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Lewis Acid-Catalyzed Cyclization Reactions of Ethenetricarboxylates via Intramolecular Hydride Transfer

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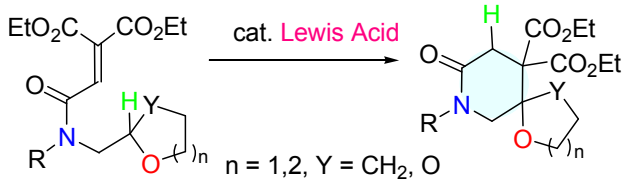
Graphical Abstract



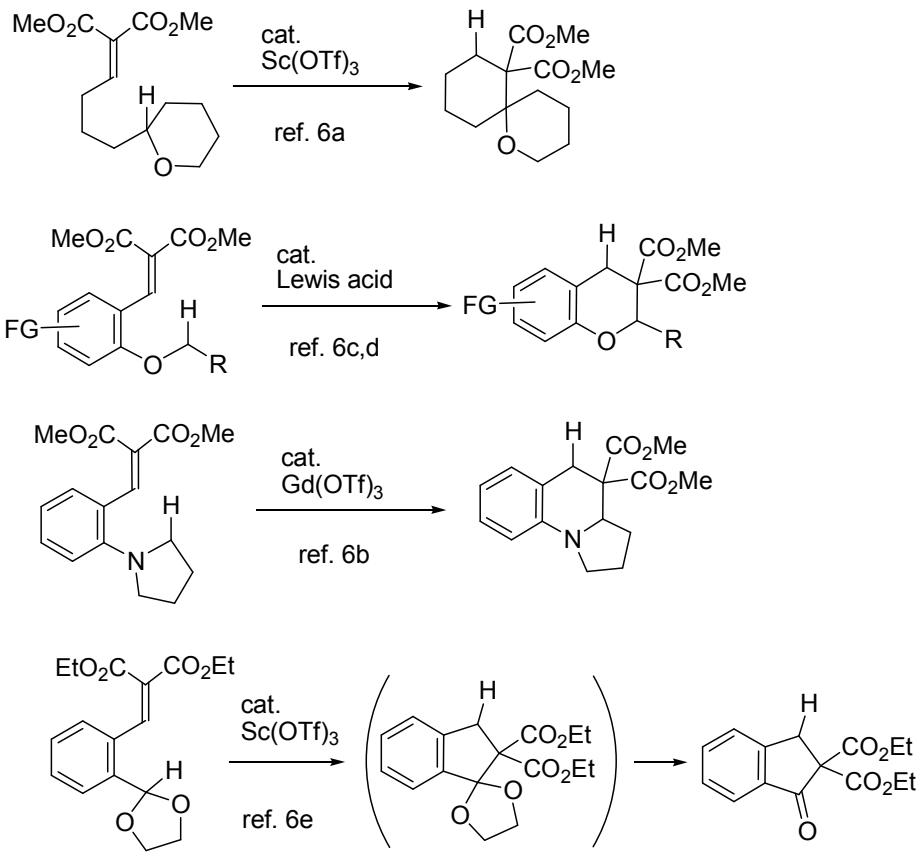
Abstract: Catalytic cyclization of amides of ethenetricarboxylate bearing ether and acetal groups has been examined. The reaction of the amides bearing cyclic ether and acetal groups in the presence of Lewis acid such as $Sc(OTf)_3$ gave spirocyclic piperidine derivatives as major products. The cyclized products may be formed via intramolecular hydride transfer. The reaction mechanism was examined by the DFT calculations. The scope and limitations of the hydride transfer/cyclization reactions of amides of ethenetricarboxylates was investigated and morpholine formation by intramolecular oxy-Michael addition was also found.

Introduction

Nitrogen-containing six-membered heterocyclic systems, such as piperidines and morpholines (1,4-oxazines), are important structures in organic chemistry because they are

present in a large number of biologically active compounds.[1,2] The development of new efficient synthetic strategies for the construction of these heterocycles has attracted considerable interest.[3,4]

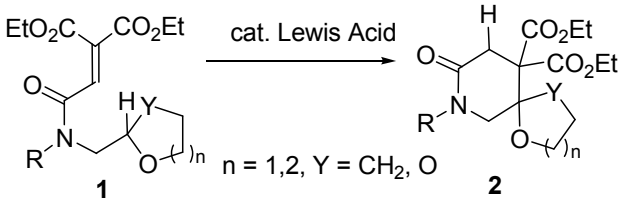
Recently, various cyclization methods involving intramolecular hydride transfer of ethers, amines and acetals as hydride donors have been developed.[5] Among the methods developed, alkylidene or arylidenemalonates have been effectively utilized as hydride acceptors (Scheme 1).[6] However, the structures of substrates for cyclization are still limited. While many of these reactions including various substrates are effective for the formation of benzo-annulated cyclic compounds,[6b,6g,7] few general methods have been reported for the formation of monocyclic six-membered nitrogen heterocycles such as piperidines.[8]



Scheme 1[6]

We have developed various ring formation reactions utilizing ethenetricarboxylates as highly electrophilic C=C components.[9] In order to develop general synthetic methodology for

the construction of the heterocycles, we have investigated the use of more reactive electrophilic substrates than alkylidene and arylidenemalonates, ethenetricarboxylates.

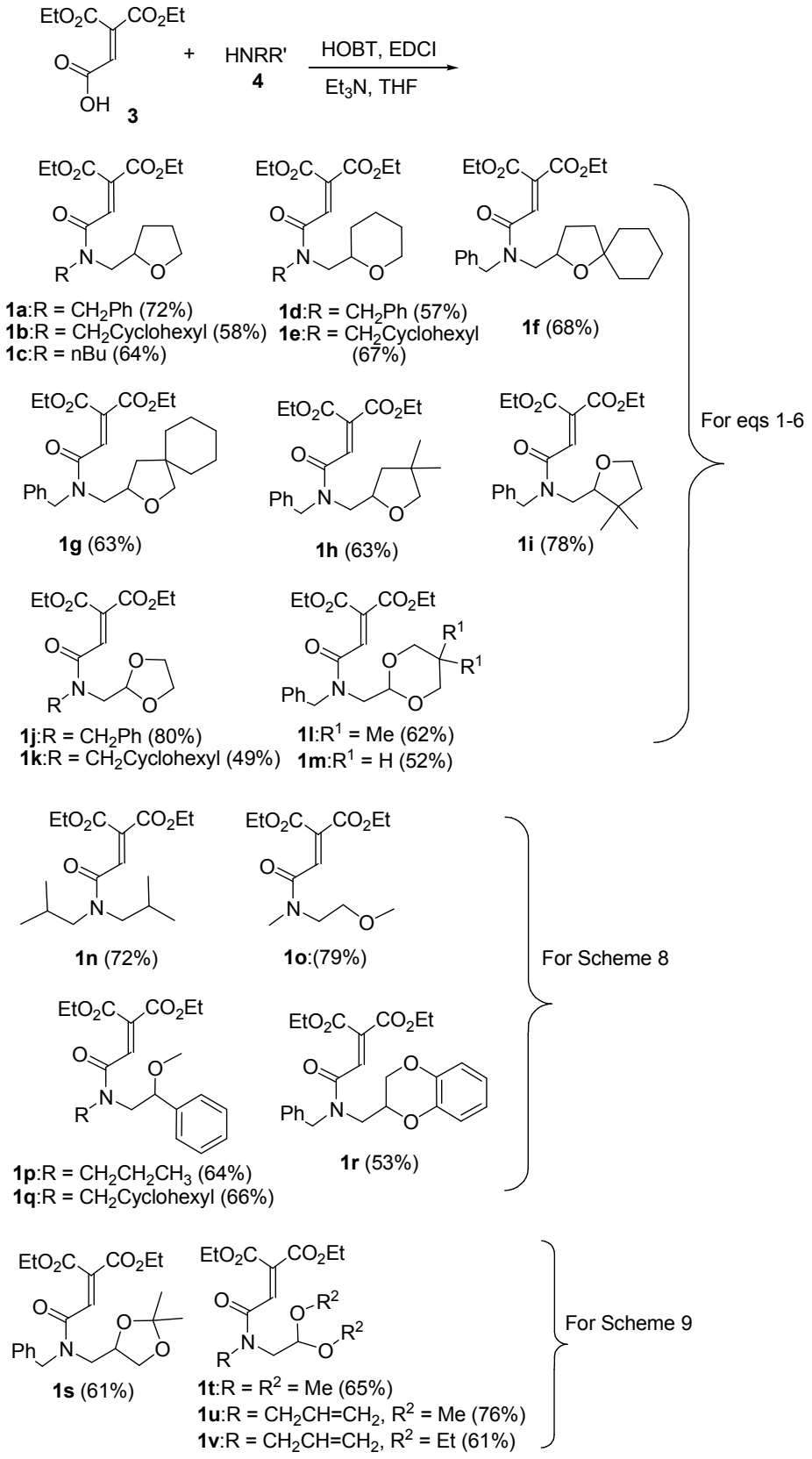


Scheme 2

In this study, catalytic cyclization of amides of ethenetricarboxylate bearing ether and acetal groups **1** has been examined (Scheme 2). The reaction of the amides **1** in the presence of Lewis acid gave piperidine derivatives as major products. The cyclized products may be formed via intramolecular hydride transfer. The scope and limitations of the hydride transfer/cyclization reactions of amides of ethenetricarboxylates have been studied.

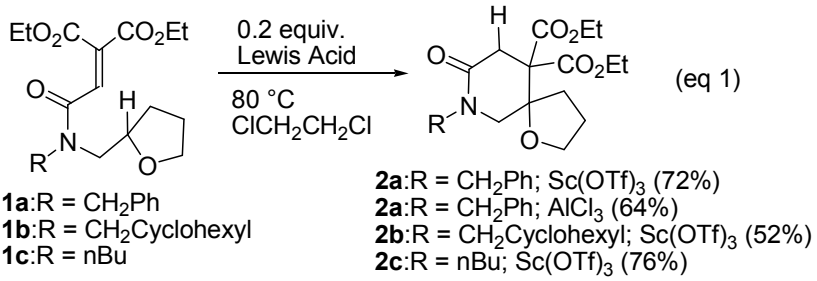
Results and Discussion

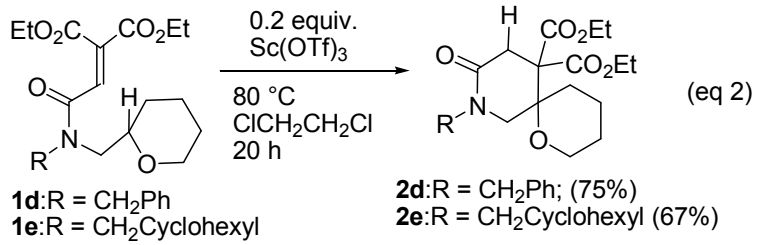
Amide precursors **1** for cyclization in this study were prepared by the condensation reaction of 1,1-diethyl 2-hydrogen ethenetricarboxylate **3** with the corresponding amines **4** in the presence of HOBT, EDCI and Et_3N in 49-80% yields (Scheme 3). Use of ethenetricarboxylate **3** is beneficial for ready introduction of various functional groups into 2-carboxyl position.


EtO2C
CO2Et
O
OH
3
+
HNRR'
4
HOBT, EDCI
Et3N, THF
1a:R = CH2Ph (72%)
1b:R = CH2Cyclohexyl (58%)
1c:R = nBu (64%)
1d:R = CH2Ph (57%)
1e:R = CH2Cyclohexyl (67%)
1f (68%)
1g (63%)
1h (63%)
1i (78%)
For eqs 1-6
1j:R = CH2Ph (80%)
1k:R = CH2Cyclohexyl (49%)
1l:R1 = Me (62%)
1m:R1 = H (52%)
1n (72%)
1o:(79%)
For Scheme 8
1p:R = CH2CH2CH3 (64%)
1q:R = CH2Cyclohexyl (66%)
1r (53%)
1s (61%)
1t:R = R2 = Me (65%)
1u:R = CH2CH=CH2, R2 = Me (76%)
1v:R = CH2CH=CH2, R2 = Et (61%)
For Scheme 9

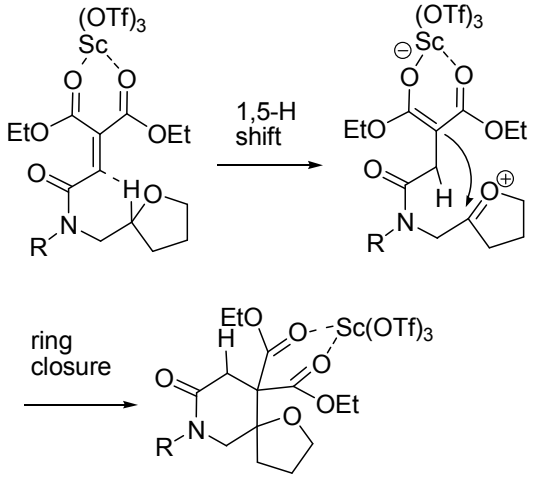
Scheme 3

Catalytic cyclization of amides of ethenetricarboxylate bearing ether groups **1** has been examined. The reaction of the amides bearing 5- and 6-membered cyclic ethers **1a-e** in the presence of Lewis acid such as $Sc(OTf)_3$ gave spirocyclic piperidine products **2a-e** selectively (eqs 1-2). The cyclized products may be formed via intramolecular hydride transfer.



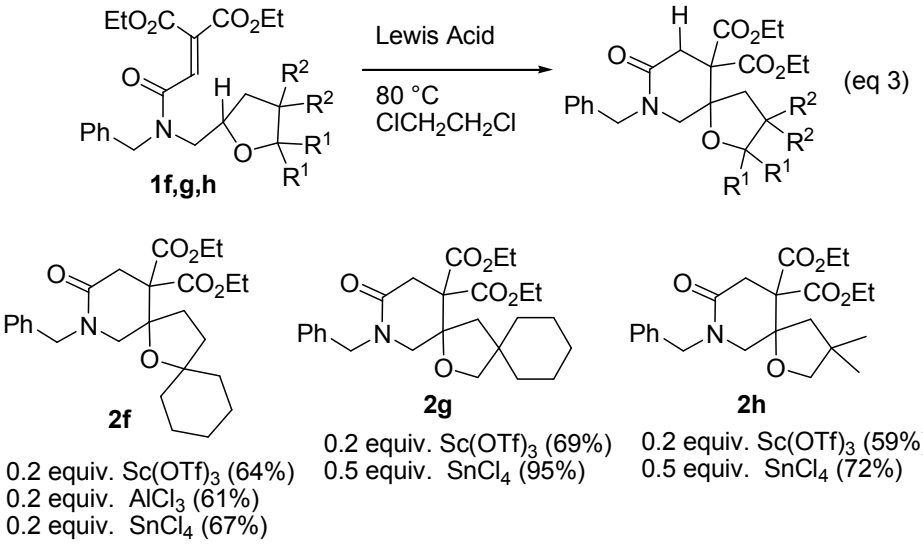


Activation of an electron-deficient alkene by a Lewis acid triggers a 1,5-hydride transfer and formation of a zwitterionic intermediate, which is followed by cyclization via ionic C-C bond formation (Scheme 4).

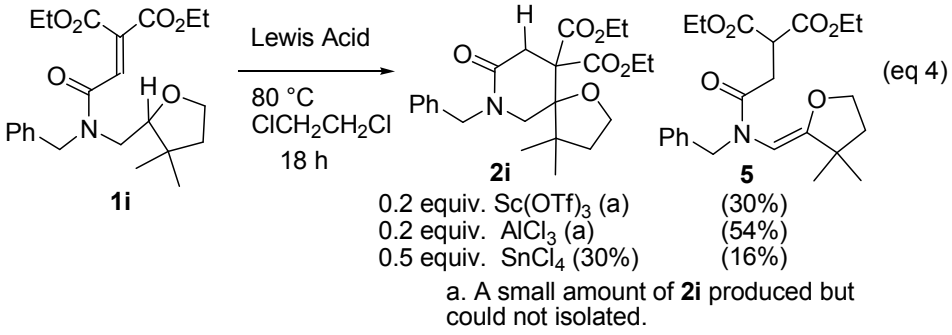


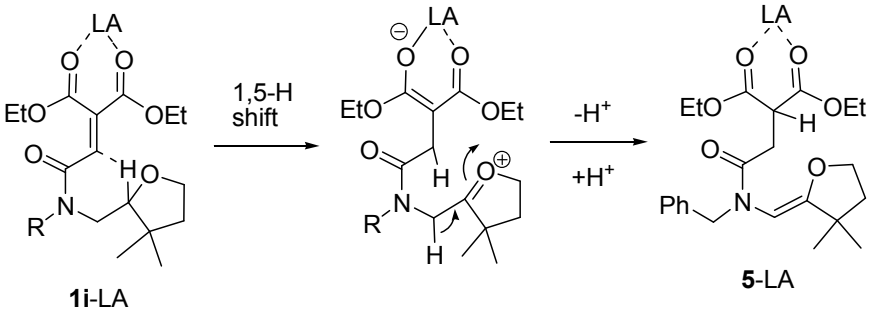
Scheme 4

The scope and generality of the reaction were investigated using variously substituted tetrahydrofuran-based substrates.[10] The reaction of **1f,g,h** with Lewis acids such as $Sc(OTf)_3$ and $SnCl_4$ gave the cyclized products **2f,g,h** efficiently (eq 3).



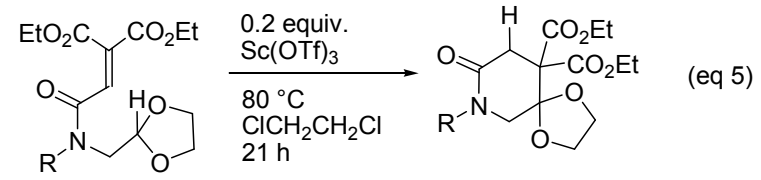
However, the reaction of **1i** with Lewis acids gave a small amount of cyclized product **2i** along with byproduct **5** (eq 4). The byproduct **5** may be formed via intramolecular hydride transfer and the subsequent deprotonation to form alkene from the resulting zwitterion intermediate (Scheme 5). Probably 3,3-dimethyl groups of tetrahydrofuran ring interfere with cyclization sterically.

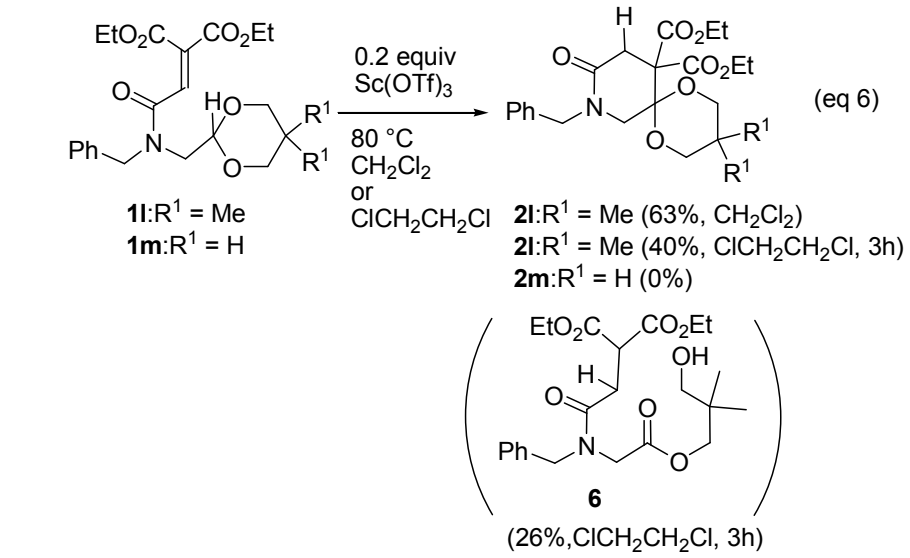


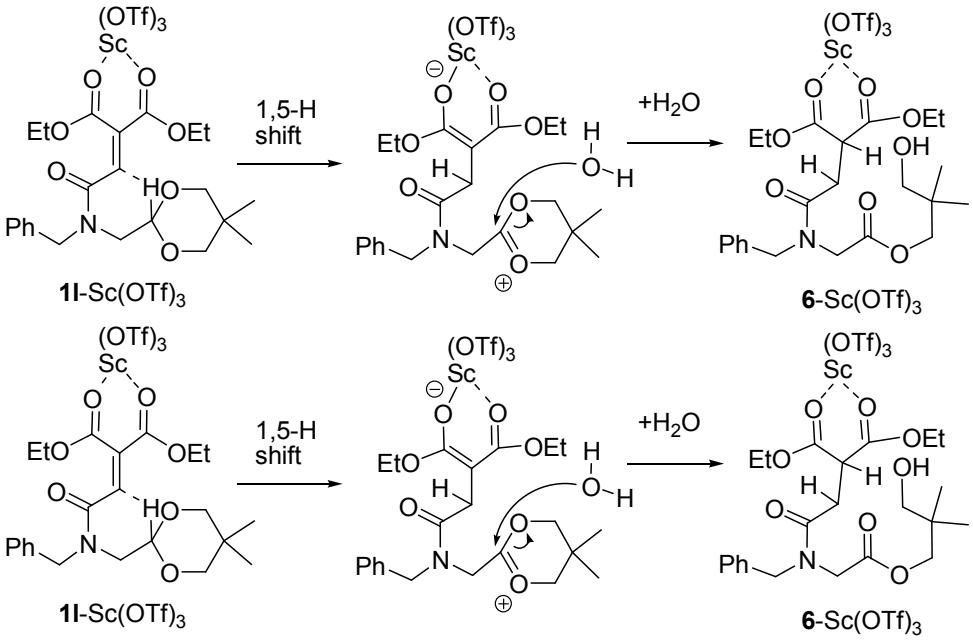


Scheme 5

The reaction of the amides bearing cyclic acetal, dioxolane derivatives **1j,k** in the presence of $Sc(OTf)_3$ gave piperidine derivatives **2j,k** similarly (eq 5). Reaction of 5,5-dimethyl-1,3-dioxolane derivative **1l** gave a cyclic compound as a major product upon heating in CH_2Cl_2 (eq 6). However, upon heating in 1,2-dichloroethane the byproduct **6** was also formed. The byproduct **6** may be formed via intramolecular hydride transfer and the subsequent reaction of the resulting zwitterion intermediate with water in situ (Scheme 6). Reaction of 1,3-dioxane derivative **1m** gave a complex mixture. This is probably because the deacetalization (hydrolysis by water *in situ*) competes with hydride transfer and/or cyclization.

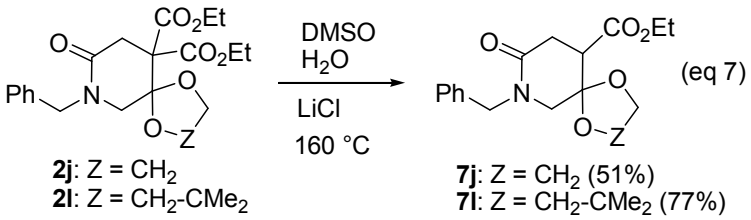






Scheme 6

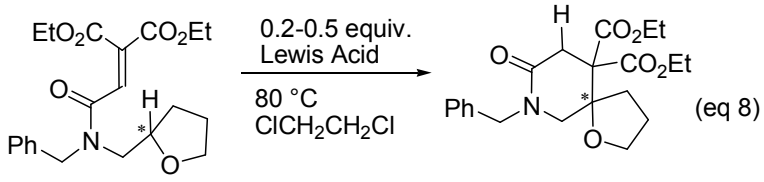
Product elaboration was next investigated. The acetal/malonate derivatives **2j,l** underwent monodecarboxylation in wet DMSO in the presence of LiCl under Krapcho conditions[11] to afford monoester derivatives **7j,l** (eq 7). Further selective transformation is under investigation.



