Silylative Dieckmann-like Cyclizations of Ester-Imides (and Diesters)

Thomas R. Hoye*, Vadims Dvornikovs, Elena Sizova

Department of Chemistry, University of Minnesota, Minneapolis, MN 55455
hoye@chem.umn.edu

Supporting Information

Spectroscopic characterization data and procedures for preparation of all new compounds (**4**, **6**, **12-15**, **17-21**, **24**, **25**, **28**, and **31**; 25 pages). Intermediates that are new compounds and that were synthesized in the course of preparing the above numbered compounds are also described here. These have been given the Roman numerals **I-VI**.

General Experimental Protocols.

All glassware was flame- or/and oven-dried before use. Tetrahydrofuran (THF) and dichloromethane were dried through Al_2O_3 columns. CH_3CN and EtOAc were distilled over P_2O_5 and stored over 3 Å MS. MeOH was distilled over Mg and stored over 3 Å MS. Et_3N was distilled from CaH_2 and stored over 4 Å MS. Other solvents were of HPLC grade and were used as received. Analytical TLC was performed using TLC plastic sheets with F_{254} indicator, and detection was performed by UV-light or staining with either potassium permanganate or anisaldehyde/ H_2SO_4 .

Most purifications were performed on a medium pressure chromatography unit using columns packed with 25-32 μm silica gel. Each unit is outfitted with a Waters HPLC pump and refractive index detector.

^1H and ^{13}C NMR spectra were acquired on a Varian VI-500 (500 MHz ^1H , 125.7 MHz ^{13}C), VI-300 (300 MHz ^1H , 75.4 MHz ^{13}C), or VXR-300 (300 MHz ^1H , 75.4 MHz ^{13}C) spectrometer, using CDCl_3 or C_6D_6 . Chemical shifts (δ) for spectra recorded in CDCl_3 are reported in ppm and are referenced to TMS at $\delta = 0.00$ for ^1H and CDCl_3 at $\delta = 77.23$ ppm for ^{13}C NMR spectra. The following abbreviations are used to describe multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), pent (pentet), m (multiplet), nform (non-first order multiplet), app (apparent), and br (broad). Coupling constants (J) are reported in Hz.

Infrared spectra were recorded on a Midac Corporation Prospect 4000 FT-IR spectrometer (only the most intense and/or diagnostic peaks are reported). All samples were thin films on a NaCl window.

High-resolution mass spectra were recorded on a Bruker Biotof II (ESI-TOF) instrument using PEG or PPG as an internal calibrant. Low resolution GC-MS data were collected on an Agilent 5975 XL-MSD instrument at 70 eV fitted with an HP-5 column (~15 m in length).

Methyl (1*R*,7*aS*)-rel-2,3,4,7*a*-Tetrahydro-7*a*-[(trimethylsilyl)oxy]-5(1*H*)-pyrrolizinone-1-carboxylate (4a**) and Methyl 2,5-Dihydro-2,5-dioxo-1*H*-pyrrole-1-(α-trimethylsilyl)butanoate (**6**).**

Imide ester **2** (376 mg, 1.9 mmol) was dissolved in CH₂Cl₂ (7.0 mL). Et₃N (0.66 mL, 4.7 mmol) and TMSOTf (0.69 mL, 3.8 mmol) were added sequentially at rt. The reaction mixture was stirred for 4 h, diluted with CH₂Cl₂ (20 mL), and washed sequentially with a saturated aqueous solution of NaHCO₃ and brine. The organic layer was dried over Na₂SO₄. The solution was concentrated and the residue was purified by silica gel chromatography with hexanes/EtOAc 3:1 as eluent. This provided, in order of elution, **6** (21 mg, 0.08 mmol, 4%) as white crystals and **4a** (dr 62:1 (GC-MS), 450 mg, 1.67 mmol, 88%) as white crystals.

For **6**: mp = 70-71 °C.

¹H-NMR (300 MHz, CDCl₃): δ 6.70 (s, 2H), 3.65 (s, 3H), 3.55 (app t, 2H, *J* = 7 Hz), 2.24 (dddd, 1H, *J* = 13.8, 12.1, 6.2, 6.2 Hz), 1.94 (dd, 1H, *J* = 12.1, 2.4 Hz), 1.70 (dddd, 1H, *J* = 13.7, 7.1, 7.1, 2.3 Hz), and 0.05 (s, 9H).

¹³C-NMR (75 MHz, CDCl₃): δ 175.0, 171.0, 134.3, 51.4, 38.1, 34.8, 25.6, and 4.1.

TLC: R_f (hexanes/EtOAc, 3:1) = 0.33.

IR: 2955, 1712, 1407, 1251, and 1192 cm⁻¹.

MS: ESI-MS calcd for C₁₂H₁₉NNaO₄Si (M•Na⁺) 292.0976, found 292.0973.

GC-MS (Start temp = 50 °C, run time = 21 min, temp. ramp = 11.4 °C/min): t_R = 10.3 min; m/z: 269 (M⁺), 254 (M⁺-CH₃).

A sample for single crystal x-ray analysis was obtained by preparing a saturated solution of **6** in hexanes followed by slow cooling to -20 °C. The solution was kept for 20 h at -20 °C. Needle-like crystals were collected by filtration.

For **4a**: mp = 64.5-66 °C

¹H-NMR (300 MHz, CDCl₃): δ 6.97 (d, 1H, *J* = 5.7 Hz), 5.95 (dd, 1H, *J* = 5.7, 1.0 Hz), 3.76 (ddd, 1H, *J* = 11.8, 8.9, 8.9 Hz), 3.56 (s, 3H), 3.27 (ddd, 1H, *J* = 11.3, 9.1, 2.4 Hz), 3.11 (dd, 1H, *J* = 6.9, 1.2 Hz), 2.60 (dddd, 1H, *J* = 13.2, 9.2, 9.2, 6.8 Hz), 2.56 (dddd, 1H, *J* = 12.9, 8.3, 2, 2 Hz), and 0.09 (s, 9H).

¹³C-NMR (75 MHz, CDCl₃): δ 173.9, 171.5, 148.3, 127.8, 101.0, 53.0, 52.1, 42.3, 31.3, and 1.3.

TLC: R_f (hexanes/EtOAc, 3:1) = 0.30.

IR: 3067, 2957, 2905, 1732, 1713, 1485, 1433, 1356, and 1321 cm⁻¹.

MS: ESI-MS calcd for C₁₂H₁₉NNaO₄Si (M•Na⁺) 292.0976, found 292.0965.

GC-MS (Start temp = 50 °C, run time = 21 min, temp. ramp = 11.4 °C/min): t_R = 10.1 min; m/z: 269 (M⁺), 254 (M⁺-CH₃).

Methyl *cis*- and *trans*-2-Methoxy-2-trimethylsilyloxycyclopentanecarboxylates (12a).

Dimethyl adipate **11a** (31.2 mg, 0.18 mmol) was dissolved in CDCl₃ (0.5 mL) and Et₃N (65 µL, 0.45 mmol) was added followed by TMSOTf (63 µL, 0.36 mmol). The resulting mixture was shaken to achieve adequate mixing and after 3 h filtered through a bed of silica gel with 80:20:1 hexanes/EtOAc/Et₃N to give an orange oil (46 mg, 86%, dr 2:1). This labile diastereomeric mixture of **12a** was ~95% pure (¹H NMR analysis).

TLC: R_f (hexanes/EtOAc, 4:1 + 1% Et₃N) = 0.55.

¹H-NMR (500 MHz, CDCl₃): δ 3.68 (s, 3H, minor), 3.67 (s, 3H, major), 3.28 (s, 3H, major), 3.27 (s, 3H, minor), 3.03 (dd, 1H, *J* = 8.3, 5.5 Hz, major), 2.94 (dd, 1H, *J* = 8.5, 4.6 Hz, minor), 2.02 (dddd, 1H, *J* = 13, 8, 7, 4 Hz (from 1D TOCSY), major), 1.80 (dddd, 1H, *J* = 12, 12, 8, 4 Hz (from 1D-TOCSY), major), 1.58-2.06 (m), 0.19 (s, 9H, minor), 0.13 (s, 9H, major).

¹³C-NMR (75 MHz, CDCl₃): δ 173.9, 173.8, 110.8, 110.3, 54.2, 51.5, 51.3, 51.1, 50.8, 49.1, 38.5, 36.2, 26.67, 26.61, 22.5, 21.3, 1.4, and 1.2.

IR: 2956, 1740, 1436, 1351, 1252, 844, and 757 cm⁻¹.

MS: ESI-MS calcd for $C_{11}H_{22}O_4SiNa$ ($M \cdot Na^+$) 269.1180, found 269.1185.

Methyl *cis*- and *trans*-2-Methoxy-2-trimethylsilyloxycyclohexanecarboxylates (12b).

Esters **12b** (an ca. 2:1 mixture of diastereomers, yellow oil, 98%) was obtained using the procedure above (for **12a**) with the exception that the reaction mixture was allowed to stand for 24 h before workup.

