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Access to *anti* or *syn* 2-amino-1,3-diol scaffolds from a common decarboxylative aldol adduct

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ABSTRACT: A straightforward synthetic pathway allowing the access to *anti* or *syn* 2-amino-1,3-diol scaffolds is presented. The strategy relies on a diastereoselective organocatalyzed decarboxylative aldol reaction of a *N*-Boc-hemimalonate that is easily formed from commercial *N*-Boc-diethyl malonate. Although this method has been optimized previously with the *N*-Bz-hemimalonate analogue, this key step was reinvestigated with the *N*-Boc derivative to improve the required reaction time, the yield and the diastereoselectivity. The new conditions enhance this transformation, and quantitative yields and *anti*/*syn* ratios up to 96 : 4 can be obtained. The *anti* aldol product was easily isolated in pure form, then taken forward as the key precursor in the preparation of both a set of ten *N*-/*O*-alkylated *anti* 2-amino-1,3-diol derivatives and the *syn* congeners.

INTRODUCTION

The 2-amino-1,3-diol scaffold (Figure 1) is important in organic synthesis, and it is found in the structure of many biologically active products (for example sphingosine, sphinganine and chloramphenicol)[1] as well as in chiral inductors for various enantioselective reactions.[2] Considering its most popular fragment, which has two vicinal stereogenic centers (and a primary alcohol), the *anti* and *syn* stereoisomers are found in an almost equivalent frequency over the multitude of applications, which is why methods for accessing both configurations individually need to be studied equally.

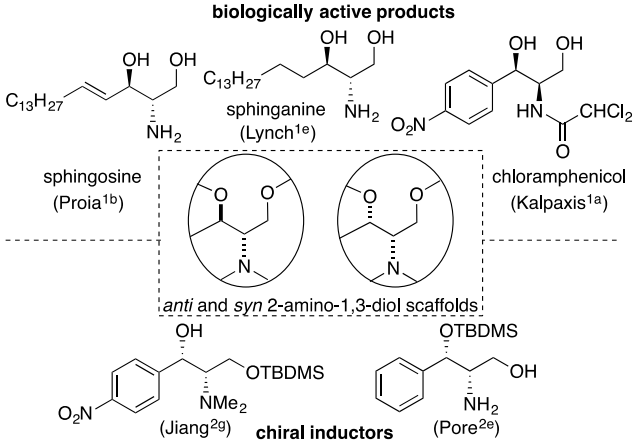
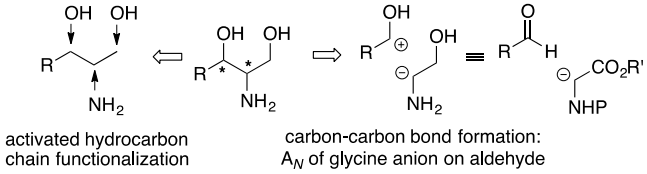


Figure 1. Targets incorporating the 2-amino-1,3-diol scaffold.

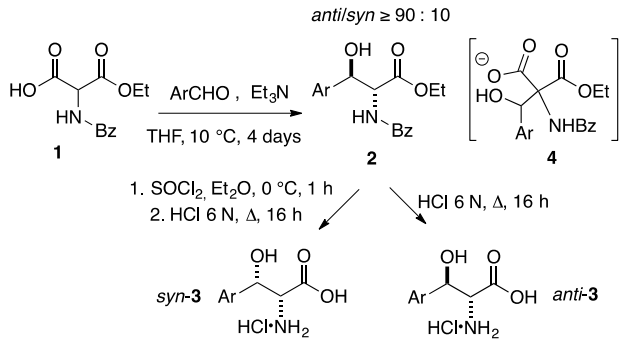
Overall, two main synthetic strategies are used to prepare these scaffolds. One consists of adding the required functional groups (*i.e.*, alcohol and amino groups) with the correct stereochemistry to a predefined carbon backbone (Scheme 1, left).[3] This strategy encompasses numerous methodologies to append a vicinal aminoalcohol moiety with a good control of the relative or absolute stereochemistry. However, its main limitation is the lack of flexibility inherent to linear syntheses, and which often require more steps than a convergent synthesis. The second approach involves the creation of the bond between the two stereogenic centers from molecular fragments bearing functional precursors of the required alcohol and amino groups (Scheme 1, right). In this context, the methodology with the highest potential involves the nucleophilic addition of a glycine anion equivalent to an aldehydes.[4] Thus, in a single step one can control the stereochemistry of the stereocenters and build an advanced scaffold containing the target 2-amino-1,3-diol motif from readily available and inexpensive precursors.[5] The main parameters that still require improvement are the diastereoselectivity (by simplifying or avoiding tedious purification steps), the nature of some reagents (solvent and base), and the operating conditions and cost.

Scheme 1. General retrosynthetic strategies for the synthesis of 2-amino-1,3-diol moieties.



In this paper, we present a simple synthetic method that follows the second strategy, and the method provides either *anti* or *syn* 2-amino-1,3-diol-substituted derivatives. The approach takes advantage of a methodology recently developed in a laboratory of our consortium, *i.e.*, a diastereoselective organocatalyzed decarboxylative aldol reaction.[6,7] Indeed, in a pioneering work from 2013, Rouden's group reported a stereoselective synthesis of *anti* or *syn* *β*-hydroxy-*α*-aminoacids (**3**, Scheme 2) under mild conditions from various aromatic aldehydes and *N*-Bz-hemimalonate **1**. The reaction mechanism followed an original aldol/decarboxylation sequence *via* characterized intermediate **4** (Scheme 2) and this reaction provided almost exclusively the *anti* stereoisomer of aldol adduct **2** (*anti*/*syn* ≥ 90:10).[6]

Scheme 2. Synthesis of *anti* or *syn* β-hydroxy-α-aminoacids **3** *via* a decarboxylative aldol reaction of *N*-Bz-hemimalonate **1**.[6]



Carrying out the reduction of the residual carbonyl group, either from **2** (CO_2Et) or **3** (CO_2H) is an elegant subsequent step for efficiently and stereoselectively accessing *anti* 2-amino-1,3-diol compounds. Otherwise, the *syn* analogues should be accessible by means of the stereoinversion of one of the carbon atoms of the *anti* aldol product. We report here the results obtained following this plan.

RESULTS AND DISCUSSION

To easily vary the *N*-substitution of the final 2-amino-1,3-diol derivatives (NH_2, NHMe and NHBn), we selected *N*-Boc-hemimalonate (**6**, Scheme 3) as the starting material instead of *N*-Bz **1**. Indeed, a Boc protecting group is more flexible than a benzamido appendage for accessing a wider variety of derivatives from a common substrate.

Thus, **6** was isolated in 79% yield following a monosaponification of commercially available *N*-Boc-malonate **5** with KOH (Scheme 3). The decarboxylative aldol reaction was then carried out on **6** in the presence of benzaldehyde **7a** first with the conditions originally used with **1** (Table 1, entry 1).[6] After 5 days of reaction, expected adduct **8a** was obtained in a satisfactory yield (59%) but with a disappointing diastereoselectivity (*anti*/*syn* 75:25). To improve the diastereoselectivity when using **6**, the conditions of this key step had to be re-examined (Table 1).

Scheme 3. Diastereoselective decarboxylative aldol reaction from *N*-Boc-hemimalonate **6**.

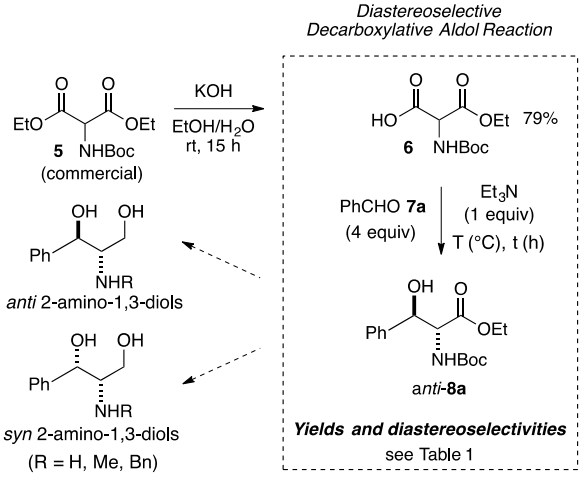


Table 1. Optimization of the diastereoselective decarboxylative aldol reaction of **6**.

Entry	Solvent	T (°C)	t (h)	yield (%)[a]	*anti*/*syn*[b]
1	THF	10	5 days	59	75:25
2	none	10	5 days	79	90:10
3	none	30	48	100	92:8
4	none	40	48	100	91:9
5	**none**	**50**	**48**	**100**	**96:4**
6	none	60	48	81	79:21

[a]Yield determined by ^{1}H NMR with 1,3,5-trimethoxybenzene as an internal standard. [b]NMR ratio measured on the crude product.

We first examined the influence of the solvent by removing THF and performing the reaction neat at 10 °C. Interestingly, after 5 days (entry 2), both the yield and the diastereoselectivity were improved (79% and 90:10, respectively). We decided to focus on the effect of increasing the temperature from 30 °C to 60 °C (entries 3 to 6) in the absence of solvent and when limiting the reaction time to 48 h. Pleasingly, the completion of the reaction and formation of the desired product could be observed with a very good 96:4 *anti*/*syn* diastereoselectivity at 50°C. Working at a higher temperature (60 °C, entry 7) did not improve the reaction outcome. The optimal reaction conditions defined with **6**, *i.e.*, no solvent, 48 h, and 50 °C, were thus used to assess the scope of this new procedure on a set of twelve aldehydes (**7b** to **7m**, Scheme 4, Table 2).

Scheme 4. Scope of the decarboxylative aldol reaction of **6** and X-ray structure of *anti*-**8c**.

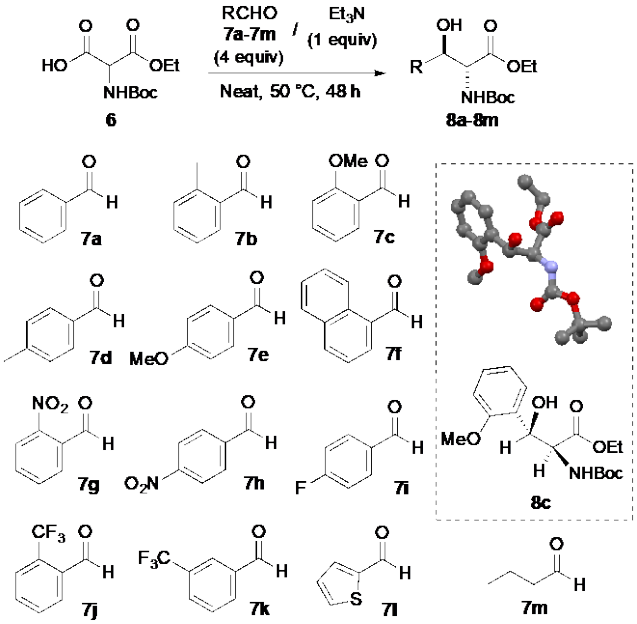


Table 2. Scope of the diastereoselective decarboxylative aldol reaction of **6**.