2j: Z = CH_2
2l: Z = CH_2-CMe_2

7j: Z = CH_2 (51%)
7l: Z = CH_2-CMe_2 (77%)

Next, the stereoselectivity of the cyclization reaction was studied. Reaction of enantiomeric cyclic ethers (-)-(*R*)-**1a** and (+)-(*S*)-**1a** gave products (-)-**2a** and (+)-**2a** in 42-46% ee, respectively (eq 8).[12] The chiral information remained partially.

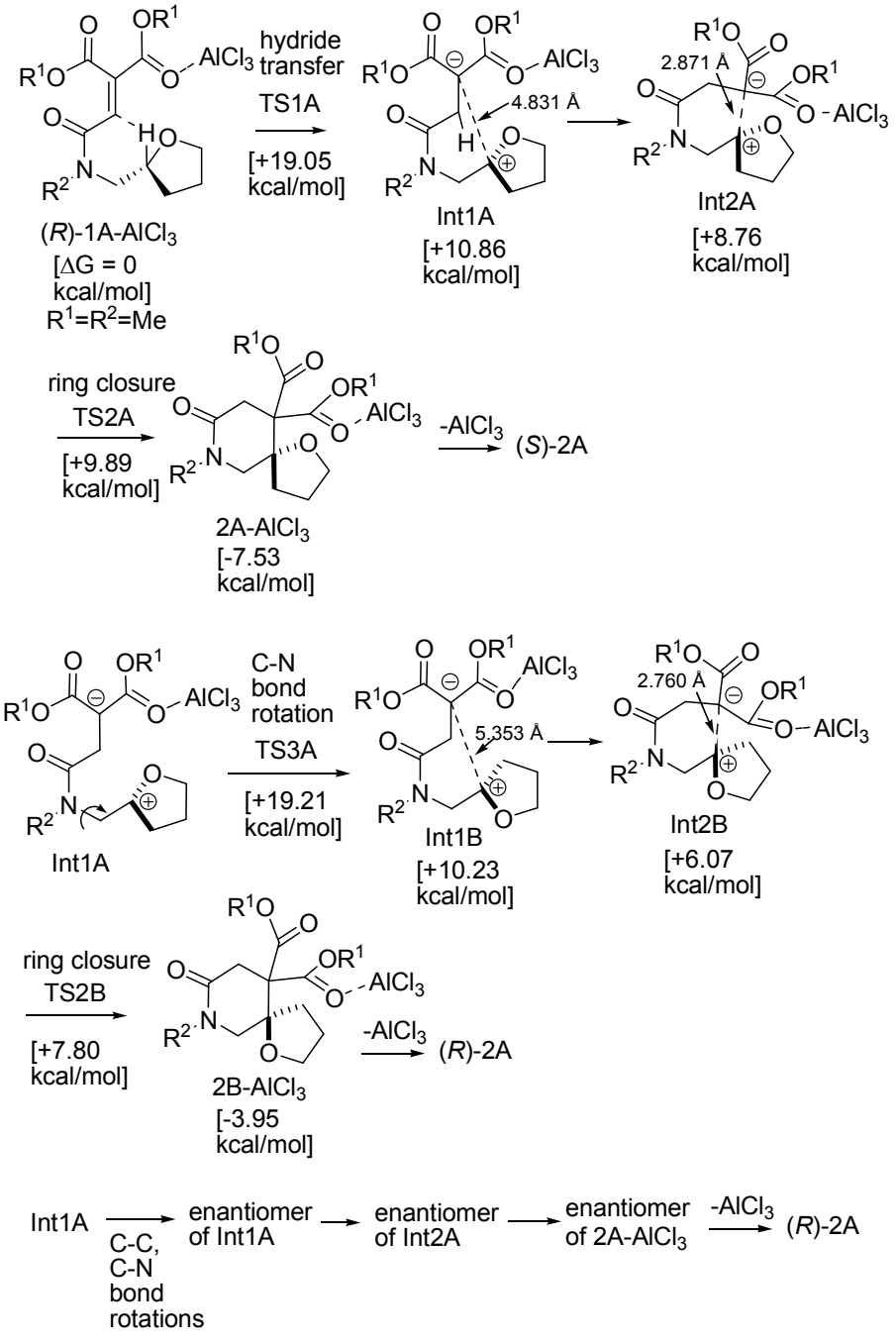


(-)-(R)-**1a** ee% >98%
0.2 eq. $Sc(OTf)_3$ (78%) (-)-**2a** 42% ee
0.5 eq. $SnCl_4$ (68%) (-)-**2a** 46% ee

(+)-(S)-**1a** ee% >98%
0.2 eq. $Sc(OTf)_3$ (82%) (+)-**2a** 43% ee
0.2 eq. $SnCl_4$ (71%) (+)-**2a** 46% ee

In order to elucidate the proposed mechanism in Scheme 4 and explain the stereochemical course, B3LYP/6-31G*[13,14] calculations including the PCM[15] solvent effect (solvent=CH_2Cl_2) were carried out. TS geometry was characterized by vibrational analysis, which checked whether the obtained geometry has single imaginary frequencies ($\nu^{\ddagger}$). From TSs, reaction paths were traced by the intrinsic reaction coordinate (IRC) method[16] to obtain the energy-minimum geometries. Relative Gibbs free energies are of RB3LYP/6-31G* SCRF = (PCM, solvent = CH_2Cl_2) (T = 353.15 K, P = 1 atm). The model compounds (R^1 = R^2 = Me and Lewis acid = $AlCl_3$) with (*R*)-configuration originally were used for the DFT calculations and the result is shown in Scheme 7 and Figure 1. The hydride transfer transition state TS1A leads to the zwitterion intermediate Int1A. A small conformational change to retain the original configuration gives Int2A, the precursor for ring closure. Int2A via transition state TS2A leads to (*S*)-2A with retention of configuration. However, Int1A may partially change to Int1B/cyclization with inversion of configuration. Moreover, the racemization of Int1A by the major conformational change could also result in the loss of chirality. For example, C-N

bond rotation via TS3A from Int1A leads to Int1B. The energy barrier for C-N rotation (19.21 kcal/mol) is only slightly higher than that of hydride transfer of TS1A. Although Reinhoudt[7b,17] and Akiyama[6g] reported high retention of chirality of their benzo-annulated substrates, in this case the chirality remained only partially. This is probably because the ethenetricarboxlates are less rigid.



Scheme 7. Reaction paths of the model compounds (R^1 = R^2 = Me; Lewis acid = $AlCl_3$). Gibbs free energies (T = 353.15 K, P = 1 atm) were obtained at the RB3LYP/6-31G* SCRF = (PCM, solvent = CH_2Cl_2) level and are relative to (*R*)-1A-$AlCl_3$.

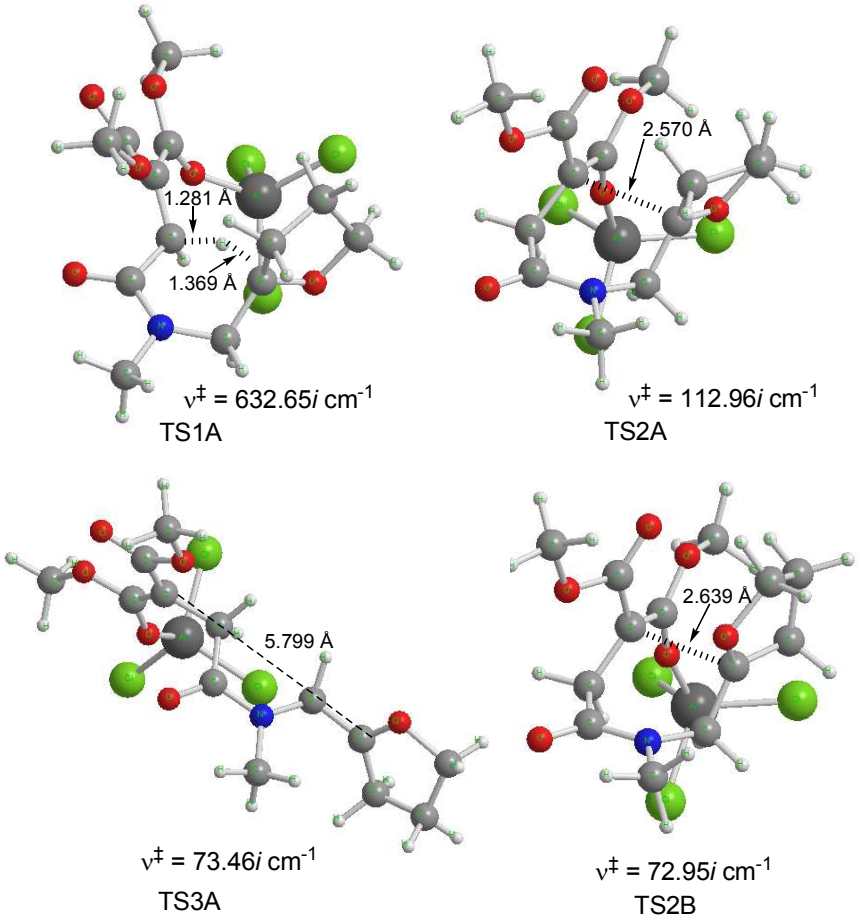
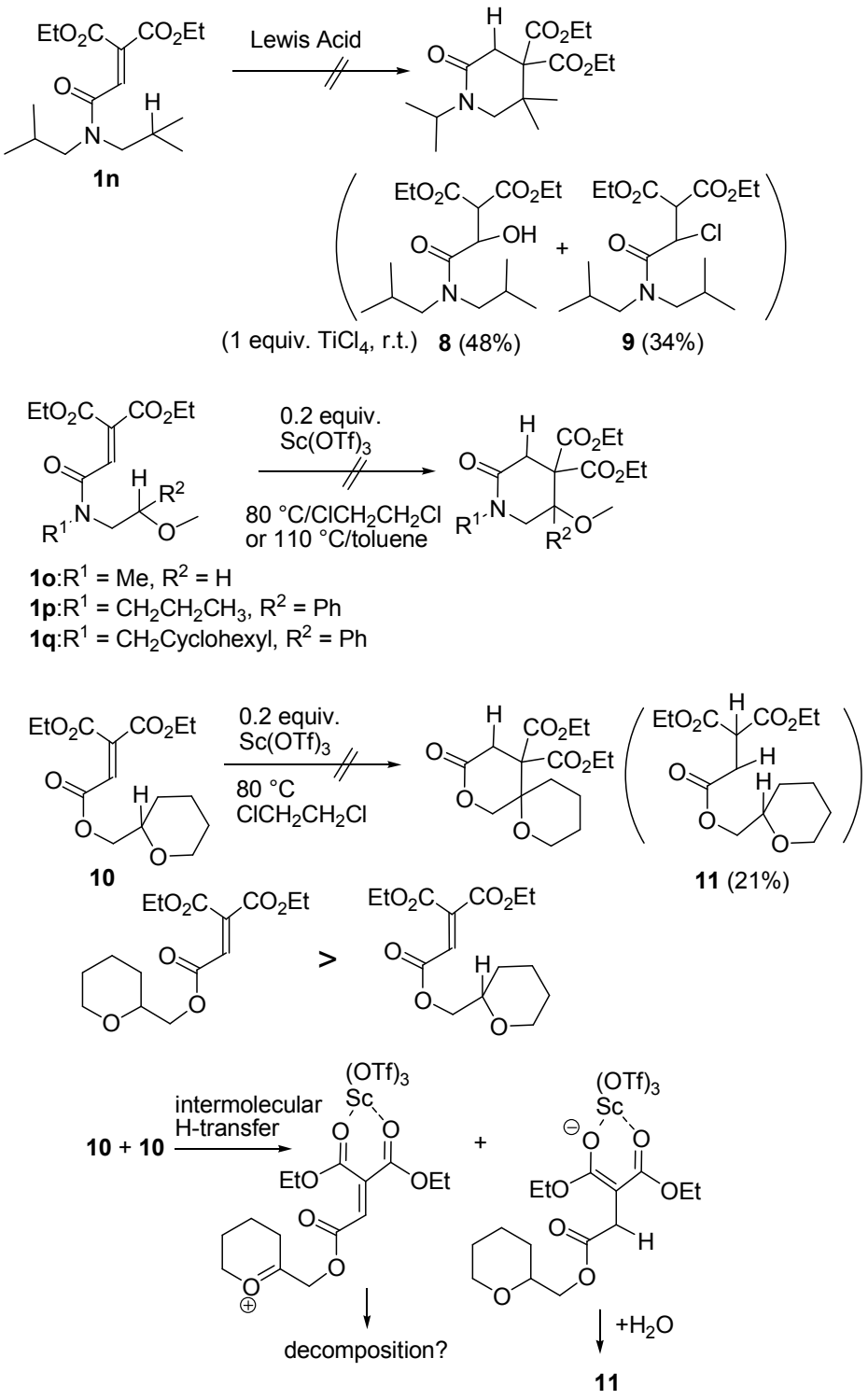


Figure 1. B3LYP/6-31G*-optimized structures of the transition states in Scheme 7.

The reactions of various substrates were also examined. As shown in Scheme 8, the cyclization reaction of diisobutylamide **1n** did not proceed.[18] The reaction of **1n** with $TiCl_4$ gave non-cyclized water and chlorine adducts as major products. The reaction of acyclic primary and secondary ethers **1o,p,q** also did not proceed under the reaction conditions. The reaction of 1,4-benzodioxane substrate **1r** (the structure is shown in Scheme 3) gave a complex mixture. Furthermore, the cyclization reaction of tetrahydropyran-2-methyl ester **10**

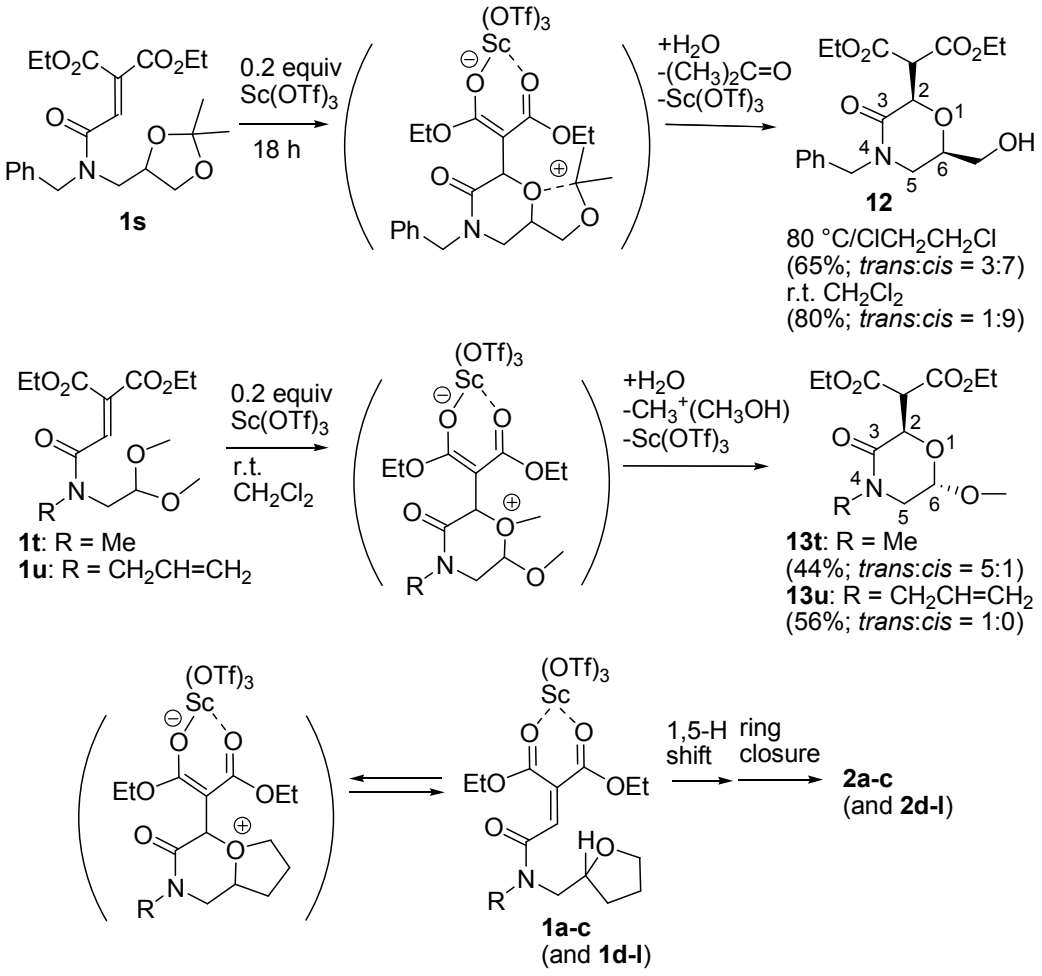
did not proceed efficiently. An isolable product is a reduced compound of C=C double bond **11**. This product **11** may be formed via intermolecular hydride transfer, although the detailed mechanism is not clear yet. The difference on reactivity between oxygen and nitrogen analogues can be explained, similar to the cyclization of other ethenetricarboxylate derivatives.[9] Triester **10** may be more stable in s-*cis* conformation, probably because of the steric repulsion. For intramolecular hydride transfer and cyclization, this must have s-*trans* conformation. In diester amides, the energy differences of s-*cis* and s-*trans* conformations may be small. The facile intramolecular reactions of amides probably originates from higher ratio of the reactive s-*trans* conformer.



Scheme 8

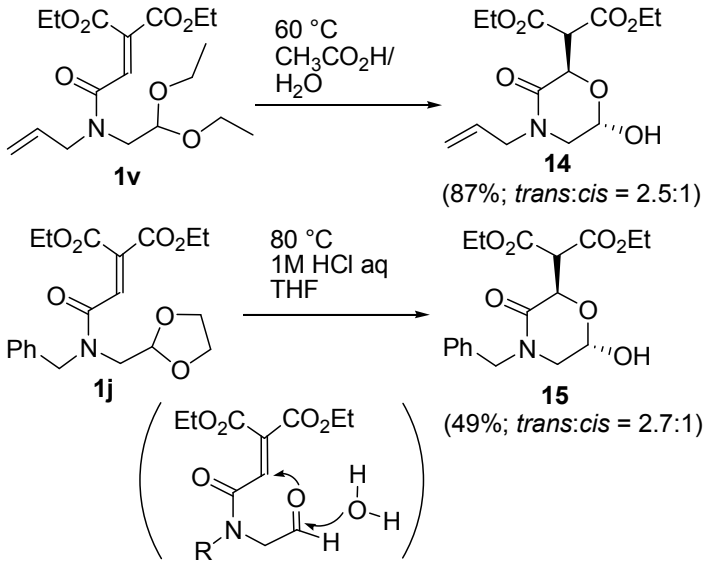
On the other hand, reaction of the amides bearing acetonide and acyclic acetals **1s**,**1t**,**1u** in the presence of $Sc(OTf)_3$ (0.2 equiv.) gave morpholine derivatives **12** and **13t,u** via nucleophilic attack of oxygen (Scheme 9). For the reaction of **1s-u**, facile C-O cleavage

occurs because of formation of tertiary carbocations (for **1s**) or demethylation (**1t,u**). Similar oxonium ion intermediates for the substrates **1a-l** may be formed reversibly, and intramolecular hydride transfer and cyclization reaction lead to **2a-l**.



Scheme 9

Acid catalyzed hydrolysis reaction of acetal amides **1v** and **1j** was also examined. The reaction of acyclic and cyclic acetals gave the cyclic hemiacetals **14** and **15**, respectively, as shown in Scheme 10. The formation of the products **14** and **15** demonstrates high electrophilicity of the ethenetricarboxylates.



Scheme 10

In summary, Lewis Acid-catalyzed cyclization reactions of ethenetricarboxylates bearing cyclic acetal and ether groups via intramolecular hydride transfer have been studied. The scope of the substrate for intramolecular hydride transfer/cyclization was expanded. The hydride transfer mechanism was examined by the DFT calculations. Reaction of enantiomeric cyclic ethers gave products with partial chirality, probably because the ethenetricaboxylates are not rigid enough. Reaction of the amides bearing acetonide and acyclic acetals in the presence of catalytic $Sc(OTf)_3$ gave morpholine derivatives via nucleophilic attack of oxygen. Further investigation on expansion of the substrate scope and improvement of the selectivity is underway.

Experimental Section

General Methods. ^1H Chemical shifts are reported in ppm relative to Me_4Si. ^{13}C Chemical shifts are reported in ppm relative to $CDCl_3$ (77.1 ppm). ^{13}C mutiplicities were determined by DEPT and HSQC. Peak assignments are made by 2D COSY, HSQC, NOESY, and HMBC spectra. Mass spectra were recorded at an ionizing voltage of 70 eV by EI, FAB, CI or ESI.

Mass analyzer type used for EI, FAB and CI is double-focusing and that for ESI is TOF in the HRMS measurements. HPLC analysis was performed with a UV detecter (detection, 254 nm light) and flow rate of 1.0 mL/min using a CHIRALPAK AS-H (0.46 cm × 250 mm) column at 30 °C. Optical rotations were measured with a 1 cm i.d. × 10 cm cell.

Amines **4a-c** were prepared from the aldehydes (benzaldehyde, cyclohexanecarboxaldehyde, and butanal) and tetrahydrofurfurylamine by reductive amination in methanol according to the literature procedure.[19]

***N*-Benzyltetrahydrofurfurylamine (4a)**: (8.9 mmol scale, 1.04 g, 61%) R_f = 0.2 (ether); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.51-1.60 (m, 1H), 1.83-1.99 (m, 4H), 2.65 (dd, *J* = 11.9, 7.5 Hz, 1H), 2.71 (dd, *J* = 11.9, 3.9 Hz, 1H), 3.71-3.76 (m, 1H), 3.81-3.86 (m, 1H), 3.82 (s, 2H), 4.03 (dddd, *J* = 7.5, 7.2, 7.2, 3.9 Hz, 1H), 7.21-7.26 (m, 1H), 7.29-7.35 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 25.8 (CH_2), 29.3 (CH_2), 53.7 (CH_2), 54.0 (CH_2), 67.9 (CH_2), 78.4 (CH), 126.9 (CH), 128.1 (CH), 128.4 (CH), 140.3 (C); IR (neat) 3325, 2971, 2867, 1604, 1495, 1453, 1361, 1132, 1072, 1028 cm^{-1}; MS (EI) m/z 191 (M^+, 5.7), 120 (75), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{12}H_{17}NO$ 191.1310; Found 191.1311.

