Supplementary Information

Efficient Synthesis of Heterocyclic Compounds using Ethenetricarboxylic Acid Diesters

Shoko Yamazaki,* Yuko Iwata and Yugo Fukushima

Department of Chemistry, Nara University of Education, Takabatake-cho, Nara 630-8528, Japan

E-mail: yamazaks@nara-edu.ac.jp

Experimental Section

General Methods. Melting points are uncorrected. IR spectra were recorded in the FT-mode. ^{1}H NMR spectra were recorded at 400 MHz. ^{13}C NMR spectra were recorded at 100.6 MHz. Chemical shifts are reported in ppm relative to Me_4Si or residual nondeuterated solvent. ^{13}C multiplicities were determined by DEPT and HSQC. Mass spectra were recorded at an ionizing voltage of 70 eV by EI or FAB. Optical rotations were measured with a 1 cm i.d. × 10 cm cell. All reactions were carried out under a nitrogen atmosphere.

N-Boc protected amino alcohols **17c,e** were prepared by the reaction of the corresponding amine and $(Boc)_2O$ in CH_2Cl_2. *O*-TBS protected amines **21a,b,d** were prepared by the reaction of the corresponding alcohol and TBSCl in the presence of imidazole in CH_2Cl_2 and **21c** was prepared by the reaction of pseudoephedorine and TBSCl in the presence of Et_3N and DMAP according to the literature method.[S1]

3b: R_f = 0.5 (hexane : ether = 1 : 4); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.02-1.43 (m, 5H), 1.295 (t, *J* = 7.1 Hz, 3H), 1.299 (t, *J* = 7.1 Hz, 3H), 1.59-1.68 (m, 2H), 1.78-1.90 (m, 3H), 2.51 (dddd, *J* = 11.3, 11.3, 3.3, 3.3 Hz, 1H), 2.82 (ddd, *J* = 12.9, 10.0, 2.9 Hz, 1H), 2.91 (ddd, *J* = 12.8, 2.9, 2.9 Hz, 1H), 3.92 (d, *J* = 4.3 Hz, 1H), 4.19 (d, *J* = 4.3 Hz, 1H), 4.21-4.33 (m, 5H), 4.41 (ddd, *J* = 10.3, 10.3, 2.7 Hz, 1H). Selected NOEs are between δ 4.19 (NC*H*C=O) and δ 2.51 (NC*H*$(CH_2)_5$-), 2.82 (NC*H*H).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ

(ppm) 13.98 (q), 14.05 (q), 25.53 (t), 25.84 (t), 26.01 (t), 26.23 (t), 31.68 (t), 41.37 (t), 55.00 (d), 59.07 (d), 60.96 (d), 61.65 (t), 61.82 (t), 67.78 (t), 167.10 (s), 167.61 (s), 169.19 (s). Selected HMBC correlations are between δ 4.19 (NC*H*C=O), 2.91 (NCH*H*) and δ 59.07 (N*C*H(CH_2)$_5$-).; IR (neat) 2932, 2856, 1738, 1452, 1373, 1276, 1190, 1151 cm^{-1}; MS (EI) *m/z* 341 (M^+, 18), 213 (26), 182 (100%); exact mass M^+ 341.1842 (calcd for $C_{17}H_{27}NO_6$ 341.1838).

3c: R_f = 0.4 (hexane : ether = 1 : 4); Colorless crystals, mp 105-108 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.25 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 3.49 (ddd, *J* = 13.4, 6.7, 3.3 Hz, 1H), 3.63 (ddd, *J* = 13.4, 6.7, 2.8 Hz, 1H), 3.93 (d, *J* = 4.0 Hz, 1H), 4.12-4.32 (m, 4H), 4.46 (ddd, *J* = 11.0, 6.7, 3.2 Hz, 1H), 4.62 (ddd, *J* = 11.0, 6.8, 2.9 Hz, 1H), 5.03 (d, *J* = 4.0 Hz, 1H), 6.97-7.01 (m, 3H), 6.32-6.36 (m, 2H). Selected NOEs are between δ 5.03 (NC*H*C=O) and δ 3.49 (NC*H*H), 6.97-7.01 (Ph).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.87 (q), 13.90 (q), 45.50 (t), 53.43 (d), 59.21 (d), 61.82 (t), 62.06 (t), 67.60 (t), 117.08 (d), 121.63 (d), 129.72 (d), 146.61 (s), 166.81 (s), 167.35 (s), 167.66 (s). Selected HMBC correlations are between δ 5.03 (NC*H*C=O) and δ 146.61 (Ph), and between δ 3.49, 3.63 (NCH_2) and δ 59.21 (N*C*HC=O).; IR (KBr) 2983, 1739, 1602, 1502, 1266, 1182, 1087, 1014 cm^{-1}; MS (EI) *m/z* 335 (M^+, 44), 243 (56), 176 (100%); exact mass M^+ 335.1371 (calcd for $C_{17}H_{21}NO_6$ 335.1369); Anal. Calcd for $C_{17}H_{21}NO_6$: C, 60.89; H, 6.31; N, 4.18. Found: C, 61.05; H, 6.37; N, 4.18.

3d: R_f = 0.5 (hexane : ether = 1 : 4); Pale yellow oil;; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.30 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 2.60 (ddd, *J* = 13.3, 10.8, 2.8 Hz, 1H), 2.85 (ddd, *J* = 10.3, 2.6, 2.6 Hz, 1H), 3.44 (d, *J* = 13.7 Hz, 1H), 3.98 (d, *J* = 4.0 Hz, 1H), 4.01 (d, *J* = 13.7 Hz, 1H), 4.02 (d, *J* = 4.0 Hz, 1H), 4.24-4.35 (m, 5H), 4.42 (ddd, *J* = 10.7, 10.7, 2.5 Hz, 1H), 7.24-7.35 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.93 (q), 14.05 (q), 47.15 (t), 54.07 (d), 59.04 (t), 61.74 (t), 61.91 (t), 63.86 (d), 67.09 (t), 127.71 (d), 128.55 (d), 128.71 (d), 136.52 (s), 166.90 (s), 167.53 (s), 168.23 (s). Selected HMBC correlations are between δ 2.85 (NC*H*HCH_2), 3.44 (NC*H*HPh) and δ 63.86 (N*C*HC=O).; IR (neat) 2982, 1747, 1255, 1373, 1291, 1208, 1159, 1058 cm^{-1}; MS (EI) *m/z* 349 (M^+, 25), 190 (49), 91 (100%); exact mass M^+ 349.1527 (calcd for $C_{18}H_{23}NO_6$ 349.1525).

5b: R_f = 0.6 (hexane : ether = 1 : 4); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.964 (dddd, *J* = 12.8, 12.8, 11.2, 4.0 Hz, 1H), 1.22-1.47 (m, 2H), 1.49-1.53 (m, 1H), 1.62-1.66 (m, 1H), 1.73-1.77 (m, 1H), 2.03 (ddd, *J* = 11.6, 11.6, 2.4 Hz, 1H), 2.46 (dddd, *J* = 10.4, 10.4, 3.0, 3.0 Hz, 1H), 2.99 (d-like, *J* = 11.4 Hz, 1H), 3.70 (d, *J* = 3.8 Hz, 1H), 3.93 (dd, *J* = 10.3, 10.3 Hz, 1H), 3.98 (dd, *J* = 10.7, 3.4 Hz, 1H), 4.01 (d, *J* = 3.8 Hz, 1H), 5.15-5.28 (m, 4H), 7.30-7.34 (m, 10H). Selected NOEs are between δ 2.46 (NC*H*) and δ 3.70 (NC*H*CO).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 23.08 (t), 24.89 (t), 26.78 (t), 52.38 (t), 53.68 (d), 56.02 (d), 64.66 (d), 67.37 (t), 67.58 (t), 71.33 (t), 128.26 (d), 128.31 (d), 128.34 (d), 128.40 (d), 128.45 (d), 128.47 (d), 135.19 (s), 135.28 (s), 166.83 (s), 167.42 (s), 168.38 (s). Selected HMBC correlations are between δ 2.03 (NC*H*H) and δ 64.66 (N*C*HCO) and between δ 3.70 (NC*H*CO) and δ 52.38 (N*C*H_2).; IR (neat) 2942, 1739, 1456, 1282, 1214, 1156 cm^{-1}; MS (EI) *m/z* 437 (M^+, 13), 302 (78), 258 (66), 244 (62), 194 (100%); HRMS M^+ 437.1838 (calcd for $C_{25}H_{27}NO_6$ 437.1838).