TLC: R_f (Hexanes/EtOAc, 4:1 + 1% Et₃N) = 0.39

¹H-NMR (500 MHz, CDCl₃): δ 3.67 (s, 3H, minor), 3.65 (s, 3H, major), 3.220 (s, 3H, major), 3.217 (s, 3H, minor), 2.89 (ddd, 1H, *J* = 4.4, 4.4, 1.8 Hz, major), 2.73 (ddd, 1H, *J* = 4.9, 4.9, 1.1 Hz, minor), 2.14 (m, 1H, minor), 2.11 (ddd, 1H, *J* = 13.3, 11.5, 4.2 Hz, (1D-TOCSY) major), 1.86-1.32 (m), 0.18 (s, 9H, minor), and 0.12 (s, 9H, major).

¹³C-NMR (75 MHz, CDCl₃): δ 173.2, 172.9, 99.6, 51.2, 51.1, 48.4, 48.1, 48.0, 33.6, 26.4, 26.2, 22.8, 22.1, 21.0, 1.74, and 1.71.

IR: 2951, 2865, 1741, 1436, 1366, 1341, 1251, 1158, 1105, 1057, 1021, and 843 cm^{-1} .

MS: ESI-MS calcd for $C_{11}H_{22}O_4SiNa (M \cdot Na^+)$ 283.1336, found 283.1346.

Methyl 2,5-Dihydro-2,5-dioxo-1H-pyrrole-1-pentanoate (13).

A solution of PPh_3 (0.393 g, 1.50 mmol) in THF (11 mL) was cooled to $-78\text{ }^\circ\text{C}$. Diethyl diazodicarboxylate (1.10 mL, 1.50 mmol) was added over 2 min. The yellow reaction mixture was stirred for 5 min. Methyl 5-hydroxypentanoate¹ (0.200 g, 1.50 mmol) was added over 5 min and the reaction mixture was stirred for 5 min. Maleimide (0.147 g, 1.50 mmol) was added to the reaction mixture as a solid. The resulting solution was allowed to remain at $-78\text{ }^\circ\text{C}$ for 5 min, the cooling bath was removed, and the solution was stirred at ambient temperature for 48 h and concentrated in vacuo. Purification of the resulting residue by chromatography on silica gel with hexanes/EtOAc 3:1 as eluent gave pure **13** (0.153 g, 0.73 mmol, 48%) as a colorless oil:

TLC: R_f (hexanes/EtOAc, 3:1) = 0.21

^1H -NMR (500 MHz, CDCl_3): δ 6.70 (s, 2H), 3.67 (s, 3H), 3.54 (t, 2H, $J = 6.5\text{ Hz}$), 2.35 (t, 2H, $J = 7.0\text{ Hz}$), 1.59-1.67 (4H, nfom).

^{13}C -NMR (125 MHz, CDCl_3): δ 173.8, 171.0, 134.3, 51.8, 37.6, 33.6, 28.1, and 22.2.

IR: 3100, 2952, 2871, 1737, 1706, 1441, 1410, 1368, 1197, 1175, 830, and 696 cm^{-1} .

MS: ESI-MS calcd for $\text{C}_{10}\text{H}_{13}\text{NO}_4\text{K}$ ($\text{M}\cdot\text{K}^+$) 250.0476, found 250.0474; for $\text{C}_{10}\text{H}_{13}\text{NO}_4\text{Na}$ ($\text{M}\cdot\text{Na}^+$) 234.0737, found 234.0749.

Methyl (1*R*,8*aS*)-rel- and (1*R*,8*aR*)-rel-2,3,4,8*a*-Tetrahydro-8*a*-[(trimethylsilyl)oxy]-6(5*H*)-indolizinone-1-carboxylate (14*a* and 15*a*).

Imide ester **13** (137 mg, 0.65 mmol) was dissolved in CH₂Cl₂ (3 mL). Et₃N (361 μL, 2.60 mmol) and TMSOTf (353 μL, 1.95 mmol) were added sequentially to the reaction mixture at 0 °C. The reaction mixture was warmed to rt and stirred for 14 h. Et₃N (136 μL, 0.98 mmol) and TMSOTf (120 μL, 0.65 mmol) were added. The resulting mixture was stirred at rt for 4 h, diluted with CH₂Cl₂ (50 mL), and washed sequentially with a saturated aqueous solution of NaHCO₃ and brine. Organic layer was dried over Na₂SO₄. Concentration under reduced pressure yielded a 5.5:1 mixture of **14a**:**15a** (GC, ¹H NMR), which was chromatographed on silica gel with CH₂Cl₂/MeOH (50:1 eluent).

Pure **14a** (118 mg, 0.42 mmol, 50%, slower eluting) was obtained as a colorless oil:

TLC: R_f (hexanes/EtOAc, 3:1) = 0.20.

¹H-NMR (300 MHz, CDCl₃): δ 6.91 (d, 1H, *J* = 5.7 Hz), 6.16 (d, 1H, *J* = 6.0 Hz), 4.12 (dd, 1H, *J* = 13.6, 4.9 Hz), 3.55 (s, 3H), 3.03 (dd, 1H, *J* = 4.8, 2.4 Hz), 2.89 (ddd, 1H, *J* = 12.7, 12.7, 3.9 Hz), 2.15 (dddd, 1H, *J* = 12.9, 12.9, 4.5, 4.5 Hz), 1.95 (dddd, 1H, *J* = 13, 13, 13, 5.4, 3.3 Hz), 1.94-1.84 (br d, 1H, *J* = 13 Hz), 1.57-1.47 (nfom, 1H), and 0.07 (s, 9H).

¹³C-NMR (75 MHz, CDCl₃): δ 171.4, 167.1, 147.6, 128.4, 88.7, 51.7, 49.0, 35.5, 21.9, 19.9, and 1.6.

IR: 2956, 1740, 1714, 1409, 1253, 1075, and 860 cm⁻¹.

MS: ESI-MS calcd for C₁₃H₂₂NO₄Si (M•H⁺) 284.1313, found 284.1314.

Pure **15a** (22 mg, 0.06 mmol, 9%, faster eluting) was obtained as a colorless oil:

TLC: R_f (hexanes/EtOAc, 3:1) = 0.20.

¹H-NMR (300 MHz, CDCl₃): δ 7.51 (d, 1H, *J* = 5.7 Hz), 6.19 (d, 1H, *J* = 6.0 Hz), 4.10 (dddd, 1H, *J* = 13.2, 5.1, 1.5, 1.5 Hz), 3.75 (s, 3H), 2.81 (ddd, 1H, *J* = 12.9, 12.9, 3.6 Hz), 2.25 (dd, 1H, *J* = 12.3, 4.5 Hz), 2.07 (dddd, 1H, *J* = 13, 13, 13, 3.6 Hz), 1.96 (dddd, 1H, *J* = 13.5, 4, 4, 4, 1.5 Hz), 1.79 (dddd, 1H, *J* = 13.5, 3.3, 3.3, 3.3, 1.5 Hz), 1.31 (dddd, 1H, *J* = 13.3, 13.3, 13.3, 5.1, 4.4 Hz), and 0.04 (s, 9H).

¹³C-NMR (75 MHz, CDCl₃): δ 171.1, 150.4, 127.1, 89.4, 55.4, 55.1, 29.9, 24.9, 22.0, and 1.39.

IR: 2956, 2926, 1744, 1710, 1407, 1253, 1126, and 846 cm⁻¹.

MS: ESI-MS calcd for C₁₃H₂₁NNaO₄Si (M•Na⁺) 306.1132, found 306.1134.

Methyl (1*R*,8*aS*)-rel- and (1*R*,8*aR*)-rel-2,3,4,8*a*-Tetrahydro-8*a*-[[tris(1-methylethyl)silyl]oxy]-6(5*H*)-indolizinone-1-carboxylate (14b** and **15b**).**

Imide ester **13** (38 mg, 0.18 mmol) was dissolved in CDCl₃ (0.6 mL). Et₃N (55 μ L, 0.40 mmol) and TIPSOTf (97 μ L, 0.36 mmol) were added sequentially to the reaction mixture at rt. The reaction mixture was stirred for 4 h, and additional Et₃N (25 μ L, 0.18 mmol) and TIPSOTf (45 μ L, 0.18 mmol) were added. The resulting mixture was stirred at rt for 15 h, diluted with CH₂Cl₂ (20 mL), and washed sequentially with saturated aqueous solution of NaHCO₃ and brine. Organic layer was dried over Na₂SO₄. The solution was concentrated and purified by silica gel chromatography with hexanes/EtOAc 3:1 as eluent. Both diastereomers **14b:15b** (dr 7.5:1, 52 mg, 0.14 mmol, 78%) coeluted and were obtained as a colorless oil.

For **14b**:

¹H-NMR (500 MHz, CDCl₃): δ 6.92 (d, 1H, J = 6.0 Hz), 6.19 (d, 1H, J = 6.5 Hz), 4.13 (br dd, 1H, J = 12.5, 5.5 Hz), 3.56 (s, 3H), 3.10 (dd, 1H, J = 4.5, 2.0 Hz), 3.02 (ddd, 1H, J = 13.0, 13.0, 4.0 Hz), 2.23 (dddd, 1H, J = 13.0, 13.0, 4.0, 4.0 Hz), 1.99 (dddd, 1H, J = 13.0, 13.0, 13.0, 5.0, 4.0 Hz), 1.92 (dddd, 1H, J = 13.0, 4.0, 2.5, 2.5, 1.5 Hz), 1.53 (dddd, 1H, J = 13.0, 4.0, 4.0, 2.5, 1.5 Hz), 1.05 (m, 9H), and 1.01 (m, 9H).