***N*-Cyclohexylmethyltetrahydrofurfurylamine (4b)**: (8.9 mmol scale, 1.06 g, 60%) R_f = 0.2 (MeOH); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.857-0.943 (m, 2H), 1.10-1.29 (m, 4H), 1.41-1.58 (m, 2H), 1.64-1.82 (m, 5H), 1.83-2.00 (m, 3H), 2.43 (dd, *J* = 11.5, 6.6 Hz, 1H), 2.46 (dd, *J* = 11.5, 6.7 Hz, 1H), 2.63 (dd, *J* = 11.9, 7.2 Hz, 1H), 2.64 (dd, *J* = 11.9, 4.3 Hz, 1H), 3.70-3.78 (m, 1H), 3.81-3.87 (m, 1H), 4.00 (dddd, *J* = 7.4, 7.2, 4.3, 4.3 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 25.6 (CH_2), 26.0 (CH_2), 26.6 (CH_2), 29.2 (CH_2), 31.3 (CH_2), 37.9 (CH), 54.6 (CH_2), 56.9 (CH_2), 67.7 (CH_2), 78.3 (CH); IR (neat) 3336, 2925, 2850, 1449, 1362, 1137, 1072 cm^{-1}; MS (FAB) m/z 198 ($[M + H]^+$); HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{12}H_{24}NO$ 198.1858; Found 198.1859, $[M - H]^+$ Calcd for $C_{12}H_{22}NO$ 196.1701; Found 196.1702.

***N*-Butyltetrahydrofurfurylamine (4c)**: (8.9 mmol scale, 0.48 g, 31%) R_f = 0.1 (ether); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.912 (t, *J* = 7.2 Hz, 3H), 1.27 (bs, 1H),

1.30-1.39 (m, 2H), 1.43-1.58 (m, 3H), 1.83-2.01 (m, 3H), 2.57-2.71 (m, 4H), 3.74 (ddd, J = 8.4, 6.8, 6.8 Hz, 1H), 3.85 (ddd, J = 8.4, 6.8, 6.8 Hz, 1H), 4.00 (tdd, J = 7.2, 7.2, 4.1 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.1 (CH_3), 20.6 (CH_2), 25.8 (CH_2), 29.4 (CH_2), 32.4 (CH_2), 50.0 (CH_2), 54.7 (CH_2), 67.9 (CH_2), 78.5 (CH); IR (neat) 3326, 2956, 1458, 1377, 1137, 1072 cm^{-1}; MS (CI) m/z 158 ([M + H]$^+$); HRMS (CI) m/z: [M + H]$^+$ Calcd for $C_9H_{20}NO$ 158.1545; Found 158.1538.

Amines **4d-m,4r,s** were prepared by reaction of benzylamine or cyclohexylamine (2 equiv. to an excess amount) with alkyl bromides or iodides (1 equiv.) at 60-80 °C according to the literature procedure.[20] Amines **4u,v** were prepared by reaction of aminoacetaldehyde dimethyl/diethyl acetal (2 equiv.) with allyl bromide in ether at room temperature according to the literature procedure.[21] 2-(Bromomethyl)tetrahydro-2*H*-pyran for **4d,e** and 2-bromomethyl-1,3-dioxolane for **4j** were purchased. The alkyl iodides for **4f,g** were prepared according to the literature.[22] 2-(Iodomethyl)-4,4-dimethyltetrahydrofuran for **4h** and 2-(iodomethyl)-3,3-dimethyltetrahydrofuran for **4i** were prepared according to the literature method.[22] 2-(Bromomethyl)-5,5-dimethyl-1,3-dioxane for **4l** and 2-(bromomethyl)-1,3-dioxane for **4m** were prepared according to the literature.[23] 4-(Bromomethyl)-2,2-dimethyl-1,3-dioxolane for **4s** was prepared according to the literature.[24]

2-(Iodomethyl)-4,4-dimethyltetrahydrofuran: (17.5 mmol scale, 1.370 g, 33%); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.10 (s, 3H), 1.12 (s, 3H), 1.46 (dd, J = 12.5, 8.8 Hz, 1H), 1.94 (ddd, J = 12.5, 6.6, 0.8 Hz, 1H), 3.23 (dd, J = 9.9, 6.5 Hz, 1H), 3.27 (dd, J = 9.9, 5.4 Hz, 1H), 3.55 (dd, J = 8.0, 0.8 Hz, 1H), 3.62 (d, J = 8.0 Hz, 1H), 4.15 (dddd, J = 8.8, 6.6, 6.5, 5.4 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 11.0 (CH_2), 26.0 (CH_3), 26.6 (CH_3), 40.5 (C), 47.2 (CH_2), 78.6 (CH), 80.7 (CH_2); IR (neat) 2958, 2867, 1465, 1368, 1168, 1047 cm^{-1}; MS (CI) m/z 241 ([M + H]$^+$); HRMS (CI) m/z: [M + H]$^+$ Calcd for $C_7H_{14}IO$ 241.0089; Found 241.0080.

2-(Iodomethyl)-3,3-dimethyltetrahydrofuran: (6.76 mmol scale, 1.622 g, quantitative yield) R_f = 0.5 (hexane-ether = 4 : 1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.946 (s, 3H), 1.12 (s, 3H), 1.80-1.91 (m, 2H), 3.10 (dd, J = 10.3, 9.6 Hz, 1H), 3.20 (dd, J =

10.3, 3.3 Hz, 1H), 3.72 (dd, *J* = 9.6, 3.3 Hz, 1H), 3.83-3.94 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 4.8 (CH_2), 21.1 (CH_3), 26.1 (CH_3), 41.6 (C), 41.8 (CH_2), 65.3 (CH_2), 87.3 (CH); IR (neat) 2958, 2871, 1464, 1414, 1389, 1369, 1183, 1109, 1021 cm^{-1}; MS (EI) m/z 240 (M^+, 1.2), 113 (59), 99 (100%); HRMS (EI) m/z: M^+ Calcd for $C_7H_{13}IO$ 240.0011; Found 240.0015.

***N*-Benzyl(tetrahydropyran-2-methyl)amine (4d)**: (10 mmol scale, 1.816 g, 86%) R_f = 0.1 (ether); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.25-1.35 (m, 1H), 1.43-1.62 (m, 4H), 1.80-1.85 (m, 2H), 2.60 (dd, *J* = 12.1, 3.5 Hz, 1H), 2.65 (dd, *J* = 12.1, 8.1 Hz, 1H), 3.39-3.49 (m, 2H), 3.79 (s, 2H), 3.97 (bd, *J* = 11.3 Hz, 1H), 7.21-7.26 (m, 1H), 7.29-7.33 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 23.3 (CH_2), 26.2 (CH_2), 29.8 (CH_2), 54.2 (CH_2), 54.9 (CH_2), 68.4 (CH_2), 77.2 (CH), 126.9 (CH), 128.2 (CH), 128.4 (CH), 140.5 (C); IR (neat) 3327, 2935, 2844, 1604, 1495, 1453, 1378, 1353, 1200, 1089, 1048 cm^{-1}; MS (EI) m/z 205 (M^+, 8.4), 120 (88), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{13}H_{19}NO$ 205.1467; Found 205.1468.

***N*-(Cyclohexylmethyl)(tetrahydropyran-2-methyl)amine (4e)**: (10 mmol scale, 1.582 g, 75%) R_f = 0.4 (MeOH); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.831-0.945 (m, 2H), 1.09-1.34 (m, 5H), 1.40-1.59 (m, 5H), 1.61-1.76 (m, 4H), 1.80-1.84 (m, 1H), 2.40 (dd, *J* = 11.5, 6.8 Hz, 1H), 2.43 (dd, *J* = 11.5, 6.6 Hz, 1H), 2.54 (dd, *J* = 12.1, 3.3 Hz, 1H), 2.62 (dd, *J* = 12.1, 8.4 Hz, 1H), 3.40-3.47 (m, 2H), 3.97 (bd, *J* = 11.1 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 23.3 (CH_2), 26.10 (CH_2), 26.12 (CH_2), 26.2 (CH_2), 26.7 (CH_2), 29.9 (CH_2), 31.48 (CH_2), 31.54 (CH_2), 38.0 (CH), 55.7 (CH_2), 57.0 (CH_2), 68.4 (CH_2), 77.2 (CH); IR (neat) 3339, 2929, 1449, 1376, 1345, 1262, 1202, 1178, 1089, 1047 cm^{-1}; MS (CI) m/z 212 ($[M + H]^+$); HRMS (CI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{26}NO$ 212.2014; Found 212.2013.

***N*-Benzyl-(1-oxaspiro[4.5]decan-2-ylmethyl)amine (4f)**: (3.5 mmol scale, 924 mg, 97%) R_f = 0.5 (ether); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.31-1.56 (m, 8H), 1.61-1.71 (m, 5H), 1.78 (bs, 1H), 1.90-1.96 (m, 1H), 2.62 (dd, *J* = 11.7, 7.0 Hz, 1H), 2.69 (dd, *J* = 11.7, 4.1 Hz, 1H), 3.80 (d, *J* = 13.4 Hz, 1H), 3.83 (d, *J* = 13.4 Hz, 1H), 4.08-4.14 (m, 1H), 7.20-7.25 (m, 1H), 7.28-7.35 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 23.8 (CH_2), 24.1 (CH_2), 25.7 (CH_2), 29.3 (CH_2), 35.9 (CH_2), 37.4 (CH_2), 38.6 (CH_2), 54.0 (CH_2), 54.5

(CH_2), 77.1 (CH), 82.8 (C), 126.7 (CH), 128.0 (CH), 128.3 (CH), 140.6 (C); IR (neat) 3327, 2928, 1495, 1454, 1359, 1314, 1131, 1074, 1028 cm^{-1}; MS (EI) m/z 259 (M^+, 51), 120 (100), 91 (71%); HRMS (EI) m/z: M^+ Calcd for $C_{17}H_{25}NO$ 259.1936; Found 259.1943.

***N*-Benzyl-(2-oxaspiro[4.5]decan-3-ylmethyl)amine (4g)**: (16.1 mmol scale, 2.896 g, 68%) R_f = 0.5 (hexane-ether = 1 : 8); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.34 (dd, *J* = 12.4, 8.9 Hz, 1H), 1.40-1.45 (m, 10H), 1.74 (bs, 1H), 1.82 (dd, *J* = 12.4, 6.6 Hz, 1H), 2.65-2.72 (m, 2H), 3.53 (d, *J* = 8.4 Hz, 1H), 3.56 (d, *J* = 8.4 Hz, 1H), 3.82 (s, 2H), 4.10 (dddd, *J* = 8.9, 6.6, 6.6, 4.9 Hz, 1H), 7.21-7.26 (m, 1H), 7.29-7.34 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 23.6 (CH_2), 24.1 (CH_2), 26.1 (CH_2), 35.6 (CH_2), 36.8 (CH_2), 42.2 (CH_2), 43.8 (C), 54.1 (CH_2), 54.2 (CH_2), 78.1 (CH), 78.4 (CH_2), 126.9 (CH), 128.2 (CH), 128.4 (CH), 140.4 (C); IR (neat) 3327, 3027, 2925, 1660, 1604, 1495, 1451, 1358, 1121, 1050 cm^{-1}; MS (CI) m/z 260 ($[M + H]^+$); HRMS (CI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{26}NO$ 260.2014; Found 260.2011.

***N*-Benzyl(tetrahydro-4,4-dimethylfuran-2-yl)methylamine (4h)**: (3.6 mmol scale, 664 mg, 68%) R_f = 0.3 (hexane-ether = 1 : 5); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.08 (s, 3H), 1.09 (s, 3H), 1.41 (dd, *J* = 12.3, 8.9 Hz, 1H), 1.74 (dd, *J* = 12.3, 6.8 Hz, 1H), 1.80 (bs, 1H), 2.69 (d, *J* = 5.7 Hz, 2H), 3.45 (d, *J* = 8.1 Hz, 1H), 3.48 (d, *J* = 8.1 Hz, 1H), 3.82 (s, 2H), 4.19 (ddt, *J* = 8.9, 6.8, 5.7 Hz, 1H), 7.21-7.26 (m, 1H), 7.29-7.35 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 26.57 (CH_3), 26.60 (CH_3), 39.6 (C), 44.6 (CH_2), 54.1 (CH_2), 54.3 (CH_2), 78.7 (CH), 80.0 (CH_2), 126.9 (CH), 128.1 (CH), 128.4 (CH), 140.4 (C); IR (neat) 3327, 3027, 2952, 1604, 1495, 1454, 1367, 1200, 1128, 1060, 1028 cm^{-1}; MS (CI) m/z 220 ($[M + H]^+$); HRMS (CI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{22}NO$ 220.1701; Found 220.1704.

***N*-Benzyl(tetrahydro-3,3-dimethylfuran-2-yl)methylamine (4i)**: (19.0 mmol scale, 474 mg, 34%) R_f = 0.3 (hexane-ether = 1 : 4); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.905 (s, 3H), 1.07 (s, 3H), 1.65 (bs, 1H), 1.63-1.83 (m, 2H), 2.59-2.66 (m, 2H), 3.55 (dd, *J* = 7.5, 4.6 Hz, 1H), 3.76-3.90 (m, 2H), 3.82 (s, 2H), 7.21-7.26 (m, 1H), 7.29-7.35 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 21.8 (CH_3), 26.0 (CH_3), 40.1 (C), 41.5 (CH_2), 50.0 (CH_2), 54.4 (CH_2), 65.7 (CH_2), 86.2 (CH), 126.9 (CH), 128.1 (CH), 128.4 (CH), 140.4

(C); IR (neat) 3326, 3027, 2956, 2871, 1495, 1453, 1386, 1368, 1102, 1026 cm^{-1}; MS (EI) m/z 219 (M^+, 3.3), 176 (3.5), 120 (98), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{14}H_{21}NO$ 219.1623; Found 219.1618.

***N*-Benzyl(1,3-dioxolan-2-yl)methylamine (4j)**: (10.7 mmol scale, 1.670 g, 81%) R_f = 0.9 (MeOH-ether = 1 : 10); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.83 (bs, 1H), 2.83 (d, *J* = 4.3 Hz, 2H), 3.84-4.02 (m, 4H), 3.85 (s, 2H), 5.02 (t, *J* = 4.3 Hz, 1H), 7.22-7.27 (m, 1H), 7.29-7.34 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 51.4 (CH_2), 54.0 (CH_2), 65.1 (CH_2), 103.4 (CH), 127.0 (CH), 128.2 (CH), 128.5 (CH), 140.0 (C); IR (neat) 3330, 3027, 2358, 1603, 1495, 1454, 1411, 1362, 1201, 1122, 1029 cm^{-1}; MS (EI) m/z 194 ([M + H]$^+$, 3.8), 193 (M^+, 2.8), 120 (52), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{11}H_{15}NO_2$ 193.1103; Found 193.1102.

***N*-Cyclohexyl(1,3-dioxolan-2-yl)methylamine (4k)**: (10 mmol scale, 1.172 g, 59%) R_f = 0.2 (ether); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.843-0.937 (m, 2H), 1.09-1.31 (m, 3H), 1.31 (bs, 1H), 1.41-1.52 (m, 1H), 1.65-1.73 (m, 5H), 2.48 (d, *J* = 6.6 Hz, 2H), 2.79 (d, *J* = 4.3 Hz, 2H), 3.83-3.92 (m, 2H), 3.94-4.02 (m, 2H), 4.99 (t, *J* = 4.3 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 26.0 (CH_2), 26.7 (CH_2), 31.3 (CH_2), 37.9 (CH), 52.5 (CH_2), 57.0 (CH_2), 65.0 (CH_2), 103.4 (CH); IR (neat) 2921, 2851, 1449, 1129, 1039 cm^{-1}; MS (FAB) m/z 222 ([M + Na]$^+$), 200 ([M + H]$^+$); HRMS (FAB) m/z: [M + H]$^+$ Calcd for $C_{11}H_{22}NO_2$ 200.1651; Found 200.1653.

***N*-Benzyl(5,5-dimethyl-1,3-dioxan-2-yl)methylamine (4l)**: (10 mmol scale, 2.961 g, 66%) R_f = 0.2 (ether); colorless crystals; mp 37-39 °C; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.707 (s, 3H), 1.18 (s, 3H), 1.66 (bs, 1H), 2.80 (d, *J* = 4.9 Hz, 2H), 3.42 (d, *J* = 10.7 Hz, 2H), 3.60 (d, *J* = 10.7 Hz, 2H), 3.81 (s, 2H), 4.57 (t, *J* = 4.9 Hz, 1H), 7.20-7.26 (m, 1H), 7.28-7.31 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 21.8 (CH_3), 23.0 (CH_3), 30.4 (C), 52.4 (CH_2), 54.0 (CH_2), 77.1 (CH_2), 100.8 (CH), 126.9 (CH), 128.2 (CH), 128.4 (CH), 140.1 (C); IR (KBr) 3326, 2953, 2839, 1468, 1453, 1412, 1398, 1144, 1123, 1097, 1025, 1011, 986 cm^{-1}; MS (EI) m/z 235 (M^+, 6.8), 115 (100), 91 (76%); HRMS (EI) m/z: M^+ Calcd for $C_{14}H_{21}NO_2$ 235.1572; Found 235.1576.

***N*-Benzyl(1,3-dioxan-2-yl)methylamine (4m)**: (10 mmol scale, 1.444 g, 70%) R_f = 0.1 (ether); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.32 (bd, *J* = 12.5 Hz, 1H), 1.71 (bs, 1H), 2.07 (dtt, *J* = 12.5, 12.5, 5.0 Hz, 1H), 2.75 (d, *J* = 4.9 Hz, 2H), 3.75 (ddd, *J* = 12.5, 11.1, 2.4 Hz, 2H), 3.79 (s, 2H), 4.09 (dd, *J* = 11.1, 5.0 Hz, 2H), 4.67 (t, *J* = 4.9 Hz, 1H), 7.20-7.25 (m, 1H), 7.27-7.33 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 25.8 (CH_2), 52.5 (CH_2), 53.9 (CH_2), 66.7 (CH_2), 100.7 (CH), 126.9 (CH), 128.1 (CH), 128.3 (CH), 140.0 (C); IR (neat) 3331, 2958, 2850, 1603, 1495, 1454, 1377, 1242, 1145, 1087, 1005 cm^{-1}; MS (EI) m/z 207 (M^+, 7.8), 120 (44), 91 (97), 87 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{12}H_{17}NO_2$ 207.1259; Found 207.1254.

***N*-Benzyl-(2,3-dihydrobenzo[*b*][1,4]dioxin-2-yl)methylamine (4r)**: (10 mmol scale, 1.582 g, 62%) R_f = 0.4 (hexane-ether = 1 : 1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.76 (bs, 1H), 2.86 (dd, *J* = 12.5, 4.7 Hz, 1H), 2.91 (dd, *J* = 12.5, 6.6 Hz, 1H), 3.84 (s, 2H), 4.02 (dd, *J* = 11.1, 7.4 Hz, 1H), 4.23-4.31 (m, 2H), 6.81-6.88 (m, 4H), 7.23-7.28 (m, 1H), 7.30-7.36 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 49.3 (CH_2), 54.0 (CH_2), 66.6 (CH_2), 72.7 (CH), 117.2 (CH), 117.4 (CH), 121.4 (CH), 121.6 (CH), 127.2 (CH), 128.2 (CH), 128.5 (CH), 140.0 (C), 143.2 (C), 143.3 (C); IR (neat) 3343, 3027, 2882, 1592, 1494, 1454, 1350, 1305, 1263, 1199, 1114, 1042 cm^{-1}; MS (EI) m/z 255 (M^+, 17), 120 (88), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{16}H_{17}NO_2$ 255.1259; Found 255.1257.

***N*-Benzyl-(2,2-dimethyl-1,3-dioxolan-4-yl)methylamine (4s)**: (10 mmol scale, 1.274 g, 66%) R_f = 0.3 (hexane-ether = 1 : 2); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.35 (s, 3H), 1.41 (s, 3H), 1.69 (bs, 1H), 2.74 (d, *J* = 5.7 Hz, 2H), 3.69 (dd, *J* = 8.0, 6.6 Hz, 1H), 3.83 (d, *J* = 13.4 Hz, 1H), 3.84 (d, *J* = 13.4 Hz, 1H), 4.04 (dd, *J* = 8.0, 6.4 Hz, 1H), 4.26 (ddt, *J* = 6.6, 6.4, 5.7 Hz, 1H), 7.23-7.28 (m, 1H), 7.29-7.34 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 25.5 (CH_3), 27.0 (CH_3), 51.8 (CH_2), 54.0 (CH_2), 67.6 (CH_2), 75.5 (CH), 109.2 (C), 127.1 (CH), 128.2 (CH), 128.5 (CH), 140.1 (C); IR (neat) 3327, 2986, 2934, 2881, 1604, 1495, 1454, 1379, 1370, 1254, 1213, 1159, 1055 cm^{-1}; MS (EI) m/z 221 (M^+, 2.6), 206 (7.8), 163 (10), 120 (83), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{13}H_{19}NO_2$ 221.1416; Found 221.1407.

***N*-(2,2-Dimethoxyethyl)-1-prop-2-enylamine (4u)**: (11.8 mmol scale, 789 mg, 46%) R_f = 0.5 (MeOH-ether = 1 : 1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.68 (bs, 1H), 2.75 (d, *J* = 5.5 Hz, 2H), 3.28 (ddd, *J* = 6.0, 1.6, 1.2 Hz, 2H), 3.39 (s, 6H), 4.49 (t, *J* = 5.5 Hz, 1H), 5.11 (dddd, *J* = 10.3, 1.6, 1.2, 1.2 Hz, 1H), 5.19 (dddd, *J* = 17.2, 1.6, 1.6, 1.6 Hz, 1H), 5.89 (ddt, *J* = 17.2, 10.3, 6.0 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 50.5 (CH_2), 52.4 (CH_2), 54.2 (CH_3), 104.0 (CH), 116.4 (CH_2), 136.5 (CH); IR (neat) 3329, 2935, 2831, 1644, 1461, 1195, 1132, 1059, 996 cm^{-1}; MS (EI) m/z 145 (M^+, 2.4), 134 (11.9), 114 (19), 75 (100%); HRMS (EI) m/z: M^+ Calcd for $C_7H_{15}NO_2$ 145.1103; Found 145.1084.

***N*-(2,2-Diethoxyethyl)-1-prop-2-enylamine (4v)**: (10.6 mmol scale, 1.583 g, 86%) R_f = 0.7 (MeOH-ether = 1 : 1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.22 (t, *J* = 7.0 Hz, 6H), 1.94 (bs, 1H), 2.75 (d, *J* = 5.5 Hz, 2H), 3.29 (ddd, *J* = 6.1, 1.6, 1.2 Hz, 2H), 3.55 (dq, *J* = 9.4, 7.0 Hz, 2H), 3.71 (dq, *J* = 9.4, 7.0 Hz, 2H), 4.63 (t, *J* = 5.5 Hz, 1H), 5.11 (dddd, *J* = 10.4, 1.4, 1.2, 1.2 Hz, 1H), 5.20 (dddd, *J* = 17.2, 1.6, 1.6, 1.4 Hz, 1H), 5.90 (ddt, *J* = 17.2, 10.4, 6.1 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 15.5 (CH_3), 51.5 (CH_2), 52.3 (CH_2), 62.6 (CH_2), 102.2 (CH), 116.5 (CH_2), 136.4 (CH); IR (neat) 3407, 2977, 2899, 1644, 1456, 1374, 1125, 1062, 1007 cm^{-1}; MS (EI) m/z 173 (M^+, 1.3), 128 (30), 103 (100%); HRMS (EI) m/z: M^+ Calcd for $C_9H_{19}NO_2$ 173.1416; Found 173.1395.

Diisopropylamine (**4n**), *N*-(2-methoxyethyl)methylamine (**4o**), and *N*-(2,2-dimethoxyethyl)-methylamine (**4t**) were purchased.