7 (trans/cis): (R_f = 0.4 (hexane : ether = 1 : 4); Colorless oil; **7**-trans ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.26-1.31 (m, 6H), 1.32-1.44 (m, 1H), 1.74-1.97 (m, 2H), 2.05 (dddd, *J* = 8.6, 8.6, 3.6, 3.6 Hz, 1H), 2.71 (ddd, *J* = 9.1, 9.1, 6.7 Hz, 1H), 3.20 (ddd, *J* = 9.2, 7.1, 2.4 Hz, 1H), 3.64 (ddd, *J* = 13.4, 9.4, 4.8 Hz, 1H), 4.04 (d, *J* = 4.8 Hz, 1H), 4.11 (d, *J* = 4.8 Hz, 1H), 4.15-4.32 (m, 6H). Selected NOEs are between δ 2.71 (NC*H*H) and δ 4.11 (NC*H*CO).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.03 (q), 14.09 (q), 23.86 (t), 26.01 (t), 53.41 (t), 54.25 (d), 55.56 (d), 60.37 (d), 61.64 (t), 69.28 (t), 167.16 (s), 167.70 (s), 169.88 (s). Selected HMBC correlations are between δ 2.71 (NC*H*H) and δ 60.37 (N*C*HCO).; **7**-cis ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.29 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.43-1.53 (m, 1H), 1.78-1.98 (m, 3H), 2.46 (ddd, *J* = 8.4, 8.4, 7.0 Hz, 1H), 2.88-2.95 (m, 1H), 3.00 (ddd, *J* = 8.2, 8.2, 4.6 Hz, 1H), 3.89 (d, *J* = 5.2 Hz, 1H), 3.98 (d, *J* = 5.2 Hz, 1H), 4.16 (dd, *J* = 10.6, 8.1Hz, 1H), 4.20-4.33 (m, 4H), 4.43 (dd, *J* = 10.6, 3.3 Hz, 1H). Selected NOEs are between δ 3.98 (NC*H*CO) and δ 2.88-2.95 (NC*H*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.96 (q), 13.98 (q), 22.72 (t), 26.80 (t), 51.87 (t), 53.57 (d), 58.16 (d), 61.71 (t), 61.85 (t), 64.07 (d), 71.67 (t), 166.98 (s), 167.10 (s), 168.77 (s). Selected HMBC correlations are between δ 2.46

(NC*H*H) and δ 58.16 (N*C*HCO), and between δ 3.98 (NC*H*CO) and δ 58.16 (N*C*HCO), 51.87 (N*C*H_2).; **7**-trans/cis mixture, IR (neat) 2980, 1742, 1465, 1372, 1266, 1207, 1164, 1036 cm^{-1}; MS (EI) *m/z* 299 (M^+, 22), 168 (88), 140 (100%); HRMS M^+ 299.1366 (calcd for $C_{14}H_{21}NO_6$ 299.1369).

8-trans (major): R_f = 0.27 (ether : MeOH = 19 : 1); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.27 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.42 (dddd, *J* = 11.7, 11.7, 11.7, 7.5 Hz, 1H), 1.80-1.92 (m, 1H), 2.00-2.07 (m, 2H), 3.37 (dd, *J* = 11.4, 10.2 Hz, 1H), 3.54 (ddd, *J* = 11.9, 9.7, 2.2 Hz, 1H), 3.65 (ddd, *J* = 11.9, 8.8, 8.8 Hz, 1H), 3.78 (dddd, *J* = 10.1, 10.1, 5.0, 5.0 Hz, 1H), 4.13 (d, *J* = 3.7 Hz, 1H), 4.18-4.31 (m, 5H), 4.54 (d, *J* = 3.7 Hz, 1H). Selected NOEs are between δ 3.37 (OC*H*H) and δ 4.54 (OC*H*C=O), and δ 4.18-4.31 (OCH*H*) and δ 3.78 (NC*H*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.99 (q), 14.03 (q), 22.28 (t), 28.79 (t), 44.86 (t), 53.86 (d), 56.62 (d), 61.60 (t), 61.68 (t), 69.11 (t), 74.76 (d), 165.86 (s), 166.60 (s), 167.33 (s). Selected HMBC correlations are between δ 3.37 (OC*H*H) and δ 74.76 (O*C*HC=O).; IR (neat) 2980, 1758-1733, 1661, 1652, 1463, 1372, 1347, 1271, 1177, 1050 cm^{-1}; MS (EI) *m/z* 299 (M^+, 28), 254 (43), 205 (84), 180 (87), 69 (100%); HRMS M^+ 299.1368 (calcd for $C_{14}H_{21}NO_6$ 299.1369).

8-cis (minor): R_f = 0.33 (ether : MeOH = 19 : 1); Colorless 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), 1.50 (dddd, *J* = 11.7, 11.7, 10.1, 7.1 Hz, 1H), 1.79-1.91 (m, 1H), 2.00-2.09 (m, 2H), 3.53 (ddd, *J* = 11.6, 8.9, 2.2 Hz, 1H), 3.60-3.67 (m, 1H), 3.70 (dd, *J* = 10.0, 10.0 Hz, 1H), 3.72-3.80 (m, 1H), 4.02 (dd, *J* = 10.2, 3.2 Hz, 1H), 4.07 (d, *J* = 6.2 Hz, 1H), 4.16-4.32 (m, 4H), 4.85 (d, *J* = 6.2 Hz, 1H). Selected NOEs are between δ 3.72-3.80 (NC*H*) and δ 4.85 (OC*H*C=O), 4.02 (OCH*H*), and between δ 3.70 (OC*H*H) and δ 4.07 (C*H*(CO_2Et)$_2$).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.08 (q), 14.10 (q), 22.63 (t), 28.92 (t), 45.31 (t), 55.10 (d), 57.36 (d), 61.67 (t), 61.77 (t), 67.05 (t), 72.75 (d), 166.09 (s), 167.32 (s), 167.35 (s). Selected HMBC correlations are between δ 4.85 (OC*H*C=O) and δ 67.05 (O*C*H_2).; IR (neat) 2980, 1738, 1660, 1455, 1371, 1258, 1176, 1035 cm^{-1}; MS (EI) *m/z* 299 (M^+, 8.1), 254 (37), 180 (65), 70 (100%); HRMS M^+ 299.1371 (calcd for $C_{14}H_{21}NO_6$ 299.1369).

