Intramolecular photocyclisation reactions of 5-*tert*-butyldimethylsilyloxymethyl-3-(3-formylpropyl)furan-2(5*H*)-one: formation of bicyclic and spirobicyclic lactones

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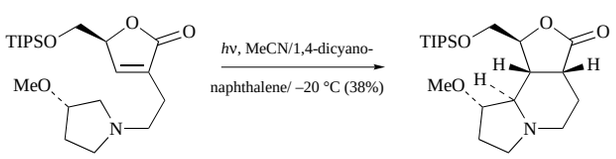
5-*tert*-Butyldimethylsilyloxymethyl-3-(3-formylpropyl)furan-2(5*H*)-one has been synthesised and upon irradiation yields either one homochiral bicyclic lactone or a mixture of spirobicyclic lactones (in modest yield) depending upon the irradiation conditions.

During the past five years we have revealed something of the scope and synthetic utility of photoinduced addition reactions of alcohols and amines to furan-2(5*H*)-ones (Scheme 1).[1] We have recently reported an intramolecular variant of one of these processes,[2] the reaction shown in Scheme 2; and in order to explore further the scope of intramolecular additions, we have prepared the substrate **1** and studied its reactions under photoirradiation.

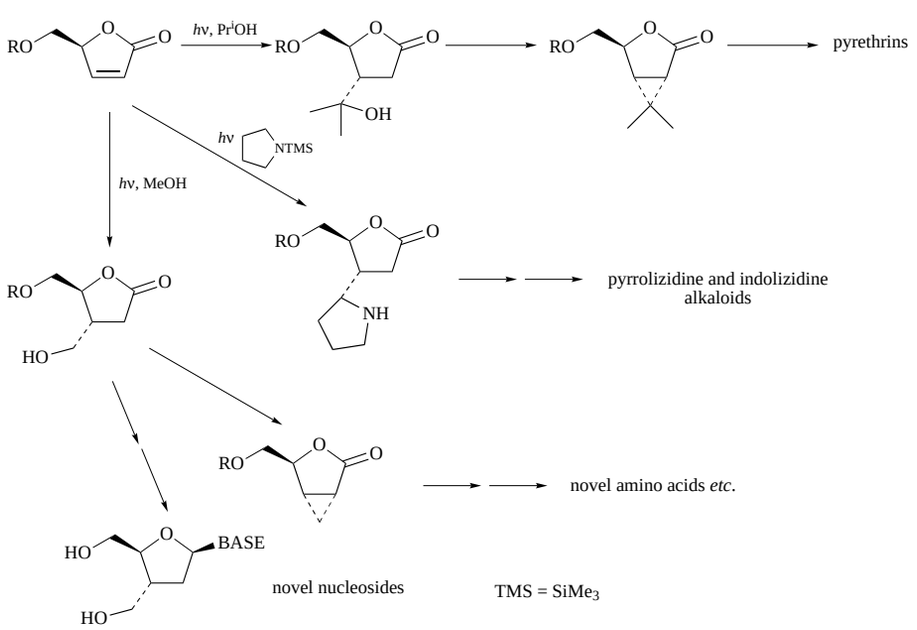
The synthetic route to compound **1** is illustrated in Scheme 3. ε-Caprolactone was converted into methyl 6-benzyloxyhexanoate **2** in a two-stage process (65% overall yield) that involved initial formation of 6-benzyloxyhexanoic acid followed by esterification with methanol. The ester enolate was produced using LDA and this was reacted with (*R*)-glyceraldehyde acetonide[3] to provide a mixture of alkylation products **3** (45% yield). From the NMR spectrum it was clear that this mixture contained all four possible stereoisomers but these were inseparable. Addition of acidic methanol effected cleavage of the acetonide moiety with concomitant formation of a mixture of lactones, and the residual primary hydroxy group was converted into its *tert*-butyldimethylsilyl (TBDMS) ether **4**, once again as an inseparable mixture (67% for the two steps). Subsequent treatment with methanesulfonyl chloride in the presence of triethylamine provided the butenolide **5** as the sole isolated product in 66% yield after chromatography. The stereochemical purity of this butenolide was assessed using the shift reagent tris[3-heptafluoropropylhydroxymethylene-(+)-camphorato]europium(III) which produced a spectrum with one discrete set of signals. The integrity of the H-5 proton was assessed further by varying the time and temperature of the elimination reaction, but this did not affect the value of the specific rotation of the isolated product.

Successful removal of the benzyl group without affecting the double bond was achieved through the use of transfer hydrogenation[4] (5% formic acid in methanol with a 5% Pd on carbon catalyst) to yield the butenolide **6** (67%). Finally, oxidation of the alcohol using pyridinium chlorochromate (PCC) in CH_2Cl_2 provided the desired substrate **1** (86%) for photoirradiation. Once again the specific rotation of this compound did not change by more than 1–2° between experiments.