Amines **4p,q** were prepared by the reduction of the corresponding amides with $LiAlH_4$. The amides, 2-methoxy-2-phenyl-*N*-propylacetamide and *N*-(cyclohexylmethyl)-2-methoxy-2-phenylacetamide for **4p,q** were prepared by the reaction of DL-α-methoxyphenylacetic acid and propylamine or cyclohexylmethylamine with EDCI/HOBt/Et_3N.

2-Methoxy-2-phenyl-*N*-propylacetamide: (10 mmol scale, 2.038 g, 98%); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.916 (t, *J* = 7.4 Hz, 3H), 1.50-1.59 (m, 2H), 3.24 (q, *J* = 6.6 Hz, 2H), 3.36 (s, 3H), 4.61 (s, 1H), 6.77 (bs, 1H), 7.28-7.41 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 11.4 (CH_3), 22.9 (CH_2), 40.7 (CH_2), 57.3 (CH_3), 83.9 (CH), 127.0 (CH), 128.4 (CH), 128.6 (CH), 137.3 (C), 170.5 (C); IR (neat) 3314, 2964, 2934, 1668, 1455,

1255, 1198, 1102 cm^{-1}; MS (EI) m/z 207 (M^+, 0.1), 177 (2.4), 121 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{12}H_{17}NO_2$ 207.1259; Found 207.1248.

***N*-(Cyclohexylmethyl)-2-methoxy-2-phenylacetamide**: (10 mmol scale, 2.618 g, 100%); colorless crystals; mp 60-61 °C; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.868-0.967 (m, 2H), 1.08-1.27 (m, 3H), 1.42-1.53 (m, 1H), 1.63-1.73 (m, 5H), 3.11 (dd, *J* = 6.5, 6.5 Hz, 2H), 3.36 (s, 3H), 4.61 (broad t, 1H), 7.28-7.40 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 25.8 (CH_2), 26.4 (CH_2), 30.77 (CH_2), 30.81 (CH_2), 37.9 (CH), 45.1 (CH_2), 57.2 (CH_3), 83.9 (CH), 127.0 (CH), 128.3 (CH), 128.5 (CH), 137.2 (C), 170.5 (C); IR (KBr) 3328, 2917, 2849, 1654, 1539, 1449, 1197, 1098, 992 cm^{-1}; MS (FAB) m/z 284 ($[M + Na]^+$), 262 ($[M + H]^+$); HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{16}H_{24}NO_2$ 262.1807; Found 262.1810; Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.26; H, 8.86; N, 5.38.

***N*-(2-methoxy-2-phenylethyl)-1-propylamine (4p)**: (2.56 mmol scale, 199 mg, 40%) R_f = 0.3 (MeOH-ether = 1 : 4); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.909 (t, *J* = 7.4 Hz, 3H), 1.46-1.56 (m, 2H), 2.02 (bs, 1H), 2.56-2.60 (m, 2H), 2.69 (dd, *J* = 12.3, 3.7 Hz, 1H), 2.86 (dd, *J* = 12.3, 9.2 Hz, 1H), 3.25 (s, 3H), 4.33 (dd, *J* = 9.2, 3.7 Hz, 1H), 7.27-7.38 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 11.8 (CH_3), 23.2 (CH_2), 51.8 (CH_2), 56.87 (CH_2), 56.89 (CH_3), 83.2 (CH), 126.8 (CH), 127.9 (CH), 128.5 (CH), 140.5 (C); IR (neat) 3327, 2933, 2822, 1674, 1493, 1454, 1356, 1103 cm^{-1}; MS (EI) m/z 193 (M^+, 1.1), 132 (6.0), 121 (12), 72 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{12}H_{19}NO$ 193.1467; Found 193.1475.

***N*-(Cyclohexylmethyl)-2-methoxy-2-phenylethylamine (4q)**: (5 mmol scale, 992 mg, 80%) R_f = 0.4 (hexane-ether = 1 : 4); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.835-0.935 (m, 2H), 1.09-1.29 (m, 3H), 1.41-1.51 (m, 1H), 1.65-1.75 (m, 5H), 2.44 (dd, *J* = 11.6, 6.6 Hz, 1H), 2.46 (dd, *J* = 11.6, 6.6 Hz, 1H), 2.66 (dd, *J* = 12.3, 3.7 Hz, 1H), 2.85 (dd, *J* = 12.3, 9.2 Hz, 1H), 3.25 (s, 3H), 4.34 (dd, *J* = 9.2, 3.7 Hz, 1H), 7.27-7.38 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 26.11 (CH_2), 26.12 (CH_2), 26.7 (CH_2), 31.48 (CH_2), 31.51 (CH_2), 38.0 (CH), 56.7 (CH_2), 56.9 (CH_3), 57.2 (CH_2), 83.2 (CH), 126.7 (CH), 127.8 (CH), 128.5 (CH), 140.6 (C); IR (neat) 3338, 2922, 2850, 1680, 1450, 1109 cm^{-1}; MS (EI) m/z 247 (M^+, 2.9), 126 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{16}H_{25}NO$ 247.1936; Found 247.1931.

Preparation of Substrates 1a-v. To a solution of 1,1-diethyl 2-hydrogen ethenetricarboxylate (238 mg, 1.1 mmol) (prepared from 1,1-diethyl 2-*tert*-butyl ethenetricarboxylate upon treatment with CF_3CO_2H) in THF (1 mL) were added *N*-benzyl ((tetrahydrofuran-2-yl)methyl)amine **4a** (192 mg, 1 mmol) in THF (0.5 mL), Et_3N (0.14 mL, 101 mg, 1 mmol), HOBt (1-hydroxybenzotriazole) (280 mg, 2.1 mmol) and EDCI (1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride) (210 mg, 1.1 mmol) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C, and was allowed to warm to room temperature and stirred overnight. The reaction mixture was concentrated under reduced pressure and the residue was diluted with CH_2Cl_2. The organic phase was washed with saturated aqueous $NaHCO_3$ solution, 2M aqueous citric acid, saturated aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified by column chromatography over silica gel eluting with hexane-ether to give **1a** (300 mg, 72%).

1a: R_f = 0.6 (ether); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.2:1) δ (ppm) 1.26-1.36 (m, 6H), 1.40-1.53 (m, 1H), 1.80-2.03 (m, 3H), 3.07 (dd, *J* = 14.0, 8.1 Hz, 1H×0.55, major rotamer), 3.24 (dd, *J* = 15.4, 3.3 Hz, 1H×0.45, minor rotamer), 3.33 (dd, *J* = 15.4, 8.3 Hz, 1H×0.45), 3.72-3.87 (m, 2H+1H×0.45), 4.04 (ddd, *J* = 8.3, 7.0, 3.2 Hz, 1H×0.45), 4.15 (ddd, *J* = 8.1, 7.4, 3.1 Hz, 1H×0.55), 4.22-4.38 (m, 4H), 4.62 (d, *J* = 15.0 Hz, 1H×0.45), 4.75 (d, *J* = 16.6 Hz, 1H×0.55), 4.79 (d, *J* = 16.6 Hz, 1H×0.55), 4.89 (d, *J* = 15.0 Hz, 1H×0.45), 7.20-7.38 (m, 5H), 7.35 (s, 1H×0.55), 7.53 (s, 1H×0.45); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.96 (CH_3), 14.00 (CH_3), 14.1 (CH_3), 25.5 (CH_2), 25.7 (CH_2), 29.29 (CH_2), 29.30 (CH_2), 48.7 (CH_2), 48.9 (CH_2), 51.4 (CH_2), 52.7 (CH_2), 61.8 (CH_2), 61.9 (CH_2), 62.07 (CH_2), 62.13 (CH_2), 67.97 (CH_2), 68.04 (CH_2), 77.0 (CH), 78.0 (CH), 127.0 (CH), 127.5 (CH), 127.9 (CH), 128.2 (CH), 128.6 (CH), 129.0 (CH), 134.0 (C), 134.4 (CH), 135.2 (C), 135.6 (CH), 136.3 (C), 136.7 (C), 163.0 (C), 163.2 (C), 164.58 (C), 164.64 (C), 164.9 (C); IR (neat) 2980, 1728, 1652, 1465, 1445, 1374, 1256, 1209, 1069 cm^{-1}; MS (EI) m/z 389 (M^+, 1.0), 343 (39), 200 (70), 190 (97), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{21}H_{27}NO_6$ 389.1838; Found 389.1843.

1b: (3 mmol scale, 690 mg, 58%) R_f = 0.6 (ether); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.3:1) δ (ppm) 0.823-0.989 (m, 2H), 1.19-1.28 (m, 3H), 1.311 (t, *J*

= 7.1 Hz, 3H×0.43, minor rotamer), 1.312 (t, *J* = 7.1 Hz, 3H×0.43), 1.317 (t, *J* = 7.1 Hz, 3H×0.57, major rotamer), 1.319 (t, *J* = 7.1 Hz, 3H×0.57), 1.43-1.55 (m, 1H), 1.59-1.76 (m, 6H), 1.80-2.05 (m, 3H), 3.10 (dd, *J* = 13.8, 7.7 Hz, 1H×0.57), 3.21 (dd, *J* = 13.4, 7.1 Hz, 1H×0.43), 3.29-3.34 (m, 2H×0.57+1H×0.43), 3.39-3.45 (m, 2H×0.43), 3.69-3.79 (m, 1H), 3.82-3.88 (m, 1H+1H×0.57), 4.03 (dddd, *J* = 7.3, 7.3, 7.3, 3.3 Hz, 1H×0.43), 4.09 (dddd, *J* = 7.3, 7.3, 7.3, 3.3 Hz, 1H×0.57), 4.26-4.36 (m, 4H), 7.36 (s, 1H×0.57), 7.47 (s, 1H×0.43); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.9 (CH_3), 14.01 (CH_3), 14.03 (CH_3), 25.4 (CH_2), 25.7 (CH_2), 25.8 (CH_2), 25.85 (CH_2), 25.89 (CH_2), 26.3 (CH_2), 26.4 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 30.68 (CH_2), 30.74 (CH_2), 30.8 (CH_2), 30.9 (CH_2), 36.1 (CH), 37.5 (CH), 50.0 (CH_2), 52.4 (CH_2), 53.1 (CH_2), 55.7 (CH_2), 61.7 (CH_2), 62.0 (CH_2), 62.1 (CH_2), 67.9 (CH_2), 68.0 (CH_2), 77.2 (CH), 77.7 (CH), 133.3 (C), 134.1 (CH), 134.7 (C), 135.9 (CH), 163.2 (C), 163.3 (C), 164.2 (C), 164.7 (C), 164.77 (C), 164.79 (C); IR (neat) 2926, 2853, 1735, 1653, 1629, 1449, 1373, 1257, 1207, 1071, 1029 cm^{-1}; MS (EI) m/z 395 (M^+, 2.7), 350 (56), 349 (88), 200 (94), 199 (76), 143 (66), 126 (71), 84 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{21}H_{33}NO_6$ 395.2308; Found 395.2309.

1c: (2 mmol scale, 456 mg, 64%) R_f = 0.4 (ether); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.5:1) δ (ppm) 0.919 (t, *J* = 7.2 Hz, 3H×0.4, minor rotamer), 0.937 (t, *J* = 7.2 Hz, 3H×0.6, major rotamer), 1.26-1.36 (m, 8H), 1.43-1.62 (m, 3H), 1.81-2.05 (m, 3H), 3.12 (dd, *J* = 13.9, 7.6 Hz, 1H×0.6), 3.29-3.55 (m, 2H+2H×0.4), 3.69-3.89 (m, 2H+1H×0.6), 4.04 (dddd, *J* = 7.2, 7.2, 7.2, 3.5 Hz, 1H×0.4), 4.08 (dddd, *J* = 7.3, 7.3, 7.3, 3.4 Hz, 1H×0.6), 4.26-4.36 (m, 4H), 7.35 (s, 1H×0.6), 7.44 (s, 1H×0.4); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.8 (CH_3), 13.9 (CH_3), 13.99 (CH_3), 14.01 (CH_3), 14.1 (CH_3), 19.9 (CH_2), 20.2 (CH_2), 25.5 (CH_2), 25.8 (CH_2), 29.3 (CH_2), 29.35 (CH_2), 29.42 (CH_2), 31.2 (CH_2), 46.4 (CH_2), 49.2 (CH_2), 49.4 (CH_2), 52.5 (CH_2), 61.77 (CH_2), 61.79 (CH_2), 62.0 (CH_2), 62.2 (CH_2), 68.0 (CH_2), 68.1 (CH_2), 77.3 (CH), 78.0 (CH), 133.4 (C), 134.1 (CH), 134.9 (C), 136.0 (CH), 163.2 (C), 163.3 (C), 164.0 (C), 164.4 (C), 164.7 (C); IR (neat) 2964, 1732, 1652, 1455, 1373, 1343, 1255, 1067, 1029 cm^{-1}; MS (EI) m/z 355 (M^+, 0.4), 354 (0.5), 326 (1.9), 310 (43), 309 (42), 200 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{18}H_{29}NO_6$ 355.1995; Found 355.1990.

1d: (2 mmol scale, 456 mg, 57%) R_f = 0.5 (ether); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1:1) δ (ppm) 1.14-1.24 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H×0.5), 1.30 (t, *J* = 7.1 Hz, 3H×0.5), 1.32 (t, *J* = 7.1 Hz, 3H×0.5), 1.35 (t, *J* = 7.1 Hz, 3H×0.5), 1.39-1.61 (m, 4H), 1.78-1.85 (m, 1H), 3.04 (dd, *J* = 13.9, 8.3 Hz, 1H×0.5), 3.08-3.15 (m, 1H×0.5), 3.25-3.42 (m, 1H+1H×0.5+1H×0.5), 3.63 (dddd, *J* = 10.9, 8.3, 2.7, 2.5 Hz, 1H×0.5), 3.70 (dd, *J* = 13.9, 2.7 Hz, 1H×0.5), 3.92-3.98 (m, 1H), 4.22-4.41 (m, 4H), 4.63 (d, *J* = 15.0 Hz, 1H×0.5), 4.70 (d, *J* = 16.7 Hz, 1H×0.5), 4.79 (d, *J* = 16.7 Hz, 1H×0.5), 4.82 (d, *J* = 15.0 Hz, 1H×0.5), 7.19-7.21 (m, 2H×0.5), 7.24-7.37 (m, 3H+2H×0.5), 7.33 (s, 1H×0.5), 7.57 (s, 1H×0.5); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.98 (CH_3), 14.02 (CH_3), 14.1 (CH_3), 23.06 (CH_2), 23.10 (CH_2), 25.7 (CH_2), 25.9 (CH_2), 29.39 (CH_2), 29.42 (CH_2), 49.1 (CH_2), 50.7 (CH_2), 52.5 (CH_2), 53.4 (CH_2), 61.8 (CH_2), 61.9 (CH_2), 62.1 (CH_2), 62.2 (CH_2), 68.3 (CH_2), 68.4 (CH_2), 75.7 (CH), 76.9 (CH), 126.9 (CH), 127.5 (CH), 127.8 (CH), 128.2 (CH), 128.6 (CH), 128.9 (CH), 134.1 (CH), 134.2 (C), 135.4 (C), 135.8 (CH), 136.5 (C), 136.9 (C), 163.0 (C), 163.3 (C), 164.5 (C), 164.7 (C), 164.8 (C), 165.1 (C); IR (neat) 2938, 2850, 1731, 1651, 1496, 1465, 1444, 1373, 1347, 1254, 1205, 1133, 1093, 1071, 1048, 1027 cm^{-1}; MS (EI) m/z 403 (M^+, 0.65), 395 (3.8), 358 (14), 204 (67), 200 (59), 120 (88), 84 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{22}H_{29}NO_6$ 403.1995; Found 403.1976.

1e: (2.4 mmol scale, 650 mg, 67%) R_f = 0.3 (hexane-ether = 1 : 1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.5:1) δ (ppm) 0.805-0.976 (m, 2H), 1.09-1.28 (m, 4H), 1.31 (t, *J* = 7.1 Hz, 6H×0.4, minor rotamer), 1.32 (t, *J* = 7.1 Hz, 3H×0.6, major rotamer), 1.33 (t, *J* = 7.1 Hz, 3H×0.6), 1.42-1.87 (m, 12H), 3.01 (dd, *J* = 13.8, 8.2 Hz, 1H×0.6), 3.17-3.23 (m, 2H×0.4), 3.29 (d, *J* = 7.2 Hz, 2H×0.6), 3.32-3.44 (m, 1H+3H×0.4), 3.59 (dddd, *J* = 10.9, 8.2, 2.5, 2.5 Hz, 1H×0.6), 3.72 (dd, *J* = 13.8, 2.8 Hz, 1H×0.6), 3.89-3.97 (m, 1H), 4.25-4.37 (m, 4H), 7.36 (s, 1H×0.6), 7.49 (s, 1H×0.4); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.01 (CH_3), 14.03 (CH_3), 14.1 (CH_3), 23.1 (CH_2), 23.2 (CH_2), 25.8 (CH_2), 25.87 (CH_2), 25.91 (CH_2), 25.94 (CH_2), 26.3 (CH_2), 26.5 (CH_2), 29.5 (CH_2), 30.7 (CH_2), 30.8 (CH_2), 30.85 (CH_2), 30.87 (CH_2), 36.1 (CH), 37.6 (CH), 51.9 (CH_2), 52.7 (CH_2), 54.1 (CH_2), 56.5 (CH_2), 61.7 (CH_2), 62.0 (CH_2), 62.2 (CH_2), 68.3 (CH_2), 68.5 (CH_2), 76.2 (CH), 76.7 (CH), 133.6 (C), 134.1 (CH), 134.8 (C), 136.0 (CH), 163.3 (C), 163.4 (C), 164.1 (C), 164.8 (C), 164.9

(C); IR (neat) 2930, 2852, 1733, 1652, 1447, 1372, 1345, 1252, 1206, 1145, 1093, 1069, 1047, 1028 cm^{-1}; MS (EI) m/z 409 (M^+, 0.06), 363 (1.3), 309 (0.8), 308 (0.5), 224 (47), 83 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{22}H_{35}NO_6$ 409.2464; Found 409.2454.

1f: (2 mmol scale, 638 mg, 68%) R_f = 0.3 (hexane-ether = 1 : 1); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.2:1) δ (ppm) 1.28 (t, *J* = 7.2 Hz, 3H×0.45, minor rotamer), 1.30 (t, *J* = 7.1 Hz, 3H×0.55, major rotamer), 1.31 (t, *J* = 7.0 Hz, 3H×0.55), 1.34 (t, *J* = 7.1 Hz, 3H×0.45), 1.27-1.76 (m, 13H), 1.88-2.04 (m, 1H), 3.02 (dd, *J* = 13.8, 7.7 Hz, 1H×0.45), 3.28 (dd, *J* = 15.2, 3.1 Hz, 1H×0.55), 3.35 (dd, *J* = 15.2, 8.1 Hz, 1H×0.55), 3.88 (dd, *J* = 13.8, 3.0 Hz, 1H×0.45), 4.06 (dddd, *J* = 8.4, 8.1, 6.3, 3.1 Hz, 1H×0.55), 4.18-4.38 (m, 4H+1H×0.45), 4.69 (d, *J* = 15.0 Hz, 1H×0.55), 4.82 (s, 2H×0.45), 4.85 (d, *J* = 15.0 Hz, 1H×0.55), 7.21-7.38 (m, 5H+1H×0.45), 7.66 (s, 1H×0.55); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.96 (CH_3), 13.99 (CH_3), 14.1 (CH_3), 23.5 (CH_2), 23.7 (CH_2), 23.9 (CH_2), 24.0 (CH_2), 25.6 (CH_2), 25.7 (CH_2), 29.3 (CH_2), 35.9 (CH_2), 36.2 (CH_2), 37.1 (CH_2), 37.4 (CH_2), 38.5 (CH_2), 38.7 (CH_2), 48.9 (CH_2), 50.0 (CH_2), 52.5 (CH_2), 52.7 (CH_2), 61.78 (CH_2), 61.83 (CH_2), 62.0 (CH_2), 62.1 (CH_2), 75.8 (CH), 77.1 (CH), 83.4 (C), 83.6 (C), 127.0 (CH), 127.4 (CH), 127.8 (CH), 128.1 (CH), 128.6 (CH), 128.9 (CH), 134.0 (C), 134.4 (CH), 135.2 (C), 135.9 (CH), 136.5 (C), 136.9 (C), 163.0 (C), 163.2 (C), 164.5 (C), 164.6 (C), 164.8 (C), 165.0 (C); IR (neat) 2931, 2857, 1730, 1496, 1447, 1374, 1257, 1209, 1063, 1027 cm^{-1}; MS (EI) m/z 457 (M^+, 2.0), 412 (24), 411 (20), 258 (34), 200 (62), 139 (81), 120 (99), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{26}H_{35}NO_6$ 457.2464; Found 457.2457.

1g: (2 mmol scale, 861 mg, 63%) R_f = 0.6 (hexane-ether = 1 : 3); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.1:1) δ (ppm) 1.18-1.43 (m, 11H), 1.28 (t, *J* = 7.1 Hz, 3H×0.52, major rotamer), 1.29 (t, *J* = 7.1 Hz, 3H×0.48, minor rotamer), 1.32 (t, *J* = 7.2 Hz, 3H×0.48), 1.34 (t, *J* = 7.1 Hz, 3H×0.52), 1.81 (dd, *J* = 12.5, 6.8 Hz, 1H×0.48), 1.89 (dd, *J* = 12.7, 6.6 Hz, 1H×0.52), 3.04 (dd, *J* = 13.9, 8.2 Hz, 1H×0.52), 3.22 (dd, *J* = 15.6, 2.9 Hz, 1H×0.48), 3.36 (dd, *J* = 15.6, 8.5 Hz, 1H×0.48), 3.51-3.58 (m, 2H), 3.84 (dd, *J* = 13.9, 2.6 Hz, 1H×0.52), 4.12 (dddd, *J* = 8.7, 8.5, 6.8, 2.9 Hz, 1H×0.48), 4.20-4.38 (m, 4H+1H×0.48), 4.59 (d, *J* = 14.8 Hz, 1H×0.48), 4.76 (d, *J* = 16.6 Hz, 1H×0.52), 4.79 (d, *J* = 16.6 Hz, 1H×0.52), 4.91 (d, *J* = 14.8 Hz, 1H×0.48), 7.20-7.38 (m, 5H), 7.34 (s, 1H×0.52), 7.55 (s,

1H×0.48); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.97 (CH_3), 14.00 (CH_3), 14.1 (CH_3), 23.5 (CH_2), 24.0 (CH_2), 24.1 (CH_2), 25.95 (CH_2), 26.00 (CH_2), 35.25 (CH_2), 35.33 (CH_2), 36.5 (CH_2), 36.6 (CH_2), 41.9 (CH_2), 43.6 (C), 43.9 (C), 48.7 (CH_2), 49.4 (CH_2), 51.7 (CH_2), 52.8 (CH_2), 61.8 (CH_2), 61.9 (CH_2), 62.05 (CH_2), 62.13 (CH_2), 76.7 (CH), 77.8 (CH), 78.1 (CH_2), 78.4 (CH_2), 127.0 (CH), 127.5 (CH), 127.8 (CH), 128.3 (CH), 128.6 (CH), 128.9 (CH), 134.0 (C), 134.3 (CH), 135.3 (C), 135.7 (CH), 136.3 (C), 136.8 (C), 163.0 (C), 163.2 (C), 164.57 (C), 164.64 (C), 164.9 (C); IR (neat) 2926, 2853, 1732, 1652, 1496, 1455, 1373, 1258, 1069, 1027 cm^{-1}; MS (CI) m/z 458 ([M + H]$^+$); HRMS (CI) m/z: [M + H]$^+$ Calcd for $C_{26}H_{36}NO_6$ 458.2543; Found 458.2545.

