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Cyclisation of 1,2-dioxines containing tethered hydroxyl and carboxylic acid functionality: synthesis of tetrahydrofurans and dihydrofuran-2(3*H*)-ones

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ABSTRACT

Herein we outline cyclisations of tethered hydroxyl and carboxylic acid moieties onto the olefinic motif of 1,2-dioxines to generate tetrahydrofurans and dihydrofuran-2(3*H*)-ones, whilst maintaining the peroxide linkage intact. This work demonstrates the first examples of intramolecular cyclisation of tethered hydroxyl groupings onto 1,2-dioxines generating functionalised THFs in a highly stereoselective manner and includes improved methods for previously reported carboxylic acid tether cyclisations. Additionally, improved methods for the oxidation of 1,2-dioxines containing tethered alcohols to furnish tethered carboxylic acids are also detailed. Subsequent reduction of the peroxide linkage enables the generation of functionalised tetrahydrofurans and dihydrofuran-2(3*H*)-ones, which are useful building blocks for the construction of natural products.

1. Introduction

The peroxide linkage of six-membered cyclic peroxides is mistakenly viewed as a very sensitive moiety with the general consensus being that installation should be conducted late in any synthetic sequence. This sensitivity is primarily due to the fact that metal-based reagents may induce fragmentation of the peroxide bond,[1] whilst ring opening occurs when the reaction medium is basic.[2] There are only a few reports where the peroxide linkage is installed early in the sequence prior to further chemical manipulation. For example, the recent synthesis of marine natural product 6-epiplakortolide E **1**[3] maintains the peroxide linkage intact throughout four subsequent synthetic steps, including oxidation with Jones Reagent, Figure 1. This example and our own experience in cyclic peroxide chemistry lead us to conclude that it is worthy to extend further the chemical manipulations of organics containing the peroxide moiety, whilst maintaining the peroxide linkage intact, particularly as there are an ever growing number of biologically active peroxide containing natural products.[4]

The Taylor group[2] and Jung et al.[3] have previously demonstrated that cyclisations onto rings containing the peroxide bond are plausible for the synthesis of tetrahydropyrans although both studies were limited in scope.

Figure 1. Synthetic approach used to synthesise 6-epiplakortolide E.

It was envisaged that intramolecular cyclisation of **3** in the presence of electrophilic reagents (NBS, NIS, PhSeCl) would lead to bicyclic fused peroxide furans or dihydrofuranones **4** (Scheme 1). The relative stereochemistry of the bicyclic system should be predictable due to the stereochemistry built into the precursor 1,2-dioxines upon their synthesis. Clearance of X within **4** would furnish bicyclic fused peroxide furans fused dihydrofuran-2(3*H*)-ones of type **5**. Such bicyclic furans and furanones are key intermediates in the synthesis of Hagen's gland lactones and form the cores of the natural products (+)-bassianolone and cephalosporolides E and F vide infra.[5]

Finally, reduction of the peroxide linkage within **5** should afford furans and lactones of type **6** in which the stereochemistry is well defined. Such furans and lactones are at the cores of numerous natural products.[5,6]

2. Results and discussion

The requisite 1,2-dioxines for this study were synthesised in a similar fashion to that outlined previously and proceeded in

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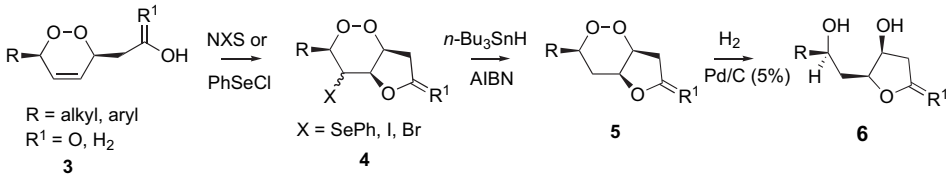
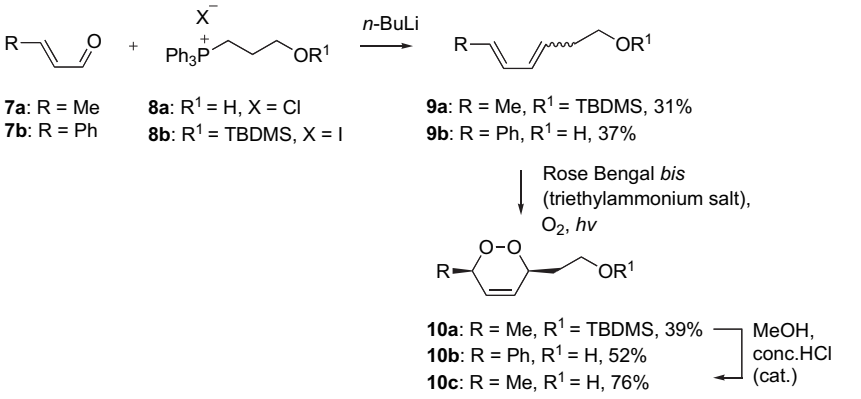


Scheme 1.