¹³C-NMR (125 MHz, CDCl₃): δ 171.2, 166.6, 146.4, 129.0, 88.0, 51.6, 49.4, 35.4, 21.8, 19.7, 18.1, 18.0, and 13.0.

For the mixture: TLC: R_f (hexanes/EtOAc, 3:1) = 0.20.

IR: 2947, 2868, 1741, 1715, 1408, 1149, 1083, and 1064 cm⁻¹.

MS: ESI-MS calcd for C₁₉H₃₄NO₄Si (M•H⁺) 368.2252, found 368.2249.

Methyl (1*R*, 8*aS*)-rel-1,2,3,5,6,7,8,8*a*-Octahydro-8*a*-[trimethylsilyl]oxy-5-oxo-(1*H*)-indolizinecarboxylate (17*a*), Methyl (1*R*, 8*aR*)-rel-1,2,3,5,6,7,8,8*a*-Octahydro-8*a*-[trimethylsilyl]oxy-5-oxo-(1*H*)-indolizinecarboxylate (18*a*), and Methyl 2,3,5,6,7,8-Hexahydro-5-oxo-1-indolizinecarboxylate (19).

Imide ester **16**² (160 mg, 0.75 mmol) was dissolved in CH₂Cl₂ (2 mL). Et₃N (173 μ L, 1.24 mmol) and TMSOTf (180 μ L, 1.00 mmol) were added sequentially at 0 °C. The reaction mixture was warmed to rt, and after 10 h Et₃N (90 μ L, 0.65 mmol) and TMSOTf (90 μ L, 0.50 mmol) were added again. After 4h the resulting mixture was diluted with CH₂Cl₂ (50 mL) and washed sequentially with saturated aqueous solution of NaHCO₃ and brine. Organic layer was dried over Na₂SO₄. Concentration under reduced pressure yielded a mixture of **17a**, **18a**, and **19** in 2:1:6 ratio, respectively. Chromatography on silica gel with hexanes/EtOAc 1:1 as eluent gave three pure components, listed in the order of elution: **19** (29 mg, 0.15 mmol, 20%) as white crystals, **17a** (13 mg, 0.08 mmol, 11%) as a colorless oil, **18a** (139 mg, 0.49 mmol, 65%) as a colorless oil.

For **19**:

mp = 91-94 °C.

TLC: R_f (hexanes/EtOAc, 1:1) = 0.20.

¹H-NMR (500 MHz, CDCl₃): δ 3.88 (t, 2H, *J* = 9.5 Hz), 3.74 (s, 3H), 2.97 (t, 2H, *J* = 6.5 Hz), 2.77 (t, 2H, *J* = 9.5 Hz), 2.49 (t, 2H, *J* = 6.5 Hz), and 1.88 (tt, 2H, *J* = 6.5, 6.5 Hz).

¹³C-NMR (125 MHz, CDCl₃): δ 168.9, 166.5, 152.5, 108.4, 51.3, 44.5, 32.4, 26.7, 23.6, and 19.5.

IR: 2954, 1694, 1675, 1621, 1407, 1260, 1241, and 1186 cm⁻¹.

MS: ESI-MS calcd for C₁₀H₁₄NO₃ (M•H⁺) 196.0968, found 196.0960.

For **17a**:

TLC: R_f (hexanes/EtOAc, 1:1) = 0.15.

¹H-NMR (500 MHz, CDCl₃): δ 3.84 (ddd, 1H, *J* = 12.0, 8.5, 8.5 Hz), 3.68 (s, 3H), 3.54 (ddd, 1H, *J* = 12.0, 10.0, 3.0 Hz), 3.18 (dd, 1H, *J* = 7.5, 1.0 Hz), 2.45 (dddd, 1H, *J* = 18.0, 6.5, 1.5, 1.5 Hz), 2.26 (ddd, 1H, *J* = 18.5, 12.0, 7.5 Hz), 2.20 (dddd, 1H, *J* = 13.0, 9.5, 9.0, 7.5 Hz), 2.00-2.14 (nfom, 3H), 1.78 (dddd, 1H, *J* = 13.0, 7.5, 3.5, 3.5, 2.0 Hz), 1.49 (ddd, 1H, *J* = 13.5, 13.5, 4.0 Hz), and 0.16 (s, 9H).

Pure **18a** TLC: R_f (hexanes/EtOAc, 1:1) = 0.11

¹H-NMR (500 MHz, CDCl₃): δ 3.74 (s, 3H, OMe), 3.59-3.55 (m, 2H, H3 β and H3 α), 2.84 (dd, 1H, *J* = 12.0, 8.0 Hz, H1 α), 2.52-2.39 (m, 3H, H2, H6 β , H8 β), 2.32 (ddd, 1H, *J* = 18.5, 11.5, 7.5, H6 α), 2.06 (dddd, 1H, *J* = 13.5, 8, 7, 3.5 Hz, H2), 1.99 (dddd, 1H, *J* =

18a (E = CO₂Me)

15.0, 14.0, 11, 7.0, 3.5 Hz, H7 β), 1.85 (dddddd, 1H, J = 13, 7.5, 3.5, 3.5, 1.0 Hz, H7 α), 1.60 (ddd, 1H, J = 13.5, 13.5, 4.0 Hz, H8 α), and 0.09 (s, 9H, TMS).

^1H -NMR (500 MHz, C_6D_6 , referenced to residual $\text{C}_6\text{D}_5\text{H}$ at δ 7.16): δ 3.45-3.34 (m, 2H, H3 β and H3 α), 3.29 (s, 3H, OMe), 2.33-2.21 (m, 4H, H2, H6 β , H8 β , H1 α), 2.00 (ddd, 1H, J = 19.0, 12.0, 7.5, H6 α), 1.69 (dddd, 1H, J = 15.0, 14.0, 11.5, 6.5, 3.5 Hz, H7 β), 1.48 (nfom, 1H, H2), 1.23 (dddddd, 1H, J = 14.0, 7.5, 3.5, 3.5, 1.5 Hz, H7 α), 1.06 (ddd, 1H, J = 13.5, 13.5, 3.5 Hz, H8 α), and 0.02 (s, 9H, TMS).

^{13}C -NMR (75 MHz, CDCl_3): δ 170.1, 169.9, 91.3, 56.6, 52.0, 44.0, 35.3, 31.1, 21.9, 16.9, and 1.5.

IR: 2954, 1741, 1655, 1400, 1253, 1042, and 842 cm^{-1} .

MS: ESI-MS calcd for $\text{C}_{13}\text{H}_{24}\text{NO}_4\text{Si}$ ($\text{M} \cdot \text{H}^+$) 286.1469, found 286.1471.

Methyl (1*R*, 8*aS*)-rel-1,2,3,5,6,7,8,8*a*-octahydro-8*a*-[tris(1-methylethyl)silyl]oxy-5-oxo-(1*H*)-indolizinecarboxylate (17*b*) and methyl (1*R*, 8*aR*)-rel-1,2,3,5,6,7,8,8*a*-octahydro-8*a*-[tris(1-methylethyl)silyl]oxy-5-oxo-(1*H*)-indolizinecarboxylate (18*b*).

Imide ester **16** (160 mg, 0.75 mmol) was dissolved in CH₂Cl₂ (2 mL). Et₃N (173 μ L, 1.24 mmol) and TIPSOTf (267 μ L, 1.00 mmol) were added sequentially to the reaction mixture at 0 °C. The reaction mixture was warmed to rt, stirred for 10 h, then additional Et₃N (90 μ L, 0.65 mmol) and TMSOTf (135 μ L, 0.50 mmol) were added. The resulting mixture was stirred at rt for 7 h, diluted with CH₂Cl₂ (50 mL), and washed sequentially with saturated aqueous solution of NaHCO₃ and brine. Organic layer was dried over Na₂SO₄. Concentration under reduced pressure yielded a mixture of **17b** and **18b** in 1.1:1 ratio, respectively. Chromatography on silica gel with hexanes/EtOAc 1:1 as eluent gave two pure components, listed in the order of elution: **17b** (128 mg, 0.35 mmol, 50%) as colorless oil, **18b** (119 mg, 0.32 mmol, 45%) as a colorless oil.

Pure **17b** TLC: R_f (hexanes/EtOAc, 1:1) = 0.25.

¹H-NMR (300 MHz, CDCl₃): δ 3.94 (ddd, 1H, J = 11.7, 8.7, 8.7 Hz), 3.65 (s, 3H), 3.50 (ddd, 1H, J = 12.6, 9.6, 3.6 Hz), 3.18 (dd, 1H, J = 7.6, 1.9 Hz), 2.42 (ddd, 1H, J = 17.4, 7.0, 2.4 Hz), 2.29-1.97 (nfom, 5H), 1.70 (dddd, 1H, J = 11.0, 7.2, 4.2, 4.2, 2.8 Hz), 1.57 (ddd, 1H, J = 12.8, 12.8, 3.7 Hz), and 1.04 (br s, 21H).