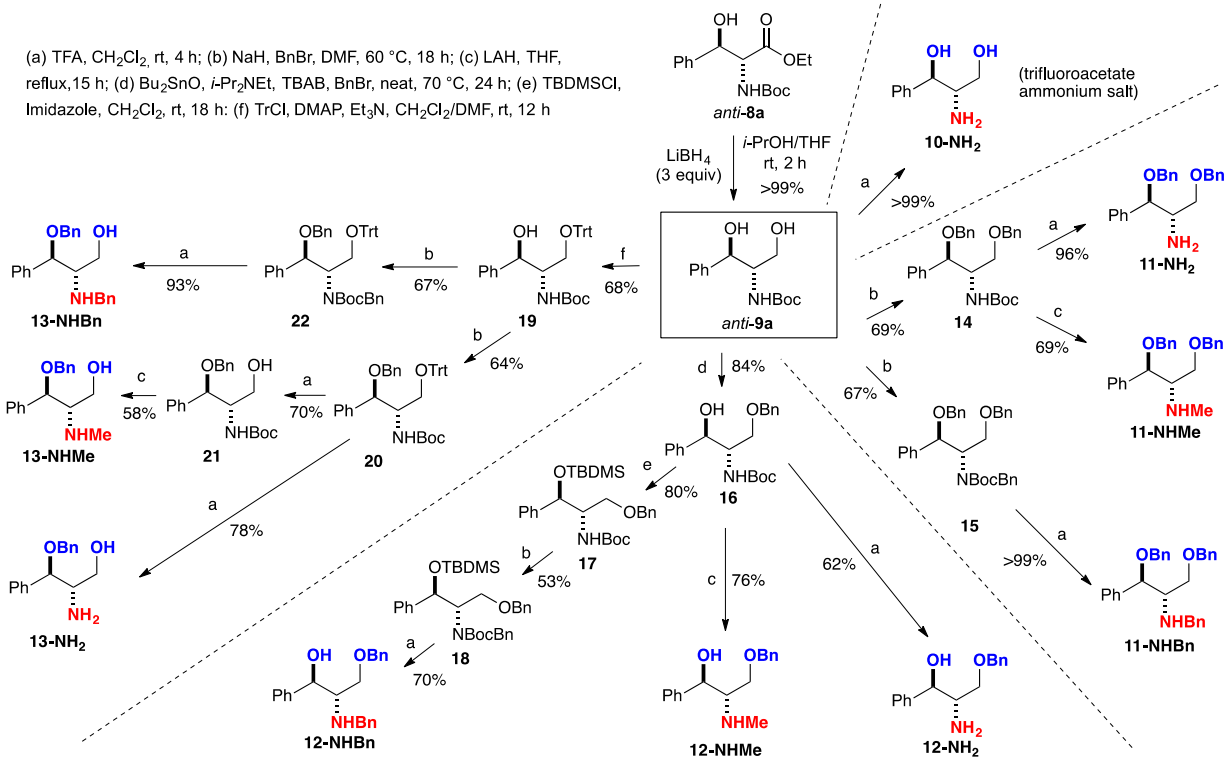
Entry	Aldehyde	Product : yield (%)[a]	*anti*/*syn*[b]
1	**7a**	**8a** : 100 (96)	96:4
2	**7b**	**8b** : 55 (46)	91:9
3	**7c**	**8c** : 73 (70)	95:5
4	**7d**	**8d** : 65 (55)	86:14
5	**7e**	**8e** : 56 (49)	89:11
6	**7f**	**8f** : 54 (39)	85:15
7	**7g**	**8g** : 100 (87)	88:12
8	**7h**[c]	**8h** : 98 (86)	87:13
9	**7i**	**8i** : 97 (70)	88:12
10	**7j**	**8j** : 94 (76)	83:17
11	**7k**	**8k** : 95 (66)	86:14
12	**7l**	**8l** : 100 (73)	87:13
13	**7m**	**8m** : 50 (38)	76:24

[a]Yield determined by ^{1}H NMR with 1,3,5-trimethoxybenzene as the internal standard. Between parentheses: isolated yield of the *anti* isomer. [b]NMR ratio measured on the crude product. [c]Diluted in 0.3 mL of THF.

Aldehydes with an *ortho* electron-donating substituent (methyl: **7b**, entry 2 and methoxy: **7c**, entry 3) provided the expected aldol products (**8b** and **8c**) with excellent diastereoselectivities (≥ 91:9). The moderate yields can be explained on the basis of the electron-donating effects as well as steric considerations. Placing the electron-donating group further away (**7d**/**8d** and **7e**/**8e**, entries 4 and 5) may lead to an improvement in the yield (a gain of approximately 10% yield is observed involving *para*-tolualdehyde instead of its *ortho* congener, entry 4 *versus* entry 2), but a slight decrease in the diastereoselectivity, with an average of a 87:13 *anti*/*syn* ratio, is observed regardless of the substituent. Working with α-naphthaldehyde (**7f**, entry 6) provided comparable results. Excellent yields are obtained with electron-withdrawing substituents as seen with NO_2, F and CF_3 (entries 7 to 11), and the products were generated with an average *anti*/*syn* ratio of 87:13 regardless of the position of the substituent (*ortho*, *meta* or *para*). Expanding the scope to non-benzaldehyde substrates such as thiophene-2-carbaldehyde **7l** and butyraldehyde **7m** (entries 12 and 13) confirmed the feasibility of the reaction as satisfactory yields and *anti*/*syn* ratios were obtained. Note that the *anti* and *syn* stereoisomers of all compounds **8** of this series were easily separated by column chromatography, and the *anti* stereoselectivity could be confirmed thanks to crystallographic data obtained from a single-crystal of **8c** (Scheme 4).

With these optimized conditions in hand, we turned our attention to our main objective; stereoselectively preparing *anti* and *syn* 2-amino-1,3-diol species. Compound *anti*-**8a** was chosen as model the compound to serve as a common precursor of both diastereomers (Scheme 3). Regarding the *anti* amino-diols series, carrying out the reduction of the ethyl ester group of *anti*-**8a** to generate the 1,3-diol appendage was the most obvious and direct method. Thus, *anti*-**8a** was reacted with excess $LiBH_4$, which quantitatively led to *N*-Boc-1,3-diol *anti*-**9a** (Scheme 5).

Scheme 5. Synthesis of 2-amino-1,3-diols *anti* derivatives **9** to **13**.



At this point, we can draw our first conclusion: *N*-Boc-protected 2-amino-1,3-diol *anti*-**9a** can be synthesized in only 3 steps from inexpensive commercially available reagents under very mild conditions in 72% overall yield. To apply this chemistry, functional group manipulations were conducted on *anti*-**9a**, which led to four sets of *anti* compounds, namely, 2-amino-1,3-diol **10**, 2-amino-1,3-diethers **11** and 2-amino-1,3-etheralcohols **12** and **13**. All transformations and yields are summarized in Scheme 5.

2-Amino-1,3-diol compound **10-NH$_2$** could be prepared from *anti*-**9a** by quantitatively removing the Boc group using trifluoroacetic acid (TFA). Thus, *anti*-**10-NH$_2$** was isolated as the trifluoroacetate ammonium salt in four synthetic steps from *N*-Boc-malonate **5** in 66% overall yield.

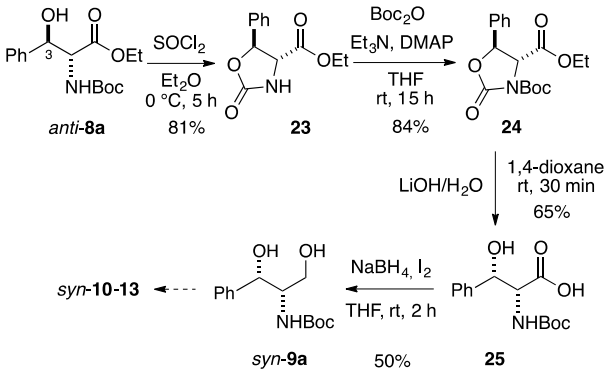
Reaching the diethereal analogues **11-NH$_2$** and **11-NHMe** required two synthetic steps from *anti*-**9a**: a dibenzylation of both hydroxy groups with NaH and BnBr (**14**) followed by either a Boc deprotection with TFA to form **11-NH$_2$** (66% yield from **9a**) or a reduction of the Boc in the presence of lithium aluminum hydride (LAH) to obtain **11-NHMe** (48% yield from **9a**). *N*-Benzyl congener **11-NHBn** was accessible through a tribenzylation of *anti*-**9a**, *i.e.*, both OH groups plus the NHBoc (**15**), followed by the addition of TFA to remove the Boc group (67% yield from **9a**). The three *anti* 2-amino-1,3-diethers **11-NH$_2$**, **11-NHMe** and **11-NHBn** were thus isolated in five synthetic steps from **5** in 50%, 36% and 53% overall yields, respectively.

The regioselective monobenzylation reactions of either the primary or the secondary alcohol (compounds *anti*-**12** and *anti*-**13**, respectively) were more tedious. The regiospecific benzylation of the primary alcohol of *anti*-**9a** was cleanly achieved *via* a cyclic dialkoxytin intermediate (Bu_2SnO, *i*-Pr_2NEt, TBAB and BnBr, **16**), affording **12-NH$_2$** in 52% yield from **9a** after amino deprotection with TFA. Compound **12-NHMe** was synthesized in 64% yield from **9a** using the same monobenzylation strategy followed by an LAH reduction of the Boc group. Preparing **12-NHBn** (25% yield from **9a**) required an additional protection of the secondary OH by a TBDMS group (**17**), enabling the *N*-benzylation of the NHBoc moiety (**18**) and a global deprotection with TFA (removal of TBDMS and Boc groups). Thus, aminoalcohols **12-NH$_2$** and **12-NHMe** were isolated in five synthetic steps from **5** in 40% and 50% overall yields, respectively, and seven steps were necessary to generate **12-NHBn** in 20% overall yield.