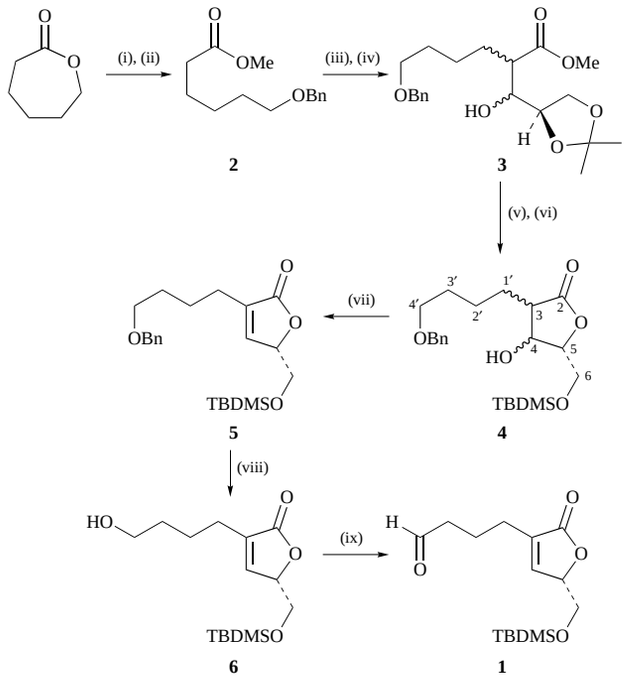
Photoexcitation of compound **1** using a low pressure mercury vapour lamp and acetonitrile as solvent, or a medium pressure lamp and acetone as solvent,[5] produced the two



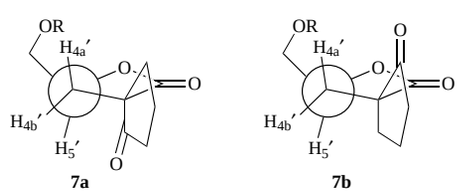
Scheme 2



Scheme 1



Scheme 3 *Reagents and conditions*: (i), Excess BnCl, excess KOH, toluene, reflux; (ii), $SOCl_2$–MeOH (65% overall two steps); (iii), LDA–THF; (iv), (2*R*)-glyceraldehyde acetonide (45% overall); (v), MeOH–acid; (vi), TBDMSCl–imidazole–CH_2Cl_2, 0 °C (67% overall); (vii), MsCl–Et_3N (66%); (viii), 5% HCO_2H–MeOH–Pd on C; (ix), PCC–CH_2Cl_2 (58% overall)



Preferred conformation of spirobicyclic isomers suggested by ^{1}H NMR spectroscopy

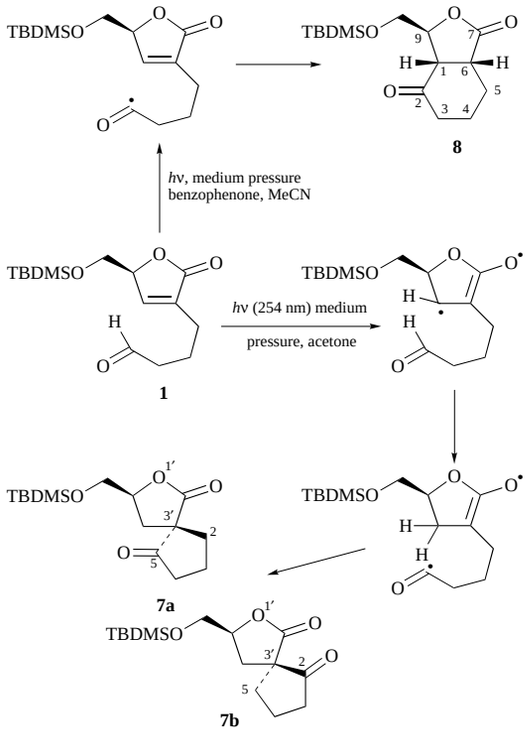
Table 1 ^{1}H NMR Chemical shifts and coupling constants for spirocycles **7a**,**b**

Proton	δ_H **7a**	δ_H **7b**
H-4a′	2.13 $J_{4',5'}$ 8.1, J_{gem} 13	2.54 $J_{4',5'}$ 7.9, J_{gem} 13
H-4b′	2.47 $J_{4',5'}$ 7.5, J_{gem} 13	2.05 $J_{4',5'}$ 7.0, J_{gem} 13
H-5′	4.73–4.77	4.52–4.58

spirobicyclic lactones **7a**,**b** in isolated yields of around 15 and 10% respectively (together with *ca.* 50% of unreacted starting material). The probable mechanism of the photoreaction is shown in Scheme 4. The identity of the two compounds was initially established through extensive NMR studies, though the structure of the lactone **7b** was subsequently confirmed by X-ray diffraction (ORTEP structure shown in Fig. 1). In the ^{1}H NMR spectrum, the signals for H-4a′ and H-4b′ † showed small but significant differences in their $J_{4',5'}$ values, and from the Karplus equation we would expect the value for H-4a′ (dihedral angle with H-5′ of *ca.* 150°) would be greater than for H-4b′ (8.1 and 7.9 Hz *versus* 7.5 and 7.0 Hz for compounds **7a** and **7b** respectively). The anisotropic effect of the carbonyl group is therefore clearly seen in the respective δ values for H-4a′ and H-4b′ in the two compounds (see Table 1).

When the aldehyde **1** was subjected to chemical photosensitisation using benzophenone in acetonitrile (medium pressure mercury vapour lamp), a 6-*endo-trig* cyclisation occurred to yield a single cycloadduct **8** in 38% isolated yield (and around 50% of unreacted starting material). That one discrete product had been produced was apparent from the ^{1}H NMR spectrum (Fig. 2), which clearly showed an absence of spurious signals, but also because the specific rotation remained constant between experiments. The stereochemistry was evident from an NOE experiment which showed a 10% enhancement between H-1 and H-6 and no enhancement between H-1 and H-9. This photocyclisation clearly needs optimisation but it does provide access to a homochiral, bicyclic species that would not be easily obtained *via* a Diels–Alder process.