¹³C-NMR (75 MHz, CDCl₃): δ 172.7, 169.5, 92.3, 57.0, 52.1, 44.1, 32.9, 31.0, 23.9, 18.3, and 13.8.

IR: 2949, 2868, 1738, 1661, 1403, 1210, and 1099 cm⁻¹.

MS: ESI-MS calcd for C₁₉H₃₆NO₄Si (M•H⁺) 370.2408, found 370.2416.

Pure **18b** TLC: R_f (hexanes/EtOAc, 1:1) = 0.20.

¹H-NMR (500 MHz, CDCl₃): δ 3.80 (ddd, 1H, J = 12.0, 9.0, 9.0 Hz, H3), 3.72 (s, 3H, OMe), 3.48 (ddd, 1H, J = 12.5, 10.0, 3.0 Hz, H3), 2.77 (dd, 1H, J = 12.0, 8.5 Hz, H1 α), 2.55 (dddd, 1H, J = 13.0, 11.5, 10.0, 9.0 Hz, H2), 2.49-2.43 (m, 2H, H6, H8), 2.33 (ddd, 1H, J = 18.0, 9.5, 6.0 Hz, H6), 2.12-2.04 (m, 2H, H8, H2), 2.01 (m, 1H, H7), 1.78 (nfom, 1H, H7), and 1.05-1.01 (m, 21H).

¹³C-NMR (75 MHz, CDCl₃): δ 170.4, 170.3, 92.3, 56.9, 52.4, 43.6, 35.2, 32.5, 22.8, 18.8, 18.7, 18.3, and 14.4.

IR: 2948, 2868, 1741, 1654, 1403, 1182, and 1045 cm⁻¹.

MS: ESI-MS calcd for C₁₉H₃₆NO₄Si (M•H⁺) 370.2408, found 370.2415.

Methyl (3*S*,4*S*)-3,4-bis(Acetyloxy)-2,5-dioxo-1-pyrrolidinebutanoate (II).

Known D-anhydride **I**³ (1.47 g, 6.8 mmol; prepared from D-tartaric acid and AcCl³) was dissolved in CH₃CN. The hydrochloride salt of methyl 4-aminobutyrate⁴ (1.10 g, 7.2 mmol) was added followed by Et₃N (1.0 μ L, 7.2 mmol). The reaction mixture was stirred for 2 h at room temperature, and the solvent was removed *in vacuo*. Acetyl chloride (10 mL) was added and the reaction mixture was stirred for 2 h at room temperature. Excess acetyl chloride was removed by distillation (at one atmosphere) and the residue was chromatographed on silica gel with hexanes/EtOAc 2:1 as eluent. Pure **II** (1.48 g, 4.7 mmol, 69%) was obtained as a pale yellow oil having an $[\alpha]_D = -68.6^\circ$ (c 8.15, CHCl₃). We also prepared a sample of the L-antipode of **II** starting from L-tartaric acid. The rotation of this sample of L-**II** was: $[\alpha]_D = +66.5^\circ$ (c 0.53, CHCl₃). The L-antipode is reported⁵ to have a rotation of: $[\alpha]_D = -57.2^\circ$ (c 1.0, CHCl₃). A search of the Beilstein database revealed other *N*-alkylated tartarimide bisesters whose specific rotation values are reported; all examples are consistent in having a positive value for each (of 6) of the L-compounds and a negative value for each (of 2) of the D-compounds.

TLC: R_f (hexanes/EtOAc, 1:1) = 0.50.

¹H-NMR (500 MHz, CDCl₃): δ 5.50 (s, 2H), 3.72-3.62 (m, 2H), 3.68 (s, 3H), 2.38 (t, 2H, 7.2 Hz), 2.20 (s, 6H), and 2.02-1.93 (m, 2H).

¹³C-NMR (75 MHz, CDCl₃): δ 173.2, 170.1, 169.6, 72.9, 51.9, 38.9, 31.2, 22.7, and 20.5.

IR: 2958, (~1750 sh), 1728, 1440, 1406, 1374, 1221, and 1060 cm⁻¹.

MS: ESI-MS calcd for C₁₃H₁₇NO₈Na (M•Na⁺) 338.0846, found 338.0842.

Methyl (3*S*,4*S*)-3,4-Dihydroxy-2,5-dioxo-1-pyrrolidinebutanoate (III**).**

bis-Acetoxy D-tartarimide **II** (163 mg, 0.52 mmol) was dissolved in methanol (15 mL) and acetyl chloride (10 μ L) was added via a syringe while stirring. The resulting reaction mixture was refluxed for 24 h and concentrated under reduced pressure to produce a white solid (104 mg, 0.45 mmol, 87%), which was essentially pure **III** by ^1H NMR and TLC analyses. This material had an $[\alpha]_{\text{D}} = -111.4^\circ$ (c 1.04, MeOH). We also prepared a sample of the L-antipode of **III** starting from L-tartaric acid (by way of the L-antipode of **II**). The rotation of this sample of L - **III** was: $[\alpha]_{\text{D}} = +107.7^\circ$ [c 0.49, MeOH]. The L-antipode (i.e., L-**III**) has been previously prepared and was reported⁵ to have a rotation of: $[\alpha]_{\text{D}} = -101.6^\circ$ (c 1.0, MeOH). A search of the Beilstein database revealed other *N*-alkylated tartarimide diols whose specific rotation values are reported; all examples are consistent in having a positive value for each (of 6) of the L-compounds and a negative value for each (of 2) of the D-compounds.

TLC: R_{f} (EtOAc) = 0.57.

mp = 86-90 $^\circ\text{C}$.

^1H -NMR (500 MHz, CDCl_3): δ 4.61 (s, 2H), 3.68 (s, 3H), 3.65 (dt, 1H, 13.2, 6.7 Hz), 3.58 (dt, 1H, 13.6, 6.9 Hz), 3.26 (br s, 2H, variable in chemical shift from sample to sample), 2.37 (t, 2H, 7.1 Hz), 1.97 (dddd, 1H, 13.7, 7, 7, 7, 7 Hz), and 1.94 (dddd, 1H, 14.1, 7, 7, 7, 7 Hz).

^{13}C -NMR (75 MHz, CDCl_3): δ 175.0, 173.9, 74.9, 52.2, 38.4, 31.3, and 22.8.

IR: 3434 (br), 2954, and 1709 cm^{-1} .

MS: ESI-MS calcd for $\text{C}_9\text{H}_{13}\text{NO}_6\text{Na}$ ($\text{M} \cdot \text{Na}^+$) 254.0635, found 254.0627.

Methyl (3*R*,4*R*)-2,5-Dioxo-3,4-bis[(trimethylsilyl)oxy]-1-pyrrolidinebutanoate (20a**).**

To a stirred solution of L-diol **III** (0.300 g, 1.30 mmol) in CH₂Cl₂ (15 mL) under a N₂ atmosphere Et₃N (0.55 mL, 3.90 mmol) and TMSCl (0.46 mL, 3.6 mmol) were added sequentially at 0° C. The resulting solution was warmed up to rt, stirred for 14 h, diluted with CH₂Cl₂ (30 mL), and washed with a saturated solution of NaHCO₃ (10 mL). Organic layer was separated and aqueous layer was extracted back with CH₂Cl₂. Organic layers were combined, washed with brine, dried over Na₂SO₄ and concentrated. The obtained residue was purified by silica gel chromatography with hexanes/EtOAc 6:1 as eluent to give the L-imide ester **20a** (0.380 g, 78%) as a colorless oil having an $[\alpha]_D^{25} = +113.9^\circ$ (c 0.79, CHCl₃). We also prepared the D-antipode **ent-20a** (structure not shown). Its rotation was: $[\alpha]_D^{25} = -109.6^\circ$ (c 1.70, CHCl₃). The L-antipode (i.e., **20a**) is reported⁵ to have a rotation of: $[\alpha]_D^{25} = -109.6^\circ$ (c 1.0, CHCl₃). A search of the Beilstein database revealed two other *N*-alkylated tartarimide bis-silyl ethers whose specific rotation values are reported; both of these -compounds have a positive value.

TLC: R_f (hexanes/EtOAc, 6:1) = 0.35.

¹H-NMR (500 MHz, CDCl₃): δ 4.43 (s, 2H), 3.67 (s, 3H), 3.59 (ddd, 1H, *J* = 13.3, 6.7, 6.7 Hz), 3.51 (ddd, 1H, *J* = 13.4, 7.0, 7.0 Hz), 2.33 (t, 2H, *J* = 7.3 Hz), 2.10 (dddd, 1H, *J* = 14.4, 7.2, 7.2, 7.2 Hz), 1.90 (dddd, 1H, *J* = 13.9, 7.5, 7.5, 7.5 Hz), and 0.24 (s, 18H).

¹³C-NMR (125 MHz, CDCl₃): δ 173.5, 173.2, 76.9, 52.0, 38.2, 31.6, 23.1, and 0.2.