An initial regioselective protection of the primary OH was achieved with a trityl group (**19**) in the synthesis of compounds **13**. Benzylation reactions were next carried out with either one equivalent or excess BnBr to afford the OBn (monobenzylated **20**) or the OBn-N(Bn)Boc (dibenzylated **22**) synthetic intermediates, respectively. A double cleavage of the trityl and Boc groups with a large excess of TFA converted the monobenzylated intermediate into **13-NH$_2$** in 34% yield from **9a**, while **13-NHMe** was obtained after the selective removal of the trityl moiety in the presence of only three equivalents of TFA (**21**) followed by the LAH reduction of the Boc group to a methyl substituent. Compound **13-NHMe** was thus isolated in 18% yield from **9a**. Compound **13-NHBn** was produced in 42% yield from **9a** by reacting the trityl dibenzylated species mentioned earlier (**22**) with a large excess of TFA. All three compounds **13-NH$_2$**, **13-NHMe** and **13-NHBn** were synthesized from **5** in six or seven synthetic steps in 27%, 14% and 33% overall yields, respectively.

The second aim of this work was to also access *syn* 2-amino-1,3-diol derivatives, thus we investigated the stereoinversion of one of the stereogenic carbon atom of *anti*-**8a**. The strategy involved anchimeric assistance from the *N*-Boc protecting group (Scheme 6).[8]

Scheme 6. Synthesis of *syn*-**9a** from *anti*-**8a**



Reacting *anti*-**8a** with thionyl chloride in Et_2O at 0 °C for five hours enabled the complete stereochemical inversion of C^3 by forming oxazolidinone **23** in 81% yield. To avoid epimerization of **23** during hydrolysis of the oxazolidinone ring in a strong acidic solution, we used an alternative route developed by Davies.[9] Thus, compound **23** was first converted into *N*-Boc oxazolidinone **24** in 84% yield, and then treatment of the latter by an aqueous LiOH solution led to *N*-Boc β-hydroxyacid **25** in 65% yield. Reduction of the acidic group of **25** with $NaBH_4$ allowed the isolation of *syn*-**9a** in 50% yield. In summary, *syn*-**9a**, the putative precursor of the *syn* congeners of compounds **10** to **13** in Scheme 4, is easily accessible from *anti*-**8a** in four synthetic steps.

CONCLUSION

In conclusion, we report in this paper a rapid and flexible strategy diastereoselectively leading to either the *anti* or *syn* 2-amino-1,3-diol scaffolds. The strategy is based on a diastereoselective organocatalyzed[10] decarboxylative aldol reaction from inexpensive commercially available *N*-Boc-aminomalonate. The main intermediate, the *N*-Boc protected 2-amino-1,3-diol, was synthesized in only 3 steps in a 72% overall yield from commercially available inexpensive reagents. Moreover, the reaction conditions for the key reaction, *i.e.*, the decarboxylative aldol reaction, are very mild and simple (no strong base, no low or high temperature, no solvent, and operationally simple reaction, work up and purification). This very short preparation of 2-amino-1,3-diol is arguably one of the most efficient methods described to date in the literature. As an application, subsequent chemical transformations of the *anti* aldol adduct allowed the isolation of ten *anti* 2-amino-1,3-diol derivatives in two to five steps in good yields. An appropriate stereoinversion on the same *anti* aldol adduct *via* neighboring group participation was also cleanly achieved, which allowed the synthesis of *syn* congeners. As part of our continuing interest in the use of main group metal nucleophiles in enantioselective addition reactions,[11] we plan

to develop an enantioselective version of the strategy depicted in this work and then use the obtained compounds as chiral ligands for organometallics such as organolithium, magnesium or zinc.[11a] Beyond this project, we believe that our methodology for the synthesis of the priviledged scaffold, *i.e.*, 2-amino-1,3-diol, combines all the properties (rapid, mild, operationally simple, selective and inexpensive) that make a process very attractive to the organic and medicinal chemistry communities.

EXPERIMENTAL SECTION

General details. All reagents were purchased from Acros Organics, Sigma Aldrich, Alfa Aesar, TCI or Fluka and were used without further purification. RPE grade solvents were used as received. Anhydrous solvents were obtained from a PURESOLV SPS400 apparatus developed by Innovative Technology Inc. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX 300 MHz or a Bruker DRX 400 MHz spectrometer. Samples were dissolved in a deuterated solvent that was deuteriochloroform ($CDCl_3$) with a calibration at 7.26 ppm for ^{1}H spectra and 77.16 ppm for ^{13}C spectra, tetradeuteromethanol (CD_3OD) with a calibration at 3.31 ppm for ^{1}H spectra and 49.00 ppm for ^{13}C spectra or deuterium oxide (D_2O) with a calibration at 4.79 ppm for ^{1}H spectra. The chemical shifts (δ) are expressed in ppm and coupling constants are indicated in Hz. Abbreviations for signal coupling are as follows: s = singlet; d = doublet; dd = doublet of doublets; t = triplet; dt = doublet of triplets; q = quartet; quin = quintet; m = multiplet; br = broad signal. Additional 2D NMR experiments (COSY, HSQC, HMBC) and NOESY experiments were performed to ensure correct structural determination. Mass spectra were obtained on a GC/MS Saturn 2000 spectrometer. High-resolution mass spectra (HRMS) were performed on Q-TOF Micro WATERS by electrospray ionisation (ESI). Infrared (IR) spectra were recorded with a Perkin Elmer 16 PC FT-IR ATR spectrometer. Pre-coated aluminium plates of silica gel 60 F-254 (Merck) were used to perform Thin Layer Chromatography (TLC). Flash chromatography was performed on silica gel column (Merck silica gel, 40-63 μm) using air pressure.

Experimental procedures and characterization data.

2-[(Tert-butoxycarbonyl)amino]-3-ethoxy-3-oxopropanoic acid (or N-Boc-hemimalonate) ***6***. A solution of KOH (2.2 g, 39.2 mmol) in distillated water (8.6 mL) was added dropwise to a solution of diethyl(boc-amino)malonate **5** (10 mL, 39.2 mmol) in ethanol (87 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 15 h. Ethanol was evaporated then the crude was extracted with diethyl ether (3×20 mL) to avoid the presence of starting material or decarboxylation product. A 1 M HCl aqueous solution was added dropwise until pH = 1, then the mixture was saturated with NaCl and extracted with ethyl acetate (3×15 mL). The organic layers were combined, dried over $MgSO_4$ and, after filtration, the solvents were removed under reduced pressure. The N-Boc-hemimalonate **6** was obtained without further purification with the 79% yield (7.68 g, 31.2 mmol) as a white solid. The characterization data of **6** (presence of two rotamers) are identical to those reported in the literature.[12] ^{1}H ($CDCl_3$, 400 MHz) δ 11.85 (bs, 1H), 7.73/5.64 (d, J = 4.5 Hz, 1H), 4.98/4.76 (d, J = 7.5 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 1.44/1.42 (s, 9H), 1.30 (t, J = 7.1 Hz, 3H); ^{13}C ($CDCl_3$, 100 MHz) δ 170.0/168.4, 166.7/166.6, 156.8/155.3, 82.8/81.4, 63.0/62.4, 58.8/57.5, 28.2 (3C), 14.2.

General procedure for the decarboxylative aldolisation. After mixing the *N*-Boc-hemimalonate **6** with triethylamine and aldehyde **7**, the reaction mixture was stirred for 48 hours at 50 °C. The reaction mixture was then concentrated and the residue was purified by flash chromatography on silica gel (pentane/ethyl acetate 90:10) to afford compound **8** *anti*.

*Ethyl 2-[(tert-butoxycarbonyl)amino]-3-hydroxy-3-phenylpropanoate anti-****8a***. Triethylamine (17 μL, 0.122 mmol) then benzaldehyde **7a** (50 μL, 0.488 mmol) were added to **6** (30 mg, 0.122 mmol) according to the general procedure above. After purification, compound *anti*-**8a** was isolated with the 96% yield (36 mg, 0.117 mmol) as a white solid. The characterization data of *anti*-**8a** are identical to those reported in the literature.[13] ^{1}H ($CDCl_3$, 300 MHz) δ 7.36-7.28 (m, 5H), 5.28 (d, J = 6.4 Hz, 1H), 5.20 (m, 1H), 4.70 (m, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.95 (d, J = 5.8 Hz, 1H), 1.43 (s, 9H), 1.19 (t, J = 7.1 Hz, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 169.9, 156.6, 139.4, 128.4 (2C), 128.1, 126.2 (2C), 80.8, 75.3, 61.9, 59.9, 28.4 (3C), 14.1.

*Ethyl 2-[(tert-butoxycarbonyl)amino]-3-hydroxy-3-(o-tolyl) propanoate anti-****8b***. Triethylamine (34 μL, 0.244 mmol) then *o*-tolualdehyde **7b** (113 μL, 0.976 mmol) were added to **6** (60 mg, 0.244 mmol) according to the general procedure. After purification, compound *anti*-**8b** (presence of two rotamers) was isolated with the 46% yield (36 mg, 0.112 mmol) as a white solid. m.p. 96-98 °C; ^{1}H ($CDCl_3$, 300 MHz) δ 7.39-7.36 (m, 1H), 7.20-7.12 (m, 3H), 5.46-5.44 (m, 1H), 5.30-5.25 (m, 1H), 4.57-4.53 (m, 1H), 4.13-3.96 (m, 2H), 3.25 (br, 1H), 2.37 (s, 3H), 1.44/1.43 (s, 9H), 1.06 (t, J = 7.1 Hz, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 170.6, 155.6, 137.6, 135.1, 130.6, 127.9, 126.0 (2C), 80.5, 71.8, 61.5, 58.1, 28.4 (3C), 19.2, 13.9; IR (ATR) ν (cm^{-1}) 3504, 3379, 2979, 2856, 2113, 1699; HRMS (ESI) *m/z* calculated for $C_{17}H_{26}NO_5$ $[M+H]^+$ 324.1811, found 324.1813.

*Ethyl 2-[(tert-butoxycarbonyl)amino]-3-hydroxy-3-(2-methoxy phenyl)propanoate anti-****8c***. Triethylamine (34 μL, 0.244 mmol) then *o*-anisaldehyde **7c** (118 μL, 0.976 mmol) were added to **6** (60 mg, 0.244 mmol) according to the general procedure. After purification, compound *anti*-**8c** was isolated with the 70% yield (58 mg, 0.171 mmol) as a yellowish solid. The characterization data of *anti*-**8c** are identical to those reported in the literature.[14] ^{1}H ($CDCl_3$, 300 MHz) δ 7.32-7.23 (m, 2H), 6.97-6.92 (m, 1H), 6.87-6.83 (m, 1H), 5.37-5.34 (m, 1H), 5.31-5.22 (m, 1H), 4.69-4.66 (m, 1H), 4.19-4.03 (m, 2H), 4.01-3.97 (m, 1H), 3.81 (s, 3H), 1.37/1.31 (s, 9H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 171.4, 170.8, 156.4, 156.0, 129.0, 127.6, 120.8, 110.3, 80.2, 71.9, 61.4, 58.8, 55.5, 28.4 (3C), 14.1.