† For the purposes of assignments in the ^{1}H NMR spectra, see Scheme 3 (compound **4**) and Scheme 4 (compound **7a**). However, the IUPAC numbering system has been used for the construction of names.



Scheme 4

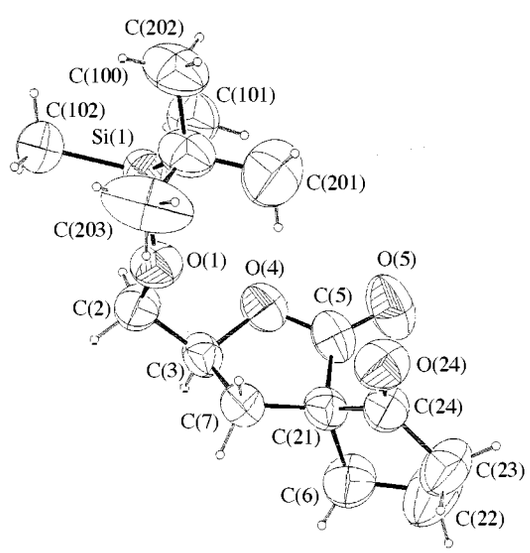


Fig. 1 ORTEP structure of **7b**

Experimental

IR spectra were recorded using a Perkin-Elmer 881 series double beam spectrophotometer. Low resolution and accurate mass data were recorded on VG Autospec or VG7070F spectrometers. Elemental analyses were carried out by Medac Ltd.

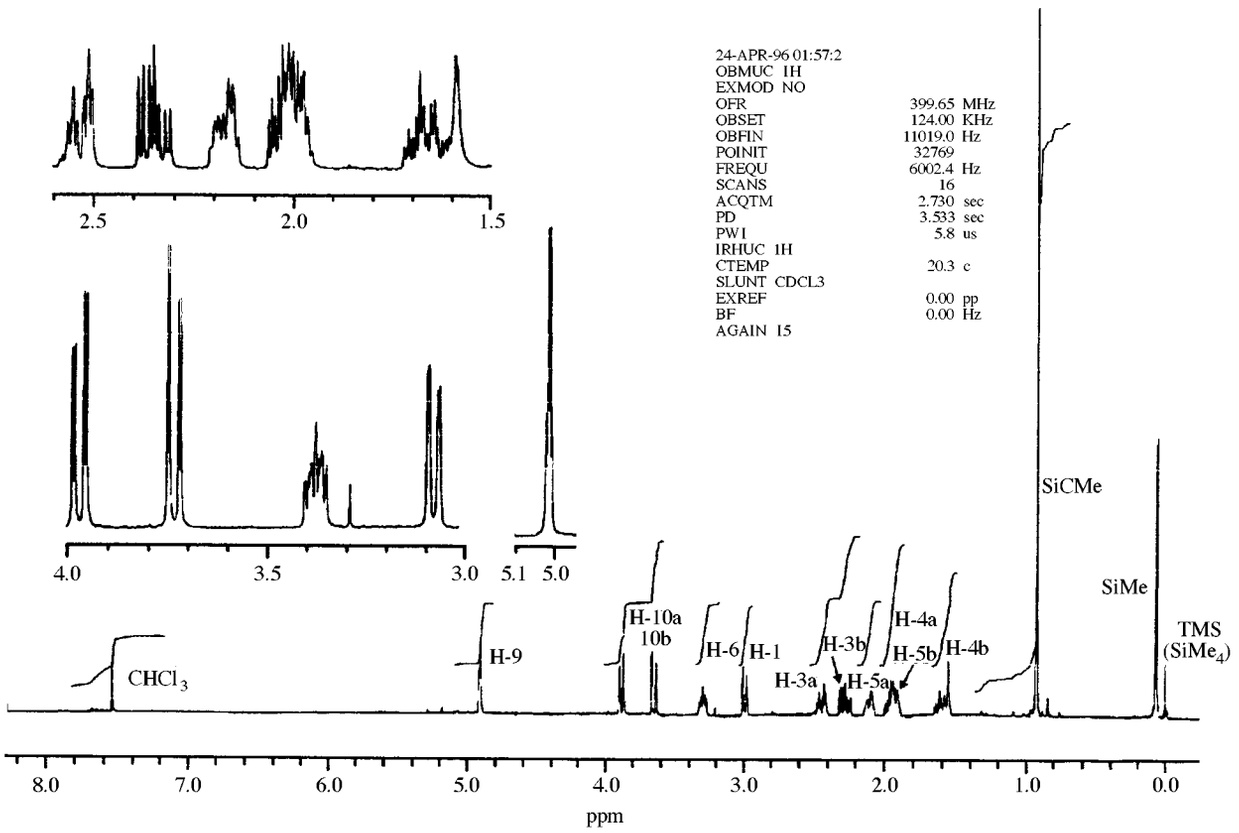


Fig. 2 400 MHz ^{1}H NMR Spectrum of (1*S*,6*R*,9*S*)-9-*tert*-butyldimethylsilyloxymethyl-8-oxabicyclo[4.3.0]nonane-2,7-dione **8**

Optical rotations were measured at room temperature on a Perkin-Elmer 341 polarimeter. NMR spectra were recorded using JEOL EX400, Bruker DPX 250 or Bruker WM250 spectrometers; NOE experiments were carried out at the University of Edinburgh on a Varian VXR600S instrument. *J* Values are given in Hz. All compounds (for which data are provided) were homogeneous by TLC using two solvent systems and by two-dimensional TLC analysis. Light petroleum refers to the fraction boiling between 40–60 °C.