10a: R_f = 0.4 (hexane : ether = 1 : 4); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.28 (t, *J* = 7.0 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 2.43 (ddd, *J* = 12.7, 9.5, 3.5 Hz, 1H), 2.85 (ddd, *J* = 12.5, 3.9, 3.9 Hz, 1H), 3.04 (ddd, *J* = 12.0, 3.8, 3.8 Hz, 1H), 3.20 (ddd, *J* = 12.5, 9.5, 3.7 Hz, 1H), 3.42 (d, *J* = 13.4 Hz, 1H), 4.00 (d, *J* = 4.7 Hz, 1H), 4.04 (d, *J* = 13.4 Hz, 1H), 4.17 (d, *J* = 4.7 Hz, 1H), 4.22-4.31 (m, 4H), 4.48 (d, *J* = 14.7 Hz, 1H), 4.80 (d, *J* = 14.7 Hz, 1H), 7.22-7.34 (m, 10H). Selected NOEs are between δ 4.00 (NC*H*) and δ 2.43 (NC*H*HCH$_2$N), 4.04 (NC*H*HPh).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.09 (q), 14.14 (q), 44.01 (t), 46.38 (t), 50.08 (t), 54.12 (d), 58.91 (t), 61.33 (t), 61.45 (t), 64.76 (d), 127.39 (d), 127.48 (d), 128.32 (d), 128.35 (d), 128.55 (d), 128.74 (d), 136.45 (s), 137.42 (s), 167.45 (s), 167.73 (s), 167.80 (s). Selected HMBC correlations are between δ 4.00 (NC*H*) and δ 58.91 (N*C*H$_2$Ph) and between δ 2.43, 2.85 (NC*H*$_2$CH$_2$N) and δ 64.76 (N*C*H).; IR (neat) 2981, 1737, 1652, 1495, 1454, 1264, 1157, 1041 cm^{-1}; MS (EI) *m/z* 438 (M^+, 24), 347 (30), 279 (59), 91 (100%); HRMS M^+ 438.2154 (calcd for $C_{25}H_{30}N_2O_5$ 438.2155).

10b: R_f = 0.3 (hexane : ether = 1 : 4); Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.96 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.35-1.41 (m, 1H), 1.86-1.97 (m, 1H), 2.34-2.42 (m, 1H), 2.49-2.58 (m, 1H), 2.88 (ddd, *J* = 13.9, 13.9, 2.7 Hz, 1H), 3.23-3.33 (m, 3H), 3.60 (dq, *J* = 13.6, 7.1 Hz, 1H), 3.85 (dd, *J* = 15.4, 11.9 Hz, 1H), 4.11-4.29 (m, 4H), 4.13 (d, *J* = 11.2 Hz, 1H), 4.45 (d, *J* = 11.2 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.39 (q), 13.46 (q), 13.95 (q), 14.14 (q), 22.51 (t), 38.74 (t), 43.20 (t), 48.37 (t), 51.88 (t), 53.10 (d), 61.08 (t), 61.31 (t), 64.53 (d), 167.97 (s), 168.08 (s), 171.24 (s). Selected HMBC correlations are between δ 4.45 (NC*H*C=O) and δ 51.88 (N*C*H$_2$CH$_2$CH$_2$N), 38.74 (N*C*H$_2$CH$_3$).; IR (neat) 2977, 2938, 1752, 1734, 1647, 1369, 1302, 1192, 1035 cm^{-1}; MS (EI) *m/z* 328 (M^+, 40), 169 (92), 141 (100%); HRMS M^+ 328.2004 (calcd for $C_{16}H_{28}N_2O_5$ 328.1998).

12b: R_f = 0.6 (hexane : ether = 1 : 2); Yellow crystals; mp 101-103 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.18 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 2.25 (s, 3H), 4.08-4.16 (m, 2H), 4.21 (d, *J* = 4.6 Hz, 1H), 4.23-4.36 (m, 2H), 4.61 (d, *J* = 4.6 Hz, 1H), 4.80 (bs, 1H), 6.56

(d, *J* = 1.6 Hz, 1H), 6.61 (ddd, *J* = 8.2, 2.0, 0.5 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.83 (q), 13.99 (q), 20.93 (q), 53.41 (d), 54.28 (d), 62.31 (t), 62.42 (t), 115.63 (d), 116.49 (d), 120.76 (d), 130.79 (s), 135.18 (s), 138.23 (s), 164.65 (s), 166.77 (s), 167.92 (s). Selected HMBC correlations are between δ 4.61 (NHC*H*) and δ 130.79 (NH*C*).; IR (KBr) 3370, 2987, 1758, 1737, 1721, 1622, 1518, 1373, 1348, 1287, 1239, 1186, 1037 cm^{-1}; MS (EI) *m/z* 321 (M^+); HRMS M^+ 321.1212 (calcd for $C_{16}H_{19}NO_6$ 321.1212); Anal. Calcd for $C_{16}H_{19}NO_6$: C, 59.81; H, 5.96; N, 4.36. Found: C, 59.73; H, 5.97; N, 4.27.

12c: R_f = 0.7 (hexane : ether = 1 : 4); Pale yellow crystals; mp 90-92 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.19 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 2.26 (s, 3H), 4.11-4.16 (m, 2H), 4.21 (d, *J* = 4.7 Hz, 1H), 4.22-4.36 (m, 2H), 4.59 (dd, *J* = 4.7, 3.0 Hz, 1H), 4.81 (bd, *J* = 3.0 Hz, 1H), 6.65 (d, *J* = 7.9 Hz, 1H), 6.79 (ddd, *J* = 7.9, 1.8, 0.7 Hz, 1H), 6.82 (bs, 1H). Selected NOEs are between δ 4.81 (N*H*) and δ 4.59 (NC*H*), 6.65 (C5-*H*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.85 (q), 13.98 (q), 20.58 (q), 53.28 (d), 54.44 (d), 62.29 (t), 62.38 (t), 115.24 (d), 117.17 (d), 125.77 (d), 128.65 (s), 130.24 (s), 140.30 (s), 164.77 (s), 166.82 (s), 167.86 (s); IR (KBr) 3374, 2985, 1763, 1735, 1721, 1523, 1374, 1350, 1186, 1037 cm^{-1}; MS (EI) *m/z* 321 (M^+, 54), 201 (60), 162 (78), 134 (100%); HRMS M^+ 321.1208 (calcd for $C_{16}H_{19}NO_6$ 321.1212).

12d: R_f = 0.7 (hexane : ether = 1 : 4); Brown crystals; mp 59-61 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.18 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 2.18 (s, 3H), 4.01-4.15 (m, 2H), 4.19 (d, *J* = 4.6 Hz, 1H), 4.24-4.37 (m, 2H), 4.63 (dd, *J* = 4.6, 2.7 Hz, 1H), 4.95 (bd, *J* = 2.7 Hz, 1H), 6.74 (t-like, *J* = 8.0 Hz, 1H), 6.86-6.90 (m, 2H). Selected NOEs are between δ 4.95 (N*H*) and δ 4.63 (NC*H*), 2.18 (C5-CH_3).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.80 (q), 14.01 (q), 16.39 (q), 53.23 (d), 54.32 (d), 62.32 (t), 62.44 (t), 114.63 (d), 119.64 (d), 123.65 (d), 126.47 (s), 129.48 (s), 140.25 (s), 164.62 (s), 166.82 (s), 167.91 (s); IR (KBr) 3403, 2994, 1763-1721, 1625, 1591, 1509, 1483, 1320, 1130, 1038 cm^{-1}; MS (EI) *m/z* 321 (M^+, 15), 201 (46), 162 (71), 133 (100%); HRMS M^+ 321.1212 (calcd for $C_{16}H_{19}NO_6$ 321.1212).