IR: 2957, 2902, 1727, 1362, 1253 1164, 1133, and 847 cm⁻¹.

MS: ESI-MS calcd for C₁₅H₂₉NNaO₆Si₂ (M•Na⁺) 398.1426, found 398.1426.

Methyl (3*R*,4*R*)-2,5-Dioxo-3,4-bis[(triethylsilyl)oxy]-1-pyrrolidinebutanoate (20b).

To a stirred solution of L-diol **III** (0.150 g, 0.650 mmol) in DMF (2 mL) under a N₂ atmosphere imidazole (0.133 g, 1.96 mmol) and TESCl (0.255 g, 1.69 mmol) were added sequentially. The resulting solution was stirred for 48 h at ambient temperature and poured into ice-cold water (10 mL), which was then extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine (2×10 mL), dried over Na₂SO₄, and concentrated in vacuo. The obtained residue was purified by silica gel chromatography with hexanes/EtOAc 6:1 as eluent to give the L-imide ester **20b** (0.178 g, 59%) as a colorless oil.

$[\alpha]_D = +109.8^\circ$ (c 0.52, CHCl₃).

TLC: R_f (hexanes/EtOAc, 6:1) = 0.32.

¹H-NMR (500 MHz, CDCl₃): δ 4.46 (s, 2H), 3.67 (s, 3H), 3.58 (ddd, 1H, *J* = 13.7, 7.0, 7.0 Hz), 3.50 (ddd, 1H, *J* = 13.6, 6.9, 6.9 Hz), 2.34 (t, 2H, *J* = 7.2 Hz), 2.10 (dddd, 1H, *J* = 14.4, 7.1, 7.1, 7.1, 7.1 Hz), 2.05 (dddd, 1H, *J* = 14.1, 7.1, 7.1, 7.1, 7.1 Hz), 1.00 (t, 18H, *J* = 7.8 Hz), 0.90 (dq, 6H, *J* = 15.4, 7.5 Hz), and 0.86 (dq, 6H, *J* = 15.7, 8.0 Hz).

¹³C-NMR (125 MHz, CDCl₃): δ 173.7, 173.2, 77.0, 51.9, 38.1, 31.6, 23.1, 6.8, and 5.0.

IR: 2956, 2914, 2879, 1725, 1164, 1133, and 743 cm⁻¹.

MS: ESI-MS calcd for C₂₁H₄₁NNaO₆Si₂ (M•Na⁺) 482.2365, found 482.2357.

Methyl (3*R*,4*R*)-2,5-dioxo-3,4-bis(benzyloxy)-1-pyrrolidinebutanoate (20b).

To a stirred suspension of methyl γ -aminobutyrate hydrochloride (0.307 g, 2.00 mmol) and L-anhydride **IV**⁶ in CH₃CN (20 mL), Et₃N (0.278 mL, 2.00 mmol) was added. This solution was stirred for 3 h at rt and concentrated under reduced pressure. To the resulting residue AcCl (20 mL) was added, and the solution was heated under reflux overnight, cooled to rt, and filtered through a 2 cm layer of silica gel with EtOAc. The filtrate was concentrated and purified by silica gel chromatography with hexanes/EtOAc 3:1 as eluent, yielding the L-imide **20c** (0.501 g, 61%) as a colorless oil.

$[\alpha]_D = +98.3^\circ$ (c 0.23, CDCl₃).

TLC: R_f (hexanes/EtOAc, 3:1) = 0.30.

¹H-NMR (500 MHz, CDCl₃): δ 7.37–7.31 (m, 10H), 4.98 (d, 2H, $J = 11.0$ Hz), 4.75 (d, 2H, $J = 11.5$ Hz), 4.38 (s, 2H), 3.64 (s, 3H), 3.60 (ddd, 1H, $J = 13.1, 6.8, 6.8$ Hz), 3.53 (ddd, 1H, $J = 13.7, 7.2, 7.2$ Hz), 2.33 (t, 2H, $J = 7.1$ Hz), 1.94 (dddd, 1H, $J = 14.0, 7.1, 7.1, 7.1, 7.1$ Hz), 1.88 (dddd, 1H, $J = 13.9, 7.1, 7.1, 7.1, 7.1$ Hz).

¹³C-NMR (125 MHz, CDCl₃): δ 172.9, 172.8, 136.6, 128.6, 128.3, 78.8, 73.5, 51.8, 38.0, 31.3, and 22.8.

IR: 3064, 3032, 2951, 2876, 1724, 1349, 1121, and 1079 cm⁻¹.

MS: ESI-MS calcd for C₂₃H₂₅NNaO₆ (M•Na⁺) 434.1574, found 434.1584.

Methyl (1*R*,6*R*,7*R*,7*aR*)-7*a*-[[(Trimethylsilyl)oxy]hexahydro-5-oxo-6,7-bis[(trimethylsilyl)oxy]-1*H*-pyrrolizine-1-carboxylate (21*a*) and Methyl (1*S*,6*R*,7*R*,7*aS*)-7*a*-[[(Trimethylsilyl)oxy]hexahydro-5-oxo-6,7-bis[(trimethylsilyl)oxy]-1*H*-pyrrolizine-1-carboxylate (22*a*).

L-Imide ester **20a** (460 mg, 1.23 mmol) was dissolved in CH₂Cl₂ (5 mL). Et₃N (683 μ L, 4.92 mmol) and TMSOTf (666 μ L, 3.69 mmol) were added sequentially to the reaction mixture at 0 °C. The mixture was warmed to rt and stirred for 16 h. Additional Et₃N (256 μ L, 1.85 mmol) and TMSOTf (222 μ L, 1.23 mmol) were added. The resulting mixture was stirred at rt for 6 h and diluted with CH₂Cl₂ (40 mL). This solution was washed sequentially with saturated aqueous NaHCO₃ and brine and dried over Na₂SO₄. GC-MS analysis of this crude mixture indicated a 23:1 ratio of two diastereomers. Chromatography on silica gel with hexanes/EtOAc 3:1 as eluent gave, in order of elution, **21a** (383 mg, 0.86 mmol, 70%) as colorless oil and **22a** (19 mg, 0.05 mmol, 4%) as white crystals.

21a TLC: R_f (hexanes/EtOAc, 6:1) = 0.40.

$[\alpha]_{\text{D}} = +42.8^\circ$ (c 0.9, CHCl₃).

¹H-NMR (300 MHz, CDCl₃): δ 4.44 (ddd, 1H, $J = 7.7, 1.0, 1.0$ Hz), 3.89 (d, 1H, $J = 7.6$ Hz), 3.74 (ddd, 1H, $J = 10.4, 8.3, 8.3$ Hz), 3.68 (s, 3H), 3.25 (br dd, 1H, $J = 10.2, 10.2$ Hz), 3.02 (dd, 1H, $J = 7.2, 1.8$ Hz), 2.40 (dddd, 1H, $J = 13.5, 9.5, 9.5, 7.4$ Hz), 2.24 (dddd, 1H, $J = 13.2, 8.1, 2.2, 2.2$ Hz), 0.20 (s, 9H), 0.17⁺ (s, 9H), and 0.17⁻ (s, 9H).

¹³C-NMR (75 MHz, CDCl₃): δ 172.1, 170.2, 95.9, 79.0, 77.6, 53.8, 52.2, 41.0, 28.6, 2.1, 0.7, and 0.5.

IR: 2959, 2902, 1736, 1253, 1167, and 846 cm⁻¹.

MS: ESI-MS calcd for C₁₈H₃₇NNaO₆Si₃ (M•Na⁺) 470.1821, found 470.1823.

22a TLC: R_f (hexanes/EtOAc, 6:1) = 0.30.

$[\alpha]_{\text{D}} = -50.6^\circ$ (c 0.17, CHCl₃).

mp = 70-73 °C. TLC: R_f (hexanes/EtOAc, 6:1) = 0.30

¹H-NMR (500 MHz, CDCl₃): δ 4.09 (d, 1H, $J = 6.2$ Hz), 3.87 (d, 1H, $J = 6.2$ Hz), 3.68 (ddd, 1H, $J = 11.4, 8.6, 8.6$ Hz), 3.67 (s, 3H), 3.29 (ddd, 1H, $J = 11.4, 9.4, 1.5$ Hz), 3.00 (d, 1H, $J = 6.8$ Hz), 2.54 (dddd, 1H, $J = 13.2, 9.6, 9.6, 7.2$ Hz), 2.27 (dddd, 1H, $J = 13.1, 7.9, 1.9, 1.2$ Hz), 0.18 (s, 9H), 0.17 (s, 9H), and 0.16 (s, 9H).

¹³C-NMR (75 MHz, CDCl₃): δ 172.9, 169.1, 99.3, 76.0, 69.5, 53.8, 52.2, 40.6, 29.8, 2.3, 0.6, and 0.4.

IR: 2957, 1724, 1715, 1250, 1132, and 840 cm⁻¹.

MS: ESI-MS calcd for C₁₈H₃₇NNaO₆Si₃ (M•Na⁺) 470.1821, found 470.1836.