The X-ray crystallographic data were collected with Mo-Kα radiation using the MARresearch Image Plate System.‡ The crystal was positioned at 70 mm from the Image Plate and 95 frames were measured at 2° intervals with a counting time of 2 min. Data analysis was carried out with the XDS programme.[6] The structure was solved using direct methods with the SHELX86 programme.[7] The non-hydrogen atoms were defined with anisotropic thermal parameters. The hydrogen atoms were included in geometric positions and given thermal parameters equivalent to 1.2 times those of the atom to which they were attached. The structure was then refined using SHELXL.[8] All calculations were carried out on a Silicon Graphics R4000 Work Station at the University of Reading.

Methyl 6-benzyloxyhexanoate 2

ε-Caprolactone (20 g, 175 mmol) was dissolved in toluene (300 ml) and KOH pellets (85% KOH–H_2O, *ca.* 3 equiv., 34 g) were added, followed by benzyl chloride (*ca.* 3 equiv, 60 ml). The mixture was refluxed for 6 h and allowed to cool to room temp. Water (300 ml) was added and the mixture was washed with hexane (3 × 50 ml). The aqueous layer was acidified with concentrated sulfuric acid and extracted with ethyl acetate (3 × 100 ml). These extracts were dried with magnesium sulfate and filtered. Removal of the solvent under reduced pressure gave 6-benzyloxyhexanoic acid (31.2 g, 77%) as a clear yellow oil containing a small quantity (1.2 g) of benzyl alcohol; ν_{max}(neat)/cm^{-1} 3500–2500s, br, 2939vs, 2863vs, 1711vs, 1454s, 1100s, 736s, 698s; δ_H($CDCl_3$, 400 MHz) 1.39–1.47 (2H, m, 2 × H-4), 1.60–1.69 (4H, m, 2 × H-3, 2 × H-5), 2.35 (2H, t, $J_{2,3}$ 7.5, 2 × H-2), 3.47 (2H, t, $J_{6,5}$ 6.6, 2 × H-6), 4.50 (2H, s, PhCH_2), 7.27–7.37 (5H, m, PhH).

Thionyl chloride (6.5 ml, 90 mmol) was added dropwise to methanol (AnalaR; 300 ml) under argon while stirring in an ice bath. Crude 6-benzyloxyhexanoic acid (10 g) was added dropwise in methanol (AnalaR; 10 ml) and the reaction allowed to warm to room temp. overnight. The solvents were removed under reduced pressure and the residue was taken into ethyl acetate (100 ml). The solution was washed with water (3 × 50 ml) and brine (50 ml), and dried over magnesium sulfate. The solvents were removed under reduced pressure to give a slightly yellow clear oil containing the desired product and a small quantity of benzyl alcohol. Purification by dry column chromatography (gradient light petroleum ⟶ 4:1 light petroleum–diethyl ether) gave methyl 6-benzyloxyhexanoate **2** as a colourless oil (10.2 g, 95%); ν_{max}(neat)/cm^{-1} 2943s, 2860s, 1738vs, 1454s, 1436s, 1364s, 1203s, 1167s, 1102s, 737s, 698s; δ_H($CDCl_3$, 400 MHz) 1.37–1.45 (2H, m, 2 × H-4), 1.57–1.69 (4H, m, 2 × H-3, 2 × H-5), 2.31 (2H, t, $J_{2,3}$ 7.5, 2 × H-2), 3.47 (2H, t, $J_{6,5}$ 6.6, 2 × H-6), 3.66 (3H, s, OMe), 4.50 (2H, s, PhCH_2), 7.27–7.34 (5H, m, PhH).

Condensation of 2,3-*O*-isopropylidene-D-glyceraldehyde with methyl 6-benzyloxyhexanoate 2 to give methyl 6-benzyloxy-2-[(2*R*)-1-hydroxy-2,3-*O*-isopropylidenepropyl]hexanoate 3

A solution of diisopropylamine (1 equiv., 5.00 ml) in dry THF (200 ml) under argon was cooled to −78 °C, and *n*-BuLi (titrated to 2.54 M solution in hexanes, 1 equiv., 15.0 ml) was added. After stirring the solution for 30 min, methyl 6-benzyloxyhexanoate **2** (1 equiv., 9.00 g, 38.0 mmol) was added in dry THF (50 ml) at −78 °C *via* a double-headed needle. After stirring for a further

‡ Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc.*, *Perkin Trans. 1*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/158.