*Ethyl 2-[(tert-butoxycarbonyl)amino]-3-hydroxy-3-(p-tolyl) propanoate anti-****8d***. Triethylamine (34 μL, 0.244 mmol) then *p*-tolualdehyde **7d** (115 μL, 0.976 mmol) were added to **6** (60 mg, 0.244 mmol) according to the general procedure. After purification, compound *anti*-**8d** was isolated with the 55% yield (43 mg, 0.134 mmol) as a white solid (presence of two rotamers). m.p. 91-93 °C; ^{1}H ($CDCl_3$, 300 MHz) δ 7.17-7.07 (m, 4H), 5.30-5.27 (m, 1H), 5.18-5.13 (m, 1H), 4.68-4.65 (m, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.98 (bs, 1H), 2.33 (s, 3H), 1.45/1.43 (s, 9H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 170.0, 156.5, 137.8, 136.3, 129.0 (2C), 126.1 (2C), 80.7, 75.1, 61.8, 59.9, 28.4 (3C), 21.2, 14.1; IR (ATR) ν (cm^{-1}) 3476, 3335, 2969, 2932, 1725, 1679, 1519, 1160; HRMS (ESI) *m/z* calculated for $C_{17}H_{26}NO_5$ $[M+H]^+$ 324.1811, found 324.1796.

*Ethyl 2-[(tert-butoxycarbonyl)amino]-3-hydroxy-3-(4-methoxy phenyl)propanoate anti-**8e***. Triethylamine (34 μL, 0.244 mmol) then *p*-anisaldehyde **7e** (119 μL, 0.976 mmol) were added to **6** (60 mg, 0.244 mmol) according to the general procedure. After purification, compound *anti*-**8e** was isolated with the 49% yield (41 mg, 0.120 mmol) as a white solid (presence of two rotamers). m.p. 109-111 °C; ^{1}H ($CDCl_3$, 300 MHz) δ 7.29-7.17 (m, 2H), 6.87-6.83 (m, 2H), 5.28-5.26 (m, 1H), 5.16-5.09 (m, 1H), 4.65-4.64 (m, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.93 (bs, 1H), 3.79 (s, 3H), 1.43/1.35 (s, 9H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 171.1/170.0, 159.5, 156.5, 131.4, 127.4 (2C), 113.8 (2C), 80.7, 74.8, 61.8, 59.9, 55.4, 28.4 (3C), 14.2; IR (ATR) ν (cm^{-1}) 3567, 3364, 2986, 2928, 1742, 1689, 1510; HRMS (ESI) *m/z* calculated for $C_{17}H2_6NO_6$ $[M + H]^+$ 340.1760, found 340.1753.

*Ethyl 2-[(tert-butoxycarbonyl)amino]-3-hydroxy-3-(naphtha len-1-yl)propanoate anti-**8f***. Triethylamine (34 μL, 0.244 mmol) then 1-naphthaldehyde **7f** (133 μL, 0.976 mmol) were added to **6** (60 mg, 0.244 mmol) according to the general procedure. After purification, compound *anti*-**8f** was isolated with the 39% yield (34 mg, 0.095 mmol) as a white solid (presence of two rotamers). m.p 151-153 °C; ^{1}H ($CDCl_3$, 300 MHz) δ 8.17 (d, *J* = 8.6 Hz, 1H), 7.87 (d, *J* = 8.6 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.64-7.44 (m, 4H), 5.95-5.86 (m, 1H), 5.53-5.51 (m, 1H), 4.82-4.80 (m, 1H), 4.00-3.90 (m, 2H), 3.44-3.43 (m, 1H), 1.46/1.43 (s, 9H), 0.96 (t, *J* = 7.1 Hz, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 170.2, 155.8, 135.3, 133.7, 130.6, 129.0, 128.7, 126.6, 125.8, 125.2, 123.9, 122.9, 80.6, 71.7, 61.5, 59.0, 28.4 (3C), 13.8; IR (ATR) ν (cm^{-1}) 3454, 3371, 2973, 2928, 1699, 1516; HRMS (ESI) *m/z* calculated for $C_{20}H_{26}NO_5$ $[M+H]^+$ 360.1811; found 360.1810.

*Ethyl 2-[(tert-butoxycarbonyl)amino]-3-hydroxy-3-(2-nitro phenyl)propanoate anti-**8g*** Triethylamine (34 μL, 0.244 mmol) then *o*-nitrobenzaldehyde **7e** (148 mg, 0.976 mmol) in THF (0.3 mL) were added to **6** (60 mg, 0.244 mmol) according to the general procedure. After purification, compound *anti*-**8g** was isolated with the 87% yield (75 mg, 0.212 mmol) as a yellowish oil (presence of two rotamers). ^{1}H ($CDCl_3$, 300 MHz) *δ* 7.96 (d, *J* = 8.1 Hz, 1H), 7.82 (d, *J* = 7.3 Hz, 1H), 7.67-7.62 (m, 1H), 7.49-7.43 (m, 1H), 5.78-5.71 (m, 1H), 5.32 (d, *J* = 8.2 Hz, 1H), 4.69-4.64 (m, 1H), 4.30-4.10 (m, 3H), 1.4321.37 (s, 9H), 1.28-1.13 (m, 3H); ^{13}C ($CDCl_3$, 75 MHz) *δ* 170.5, 155.9, 148.2, 135.3, 133.4, 129.5, 128.9, 124.7, 80.8, 70.6, 62.1, 59.2, 30.4/28.3 (3C), 14.0; IR (ATR) ν (cm^{-1}) 3424, 2979, 2954, 1691, 1525, 1344; HRMS (ESI) *m/z* calculated for $C_{16}H_{23}N_2O_7$ $[M+H]^+$ 355.1505, found 355.1500.

*Ethyl 2-[(tert-butoxycarbonyl)amino]-3-hydroxy-3-(4-nitro phenyl)propanoate anti-**8h*** Triethylamine (34 μL, 0.244 mmol) then *p*-nitrobenzaldehyde **7f** (148 mg, 0.976 mmol) in THF (0.3 mL) were added to **6** (60 mg, 0.244 mmol) according to the general procedure. After purification, compound *anti*-**8h** was isolated with the 86% yield (74 mg, 0.207 mmol) as a white solid. The characterization data of *anti*-**8h** are identical to those reported in the literature.[6] ^{1}H ($CDCl_3$, 300 MHz) *δ* 8.19-8.17 (m, 2H), 7.47-7.44 (m, 2H), 5.37-5.32 (m, 2H), 4.69-4.68 (m, 1H), 4.48 (d, *J* = 5.3 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.44 (s, 9H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C ($CDCl_3$, 75 MHz) *δ* 169.0, 156.8, 147.7, 147.0, 127.2 (2C), 123.5 (2C), 81.4, 74.9, 62.4, 60.1, 28.3 (3C), 14.2.

*Ethyl 2-[(tert-butoxycarbonyl)amino]-3-(4-fluorophenyl)-3-hydroxypropanoate anti-**8i***. Triethylamine (34 μL, 0.244 mmol) then *p*-fluorobenzaldehyde **7i** (105 μL, 0.976 mmol) were added to **6** (60 mg, 0.244 mmol) according to the general procedure. After purification, compound *anti*-**8i** was isolated with the 70% yield (55 mg, 0.171 mmol) as a white solid. The characterization data of *anti*-**8i** are identical to those reported in the literature.[15] ^{1}H ($CDCl_3$, 300 MHz) δ 7.27-7.22 (m, 2H), 7.04-6.98 (m, 2H), 5.33-5.31 (m, 1H), 5.16 (m, 1H), 4.66-4.64 (m, 1H), 4.19 (bs, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 1.42 (s, 9H), 1.20 (t, *J* = 7.1 Hz, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 169.8, 160.9, 156.5, 135.2, 128.0, 127.9, 115.3, 115.0, 80.9, 74.7, 61.9, 59.9, 28.3 (3C), 14.1; ^{19}F ($CDCl_3$, 282 MHz) δ -114.49.

*Ethyl 2-[(tert-butoxycarbonyl)amino]-3-hydroxy-3-[2-(trifluo romethyl)phenyl]propanoate anti-**8j*** Triethylamine (34 μL, 0.244 mmol) then *o*-(trifluoromethyl)benzaldehyde **7g** (129 μL, 0.976 mmol) were added to **6** (60 mg, 0.244 mmol) according to the general procedure. After purification, compound *anti*-**8j** was isolated with the 76% yield (70 mg, 0.186 mmol) as a colorless oil (presence of two rotamers). ^{1}H ($CDCl_3$, 300 MHz) *δ* 7.76-7.74 (m, 1H), 7.65-7.62 (m, 1H), 7.60-7.55 (m, 1H), 7.43-7.38 (m, 1H), 5.38-5.35 (m, 1H), 5.22 (d, *J* = 8.9 Hz, 1H), 4.62-4.58 (m, 1H), 4.24-4.08 (m, 2H), 3.58 (bs, 1H), 1.42/1.33 (s, 9H), 1.19-1.13 (m, 3H); ^{13}C ($CDCl_3$, 75 MHz) *δ* 171.0, 155.2, 138.5, 132.1, 128.8, 128.3, 127.9 (q, J_{C-F} = 30.1 Hz), 125.6, 122.6, 80.4, 70.3, 61.8, 58.9, 30.4/28.2 (3C), 15.3/14.0; ^{19}F ($CDCl_3$, 282 MHz) *δ* – 57.48 (3F); IR (ATR) ν (cm^{-1}) 3439, 3376, 2981, 2932, 1696, 1502, 1310; HRMS (ESI) *m/z* calculated for $C_{17}H_{23}F_3NO_5$ $[M+H]^+$ 378.1528, found 378.1534.

*Ethyl 2-[(tert-butoxycarbonyl)amino]-3-hydroxy-3-[3-(trifluo romethyl)phenyl]propanoate anti-**8k***. Triethylamine (34 μL, 0.244 mmol) then *m*-(trifluoromethyl)benzaldehyde **7h** (131 μL, 0.976 mmol) were added to **6** (60 mg, 0.244 mmol) according to the general procedure. After purification, compound *anti*-**8k** was isolated with the 66% yield (61 mg, 0.162 mmol) as a white solid. m.p. 70-72 °C; ^{1}H ($CDCl_3$, 300 MHz) *δ* 7.54-7.50 (m, 2H), 7.45-7.43 (m, 2H), 5.34-5.32 (m, 1H), 5.30-5.25 (m, 1H), 4.69-4.68 (m, 1H), 4.41 (d, *J* = 5.3 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 1.43 (s, 9H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{13}C ($CDCl_3$, 75 MHz) *δ* 169.3, 156.8, 140.7, 130.7 (q, J_{C-F} = 32.3 Hz), 129.6, 128.8, 124.9 (q, J_{C-F} = 3.8 Hz), 123.3 (q, J_{C-F} = 3.9 Hz), 81.2, 75.1, 62.2, 60.0, 28.3 (3C), 14.1; ^{19}F ($CDCl_3$, 282 MHz) *δ* – 62.63 (3F); IR (ATR) ν (cm^{-1}) 3518, 3358, 2986, 2941, 1716, 1678, 1519; HRMS (ESI) *m/z* calculated for $C_{17}H_{23}F_3NO_5$ $[M + H]^+$ 378.1528, found 378.1522.