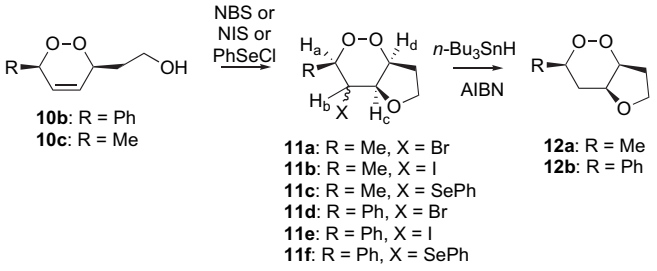
moderate to good overall yields (Scheme 2).[2] To evaluate the effectiveness of tethered hydroxyl cyclisations we chose to investigate both aryl **10b** and alkyl **10c** substituted 1,2-dioxines; noting that aryl substituted 1,2-dioxines can behave very differently under basic conditions to those of alkyl substitution due to the increased acidity of the proton adjacent the peroxide bond.[2b]

The stereochemical variation of X was assigned utilising both 1D ^{1}H NMR and 2D ^{1}H NMR techniques with typically small couplings of $J \approx 3.6$ Hz between H_a and H_b and between H_b and H_c observed. Additionally ROESY 2D ^{1}H NMR of the obtained cis fused furans **11** showed interactions between the proton α to the X group and the methyl or phenyl functional groupings. The stereochemical orientation of the X group resulting in minor amounts of the cis isomers is believed to be a result of an S_N1 process. This variation about X was, however, irrelevant as reduction of **11** resulted in formation of a single product **12a** or **12b**.



Scheme 2.

With the precursor 1,2-dioxines in hand we first examined the possibility of bicyclic furan formation employing NBS, NIS and PhSeCl to initiate cyclisation. This one-pot cyclisation proceeded well to afford bicyclic peroxide furans **11** in moderate to excellent yields (Table 1). The assisting halogen or phenylselenyl group was then removed to furnish peroxide furans **12a**,**b** through reduction with AIBN and tri-*n*-butyltin hydride (Scheme 3, Table 1). Treatment of 1,2-dioxines **10b**,**c** with NBS, NIS and phenylselenyl chloride gave cyclic peroxide furans **11** with varying stereochemistry about the X group. Based on the 1D ^{1}H NMR and 2D ^{1}H NMR analyses, the varying stereochemistry of the two isomers was seen about the group assisting cyclisation and formation of the new furan ring was always found to form in a cis fashion as expected.



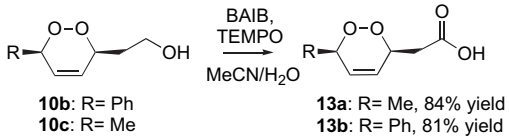
Scheme 3.

Table 1
Cyclisation and concomitant assisting group reduction of 1,2-dioxines **10b** and **10c**

Entry[a]	1,2-Dioxine	Reagent	**11a**–**f** (% Yield) ratio *cis*:*trans*	**12a**,**b** (% Yield)
1	**10b**	NBS	**11d** (51) 0:1	—
2	**10b**	NIS	**11e** (71) Trace:1	**12b** (67)
3	**10b**	PhSeCl	**11f** (38) 1:5	**12b** (55)
4	**10c**	NBS	**11a** (64) Trace:1	**12a** (66)
5	**10c**	NIS	**11b** (62) 1:4	**12a** (89)
6	**10c**	PhSeCl	**11c** (85) Trace:1	**12a** (46)

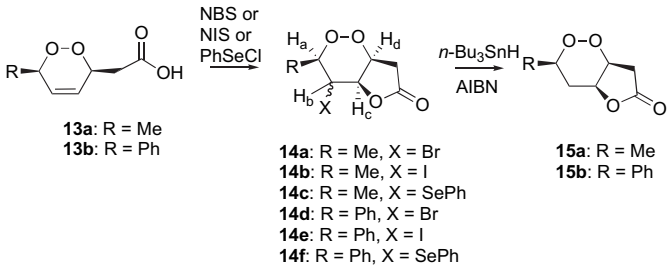
[a] Reagent (2 equiv), CH_2Cl_2. Ambient temp.

With approaches to bicyclic peroxide furans of type **12** now addressed we next turned our attention to developing methodology for the synthesis of bicyclic peroxide lactones of type **14**. Oxidation of alcohols **10b** and **10c** to the requisite carboxylic acids was accomplished with BAIB/TEMPO and proceeded in excellent yields (Scheme 4).



Scheme 4.

Employing the same cyclisation process as for the construction of bicyclic furans proved successful for all examples and provided the bicyclic peroxide lactones **14a–f** in moderate to good yields (Scheme 5, Table 2). Further reduction with tri-*n*-butyltin hydride furnished the desired furanones **15a,b**.



Scheme 5.