20 min a solution of 2,3-*O*-isopropylidene-D-glyceraldehyde (1.1 equiv., 5.45 g, 42.0 mmol) was added in dry THF (10 ml) at −78 °C. After stirring for a further 3 h at low temperature the reaction was quenched with saturated aqueous ammonium chloride (100 ml), and diethyl ether (100 ml) was added. The mixture was separated, and the aqueous layer extracted with diethyl ether (3 × 50 ml). The combined organic extracts were dried over magnesium sulfate and filtered. The solvents were removed under reduced pressure to give a cloudy yellow oil (11.2 g), which was purified by flash column chromatography (1:1 light petroleum–diethyl ether) to give recovered starting material (1.25 g, 14%), a colourless oil which corresponded to methyl 3-oxo-8-benzyloxy-2-(4-benzyloxybutyl)octanoate (1.92 g, 22%), and a colourless oil which corresponded to methyl 6-benzyloxy-2-[(2*R*)-1-hydroxy-2,3-*O*-isopropylidenepropyl]hexanoate **3** (6.20 g, 44%) as an inseparable mixture of stereoisomers. For the former compound; ν_{max}(neat)/cm^{-1} 2939vs, 2860vs, 1743vs, 1714vs, 1454s, 1363w, 1274s, 1204s, 1103vs, 737s, 698s [HRMS (CI+) Calc. for MH$^+$, 441.2641. Found MH$^+$: 441.2620]. For compound **3**: ν_{max}(neat)/cm^{-1} 3475s, br, 2986s, 2936s, 2864s, 1735vs, 1454s, 1371s, 1210s, 1067vs, 698s [HRMS (CI+) Calc. for *MH*$^+$, 367.2121. Found MH$^+$: 367.2103].

Hydrolysis and ring closure of adduct 3 to give (5*S*)-5-hydroxymethyl-3-(4-benzyloxybutyl)-4-hydroxytetrahydrofuran-2-one, followed by protection to give (5*S*)-5-*tert*-butyldimethylsilyloxymethyl-3-(4-benzyloxybutyl)-4-hydroxytetrahydrofuran-2-one 4

The ester **3** (16.8 g) was dissolved in methanolic sulfuric acid (1% soln in MeOH of 30% aqueous sulfuric acid, 200 ml) and stirred for 1$\frac{3}{4}$ h. Solid potassium carbonate was added to neutralise the solution, and the mixture was filtered. Removal of the solvent under reduced pressure gave a residue which was taken into CH_2Cl_2 and dried over magnesium sulfate. The mixture was filtered, and the solvents removed under reduced pressure to give a yellow–orange gum. Purification by flash chromatography (1:1 light petroleum–ethyl acetate) gave (5*S*)-5-hydroxymethyl-3-(4-benzyloxybutyl)-4-hydroxytetrahydrofuran-2-one (11.7 g, 87%) as an inseparable mixture of stereoisomers; ν_{max}($CHCl_3$)/cm^{-1} 3391s, br, 3016s, 2934s, 2862s, 1772vs, 1448s, 1360s, 1164s, 1092vs; δ_H($CDCl_3$, 400 MHz)† 1.52–1.72 and 1.78–1.84 (6H, 2m, H-1′, H-2′, H-3′), 2.56–2.59 (*ca.* 0.5H, m, H-3), 2.74–2.79 (*ca.* 0.5H, m, H-3), 3.30 (*ca.* 0.5H, m, H-4), 3.50–3.53 (2H, m, H-4′), 3.64–3.88 (2H, m, H-6), 4.10 (*ca.* 0.5H, m, H-4), 4.31 (*ca.* 0.5H, m, H-5), 4.37 (*ca.* 0.5H, m, H-5), 4.49 (2H, s, PhC*H*$_2$), 7.25–7.33 (5H, m, PhH) [HRMS (CI+) Calc. for *MH*$^+$, 295.1545. Found MH$^+$: 295.1532].

(5*S*)-5-Hydroxymethyl-3-(4-benzyloxybutyl)-4-hydroxytetrahydrofuran-2-one (14.6 g, 50.0 mmol) was placed under argon, dissolved in dry CH_2Cl_2 (150 ml) and cooled to 0–5 °C. Imidazole (1.1 equiv., 3.72 g) was added, followed by *tert*-butyldimethylsilyl chloride (1.1 equiv., 8.23 g). The reaction was stirred for 2 h, after which time no starting material was seen to remain. Saturated aqueous ammonium chloride (100 ml) was added, the organic layer separated and washed with water (3 × 25 ml), brine (25 ml), dried over magnesium sulfate and filtered. Removal of the solvent under reduced pressure gave an orange oil which was purified by flash column chromatography (diethyl ether–light petroleum) to give a colourless oil that corresponded to (5*S*)-5-*tert*-butyldimethylsilyloxymethyl-3-(4-benzyloxybutyl)-4-hydroxytetrahydrofuran-2-one **4** (15.6 g, 77%) as an inseparable mixture of stereoisomers: ν_{max}($CHCl_3$)/cm^{-1} 3391w, br, 3013vs, 2931s, 2859s, 2352w, 1773vs, 1460w, 1361w, 1252s, 1098s, 831vs; δ_H($CDCl_3$, 400 MHz)† 0.07, 0.08 (6H, s, $SiMe_3$), 0.88 (9H, s, SiBu^t), 1.48–1.78 (6H, m, H-1′, H-2′, H-3′), 2.58–2.66 (*ca.* 0.5H, m, H-3), 2.71–2.82 (*ca.* 0.5H, m, H-3), 3.45–3.57 (*ca.* 2.5H, m, H-4, H-4′), 3.79–3.93 (2H, m, H-6), 4.09–4.15 (*ca.* 0.5H, H-4), 4.20–4.28 (*ca.* 0.5H, m, H-5), 4.32–4.37 (*ca.* 0.5H, m, H-5), 4.50 (2H, s, PhC*H*$_2$), 7.37–7.38 (5-H, m, PhH) [HRMS (CI+) Calc. for *MH*$^+$, 409.2410. Found MH$^+$: 409.2406].