Methyl (1*S*,6*S*,7*S*,7*aS*)-7a-[(Trimethylsilyl)oxy]hexahydro-5-oxo-6,7-bis[(trimethylsilyl)oxy]-1*H*-pyrrolizine-1-carboxylate (ent-21a).

D-Tartarimide **III** (142 mg, 0.61 mmol) was dissolved in CH₂Cl₂ (3 mL). Et₃N (430 μL, 3.1 mmol) was added at rt followed by TMSOTf (440 μL, 2.44 mmol). The reaction mixture was stirred for 24 h and partitioned between CH₂Cl₂ (50 mL) and 5% aqueous solution of NaHCO₃. The aqueous layer was extracted with CH₂Cl₂ (3x25 mL) and the combined organic layers were dried over Na₂SO₄. Concentration of the extract under reduced pressure yielded a brown residue that was chromatographed on silica gel with hexanes/EtOAc 6:1 as eluent to provide **ent-21a** (204 mg, 0.46 mmol, 75%) was obtained as a pale yellow oil.

[α]_D = -42.4° (c 1.36, CHCl₃).

TLC: R_f (hexanes/EtOAc, 4:1) = 0.50.

¹H-NMR (500 MHz, CDCl₃): δ 4.44 (br d, 1H, 7.6 Hz), 3.90 (d, 1H, 7.5 Hz), 3.76 (ddd, 1H, 10.6, 8.5, 8.5 Hz), 3.69 (s, 3H), 3.27 (dddd, 1H, 10.8, 9.1, 2.3, 1.3 Hz), 3.04 (dd, 1H, 7.1, 1.7 Hz), 2.42 (dddd, 1H, 13.1, 9.1, 9.1, 7.2 Hz), 2.25 (dddd, 1H, 13.1, 7.9, 2.0, 2.0 Hz), 0.21 (s, 9H), 0.18 (s, 9H), and 0.17 (s, 9H).

¹³C-NMR (125 MHz, CDCl₃): δ 171.9, 170.0, 95.8, 78.9, 77.4, 53.6, 52.0, 40.9, 28.5, 1.9, 0.5, and 0.4.

IR: 2958, 2902, and 1734 cm⁻¹.

MS: ESI-MS calcd for C₁₈H₃₇NO₆Si₃Na (M•Na⁺) 470.1821, found 470.1826.

Methyl (1*R*,6*R*,7*R*,7*aR*)-7a-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]hexahydro-5-oxo-6,7-bis[(trimethylsilyl)oxy]-1*H*-pyrrolizine-1-carboxylate (21b).

L-Imide ester **20a** (300 mg, 0.8 mmol) was dissolved in CH_2Cl_2 (3 mL). Et_3N (390 μL , 3.6 mmol) and TBSOTf (550 μL , 3.2 mmol) were added sequentially to the reaction mixture at 0 °C. The mixture was warmed to rt and stirred for 2 h. Additional Et_3N (220 μL , 1.6 mmol) and TBSOTf (280 μL , 1.2 mmol) were added. The resulting mixture was stirred at rt for 20 h and diluted with CH_2Cl_2 (20 mL). This solution was washed sequentially with saturated aqueous NaHCO_3 and brine and dried over Na_2SO_4 . GC-MS analysis of this crude mixture indicated a 24:1 ratio of two diastereomers. MPLC on silica gel with hexanes/ EtOAc 6:1 as eluent gave **21b** (297 mg, 0.61 mmol, 76%) as a colorless oil having an $[\alpha]_{\text{D}} = +58.5^\circ$ (c 0.68, CHCl_3). Lit.⁵: $[\alpha]_{\text{D}} = +51.6^\circ$ (c 1.0, CHCl_3).

For **21b**:

TLC: R_{f} (hexanes/ EtOAc , 6:1) = 0.30.

$^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 4.45 (ddd, 1H, $J = 8.0, 1.0, 1.0$ Hz), 3.91 (d, 1H, $J = 8.0$ Hz), 3.77 (ddd, 1H, $J = 11.0, 8.5, 8.5$ Hz), 3.69 (s, 3H), 3.25 (dddd, 1H, $J = 10.5, 9.0, 3.0, 1.5$ Hz), 3.03 (dd, 1H, $J = 7.0, 2.5$ Hz), 2.41 (dddd, 1H, $J = 13.0, 9.0, 9.0, 7.5$ Hz), 2.24 (dddd, 1H, $J = 13.5, 8.0, 3.0, 3.0$ Hz), 0.88 (s, 9H), 0.21 (s, 9H), 0.17 (s, 9H), 0.16 (s, 3H), and 0.12 (s, 3H).

GC-MS (Start temp = 50 °C, run time = 21 min, temp. ramp = 11.4 °C/min): $t_{\text{R}} = 12.9$ min; m/z : 343 (M^+), 328 ($\text{M}^+ - \text{CH}_3$).

Methyl (1*R*,6*R*,7*R*,7*aR*)-7*a*-[(Trimethylsilyl)oxy]hexahydro-5-oxo-6,7-bis[(triethylsilyl)oxy]-1*H*-pyrrolizine-1-carboxylate (21c**)**

To a solution of L-imide ester **20b** (0.060 g, 0.131 mmol) in CDCl_3 (0.6 mL), Et_3N (54 μL , 0.388 mmol) and TMSOTf (63 μL , 0.318 mmol) were added sequentially. This mixture was kept at ambient temperature and monitored by ^1H NMR spectroscopy. After 48 h the reaction mixture (dr 23:1 by GC-MS) was diluted with CH_2Cl_2 (15 mL), washed sequentially with aq NaHCO_3 (2 $\times$ 15 mL) and brine (2 $\times$ 10 mL), dried over Na_2SO_4 , concentrated in vacuo, and purified by silica gel chromatography with hexanes/ EtOAc 6:1 as eluent to give **21c** (0.040 g, 58%) as a colorless oil.

$[\alpha]_{\text{D}} = +61.0^\circ$ (c 0.10, CHCl_3).

TLC: R_f (hexanes/ EtOAc , 6:1) = 0.35.

^1H -NMR (500 MHz, CDCl_3): δ 4.51 (ddd, 1H, $J = 7.0, 1, 1$ Hz), 3.91 (d, 1H, $J = 7.0$ Hz), 3.79 (ddd, 1H, $J = 10.4, 10.4, 7.9$ Hz), 3.66 (s, 3H), 3.22 (dddd, 1H, $J = 11.1, 9.3, 1.4, 1.4$ Hz), 3.02 (d, 1H, $J = 7.0$ Hz), 2.44 (dddd, 1H, $J = 13.3, 9.7, 9.7, 7.2$ Hz), 2.22 (dddd, 1H, $J = 13.2, 7.6, 1.3, 1.3$ Hz), 0.99 (t, 18H, $J = 8.0$ Hz), 0.88 (ddd, 3H, $J = 15.2, 7.6, 7.6$ Hz), 0.83 (ddd, 3H, $J = 16.2, 8.0, 8.0$ Hz), 0.81 (q, 6H, $J = 7.9$ Hz), and 0.14 (s, 9H).

^{13}C -NMR (125 MHz, CDCl_3): δ 172.3, 171.1, 95.7, 79.8, 77.1, 54.4, 52.0, 41.6, 28.3, 6.93, 6.85, 5.2, 4.9, and 1.5.

IR: 2956, 2913, 2879, 1737, 1249, 1149, 843, and 744 cm^{-1} .

MS: ESI-MS calcd for $\text{C}_{24}\text{H}_{49}\text{NNaO}_6\text{Si}_3$ ($\text{M} \cdot \text{Na}^+$) 554.2760, found 554.2744.

Methyl (1*R*,6*R*,7*R*,7*aR*)-7*a*-[(Trimethylsilyl)oxy]hexahydro-5-oxo-6,7-bis(benzyloxy)-1*H*-pyrrolizine-1-carboxylate (21*d*) and Methyl (1*S*,6*R*,7*R*,7*aS*)-7*a*-[(Trimethylsilyl)oxy]hexahydro-5-oxo-6,7-bis[(benzyl)oxy]-1*H*-pyrrolizine-1-carboxylate (22*d*).

L-Imide **20c** (74 mg, 0.18 mmol) was dissolved in CDCl_3 (0.6 mL). $i\text{Pr}_2\text{NEt}$ (103 μL , 0.59 mmol) and TMSOTf (98 μL , 0.54 mmol) were added sequentially to the reaction mixture at rt and stirred for 4 h. Additional $i\text{Pr}_2\text{NEt}$ (67 μL , 0.40 mmol) and TMSOTf (66 μL , 0.36 mmol) were added. The resulting mixture was stirred at rt for 40 h, diluted with CH_2Cl_2 (20 mL), and washed sequentially with a saturated aqueous solution of NaHCO_3 and brine. Organic layer was dried over Na_2SO_4 . The solution was concentrated and purified by silica gel chromatography with hexanes/EtOAc 4:1 as eluent, yielding a mixture (76 mg, 87%) of **21d** and **22d** in 11:1 ratio as a colorless oil.

For the major diastereomer **21d**:

$[\alpha]_{\text{D}} = +64.7^\circ$ (c 0.36, CDCl_3).

TLC: R_f (hexanes/EtOAc, 3:1) = 0.35.