Table 2
Cyclisation and concomitant assisting group reduction of 1,2-dioxines **13a** and **13b**

Entry[a]	1,2-Dioxine	Reagent	**14a–f** (% Yield) ratio *cis*:*trans*	**15a,b** (% Yield)
1	**13a**	NBS	**14a** (69) 1:1	**15a** (60)
2	**13a**	NIS	**14b** (76) 0:1	**15a** (81)
3	**13a**	PhSeCl	**14c** (57) 0:1	**15a** (68)
4	**13b**	NBS	**14d** (56) 0:1	**15b** (73)
5	**13b**	NIS	**14e** (56) 0:1	**15b** (62)
6	**13b**	PhSeCl	**14f** (55) 0:1	**15b** (45)

[a] Reagent (2 equiv), CH_2Cl_2. Ambient temp.

In all cases cyclisation proceeded to furnish cis fused lactones with a trans relationship to X as expected except for **13a** (Table 2, entry 1) where a 1:1 mixture of isomers about the X stereocentre was observed. This was irrelevant as reduction of the mixture **14a** resulted in a single product **15a**. 1D ^{1}H NMR and 2D ^{1}H NMR analyses confirmed the orientation of the newly formed lactone ring with typically small couplings of $J \approx 3.0$–4.2 Hz between H_c and H_d indicating a *syn* relationship. Interestingly 1D ^{1}H NMR of the bicyclic lactones **14** showed small couplings of $J \approx 2.4$–3.6 Hz between H_a and H_b as well as between H_b and H_c suggesting a cis relationship. However, ROESY 2D ^{1}H NMR showed interactions between the proton α to the X group and the methyl or phenyl functional groupings indicating a trans relationship.

X-ray crystallography of **14b** supported the stereochemical assignments made by both 1D and 2D ^{1}H NMR showing the X group trans to both the methyl group and lactone ring (Fig. 2).

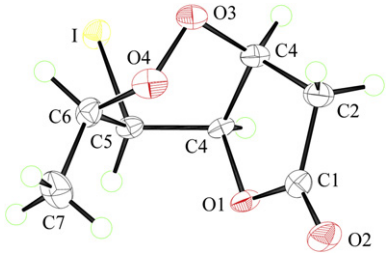
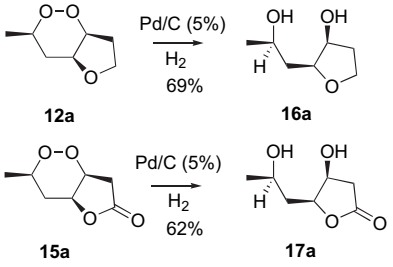


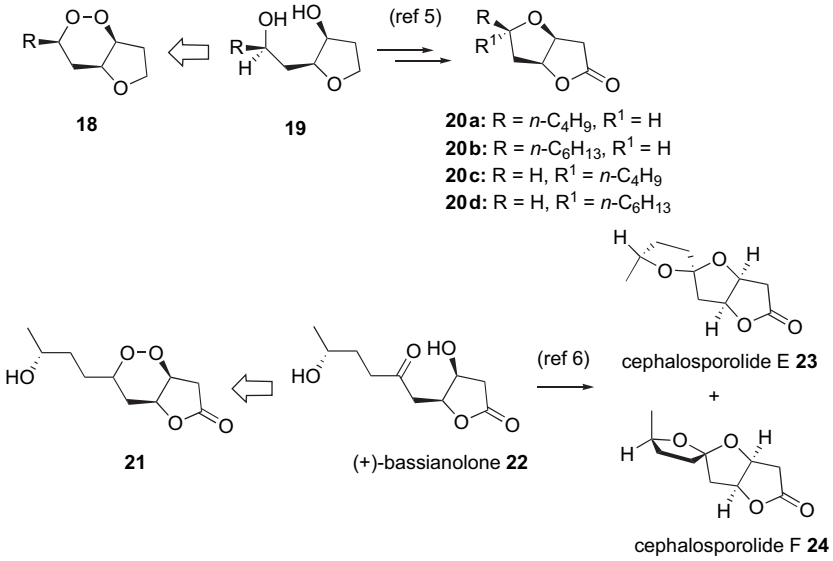
Figure 2. Molecular structure and crystallographic numbering scheme for **14b**.

Finally, the peroxide bonds of **12a** and **15a** were reduced to give diols **16a** and **17a** in 69% and 45% yields, respectively (Schemes 6).



Scheme 6.

The methodology employed to yield diols **16a** and **17a** demonstrates a useful means towards exotic furans and lactones that could be used for the short simple construction of analogues of Hagen's lactones **20**[6] or as building blocks towards natural products (+)-bassianolone **22**,[5] and cephalosporolides E **23** and F **24** (Schemes 7).[5]



Scheme 7.