(5*S*)-5-*tert*-Butyldimethylsilyloxymethyl-3-(4-benzyloxybutyl)-furan-2(5*H*)-one 5

(5*S*)-5-*tert*-Butyldimethylsilyloxymethyl-3-(4-benzyloxybutyl)-4-hydroxytetrahydrofuran-2-one **4** (638 mg, 1.56 mmol) was dissolved in dry CH_2Cl_2 (25 ml) and cooled to 0–5 °C. Dry triethylamine (50% excess, 0.33 ml) was added, followed by methanesulfonyl chloride (10% excess, 0.13 ml). After 45 min the reaction was allowed to reach room temp. and stirred for a further 1 h. Further triethylamine (1 equiv., 0.22 ml) was added. After stirring for 30 min the reaction was quenched with saturated aqueous ammonium chloride (10 ml) and the organic layer separated, washed with water (3 × 10 ml), dried over magnesium sulfate, and filtered. Removal of the solvent under reduced pressure gave a crude oil which was purified by flash column chromatography (light petroleum–diethyl ether 3:2) to give recovered starting material (63 mg, 10%) and (5*S*)-5-*tert*-butyldimethylsilyloxymethyl-3-(4-benzyloxybutyl)-2(5*H*)-one **5** as a colourless oil (335 mg, 55%); $[\alpha]_D$ −56.72 (*c* 1.175, $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 3013s, 2933w, 2849w, 1754vs, 1252s, 1112s, 830s; δ_H($CDCl_3$, 400 MHz)† 0.05 (3H, s, $SiCH_3$), 0.06 (3H, s, $SiCH_3$), 0.86 (9H, $SiCMe_3$), 1.65–1.70 (4H, m, 2 × H-2′, 2 × H-3′), 2.28–2.35 (2H, m, 2 × H-1′), 3.49 (2H, t, $J_{4',3'}$ 6.1, 2 × H-4′), 3.77 (1H, dd, J_{gem} 11.0, $J_{6,5}$ 5.1, H-6), 3.83 (1H, dd, J_{gem} 11.0, $J_{6,5}$ 4.6, H-6), 4.50 (2H, s, PhC*H*$_2$), 4.89–4.92 (1H, m, H-5), 7.03 (1H, d, $J_{4,5}$ 1.5, H-4), 7.26–7.34 (5H, m, PhH) [HRMS (CI) Calc. for *MH*$^+$, 391.2305. Found MH$^+$: 391.2293].

Debenzylation of (5*S*)-5-*tert*-butyldimethylsilyloxymethyl-3-(4-benzyloxybutyl)furan-2(5*H*)-one 5 to give (5*S*)-5-*tert*-butyldimethylsilyloxymethyl-3-(4-hydroxybutyl)furan-2(5*H*)-one 6, followed by oxidation to give (5*S*)-5-*tert*-butyldimethylsilyloxymethyl-3-(4-oxobutyl)furan-2(5*H*)-one 1

(5*S*)-5-*tert*-Butyldimethylsiloxymethyl-3-(4-benzyloxybutyl)-furan-2(5*H*)-one **5** (1.0 g, 2.46 mmol) was placed in methanol (AnalaR; 25 ml). Palladium on charcoal (5%, 300 mg) suspended in methanol (AnalaR; 5 ml) was added, followed by formic acid (1.8 ml). The reaction was vigorously stirred under argon for 5 h. A further 60 mg of catalyst suspended in methanol (AnalaR; 5 ml) was added, followed by formic acid (0.3 ml), and the reaction stirred for a further 16 h. The catalyst was removed by filtering under gravity, and the filtrate neutralised with saturated aqueous sodium hydrogen carbonate. The methanol was removed under reduced pressure and the residue taken into CH_2Cl_2 and dried with magnesium sulfate, then the mixture was filtered again and the solvent removed under reduced pressure. The residue was purified by flash column chromatography (diethyl ether) to give (5*S*)-5-*tert*-butyldimethylsilyloxymethyl-3-(4-hydroxybutyl)furan-2(5*H*)-one **6** as a colourless oil (494 mg, 67%); $[\alpha]_D$ −73.7 (*c* 0.4, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3439s, br, 2931vs, 2859vs, 1755vs, 1651w, 1469s, 1252s, 1125vs, 1062s, 836vs, 772s; δ_H($CDCl_3$, 400 MHz)† 0.06, 0.07 (2 × 3H, s, SiMe), 0.87 (9H, s, $SiCMe_3$), 1.59–1.71 (4H, m, 2 × H-2′, 2 × H-3′), 2.32–2.35 (2H, m, 2 × H-1′), 3.68 (2H, t, $J_{4',3'}$ 5.9, 2 × H-4′), 3.72 (1H, dd, J_{gem} 11.0, $J_{6,5}$ 4.4, H-6), 3.92 (1H, dd, J_{gem} 11.0, $J_{6,5}$ 5.1, H-6), 4.91–4.94 (1H, m, H-5), 7.06 (1H, dd, $J_{4,5}$ 2.9, $J_{4,1'}$ 1.5, H-4) [HRMS (CI+) Calc. for MH$^+$, 301.1385. Found MH$^+$: 301.1386].