*Ethyl 2-[(tert-butoxycarbonyl)amino]-3-hydroxy-3-(thiophen-2-yl)propanoate anti-**8l***. Triethylamine (34 μL, 0.244 mmol) then *o*-thiophencarboxaldehyde **7l** (91 μL, 0.976 mmol) were added to **6** (60 mg, 0.244 mmol) according to the general procedure. After purification, compound *anti*-**8l** was isolated with the 73% yield (56 mg, 0.178 mmol) as a pale pink oil. The characterization data of *anti*-**8l** are identical to those reported in the literature.[15] ^{1}H ($CDCl_3$, 300 MHz) δ 7.25 (dd, *J* = 1.2 and 5.0 Hz, 1H), 6.96 (dd, *J* = 3.5 and 5.0 Hz, 1H), 6.91-6.86 (m, 1H), 5.50-5.44 (m, 1H), 5.40-5.38 (m, 1H), 4.77-4.71 (m, 1H), 4.49-4.45 (bs, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 1.45 (s, 9H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ : 169.3, 157.0, 142.9, 126.7, 125.2, 124.4, 81.1, 72.2, 62.0, 59.8, 28.4 (3C), 14.2.

*Ethyl 2-[(tert-butoxycarbonyl)amino]-3-hydroxyhexanoate anti-**8m***. Triethylamine (34 μL, 0.244 mmol) then butyraldehyde **7m** (88 μL, 0.976 mmol) were added to **6** (60 mg, 0.244

mmol) according to the general procedure. After purification, compound *anti*-**8m** was isolated with the 38% yield (26 mg, 0.093 mmol) as a colorless oil (presence of two rotamers). The characterization data of *anti*-**8m** are identical to those reported in the literature.[16] ^{1}H ($CDCl_3$, 300 MHz) 5.51-5.38 (m, 1H), 4.39-4.31 (m, 1H), 4.34-4.17 (m, 2H), 3.95-3.85 (m, 1H), 2.75 (br, 1H), 1.53-1.36 (13H), 1.28 (t, J = 8.1 Hz, 3H), 0.91 (t, J = 6.8 Hz, 3H); ^{13}C ($CDCl_3$, 75 MHz) 170.8, 156.2, 80.5, 73.0, 61.8, 58.6, 35.5, 30.5/28.4 (3C), 19.1, 14.3, 14.0.

*Tert-butyl (1,3-dihydroxy-1-phenylpropan-2-yl)carbamate anti-**9a***. $LiBH_4$ (140 mg, 6.41 mmol) was added at 0 °C to a solution of *anti*-**8a** (662 mg, 2.13 mmol) in *i*-PrOH/THF (1:2) (13 mL). The reaction mixture was allowed to warm to room temperature for 2 hours. Water (10 mL) was added and the mixture was extracted with ethyl acetate (3×15 mL). The organic layers were combined then washed with a saturated aqueous $NaHCO_3$ solution and brine then dried over $MgSO_4$. After filtration, the solvents were removed under reduced pressure and *anti*-**9a** was isolated without further purification in a quantitative yield (569 mg, 2.13 mmol) as a white solid. The characterization data of *anti*-**9a** are identical to those reported in the literature.[17] ^{1}H ($CDCl_3$, 300 MHz) δ 7.41-7.28 (m, 5H), 5.38 (bs, 1H), 5.06 (bs, 1H), 3.81 (m, 2H), 3.62 (m, 1H), 3.08 (bs, 1H), 2.47-2.43 (m, 1H), 1.45 (s, 9H); ^{13}C ($CDCl_3$, 75 MHz) δ 156.2, 141.2, 128.6 (2C), 127.8, 126.0 (2C), 80.1, 76.2, 62.0, 56.5, 28.5 (3C).

*Three general procedures used to transform anti-**9a** to compounds **10**-**13***.

General procedure A: N-Boc deprotection with TFA. Trifluoroacetic acid was added to a solution of *N*-Boc compound in DCM at room temperature. The reaction mixture was stirred for the indicated period. Volatiles were evaporated under reduced pressure. The crude product was diluted in a mixture diethyl ether/water (2:1) (3 mL). To this solution was slowly added solid sodium hydrogen carbonate. The mixture was stirred until the solid was all disappeared then extracted with diethyl ether (3×10 mL). The organic layers were combined, dried over $MgSO_4$ and filtrated. The solvents were removed under reduced pressure. The residue was purified by flash chromatography under silica gel (100% ethyl acetate or cyclohexane/diethyl ether) to afford the desired *N*-Boc deprotected compound.

General procedure B: benzylation reactions with NaH and benzyl bromide. NaH (60% in oil) then benzyl bromide were added to a solution of *N*-Boc compound in DMF at 0 °C. The reaction mixture was allowed to stir for 18 h at 60 °C. Water was added to the medium and the mixture was extracted with ethyl acetate (3×20 mL). The organic layers were combined and washed with a saturated aqueous $NaHCO_3$ solution, brine then dried over $MgSO_4$. After filtration, the solvents were removed under reduced pressure. The crude product was purified by flash chromatography under silica gel (pentane or cyclohexane/diethyl ether) to afford the desired mono-, di- or tri-benzylated compound.

General procedure C: *N-Boc reduction with LAH*. $LiAlH_4$ (LAH) was added to a solution of *N*-Boc compound in THF at 0 °C. The reaction mixture was allowed to reach the reflux temperature of THF and stirred for the indicated period. A Rochelle-salt solution (10%) was added at 0 °C and stirred for1 h at room temperature. The crude product was extracted with ethyl acetate (3×15 mL), then the combined organic layers were washed with a saturated aqueous $NaHCO_3$ solution, brine and dried over $MgSO_4$. After filtration, the solvents were removed under reduced pressure. The residue was purified by flash chromatography under silica gel (pentane/ethyl acetate) to afford the desired *N*-methyl compound.

*1,3-Dihydroxy-1-phenylpropan-2-ammonium 2,2,2-trifluoroacetate anti-**10-NH$_2$***. Compound *anti*-**9a** (100 mg, 0.373 mmol) and TFA (1.14 mL, 14.91 mmol) were mixed in DCM (3.7 mL) for 4 hours following *General procedure A*. Pure 2-amino-1,3-diol *anti*-**10-NH$_2$** was isolated in its trifluoroacetic ammonium salt in a quantitative yield (106 mg, 0.373 mmol) as a colorless oil. ^{1}H (D_2O, 300 MHz) δ 7.45-7.38 (m, 5H), 6.97 (d, J = 6.3 Hz, 1H), 3.81-3.68 (m, 2H), 3.62-3.57 (m, 1H); ^{13}C (D_2O, 75 MHz) δ 162.9 ($J^2_{C\text{-}F}$ = 35.5 Hz), 138.0, 129.1 (2C), 128.9, 126.3 (2C), 116.3 ($J^1_{C\text{-}F}$ = 291.7 Hz), 70.4, 57.9, 57.2; ^{19}F (D_2O, 282 MHz) δ – 73.09; IR (ATR) ν (cm^{-1}) 3068, 2901, 2379, 1659, 1453, 1132; HRMS (ESI) *m/z* calculated for $C_9H_{14}NO_2$ $[M+H]^+$ 168.1025, found 168.1018.

*Tert-butyl [1,3-bis(benzyloxy)-1-phenylpropan-2-yl] carbamate **14***. Compound *anti*-**9a** (85 mg, 0.32 mmol), NaH (31 mg, 0.77 mmol) and benzyl bromide (80 µL, 0.70 mmol) were mixed in DMF (1.6 mL) following *General procedure B*. After purification by flash chromatography under silica gel (pentane/diethyl ether 90:10), compound **14** was isolated with the 69% yield (96 mg, 0.22 mmol) as a white solid (presence of two rotamers). m.p. 67-69 °C; ^{1}H ($CDCl_3$, 400 MHz) δ 7.33-7.22 (m, 15H), 4.82 (d, J = 9.5 Hz, 1H), 4.52-4.36 (m, 4H), 4.23 (d, J = 11.7 Hz, 1H [B part of AB system]), 4.08-3.98 (m, 1H), 3.85 (dd, J = 4.2 and 9.3 Hz, 1H [A' part of AB' system]), 3.47 (dd, J = 4.2 and 9.9 Hz, 1H [B' part of AB' system]), 1.23/1.15 (s, 9H); ^{13}C ($CDCl_3$, 75 MHz) δ 155.1, 138.9, 138.4 (2C), 128.5 (3C), 128.4 (2C), 127.9 (2C), 127.8 (4C), 127.7 (4C), 80.7, 79.1, 73.3, 71.1, 68.9, 54.8, 28.4 (3C); IR (ATR) ν (cm^{-1}) 3377, 3091, 3083, 1687, 1519; HRMS (ESI) *m/z* calculated for $C_{28}H_{33}NO_4$ $[M + H]^+$ 448.2488, found 448.2479.

*1,3-Bis(benzyloxy)-1-phenylpropan-2-amine anti-**11-NH$_2$***. Compound **14** (285 mg, 0.64 mmol) and TFA (2 mL, 25.6 mmol) were mixed in DCM (6.5 mL) for 4 h following *General procedure A*. After purification by flash chromatography under silica gel (pentane/ethyl acetate 30:70), 2-amino-1,3-diether *anti*-**11-NH$_2$** was isolated with the 96% yield (213 mg, 0.614 mmol) as a yellowish oil. ^{1}H ($CDCl_3$, 300 MHz) δ 7.27-7.13 (m, 15H), 4.38-4.37 (m, 2H), 4.34 (m, 1H), 4.31 (d, J = 11.5 Hz, 1H [A part of AB system]), 4.14 (d, J = 11.5 Hz, 1H [B part of AB system]), 3.51-3.50 (m, 2H), 3.21-3.16 (m, 1H), 2.95 (bs, 2H); ^{13}C ($CDCl_3$, 75 MHz) δ 138.5, 138.1 (2C), 128.7 (2C), 128.5 (2C), 128.4 (2C), 128.3, 127.9 (4C), 127.8 (3C), 127.7, 81.8, 73.4, 70.8, 70.7, 55.9; IR (ATR) ν (cm^{-1}) 3460, 3398, 2863, 1682, 1453; HRMS (ESI) *m/z* calculated for $C_{23}H_{26}NO_2$ $[M + H]^+$ 348.1964, found 348.1956.