3. Conclusion

In conclusion, we have shown the versatility of cyclic peroxides with tethered functionality to afford novel tetrahydrofurans and dihydrofuran-2(3*H*)-ones whilst maintaining the peroxide linkage intact. Subsequent removal of the assisting halogen or phenylselenyl group afforded bicyclic peroxide furans or peroxide furanones, which are at the cores of numerous natural products. Reduction of the peroxide linkage to diols of type **16** and **17** has allowed for the generation of a simple methodology towards the synthesis of Hagen's lactones[6] and natural products (+)-bassianolone,[5] and cephalosporolides E and F.[5]

4. Experimental

4.1. General methods

Solvents were dried and purified where needed and according to literature methods. Thin Layer Chromatography (TLC) using Silica gel F_{254} (30 mm×60 mm) from Merck and visualised under 254 nm light or developed in vanillin or permanganate dip. Flash chromatography was conducted using Merck Silica gel 60 of particle size 0.040–0.063 mm. ^{1}H NMR and ^{13}C NMR spectra were conducted in deuterated chloroform on the 300 MHz Brucker ACP-30 or on the 600 MHz Varian INOVA. TMS (0.00 ppm) and $CDCl_3$ (77.00 ppm) were used as internal standards for ^{1}H NMR and ^{13}C NMR analysis. Melting points were taken on a *Reichert* Thermovar Kofler apparatus and are uncorrected. Infrared spectra were recorded on an ATI Mattson Genesis Series FTIR spectrophotometer as either Nujol mulls or neat as denoted. All yields reported are isolated yields judged to be homogeneous by TLC and NMR spectroscopy.

4.2. General procedure for Witting reaction: synthesis of 9a,b

To a stirred solution of the appropriate phosphonium salt (1.1 equiv) in dry THF (4 mL/1 g of salt) under a stream of nitrogen at 0 °C was added dropwise *n*-BuLi (1.1 equiv). After 30 min a solution of the respective aldehyde (1 equiv) in THF (5 mL/1 g of aldehydes) was added dropwise to the solution and stirred for 16 h. Volatiles were removed in vacuo and the crude residue was filtered through a pad of silica. Volatiles were removed in vacuo and the crude residue purified via column chromatography to give the 1,3-butadienes **9a**,**b** as a mixture of *E*/*E* and *E*/*Z* isomers. 1,3-Butadiene **9b**,[7,8] has previously been reported.

*4.2.1. (±) tert-Butyl-[((E)-hepta-3,5-dienyl)oxy]-dimethyl-silane (**9a**).* Yield: 9.5 g, 31% as a yellow oil; R_f 0.40 (1:99 ethyl acetate/hexane); ν_{max} (film)/cm^{-1} 2897, 1610, 1463, 1256, 1104; δ_H (300 MHz; $CDCl_3$) 0.06 (12H, s), 0.89 (18H, s), 1.73 (3H, d, *J*=6.68 Hz), 1.77 (3H, d, *J*=6.72 Hz), 2.33–2.43 (4H, m), 3.56–3.70 (4H, t, *J*=6.9 Hz), 5.30 (1H, q, *J*=7.8 Hz), 5.48–5.77 (3H, m), 5.94–6.1 (3H, m), 6.24–6.42 (1H, m); δ_C (75 MHz; $CDCl_3$) 132.2, 131.6, 130.3, 129.5, 127.9, 127.3, 127.1, 125.3, 63.1, 62.9, 36.3, 31.5, 25.9, 18.4, 18.2, 17.9, −5.3. *Could not obtain *m*/*z* nor HRMS due to rapid decomposition of compound **9a**.

4.3. General procedure for the synthesis of 1,2-dioxines 10a,b

A solution of appropriate 1,3-butadiene (1 equiv) in anhydrous dichloromethane (25 mL/1 g of 1,3-butadiene) was irradiated with light from 3×500 W tungsten–halogen lamps at 0 °C in the presence of rose bengal bis(triethylammonium) salt (0.01 equiv) with oxygen bubbled through the solution for 6 h. The solution was concentrated and the resulting residue purified by flash column chromatography using 1:19 ethyl acetate/hexanes as eluent to yield pure 1,2-dioxine **10a**,**b**.

*4.3.1. (±) tert-Butyl-dimethyl-[2-((3S,6R)-6-methyl-3,6-dihydro-[1,2]-dioxin-3-yl)ethoxy]-silane (**10a**).* Yield: 4.04 g, 39% colourless oil; R_f 0.37 (1:19 ethyl acetate/hexane); ν_{max} (film)/cm^{-1} 2957, 1471, 1255, 1096, 777; δ_H (300 MHz; $CDCl_3$) 0.07 (6H, s), 0.89 (9H, s), 1.23 (3H, d, *J*=6.6 Hz), 1.69–1.79 (1H, m), 1.85–1.95 (1H, m), 3.71–3.81 (2H, m), 4.53–4.58 (1H, m), 4.64–4.71 (1H, m), 5.83–5.91 (2H, m); δ_C (75 MHz; $CDCl_3$) 128.9, 127.7, 75.1, 74.3, 59.1, 36.1, 25.91, 18.3, 18.0, −5.4; HRMS (ESI) $C_{13}H_{26}O_3Si$+Na requires 258.1651, found 258.1656.