1h: (2 mmol scale, 517 mg, 63%) R_f = 0.6 (hexane-ether = 1 : 7); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.1:1) δ (ppm) 1.06 (s), 1.080 (s), 1.084 (s), (6H), 1.25-1.36 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H×0.52, major rotamer), 1.30 (t, *J* = 7.1 Hz, 3H×0.48, minor rotamer), 1.32 (t, *J* = 7.1 Hz, 3H×0.48), 1.34 (t, *J* = 7.1 Hz, 3H×0.52), 1.74 (dd, *J* = 12.3, 7.0 Hz, 1H×0.48), 1.80 (dd, *J* = 12.4, 6.7 Hz, 1H×0.52), 3.06 (dd, *J* = 13.9, 8.2 Hz, 1H×0.52), 3.22 (dd, *J* = 15.4, 2.7 Hz, 1H×0.48), 3.38 (dd, *J* = 15.4, 8.3 Hz, 1H×0.48), 3.43-3.51 (m, 2H), 3.83 (dd, *J* = 13.9, 2.7 Hz, 1H×0.52), 4.17-4.37 (m, 5H), 4.58 (d, *J* = 14.9 Hz, 1H×0.48), 4.77 (d, *J* = 16.6 Hz, 1H×0.52), 4.80 (d, *J* = 16.6 Hz, 1H×0.52), 4.93 (d, *J* = 14.9 Hz, 1H×0.48), 7.21-7.38 (m, 5H), 7.35 (s, 1H×0.52), 7.56 (s, 1H×0.48); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.95 (CH_3), 13.99 (CH_3), 14.1 (CH_3), 26.2 (CH_3), 26.4 (CH_3), 39.4 (C), 39.8 (C), 44.1 (CH_2), 44.4 (CH_2), 48.6 (CH_2), 49.4 (CH_2), 51.7 (CH_2), 52.8 (CH_2), 61.81 (CH_2), 61.84 (CH_2), 62.0 (CH_2), 62.1 (CH_2), 77.2 (CH), 78.3 (CH), 79.7 (CH), 79.9 (CH), 127.0 (CH), 127.5 (CH), 127.8 (CH), 128.2 (CH), 128.6 (CH), 128.9 (CH), 134.0 (C), 134.3 (CH), 135.2 (C), 135.7 (CH), 136.3 (C), 136.7 (C), 162.9 (C), 163.2 (C), 164.5 (C), 164.58 (C), 164.62 (C), 164.9 (C); IR (neat) 2961, 2871, 1732, 1649, 1496, 1466, 1372, 1254, 1070, 1027 cm^{-1}; MS (CI) m/z 418 ([M + H]$^+$); HRMS (CI) m/z: [M + H]$^+$ Calcd for $C_{23}H_{32}NO_6$ 418.2230; Found 418.2234.

1i: (2 mmol scale, 686 mg, 78%) R_f = 0.3 (hexane-ether = 1 : 1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.1:1) δ (ppm) 0.853 (s, 3H×0.52, major rotamer), 0.868 (s, 3H×0.48, minor rotamer), 1.03 (s, 3H×0.52), 1.11 (s, 3H×0.48), 1.28 (t, *J* = 7.1 Hz,

3H×0.48), 1.305 (t, *J* = 7.1 Hz, 3H×0.52), 1.308 (t, *J* = 7.1 Hz, 3H×0.52), 1.34 (t, *J* = 7.1 Hz, 3H×0.48), 1.64-1.81 (m, 2H), 2.77 (dd, *J* = 13.8, 9.6 Hz, 1H×0.48), 3.19 (dd, *J* = 15.4, 2.3 Hz, 1H×0.52), 3.24 (dd, *J* = 15.4, 9.0 Hz, 1H×0.52), 3.52 (dd, *J* = 9.0, 2.3 Hz, 1H×0.52), 3.64 (dd, *J* = 9.6, 1.6 Hz, 1H×0.48), 3.76-3.95 (m, 2H), 4.00 (d, *J* = 13.8 Hz, 1H×0.48), 4.24-4.39 (m, 4H), 4.69 (d, *J* = 14.8 Hz, 1H×0.52), 4.72 (d, *J* = 16.6 Hz, 1H×0.48), 4.76 (d, *J* = 16.6 Hz, 1H×0.48), 4.79 (d, *J* = 14.8 Hz, 1H×0.52), 7.21-7.38 (m, 5H), 7.34 (s, 1H×0.48), 7.56 (s, 1H×0.52); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.96 (CH_3), 13.97 (CH_3), 14.02 (CH_3), 14.1 (CH_3), 21.2 (CH_3), 21.4 (CH_3), 25.0 (CH_3), 25.4 (CH_3), 40.4 (C), 40.8 (C), 41.95 (CH_2), 41.04 (CH_2), 46.0 (CH_2), 47.9 (CH_2), 48.5 (CH_2), 52.5 (CH_2), 61.9 (CH_2), 62.0 (CH_2), 62.1 (CH_2), 65.8 (CH_2), 65.9 (CH_2), 85.1 (CH), 85.5 (CH), 127.0 (CH), 127.5 (CH), 127.8 (CH), 128.4 (CH), 128.6 (CH), 128.9 (CH), 134.0 (C), 134.6 (CH), 135.0 (C), 135.7 (CH), 136.5 (C), 136.8 (C), 163.0 (C), 163.1 (C), 164.4 (C), 164.6 (C), 164.7 (C); IR (neat) 2961, 2874, 1728, 1652, 1496, 1466, 1453, 1371, 1255, 1208, 1069, 1025 cm^{-1}; MS (EI) m/z 417 (M^+, 0.8), 371 (43), 218 (75), 99 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{23}H_{31}NO_6$ 417.2151; Found 417.2137.

1j: (3.11 mmol scale, 1.035 g, 80%) R_f = 0.4 (hexane-ether = 1 : 4); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.8:1) δ (ppm) 1.28 (t, *J* = 7.0 Hz, 3H×0.36, minor rotamer), 1.29 (t, *J* = 7.1 Hz, 3H×0.64, major rotamer), 1.32 (t, *J* = 7.0 Hz, 3H×0.64), 1.34 (t, *J* = 7.1 Hz, 3H×0.36), 3.45 (d, *J* = 3.1 Hz, 2H×0.64), 3.54 (d, *J* = 4.5 Hz, 2H×0.36), 3.84-4.00 (m, 4H), 4.23-4.38 (m, 4H), 4.73 (s, 2H×0.36), 4.79 (s, 2H×0.64), 4.99 (t, *J* = 3.1 Hz, 1H×0.64), 5.10 (t, *J* = 4.5 Hz, 1H×0.36), 7.20-7.38 (m, 5H), 7.33 (s, 1H×0.36), 7.55 (s, 1H×0.64); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.99 (CH_3), 14.04 (CH_3), 14.1 (CH_3), 47.5 (CH_2), 48.6 (CH_2), 49.7 (CH_2), 52.7 (CH_2), 61.9 (CH_2), 62.0 (CH_2), 62.1 (CH_2), 62.2 (CH_2), 64.9 (CH_2), 65.3 (CH_2), 101.9 (CH), 102.3 (CH), 127.1 (CH), 127.6 (CH), 128.0 (CH), 128.5 (CH), 128.7 (CH), 129.0 (CH), 134.3 (CH), 134.5 (C), 135.3 (CH), 136.0 (C), 136.7 (C), 162.9 (C), 163.2 (C), 164.5 (C), 164.8 (C), 165.0 (C), 165.4 (C); IR (neat) 2983, 2895, 1728, 1652, 1496, 1465, 1444, 1374, 1256, 1203, 1134, 1068, 1022 cm^{-1}; MS (EI) m/z 391 (M^+, 2.1), 346 (9.9), 192 (35), 91 (58), 73 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{20}H_{25}NO_7$ 391.1631; Found 391.1631.

1k: (2 mmol scale, 393 mg, 49%) R_f = 0.6 (ether); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.5:1) δ (ppm) 0.849-0.979 (m, 2H), 1.12-1.28 (m, 3H), 1.313 (t, *J* = 7.2 Hz, 6H×0.6, major rotamer), 1.318 (t, *J* = 7.1 Hz, 3H×0.4, minor rotamer), 1.322 (t, *J* = 7.1 Hz, 3H×0.4), 1.59-1.76 (m, 6H), 3.30 (d, *J* = 7.2 Hz, 2H×0.4), 3.36 (d, *J* = 7.4 Hz, 2H×0.6), 3.54 (d, *J* = 3.1 Hz, 2H×0.6), 3.56 (d, *J* = 4.7 Hz, 2H×0.4), 3.83-3.99 (m, 4H), 4.26-4.35 (m, 4H), 5.01 (t, *J* = 3.1 Hz, 1H×0.6), 5.03 (t, *J* = 4.7 Hz, 1H×0.4), 7.34 (s, 1H×0.4), 7.48 (s, 1H×0.6); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.8 (CH_3), 13.85 (CH_3), 13.91 (CH_3), 13.93 (CH_3), 25.7 (CH_2), 25.8 (CH_2), 26.1 (CH_2), 26.3 (CH_2), 30.6 (CH_2), 36.0 (CH), 37.3 (CH), 48.7 (CH_2), 50.7 (CH_2), 53.3 (CH_2), 55.5 (CH_2), 61.6 (CH_2), 61.7 (CH_2), 61.9 (CH_2), 62.0 (CH_2), 64.8 (CH_2), 65.2 (CH_2), 101.5 (CH), 102.2 (CH), 133.5 (C), 133.8 (CH), 134.8 (C), 135.5 (CH), 163.0 (C), 163.1 (C), 164.4 (C), 164.5 (C), 164.7 (C), 165.0 (C); IR (neat) 2927, 2853, 1732, 1652, 1632, 1467, 1449, 1373, 1257, 1204, 1131, 1069, 1024 cm^{-1}; MS (FAB) m/z 420 ($[M + Na]^+$), 398 ($[M + H]^+$); HRMS (FAB) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{31}NO_7Na$ 420.1998; Found 420.2001.

1l: (2 mmol scale, 580 mg, 62%) R_f = 0.6 (hexane-ether = 1 : 2); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.5:1) δ (ppm) 0.710 (s, 3H), 1.16 (s, 3H×0.4, minor rotamer), 1.17 (s, 3H×0.6, major rotamer), 1.27 (t, *J* = 7.1 Hz, 3H×0.4), 1.29 (t, *J* = 7.1 Hz, 3H×0.6), 1.31 (t, *J* = 7.0 Hz, 3H×0.6), 1.35 (t, *J* = 7.2 Hz, 3H×0.4), 3.33 (d, *J* = 10.7 Hz, 2H×0.6), 3.40 (d, *J* = 10.7 Hz, 2H×0.4), 3.41 (d, *J* = 4.3 Hz, 2H×0.6), 3.51 (d, *J* = 4.9 Hz, 2H×0.4), 3.58 (d, *J* = 10.7 Hz, 2H×0.4), 3.60 (d, *J* = 10.7 Hz, 2H×0.6), 4.22-4.39 (m, 4H), 4.45 (t, *J* = 4.3 Hz, 1H×0.6), 4.71 (t, *J* = 4.9 Hz, 1H×0.4), 4.72 (s, 2H×0.4), 4.77 (s, 2H×0.6), 7.19-7.21 (m, 2H×0.4), 7.24-7.38 (m, 5H×0.6+3H×0.4+1H×0.4), 7.60 (s, 1H×0.6); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.9 (CH_3), 13.99 (CH_3), 14.03 (CH_3), 21.7 (CH_3), 21.9 (CH_3), 22.9 (CH_3), 23.0 (CH_3), 30.2 (C), 30.3 (C), 48.7 (CH_2), 49.6 (CH_2), 50.0 (CH_2), 53.2 (CH_2), 61.77 (CH_2), 61.83 (CH_2), 62.0 (CH_2), 62.1 (CH_2), 77.95 (CH_2), 77.01 (CH_2), 99.0 (CH), 99.2 (CH), 127.0 (CH), 127.5 (CH), 127.9 (CH), 128.4 (CH), 128.6 (CH), 128.9 (CH), 133.8 (CH), 134.2 (C), 135.6 (C), 135.7 (CH), 136.1 (C), 136.7 (C), 162.9 (C), 163.1 (C), 164.6 (C), 164.7 (C), 165.4 (C); IR (neat) 2958, 2870, 1735, 1654, 1496, 1466, 1395, 1374, 1258,

1202, 1132, 1069, 1025 cm^{-1}; MS (EI) m/z 433 (M^+, 42), 388 (53), 234 (78), 115 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{23}H_{31}NO_7$ 433.2101; Found 433.2088.

1m: (2 mmol scale, 415 mg, 52%) R_f = 0.8 (ether); pale yellow oil;^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.4:1) δ (ppm) 1.26-1.37 (m, 7H), 2.00-2.13 (m, 1H), 3.36 (d, *J* = 4.5 Hz, 2H×0.58, major rotamer), 3.46 (d, *J* = 5.1 Hz, 2H×0.42, minor rotamer), 3.68 (ddd, *J* = 12.2, 12.2, 2.2 Hz, 2H×0.58), 3.75 (ddd, *J* = 12.2, 12.2, 2.1 Hz, 2H×0.42), 4.05-4.12 (m, 2H), 4.25 (q, *J* = 7.1 Hz, 2H×0.42), 4.29 (q, *J* = 7.2 Hz, 2H×0.58), 4.31 (q, *J* = 7.2 Hz, 2H×0.58), 4.37 (q, *J* = 7.1 Hz, 2H×0.42), 4.56 (t, *J* = 4.5 Hz, 1H×0.58), 4.71 (s, 2H×0.42), 4.75 (s, 2H×0.58), 4.82 (t, *J* = 5.1 Hz, 1H×0.42), 7.19-7.21 (m, 2H×0.42), 7.24-7.37 (m, 3H+2H×0.58), 7.33 (s, 1H×0.42), 7.57 (s, 1H×0.58); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.97 (CH_3), 14.02 (CH_3), 14.1 (CH_3), 25.5 (CH_2), 25.8 (CH_2), 48.9 (CH_2), 49.6 (CH_2), 50.4 (CH_2), 53.3 (CH_2), 61.8 (CH_2), 61.9 (CH_2), 62.1 (CH_2), 62.2 (CH_2), 66.7 (CH_2), 66.9 (CH_2), 99.27 (CH), 99.30 (CH), 127.0 (CH), 127.6 (CH), 127.9 (CH), 128.4 (CH), 128.6 (CH), 128.9 (CH), 133.9 (CH), 134.4 (C), 135.6 (C), 135.7 (CH), 136.1 (C), 136.7 (C), 162.9 (C), 163.2 (C), 164.6 (C), 164.7 (C), 164.8 (C), 165.3 (C); IR (neat) 2980, 2858, 1730, 1652, 1496, 1466, 1445, 1374, 1258, 1206, 1136, 1068, 1020 cm^{-1}; MS (FAB) m/z 428 ([M + Na]$^+$), 406 ([M + H]$^+$); HRMS (FAB) m/z: [M + Na]$^+$ Calcd for $C_{21}H_{27}NO_7Na$ 428.1685; Found 428.1688.

1n: (3 mmol scale, 704 mg, 72%) R_f = 0.4 (hexane-ether = 1 : 1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.895 (d, *J* = 6.8 Hz, 6H), 0.920 (d, *J* = 6.6 Hz, 6H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.88-2.08 (m, 2H), 3.14 (d, *J* = 7.6 Hz, 2H), 3.23 (d, *J* = 7.6 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 7.35 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.00 (CH_3), 14.01 (CH_3), 20.1 (CH_3), 20.2 (CH_3), 26.6 (CH), 28.2 (CH), 53.2 (CH_2), 56.3 (CH_2), 61.8 (CH_2), 62.2 (CH_2), 134.4 (C), 134.8 (CH), 163.3 (C), 164.3 (C), 164.8 (C); IR (neat) 2961, 2872, 1728, 1650, 1468, 1444, 1389, 1370, 1338, 1260, 1212, 1149, 1068, 1028 cm^{-1}; MS (EI) m/z 327 (M^+, 0.8), 312 (1.2), 281 (44), 199 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{17}H_{29}NO_5$ 327.2046; Found 327.2052.

1o: (2 mmol scale, 454 mg, 79%) R_f = 0.3 (ether); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1:1) δ (ppm) 1.30-1.34 (m, 6H), 3.03 (s, 3H×0.5), 3.14 (s, 3H×0.5),

3.34 (s, 3H×0.5), 3.35 (s, 3H×0.5), 3.51-3.52 (m, 2H×0.5+2H×0.5), 3.54-3.62 (m, 2H×0.5+2H×0.5), 4.26-4.36 (m, 4H), 7.35 (s, 1H×0.5), 7.42 (s, 1H×0.5); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.0 (CH_3), 14.1 (CH_3), 33.8 (CH_3), 37.5 (CH_3), 47.7 (CH_2), 50.3 (CH_2), 58.9 (CH_3), 59.2 (CH_3), 61.78 (CH_2), 61.84 (CH_2), 62.0 (CH_2), 62.2 (CH_2), 70.1 (CH_2), 70.9 (CH_2), 134.1 (C), 134.3 (C), 134.7 (CH), 135.3 (CH), 163.1 (C), 163.2 (C), 164.1 (C), 164.5 (C), 164.6 (C), 164.7 (C); IR (neat) 2984, 2937, 1735, 1654, 1466, 1405, 1373, 1342, 1254, 1118, 1069, 1021 cm^{-1}; MS (EI) m/z 287 (M^+); HRMS (EI) m/z: M^+ Calcd for $C_{13}H_{21}NO_6$ 287.1369; Found 287.1368.

1p: (1.82 mmol scale, 459 mg, 64%) R_f = 0.5 (hexane-ether = 1 : 2); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1:1) δ (ppm) 0.871 (t, *J* = 7.4 Hz, 3H×0.5), 0.903 (t, *J* = 7.4 Hz, 3H×0.5), 1.29-1.36 (m, 6H), 1.52-1.65 (m, 2H), 3.13-3.50 (m, 3H), 3.23 (s, 3H×0.5), 3.24 (s, 3H×0.5), 3.59 (dd, *J* = 15.4, 8.2 Hz, 1H×0.5), 3.69 (dd, *J* = 13.7, 3.9 Hz, 1H×0.5), 4.26-4.39 (m, 4H+1H×0.5), 4.55 (dd, *J* = 8.6, 3.9 Hz, 1H×0.5), 7.22 (s, 1H×0.5), 7.27-7.40 (m, 5H+1H×0.5); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 11.1 (CH_3), 11.3 (CH_3), 13.99 (CH_3), 14.00 (CH_3), 14.03 (CH_3), 14.1 (CH_3), 20.6 (CH_2), 22.3 (CH_2), 48.5 (CH_2), 52.0 (CH_2), 53.4 (CH_2), 55.0 (CH_2), 57.0 (CH_3), 57.1 (CH_3), 61.7 (CH_2), 61.8 (CH_2), 61.9 (CH_2), 62.2 (CH_2), 81.7 (CH), 82.4 (CH), 126.58 (CH), 126.64 (CH), 128.0 (CH), 128.5 (CH), 128.6 (CH), 129.0 (CH), 133.3 (C), 134.3 (CH), 135.0 (C), 135.8 (CH), 138.7 (C), 139.7 (C), 163.17 (C), 163.20 (C), 164.0 (C), 164.6 (C), 164.7 (C); IR (neat) 2981, 1732, 1652, 1455, 1373, 1342, 1254, 1105, 1069, 1024 cm^{-1}; MS (EI) m/z 391 (M^+, 1.0), 346 (9.3), 270 (10), 199 (48), 121 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{21}H_{29}NO_6$ 391.1995; Found 391.2005.

1q: (3 mmol scale, 883 mg, 66%) R_f = 0.8 (hexane-ether = 1 : 2); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1:1) δ (ppm) 0.806-0.976 (m, 2H), 1.10-1.28 (m, 3H), 1.29-1.36 (m, 6H), 1.54-1.74 (m, 6H), 3.05 (dd, *J* = 14.9, 7.3 Hz, 1H×0.5), 3.15-3.41 (m, 2H+1H×0.5), 3.225 (s, 3H×0.5), 3.228 (s, 3H×0.5), 3.61 (dd, *J* = 15.4, 8.4 Hz, 1H×0.5), 3.70 (dd, *J* = 13.7, 3.9 Hz, 1H×0.5), 4.26-4.40 (m, 4H+1H×0.5), 4.58 (dd, *J* = 8.6, 3.9 Hz, 1H×0.5), 7.26-7.40 (m, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.0 (CH_3), 14.05 (CH_3), 14.08 (CH_3), 14.12 (CH_3), 25.8 (CH_2), 25.86 (CH_2), 25.90 (CH_2), 25.93 (CH_2), 26.3

(CH_2), 26.5 (CH_2), 30.7 (CH_2), 30.8 (CH_2), 30.9 (CH_2), 36.3 (CH), 37.6 (CH), 52.8 (CH_2), 54.1 (CH_2), 55.7 (CH_2), 56.7 (CH_2), 57.0 (CH_3), 57.2 (CH_3), 61.75 (CH_2), 61.79 (CH_2), 62.0 (CH_2), 62.2 (CH_2), 81.6 (CH), 82.5 (CH), 126.6 (CH), 126.7 (CH), 128.0 (CH), 128.5 (CH), 128.6 (CH), 129.0 (CH), 133.5 (C), 134.3 (CH), 134.9 (C), 135.6 (CH), 138.7 (C), 139.8 (C), 163.3 (C), 164.3 (C), 164.8 (C), 164.86 (C), 164.93 (C); IR (neat) 2925, 2852, 1729, 1651, 1450, 1372, 1253, 1106, 1068, 1025 cm^{-1}; MS (EI) m/z 445 (M^+, 2.3), 400 (18), 324 (47), 199 (96), 171 (86), 121 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{25}H_{35}NO_6$ 445.2464; Found 445.2469.