(5*S*)-5-*tert*-Butyldimethylsilyloxymethyl-3-(4-hydroxybutyl)-furan-2(5*H*)-one (200 mg, 0.67 mmol) was dissolved in CH_2Cl_2 (5 ml), and added to a suspension of PCC (1.1 equiv., 160 mg) in CH_2Cl_2 (10 ml). The reaction was stirred for 4 h. Diethyl ether (50 ml) was added, and the mixture filtered and washed with further diethyl ether (3 × 10 ml). The combined filtrates were evaporated under reduced pressure to leave a residue which was purified by flash column chromatography (diethyl ether–light petroleum 3:2) to give (5*S*)-5-*tert*-butyldimethylsilyloxymethyl-3-(4-oxobutyl)furan-2(5*H*)-one **1** (170 mg, 86%) as a colourless oil; $[\alpha]_D$ −73.1 (*c* 1.42, $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 2922w, 2850w, 1750vs, 1711s, 1252w, 1125s, 831s; δ_H($CDCl_3$, 250 MHz)† 0.05, 0.07 (2 × 3H, s, SiMe), 0.87 (9H, s,

$SiCMe_3$), 1.88–1.97 (2H, m, H-2′), 2.31–2.38 (2H, m, H-3′), 2.50–2.56 (2H, m, H-1′), 3.73 (1H, dd, J_{gem} 10.8, $J_{6,5}$ 5.0, H-6), 3.93 (1H, dd, J_{gem} 10.8, $J_{6,5}$ 4.4, H-6), 4.94 (1H, m, H-5), 7.09 (1H, dd, $J_{4,5}$ 3.0, $J_{4,1'}$ 1.5, H-4), 9.79–9.80 (1H, m, H-4′) [HRMS (CI+) Calc. for MH^+, 299.1679. Found MH^+: 299.1695]; λ_{max}(EtOH)/nm 223 (ε/dm^3 mol^{-1} cm^{-1} 2600), 273 (160).

Cyclisation of (5*S*)-5-*tert*-butyldimethylsilyloxymethyl-3-(4-oxobutyl)furan-2(5*H*)-one 1a using direct irradiation to give (3*S*,5*S*)-3-*tert*-butyldimethylsilyloxymethyl-2-oxaspiro[4.4]-nonane-1,6-dione 7a and (3*R*,5*S*)-3-*tert*-butyldimethylsilyloxy-methyl-2-oxaspiro[4.4]nonane-1,6-dione 7b

A solution of (5*S*)-5-*tert*-butyldimethylsilyloxymethyl-3-(4-oxobutyl)furan-2(5*H*)-one **1** (50 mg, 0.17 mmol) in acetonitrile (20 ml) was placed in a quartz tube and degassed with a stream of argon for 1 h. The solution was irradiated using low pressure Hg vapour lamps for 1 h. Removal of the solvent and purification of the resultant mixture by flash column chromatography (diethyl ether–hexane) gave (3*S*,5*S*)-3-*tert*-butyldimethylsilyloxymethyl-2-oxaspiro[4.4]nonane-1,6-dione **7a** (5 mg, 10%) as a colourless oil, (3*R*,5*S*)-3-*tert*-butyldimethylsilyloxymethyl-2-oxaspiro[4.4]nonane-1,6-dione **7b** (5 mg, 10%) as colourless crystalline rods, and recovered starting material (*ca.* 25 mg).

7a; $[a]_D$ +45 (*c* 0.20, $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 2954s, 2929s, 1768vs, 1734vs, 1471w, 1462w, 1129s, 387vs; δ_H($CDCl_3$, 400 MHz)† 0.07 (s, 3H, SiMe), 0.08 (3H, s, SiMe), 0.89 (9H, s, $SiCMe_3$), 1.95–2.02 (2H, m), 2.13 (1H, dd, J_{gem} 11.8, $J_{4,4}$ 7.1, H-4′), 2.29–2.39 (2H, m), 2.44–2.51 (1H, m, 1 × H-4′), 2.54–2.61 (2H, m), 3.75 (1H, dd, J_{gem} 11.4, $J_{6,5}$ 3.1, H-6′), 3.81 (1H, dd, J_{gem} 11.6, $J_{6,5}$ 1.7, H-6′), 4.73–4.77 (1H, m, H-5′); δ_C($CDCl_3$, 100 MHz) −5.03 (SiMe), −4.93 (SiMe), 18.75 (Si*C*Me_3), 20.17, 26.24 (C*Me*$_3$), 34.18 (C-4′), 34.95, 37.87, 58.51 (C-1), 63.94 (C-6′), 78.48 (C-5′), 174.40 (C-2′), 214.92 (C-2) [HRMS (EI+) Calc. for M^+ − Bu^t, 241.0896. Found M^+ − Bu^t: 241.0892].

7b; $[a]_D$ +10.3 (*c* 0.845, $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 2954s, 2929s, 1769vs, 1737vs, 1471w, 1462w, 1111s, 838vs; δ_H($CDCl_3$, 400 MHz) 0.09 (6H, s, 2 × SiMe), 0.90 (9H, s, $SiCMe_3$), 1.94–2.07 (3H, m), 2.27–2.37 (2H, m), 2.51–2.60 (3H, m), 3.78–3.87 (2H, m, 2 × H-6′), 4.52–4.58 (1H, m, H-5′); δ_C($CDCl_3$, 100 MHz) −5.42 (SiMe), −5.37 (SiMe), 18.26 (Si*C*Me_3), 19.41, 25.79 (C*Me*$_3$), 34.12 (C-4′), 35.38, 37.43, 56.96 (C-1), 64.45 (C-6′), 78.37 (C-5′), 175 (C-2′), 213.65 (C-5) [HRMS (CI+) Calc. for MH^+, 299.1679. Found MH^+: 299.1668].