12e: R_f = 0.7 (hexane : ether = 1 : 4); Pale yellow crystals; mp 95-97 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.18 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 4.10-4.15 (m, 2H), 4.22 (d, *J* = 4.1 Hz, 1H), 4.23-4.37 (m, 2H), 4.66 (d, *J* = 4.1 Hz, 1H), 5.08 (bs, 1H), 6.74 (s, 1H), 6.75 (dd, *J* = 7.7, 2.4 Hz, 1H), 6.90-6.93 (m, 1H). Selected NOEs are between δ 5.08 (N*H*) and δ 4.66 (NC*H*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.80 (q), 13.97 (q), 53.54 (d), 53.78 (d), 62.45 (t), 62.57 (t), 114.73 (d), 117.77 (d), 119.66 (d), 130.31 (s), 131.98 (s), 138.49 (s), 163.77 (s), 166.47 (s), 166.87 (s); IR (KBr) 3378, 2986, 1766, 1737, 1721, 1618, 1507, 1347, 1285, 1239, 1188, 1036 cm^{-1}; MS (EI) *m/z* 343 (M^+, 45), 341 (M^+, 75), 221 (45), 154 (100%); HRMS M^+ 341.0666 (calcd for $C_{15}H_{16}N^{35}ClO_6$ 341.0666), 343.0631 (calcd for $C_{15}H_{16}N^{37}ClO_6$ 343.0637); Anal. Calcd for $C_{15}H_{16}NClO_6$: C, 52.72; H, 4.72; N, 4.10. Found: C, 52.63; H, 4.68; N, 4.05.

12f: R_f = 0.6 (hexane : ether = 1 : 4); Pale yellow crystals; mp 114-117 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.19 (t, *J* = 7.1 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H), 4.15 (q, *J* = 7.1 Hz, 2H), 4.28-4.40 (m, 2H), 4.27 (d, *J* = 3.8 Hz, 1H), 4.78 (dd, *J* = 3.8, 2.5 Hz, 1H), 5.45 (bd, *J* = 2.2 Hz, 1H), 7.10 (d, *J* = 8.8 Hz, 1H), 7.65 (d, *J* = 2.5 Hz, 1H), 7.69 (dd, *J* = 8.8, 2.5 Hz, 1H). Selected NOEs are between δ 5.45 (N*H*) and δ 4.78 (NC*H*), 4.27 (C*H*($CO_2Et)_2$).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.80 (q), 13.96 (q), 53.46 (d), 53.76 (d), 62.63 (t), 62.76 (t), 109.82 (d), 115.23 (d), 117.19 (d), 131.51 (s), 143.69 (s), 145.01 (s), 162.82 (s), 166.23 (s), 167.76 (s); IR (KBr) 3328, 2992, 1772, 1739, 1715, 1600, 1540, 1346, 1183 cm^{-1}; MS (EI) *m/z* 352 (M^+, 74), 278 (83), 232 (100%); HRMS M^+ 352.0909 (calcd for $C_{15}H_{16}N_2O_8$ 352.0907); Anal. Calcd for $C_{15}H_{16}N_2O_8$: C, 51.14; H, 4.58; N, 7.95. Found: C, 51.29; H, 4.68; N, 7.77.

12g: R_f = 0.7 (hexane : ether = 1 : 4); Pale yellow crystals; mp 90-93 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 4.34 (d, *J* = 4.5 Hz, 1H), 4.62 (dd, *J* = 4.5, 1.9 Hz, 1H), 4.85 (bs, 1H), 5.05 (d, *J* = 12.3 Hz, 1H), 5.07 (d, *J* = 12.3 Hz, 1H), 5.18 (d, *J* = 12.2 Hz, 1H), 5.22 (d, *J* = 12.2 Hz, 1H), 6.64 (dd, *J* = 7.8, 1.5 Hz, 1H), 6.78 (ddd, *J* = 8.6, 7.3, 1.5 Hz, 1H), 6.90-6.96 (m, 2H), 7.17-7.33 (m, 10H). Selected NOEs are between δ 4.85 (N*H*) and δ 4.62 (NC*H*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 53.48 (d), 54.20 (d), 67.93 (t), 68.03 (t), 115.24 (d), 116.81 (d), 120.24 (d), 125.27 (d), 128.15 (d), 128.37 (d), 128.45 (d), 128.50 (d), 128.59 (d),

128.62 (d), 131.03 (s), 134.52 (s), 134.72 (s), 140.19 (s), 164.33 (s), 166.41 (s), 167.56 (s); IR (KBr) 3350, 1741, 1724, 1309, 1266, 1206, 1153 cm^{-1}; MS (EI) *m/z* 431 (M^+, 6.6), 193 (15), 107 (86), 91 (100%); HRMS (FAB) $(M+Na)^+$ 454.1257 (calcd for $C_{25}H_{21}NO_6Na$ 454.1267); Anal. Calcd for $C_{25}H_{21}NO_6$: C, 69.60; H, 4.91; N, 3.25. Found: C, 69.37; H, 4.92; N, 3.25.

12'a: R_f = 0.5 (hexane : ether = 1 : 4); brown crystals; mp 116-119 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.345 (t, *J* = 7.1 Hz, 3H), 1.346 (t, *J* = 7.1 Hz, 3H), 4.27 (q, *J* = 7.1 Hz, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 6.90 (ddd, *J* = 8.3, 6.8, 2.3 Hz, 1H), 6.96-7.02 (m, 2H), 7.20 (d-like, *J* = 8.3 Hz, 1H), 7.85 (bs, 1H), 8.60 (d, *J* = 14.3 Hz, 1H), 11.21 (d, *J* = 14.3 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.35 (q), 14.46 (q), 60.48 (t), 60.61 (t), 92.73 (s), 114.92 (d), 116.17 (d), 120.82 (d), 125.23 (d), 127.45 (s), 146.38 (s), 151.04 (d), 166.85 (s), 168.71 (s); IR (KBr) 3156, 2979, 1684, 1661, 1631, 1590, 1287, 1214, 1091 cm^{-1}; MS (EI) *m/z* 279 (M^+, 64), 233 (71), 187 (76), 159 (100%); HRMS M^+ 279.1108 (calcd for $C_{14}H_{17}NO_6$ 279.1107).

12'g: R_f = 0.4 (hexane : ether = 1 : 4); pale brown crystals; mp 121-123 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.27 (s, 2H), 5.30 (s, 2H), 6.83-6.94 (m, 3H), 7.14 (d, *J* = 7.1 Hz, 1H), 7.24-7.37 (m, 10H), 8.64 (d, *J* = 14.3 Hz, 1H), 11.26 (d, *J* = 14.3 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 66.07 (t), 66.31 (t), 92.53 (s), 115.36 (d), 116.23 (d), 121.12 (d), 125.45 (d), 127.32 (s), 127.85 (d), 127.88 (d), 127.99 (d), 128.02 (d), 128.49 (d), 128.56 (d), 136.26 (s), 136.52 (s), 146.12 (s), 151.95 (d), 166.73 (s), 168.55 (s); IR (KBr) 3295, 3025, 1685, 1637, 1577, 1470, 1429, 1356, 1277, 1231, 1088 cm^{-1}; MS (EI) *m/z* 403 (M^+, 19), 295 (14), 120 (69), 91 (100%); HRMS (FAB) $(M+Na)^+$ 426.1324 (calcd for $C_{24}H_{21}NO_5Na$ 426.1317).