*4.3.2. (±) 2-((3S,6S)-6-Phenyl-3,6-dihydro-[1,2]dioxin-3-yl)-ethanol (**10b**).* Yield: 1.27 g, 52% as a colourless oil; R_f 0.40 (2:3 ethyl acetate/hexane); ν_{max} (film)/cm^{-1} 3120–3610, 1676, 1602; δ_H (300 MHz; $CDCl_3$) 1.89–2.31 (2H, m), 2.34 (1H, br s), 3.75–3.89 (2H, m), 4.76–4.79 (1H, m), 5.59 (1H, d, *J*=1.5), 6.08–6.16 (2H, m), 7.29–7.48 (5H, m); δ_C (75 MHz; $CDCl_3$) 136.9, 129.0, 128.6 (×2), 128.2, 126.9, 80.4, 76.6, 59.5, 35.7; *m*/*z* (EI) (M^+ 206, 6%), 174(100), 143(73), 105(41), 77(56); HRMS (ESI) $C_{12}H_{14}O_3$+Na requires 229.0841, found 229.0837.

4.4. General procedure for deprotection of 1,2-dioxines: synthesis of 1,2-dioxines 10c

To a solution of 1,2-dioxine (1 equiv) in methanol (10 mL/1 g of 1,2-dioxine) was added concentrated HCl (four drops/1 g of 1,2-dioxine) and stirred until complete via TLC. The volatiles were removed in vacuo and the crude residue was purified by column chromatography to give the desired 1,2-dioxines **10c**.

*4.4.1. (±) 2-((3S,6R)-6-Methyl-3,6-dihydro-[1,2]dioxin-3-yl)-ethanol (**10c**).* Yield: 1.71 g, 76% as a colourless oil; R_f 0.51 (2:3 ethyl acetate/hexane); ν_{max} (film)/cm^{-1} 3100–3580, 3043, 2932, 2876, 1657; δ_H (300 MHz; $CDCl_3$) 1.25 (3H, d, *J*=6.6 Hz), 1.82–2.09 (3H, m), 3.79–3.86 (2H, m), 4.61–4.65 (1H, m), 4.68–4.75 (1H, m), 5.86–5.89 (2H, m); δ_C (75 MHz; $CDCl_3$) 129.3, 127.0, 76.5, 74.4, 59.5, 35.7, 17.9; *m*/*z* (EI) (M+H^+ 145, 9%), 112(100), 95(13), 81(58), 71(7), 55(4); HRMS (ESI) $C_7H_{12}O_3$+Na requires 167.0684, found 167.0680.

4.5. General procedure for formation of 1,2-dioxines 13a,b

To a solution of 1,2-dioxine (1 equiv) in acetonitrile/water (1:1, 20 mL/1 g of 1,2-dioxine) was added BAIB (2.2 equiv) and TEMPO (0.2 equiv) in a single portion, protected from light and stirred until complete via TLC. The mixture was extracted using ethyl acetate (4×30 mL) followed by 5% $NaHCO_3$ (4×30 mL). The aqueous solution was acidified using concentrated HCl and extracted using ethyl acetate (4×30 mL). The organic layer was then dried ($MgSO_4$), filtered and the volatiles were removed in vacuo. The crude residue was purified by column chromatography to give the desired 1,2-dioxines **13a**,**b**.

*4.5.1. (±) ((3S,6R)-6-Methyl-3,6-dihydro-[1,2]dioxin-3-yl)-acetic acid (**13a**).* Yield: 689 mg as a colourless oil, 84%; R_f 0.19 (2:3 ethyl acetate/hexane); ν_{max} (film)/cm^{-1} 3441, 2360, 1715, 1274, 1043; δ_H (300 MHz; $CDCl_3$) 1.21(3H, d, *J*=6.9 Hz), 2.69 (1H, dd, *J*=5.1, 17.7 Hz), 2.94 (1H, dd, *J*=7.8, 16.2 Hz), 4.60–5.00 (2H, m), 5.89–6.00 (2H, m); δ_C (75 MHz; $CDCl_3$) 176.6, 130.4, 125.6, 74.3, 74.2, 38.3, 17.5; *m*/*z* (EI) (M^+ 158, 1%), 143(56), 117(59), 87(100), 71(100), 45(50); HRMS (ESI) $C_7H_{10}O_4$+Na requires 181.0477, found 181.0480.

*4.5.2. (±) ((3S,6S)-6-Phenyl-3,6-dihydro-[1,2]dioxin-3-yl)-acetic acid (**13b**).* Yield: 291 mg, 81% as a colourless oil; R_f 0.21 (2:3 ethyl acetate/hexane); ν_{max} (film)/cm^{-1} 3064, 1731, 1694, 1453, 1285; δ_H

(300 MHz; $CDCl_3$) 2.79 (1H, dd, *J*=5.7, 16.4 Hz), 3.03 (1H, dd, *J*=7.5, 16.4 Hz), 4.93–5.00 (1H, m), 5.65–5.67 (1H, m), 6.10–6.22 (2H, m), 7.33–7.38 (5H, m); δ_C (75 MHz; $CDCl_3$) 176.1, 136.0, 129.2, 128.7, 128.7, 128.3, 126.7, 80.6, 74.5, 38.3; *m*/*z* (EI) (M^+ 220, 1%), 176(12), 161(27), 133(15), 105(100), 77(46); HRMS (ESI) $C_{12}H_{12}O_4$−H requires 219.0657, found 219.0658.