*1,3-Bis(benzyloxy)-N-methyl-1-phenylpropan-2-amine anti-**11-NHMe***. Compound **14** (65 mg, 0.15 mmol) and $LiAlH_4$ (17 mg, 0.44 mmol) were mixed in THF (1.6 mL) for 6 h following *General procedure C*. After purification by flash chromatography under silica gel (pentane/ethyl acetate 70:30), 2-amino-1,3-diether *anti*-**11-NHMe** was isolated with the 69% yield (37 mg, 0.104 mmol) as a yellowish oil. ^{1}H ($CDCl_3$, 400 MHz) δ 7.33-7.20 (m, 15H), 4.48 (d, J = 6.0 Hz, 1H), 4.45 (m, 2H), 4.41 (d, J = 11.7 Hz, 1H [A part of AB system]), 4.22 (d, J = 11.7 Hz, 1H [B part of AB system]), 3.60 (dd, J = 5.5 and 9.7 Hz, 1H [A' part of AB' system]), 3.53 (dd, J = 4.2 and 9.7 Hz, 1H [B' part of AB' system]), 2.93-2.89 (m, 1H), 2.24 (s,

3H), 1.96 (bs, 1H); ^{13}C ($CDCl_3$, 100 MHz) δ 139.5, 138.5 (2C), 128.5 (2C), 128.4 (4C), 127.9, 127.8 (6C), 127.6 (2C), 81.0, 73.3, 70.9, 68.7, 64.5, 34.8; IR (ATR) ν (cm^{-1}) 3389, 2925, 2852, 1737, 1452; HRMS (ESI) *m/z* calculated for $C_{24}H_{28}NO_2$ $[M + H]^+$ 362.2120, found 362.2126.

*Tert-butylbenzyl[1,3-bis(benzyloxy)-1-phenylpropan-2-yl]carbamate **15***. Compound *anti*-**9a** (134 mg, 0.50 mmol), NaH (90 mg, 2.25 mmol) and benzyl bromide (0.27 mL, 2.25 mmol) were mixed in DMF (2.5 mL) following *General procedure B*. After purification by flash chromatography under silica gel (pentane/diethyl ether 95:5), compound **15** was isolated with the 67% yield (179 mg, 0.335 mmol) as a yellow oil (presence of two rotamers). ^{1}H ($CDCl_3$, 300 MHz) δ 7.34-7.00 (m, 20H), 4.83-4.58 (m, 1H), 4.46-3.79 (m, 9H), 1.30/1.20 (s, 9H); ^{13}C ($CDCl_3$, 75 MHz) δ 155.7, 139.7, 139.3, 138.6, 138.4, 128.5, 128.4, 128.3 (2C), 128.2 (2C), 128.0 (4C), 127.7 (5C), 127.6 (2C), 127.4, 127.1, 126.3, 80.8, 80.1, 79.6, 72.9, 71.0, 69.1, 53.5, 28.3 (3C); IR (ATR) ν (cm^{-1}) 3030, 2975, 2868, 1738, 1688; HRMS (ESI) *m/z* calculated for $C_{35}H_{40}NO_4$ $[M + H]^+$ 538.2957, found 538.2953.

*N-Benzyl-1,3-bis(benzyloxy)-1-phenylpropan-2-amine anti-**11-NHBn***. Compound **15** (70 mg, 0.13 mmol) and TFA (0.4 mL, 5.21 mmol) were mixed in DCM (1.5 mL) for 3 h following *General procedure A*. After purification by flash chromatography under silica gel (cyclohexane/diethyl ether 90:10), 2-amino-1,3-diether *anti*-**11-NHBn** was isolated in a quantitative yield (56 mg, 0.13 mmol) as a yellowish oil. ^{1}H ($CDCl_3$, 300 MHz) δ 7.37-7.06 (m, 20H), 4.50-4.49 (m, 3H), 4.45 (d, *J* = 11.7 Hz, 1H [A part of AB system]), 4.25 (d, *J* = 11.7 Hz, 1H [B part of AB system]), 3.70-3.53 (m, 4H), 3.08-3.03 (m, 1H), 1.66 (bs, 1H); ^{13}C ($CDCl_3$, 75 MHz) δ 140.7, 139.8, 138.6 (2C), 128.4 (3C), 128.3, 128.2 (4C), 128.0 (2C), 127.9, 127.8 (4C), 127.6 (4C), 126.8, 81.5, 73.2, 70.8, 69.3, 61.4, 51.9; IR (ATR) ν (cm^{-1}) 3379, 3028, 2901, 2858, 1494; HRMS (ESI) *m/z* calculated for $C_{30}H_{32}NO_2$ $[M + H]^+$ 438.2433, found 438.2431.

*Tert-butyl (3-benzyloxy-1-hydroxy-1-phenylpropan-2-yl) carbamate **16***. DIPEA (1.82 mL, 10.5 mmol) and benzyl bromide (1.25 mL, 10.5 mmol) were sequentially added in a round-bottomed flask to a mixture of *anti*-**9a** (700 mg, 2.62 mmol), Bu_2SnO (65 mg, 0.26 mmol) and TBAB (253 mg, 0.79 mmol). The flask was sealed and reach to 70 °C for 24 hours. After purification by flash chromatography on silica gel (cyclohexane/ethyl acetate 80:20), compound **16** was isolated with the 84% yield (790 mg, 2.20 mmol) as a white solid (presence of two rotamers). m.p. 62-64 °C; ^{1}H ($CDCl_3$, 300 MHz) δ 7.39-7.20 (m, 10H), 5.41-5.28 (m, 1H), 4.97-4.89 (m, 1H), 4.46 (d, *J* = 11.6 Hz, 1H [A part of AB system]), 4.40 (d, *J* = 11.6 Hz, 1H [B part of AB system]), 4.03-3.92 (m, 1H), 3.82-3.69 (m, 1H), 3.58-3.45 (m, 2H), 1.43 (s, 9H); ^{13}C ($CDCl_3$, 75 MHz) δ 155.7, 141.4, 137.1, 128.7 (2C), 128.6 (2C), 128.3, 128.1 (2C), 127.9, 127.4, 125.7, 79.7, 75.9, 73.9, 69.7, 54.8, 28.4 (3C); IR (ATR) ν (cm^{-1}) 3424, 3380, 2974, 1753, 1518; HRMS (ESI) *m/z* calculated for $C_{21}H_{28}NO_4$ $[M + H]^+$ 358.2018, found 358.2013.

*2-Amino-3-benzyloxy-1-phenylpropan-1-ol anti-**12-NH$_2$***. Compound **16** (302 mg, 0.85 mmol) and TFA (2.62 mL, 34 mmol) were mixed in DCM (8.5 mL) for 4 h following *General procedure A*. After purification by flash chromatography under silica gel (pentane/ethyl acetate 30:70), compound *anti*-**12-NH$_2$** was isolated with the 62% yield (136 mg, 0.53 mmol) as a colorless oil. ^{1}H ($CDCl_3$, 300 MHz) δ 7.30-7.19 (m, 10H), 4.63 (d, *J* = 5.6 Hz, 1H), 4.43 (d, *J* = 11.7 Hz, 1H [A part of AB system]), 4.39 (d, *J* = 11.7 Hz, 1H [B part of AB system]), 3.45-3.35 (m, 2H), 3.21-3.16 (m, 1H), 2.30 (bs, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 141.4, 137.9, 128.6 (2C), 128.5 (2C), 128.0, 127.9 (2C), 127.8, 126.4 (2C), 75.9, 73.6, 71.9, 56.0; IR (ATR) ν (cm^{-1}) 3356, 3298, 2916, 2849, 1671; HRMS (ESI) *m/z* calculated for $C_{16}H_{20}NO_2$ $[M + H]^+$ 258.1494, found 258.1490.

*3-Benzyloxy-2-methylamino-1-phenylpropan-1-ol anti-**12-NHMe***. Compound **16** (381 mg, 1.096 mmol) and $LiAlH_4$ (125 mg, 3.288 mmol) were mixed in THF (11 mL) for 15 h following *General procedure C*. After purification by flash chromatography under silica gel (pentane/ethyl acetate 30:70), compound *anti*-**12-NHMe** was isolated with the 76% yield (227 mg, 0.833 mmol) as a yellowish oil. ^{1}H ($CDCl_3$, 300 MHz) δ 7.27-7.18 (m, 10H), 4.94 (d, *J* = 3.9 Hz, 1H), 4.34 (d, *J* = 11.7 Hz, 1H [A part of AB system]), 4.29 (d, *J* = 11.7 Hz, 1H [B part of AB system]), 3.95 (bs, 2H), 3.41 (dd, *J* = 5.4 and 9.7 Hz, 1H [A' part of AB' system]), 3.22 (dd, *J* = 5.4 and 9.7 Hz, 1H [B' part of AB' system]), 2.91-2.86 (m, 1H), 2.48 (s, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 141.0, 137.7, 128.6 (2C), 128.4 (2C), 128.0, 127.9 (2C), 127.3, 125.8 (2C), 73.6, 71.2, 68.5, 64.4, 33.9; IR (ATR) ν (cm^{-1}) 3367, 3029, 2856, 1736, 1561; HRMS (ESI) *m/z* calculated for $C_{17}H_{22}NO_2$ $[M + H]^+$ 272.1651, found 272.1641.

*Tert-butyl (3-benzyloxy-1-tert-butyldimethylsilyloxy-1-phenyl propan-2-yl)carbamate **17***. Imidazole (48 mg, 0.70 mmol), 4-dimethylaminopyridine (11 mg, 0.09 mmol) and TBDMSCl (81 mg, 0.54 mmol) were added to a solution of **16** (100 mg, 0.28 mmol) in DMF (1.4 mL). The reaction mixture was stirred at room temperature for 18 h. After addition of water (10 mL), the reaction mixture was extracted with DCM (3×15 mL). The organic layers were combined, dried over $MgSO_4$ and, after filtration, the solvents were removed under reduced pressure. The residue was purified by flash chromatography on silica gel (cyclohexane/diethyl ether 90:10). Compound **17** was isolated with the 80% yield (105 mg, 0.22 mmol) as a colorless oil (presence of two rotamers). ^{1}H ($CDCl_3$, 300 MHz) δ 7.28-7.15 (m, 10H), 4.87 (d, *J* = 5.3 Hz, 1H), 4.76 (d, *J* = 8.6 Hz, 1H), 4.45-4.34 (m, 2H), 3.91 (m, 1H), 3.69 (dd, *J* = 5.8 and 10.1 Hz, 1H [A' part of AB' system]), 3.37 (dd, J = 4.0 and 10.1 Hz, 1H [B' part of AB' system]), 1.30/1.22 (s, 9H), 0.84 (s, 9H), -0.01 (s, 3H), -0.23 (s, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 155.4, 141.8, 138.2, 128.5 (2C), 128.0 (3C), 127.9 (2C), 127.8, 127.4, 126.8, 79.1, 74.4, 73.1, 68.2, 56.4, 28.4 (3C), 25.9 (3C), 18.3, -4.6, -5.1; IR (ATR) ν (cm^{-1}) 3453, 2929, 2857, 1710, 1495; HRMS (ESI) *m/z* calculated for $C_{27}H_{42}NO_4Si$ $[M + H]^+$ 472.2883, found 472.2885.

