Stereoselective synthesis of bicyclic lactones by annelation with functionalised orthoesters.

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Electronic Supporting Information.

Instrumentation and procedures.
Routine nuclear magnetic resonance (NMR) spectra were recorded on a VARIAN GEMINI-300 (\(^1\)H 300MHz and \(^{13}\)C 75MHz). \(^1\)H NMR chemical shifts (\(\delta_{\text{H}}\)) are reported in ppm downfield from internal tetramethyl silane (TMS). \(^{13}\)C NMR spectra were recorded using CDCl\(_3\) as the internal standard. Splitting patterns in \(^1\)H spectra are designed as s, singlet; d, doublet; t, triplet; b, broad and m, multiplet.

Low resolution mass spectra (EI) were recorded using VARIAN MATT-44 and FINNIGAN MAT-TSQ 70 spectrometers.

Infra-red spectra (IR) were taken as thin films on a SHIMADZU spectrometer and recorded in cm\(^{-1}\).

Thin layer chromatography (TLC) was performed on MERCK silica gel 60 F\(_{254}\) aluminum-backed plates. The plates were visualised using 254 nm UV light and developed using an alkaline KMnO\(_4\) solution (1% KMnO\(_4\)/5% Na\(_2\)CO\(_3\)). Flash chromatography was performed using Rocc silica gel 60 (40-63 µm) under pressure with the stated solvents.

All solvents were routinely distilled prior to use. Reactions were performed under a dry, inert atmosphere of argon unless stated otherwise.

The following abbreviations are used: rt, room temperature; hr, hour; min, minute; mmol, millimole; mol, mole; mg, milligram; g, gram; mL, milliliter, µL, microliter.
Typical experimental procedures.

Condensation step: Preparation of 7c

![Chemical structure of 7c]

To a suspension of ZnCl$_2$ (116 mg, 0.85 mmol, 0.7 eq.) in CH$_2$Cl$_2$ (5 mL) at -78°C are sequentially added with stirring orthoester 6c (480 mg, 1.82 mmol, 1.5 eq.) and furan derivative 5a (0.2 mL, 1.2 mmol, 1 eq.). The mixture is slowly warmed to rt and monitored by TLC. Upon completion, the reaction is quenched by adding 5 mL of a sat. NaHCO$_3$ solution. The aqueous layer is repeatedly extracted with CH$_2$Cl$_2$, dried (MgSO$_4$) and concentrated under reduced pressure. Purification by rapid flash chromatography (silica, PE/AcOEt 4:1) afforded 7c (385 mg, 95%).

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.54 (dd, $J = 5.7$, 1.8 Hz, 1 H), 6.126 (dd, $J = 5.7$, 2.1 Hz, 1 H), 5.08 (br s, 1 H), 3.61-3.22 (m, 6 H), 1.92-1.66 (m, 4 H), 1.24-1.11 (m, 6 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 172.7, 154.5, 122.0, 100.8, 84.0, 56.8, 56.7, 33.9, 27.2, 21.1, 15.5, 15.1; IR(cm$^{-1}$): 2975, 2362, 1759, 1732, 1596, 1443, 1375; MS (APCI+ev): m/z (%): 262 (100) [M-OEt]$^+$, 233 (50), 227 (25), 181 (20), 153 (20), 111 (15); HRMS (ES) calcd. for C$_{12}$H$_{19}$O$_4$NaBr (M+Na): 329.0364; found 329.0363.

Cyclisation step: Preparation of 8b

![Chemical structure of 8b]

To a solution of 7c (200 mg, 0.65 mmol, 1 eq.) in benzene (6.5 mL) were sequentially added in one portion TTMSS (0.31 mL, 1.0 mmol, 1.5 eq) and AIBN (16 mg, 0.1 mmol, 0.15 eq.) and the mixture was refluxed for 2 hours. After cooling, removal of the solvent under reduced pressure and flash chromatography of the residue (silica, PE/AcOEt 6:1) afforded 8b (130 mg, 88%).

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 4.36 (d, $J = 3.9$ Hz, 1 H), 3.60-3.45 (m, 4 H), 2.60-5.52 (m, 2 H), 2.34-2.28 (m, 1 H), 1.82-1.40 (m, 6 H), 1.23-1.17 (m, 6 H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 176.7, 98.1, 79.9, 55.5, 55.4, 36.8, 35.0, 28.5, 26.6, 19.2, 15.3, 15.2; IR(cm$^{-1}$): 2972, 2927, 2854, 1786, 1662; MS (APCI+ev): m/z (%): 183 (100) [M-OEt]$^+$, 169 (25), 155 (35), 137 (15), 123 (15), 109 (20), 95 (30), 81 (12); Elemental analysis calcd. for C$_{12}$H$_{20}$O$_4$: C 63.18%; H 8.84%; found C 62.74%; H 8.86%. 