4.6. General procedure for cyclisation: synthesis of 11a–f and 14a–f

Method 1: to a solution of 1,2-dioxine (1 equiv) in dry dichloromethane (10 mL/1 g 1,2-dioxine) was added *N*-iodosuccinimide (2 equiv) in one portion and stirred until product formation was complete by TLC. The solution was washed with saturated $NaHCO_3$ (2×30 mL) followed by saturated $Na_2S_2O_3$ (2×30 mL) and water (2×30 mL). The organic layer was then dried ($MgSO_4$), filtered and the volatiles were removed in vacuo. The crude residue was purified by column chromatography to give the desired 1,2-dioxines **11b**,**e** and **14b**,**e**.

Method 2: to a solution of 1,2-dioxine (1 equiv) in dry dichloromethane (10 mL/1 g 1,2-dioxine) was added *N*-bromosuccinimide (2 equiv) in one portion and stirred until product formation was complete by TLC. The solution was washed with saturated $NaHCO_3$ (2×30 mL) followed by water (2×30 mL). The organic layer was then dried ($MgSO_4$), filtered and the volatiles were removed in vacuo. The crude residue was purified by column chromatography to give the desired 1,2-dioxines **11a**,**d** and **14a**,**d**.

Method 3: to a solution of 1,2-dioxine (1 equiv) in dry dichloromethane (10 mL/1 g 1,2-dioxine) was added phenylselenyl chloride (2 equiv) in one portion and stirred until product formation was complete by TLC. The volatiles were removed in vacuo and the crude residue was purified by column chromatography to give the desired 1,2-dioxines **11c**,**f** and **14c**,**f**.

*4.6.1. (±) (3R,4S,4aR,7aS)-4-Bromo-3-methyl-hexahydro-furo[3,2-c][1,2]dioxine (**11a**).* Yield: 109 mg, 64% as a yellow oil; R_f 0.51 (2:3 ethyl acetate/hexane); ν_{max} (film)/cm^{-1} 2980, 2360, 1438, 1142, 1067; δ_H (600 MHz; $CDCl_3$) 1.51 (3H, d, *J*=6.6 Hz), 2.02–2.11 (1H, m), 2.13–2.23 (1H, m), 3.91 (1H, ddd, *J*=4.8, 9.0, 9.0 Hz), 4.05 (1H, q, *J*=9.0 Hz), 4.11 (1H, t, *J*=3.0 Hz), 4.14 (1H, t, *J*=3.0 Hz), 4.44 (1H, dq, *J*=3.0, 6.6 Hz), 4.97 (1H, d quin, *J*=3.0, 12.0 Hz); δ_C (75 MHz; $CDCl_3$) 79.8, 79.2, 78.5, 66.7, 47.8, 29.9, 18.2; *m*/*z* (EI) (M^+ 223, 1%), 179(20), 143(70), 120(60), 101(68), 83(100), 69(30), 55(27); HRMS (ESI) $C_7H_{11}O_4Br$+K requires 260.9529, found 260.9568. *Trace amounts of the minor isomer were observed by 1D ^{1}H NMR however the isomer could not be isolated since formed on a small scale.

*4.6.2. (±) (3R,4S,4aR,7aS)-4-Iodo-3-methyl-hexahydro-furo[3,2-c][1,2]dioxine/(±) (3R,4R,4aR,7aS)-4-iodo-3-methyl-hexahydro-furo[3,2-c][1,2]dioxine (**11b**).* Yield: 233 mg, 62%; ratio 4:1. *(±) (3R,4S,4aR,7aS)-4-Iodo-3-methyl-hexahydro-furo[3,2-c][1,2]dioxine* (**11b**): yield: 186 mg as a colourless oil; ν_{max} (film)/cm^{-1} 2935, 2886, 1439, 1372; R_f 0.42 (dichloromethane); δ_H (300 MHz; $CDCl_3$) 1.51 (3H, d, *J*=6.6 Hz), 2.03–2.22 (2H, m), 3.91 (1H, ddd, *J*=5.1, 8.4, 8.4 Hz), 4.07 (1H, q, *J*=8.4 Hz), 4.23 (1H, t, *J*=3.6 Hz), 4.29 (1H, t, *J*=3.6 Hz), 4.48 (1H, dq, *J*=6.6, 3.6 Hz), 4.99 (1H, dt, *J*=3.0, 6.0 Hz); δ_C (75 MHz; $CDCl_3$) 80.9, 79.9, 79.4, 66.7, 29.5, 27.4, 19.2; *m*/*z* (EI) (M^+ 270, 9%), 254(40), 170(47), 143(100), 127(18), 57(33); HRMS (ESI) $C_7H_{11}O_4I$+Na requires 292.9651, found 292.9656. *(±) (3R,4R,4aR,7aS)-4-Iodo-3-methyl-hexahydro-furo[3,2-c][1,2]dioxine* (**11b**): yield: 47 mg as colourless crystals; R_f 0.40 (dichloromethane); Mp 99–101 °C; ν_{max} (Nujol)/cm^{-1} 2935, 2886, 1439, 1372; δ_H (600 MHz; $CDCl_3$) 1.77 (3H, d, *J*=6.6 Hz), 2.02–2.05 (1H, m), 2.19–2.21 (1H, m), 3.89–3.93 (2H, m), 4.12 (1H, q, *J*=8.4 Hz), 4.25 (1H, pentet, *J*=6.3, 6.6 Hz), 4.59 (1H, dd, *J*=3.6, 5.7 Hz), 4.86 (1H, dd, *J*=1.8, 5.4 Hz); δ_C (75 MHz; $CDCl_3$) 82.3, 78.2, 76.6, 65.9, 31.9, 23.6, 16.6; *m*/*z* (EI) (M^+ 270, 9%), 254(40), 170(47), 143(100), 127(18), 57(33); HRMS (ESI) $C_7H_{11}O_4I$+Na requires 292.9651, found 292.9656.