1r: (2 mmol scale, 478 mg, 53%) R_f = 0.3 (hexane-ether = 1 : 1); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 2.4:1) δ (ppm) 1.29 (t, *J* = 7.1 Hz, 3H×0.71, major rotamer), 1.30 (t, *J* = 7.1 Hz, 3H×0.29, minor rotamer), 1.31 (t, *J* = 7.1 Hz, 3H×0.29), 1.33 (t, *J* = 7.1 Hz, 3H×0.71), 3.39 (dd, *J* = 15.6, 4.2 Hz, 1H×0.29), 3.44 (dd, *J* = 14.3, 7.0 Hz, 1H×0.71), 3.62 (dd, *J* = 15.6, 8.4 Hz, 1H×0.29), 3.81 (dd, *J* = 14.3, 4.0 Hz, 1H×0.7), 3.94 (dd, *J* = 11.5, 5.9 Hz, 1H×0.3), 3.97 (dd, *J* = 11.5, 6.4 Hz, 1H×0.71), 4.14 (dd, *J* = 11.5, 2.3 Hz, 1H×0.29), 4.24-4.38 (m, 4H+1H×0.71+1H×0.29), 4.52 (dddd, *J* = 7.0, 6.4, 4.0, 2.3 Hz, 1H×0.71), 4.64 (d, *J* = 16.4 Hz, 1H×0.71), 4.66 (d, *J* = 14.9 Hz, 1H×0.29), 4.80 (d, *J* = 16.4 Hz, 1H×0.71), 4.89 (d, *J* = 14.9 Hz, 1H×0.29), 6.84-6.90 (m, 4H), 7.13-7.15 (m, 2H×0.71), 7.24-7.37 (m, 3H+1H+2H×0.29); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.02 (CH_3), 14.03 (CH_3), 14.1 (CH_3), 45.8 (CH_2), 47.3 (CH_2), 48.9 (CH_2), 53.5 (CH_2), 62.0 (CH_2), 62.1 (CH_2), 62.2 (CH_2), 62.3 (CH_2), 65.1 (CH_2), 65.9 (CH_2), 70.8 (CH), 72.1 (CH), 117.3 (CH), 117.4 (CH), 117.7 (CH), 121.7 (CH), 121.8 (CH), 121.9 (CH), 122.2 (CH), 127.2 (CH), 127.9 (CH), 128.2 (CH), 128.4 (CH), 128.9 (CH), 129.1 (CH), 134.1 (CH), 134.7 (CH), 134.8 (C), 135.6 (C), 136.1 (C), 142.0 (C), 142.5 (C), 142.8 (C), 143.1 (C), 162.8 (C), 162.9 (C), 164.4 (C), 165.2 (C); IR (neat) 2983, 2938, 1732, 1651, 1593, 1495, 1467, 1446, 1373, 1264, 1068, 1022 cm^{-1}; MS (EI) m/z 453 (M^+, 25), 408 (13), 407 (13), 254 (22), 148 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{25}H_{27}NO_7$ 453.1788; Found 453.1788.

1s: (2 mmol scale, 519 mg, 61%) R_f = 0.8 (ether); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.7:1) δ (ppm) 1.27-1.36 (m, 9H), 1.42 (s, 3H×0.63, major rotamer), 1.46 (s, 3H×0.37, minor rotamer), 3.18 (dd, *J* = 13.9, 7.2 Hz, 1H×0.63), 3.27 (dd, *J*

= 15.3, 3.0 Hz, 1H×0.37), 3.46 (dd, *J* = 15.3, 8.6 Hz, 1H×0.37), 3.51 (dd, *J* = 8.6, 6.7 Hz, 1H×0.37), 3.59 (dd, *J* = 8.6, 6.8 Hz, 1H×0.63), 3.83 (dd, *J* = 13.9, 3.3 Hz, 1H×0.63), 4.01 (dd, *J* = 8.6, 6.7 Hz, 1H×0.37), 4.05 (dd, *J* = 8.6, 6.3 Hz, 1H×0.63), 4.21-4.40 (m, 5H), 4.63 (d, *J* = 15.0 Hz, 1H×0.37), 4.72 (d, *J* = 16.6 Hz, 1H×0.63), 4.80 (d, *J* = 16.6 Hz, 1H×0.63), 4.88 (d, *J* = 15.0 Hz, 1H×0.37), 7.20-7.22 (m, 2H×0.63), 7.25-7.39 (m, 2H×0.37+3H), 7.35 (s, 1H×0.63), 7.57 (s, 1H×0.37); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.9 (CH_3), 14.0 (CH_3), 14.1 (CH_3), 25.2 (CH_3), 25.4 (CH_3), 26.7 (CH_3), 26.9 (CH_3), 47.8 (CH_2), 48.7 (CH_2), 50.4 (CH_2), 53.0 (CH_2), 61.87 (CH_2), 61.91 (CH_2), 62.1 (CH_2), 62.2 (CH_2), 66.9 (CH_2), 67.3 (CH_2), 73.8 (CH), 74.9 (CH), 109.4 (C), 110.2 (C), 127.0 (CH), 127.7 (CH), 128.0 (CH), 128.2 (CH), 128.7 (CH), 129.0 (CH), 134.1 (CH), 134.3 (C), 135.5 (CH), 135.9 (C), 136.4 (C), 162.8 (C), 163.0 (C), 164.4 (C), 164.5 (C), 164.9 (C), 165.0 (C); IR (neat) 2985, 2938, 1732, 1652, 1496, 1451, 1372, 1343, 1256, 1157, 1071, 1026 cm^{-1}; MS (EI) m/z 419 (M^+, 0.5), 404 (26), 374 (23), 373 (18), 220 (52), 200 (56), 120 (50), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{22}H_{29}NO_7$ 419.1944; Found 419.1932.

1t: (2.8 mmol scale, 575 mg, 65%) R_f = 0.1 (CH_2Cl_2); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.3:1) δ (ppm) 1.30-1.34 (m, 6H), 3.05 (s, 3H×0.43, minor rotamer), 3.13 (s, 3H×0.57, major rotamer), 3.41 (s, 6H×0.57), 3.42 (s, 6H×0.43), 3.45 (d, *J* = 5.1 Hz, 2H×0.43), 3.51 (d, *J* = 5.5 Hz, 2H×0.57), 4.27-4.36 (m, 4H), 4.44 (t, *J* = 5.1 Hz, 1H×0.43), 4.53 (t, *J* = 5.5 Hz, 1H×0.57), 7.35 (s, 1H×0.57), 7.42 (s, 1H×0.43); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.8 (CH_3), 13.9 (CH_3), 34.6 (CH_3), 37.4 (CH_3), 49.6 (CH_2), 52.5 (CH_2), 54.6 (CH_3), 55.1 (CH_3), 61.57 (CH_2), 61.63 (CH_2), 61.9 (CH_2), 62.0 (CH_2), 102.5 (CH), 103.0 (CH), 134.1 (C), 134.5 (CH), 134.8 (CH), 162.8 (C), 162.9 (C), 164.2 (C), 164.4 (C), 164.6 (C); IR (neat) 2985, 2940, 1734, 1653, 1465, 1405, 1373, 1256, 1218, 1123, 1072 cm^{-1}; MS (EI) m/z 317 (M^+); HRMS (EI) m/z: M^+ Calcd for $C_{14}H_{23}NO_7$ 317.1475; Found 317.1475.

1u: (2.94 mmol scale, 662 mg, 76%) R_f = 0.3 (hexane-ether = 1 : 4); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.8:1) δ (ppm) 1.29-1.35 (m, 6H), 3.406 (s, 6H×0.64, major rotamer), 3.408 (s, 6H×0.36, minor rotamer), 3.41 (d, *J* = 5.1 Hz, 2H×0.36), 3.47 (d, *J* = 5.3 Hz, 2H×0.64), 4.07 (ddd, *J* = 5.1, 1.6, 1.6 Hz, 2H×0.64), 4.11 (ddd, *J* = 6.0,

1.3, 1.3 Hz, 2H×0.36), 4.26-4.37 (m, 4H), 4.42 (t, J = 5.1 Hz, 1H×0.36), 4.53 (t, J = 5.3 Hz, 1H×0.64), 5.15-5.26 (m, 2H), 5.72-5.84 (m, 1H), 7.26 (s, 1H×0.64), 7.46 (s, 1H×0.36); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.96 (CH_3), 14.01 (CH_3), 47.9 (CH_2), 49.0 (CH_2), 49.7 (CH_2), 51.9 (CH_2), 55.0 (CH_3), 55.2 (CH_3), 61.8 (CH_2), 62.1 (CH_2), 62.2 (CH_2), 103.0 (CH), 103.4 (CH), 117.6 (CH_2), 118.0 (CH_2), 132.4 (CH), 132.5 (CH), 134.0 (CH), 134.4 (C), 135.1 (CH), 135.2 (C), 163.0 (C), 163.1 (C), 164.56 (C), 164.59 (C), 164.7 (C); IR (neat) 2984, 2940, 1729, 1656, 1466, 1446, 1373, 1257, 1206, 1126, 1070, 1024 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{25}NO_7Na$ 366.1529; Found 366.1528.

1v: (1.44 mmol scale, 328 mg, 61%) R_f = 0.5 (hexane-ether = 1 : 4); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 1.4:1) δ (ppm) 1.21 (t, J = 7.0 Hz, 3H×0.58, major rotamer), 1.22 (t, J = 7.0 Hz, 3H×0.42, minor rotamer), 1.29-1.35 (m, 6H), 3.42 (d, J = 5.1 Hz, 2H×0.42), 3.46 (d, J = 5.5 Hz, 2H×0.58), 3.48-3.58 (m, 2H), 3.69-3.77 (m, 2H), 4.09 (ddd, J = 4.9, 1.7, 1.7 Hz, 2H×0.58), 4.12 (bd, J = 6.1 Hz, 2H×0.42), 4.26-4.37 (m, 4H), 4.54 (t, J = 5.1 Hz, 1H×0.42), 4.66 (t, J = 5.5 Hz, 1H×0.58), 5.15-5.25 (m, 2H), 5.72-5.84 (m, 1H), 7.26 (s, 1H×0.58), 7.52 (s, 1H×0.42); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.0 (CH_3), 14.07 (CH_3), 14.08 (CH_3), 15.4 (CH_3), 15.5 (CH_3), 49.1 (CH_2), 49.2 (CH_2), 50.6 (CH_2), 52.1 (CH_2), 61.8 (CH_2), 62.1 (CH_2), 62.2 (CH_2), 63.7 (CH_2), 63.9 (CH_2), 101.2 (CH), 101.5 (CH), 117.6 (CH_2), 118.0 (CH_2), 132.6 (CH), 134.0 (CH), 134.4 (C), 135.2 (CH), 135.4 (C), 163.1 (C), 163.2 (C), 164.5 (C), 164.6 (C), 164.8 (C); IR (neat) 2979, 2935, 1732, 1652, 1463, 1445, 1374, 1256, 1207, 1125, 1067 cm^{-1}; MS (CI) m/z 372 ($[M + H]^+$); HRMS (CI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{30}NO_7$ 372.2022; Found 372.2007.

Typical experimental procedure (eq 1). To a solution of **1a** (223 mg, 0.57 mmol) in CH_2ClCH_2Cl (2 mL) was added $Sc(OTf)_3$ (57 mg, 0.12 mmol). The mixture was heated at 80 °C for 22 h and cooled to 0 °C. The reaction mixture was quenched by water and then saturated aqueous $NaHCO_3$. The mixture was extracted with dichloromethane and the organic phase was dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified by column chromatography over silica gel with hexane-ether as eluent to give **2a** (160 mg, 72%).

2a: R_f = 0.3 (hexane-ether = 1 : 4); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.21 (t, *J* = 7.1 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.64 (ddd, *J* = 13.7, 7.8, 7.8 Hz, 1H), 1.79-1.90 (m, 2H), 2.72-2.79 (m, 1H), 3.04 (d, *J* = 17.5 Hz, 1H), 3.05 (d, *J* = 13.2 Hz, 1H), 3.336 (d, *J* = 17.5 Hz, 1H), 3.341 (d, *J* = 13.2 Hz, 1H), 3.64 (ddd, *J* = 8.4, 7.1, 7.1 Hz, 1H), 3.93 (ddd, *J* = 8.4, 6.3, 6.3 Hz, 1H), 4.09-4.27 (m, 4H), 4.57 (d, *J* = 15.0 Hz, 1H), 4.60 (d, *J* = 15.0 Hz, 1H), 7.21-7.26 (m, 3H), 7.28-7.33 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.8 (CH_3), 14.0 (CH_3), 25.9 (CH_2), 32.2 (CH_2), 35.9 (CH_2), 49.4 (CH_2), 54.5 (CH_2), 59.3 (C), 61.8 (CH_2), 61.9 (CH_2), 68.1 (CH_2), 81.3 (C), 127.3 (CH), 127.7 (CH), 128.5 (CH), 136.4 (C), 167.3 (C), 167.7 (C), 169.0 (C); IR (neat) 2980, 1732, 1649, 1496, 1454, 1366, 1240, 1096, 1057, 1025 cm^{-1}; MS (FAB) m/z 412 ($[M + Na]^+$), 390 ($[M + H]^+$); HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{21}H_{28}NO_6$ 390.1917; Found 390.1917, $[M + Na]^+$ Calcd for $C_{21}H_{27}NO_6Na$ 412.1736; Found 412.1746.

2b: (0.3 mmol scale, 0.2 equiv. $Sc(OTf)_3$, 62 mg, 52%) R_f = 0.6 (ether); colorless oil;^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.881-0.964 (m, 2H), 1.08-1.21 (m, 3H), 1.24 (t, *J* = 7.0 Hz, 3H), 1.26 (t, *J* = 7.0 Hz, 3H), 1.63-1.79 (m, 7H), 1.82-1.99 (m, 2H), 2.79 (ddd, *J* = 14.0, 8.7, 5.9 Hz, 1H), 2.95 (d, *J* = 17.6 Hz, 1H), 3.08 (dd, *J* = 13.5, 6.6 Hz, 1H), 3.12 (d, *J* = 12.9 Hz, 1H), 3.26 (dd, *J* = 13.5, 7.8 Hz, 1H), 3.27 (d, *J* = 17.6 Hz, 1H), 3.50 (d, *J* = 12.9 Hz, 1H), 3.77 (ddd, *J* = 8.4, 7.1, 7.1 Hz, 1H), 3.95 (ddd, *J* = 8.4, 6.9, 5.6 Hz, 1H), 4.11-4.27 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.9 (CH_3), 14.0 (CH_3), 25.86 (CH_2), 25.91 (CH_2), 26.0 (CH_2), 26.5 (CH_2), 30.5 (CH_2), 30.7 (CH_2), 32.5 (CH_2), 35.7 (CH), 35.9 (CH_2), 52.9 (CH_2), 56.2 (CH_2), 59.3 (C), 61.9 (CH_2), 62.0 (CH_2), 68.2 (CH_2), 81.5 (C), 167.3 (C), 167.9 (C), 169.2 (C); IR (neat) 2925, 2852, 1734, 1647, 1495, 1449, 1367, 1240, 1187, 1056 cm^{-1}; MS (EI) m/z 395 (M^+, 30), 350 (17), 322 (42), 205 (25), 84 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{21}H_{33}NO_6$ 395.2308; Found 395.2302.

2c: (0.5 mmol scale, 0.2 equiv. $Sc(OTf)_3$, 135 mg, 76%) R_f = 0.5 (ether); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.912 (t, *J* = 7.3 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.22-1.34 (m, 2H), 1.42-1.52 (m, 2H), 1.76 (ddd, *J* = 13.5, 8.6, 6.7 Hz, 1H), 1.83-2.00 (m, 2H), 2.79 (ddd, *J* = 13.5, 8.7, 5.9 Hz, 1H), 2.91 (d, *J* = 17.6 Hz, 1H), 3.13 (d, *J* = 12.9 Hz, 1H), 3.22 (dt, *J* = 13.5, 7.2 Hz, 1H), 3.24 (d, *J* = 17.6 Hz, 1H), 3.41 (dt, *J* = 13.5,

7.5 Hz, 1H), 3.49 (d, *J* = 12.9 Hz, 1H), 3.79 (ddd, *J* = 8.4, 7.0, 7.0 Hz, 1H), 3.95 (ddd, *J* = 8.4, 6.8, 5.7 Hz, 1H), 4.12-4.27 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.9 (CH_3), 14.0 (CH_3), 14.1 (CH_3), 20.0 (CH_2), 26.0 (CH_2), 28.8 (CH_2), 32.6 (CH_2), 36.0 (CH_2), 46.4 (CH_2), 55.5 (CH_2), 59.4 (C), 61.88 (CH_2), 61.92 (CH_2), 68.3 (CH_2), 81.5 (C), 166.8 (C), 168.0 (C), 169.2 (C); IR (neat) 2959, 2873, 1735, 1650, 1497, 1466, 1367, 1241, 1057 cm^{-1}; MS (EI) m/z 355 (M^+, 47), 310 (38), 282 (100), 205 (62%); HRMS (EI) m/z: M^+ Calcd for $C_{18}H_{29}NO_6$ 355.1995; Found 355.2000.

2d: (0.57 mmol scale, 0.2 equiv. $Sc(OTf)_3$, 203 mg, 75%) R_f = 0.3 (hexane-ether = 1 : 4); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.21 (t, *J* = 7.1 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.32-1.40 (m, 2H), 1.46-1.58 (m, 1H), 1.63-1.67 (m, 1H), 1.73 (d, *J* = 14.0 Hz, 1H), 2.38 (ddd, *J* = 14.0, 13.7, 4.8 Hz, 1H), 2.93 (d, *J* = 17.7 Hz, 1H), 3.17 (ddd, *J* = 12.3, 12.0, 2.3 Hz, 1H), 3.27 (d, *J* = 13.8 Hz, 1H), 3.34 (d, *J* = 17.7 Hz, 1H), 3.64 (dd, *J* = 12.0, 5.0 Hz, 1H), 3.74 (d, *J* = 13.8 Hz, 1H), 4.10-4.28 (m, 4H), 4.37 (d, *J* = 14.8 Hz, 1H), 4.85 (d, *J* = 14.8 Hz, 1H), 7.25-7.29 (m, 3H), 7.31-7.36 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.9 (CH_3), 14.1 (CH_3), 19.1 (CH_2), 24.9 (CH_2), 27.6 (CH_2), 35.5 (CH_2), 46.8 (CH_2), 49.6 (CH_2), 60.7 (C), 61.6 (CH_2), 61.7 (CH_2), 61.9 (CH_2), 72.7 (C), 127.5 (CH), 128.0 (CH), 128.6 (CH), 136.9 (C), 167.6 (C), 167.8 (C), 169.0 (C); IR (neat) 2989, 2871, 1732, 1650, 1497, 1454, 1240, 1089, 1073, 1052, 1028 cm^{-1}; MS (EI) m/z 403 (M^+, 60), 358 (22), 330 (54), 83 (100%); HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{29}NO_6Na$ 426.1893; Found 426.1893.

2e: (0.5 mmol scale, 0.2 equiv. $Sc(OTf)_3$, 138 mg, 67%) R_f = 0.7 (ether); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.916-1.02 (m, 2H), 1.13-1.31 (m, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.52-1.84 (m, 11H), 2.42 (ddd, *J* = 13.1, 13.1, 4.2 Hz, 1H), 2.82 (d, *J* = 17.7 Hz, 1H), 3.12 (dd, *J* = 13.4, 7.1 Hz, 1H), 3.26 (d, *J* = 17.7 Hz, 1H), 3.35 (dd, *J* = 13.4, 7.4 Hz, 1H), 3.39 (d, *J* = 13.9 Hz, 1H), 3.59 (dd, *J* = 11.5, 11.5 Hz, 1H), 3.78-3.82 (m, 1H), 3.81 (d, *J* = 13.9 Hz, 1H), 4.11-4.27 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.9 (CH_3), 14.0 (CH_3), 19.1 (CH_2), 25.0 (CH_2), 25.8 (CH_2), 25.9 (CH_2), 26.4 (CH_2), 27.6 (CH_2), 30.4 (CH_2), 30.6 (CH_2), 35.5 (CH_2), 35.9 (CH), 48.0 (CH_2), 52.8 (CH_2), 60.6 (C), 61.5 (CH_2), 61.7 (CH_2), 72.8 (C), 167.6 (C), 167.7 (C), 169.1 (C); IR (neat) 2927, 2852, 1732,

1645, 1504, 1449, 1367, 1284, 1241, 1205, 1181, 1092, 1071, 1051 cm^{-1}; MS (EI) m/z 409 (M^+, 40), 364 (33), 336 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{22}H_{35}NO_6$ 409.2464; Found 409.2467.

2f: (0.46 mmol scale, 0.2 equiv. $SnCl_4$, 140 mg, 67%) R_f = 0.5 (hexane-ether = 1 : 4); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.17-1.50 (m, 9H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.55-1.63 (m, 2H), 1.69 (ddd, *J* = 12.7, 8.2, 7.0 Hz, 1H), 1.90 (ddd, *J* = 13.9, 8.2, 6.6 Hz, 1H), 2.81 (ddd, *J* = 13.9, 8.8, 7.0 Hz, 1H), 3.02 (d, *J* = 17.7 Hz, 1H), 3.06 (d, *J* = 12.7 Hz, 1H), 3.56 (d, *J* = 17.7 Hz, 1H), 3.59 (d, *J* = 12.7 Hz, 1H), 4.08-4.22 (m, 5H), 4.90 (d, *J* = 14.8 Hz, 1H), 7.20-7.24 (m, 3H), 7.27-7.31 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.8 (CH_3), 13.9 (CH_3), 23.39 (CH_2), 23.41 (CH_2), 25.4 (CH_2), 31.5 (CH_2), 35.7 (CH_2), 36.2 (CH_2), 38.0 (CH_2), 38.6 (CH_2), 49.3 (CH_2), 56.9 (CH_2), 59.8 (C), 61.8 (CH_2), 61.9 (CH_2), 81.6 (C), 84.2 (C), 127.3 (CH), 127.9 (CH), 128.5 (CH), 136.4 (C), 167.6 (C), 167.7 (C), 169.1 (C); IR (neat) 2930, 2858, 1732, 1652, 1496, 1454, 1240, 1094, 1046 cm^{-1}; MS (EI) m/z 457 (M^+, 33), 439 (37), 344 (35), 211 (37), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{26}H_{35}NO_6$ 457.2464; Found 457.2457.

2g: (0.3 mmol scale, 0.5 equiv. $SnCl_4$, 131 mg, 95%) R_f = 0.3 (hexane-ether = 1 : 2); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.22 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7,1 Hz, 3H), 1.25-1.41 (m, 10H), 1.56 (d, *J* = 14.3 Hz, 1H), 2.61 (d, *J* = 14.3 Hz, 1H), 3.04 (d, *J* = 17.6 Hz, 1H), 3.21 (d, *J* = 13.2 Hz, 1H), 3.37 (d, *J* = 13.2 Hz, 1H), 3.40 (d, *J* = 9.0 Hz, 1H), 3.42 (d, *J* = 17.6 Hz, 1H), 3.64 (d, *J* = 9.0 Hz, 1H), 4.08-4.30 (m, 4H), 4.54 (d, *J* = 15.0 Hz, 1H), 4.60 (d, *J* = 15.0 Hz, 1H), 7.20-7.33 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.9 (CH_3), 14.0 (CH_3), 23.7 (CH_2), 23.8 (CH_2), 25.7 (CH_2), 35.9 (CH_2), 36.4 (CH_2), 37.2 (CH_2), 43.5 (C), 44.3 (CH_2), 49.4 (CH_2), 54.0 (CH_2), 60.0 (C), 61.97 (CH_2), 62.04 (CH_2), 77.7 (CH_2), 82.1 (C), 127.4 (CH), 127.8 (CH), 128.6 (CH), 136.5 (C), 167.4 (C), 167.8 (C), 169.1 (C); IR (neat) 2928, 2853, 1738, 1643, 1496, 1453, 1367, 1240, 1096, 1049 cm^{-1}; MS (EI) m/z 457 (M^+, 10), 344 (42), 205 (30), 120 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{26}H_{35}NO_6$ 457.2464; Found 457.2468.

