, 1456, 1416, 1367, 1255, 1165, 1072, 1031, 864, 798 cm^{-1}. ESIMS: *m*/*z* 362 $(M + H)^+$, 384 $(M + Na)^+$. Anal. Calcd for $C_{17}H_{31}NO_7$: C, 56.49; H, 8.65. Found: C, 56.41; H, 8.70.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*S*,4*S*,5*S*)-2-Benzyl-3,4,5-trihydroxyhexahydro-1,4-pyridinedicarboxylate (14d). To a solution of **13d** (0.1 g, 0.259 mmol) in acetone−water (1.6:1) was added a 5% OsO_4 solution in toluene (0.13 mL, 0.026 mmol). After 15 min, an aqueous 50% NMMO solution (0.121 mL, 0.52 mmol) was added and the mixture was stirred for 43 h. Then the reaction mixture was worked up and purified as described for **14a** to afford the **14d** (silica gel 60–120 mesh, *n*-hexane−EtOAc, 6.0:4.0) single diastereomer (0.105 g, 97%) as a white syrup. $[\alpha]_D = -0.39$ (*c* 1.82, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 7.30–7.14 (m, 5H), 4.29 (q, 2H, $J = 7.55$ Hz), 4.14–4.05 (m, 2H), 3.85 (dd, 1H, $J = 5.28$ and 12.84 Hz), 3.69–3.56 (m, 2H), 3.53 (br s, 1H, OH), 3.02–3.00 (m, 2H), 1.25 (s, 9H), 0.88 (t, 3H, $J = 6.78$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 173.1, 155.4, 137.9,129.3, 128.3, 126.3, 80.36, 74.6, 71.9, 69.5, 65.5, 62.7, 59.6, 57.9, 40.79, 39.5, 35.8, 31.9, 29.6, 14.1. IR (neat): 3425, 2899, 1726, 1683, 1401, 1283, 1079, 801 cm^{-1}. ESIMS: *m*/*z* 396 $(M + H)^+$, 418 $(M + Na)^+$. Anal. Calcd for $C_{17}H_{31}NO_7$: C, 60.74; H, 7.39. Found: C, 60.82; H, 7.50.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*R*,4*R*,5*R*)-2-Benzyl-3,4,5-trihydroxyhexahydro-1,4-pyridinedicarboxylate (14d′). To a solution of **13d′** (0.1 g, 0.259 mmol) in acetone−water (1.6:1) was added a 5% OsO_4 solution in toluene (0.13 mL, 0.026 mmol). After 15 min, an aqueous 50% NMMO solution (0.121 mL, 0.52 mmol) was added and the mixture was stirred for 40 h. Then the reaction mixture was worked up and purified as described for **14a** to afford the **14d′** (silica gel 60–120 mesh, *n*-hexane−EtOAc, 6.2:3.8) single diastereomer (0.99 g, 92%) as a light-yellow syrup. $[\alpha]_D = +0.66$ (*c* 0.87, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.25–7.10 (m, 5H), 4.28 (q, 2H, $J = 7.55$ Hz), 4.15 (dt, 1H, $J = 4.53$ and 7.55 Hz), 4.06 (t, 1H, $J = 3.77$ Hz), 3.92 (d, 1H, $J = 4.53$ Hz), 3.75 (d, 1H, $J = 3.77$ Hz), 3.44 (br s, 1H, OH), 2.98 (m, 2H), 1.36 (s, 9H), 1.31 (t, 3H, $J = 6.80$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 173.6, 156.6, 138.7, 129.2, 128.2, 126.1, 80.2, 75.2, 70.7, 67.9, 62.4, 57.1, 44.56, 32.9, 29.6, 28.0, 13.9. IR (neat): 3309, 2980, 2946, 1710, 1398, 1246, 1087, 755 cm^{-1}. ESIMS: *m*/*z* 396 $(M + H)^+$, 418 $(M + Na)^+$. Anal. Calcd for $C_{17}H_{31}NO_7$: C, 60.74; H, 7.39. Found: C, 60.88; H, 7.51.