*4.6.3. (±) (3R,4S,4aR,7aS)-3-Methyl-4-phenylselanyl-hexahydro-furo-[3,2-c][1,2]dioxine (**11c**).* Yield: 199 mg, 85% as a yellow oil; R_f 0.53 (dichloromethane); ν_{max} (film)/cm^{-1} 2976, 2934, 2884, 1579, 1060; δ_H (600 MHz; $CDCl_3$) 1.52 (3H, d, *J*=6.6 Hz), 1.97–2.04 (1H, m), 2.11–2.17 (1H, m), 3.47 (1H, t, *J*=3.0 Hz), 3.82 (1H, ddd, *J*=4.8, 8.4, 8.4 Hz), 4.00 (1H, t, *J*=3.6 Hz), 4.04 (1H, q, *J*=7.8 Hz), 4.37 (1H, dq, *J*=3, 6.6 Hz), 4.92 (1H, dt, *J*=3.0, 6.0 Hz), 7.25–7.31 (3H, m), 7.55–7.58 (2H, m); δ_C (75 MHz; $CDCl_3$) 134.1, 129.4, 129.4, 127.9, 79.5, 78.6, 77.6, 66.4, 43.1, 30.6, 19.5; *m*/*z* (EI) (M^+ 300, 55%), 214(30), 157(68), 83(100), 55(30); HRMS (ESI) $C_{13}H_{16}O_3Se$+H requires 301.0343, found 301.0340. *Trace amounts of the minor isomer were observed by 1D ^{1}H NMR however the isomer could not be isolated since formed on a small scale.

*4.6.4. (±) (3R,4S,4aR,7aS)-4-Bromo-3-phenyl-hexahydro-furo[3,2-c][1,2]dioxine (**11d**).* Yield: 79 mg, 51% as a yellow oil; R_f 0.77 (dichloromethane); ν_{max} (film)/cm^{-1} 2954, 2883, 1723, 1688, 1068; δ_H (600 MHz; $CDCl_3$) 2.20–2.24 (2H, m), 3.92 (1H, ddd, *J*=6.6, 7.8, 7.8 Hz), 3.95 (1H, ddd, *J*=7.8 Hz), 4.44 (1H, t, *J*=5.4 Hz), 4.52 (1H, t, *J*=5.4 Hz), 5.05 (1H, q, *J*=5.4 Hz), 5.36 (1H, d, *J*=5.4 Hz), 7.33–7.50 (5H, m); δ_C (75 MHz; $CDCl_3$) 29.8, 48.1, 66.6, 78.9, 81.3, 85.6, 127.5, 128.7, 128.8, 136.6; *m*/*z* (EI) (M^+ 285, 1%), 205(33), 105(100), 77(33), 51(8); HRMS (ESI) $C_{12}H_{13}O_3$+Na requires 306.9946, found 306.9941.

*4.6.5. (±) (3R,4S,4aR,7aS)-4-Iodo-3-phenyl-hexahydro-furo[3,2-c]-[1,2]dioxine (**11e**).* Yield: 231 mg, 71% as a colourless oil; R_f 0.76 (dichloromethane); ν_{max} (film)/cm^{-1} 2953, 2888, 1713, 1578, 1063; δ_H (600 MHz; $CDCl_3$) 2.15–2.36 (2H, m), 3.90–3.94 (1H, ddd, *J*=6.0, 8.4, 8.4 Hz), 3.99–4.04 (1H, ddd, *J*=6.6, 8.1, 8.1 Hz), 4.54–4.56 (1H, t, *J*=6.0 Hz), 4.58–4.61 (1H, t, *J*=6.0 Hz), 4.99–5.02 (1H, m), 5.40 (1H, d, *J*=6.0 Hz), 7.33–7.45 (5H, m); δ_C (75 MHz; $CDCl_3$) 136.9, 128.9, 128.5, 127.6, 86.8, 81.7, 80.2, 66.4, 29.2, 27.4; *m*/*z* (EI) (M^+ 332, 1%), 147 (31), 119 (23), 91(100), 77(15); HRMS (ESI) $C_{12}H_{13}O_3$+Na requires 354.9807, found 354.9802. *Trace amounts of the minor isomer were observed by 1D ^{1}H NMR however the isomer could not be isolated since formed on a small scale.