2h: (0.3 mmol scale, 0.2 equiv. $SnCl_4$, 95 mg, 72%) R_f = 0.3 (hexane-ether = 1 : 2); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.998 (s, 3H), 1.02 (s, 3H), 1.21 (t, *J* = 7.1

Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.56 (d, *J* = 14.2 Hz, 1H), 2.66 (d, *J* = 14.2 Hz, 1H), 3.04 (d, *J* = 17.8 Hz, 1H), 3.26 (d, *J* = 13.1 Hz, 1H), 3.37 (d, *J* = 8.8 Hz, 1H), 3.38 (d, *J* = 13.1 Hz, 1H), 3.42 (d, *J* = 17.8 Hz, 1H), 3.57 (d, *J* = 8.8 Hz, 1H), 4.08-4.29 (m, 4H), 4.55 (d, *J* = 15.0 Hz, 1H), 4.60 (d, *J* = 15.0 Hz, 1H), 7.21-7.33 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.9 (CH_3), 14.0 (CH_3), 27.2 (CH_3), 28.1 (CH_3), 35.9 (CH_2), 39.3 (C), 46.7 (CH_2), 49.4 (CH_2), 54.3 (CH_2), 60.1 (C), 61.96 (CH_2), 62.01 (CH_2), 79.9 (CH_2), 82.7 (C), 127.4 (CH), 127.8 (CH), 128.6 (CH), 136.5 (C), 167.2 (C), 167.9 (C), 169.0 (C); IR (neat) 2960, 2871, 1732, 1660, 1651, 1496, 1455, 1367, 1239, 1096, 1050 cm^{-1}; MS (EI) m/z 417 (M^+, 24), 372 (12), 344 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{23}H_{31}NO_6$ 417.2151; Found 417.2135.

2i: (0.5 mmol scale, 0.5 equiv. $SnCl_4$, 59 mg, 30%) R_f = 0.1 (CH_2Cl_2-ether = 10 : 1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.08 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.27 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.74-1.78 (m, 2H), 2.98 (d, *J* = 12.9 Hz, 1H), 2.99 (d, *J* = 17.2 Hz, 1H), 3.49 (d, *J* = 12.9 Hz, 1H), 3.51 (d, *J* = 17.2 Hz, 1H), 3.77 (ddd, *J* = 7.8, 7.8, 5.9 Hz, 1H), 3.89 (ddd, *J* = 7.8, 7.8, 7.8 Hz, 1H), 4.10-4.23 (m, 4H), 4.54 (d, *J* = 14.9 Hz, 1H), 4.60 (d, *J* = 14.9 Hz, 1H), 7.21-7.33 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.8 (CH_3), 13.9 (CH_3), 24.1 (CH_3), 25.7 (CH_3), 38.9 (CH_2), 42.3 (CH_2), 45.3 (C), 49.8 (CH_2), 54.3 (CH_2), 60.3 (C), 61.8 (CH_2), 62.0 (CH_2), 65.2 (CH_2), 85.3 (C), 127.3 (CH), 127.8 (CH), 128.5 (CH), 136.6 (C), 167.3 (C), 169.1 (C), 169.9 (C); IR (neat) 2979, 1728, 1651, 1497, 1475, 1454, 1367, 1241, 1126, 1090, 1059 cm^{-1}; MS (EI) m/z 417 (M^+, 13), 372 (20), 256 (10), 205 (26), 84 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{23}H_{31}NO_6$ 417.2151; Found 417.2155.

5: (0.5 mmol scale, 0.2 equiv. $AlCl_3$, 104 mg, 54%) R_f = 0.5 (CH_2Cl_2-ether = 10 : 1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.13 (s, 6H), 1.26 (t, *J* = 7.1 Hz, 6H), 1.80 (t, *J* = 6.8 Hz, 2H), 2.99 (d, *J* = 7.4 Hz, 2H), 3.97 (t, *J* = 7.4 Hz, 1H), 4.10 (t, *J* = 6.8 Hz, 2H), 4.14-4.27 (m, 4H), 4.67 (s, 2H), 4.92 (s, 1H), 7.18-7.28 (m, 5H). Selected NOEs are between δ 4.92 (C*H*=) and δ 1.13 (C(CH_3)$_2$C).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.1 (CH_3), 26.9 (CH_3), 33.1 (CH_2), 39.6 (CH_2), 40.5 (C), 48.4 (CH), 50.0 (CH_2), 61.5 (CH_2), 68.6 (CH_2), 96.4 (CH), 127.0 (CH), 128.1 (CH), 128.6 (CH), 137.8 (C), 163.4 (C), 165.5 (C), 170.3 (C);

IR (neat) 2965, 1732, 1653, 1496, 1455, 1415, 1370, 1267, 1176, 1096, 1030 cm^{-1}; MS (EI) m/z 417 (M^+, 10), 372 (6.0), 246 (49), 205 (66), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{23}H_{31}NO_6$ 417.2151; Found 417.2144.

2j: (1.01 mmol scale, 0.2 equiv. $Sc(OTf)_3$, 350 mg, 88%) R_f = 0.6 (ether); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.24 (t, *J* = 7.1 Hz, 6H), 3.21 (s, 2H), 3.30 (s, 2H), 3.89-3.95 (m, 2H), 4.04-4.10 (m, 2H), 4.17-4.25 (m, 4H), 4.58 (s, 2H), 7.22-7.34 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.0 (CH_3), 37.2 (CH_2), 49.7 (CH_2), 52.1 (CH_2), 59.4 (C), 62.1 (CH_2), 65.7 (CH_2), 105.6 (C), 127.5 (CH), 127.9 (CH), 128.7 (CH), 136.2 (C), 166.7 (C), 167.3 (C); IR (neat) 2979, 2905, 1733, 1652, 1496, 1454, 1367, 1272, 1243, 1181, 1075, 1050 cm^{-1}; MS (EI) m/z 391 (M^+, 49), 346 (15), 205 (25), 199 (28), 91 (60), 84 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{20}H_{25}NO_7$ 391.1631; Found 391.1628.

2k: (0.5 mmol scale, 0.2 equiv. $Sc(OTf)_3$, 150 mg, 75%) R_f = 0.5 (ether); colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.882-0.974 (m, 2H), 1.10-1.33 (m, 3H), 1.26 (t, *J* = 7.1 Hz, 6H), 1.63-1.74 (m, 6H), 3.12 (s, 2H), 3.17 (d, *J* = 7.2 Hz, 2H), 3.43 (s, 2H), 4.02-4.14 (m, 4H), 4.19-4.26 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.0 (CH_3), 25.9 (CH_2), 26.5 (CH_2), 30.6 (CH_2), 35.6 (CH), 37.2 (CH_2), 53.0 (CH_2), 53.8 (CH_2), 59.3 (C), 62.1 (CH_2), 65.8 (CH_2), 105.7 (C), 166.6 (C), 167.4 (C); IR (neat) 2925, 2852, 1733, 1648, 1491, 1449, 1367, 1284, 1246, 1181, 1076, 1050 cm^{-1}; MS (EI) m/z 397 (M^+, 47), 352 (14), 324 (17), 171 (20), 114 (29), 84 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{20}H_{31}NO_7$ 397.2101; Found 397.2102.

2l: (0.5 mmol scale, 0.2 equiv. $Sc(OTf)_3/CH_2Cl_2$, 134 mg, 63%) R_f = 0.3 (hexane-ether = 1 : 3); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.587 (s, 3H), 1.10 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 6H), 3.22 (s, 2H), 3.29 (d, *J* = 11.8 Hz, 2H), 3.38 (d, *J* = 11.8 Hz, 2H), 3.82 (s, 2H), 4.16-4.31 (m, 4H), 4.60 (s, 2H), 7.24-7.30 (m, 3H), 7.32-7.34 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.0 (CH_3), 22.0 (CH_3), 22.8 (CH_3), 29.6 (C), 36.7 (CH_2), 43.5 (CH_2), 49.6 (CH_2), 60.3 (C), 62.0 (CH_2), 70.7 (CH_2), 95.2 (C), 127.7 (CH), 128.1 (CH), 128.7 (CH), 136.5 (C), 167.1 (C), 167.3 (C); IR (neat) 2960, 2872, 1733, 1645, 1497, 1455, 1366, 1294, 1244, 1186, 1140, 1088, 1053 cm^{-1}; MS (EI) m/z 433 (M^+, 86), 388 (40), 347 (62), 274 (62), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{23}H_{31}NO_7$ 433.2101; Found 433.2098.

6: (0.3 mmol scale, 0.2 equiv. $Sc(OTf)_3/ClCH_2CH_2Cl$, 40 mg, 26%) R_f = 0.3 (hexane-ether = 1 : 3); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 2.5:1) δ (ppm) 0.892 (s, 6H×0.71, major rotamer), 0.908 (s, 6H×0.29, minor rotamer), 1.28 (t, *J* = 7.1 Hz, 6H×0.71), 1.29 (t, *J* = 7.1 Hz, 6H×0.29), 2.02 (bs, 1H), 2.95 (d, *J* = 7.2 Hz, 2H×0.29), 3.11 (d, *J* = 7.4 Hz, 2H×0.71), 3.29 (s, 2H×0.71), 3.30 (s, 2H×0.29), 3.95 (s, 2H×0.71), 3.99-4.06 (m, 3H+2H×0.29), 4.15-4.28 (m, 4H), 4.65 (s, 2H×0.29), 4.66 (s, 2H×0.71), 7.20-7.41 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.1 (CH_3), 21.55 (CH_3), 21.57 (CH_3), 32.5 (CH_2), 32.7 (CH_2), 36.2 (C), 36.4 (C), 47.4 (CH_2), 48.1 (CH), 48.3 (CH), 48.6 (CH_2), 50.1 (CH_2), 52.2 (CH_2), 61.8 (CH_2), 62.0 (CH_2), 67.9 (CH_2), 68.1 (CH_2), 70.1 (CH_2), 70.4 (CH_2), 127.1 (CH), 127.9 (CH), 128.2 (CH), 128.5 (CH), 128.8 (CH), 129.2 (CH), 135.4 (C), 136.3 (C), 169.1 (C), 169.2 (C), 169.3 (C), 169.6 (C), 170.5 (C), 170.9 (C); IR (neat) 3478, 2963, 1742, 1732, 1651, 1497, 1446, 1372, 1179, 1097, 1031 cm^{-1}; MS (EI) m/z 451 (M^+, 5.0), 406 (8.8), 250 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{23}H_{33}NO_8$ 451.2206; Found 451.2203.

Preparation of 7 (eq 7). The diester **2j** (166 mg, 0.424 mmol), LiCl (41 mg, 0.967 mmol), water (0.11 mL) and DMSO (1.95 ml) were heated at 160 °C for 18 h. The reaction mixture was cooled to 0 °C, diluted with EtOAc (20 mL) and saturated aqueous NH_4Cl (20 mL) was added to the mixture. The mixture was extracted with EtOAc (20 mL×4). The combined extracts were washed with water (8 mL) and brine (8 mL), dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified by column chromatography over silica gel eluting with ether -MeOH to give **7j** (69 mg, 51%).

7j: R_f = 0.3 (ether); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.23 (t, *J* = 7.1 Hz, 3H), 2.82 (dd, *J* = 17.3, 6.6 Hz, 1H), 2.89 (dd, *J* = 17.3, 6.3 Hz, 1H), 3.04 (ddd, *J* = 6.6, 6.3, 1.1 Hz, 1H), 3.11 (dd, *J* = 12.7, 1.1 Hz, 1H), 3.39 (d, *J* = 12.7 Hz, 1H), 3.87-4.05 (m, 4H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.52 (d, *J* = 14.9 Hz, 1H), 4.69 (d, *J* = 14.9 Hz, 1H), 7.24-7.28 (m, 3H), 7.31-7.35 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.2 (CH_3), 32.8 (CH_2), 46.6 (CH), 50.1 (CH_2), 52.4 (CH_2), 61.3 (CH_2), 65.1 (CH_2), 65.4 (CH_2), 104.8 (C), 127.5 (CH), 128.0 (CH), 128.7 (CH), 136.4 (C), 167.6 (C), 170.3 (C); IR (neat) 2977, 2898, 1733,

1652, 1486, 1454, 1374, 1276, 1198, 1137, 1036 cm^{-1}; MS (EI) m/z 319 (M^+, 16), 274 (5), 171 (10), 83 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{17}H_{21}NO_5$ 319.1420; Found 319.1426.

7l: (0.4 mmol scale, 112 mg, 77%) R_f = 0.3 (ether); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.920 (s, 3H), 0.935 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 2.65 (dd, *J* = 17.6, 6.7 Hz, 1H), 2.74 (dd, *J* = 17.6, 3.9 Hz, 1H), 3.27 (dd, *J* = 12.7, 1.7 Hz, 1H), 3.28 (dd, *J* = 11.6, 1.4 Hz, 1H), 3.38 (dd, *J* = 11.6, 1.4 Hz, 1H), 3.47-3.56 (m, 3H), 3.65 (d, *J* = 11.6 Hz, 1H), 4.10-4.18 (m, 2H), 4.35 (d, *J* = 14.9 Hz, 1H), 4.89 (d, *J* = 14.9 Hz, 1H), 7.24-7.35 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.1 (CH_3), 22.4 (CH_3), 22.7 (CH_3), 30.0 (C), 31.7 (CH_2), 42.7 (CH), 50.3 (CH_2), 50.8 (CH_2), 61.2 (CH_2), 70.5 (CH_2), 70.7 (CH_2), 94.3 (C), 127.5 (CH), 128.1 (CH), 128.6 (CH), 136.5 (C), 167.7 (C), 170.9 (C); IR (neat) 2959, 2872, 1732, 1651, 1495, 1454, 1372, 1276, 1197, 1122, 1086, 1046 cm^{-1}; MS (EI) m/z 361 (M^+, 6.3), 213 (11), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{20}H_{27}NO_5$ 361.1889; Found 361.1887.

8 (Scheme 8): (0.42 mmol scale, 69 mg, 48%) R_f = 0.4 (hexane-ether = 1 : 1); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.861 (d, *J* = 6.6 Hz, 3H), 0.872 (d, *J* = 6.6 Hz, 3H), 0.940 (d, *J* = 6.6 Hz, 3H), 0.948 (d, *J* = 6.6 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.91-2.05 (m, 2H), 3.15 (dd, *J* = 7.6, 3.7 Hz, 1H), 3.24 (dd, *J* = 7.4, 5.5 Hz, 1H), 3.29 (d, *J* = 7.6 Hz, 2H), 3.85 (d, *J* = 6.1 Hz, 1H), 4.13-4.35 (m, 4H), 4.98 (d, *J* = 6.1 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.0 (CH_3), 20.0 (CH_3), 20.09 (CH_3), 20.12 (CH_3), 26.3 (CH), 27.6 (CH), 53.1 (CH_2), 54.9 (CH_2), 55.0 (CH), 61.9 (CH_2), 69.1 (CH), 167.4 (C), 169.0 (C), 171.0 (C); IR (neat) 3366, 2962, 2873, 1754, 1733, 1645, 1468, 1389, 1370, 1260, 1153, 1099, 1066, 1032 cm^{-1}; MS (FAB) m/z 368 ($[M + Na]^+$), 346 ($[M + H]^+$); HRMS (FAB) m/z: $[M + H]^+$ Calcd for $C_{17}H_{32}NO_6$ 346.2230; Found 346.2229, $[M + Na]^+$ Calcd for $C_{17}H_{31}NO_6Na$ 368.2049; Found 368.2051.

9 (Scheme 8): (0.42 mmol scale, 52 mg, 34%) R_f = 0.6 (hexane-ether = 1 : 1); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.871 (d, *J* = 6.8 Hz, 3H), 0.891 (d, *J* = 6.6 Hz, 3H), 1.00 (d, *J* = 6.6 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.99-2.16 (m, 2H), 2.85 (dd, *J* = 13.5, 7.4 Hz, 1H), 3.09 (dd, *J* = 14.8, 7.2 Hz, 1H), 3.39 (dd, *J* = 14.8, 8.0 Hz, 1H), 3.57 (dd, *J* = 13.5, 7.7 Hz, 1H), 4.10-4.32 (m, 4H), 4.29

(d, J = 10.7 Hz, 1H), 4.99 (d, J = 10.7 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.0 (CH_3), 14.1 (CH_3), 19.9 (CH_3), 20.1 (CH_3), 20.2 (CH_3), 20.5 (CH_3), 26.4 (CH), 28.1 (CH), 51.1 (CH), 54.0 (CH_2), 55.7 (CH_2), 56.7 (CH), 62.1 (CH_2), 62.2 (CH_2), 166.5 (C), 166.8 (C), 167.3 (C); IR (neat) 2963, 2873, 1752, 1654, 1468, 1447, 1389, 1370, 1339, 1297, 1184, 1148, 1100, 1030 cm^{-1}; MS (FAB) m/z 388, 386 ([M + Na]$^+$), 366, 364 ([M + H]$^+$); HRMS (FAB) m/z: [M + H]$^+$ Calcd for $C_{17}H_{31}ClNO_5$ 364.1891, 366.1861; Found 364.1892, 366.1862.

Ethenetricarboxylate **10** was prepared by the reaction of diethyl ketomalonate with the corresponding (triphenylphosphoranylidne)acetate according to the literature procedure.[9b,25] The (triphenylphosphoranylidne)acetate ester was prepared by the corresponding chloroacetate and triphenylphosphine in benzene and subsequent treatment with NaOH. The chloroacetate was prepared by the reaction of tetrahydropyran-2-methanol (1 equiv) and chloroacetyl chloride (1 equiv) in the presence of pyridine (1 equiv) in ether at 0 °C. Data of the ethenetricarboxylate **10** and chloroacetate for the (triphenylphosphoranylidne)acetate ester are shown below.

Tetrahydropyran-2-methyl 2-chloroacetate: (30.4 mmol scale, 5.774 g, 99%); colorless oil (bp. 85 °C/1 mmHg for analytical data); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.30-1.39 (m, 1H), 1.46-1.65 (m, 4H), 1.86-1.92 (m, 1H), 3.45 (ddd, J = 11.4, 11.4, 2.7 Hz, 1H), 3.57 (dddd, J = 12.3, 6.7, 3.4, 2.3 Hz, 1H), 4.01 (bd, J = 11.4 Hz, 1H), 4.11 (s, 2H), 4.13 (dd, J = 11.6, 6.7 Hz, 1H), 4.18 (dd, J = 11.6, 3.4 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 23.0 (CH_2), 25.7 (CH_2), 27.8 (CH_2), 41.0 (CH_2), 68.5 (CH_2), 69.0 (CH_2), 75.2 (CH), 167.5 (C); IR (neat) 2942, 2850, 1760, 1442, 1414, 1315, 1177, 1095, 1049, 1006 cm^{-1}; MS (CI) m/z 195, 193 ([M + H]$^+$); HRMS (CI) m/z: [M + H]$^+$ Calcd for $C_8H_{14}ClO_3$ 193.0631, 195.0602; Found 193.0635, 195.0602.

10 (Scheme 8): (17.3 mmol scale, 2.803 g, 52%) R_f = 0.7 (hexane-ether = 1 : 4); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.29-1.39 (m, 1H), 1.32 (t, J = 7.1 Hz, 3H), 1.35 (t, J = 7.1 Hz, 3H), 1.46-1.65 (m, 4H), 1.86-1.89 (m, 1H), 3.44 (ddd, J = 11.4, 11.4, 2.7 Hz, 1H), 3.57 (dddd, J = 11.1, 6.8, 3.4, 2.1 Hz, 1H), 4.00 (bd, J = 11.4 Hz, 1H), 4.11 (dd, J =

11.7, 6.8 Hz, 1H), 4.19 (dd, *J* = 11.7, 3.4 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 3H), 4.37 (q, *J* = 7.1 Hz, 3H), 6.94 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.9 (CH_3), 14.0 (CH_3), 22.9 (CH_2), 25.6 (CH_2), 27.7 (CH_2), 62.1 (CH_2), 62.5 (CH_2), 68.4 (CH_2), 68.5 (CH_2), 75.1 (CH), 129.7 (CH), 139.3 (C), 162.2 (C), 163.6 (C), 164.2 (C); IR (neat) 2942, 2850, 1728, 1651, 1446, 1375, 1345, 1263, 1067, 1024 cm^{-1}; MS (CI) m/z 315 ($[M + H]^+$); HRMS (CI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{23}O_7$ 315.1444; Found 315.1444.

11 (Scheme 8): (0.52 mmol scale, 35 mg, 21%) R_f = 0.7 (hexane-ether = 1 : 4); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.24-1.37 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.45-1.61 (m, 4H), 1.85-1.89 (m, 1H), 2.99 (d, *J* = 7.4 Hz, 2H), 3.44 (ddd, *J* = 11.5, 11.5, 2.7 Hz, 1H), 3.53 (dddd, *J* = 12.5, 6.1, 3.5, 2.1 Hz, 1H), 3.83 (t, *J* = 7.4 Hz, 1H), 3.98-4.03 (m, 1H), 4.04 (dd, *J* = 11.5, 6.6 Hz, 1H), 4.10 (dd, *J* = 11.5, 3.5 Hz, 1H), 4.16-4.30 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.0 (CH_3), 23.0 (CH_2), 25.7 (CH_2), 27.8 (CH_2), 33.1 (CH_2), 47.9 (CH), 61.8 (CH_2), 68.0 (CH_2), 68.4 (CH_2), 75.3 (CH), 168.38 (C), 168.41 (C), 170.9 (C); IR (neat) 2941, 2852, 1735, 1446, 1370, 1266, 1164, 1095, 1049, 1030 cm^{-1}; MS (EI) m/z 317 ($[M + H]^+$); HRMS (CI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{25}O_7$ 317.1600; Found 317.1620.

Diethyl 2-(4-benzyl-6-(hydroxymethyl)-3-oxomorpholin-2-yl)malonate (12) (Scheme 9): ($ClCH_2CH_2Cl$, r.t., 0.5 mmol scale, 160 mg, 80%, *trans* : *cis* = 1 : 9) R_f = 0.3 (ether); pale yellow oil; The *trans* : *cis* ratio was determined by ^{1}H NMR of the product mixture. The *cis* product was partially isolated. For the major *cis* product, ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.24 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 2.10 (bs, 1H), 3.05 (dd, *J* = 12.0, 2.8 Hz, 1H), 3.41 (dd, *J* = 12.0, 10.9 Hz, 1H), 3.57 (dd, *J* = 12.0, 5.4 Hz, 1H), 3.64 (dd, *J* = 12.0, 3.7 Hz, 1H), 3.92 (dddd, *J* = 10.9, 5.4, 3.7, 2.8 Hz, 1H), 4.13-4.31 (m, 4H), 4.20 (d, *J* = 3.9 Hz, 1H), 4.52 (d, *J* = 14.7 Hz, 1H), 4.72 (d, *J* = 14.7 Hz, 1H), 4.80 (d, *J* = 3.9 Hz, 1H), 7.27-7.36 (m, 5H). Selected NOEs are between δ 4.80 (H-2) and δ 3.92 (H-6).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.08 (CH_3), 14.12 (CH_3), 46.9 (CH_2), 50.2 (CH_2), 54.2 (CH), 61.7 (CH_2), 61.78 (CH_2), 62.80 (CH_2), 73.7 (CH), 75.4 (CH), 127.9 (CH), 128.5 (CH), 128.8 (CH), 136.0 (C), 166.7 (C), 167.3 (C); IR (neat) 3441, 2983, 2936, 1733, 1652, 1495, 1455,

1373, 1277, 1178, 1036 cm^{-1}; MS (EI) m/z 379 (M^+, 28), 334 (15), 249 (36), 205 (39), 159 (64), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{19}H_{25}NO_7$ 379.1631; Found 379.1630.