*Tert-butylbenzyl(3-benzyloxy-1-tert-butyldimethylsilyloxy-1-phenylpropan-2-yl)carbamate **18***. Compound **17** (43 mg, 0.09 mmol), NaH (5 mg, 0.12 mmol) and benzyl bromide (12 μL, 0.10 mmol) were mixed in DMF (0.5 mL) following *General procedure B*. After purification by flash chromatography under silica gel (cyclohexane/diethyl ether 97:3), compound **18** was isolated with the 53% yield (27 mg, 0.048 mmol) as a colorless oil (presence of two rotamers). ^{1}H ($CDCl_3$, 300 MHz) δ 7.32-6.98 (m, 15H), 5.08-4.82 (m, 1H), 4.31-3.82 (m, 7H), 1.26/1.21 (s, 9H), 0.82 (s, 9H), -0.03 (s, 3H), -0.32 (s, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 155.7/155.5, 142.4, 139.7, 138.4, 128.2 (2C), 128.1, 127.9 (2C), 127.9 (2C), 127.8, 127.7, 127.5, 127.4, 127.2 (2C), 127.1, 126.3, 79.5, 74.2, 73.7, 73.0, 72.9, 69.3, 28.3 (3C), 25.9 (3C), 18.1, -4.5, -5.0; IR (ATR) ν

(cm^{-1}) 3056, 3031, 2956, 1689, 1495; HRMS (ESI) *m/z* calculated for $C_{34}H_{48}NO_4Si$ $[M + H]^+$ 562.3353, found 562.3340.

*2-Benzylamino-3-benzyloxy-1-phenylpropan-1-ol anti-**12-NHBn***. Compound **18** (27 mg, 0.048 mmol) and TFA (0.15 mL, 1.92 mmol) were mixed in DCM (0.25 mL) for 4 h following *General procedure A*. After purification by flash chromatography under silica gel (cyclohexane/diethyl ether 70:30), compound *anti*-**12-NHBn** was isolated with the 70% yield (12 mg, 0.034 mmol) as a colorless oil. ^1H ($CDCl_3$, 300 MHz) δ 7.28-7.15 (m, 15H), 4.89 (d, J = 4.2 Hz, 1H), 4.32 (d, J = 11.7 Hz, 1H [A part of AB system]), 4.26 (d, J = 11.7 Hz, 1H [B part of AB system]), 3.88 (d, J = 13.3 Hz, 1H [A" part of AB" system]), 3.79 (d, J = 13.3 Hz, 1H [B" part of AB" system]), 3.38 (dd, J = 7.4 and 9.7 Hz, 1H [A' part of AB' system]), 3.18 (dd, J = 4.1 and 9.7 Hz, 1H [B' part of AB' system]), 3.05-2.99 (m, 1H), 2.69 (bs, 2H); ^{13}C ($CDCl_3$, 75 MHz) δ 141.0 (2C), 137.9, 128.7 (2C), 128.6 (2C), 128.4 (2C), 128.3 (2C), 127.9, 127.8 (2C), 127.3 (2C), 125.8 (2C), 73.5, 71.8, 69.2, 61.4, 51.3; IR (ATR) ν (cm^{-1}) 3536, 3335, 2862, 1736, 1452; HRMS (ESI) *m/z* calculated for $C_{23}H_{26}NO_2$ $[M + H]^+$ 348.1964, found 348.1978.

*Tert-butyl (1-hydroxy-1-phenyl-3-trityloxypropan-2-yl) carbamate **19***. 4-Dimethylaminopyridine (6 mg, 0.05 mmol) then triethylamine (70 µL, 0.5 mmol) were added at 0 °C to a solution of *anti*-**9a** (134 mg, 0.5 mmol) and trityl chloride (139 mg, 0.5 mmol) in DCM/DMF (3:1) (2 mL). The reaction mixture was allowed to warm to room temperature for 12 h. After extractions with ethyl acetate (3×15 mL), the organic layers were combined, washed with brine, dried over $MgSO_4$ and filtrated. The solvents were removed under reduced pressure and the residue was purified by flash chromatography on silica gel (cyclohexane/ethyl acetate 80:20). Compound **19** was obtained with the 68% yield (173 mg, 0.34 mmol) as a white solid (presence of two rotamers). m.p. 153-155 °C; ^1H ($CDCl_3$, 300 MHz) δ 7.39-7.13 (m, 20H), 5.23 (d, J = 8.9 Hz, 1H), 4.96 (dd, J = 3.3 and 7.4 Hz, 1H), 4.04-4.02 (m, 1H), 3.73 (d, J = 7.4 Hz, 1H), 3.26 (dd, J = 4.3 and 9.6 Hz, 1H [A' part of AB' system]), 3.11-3.08 (m, 1H [B' part of AB' system]), 1.46/1.38 (s, 9H); ^{13}C ($CDCl_3$, 75 MHz) δ 156.0, 143.6, 143.3 (3C), 128.6 (6C), 128.3, 128.1 (10C), 127.4 (2C), 126.0, 87.6, 79.9, 76.0, 62.9, 55.3, 28.6 (3C); IR (ATR) ν (cm^{-1}) 3437, 3346, 2960, 1686, 1500; HRMS (ESI) *m/z* calculated for $C_{33}H_{35}NO_4$,Na $[M + Na]^+$ 532.2464, found 532.2460.

*Tert-butyl (1-benzyloxy-1-phenyl-3-trityloxypropan-2-yl) carbamate **20***. Compound **19** (150 mg, 0.29 mmol), NaH (13 mg, 0.32 mmol) and benzyl bromide (37 µL, 0.31 mmol) were mixed in DMF (2.9 mL) following *General procedure B*. After purification by flash chromatography under silica gel (pentane/diethyl ether 90:10), compound **20** was isolated with the 64% yield (112 mg, 0.19 mmol) as a colorless oil (presence of two rotamers). ^1H ($CDCl_3$, 300 MHz) δ 7.41-7.38 (m, 5H), 7.31-7.19 (m, 20H), 4.80 (d, J = 10.0 Hz, 1H), 4.65 (d, J = 6.8 Hz, 1H), 4.47 (d, J = 11.6 Hz, 1H [A part of AB system]), 4.29 (d, J = 11.6 Hz, 1H [B part of AB system]), 4.11-4.05 (m, 1H), 3.49 (dd, J = 4.2 and 9.2 Hz, 1H [A' part of AB' system]), 3.16 (dd, J = 4.2 and 9.2 Hz, 1H [B' part of AB' system]), 1.31/1.26 (s, 9H); ^{13}C ($CDCl_3$, 75 MHz) δ 155.3, 144.1 (3C), 138.8, 138.4, 129.0 (6C), 128.5 (2C), 128.4, 128.0 (10C), 127.9 (2C), 127.8, 127.7, 127.2 (2C), 86.8, 81.4, 79.2, 71.2, 62.3, 55.2, 28.6 (3C); IR (ATR) ν (cm^{-1}) 3386, 3030, 2967, 1702, 1597; HRMS (ESI) *m/z* calculated for $C_{40}H_{41}NO_4$,Na $[M + Na]^+$ 622.2933, found 622.2904.

*2-Amino-3-benzyloxy-3-phenylpropan-1-ol anti-**13-NH$_2$***. Compound **20** (33 mg, 0.055 mmol) and TFA (0.31 mL, 4.016 mmol) were mixed in DCM (1 mL) for 3 h following *General procedure A*. After purification by flash chromatography under silica gel (cyclohexane/diethyl ether 90:10), compound *anti*-**13-NH$_2$** was isolated with the 78% yield (11 mg, 0.043 mmol) as a colorless oil. ^1H ($CDCl_3$, 300 MHz) δ 7.32-7.15 (m, 10H), 4.37 (d, J = 11.5 Hz, 1H [A part of AB system]), 4.20 (d, J = 6.8 Hz, 1H), 4.15 (d, J = 11.5 Hz, 1H [B part of AB system]), 3.63 (dd, J = 4.6 and 11.0 Hz, 1H [A' part of AB' system]), 3.49 (dd, J = 6.0 and 11.0 Hz, 1H [B' part of AB' system]), 3.02-2.99 (m, 1H), 2.36 (bs, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 138.9, 138.0, 128.8 (2C), 128.5 (2C), 128.4, 127.9 (3C), 127.6 (2C), 83.7, 70.9, 63.6, 57.4; IR (ATR) ν (cm^{-1}) 3406, 3367, 2918, 2863, 1584; HRMS (ESI) *m/z* calculated for $C_{16}H_{20}NO_2$ $[M + H]^+$ 258.1494, found 258.1495.

*Tert-butyl (1-benzyloxy-3-hydroxy-1-phenylpropan-2-yl) carbamate **21***. Trifluoroacetic acid (28 µL, 0.364 mmol) was added to a solution of compound **20** (31 mg, 0.052 mmol) in DCM (0.26 mL) at room temperature. The reaction mixture was stirred overnight. After completion of the reaction, the reaction mixture was quenched by addition of a saturated sodium hydrogen carbonate solution (10 mL). After extraction with dichloromethane (3×10 mL), the combined organic layers were washed with brine (2×10 mL), dried over $MgSO_4$ then filtrated. The solvents were removed under reduced pressure. The residue was purified by flash chromatography under silica gel (cyclohexane/ethyl acetate 85:25) to afford compound **21** with the 70% yield (13 mg, 0.036 mmol) as a white solid (presence of two rotamers). m.p. 65-67 °C; ^1H ($CDCl_3$, 300 MHz) δ 7.41-7.30 (m, 10H), 5.37 (d, J = 7.5 Hz, 1H), 4.78-4.77 (m, 1H), 4.62 (d, J = 11.7 Hz, 1H [A part of AB system]), 4.30 (d, J = 11.7 Hz, 1H [B part of AB system]), 3.89 (dd, J = 3.3 and 11.5 Hz, 1H [A' part of AB' system]), 3.74-3.68 (m, 1H), 3.52 (m, 1H [B' part of AB' system]), 2.84 (bs, 1H), 1.43/1.40 (s, 9H); ^{13}C ($CDCl_3$, 75 MHz) δ 155.8, 138.5, 137.7, 128.7 (2C), 128.6 (2C), 128.0 (2C), 127.8 (2C), 126.9 (2C), 83.2, 79.5, 71.8, 61.4, 56.4, 28.4 (3C); IR (ATR) ν (cm^{-1}) 3346, 3241, 3063, 1670, 1549; HRMS (ESI) *m/z* calculated for $C_{21}H_{28}NO_4$ $[M + H]^+$ 358.2018, found 358.2026.