14: R_f = 0.6 (hexane : ether = 1 : 4); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.30 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.3 Hz, 3H), 3.96 (d, *J* = 7.9 Hz, 1H), 4.20-4.33 (m, 4H), 4.65 (bs, 1H), 4.94 (d, *J* = 14.3 Hz, 1H), 5.20 (d, *J* = 7.9 Hz, 1H), 5.87 (d, *J* = 14.3 Hz, 1H), 6.70 (dd, *J* = 8.1, 1.1 Hz, 1H), 6.80 (td, *J* = 7.4, 1.0 Hz, 1H), 7.04 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.17 (td, *J* = 7.7, 1.5 Hz, 1H). Selected NOEs are between δ 4.65 (N*H*) and δ 3.96 (C*H*($CO_2Et)_2$).;

^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.00 (q), 14.07 (q), 52.74 (d), 54.32 (d), 62.33 (t), 62.35 (t), 70.20 (t), 118.61 (d), 120.03 (d), 120.38 (s), 129.93 (d), 130.17 (d), 144.35 (s), 167.01 (s), 167.60 (s), 170.39 (s). Selected HMBC correlations are between δ 4.94, 5.87 (OC*H*$_2$Ar) and δ 170.39 (*C*=O).; IR (neat) 3351, 2983, 1746, 1608, 1595, 1494, 1265, 1175, 1032 cm^{-1}; MS (EI) *m/z* 321 (M^+, 20), 276 (34), 118 (87), 84 (100%); HRMS M^+ 321.1222 (calcd for $C_{16}H_{19}NO_6$ 321.1212).

16: R_f = 0.7 (hexane : ether = 1 : 4); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.29 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 4.19 (d, *J* = 6.0 Hz, 1H), 4.24-4.33 (m, 4H), 5.21 (d, *J* = 6.0 Hz, 1H), 6.99-7.11 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.91 (q), 53.69 (d), 62.33 (t), 72.69 (d), 117.17 (d), 117.27 (d), 123.47 (d), 125.46 (d), 140.63 (s), 141.53 (s), 163.18 (s), 165.25 (s), 165.50 (s). Selected HMBC correlations are between δ 5.21 (OC*H*) and δ 141.53 (O*C*(Ar)).; IR (neat) 2984, 1784, 1747, 1740, 1497, 1270, 1179, 1031 cm^{-1}; MS (EI) *m/z* 308 (M^+, 29), 189 (18), 121 (100%); HRMS M^+ 308.0894 (calcd for $C_{15}H_{16}O_7$ 308.0896).

17c: 98% yield; R_f = 0.5 (CH_2Cl_2 : AcOEt = 2 : 1); Colorless crystals; mp 56.1-57.2 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.25 (s, 6H), 1.44 (s, 9H), 3.59 (s, 2H), 4.69 (bs, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 24.79 (q), 28.42 (q), 54.40 (s), 71.01 (d), 79.88 (s), 156.27 (s); IR (neat) 3481, 3303, 2976, 1690, 1538, 1367, 1305, 1176, 1086, 1044 cm^{-1}; MS (EI) *m/z* 190 $(M+H)^+$, 189 (M^+); HRMS M^+ 189.1369 (calcd for $C_9H_{19}NO_3$ 189.1365); Anal. Calcd for $C_9H_{19}NO_3$: C, 57.12; H, 10.12; N, 7.40. Found: C, 56.88; H, 10.06; N, 7.44.

Preparation of 18a (eq 8). To a solution of 1,1-diethyl 2-hydrogen ethenetricarboxylate **1a** (649 mg, 3 mmol) (prepared from 2-*tert*-butyl 1,1-diethyl ethenetricarboxylate upon treatment with CF_3CO_2H) in ether (3 mL) were added diethyl azodicarboxylate 40% in toluene (1.17 mL, 3 mmol), PPh_3 (780 mg, 3 mmol) and a solution of *N*-(hydroxyethyl)carbamic acid *tert*-butyl ester **17a** (725 mg, 4.5 mmol) in ether (3 mL) at room temperature. The reaction mixture was stirred for 18 h. After removal of the solvent

under reduced pressure, the residue was purified by column chromatography over silica gel with hexane-ether (1 : 4) as eluent to give **18a** (763 mg, 71%).

18a: R_f = 0.5 (hexane : ether = 1 : 4); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.33 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.45 (s, 9H), 3.42 (m, 2H), 4.25 (t, *J* = 5.1 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 4.88 (bs, 1H), 6.88 (s, 1H).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.98 (q), 13.99 (q), 28.39 (q), 39.46 (t), 62.26 (t), 62.64 (t), 65.11 (t), 79.76 (s), 129.66 (d), 139.22 (s), 155.77 (s), 162.20 (s), 163.37 (s), 164.39 (s); IR (neat) 3403, 2981, 1729, 1517, 1368, 1255, 1167, 1068 cm^{-1}; MS (FAB) *m/z* 360 $(M+H)^+$, 382 $(M+Na)^+$; HRMS (FAB) $(M+H)^+$ 360.1660 (calcd for $C_{16}H_{26}NO_8$ 360.1658).

18b: R_f = 0.6 (hexane : ether = 1 : 9); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.17 (d, *J* = 6.8 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.44 (s, 9H), 3.99 (bs, 1H), 4.14 (dd, *J* = 11.2, 4.4 Hz, 1H), 4.20 (dd, *J* = 11.2, 4.8 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 4.39 (q, *J* = 7.1 Hz, 2H), 4.61 (bs, 1H), 6.89 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.00 (q), 14.03 (q), 17.66 (q), 28.43 (q), 45.36 (d), 62.28 (t), 62.65 (t), 68.53 (t), 79.73 (s), 129.56 (d), 139.34 (s), 155.11 (s), 162.26 (s), 163.48 (s), 164.32 (s); IR (neat) 3393, 2980, 1729, 1516, 1368, 1254, 1166, 1067, 1024 cm^{-1}; MS (EI) *m/z* 373 (M^+, 1.1), 343 (10), 300 (12), 200 (61), 144 (100%); HRMS (EI) M^+ 373.1729 (calcd for $C_{17}H_{27}NO_8$ 373.1737).

18c: R_f = 0.3 (hexane : ether = 1 : 4); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.31 (s, 6H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.43 (s, 9H), 4.28 (s, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 4.63 (bs, 1H), 6.91 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.84 (q), 13.90 (q), 24.30 (q), 51.85 (s), 62.09 (t), 62.50 (t), 69.97 (t), 79.26 (s), 129.54 (d), 139.15 (s), 154.31 (s), 162.17 (s), 163.24 (s), 164.08 (s); IR (neat) 1396, 2980, 1727, 1513, 1368, 1258, 1166, 1069, 1024 cm^{-1}; MS (EI) *m/z* 387 (M^+, 0.2), 357 (1.9), 158 (91), 102 (100%); HRMS (EI) M^+ 387.1902 (calcd for $C_{18}H_{29}NO_8$ 387.1893).

18d: R_f = 0.6 (hexane : ether = 1 : 4); Colorless oil; $[\alpha]^{28}_D$ = -37° (c 1.55, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.32 (t, *J* = 7.1 Hz, 3H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.46 (s, 9H), 1.80-2.02 (m, 4H), 3.36 (bs, 2H), 4.01 (bs, 1H), 4.08-4.22 (broad m, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 6.87 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.98

(q), 14.02 (q), 23.01 (t), 28.52 (q), 28.79 (t), 46.65 (t), 55.43 (d), 62.21 (t), 62.62 (t), 65.82 (t), 79.80 (s), 129.69 (d), 139.38 (s), 154.51 (s), 162.29 (s), 163.45 (s), 164.24 (s); IR (neat) 2979, 1732, 1695, 1394, 1257, 1167, 1067 cm^{-1}; MS (EI) *m/z* 399 (M^+, 2.0), 298 (20), 170 (51), 114 (100%); HRMS (EI) M^+ 399.1897 (calcd for $C_{19}H_{29}NO_8$ 399.1893).