Diethyl 2-(6-methoxy-4-methyl-3-oxomorpholin-2-yl)malonate (13t) (Scheme 9): (0.59 mmol scale, 79 mg, 44%, *trans* : *cis* = 5 : 1) R_f = 0.1 (CH_2Cl_2); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.28 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 2.96 (s, 3H×0.17, minor isomer), 2.97 (s, 3H×0.83, major isomer), 3.22 (d, *J* = 12.4 Hz, 1H×0.83), 3.34 (dd, *J* = 11.7, 3.0 Hz, 1H×0.17), 3.43 (dd, *J* = 11.7, 7.4 Hz, 1H×0.17), 3.46 (s, 3H×0.83), 3.48 (s, 3H×0.17), 3.71 (dd, *J* = 12.4, 3.6 Hz, 1H×0.83), 4.05 (d, *J* = 5.9 Hz, 1H×0.17), 4.15 (d, *J* = 4.6 Hz, 1H×0.83), 4.20-4.29 (m, 4H), 4.75 (d, *J* = 4.6 Hz, 1H×0.83), 4.79 (d, *J* = 5.9 Hz, 1H×0.17), 4.83 (dd, *J* = 7.4, 3.0 Hz, 1H×0.17), 4.88 (d, *J* = 3.6 Hz, 1H×0.83). Selected NOEs for major isomer are between δ 3.46 (OC*H*$_3$) and δ 4.75 (H-2), 4.88 (H-6), and between δ 4.15 (C*H*(CO_2Et)$_2$) and δ 4.88 (H-6).; ^{13}C NMR (100.6 MHz, $CDCl_3$) (For major isomer) δ (ppm) 14.0 (CH_3), 14.1 (CH_3), 34.2 (CH_3), 52.0 (CH_2), 53.6 (CH), 55.1 (CH_3), 61.6 (CH_2), 61.7 (CH_2), 68.7 (CH), 94.8 (CH), 166.2 (C), 166.8 (C), 167.2 (C); IR (neat) 2983, 2939, 1738, 1661, 1508, 1447, 1371, 1267, 1178, 1156, 1092, 1061 cm^{-1}; MS (EI) m/z 303 (M^+, 11), 271 (94), 258 (97), 200 (99), 127 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{13}H_{21}NO_7$ 303.1318; Found 303.1324.

Diethyl 2-(4-allyl-6-methoxy-3-oxomorpholin-2-yl)malonate (13u) (Scheme 9): (0.56 mmol scale, 130 mg, 56%, *trans*) R_f = 0.3 (hexane-ether = 1 : 4); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.28 (t, *J* = 7.2 Hz, 3H), 1.30 (t, *J* = 7.0 Hz, 3H), 3.20 (d, *J* = 12.5 Hz, 1H), 3.45 (s, 3H), 3.64 (dd, *J* = 12.5, 3.5 Hz, 1H), 3.98 (dddd, *J* = 15.2, 5.9, 1.4, 1.4 Hz, 1H), 4.05 (dddd, *J* = 15.2, 5.9, 1.4, 1.4 Hz, 1H), 4.18 (d, *J* = 4.4 Hz, 1H), 4.16-4.31 (m, 4H), 4.76 (d, *J* = 4.4 Hz, 1H), 4.89 (d, *J* = 3.5 Hz, 1H), 5.22 (dddd, *J* = 11.7, 1.5, 1.4, 1.4 Hz, 1H), 5.27 (dddd, *J* = 17.2, 1.5, 1.4, 1.4 Hz, 1H), 5.74 (ddt, *J* = 17.2, 11.7, 5.9 Hz, 1H). Selected NOEs are between δ 3.45 (OC*H*$_3$) and δ 4.76 (H-2), 4.89 (H-6).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.1 (CH_3), 14.2 (CH_3), 48.8 (CH_2), 49.3 (CH_2), 53.6 (CH), 55.2 (CH), 61.7 (CH_2), 61.8 (CH_2), 68.8 (CH), 95.1 (CH), 118.3 (CH_2), 131.7 (CH), 166.2 (C), 166.9 (C), 167.3 (C); IR (neat) 2983, 2937, 1747, 1661, 1494, 1446, 1371, 1279, 1178, 1068, 1041 cm^{-1}; MS

(FAB) m/z 330 ([M + H]$^+$); HRMS (FAB) m/z: [M + H]$^+$ Calcd for $C_{15}H_{24}NO_7$ 330.1553; Found 330.1541.

Formation of 14 (Scheme 10). A mixture of 0.7 mL AcOH and 0.7 mL H_2O was added at room temperature to **1v** (273 mg, 0.732 mmol). The mixture was heated at 60 °C for 21 h. After cooling to room temperature, 20 mL CH_2Cl_2 and 20 mL H_2O were added. The organic phase was washed once with 20 mL H_2O, once with 20 mL saturated $NaHCO_3$, then dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography over silica gel with hexane-ether as eluent to give **14** (201 mg, 87%, *trans* : *cis* = 2.5 : 1).

Diethyl 2-(4-allyl-6-hydroxy-3-oxomorpholin-2-yl)malonate (14): R_f = 0.4 (ether); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.25-1.30 (m, 6H), 3.21 (dd, *J* = 12.3, 0.8 Hz, 1H×0.71, major isomer), 3.36-3.38 (m, 2H×0.29, minor isomer), 3.63 (dd, *J* = 12.3, 3.2 Hz, 1H×0.71), 3.97-4.08 (m, 2H), 4.10 (d, *J* = 5.1 Hz, 1H×0.29), 4.13 (d, *J* = 4.2 Hz, 1H×0.71), 4.18-4.31 (m, 4H), 4.84 (d, *J* = 5.1 Hz, 1H×0.29), 4.96 (d, *J* = 4.2 Hz, 1H×0.71), 5.20-5.31 (m, 2H+1H×0.29), 5.41 (bd, *J* = 3.2 Hz, 1H×0.71), 5.71-5.81 (m, 1H). Selected NOEs are between δ 4.13 (C*H*(CO_2Et)$_2$) and δ 5.41 (H-6) for major isomer, and between δ 4.84 (H-2') and δ 5.20-5.31 (H-6', overlapped) for minor isomer.; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.97 (CH_3), 14.01 (CH_3), 48.8 (CH_2), 49.2 (CH_2), 49.7 (CH_2), 50.5 (CH_2), 53.8 (CH), 54.5 (CH), 61.7 (CH_2), 61.75 (CH_2), 61.83 (CH_2), 61.9 (CH_2), 69.1 (CH), 72.8 (CH), 88.6 (CH), 90.4 (CH), 118.3 (CH_2), 118.8 (CH_2), 131.6 (CH), 131.7 (CH), 166.2 (C), 166.3 (C), 166.9 (C), 167.1 (C), 167.2 (C), 167.5 (C); IR (neat) 3379, 2983, 2939, 1747, 1651, 1497, 1514, 1420, 1372, 1278, 1178, 1080, 1037 cm^{-1}; MS (EI) m/z 315 (M$^+$, 31), 270 (55), 224 (43), 196 (40), 127 (99), 84 (100%); HRMS (EI) m/z: M$^+$ Calcd for $C_{14}H_{21}NO_7$ 315.1318; Found 315.1317.

Diethyl 2-(4-benzyl-6-hydroxy-3-oxomorpholin-2-yl)malonate (15) (Scheme 10): (0.51 mmol scale, 90 mg, 49%, *trans* : *cis* = 2.7 : 1) R_f = 0.6 (ether); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.21-1.29 (m, 6H), 3.13 (d, *J* = 12.3 Hz, 1H×0.73, major isomer), 3.28 (d, *J* = 4.6 Hz, 2H×0.27, minor isomer), 3.53 (dd, *J* = 12.3, 3.3 Hz, 1H×0.73), 4.14-4.28 (m,

5H), 4.49 (d, *J* = 14.8 Hz, 1H×0.27), 4.57 (d, *J* = 14.8 Hz, 1H×0.73), 4.68 (d, *J* = 14.8 Hz, 1H), 4.87 (d, *J* = 4.9 Hz, 1H×0.27), 5.02 (d, *J* = 4.1 Hz, 1H×0.73), 5.18 (dd, *J* = 4.6, 4.6 Hz, 1H×0.27), 5.33 (d, *J* = 3.3 Hz, 1H×0.73), 7.24-7.35 (m, 5H). Selected NOEs are between δ 4.14-4.28 (C*H*(CO_2Et)$_2$, overlapped) and δ 5.33 (H-6) for major isomer, and between δ 4.87 (H-2') and δ 5.18 (H-6') for minor isomer.; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.98 (CH_3), 14.02 (CH_3), 49.7 (CH_2), 49.8 (CH_2), 50.2 (CH_2), 50.5 (CH_2), 53.8 (CH), 54.5 (CH), 61.7 (CH_2), 61.8 (CH_2), 61.9 (CH_2), 62.0 (CH_2), 69.1 (CH), 72.9 (CH), 88.6 (CH), 90.4 (CH), 127.6 (CH), 127.9 (CH), 128.2 (CH), 128.4 (CH), 128.7 (CH), 128.8 (CH), 135.7 (C), 135.8 (C), 166.4 (C), 166.6 (C), 167.0 (C), 167.1 (C), 167.3 (C), 167.6 (C); IR (neat) 3374, 2981, 1749, 1734, 1652, 1497, 1455, 1371, 1277, 1178, 1094, 1029 cm^{-1}; MS (EI) m/z 365 (M^+, 43), 205 (36), 176 (45), 148 (94), 115 (89), 91 (100%); HRMS (EI) m/z: M^+ Calcd for $C_{18}H_{23}NO_7$ 365.1475; Found 365.1472.

Enantiomeric substrates (-)-(*R*)-**4a** and (+)-(*S*)-**4a** were synthesized by reaction with (-)-(*R*)- and (+)-(*S*)-tetrahydrofurfurylamine, respectively.

(-)-(*R*)-**4a**: (9.9 mmol scale, 1.37 g, 73%); pale yellow oil; HPLC (hexane-*i*PrOH = 9:1) major peak t_{R1} 5.1 min, >98% ee; $[\alpha]_D^{20}$ –8.3 (c 1.00, $CHCl_3$).

(+)-(*S*)-**4a**: (9.9 mmol scale, 1.84 g, 97%); pale yellow oil; HPLC (hexane-*i*PrOH = 9:1) major peak t_{R2} 6.0 min, >98% ee; $[\alpha]_D^{17}$ +11.1 (c 0.97, $CHCl_3$).

Enantiomeric substrates (-)-(*R*)-**1a** and (+)-(*S*)-**1a** were synthesized by reaction with (-)-(*R*)-**4a** and (+)-(*S*)-**4a**, respectively.

(-)-(*R*)-**1a**: (1.6 mmol scale, 306 mg, 50%); pale yellow oil; HPLC (hexane-*i*PrOH = 19:1) major peak t_{R1} 24.5 min, >98% ee; $[\alpha]_D^{17}$ –36.4 (c 0.97, $CHCl_3$).

(+)-(*S*)-**1a**: (3.0 mmol scale, 666 mg, 63%); pale yellow oil; HPLC (hexane-*i*PrOH = 19:1) major peak t_{R2} 32.2 min, >98% ee; $[\alpha]_D^{17}$ +35.9 (c 0.99, $CHCl_3$).

Enantioenriched (-)-**2a** and (+)-**2a** were synthesized by the reaction of (-)-(*R*)-**1a** and (+)-(*S*)-**1a**, respectively.

(-)-**2a**: (0.5 mmol scale, 0.2 equiv. $Sc(OTf)_3$, 153 mg, 78%); pale yellow oil; HPLC (hexane-*i*PrOH = 9:1) major peak t_{R1} 18.8 min, minor peak t_{R2} 29.5 min, 42% ee; $[\alpha]_D^{17}$ –25.0 (c 1.02, $CHCl_3$).

(+)-**2a**: (0.5 mmol scale, 0.2 equiv. $Sc(OTf)_3$, 158 mg, 82%); pale yellow oil; HPLC (hexane-*i*PrOH = 9:1) minor peak t_{R1} 19.6 min, major peak t_{R2} 31.3 min, 43% ee; $[\alpha]_D^{16}$ –25.7 (c 1.12, $CHCl_3$).

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Supporting Information Available: ^1H and ^{13}C NMR spectral data and Cartesian coordinates of the optimized geometries. This information is available free of charge via the Internet at http://pubs.acs.org.

References and notes

[1] For examples of piperidines, see: (a) O'Hagan, D. *Nat. Prod. Rep.* **2000**, *17*, 435. (b) Källström, S.; Leino, R. *Bioorg. Med. Chem.* **2008**, *16*, 601. (c) Kesting, J. R.; Tolderlund, I.-L.; Pedersen, A. F.; Witt, M.; Jaroszewski, J. W.; Staerk, D. *J. Nat. Prod.* **2009**, *72*, 312. (d) Dragutan, I.; Dragutan, V.; Demonceau, A. *RSC Adv.* **2012**, *2*, 719. (e) Still, P. C.; Yi, B.; González-Cestari, T. F.; Pan, L.; Pavlovicz, R. E.; Chai, H.-B.; Ninh, T. N.; Li, C.; Soejarto, D. D.; McKay, D. B.; Kinghorn, A. D. *J. Nat. Prod.* **2013**, *76*, 243. (f) Taylor, R. D.; MacCoss, M.; Lawson, A. D. G. *J. Med. Chem.* **2014**, *57*, 5845. (g) Vitaku, E.; Smith, D. T.; Njardarson, J. T. *J. Med. Chem.* **2014**, *57*, 10257.

[2] For examples of morpholines, see: (a) Wijtmans, R.; Vink, M. K. S.; Schoemaker, H. E.; van Delft, F. L.; Blaauw, R. H.; Rutjes, F. P. J. T. *Synthesis* **2004**, 641. (b) Wilhelm, A.; Kendrekar, P.; Noreljaleel, A. E. M.; Abay, E. T.; Bonnet, S. L.; Wiesner, L.; de Kock, C.; Swart, K. J.; van der Westhuizen, J. H. *J. Nat. Prod.* **2015**, *78*, 1848. (c) Rombouts, F. J. R.; Tresadern, G.; Delgado, O.; Martínez-Lamenca, C.; Van Gool, M.; García-Molina, A.; de Diego, S. A. A.; Oehlrich, D.; Prokopcova, H.; Alonso, J. M.; Austin, N.; Borghys, H.; Van Brandt, S.; Surkyn, M.; De Cleyn, M.; Vos, A.; Alexander, R.; Macdonald, G.; Moechars, D.; Gijsen, H.; Trabanco, A. A. *J. Med. Chem.* **2015**, *58*, 8216. (d) Zhao, Z.; Pissarnitski, D. A.; Josien, H. B.; Bara, T. A.; Clader, J. W.; Li, H.; McBriar, M. D.; Rajagopalan, M.; Xu, R.; Terracina, G.; Hyde, L.; Song, L.; Zhang, L.; Parker, E. M.; Osterman, R.; Buevich, A. V. *Euro. J. Med. Chem*. **2016**, *124*, 36. (e) Witt, J. O.; McCollum, A. L.; Hurtado, M. A.; Huseman, E. D.; Jeffries, D. E.; Temple, K. J.; Plumley, H. C.; Blobaum, A. L.; Lindsley, C. W.; Hopkins, C. R. *Bioorg. Med. Chem. Lett*. **2016**, *26*, 2481.

[3] For the synthesis of piperidines, see: (a) Laschat, S.; Dickner, T. *Synthesis* **2000**, 1781. (b) Weintraub, P. M.; Sabol, J. S.; Kane, J. M.; Borcherding, D. R. *Tetrahedron* **2003**, *59*, 2953. (c) Felpin, F.-X.; Lebreton, J. *Eur. J. Org. Chem*. **2003**, 3693. (d) Buffat, M. G. P. *Tetrahedron* **2004**, *60*, 1701. (e) Källström, S.; Leino, R. *Bioorg. Med. Chem*. **2008**, *16*, 601. (f) Kim, H.; Rhee, Y. H. *J. Am. Chem. Soc.* **2012**, *134*, 4011. (g) Yang, Y. *RSC Adv*. **2015**, *5*, 18894. (h) Penk, D. N.; Robinson, N. A.; Hill, H. M.; Turlington, M. *Tetrahedron Lett*. **2017**, *58*, 470.

[4] For the synthesis of morpholines, see: (a) Lu, Z.; Stahl, S. S. *Org. Lett.* **2012**, *14*, 1234. (b) Ghosh, P.; Deka, M. J.; Saikia, A. K. *Tetrahedron* **2016**, *72*, 690 and references therein.

[5] (a) Mátyus, P.; Éliás, O.; Tapolcsányi, P.; Polonka-Bálint, Á.; Halász-Dajka, B. *Synthesis* **2006**, 2625. (b) Wang, M. *ChemCatChem* **2013**, *5*, 1291. (c) Peng, B.; Maulide, N. *Chem. Eur. J.* **2013**, 19, 13274. (d) Wang, L.; Xiao, J. *Adv. Synth. Catal*. **2014**, *356*, 1137. (e) Haibach, M. C.; Seidel, D. *Angew. Chem. Int. Ed.* **2014**, *53*, 5010. (f) Kwon, S. J.; Kim, D. Y. *Chem. Rec*. **2016**, *16*, 1191.

[6] (a) Pastine, S. J.; McQuaid, K. M.; Sames, D. *J. Am. Chem. Soc*. **2005**, *127*, 12180. (b) Murarka, S.; Zhang, C.; Konieczynska, M. D.; Seidel, D. *Org. Lett*. **2009**, *11*, 129. (c) McQuaid, K. M.; Long, J. Z.; Sames, D. *Org. Lett*. **2009**, *11*, 2972. (d) Mori, K.; Kawasaki, T.; Sueoka, S.; Akiyama, T. *Org. Lett.*, **2010**, *12*, 1732. (e) Alajarin, M.; Marin-Luna, M.; Vidala, A. *Adv. Synth. Catal*. **2011**, *353*, 557. (f) Cao, W.; Liu, X.; Wang, W.; Lin, L.; Feng, X. *Org. Lett.* **2011**, *13*, 600. (g) Mori, K.; Ehara, K.; Kurihara, K.; Akiyama, T. *J. Am. Chem. Soc*. **2011**, *133*, 6166. (h) Zhang, L.; Chen, L.; Lv, J.; Cheng. J.-P.; Luo, S. *Chem. Asian J*. **2012**, *7*, 2569. (i) Chen, L.; Zhang, L.; Lv, J.; Cheng, J.-P.; Luo, S. *Chem. Eur. J*. **2012**, *18*, 8891.

[7] For the formation of benzo-condensed six-membered nitrogen heterocycles, quinolines (a) Verboom, W.; Reinhoudt, D. N.; Visser, R.; Harkema, S. *J. Org. Chem.* **1984**, *49*, 269. (b) Nijhuis, W. H. N.; Verboom, W.; Reinhoudt, D. N.; Harkema, S. *J. Am. Chem. Soc*. **1987**, *109*, 3136. (c) Alajarin, M.; Bonillo, B.; Ortin, M.-M.; Sanchez-Andrada, P.; Vidal, A.; Orenes, R.-A. *Org. Biomol. Chem.* **2010**, *8*, 4690. (d) Alajarin, M.; Bonillo, B.; Marin-Luna, M.; Sanchez-Andrada, P.; Vidal, A.; Orenes, R.-A. *Tetrahedron* **2012**, *68*, 4672. (e) Cao, W.; Liu, X.; Guo, J.; Lin, L.; Feng, *Chem. Eur. J*. **2015**, *21*, 1632.

[8] Vadola, P. A.; Carrera, I.; Sames, D. *J. Org. Chem*. **2012**, *77*, 6689.

[9] (a) Yamazaki, S. *Heterocycles*, **2016**, *92*, 1561. (b) Yamazaki, S.; Fujinami, K.; Maitoko, Y.; Ueda, K.; Kakiuchi, K. *J. Org. Chem.* **2013**, *78*, 8405-8416. (c) Yamazaki, S.; Ueda, K.; Fukushima, Y.; Ogawa, A.; Kakiuchi, K. *Eur. J. Org. Chem.* **2014**, 7023-7033.

[10] The effect of R groups installed on nitrogen of **1a-e** in the hydride transfer/cyclization has not been examined in detail yet. For other cyclizations of amides of ethenetricarboxylate with various R groups, see reference 9 and (a) Yamazaki, S.; Morikawa, S.; Iwata, Y.; Yamamoto, M.; Kuramoto, K. *Org. Biomol. Chem*. **2004**, *2*, 3134. (b) Yamazaki, S.; Yamamoto, M.; Morikawa, S. *Heterocycles* **2006**, *67*, 269.

[11] Krapcho, A. P. *Synthesis* **1982**, 805 and 893.

[12] The absolute stereochemistries of the products were not determined.

[13] (a) Becke, A. D. *J. Chem. Phys*. **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1998**, *37*, 785.

[14] Gaussian 09, Revision D.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.

[15] (a) Cancès, E.; Mennucci, B.; Tomasi, J. *J. Chem. Phys.* **1997**, *107*, 3032. (b) Cossi, M.; Barone, V.; Mennucci, B.; Tomasi, J. *Chem. Phys. Lett*. **1998**, *286*, 253. (c) Mennucci, B.; Tomasi, J. *J. Chem. Phys*. **1997**, *106*, 5151.

[16] (a) Fukui, K. *J. Phys. Chem.* **1970**, *74*, 4161. (b) Gonzalez, C.; Schlegel, H. B. *J. Phys. Chem.* **1989**, *90*, 2154.

[17] Nijhuis, W. H. N.; Verboom, W.; El-Fadl, A. A.; Van Hummel, G. J.; Reinhoudt, D. N. *J. Org. Chem.* **1989**, *54*, 209.

[18] Mori, K.; Sueoka, S.; Akiyama, T. *J. Am. Chem. Soc.* **2011**, *133*, 2424.

[19] (a) Anan, H.; Tanaka, A.; Tsuzuki, R.; Yokota, M.; Yatsu, T.; Fujikura, T. *Chem. Pharm. Bull*. **1996**, *44*, 1865. (b) Abdel-Magid, A. F.; Carson, K. G.; Harris, B. D.; Maryanoff, C. A.; Shah, R. D. *J. Org. Chem.* **1996**, *61*, 3849.

[20] (a) Newcomb, M.; Kumar, M. U. *Tetrahedron Lett*. **1990**, *31*, 1675. (b) Labrecque, D.; Nwe, K. T.; Chan, T. H. *Organometallics* **1994**, *13*, 332.

[21] Wu, H.-P.; Aumann, R.; Fröhlich, R.; Wegelius, E. *Organometallics* **2001**, *20*, 2183.

[22] Jiao, Z.-W.; Zhang, S.-Y.; He, C.; Tu, Y.-Q.; Wang, S.-H.; Zhang, F.-M.; Zhang, Y.-Q.; Li, H. *Angew. Chem. Int. Ed*. **2012**, *51*, 8811.

[23] (a) MacCorquodale, F.; Walton, J. C.; Hughes, L.; Ingold, K. U. *J. Chem. Soc., Perkin Trans. 2* **1991**, 1893. (b) Eccleston, G.; Walsh, B.; Wyn-Jones, E.; Morris, H. *Trans. Faraday Soc*. **1971**, *67*, 3223.

[24] Sugai, S.; Ikawa, H.; Hasegawa, Y.; Yoshida, S.; Kutsuma, T.; Akaboshi, S. *Chem. Pharm. Bull*. **1984**, *32*, 967.

[25] (a) Yamazaki, S.; Ohmitsu, K.; Ohi, K.; Otsubo, T.; Moriyama, K. *Org. Lett*. **2005**, *7*, 759. (b) Yamazaki, S.; Takebayashi, M. *J. Org. Chem*. **2011**, *76*, 6432.