^1H -NMR (500 MHz, CDCl_3): δ 7.39–7.27 (m, 10H), 4.99 (d, 1H, $J = 12.0$ Hz), 4.76 (d, 1H, $J = 12.0$ Hz), 4.70 (d, 1H, $J = 11.5$ Hz), 4.49 (dt, 1H, $J = 8.0, 1.2$ Hz), 4.46 (d, 1H, $J = 11.0$ Hz), 3.86 (d, 1H, $J = 7.5$ Hz), 3.82 (ddd, 1H, $J = 10.6, 8.6, 8.6$ Hz), 3.57 (s, 3H), 3.26 (dddd, 1H, $J = 11.2, 9.3, 1.7, 1.7$ Hz), 3.08 (dd, 1H, $J = 7.1, 1.5$ Hz), 2.45 (dddd, 1H, $J = 13.1, 9.2, 9.2, 7.3$ Hz), 2.28 (dddd, 1H, $J = 13.2, 8.0, 1.7, 1.7$ Hz), and 0.08 (s, 9H).

^{13}C -NMR (75 MHz, CDCl_3): δ 172.1, 170.3, 137.9, 137.7, 128.51, 128.49, 128.4, 128.03, 127.94, 127.91, 95.2, 82.4, 81.0, 72.7, 72.3, 55.1, 52.3, 41.5, 28.6, and 1.2.

IR: 3063, 3031, 2954, 2901, 1731, 1721, 1355, 1115, and 842 cm^{-1} .

MS: ESI-MS calcd for $\text{C}_{26}\text{H}_{34}\text{NO}_6\text{Si}$ ($\text{M} \cdot \text{H}^+$) 484.2150, found 484.2150.

Resonances from the minor isomer consistent with structure **22d** (cf. ^1H NMR data from **22a**): δ 4.18 (d, 1H, $J = 4.0$ Hz) 4.02 (d, 1H, $J = 4.0$ Hz), 3.30 (m, 1H), 3.00 (d, 1H, $J = 8.4$ Hz), ~ 2.55 (m, 1H), and 2.10 (br dd, 1H, $\Sigma J = 21$ Hz).

Methyl (1*R*,6*R*,7*R*,7*aR*)-7a-[(1,1-Dimethylethyl)dimethylsilyl]oxy}hexahydro-5-oxo-6,7-dihydroxy-1*H*-pyrrolizine-1-carboxylate (24**).**

A solution of *bis*-trimethylsilyl ether **21b**⁵ (220 mg, 0.45 mmol) in THF (6 mL) was treated with AcOH (0.2 mL) and aqueous HCl (1.0 M, 0.2 mL) at 0 °C. The resulting solution was stirred for 20 min at rt, diluted with EtOAc (20 mL), washed sequentially with water (2×2 mL) and aqueous NaHCO₃ (1 mL), dried over Na₂SO₄, and concentrated in vacuo. The resulting residue was purified by silica gel chromatography with EtOAc as eluent, yielding pure **24** (65 mg, 42%) as white crystals.

mp = 111-115 °C.

[α]_D = +17.0° (c 0.27, MeOH).

TLC: R_f (hexanes/EtOAc, 1:1) = 0.20.

¹H-NMR (500 MHz, CDCl₃): δ 4.40 (ddd, 1H, *J* = 8.5, 3.3, 1.0 Hz), 3.98 (ddd, 1H, *J* = 11.9, 7.8, 3.7 Hz), 3.89 (dd, 1H, *J* = 8.7, 8.5 Hz), 3.76 (s, 3H), 3.19 (dddd, 1H, *J* = 11.4, 8.8, 6.9, 1.3 Hz), 3.14 (dd, 1H, *J* = 8.9, 7.4 Hz), 2.85 (d, 1H, *J* = 8.9 Hz), 2.61 (d, 1H, *J* = 3.3 Hz), 2.28 (dddd, 1H, *J* = 13.3, 7.5, 6.9, 3.7 Hz), 2.17 (dddd, 1H, *J* = 13.1, 8.7, 8.7, 7.7 Hz), 0.94 (s, 9H), 0.22 (s, 3H), and 0.15 (s, 3H).

¹³C-NMR (125 MHz, CDCl₃): δ 173.5, 170.7, 95.4, 78.8, 76.2, 54.1, 52.8, 43.0, 29.3, 25.8, 18.3, -3.15 and -3.05.

IR: 3425, 3292, 2953, 2930, 2859, 1732, 1713, 1354, 1291, 1223, and 1120 cm⁻¹.

MS: ESI-MS calcd for C₁₅H₂₇NNaO₆Si (M•Na⁺) 368.1500, found 368.1499.

A sample for single crystal x-ray analysis was obtained by dissolving 20 mg of **24** in ~1.0 mL of ethyl acetate in a small test tube. The tube was immersed in a larger screw-capped jar containing hexanes to a depth of ~1 cm. The jar was capped and stored at room temperature. After several days, suitable crystals had grown inside the tube.

Methyl (3*S*)-3-Acetyloxy-2,5-dioxo-1-pyrrolidinebutanoate (VI).

Anhydride **V**⁷ (1.19 g, 7.5 mmol) was dissolved in CH₃CN and the hydrochloride salt of methyl 4-aminobutyrate (1.21 g, 7.9 mmol) was added followed by Et₃N (1.1 mL, 7.9 mmol). The reaction mixture was stirred for 2 h, and the solvent was removed *in vacuo*. Acetyl chloride (15 mL) was added and the reaction mixture was stirred for 2 h. Excess acetyl chloride was removed by distillation (at one atmosphere), and the residue was chromatographed on silica gel with hexanes/EtOAc 2:1 as eluent. Imide **VI** (1.30 g, 5.1 mmol, 67%) was obtained as pale yellow oil.

$[\alpha]_D = -12.5^\circ$ (c 3.12, CHCl₃).

TLC: R_f (hexanes/EtOAc, 1:1) = 0.29.

¹H-NMR (500 MHz, CDCl₃): δ 5.40 (dd, 1H, *J* = 8.7, 4.8 Hz), 3.68 (s, 3H), 3.63 (ddd, 1H, *J* = 13.5, 6.7, 6.7 Hz), 3.62 (ddd, 1H, *J* = 13.6, 6.7, 6.7 Hz), 3.15 (dd, 1H, *J* = 18.3, 8.8 Hz), 2.68 (dd, 1H, *J* = 18.3, 4.5 Hz), 2.37 (t, 2H, *J* = 7.3 Hz), 2.17 (s, 3H), and 1.95 (pent, 2H, *J* = 7 Hz).

¹³C-NMR (75 MHz, CDCl₃): δ 173.7, 173.4, 173.1, 170.0, 67.7, 51.8, 38.4, 35.7, 31.3, 22.8, and 20.6.

IR: 2953, 1714 cm⁻¹.

MS: ESI-MS calcd for C₁₁H₁₅NO₆Na (M•Na⁺) 280.0792, found 280.0790.

Methyl (3*S*)-3-Hydroxy-2,5-dioxo-1-pyrrolidinebutanoate (25).

Acetate **VI** (287 mg, 1.12 mmol) was dissolved in methanol (20 mL) and acetyl chloride (10 μ L) was added while stirring. The resulting reaction mixture was heated under reflux for 48 h, cooled, and concentrated under reduced pressure to produce **25** as a clear oil (208 mg, 0.97 mmol, 86%) that was of excellent purity (^1H NMR and TLC analyses).

$[\alpha]_{\text{D}} = -56.0^\circ$ (c 3.16, CHCl_3).

TLC: R_{f} (EtOAc) = 0.54.

^1H -NMR (500 MHz, CDCl_3): δ 4.63 (m, 1H), 3.68 (s, 3H), 3.60 (ddd, 1H, $J = 13.5, 6.8, 6.8$ Hz), 3.59 (ddd, 1H, $J = 13.5, 6.7, 6.7$ Hz), 3.06 (dd, 1H, $J = 18.2, 8.4$ Hz), 2.97 (br s, 1H), 2.68 (dd, 1H, $J = 18.2, 4.7$ Hz), 2.36 (t, 2H, $J = 7.2$ Hz), and 1.94 (pent, 2H, $J = 7.1$ Hz).

^{13}C -NMR (125 MHz, CDCl_3): δ 178.8, 174.7, 173.3, 66.9, 51.9, 38.1, 37.4, 31.3, and 22.8.

IR: 3461 (br), 2953, $\sim$ 1725 (sh), and 1703 cm^{-1} .

MS: ESI-MS calcd for $\text{C}_9\text{H}_{13}\text{NO}_5\text{Na}$ ($\text{M} \cdot \text{Na}^+$) 238.0686, found 238.0687.