18e: R_f = 0.7 (hexane : ether = 1 : 4); Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.31 (t, *J* = 7.1 Hz, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.45 (s, 9H), 1.39-1.51 (m, 2H), 1.59-1.70 (m, 4H), 2.79 (broad t, *J* = 12.7 Hz, 1H), 4.01-4.04 (m, 1H), 4.23-4.34 (m, 2H), 4.52 (bs, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 6.85 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.94 (q), 13.96 (q), 19.27 (t), 25.15 (t), 25.23 (t), 28.39 (q), 39.48 (t), 48.57 (d), 62.15 (t), 62.53 (t), 62.92 (t), 79.79 (s), 129.53 (d), 139.47 (s), 155.03 (s), 162.17 (s), 163.45 (s), 164.18 (s); IR (neat) 2979, 2939, 1729, 1694, 1415, 1366, 1257, 1177, 1067 cm^{-1}; MS (EI) *m/z* 413 (M^+, 0.15), 312 (1.6), 268 (3.1), 200 (4.4), 128 (100%); HRMS (EI) M^+ 413.2058 (calcd for $C_{20}H_{31}NO_8$ 413.2050).

20b: The diastereomer ratio of **20b** changed from 1.7:1 to 1:0 on standing. For the major product, R_f = 0.6 (CH_2Cl_2 : ether = 1 : 1); Colorless crystals, mp 68-69 ºC; $[\alpha]^{28}_D$ = +40° (c 2.47, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.09 (d, *J* = 6.4 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 2.46 (bs, 1H), 3.23-3.31 (m, 1H), 4.03 (t, *J* = 10.5 Hz, 1H), 4.15 (d, *J* = 3.1 Hz, 1H), 4.20-4.33 (m, 6H). Selected NOEs are between δ 3.23-3.31 (NC*H*CH_3) and δ 4.15 (can be assigned to NC*H*$CH(CO_2Et)_2$).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.67 (q), 16.46 (q), 46.92 (d), 53.79 (d), 57.27 (d), 61.53 (t), 74.93 (t), 167.27 (s), 167.92 (s), 168.04 (s); IR (neat) 3320, 2996, 1744, 1728, 1467, 1376, 1306, 1213, 1181, 1045 cm^{-1}; MS (EI) *m/z* 273 (M^+, 50), 160 (49), 142 (100); HRMS M^+ 273.1208 (calcd for $C_{12}H_{19}NO_6$ 273.1212). The stereochemistry of the major product is not decisive by NMR spectra, because of the overlap of peaks. However, due to the stability of diequatorial conformation, 1,3-cis stereochemistry is assumed.

20c: R_f = 0.7 (CH_2Cl_2 : MeOH = 4 : 1); Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.15 (s, 3H), 1.27 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 2.11 (bs, 1H), 4.05 (d, *J* = 10.7 Hz, 1H), 4.13 (d, *J* = 3.9 Hz, 1H), 4.17 (d, *J* = 3.9 Hz, 1H), 4.18 (d, *J* = 10.7

Hz, 1H), 4.21-4.29 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.04 (q), 14.07 (q), 22.90 (q), 26.54 (q), 48.66 (s), 53.80 (d), 53.82 (d), 61.97 (t), 77.62 (t), 167.86 (s), 168.06 (s), 169.55 (s); IR (neat) 2980, 1742, 1467, 1372, 1231, 1179, 1043 cm^{-1}; MS (EI) *m/z* 287 (M^+); HRMS M^+ 287.1372 (calcd for $C_{13}H_{21}NO_6$ 287.1369).

21a: 98% yield; R_f = 0.5 (AcOEt : MeOH = 1 : 1); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.065 (s, 6H), 0.899 (s, 9H), 1.73 (bs, 1H), 2.68 (dd, *J* = 5.3, 5.3 Hz, 2H), 3.72 (dd, *J* = 5.3, 5.3 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) -5.28 (q), 18.40 (s), 26.00 (q), 36.38 (q), 53.87 (t), 62.25 (t); IR (neat) 3418, 2955, 2929, 2858, 1472, 1256, 1092 cm^{-1}; MS (FAB) *m/z* 190 $(M+H)^+$; HRMS $(M+H)^+$ 190.1631 (calcd for $C_9H_{24}NOSi$ 190.1627).

21b: 96% yield; R_f = 0.2 (ether : MeOH = 4 : 1); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.030 (s, 6H), 0.871 (s, 9H), 1.05 (dddd, *J* = 12.5, 12.5, 11.0, 3.8 Hz, 1H), 1.25-1.51 (m, 3H), 1.56-1.60 (m, 1H), 1.74-1.79 (m, 1H), 2.17 (bs, 1H), 2.54-2.64 (m, 2H), 3.03-3.08 (m, 1H), 3.37 (dd, *J* = 9.7, 8.3 Hz, 1H), 3.51 (dd, *J* = 9.7, 3.8 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) -5.32 (q), 18.37 (s), 24.51 (t), 25.99 (q), 26.53 (t), 28.54 (t), 46.71 (t), 58.35 (d), 68.01 (t); IR (neat) 2929, 2857, 1672, 1329, 1256, 1088 cm^{-1}; MS (EI) *m/z* 229 (M^+, 2.6), 172 (25), 84 (100); HRMS M^+ 229.1862 (calcd for $C_{12}H_{27}NOSi$ 229.1862).

21c: (75%) R_f = 0.3 (ether : MeOH = 4 : 1); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) -0.318 (s, 3H), -0.028 (s, 3H), 0.727 (d, *J* = 6.4 Hz, 3H), 0.813 (s, 9H), 2.18 (bs, 1H), 2.39 (s, 3H), 2.65 (dq, *J* = 7.9, 6.4, 1H), 4.32 (d, *J* = 7.9 Hz, 1H), 7.18-7.27 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) -5.04 (q), -4.48 (q), 14.87 (q), 18.17 (s), 25.87 (q), 33.71 (q), 61.67 (d), 79.35 (d), 127.39 (d), 127.51 (d), 127.99 (d), 142.55 (s); IR (neat) 3349, 2955, 2929, 2857, 1472, 1258, 1079, 1065 cm^{-1}; MS (EI) *m/z* 279 (M^+, 11), 264 (24), 222 (100); HRMS M^+ 279.2015 (calcd for $C_{16}H_{29}NOSi$ 279.2018).

21d: (78%) R_f = 0.1 (ether : MeOH = 4 : 1); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.018 (s, 6H), 0.856 (s, 9H), 1.16 (dddd, *J* = 12.6, 12.6, 10.8, 3.7 Hz, 1H), 1.26-1.67 (m, 6H), 1.72-1.78 (m, 1H), 2.58-2.66 (m, 2H), 3.02-3.07 (m, 1H), 3.24 (bs, 1H), 3.63-3.73 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) -5.39 (q), -5.32 (q), 18.28 (s), 24.71 (t),

25.95 (q), 26.06 (t), 32.66 (t), 39.45 (t), 46.85 (t), 55.11 (d), 60.93 (t); IR (neat) 2929, 2856, 1472, 1255, 1100 cm^{-1}; MS (EI) *m/z* 243 (M^+, 28), 186 (100); HRMS M^+ 243.2024 (calcd for $C_{13}H_{29}NOSi$ 243.2018).

Preparation of 22a (eq 9). To a solution of 1,1-diethyl 2-hydrogen ethenetricarboxylate **1a** (290 mg, 1.3 mmol) (prepared from 1,1-diethyl 2-*tert*-butyl ethenetricarboxylate upon treatment with CF_3CO_2H)[5d] in THF (5.2 mL) were added *N*-(2-(*tert*-butyldimethylsilyloxy)ethyl)methylamine **21a** (254 mg, 1.3 mmol), HOBt (181 mg, 1.3 mmol) and EDCI (257 mg, 1.3 mmol) at 0 °C. The reaction mixture was allowed to warm to rt and stirred for overnight. The mixture was concentrated *in vacuo* 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 CH_2Cl_2-AcOEt to give **22a** (358 mg, 69%).