*3-Benzyloxy-2-methylamino-3-phenylpropan-1-ol anti-**13-NHMe***. Compound **21** (214 mg, 0.616 mmol) and $LiAlH_4$ (70 mg, 1.85 mmol) were mixed in THF (6 mL) for 15 h following *General procedure C*. After purification by flash chromatography under silica gel (pentane/ethyl acetate 30:70), compound *anti*-**13-NHMe** was isolated with the 58% yield (97 mg, 0.357 mmol) as a yellowish oil. ^1H ($CDCl_3$, 300 MHz) δ 7.40-7.29 (m, 10H), 4.62 (d, J = 5.7 Hz, 1H), 4.51 (d, J = 11.5 Hz, 1H [A part of AB system]), 4.47 (bs, 2H), 4.28 (d, J = 11.5 Hz, 1H [B part of AB system]), 3.75 (dd, J = 5.1 and 11.5 Hz, 1H [A' part of AB' system]), 3.63 (dd, J = 4.2 and 11.5 Hz, 1H [B' part of AB' system]), 2.79-2.74 (m, 1H), 2.33 (s, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 138.6, 137.8, 129.0 (2C), 128.6 (2C), 128.4, 128.1 (2C), 128.0, 127.3 (2C), 80.8, 71.3, 65.4, 59.1, 33.5; IR (ATR) ν (cm^{-1}) 3410, 3367, 2863, 1735, 1554; HRMS (ESI) *m/z* calculated for $C_{17}H_{22}NO_2$ $[M + H]^+$ 272.1651, found 272.1642.

*Tert-butylbenzyl(1-benzyloxy-1-phenyl-3-trityloxypropan-2-yl) carbamate **22***. Compound **19** (60 mg, 0.12 mmol), NaH (10 mg, 0.24 mmol) and benzyl bromide (28 µL, 0.24 mmol) were mixed in DMF (0.6 mL) following *General procedure B*. After purification by flash chromatography under silica gel

(cyclohexane/diethyl ether 97:3), compound **22** was isolated with the 67% yield (55 mg, 0.08 mmol) as a colorless oil (presence of two rotamers). ^{1}H ($CDCl_3$, 300 MHz) δ 7.39-7.38 (m, 4H), 7.32-7.22 (m, 16H), 7.09-6.87 (m, 10H), 4.73-4.71 (m, 1H), 4.42-4.37 (m, 1H), 4.21-3.97 (m, 4H), 3.65-3.62 (m, 2H), 1.29/1.26 (s, 9H); ^{13}C ($CDCl_3$, 75 MHz) δ 156.8, 147.0 (3C), 144.2, 139.2, 138.1, 128.9 (6C), 128.5, 128.2 (2C), 128.1 (9C), 127.8 (6C), 127.5, 127.4 (2C), 126.9 (2C), 82.1, 80.7, 79.7, 71.4, 70.6, 70.0, 29.8, 28.5 (3C); IR (ATR) ν (cm^{-1}) 3060, 3030, 2954, 1696, 1598; HRMS (ESI) *m/z* calculated for $C_{47}H_{47}NO_4$,Na $[M + Na]^+$ 712.3403, found 712.3420.

*2-Benzylamino-3-benzyloxy-3-phenylpropan-1-ol anti-**13-NHBn***. Compound **22** (41 mg, 0.059 mmol) and TFA (0.36 mL, 4.70 mmol) were mixed in DCM (1 mL) for 4 h following *General procedure A*. After purification by flash chromatography under silica gel (cyclohexane/diethyl ether 60:40), compound *anti*-**13-NHBn** was isolated with the 93% yield (19 mg, 0.056 mmol) as a colorless oil. ^{1}H ($CDCl_3$, 300 MHz) δ 7.33-7.15 (m, 13H), 7.06-7.04 (m, 2H), 4.48 (d, J = 5.9 Hz, 1H), 4.46 (d, J = 11.6 Hz, 1H [A part of AB system]), 4.20 (d, J = 11.6 Hz, 1H [B part of AB system]), 3.66-3.51 (m, 4H), 2.82-2.77 (m, 1H), 2.53 (bs, 2H); ^{13}C ($CDCl_3$, 75 MHz) δ 139.5, 138.9, 137.9, 128.8 (2C), 128.6 (2C), 128.5 (2C), 128.3, 128.2 (2C), 128.0 (2C), 127.9, 127.3 (3C), 81.0, 71.1, 62.8, 59.9, 51.2; IR (ATR) ν (cm^{-1}) 3445, 3256, 3029, 2869, 1736; HRMS (ESI) *m/z* calculated for $C_{23}H_{26}NO_2$ $[M + H]^+$ 348.1964, found 348.1961.

*Ethyl 2-oxo-5-phenyloxazolidine-4-carboxylate **23***. Compound *anti*-**8a** (172 mg, 0.556 mmol) was diluted in dry Et_2O (2.8 mL) and cooled to 0 °C. $SOCl_2$ (0.37 mL, 5 mmol) was added and the solution was stirred for 5 h at this temperature. An aqueous solution of $NaHCO_3$ was added and the mixture was extracted with AcOEt (2×5 mL). The combined organic layers were dried over $MgSO_4$ and after filtration, the solvent was removed under reduced pressure. The residue was purified by flash chromatography under silica gel (pentane/ethyl acetate 80:20), which led to pure oxazolidin-2-one **23** with the 81% yield (106 mg, 0.45 mmol) as a colorless oil. The characterization data of **23** are identical to those reported in the literature.[18] ^{1}H ($CDCl_3$, 300 MHz) δ 7.44-7.35 (m, 5H), 6.65 (bs, 1H), 5.63 (d, J = 5.1 Hz, 1H), 4.38-4.23 (m, 3H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 169.8, 159.0, 138.2, 129.2, 129.1 (2C), 125.5 (2C), 79.6, 62.6, 61.5, 14.2.

*3-Tert-butyl 4-ethyl 2-oxo-5-phenyloxazolidine-3,4-dicarboxylate **24***. Triethylamine (92 µL, 0.663 mmol), di-*tert*-butyl-dicarbonate (0.35 mL, 1.527 mmol) and DMAP (12 mg, 0.101 mmol) were added to a solution of oxazolidin-2-one **23** (78 mg, 0.332 mmol) in THF (4.2 mL). The reaction mixture was stirred for 15 hours at room temperature. After completion of the reaction, the reaction mixture was concentrated under reduced pressure. The residue was diluted in $CHCl_3$, washed with a saturated aqueous solution of $NaHCO_3$ (2×10 mL) and the organic layer was washed with brine (2×10 mL) and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure. The residue was purified by flash chromatography under silica gel (cyclohexane/ethyl acetate 95:5), which led to pure oxazolidine-3,4-dicarboxylate **24** with the 84% yield (93 mg, 0.278 mmol) as a yellow oil. ^{1}H ($CDCl_3$, 300 MHz) δ 7.46-7.35 (m, 5H), 5.36 (d, J = 4.3 Hz, 1H), 4.61 (d, J = 4.3 Hz, 1H), 4.42-4.26 (m, 2H), 1.49 (s, 9H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C ($CDCl_3$, 75 MHz) δ 169.6, 150.9, 148.6, 137.3, 129.5, 129.3 (2C), 125.1 (2C), 84.9, 76.1, 63.9, 62.7, 27.9 (3C), 14.3; IR (ATR) ν (cm^{-1}) 2982, 2936, 1825, 1728, 1322, 1153; HRMS (ESI) *m/z* calculated for $C_{17}H_{25}N_2O_6$ $[M + NH_4]^+$ 353.1713, found 353.1707.

*2-Tert-butoxycarbonylamino-3-hydroxy-3-phenylpropanoic acid **25***. A 2 M aqueous solution of lithium hydroxide (1,27 mL, 2.53 mmol) was added to a solution of **24** (85 mg, 0.253 mmol) in 1,4-dioxane (6.3 mL). The reaction mixture was stirred for 30 minutes at room temperature then concentrated under reduced pressure. The residue was purified by flash chromatography under silica gel (dichloromethane/methanol 93:7), which led to **25** with the 65% yield (46 mg, 0.165 mmol) as a white solid (presence of two rotamers). The characterization data of **25** are identical to those reported in the literature.[19] ^{1}H (CD_3OD, 300 MHz) δ 7.41-7.22 (m, 5H), 5.26 (bs, 1H), 4.36 (bs, 1H), 1.32/1.15 (s, 9H); ^{13}C (CD_3OD, 75 MHz) δ 176.4, 157.7, 142.8, 129.0 (2C), 128.3, 127.4 (2C), 81.1/80.4, 75.0/74.7, 61.4, 28.6/28.2 (3C).

*Tert-butyl(1,3-dihydroxy-1-phenylpropan-2-yl)carbamate syn-**9a***. Sodium borohydride (4 mg, 0.105 mmol) was added to a solution of **25** (24 mg, 0.089 mmol) in THF (0.44 mL) at 0 °C for 10 minutes then I_2 was added (11 mg, 0.044 mmol). After 20 minutes, the reaction mixture was warm up at room temperature and stirred for 2 hours. After quenching with water (3 mL), the pH was adjusted until reaching pH = 4 with an 1 M hydrochloride aqueous solution (about 0.2 mL). The suspension was extracted with ethyl acetate (3×5 mL) and the combined organic layers were washed with a 2 M aqueous solution of sodium hydroxide (3×5 mL) then brine (2×5 mL). The organic layer was dried over Na_2SO_4 and filtrated. The solvents were removed under reduced pressure. The residue was purified by flash chromatography under silica gel (*n*-pentane/ethyl acetate 50:50) to afford *syn*-**9a** with the 50% yield (12 mg, 0.045 mmol) as a colorless oil. The characterization data of *syn*-**9a** are identical to those reported in the literature (presence of two rotamers).[20] ^{1}H ($CDCl_3$, 300 MHz) δ 7.36-7.16 (m, 5H), 5.21 (d, J = 7.4 Hz, 1H), 4.98 (d, J = 3.4 Hz, 1H), 3.81-3.76 (m, 3H), 3.25 (bs, 1H), 2.56 (bs, 1H), 1.35/1.26 (s, 9H); ^{13}C ($CDCl_3$, 75 MHz) δ 156.6, 141.3, 129.2/128.4, 128.6/127.9 (2C), 126.2/125.4 (2C), 80.0, 74.7, 64.2, 57.3, 29.8/28.4 (3C).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

^{1}H and ^{13}C NMR spectra for new compounds (PDF)

X-ray crystallography data for compound *anti*-**8c**

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