Cyclisation of (5*S*)-5-*tert*-butyldimethylsilyloxymethyl-3-(4-oxobutyl)furan-2(5*H*)-one 1 using triplet-sensitising irradiation to give (3*S*,5*S*)-3-*tert*-butyldimethylsilyloxymethyl-2-oxaspiro[4.4]nonane-1,6-dione 7a and (3*R*,5*S*)-3-*tert*-butyl-dimethylsilyloxymethyl-2-oxaspiro[4.4]nonane-1,6-dione 7b

A solution of (5*S*)-5-*tert*-butyldimethylsilyloxymethyl-3-(4-oxobutyl)furan-2(5*H*)-one **1** (50 mg, 0.17 mmol) in freshly distilled acetone (20 ml) was placed in a Pyrex tube, cooled to −40 °C with the aid of an acetonitrile–dry ice slush bath, and degassed with a stream of argon for 1 h. The solution was irradiated using a high pressure Hg vapour lamp for 5 h. Removal of the solvent and purification of the resultant mixture by flash column chromatography (diethyl ether–hexane) gave (3*S*,5*S*)-3-*tert*-butyldimethylsilyloxymethyl-2-oxaspiro-[4.4]nonane-1,6-dione **7a** (8 mg, 16%) as a colourless oil, and (3*R*,5*S*)-3-*tert*-butyldimethylsilyloxymethyl-2-oxaspiro[4.4]-nonane-1,6-dione **7b** (5 mg, 10%) as colourless crystalline rods.

Cyclisation of (5*S*)-5-*tert*-butyldimethylsilyloxymethyl-3-(4-oxobutyl)furan-2(5*H*)-one 1 using chemical-sensitising irradiation to give (1*S*,6*R*,9*S*)-9-*tert*-butyldimethylsilyloxy-methyl-8-oxabicyclo[4.3.0]nonane-2,7-dione 8

A solution of (5*S*)-5-*tert*-butyldimethylsilyloxymethyl-3-(4-oxobutyl)furan-2(5*H*)-one **1** (340 mg, 1.14 mmol) and benzophenone (1 equiv., 208 mg) in acetonitrile (80 ml) was placed in a Pyrex reaction vessel and degassed with a stream of argon for 1 h. The solution was irradiated by a high pressure Hg vapour lamp for $1\frac{1}{4}$ h. Removal of the solvent and purification by flash column chromatography gave recovered starting material (160 mg, *ca.* 45%) and (1*S*,6*R*,9*S*)-9-*tert*-butyl-dimethylsilyloxymethyl-8-oxabicyclo[4.3.0]nonane-2,7-dione **8** (128 mg, 38%) as a colourless oil; $[a]_D$ −14.9 (*c* 0.645, $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 2953s, 2929s, 1768vs, 1712vs, 1470w, 1462w, 1256s, 1170s, 1128s, 837vs, 788vs, 668s; δ_H($CDCl_3$, 400 MHz)† 0.06, 0.07 (2 × 3H, s, SiMe), 0.88 (9H, s, $SiCMe_3$), 1.63–1.71 (1H, m, H-4), 1.97–2.06 (2H, m, H-4, H-5), 2.15–2.19 (1H, m, H-5), 2.51–2.39 (1H, m, H-3), 2.48–2.56 (1H, m, H-3), 3.08 (1H, dd, $J_{1,6}$ 10.7, $J_{1,9}$ 1.5, H-1), 3.29–3.41 (1H, m, H-6), 3.72–3.75 (1H, m, H-10), 3.97 (1H, dd, J_{gem} 11.7, $J_{10,9}$ 2.6, H-10), 5.01–5.03 (1H, m, H-9); δ_C($CDCl_3$, 100 MHz) −5.63, −5.51 (2 × SiMe), 18.23 (Si*C*Me_3), 21.67 (C-4), 23.48 (C-5), 25.80 (SiC*Me*$_3$), 40.53 (C-3), 40.87 (C-6), 49.10 (C-1), 64.83 (C-10), 78.42 (C-9), 177.43 (lactone CO), 208.06 (ketone CO) [HRMS (CI+) Calc. for MNH_4^+, 316.1944. Found MNH_4^+: 316.1942].

Table 2 X-Ray crystal data and structure refinement for compound **7b**

Empirical formula	$C_{15}H_{26}O_4Si$
Formula weight	298.45
Temperature/K	293(2)
Wavelength/Å	0.710 73
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions/Å	a = 6.304(9), b = 12.058(12), c = 24.24(2)
Volume/Å^3	1843(4)
Z	4
Density (calculated)/Mg m^{-3}	1.076
Absorption coefficient/mm	0.136
F(000)	648
θ range for data collection (°)	3.34 to 24.89
Index ranges	$0 \leqslant h \leqslant 7$, $-13 \leqslant k \leqslant 13$, $-28 \leqslant I \leqslant 28$
Reflections collected	4044
Independent reflections	2642 [R(int) = 0.0824]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2642/0/187
Goodness-of-fit on F^2	0.960
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0828, wR_2 = 0.2117
R indices (all data)	R_1 = 0.1212, wR_2 = 0.2542
Largest diff. peak and hole/Å^{-3}	0.338 and −0.612e

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