General Procedure for Compounds 13′a and 13′b. To a solution of **13d** (0.1 g, 0.277 mmol) in ethyl acetate (1 mL) was added 10% Pd−C under a hydrogen atmosphere, and the mixture was stirred for 8 h. Then the reaction mixture was filtered through a Celite pad, and the filterate was evaporated under reduced pressure to obtain a residue, which was subjected to chromatography (silica gel 60–120 mesh, *n*-hexane−EtOAc, 6.4:3.6) to afford the separable diastereomers **13′a**(0.06 g, 70%) and **13′b** (0.025 g, 70%).

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*R*,4*S*)-2-Benzyl-3-hydroxyhexahydro-1,4-pyridinedicarboxylate (13′a). $[\alpha]_D = +11.08$ (*c* 0.75, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$, TMS): δ 7.32–7.10 (m, 5H), 4.27–4.06 (m, 4H), 4.06–3.76 (br dd, 1H, $J = 6.49$ and 14.28 Hz), 3.08–2.87 (m, 1H), 2.76–2.73 (d, 2H, $J = 6.49$ Hz), 2.67–2.60 (m, 1H), 2.10–1.90 (m, 1H), 1.89–1.76 (m, 1H), 1.33 (t, 3H, $J = 7.79$ Hz), 1.25 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 173.5, 155.5, 137.9, 130.9, 129.3, 129.0, 128.5, 126.4, 123.1, 118.8, 79.9, 69.2, 67.2, 60.9, 59.8, 58.7, 43.4, 41.3, 37.4, 35.9, 35.1, 31.9, 29.6, 28.1, 22.0, 14.1. LCMS: *m*/*z* 386 $(M + Na)^+$. Anal. Calcd for $C_{20}H_{29}NO_5$: C, 66.09; H, 8.04. Found: C, 66.20; H, 7.98.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*R*,4*R*)-2-Benzyl-3-hydroxyhexahydro-1,4-pyridinedicarboxylate (13′b). $[\alpha]_D = +36.11$ (*c* 0.83, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$, TMS): δ 7.33–7.16 (m, 1H), 4.45–4.32 (m, 2H), 4.20–4.07 (q, 2H, $J = 7.79$ Hz), 4.01–3.87 (m, 1H), 3.24 (q, 1H, $J = 9.09$ Hz), 2.88–2.83 (m, 1H), 2.38–2.31 (m, 1H), 1.33 (s, 9H), 1.24 (t, 3H, $J = 9.09$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 172.7, 155.0, 136.9, 130.1, 129.4, 128.5, 127.0, 123.3, 119.0, 80.4, 69.1, 62.9, 61.5, 52.8, 44.7, 42.5, 39.6, 36.6, 33.8, 33.0, 31.9, 29.6, 28.2, 22.7, 14.3. LCMS: *m*/*z* 386 $(M + Na)^+$. Anal. Calcd for $C_{20}H_{29}NO_5$: C, 66.09; H, 8.04. Found: C, 66.12; H, 8.16.

General Procedure for Compounds 13′c and 13′d. To a solution of **13d** in THF was added nitromethane (0.017 g, 0.28 mmol) followed by K_2Co_3 (0.008 g, 0.067 mL) and TBAF (0.07 mL, 0.07 mmol), and the reaction mixture was stirred at room temperature for 1 h. Then the reaction reaction mixture was diluted with water (2 × 5 mL) and extracted with ethyl acetate (2 × 10 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure to get a residue, which was purified by column chromatography (silica gel 60–120 mesh, *n*-hexane−EtOAc, 8.4:1.6) to afford the diastereomers **13′c** (0.0122 g, 55%) and **13′d** (0.01 g, 45%).

1-(*tert*-Butyl) 4-ethyl (2*S*,3*R*,4*S*,5*S*)-2-benzyl-3-hydroxy-5-(nitromethyl)hexahydro-1,4-pyridinedicarboxylate (13′c). $[\alpha]_D = -2.92$ (*c* 0.7, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$, TMS): δ 7.35–7.06 (m, 5H), 4.82 (dd, 1H, $J = 9.97$ and 14.54 Hz), 4.72–4.61 (m, 1H), 4.47 (dd, 1H, $J = 14.95$ and 23.68 Hz), 4.22 (q, 2H, $J = 7.06$ Hz), 4.16–4.02 (m, 2H), 3.21–3.04 (br d, 2H, $J = 14.12$ Hz), 2.90 (br s, 1H), 2.77 (d, 2H, $J = 8.31$ Hz), 1.34 (s, 9H), 1.30 (t, 3H, $J = 4.98$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 172.1, 155.0, 137.2, 129.2, 128.3, 126.8, 68.5, 61.8, 46.4, 38.4, 35.6, 34.3, 29.7, 28.2, 14.0. IR (neat): 3432, 2975, 2928, 1731, 1676, 1550, 1423, 1369, 1169 cm^{-1}. ESIMS: *m*/*z* 445 $(M + Na)^+$. Anal. Calcd for $C_{21}H_{30}N_2O_7$: C, 59.70; H, 7.16. Found: C, 59.72; H, 7.15.