22a: R_f = 0.3 (CH_2Cl_2 : AcOEt = 1 : 1); Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 6:4) δ (ppm) 0.049 (s, 0.4×6H), 0.056 (s, 0.4×6H), 0.885 (s, 0.6×9H), 0.887 (s, 0.4×9H), 1.29-1.34 (m, 6H), 3.02 (s, 0.6×3H), 3.17 (s, 0.4×3H), 3.49 (t, *J* = 5.1 Hz, 0.6×2H), 3.54 (t, *J* = 5.3 Hz, 0.4×2H), 3.75 (t, *J* = 5.1 Hz, 0.6×2H), 3.79 (t, *J* = 5.3 Hz, 0.6×2H), 4.26-4.36 (m, 4H), 7.35 (s, 0.4×1H), 7.47 (s, 0.6×1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) -5.55 (q), -5.45 (q), 13.97 (q), 14.05 (q), 18.16 (s), 18.23 (s), 25.85 (q), 33.57 (q), 37.97 (q), 50.56 (t), 52.51 (t), 60.39 (t), 61.61 (t), 61.70 (t), 61.76 (t), 62.01 (t), 62.16 (t), 134.15 (s), 134.35 (d), 134.43 (s), 134.93 (d), 163.10 (s), 163.84 (s), 164.52 (s), 164.58 (s), 164.81 (s); IR (neat) 2955, 2931, 1732, 1653, 1472, 1254, 1101, 1068 cm^{-1}; MS (FAB) *m/z* 388 $(M+H)^+$; HRMS $(M+H)^+$ 388.2155 (calcd for $C_{18}H_{34}NO_6Si$ 388.2155).

22b: R_f = 0.5 (hexane : ether = 1 : 4); Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 8:2) δ (ppm) 0.026 (s, 0.8×3H), 0.038 (s, 0.2×3H), 0.044 (s, 3H), 0.864 (s, 9H), 1.27-1.32 (m, 6H), 1.39-1.57, 1.62-1.72, 1.91-1.95 (m, 6H), 2.64 (ddd, *J* = 13.2, 13.2, 2.9 Hz, 0.8×1H), 3.17 (ddd, *J* = 13.2, 13.2, 3.2 Hz, 0.2×1H), 3.55 (dd, *J* = 10.1, 4.8 Hz, 0.8×1H), 3.56-3.61 (m, 0.2×1H), 3.63 (dd, *J* = 15.7, 5.6 Hz, 0.2×1H), 3.74 (dd, *J* = 10.0, 8.2 Hz,

0.2×1H), 3.86 (dd, *J* = 9.7, 9.7 Hz, 0.8×1H), 3.92-3.97 (m, 0.8×1H), 4.22-4.37 (m, 4H), 4.50 (bd, *J* = 14.3 Hz, 0.8×1H), 4.61-4.66 (m, 0.2×1H), 7.32 (s, 0.2×1H), 7.47 (s, 0.8×1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) For a major rotamer, δ (ppm) -5.48 (q), -5.46 (q), 14.05 (q), 14.09 (q), 18.22 (s), 19.99 (t), 25.01 (t), 25.86 (t), 25.89 (q), 37.00 (t), 55.70 (d), 60.97 (t), 61.29 (t), 61.71 (t), 61.90 (t), 132.14 (s), 137.71 (d), 163.23 (s), 164.39 (s), 164.57 (s); IR (neat) 2936, 2858, 1728, 1643, 1443, 1254, 1098, 1070 cm^{-1}; MS (FAB) *m/z* 428 $(M+H)^+$; HRMS $(M+H)^+$ 428.2477 (calcd for $C_{21}H_{38}NO_6Si$ 428.2468).

22c: R_f = 0.5 (hexane : ether = 1 : 4); Pale yellow oil; $[\alpha]^{27}_D$ = +48° (c 0.77, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 9:1) For a major rotamer, δ (ppm) -0.281 (s, 3H), -0.014 (s, 3H), 0.822 (s, 9H), 1.06 (d, *J* = 6.8 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 2.95 (d, *J* = 0.4 Hz, 3H), 3.86 (dq, *J* = 7.0, 7.0 Hz, 1H), 4.19-4.34 (m, 4H), 4.50 (d, *J* = 7.1 Hz, 1H), 7.11 (s, 1H), 7.21-7.24 (m, 2H), 7.27-7.35 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) For a major rotamer, δ (ppm) -5.16 (q), -4.73 (q), 14.00 (q), 14.11 (q), 15.31 (q), 17.95 (s), 25.72 (q), 27.44 (q), 59.96 (d), 61.65 (t), 61.84 (t), 77.12 (d), 126.82 (d), 128.26 (d), 128.65 (d), 131.44 (s), 138.55 (d), 141.69 (s), 163.16 (s), 164.21 (s), 165.64 (s); IR (neat) 2956, 2931, 2858, 1732, 1642, 1472, 1455, 1254, 1069 cm^{-1}; MS (FAB) *m/z* 500 $(M+Na)^+$; HRMS $(M+Na)^+$ 500.2431 (calcd for $C_{25}H_{39}NO_6SiNa$ 500.2444).

22d: R_f = 0.5 (hexane : ether = 1 : 4); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 2:1) δ (ppm) 0.013 (s), 0.019 (s), 0.027 (s), 6H, 0.848 (s), 0.854 (s), 9H, 1.278 (t, *J* = 7.1 Hz), 1.287 (t, *J* = 7.1 Hz), 1.290 (t, *J* = 7.1 Hz), 6H, 1.38-1.48 (m), 1.54-1.79 (m), 1.86-2.01 (m), 8H, 2.62 (td, *J* = 13.8, 13.8, 2.9 Hz), 3.19 (td, *J* = 13.6, 13.6, 2.4 Hz), 1H, 3.50-3.65 (m), 4.45 (dd, *J* = 13.8, 3.9 Hz), 3H, 4.04-4.09 (m), 4.73-4.47 (m), 1H, 4.18-4.35 (m, 4H), 7.29 (s), 7.43 (s), 1H; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) -5.39 (q), -5.38 (q), -5.35 (q), 13.98 (q), 14.04 (q), 14.06 (q), 18.24 (s), 18.35 (s), 19.11 (t), 19.23 (t), 25.31 (t), 25.92 (q), 25.96 (q), 26.12 (t), 28.37 (t), 29.01 (t), 32.72 (t), 32.81 (t), 36.87 (t), 42.43 (t), 46.24 (d), 50.87 (d), 59.35 (t), 60.83 (t), 61.65 (t), 61.74 (t), 61.87 (t), 62.01 (t), 132.61 (s), 133.43 (s), 136.86 (d), 137.21 (d), 163.11 (s), 163.20 (s), 163.58 (s), 164.16 (s), 164.57 (s); IR (neat) 2936, 2857, 1729, 1640, 1446, 1254, 1211, 1096, 1069 cm^{-1}; MS (FAB) *m/z* 442 $(M+H)^+$; HRMS $(M+H)^+$ 442.2614 (calcd for $C_{22}H_{40}NO_6Si$ 442.2625).