(4*R*,5*R*)-*rel*-5-Methoxy-4,5-bis[(trimethylsilyl)oxy]-1,3(2*H*,5*H*)-indolizinedione (28**).**

Malimide **25** (39 mg, 0.18 mmol) was dissolved in CDCl₃ (0.5 mL) and the solution was transferred to an NMR tube. Et₃N (125 μL, 0.90 mmol) was added and the tube was shaken to ensure proper mixing. TMSOTf (129 μL, 0.72 mmol) was added and the tube was capped and shaken well. After the disappearance of the *in situ* and immediately formed *O*-TMS ether of **25** was observed (ca. 1 h) by ¹H NMR analysis (by disappearance of CHOTMS), the solution was partitioned between 5% aqueous NaHCO₃ (30 mL) and CH₂Cl₂ (40 mL). The aqueous layer was extracted with more CH₂Cl₂ (2x20 mL) and dried over Na₂SO₄. This extract was concentrated and GC-MS analysis of the residue showed only one peak with *m/z* corresponding to the molecular ion and the fragmentation pattern consistent with **28**. The residue was filtered through a plug of silica gel with hexanes/EtOAc/Et₃N 40:10:1 as eluent to give **28** (55 mg, 0.18 mmol, 100%, d.r. 14:1⁸) that was ca. 90% pure by ¹H NMR analysis. Attempts to further purify **28** on a preparative MPLC column with the same eluent resulted in 24 mg (44% recovery) of **28** having essentially the same level of purity. Such behavior suggests decomposition on silica gel.

[α]_D = -2.1° (c 1.17, CHCl₃). If it arises entirely by the mechanism offered in Scheme 7 of the manuscript, then the sample of **28** should be racemic. We would suggest that the observed small rotation arises from residual amounts of chiral, non-racemic impurities. The lability of this silyloxy ketal precluded more extensive purification.

TLC: R_f (hexanes/EtOAc, 1:1) = 0.66.

¹H-NMR (500 MHz, CDCl₃): δ 4.21 (ddd, 1H, *J* = 13.2, 4.4, 1.5 Hz), 3.11 (s, 3H), 3.06 (d, 1H, *J* = 21.4 Hz), 2.82 (dd, 1H, *J* = 22.0, 1.5 Hz), 2.77 (dddd, 1H, *J* = 13.2, 13.2, 2.9, 1.5 Hz), 1.94-1.91 [nfom, 2H (*J*s from spectrum in 1:1 C₆D₆:CDCl₃ are: ddd, 1H, 13.7, 13.7, 3.9 Hz and dddd, 1H, 13.9, 4.0, 3.0, 1.1 Hz)], 1.68 [dddd, 1H, *J* = 13.2, 13.2, 13.2, 5.1, 3.9 Hz (*J*s from spectrum in 1:1 C₆D₆:CDCl₃)], 1.56 (dddd, 1H, *J* = 13.3, 3.6, 3.6, 3.6, 1.5 Hz), 0.21 (s, 9H), and 0.13 (s, 9H).

¹³C-NMR (125 MHz, CDCl₃): δ 204.2, 168.2, 105.0, 100.1, 48.2, 41.8, 35.4, 28.1, 22.3, 2.3, and 1.4.

IR: 2957, 1782, 1711 cm⁻¹.

MS: ESI-MS calcd for C₁₅H₂₉NO₅Si₂Na (M•Na⁺) 382.1476, found 382.1495.

Methyl 2,5-Dioxo-3-trimethylsilyl-1-pyrrolidinebutanoate (31a), Methyl (3*R*, α *R*)-rel-2,5-Dioxo-3-trimethylsilyl-1-pyrrolidine(α -trimethylsilyl)butanoate (31b) and Methyl (3*S*, α *R*)-rel-2,5-Dioxo-3-trimethylsilyl-1-pyrrolidine(α -trimethylsilyl)butanoate (31c).

Succinimide ester **29** (40 mg, 0.24 mmol) was dissolved in CDCl_3 (0.5 mL), and Et_3N (100 μL , 0.7 mmol) and TMSOTf (126 μL , 0.69 mmol) were added at rt. The reaction mixture was stirred for 24 h, and additional Et_3N (55 μL , 0.22 mmol) and TMSOTf (72 μL , 0.20 mmol) were added. The mixture was stirred at rt for 48 h, diluted with CH_2Cl_2 (10 mL), and washed sequentially with a saturated aqueous solution of NaHCO_3 and brine. The organic layer was dried over Na_2SO_4 . The solution was concentrated and purified by silica gel chromatography with hexanes/ EtOAc 3:1 as eluent, yielding, in order of elution, **31b** (28 mg, 0.088 mmol, 30%), **31c** (26 mg, 0.076 mmol, 30%), and **31a** (9 mg, 0.033 mmol, 13%), as colorless oils. Compounds **31b** and **31c** are separable by silica gel chromatography, however, we could not assign their relative configurations.

For **31b**:

TLC: R_f (hexanes/ EtOAc , 3:1) = 0.25.

^1H -NMR (500 MHz, CDCl_3): δ 3.67 (s, 3H), 3.51 (app t, 2H, J = 7 Hz), 2.85 (dd, 1H, J = 18.5, 9.8 Hz), 2.50 (dd, 1H, J = 18.8, 3.6 Hz), 2.35 (dd, 1H, J = 9.6, 3.4 Hz), 2.06 (dddd, 1H, J = 13.6, 12.2, 6.2, 6.2 Hz), 1.96 (dd, 1H, J = 12.2, 2.7 Hz), 1.68 (dddd, 1H, J = 13.4, 7.4, 7.4, 2.5 Hz), 0.15 (s, 9H), and 0.06 (s, 9H).

^{13}C NMR (75 MHz, CDCl_3): δ 179.6, 177.6, 175.0, 51.3, 38.8, 34.9, 31.8, 31.1, 25.0, -2.5, and -3.0.

IR: 2954, 2901, 1763, 1692, 1398, 1252, and 1193 cm^{-1} .

MS: ESI-MS calcd for $\text{C}_{15}\text{H}_{29}\text{NNaO}_4\text{Si}_2$ ($\text{M}\cdot\text{Na}^+$) 366.1527, found 366.1527.

GC-MS (Start temp = 50 $^\circ\text{C}$, run time = 21 min, temp. ramp = 11.4 $^\circ\text{C}/\text{min}$): t_R = 11.0 min; m/z : 343 (M^+), 328 ($\text{M}^+ - \text{CH}_3$).

For **31c**:

TLC: R_f (hexanes/ EtOAc , 3:1) = 0.22.

^1H -NMR (500 MHz, CDCl_3): δ 3.69 (s, 3H), 3.55 (ddd, 1H, J = 13.0, 7.3, 4.7 Hz), 3.48 (ddd, 1H, J = 13.3, 7.3, 7.3 Hz), 2.84 (dd, 1H, J = 18.5, 9.6 Hz), 2.52 (dd, 1H, J = 18.6, 3.2 Hz), 2.36 (dd, 1H, J = 9.7, 3.3 Hz), 2.05 (dddd, 1H, J = 13.5, 12.0, 7.3, 4.9 Hz), 1.96 (dd, 1H, J = 12.2, 2.6 Hz), 1.67 (dddd, 1H, J = 13.5, 7.3, 7.3, 2.4 Hz), 0.14 (s, 9H), and 0.06 (s, 9H).

^{13}C -NMR (75 MHz, CDCl_3): δ 179.7, 177.7, 175.0, 52.0, 38.8, 34.8, 31.3, 31.0, 25.0, -2.5, and -3.0.

IR: 2957, 1717, 1693, 1399, 1252, and 1194 cm^{-1} .

MS: ESI-MS calcd for $\text{C}_{15}\text{H}_{29}\text{NNaO}_4\text{Si}_2$ ($\text{M}\cdot\text{Na}^+$) 366.1527, found 366.1531.

GC-MS (Start temp = 50 °C, run time = 21 min, temp. ramp = 11.4 °C/min): t_R = 11.1 min; m/z : 343 (M^+), 328 ($M^+ - CH_3$).

For **31a**:

TLC: R_f (hexanes/EtOAc, 3:1) = 0.12.

1H -NMR (500 MHz, $CDCl_3$): δ 3.67 (s, 3H), 3.56 (ddd, 1H, J = 13.3, 7.0, 7.0 Hz), 3.53 (ddd, 1H, J = 13.3, 7.0, 7.0 Hz), 2.86 (dd, 1H, J = 18.6, 9.7 Hz), 2.51 (dd, 1H, J = 18.6, 3.2 Hz), 2.35 (dd, 1H, J = 9.7, 3.2 Hz), 2.31 (t, 2H, J = 7.4 Hz), 1.87 (pent, 2H, J = 7.2 Hz), and 0.12 (s, 9H).

^{13}C -NMR (125 MHz, $CDCl_3$): δ 179.6, 177.6, 173.2, 51.9, 38.0, 31.8, 31.5, 31.1, 23.3, and -3.0.

IR: 2957, 1760, 1738, 1690, 1437, 1399, 1252, and 1175 cm^{-1} .

MS: ESI-MS calcd for $C_{12}H_{21}NNaO_4Si$ ($M \cdot Na^+$) 294.1132, found 294.1127.

GC-MS (Start temp = 50 °C, run time = 21 min, temp. ramp = 11.4 °C/min): t_R = 11.1 min; m/z : 271 (M^+), 256 ($M^+ - CH_3$).

Supporting Information References

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- ⁸ Resonances consistent with a second (minor) diastereomer were observed in the 1H and ^{13}C NMR spectra; however, a second peak was not observed by capillary GC.