1-(*tert*-Butyl) 4-Ethyl (2*S*,3*R*,4*R*,5*R*)-2-Benzyl-3-hydroxy-5-(nitromethyl)hexahydro-1,4-pyridinedicarboxylate (13′d). $[\alpha]_D = -62.11$ (*c* 1.1, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$, TMS): δ 7.33–7.08 (m, 5H), 4.70–4.53 (m, 1H), 4.43 (dd, 1H, $J = 4.78$ and 13.96 Hz), 4.23 (q, 2H, $J = 7.34$ Hz), 4.15 (dd, 2H, $J = 5.87$ and 11.85 Hz), 3.82 (d, 1H, $J = 14.32$ Hz), 3.01–2.72 (m, 5H), 1.37 (s, 9H), 1.29 (d, 3H, $J = 7.34$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 172.6, 156.0, 137.3, 129.5, 128.1, 125.9, 70.0, 61.7, 47.1, 38.2, 34.4, 29.7, 28.0, 15.4. IR (neat): 3430, 2930, 2927, 1735, 1675, 1545, 1423, 1370,1162 cm^{-1}. ESIMS: *m*/*z* 423 $(M + H)^+$, 445 $(M + Na)^+$. Anal. Calcd for $C_{21}H_{30}N_2O_7$: C, 59.70; H, 7.16. Found: C, 59.77; H, 7.34.

3-(*tert*-Butyl) 5a-Ethyl (1a*S*,4*S*,5*S*,5a*R*)-4-Benzyl-5-hydroxyperhydrooxireno[2,3-*c*]pyridine-3,5a-dicarboxylate (13′e). To a dichloroethane solution of **13d** (0.01 g, 0.027mmol) was added a solution of DBU (0.005 mL, 0.033 mmol) and *t*-BuOOH at 0 °C. The reaction mixture was stirred at room temperature for 5 h. Then the reaction mixture was diluted with chloroform (2 × 5 mL) and water (1 × 5 mL) was added, followed by the addition of sodium metasulfite, stirring for 20 min, and then extraction with chloroform (2 × 10 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure to get a residue, which was purified by column chromatography (silica gel 60–120 mesh, *n*-hexane−EtOAc, 8.4:1.6) to afford the inseparable diastereomers (0.006 g, 57.5%) as a semisolid. $[\alpha]_D = -2.92$ (*c* 0.7, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$, TMS): δ 7.34–7.08 (m, 5H), 4.87 (dd, 0.4H, $J = 7.89$ and 23.26 Hz), 4.70 (dd, 0.6H, $J = 4.98$ and 9.55 Hz), 4.32 (q, 2H, $J = 7.06$ Hz), 4.20 (q, 1H, $J = 7.06$ Hz), 4.12–4.05 (m, 1H), 3.34 (br s, OH), 3.03 (dd, 1H, $J = 5.40$ and 13.71 Hz), 2.92–2.70 (m, 1H), 2.56 (dd, 2H, $J = 8.31$ and 12.88 Hz), 1.52 (s, 9H), 1.41 (t, 1.2H, $J = 8.31$ Hz), 1.30 (t, 3H, $J = 10.30$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ 170.2, 146.3, 131.8, 129.4, 128.8, 127.0, 62.1, 61.2, 41.3, 39.1, 28.0, 14.0. IR (neat): 3447, 2970, 1689, 1455, 1365, 1171 cm^{-1}.

ESIMS: *m*/*z* 400 $(M + Na)^+$. Anal. Calcd for $C_{20}H_{27}NO_6$: C, 63.64; H, 7.21. Found: C, 63.68; H, 7.19.

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