23b-trans: R_f = 0.3 (hexane : ether = 1 : 4); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.988-1.09 (m, 1H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.27-1.37 (m, 2H), 1.59 (bd, *J* = 13.2 Hz, 1H), 1.67-1.74 (m, 1H), 1.75-1.82 (m, 1H), 2.46 (ddd, *J* = 12.9, 12.9, 3.1 Hz, 1H), 3.43 (dd, *J* = 10.4, 10.4 Hz, 1H), 3.49 (dddd, *J* = 10.4, 10.4, 3.1, 3.1 Hz, 1H), 3.94-3.97 (m, 1H), 4.02 (d, *J* = 4.8 Hz, 1H), 4.10-4.24 (m, 4H), 4.55 (bd, *J* = 13.6 Hz, 1H), 4.60 (d, *J* = 4.8 Hz, 1H). Selected NOEs are between δ 3.43 (OC*H*H) and δ 4.60 (OC*H*C=O), 0.988-1.09 (NCHC*H*HCH$_2$) and between δ 1.59 (NCHCH*H*CH$_2$) and δ 3.49 (NC*H*), 3.94-3.97 (OCH*H*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.05 (q), 22.76 (t), 24.77 (t), 27.82 (t), 40.93 (t), 54.20 (d), 54.38 (d), 61.60 (t), 61.68 (t), 69.29 (t), 75.95 (d), 166.70 (s), 166.76 (s), 167.24 (s). Selected HMBC correlations are between δ 3.43, 3.94-3.97 (OC*H*$_2$) and δ 75.95 (O*C*HC=O).; IR (neat) 2982, 2938, 2860, 1750, 1658, 1447, 1369, 1271, 1174, 1157 cm^{-1}; MS (EI) *m/z* 313 (M^+, 11), 268 (24), 240 (44), 194 (83), 98 (100); HRMS M^+ 313.1526 (calcd for $C_{15}H_{23}NO_6$ 313.1525).

23b-cis: R_f = 0.2 (hexane : ether = 1 : 4); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.28 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.53-1.63 (m, 4H), 1.96-2.07 (m, 2H), 2.52 (ddd, *J* = 11.9, 11.9, 3.6 Hz, 1H), 3.24 (bd, *J* = 12.1 Hz, 1H), 3.81 (dd, *J* = 12.1, 1.2 Hz, 1H), 3.95 (dd, *J* = 12.1, 3.8 Hz, 1H), 4.14 (d, *J* = 4.6 Hz, 1H), 4.17-4.30 (m, 4H), 4.62 (d, *J* = 4.6 Hz, 1H), 4.66 (bd, *J* = 12.8 Hz, 1H). Selected NOEs are between δ 3.95 (OC*H*H) and δ 4.62 (OC*H*C=O), 3.24 (NC*H*).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.10 (q), 24.71 (t), 24.93 (t), 30.09 (t), 44.10 (t), 53.95 (d), 56.62 (d), 61.62 (t), 61.67 (t), 67.78 (t), 75.98 (d), 165.76 (s), 166.66 (s), 167.29 (s). Selected HMBC correlations are between δ 3.95, 3.81 (OC*H*$_2$) and δ 75.98 (O*C*HC=O) and between δ 4.62 (OC*H*C=O) and δ 67.78 (O*C*H$_2$).; IR (neat) 2938, 1758, 1738, 1652, 1471, 1444, 1271, 1178, 1036 cm^{-1}; MS (EI) *m/z* 313 (M^+, 16), 268 (29), 240 (34), 194 (88), 84 (100); HRMS M^+ 313.1524 (calcd for $C_{15}H_{23}NO_6$ 313.1525).

23c (1,3-trans:cis 3:1 mixture): R_f = 0.2 (hexane : ether = 1 : 4); Colorless oil; $[\alpha]^{25}_D$ = -57° (c 0.76, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.08 (d, *J* = 6.4 Hz, 0.25×3H), 1.23-1.29 (m, 6H), 1.52 (d, *J* = 6.6 Hz, 0.75×3H), 3.00 (d, *J* = 0.4 Hz, 0.25×3H), 3.09 (d, *J* = 0.5 Hz, 0.75×3H), 3.65 (dq, *J* = 9.3, 6.4 Hz, 0.25×1H), 3.89 (qd, *J* = 6.6, 2.0 Hz, 0.75×1H), 4.05

(d, *J* = 5.1 Hz, 0.25×1H), 4.08 (d, *J* = 4.6 Hz, 0.75×1H), 4.13-4.30 (m, 4H), 4.36 (d, *J* = 9.5 Hz, 0.25×1H), 4.38 (dd, *J* = 4.5, 0.5 Hz, 0.75×1H), 4.84 (d, *J* = 1.8 Hz, 0.75×1H), 4.87 (ddd, *J* = 5.1, 0.5, 0.5 Hz, 0.25×1H), 7.32-7.41 (m, 5H). Selected NOEs are between δ 4.36 (OC*H*Ph, 1,3-cis isomer) and δ 4.87 (OC*H*C=O, 1,3-cis isomer), 1.08 (NCHCH_3, 1,3-cis isomer), and between δ 4.84 (OC*H*Ph, 1,3-trans isomer) and δ 1.52 (NCHCH_3, 1,3-trans isomer).; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 14.00 (q), 14.06 (q), 16.00 (q), 18.03 (q), 30.51 (q), 32.76 (q), 53.88 (d), 54.57 (d), 54.82 (d), 58.43 (d), 61.54 (t), 61.57 (t), 61.61 (t), 61.63 (t), 70.81 (d), 75.79 (d), 76.63 (d), 82.52 (d), 127.49 (d), 127.64 (d), 128.58 (d), 128.65 (d), 128.85 (d), 128.90 (d), 136.37 (s), 137.86 (s), 166.58 (s), 166.76 (s), 166.82 (s), 166.97 (s), 167.21 (s), 167.67 (s). Selected HMBC correlations are between δ 3.09 (NCH_3, 1,3-trans) and δ 166.82 (N-*C*=O, 1,3-trans), between δ 3.00 (NCH_3, 1,3-cis) and δ 167.67 (N-*C*=O, 1,3-cis), and between δ 4.84 (OC*H*Ph, 1,3-trans) and δ 70.81 (O*C*HC=O, 1,3-trans).; IR (neat) 2982, 2937, 1753, 1657, 1454, 1372, 1268, 1156, 1035 cm^{-1}; MS (FAB) *m/z* 386 $(M+Na)^+$; HRMS $(M+Na)^+$ 386.1578 (calcd for $C_{19}H_{25}NO_6Na$ 386.1580).

24d: R_f = 0.7 (ether : MeOH = 9 : 1); Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) (2 rotamers, ratio 2:1) δ (ppm) 1.29-1.34 (m, 6H), 1.47-2.03 (m), 2.23-2.38 (m), 8H, 2.73 (broad t, *J* = 12.5 Hz), 3.24 (td, *J* = 13.5, 2.5 Hz), 3.62 (broad t, *J* = 13.7 Hz), 4.22-4.53 (m), 8H, 4.02-4.07 (m), 4.88-4.92 (m), 1H, 7.28 (s), 7.32 (s), 1H, 9.27 (bs, OH, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.87 (q), 13.91 (q), 14.01 (q), 18.94 (t), 18.97 (t), 25.13 (t), 25.75 (t), 28.42 (t), 28.51 (t), 28.67 (t), 28.96 (t), 37.42 (t), 42.68 (t), 46.13 (d), 51.40 (d), 62.23 (t), 62.28 (t), 62.37 (t), 62.40 (t), 64.45 (t), 65.44 (t), 133.13 (s), 134.38 (s), 135.82 (d), 136.75 (d), 162.76 (s), 162.98 (s), 163.99 (s), 164.08 (s); IR (neat) 3445, 2985, 2946, 1788, 1732, 1642, 1615, 1449, 1374, 1261, 1214, 1170 cm^{-1}; MS (EI) *m/z* 327 (M^+, 5), 282 (75), 143 (58), 84 (100); HRMS M^+ 327.1681 (calcd for $C_{16}H_{25}NO_6$ 327.1682).

References

[S1] E. W. Colvin, *Silicon Reagents in Organic Synthesis*, Academic Press, London, 1988.