*4.6.6. (±) (3R,4S,4aR,7aS)-3-Phenyl-4-phenylselanyl-hexahydro-furo-[3,2-c][1,2]dioxine/(±) (3R,4R,4aR,7aS)-3-phenyl-4-phenylselanyl-hexahydro-furo[3,2-c][1,2]dioxine (**11f**).* Yield: 173 mg, 38%; ratio 5:1. *(±) (3R,4S,4aR,7aS)-3-Phenyl-4-phenylselanyl-hexahydro-furo-[3,2-c][1,2]dioxine* (**11f**): yield: 140 mg as a yellow oil; R_f 0.41 (1:5 ethyl acetate/hexane); ν_{max} (film)/cm^{-1} 3059, 2953, 2887, 1712, 1063, 739; δ_H (600 MHz; $CDCl_3$) 2.04–2.23 (2H, m), 3.82 (1H, ddd, *J*=4.8, 8.1, 8.1 Hz), 3.89 (1H, dd, *J*=4.8 Hz), 3.94 (1H, ddd, *J*=7.8 Hz), 4.28 (1H, t, *J*=4.8 Hz), 5.00 (1H, ddd, *J*=3.3, 4.8, 6.6 Hz), 5.25 (1H, d, *J*=4.8 Hz), 7.25–7.35 (6H, m), 7.40–7.50 (4H, m); δ_C (75 MHz; $CDCl_3$) 138.3, 134.9, 129.3, 128.3, 128.3, 128.3, 128.2, 127.8, 84.6, 81.1, 77.4, 66.5, 43.3, 30.9; *m*/*z* (EI) (M^+ 362, 11%), 256(18), 157(22), 99(100), 77(47); HRMS (ESI) $C_{18}H_{18}O_3Se$+Na requires 385.0319, found 385.0355. *(±) (3R,4R,4aR,7aS)-3-Phenyl-4-phenylselanyl-hexahydro-furo*[3,2-*c*][1,2]*dioxine* (**11f**): yield: 33 mg as white needles; Mp 150–152 °C; R_f 0.35 (1:5 ethyl acetate/hexane); ν_{max} (Nujol)/cm^{-1} 1718, 1131, 1056, 742; δ_H (600 MHz; $CDCl_3$) 1.95–2.04 (1H, ddd, *J*=3.9, 7.95, 14.33 Hz), 2.18–2.30 (1H, m), 3.61 (1H, dd, *J*=3.6, 11.1 Hz), 3.90 (1H, ddd, *J*=4.2, 8.4, 9.6 Hz), 4.2 (1H, q, *J*=8.4 Hz), 4.30 (1H, dd, *J*=1.8, 3.6 Hz), 4.90 (1H, dd, *J*=1.8, 4.8 Hz), 5.35 (1H, d, *J*=11.1 Hz), 6.91–7.04 (4H, m), 7.07–7.34 (6H, m); δ_C (75 MHz; $CDCl_3$) 135.2, 135.0, 129.3,

129.0, 128.5, 128.4, 128.2, 127.5, 84.4, 82.4, 78.5, 66.8, 47.3, 31.2; *m*/*z* (EI) (M^+ 362, 1%), 157(33), 105(100), 77(75), 51(22); HRMS (ESI) $C_{18}H_{18}O_3Se$+Na requires 385.0319, found 385.0317.

*4.6.7. (±) (3R,4R,4aR,7aS)-4-Bromo-3-methyl-tetrahydro-furo[3,2-c][1,2]dioxin-6-one/(±) (3R,4S,4aR,7aS)-4-bromo-3-methyl-tetrahydro-furo[3,2-c][1,2]dioxin-6-one (**14a**).* Yield: 201 mg, 69% as a colourless oil; ratio 1:1; R_f 0.57 (2:3 ethyl acetate/hexane). *(±) 3R,4R,4aR,7aS)-4-bromo-3-methyl-tetrahydro-furo*[3,2-*c*][1,2]*dioxin*-6 *-one* (**14a**): ν_{max} (film)/cm^{-1} 1789, 1149, 1023, 849; δ_H (600 MHz; $CDCl_3$) 1.46 (3H, d, *J*=6.6 Hz), 2.54 (2H, dd, *J*=2.4, 13.2 Hz), 4.22 (1H, dd, *J*=3.6 Hz), 4.62 (1H, dq, *J*=2.74, 6.6 Hz), 4.82 (1H, dd, *J*=3 Hz), 5.12 (1H, m); δ_C (150 MHz; $CDCl_3$) 172.8, 80.7, 77.9, 75.4, 44.7, 33.7, 18.4; *m*/*z* (EI) (M^+ 237, 1%), 195(15), 139(17), 115 (50), 71(100), 55 (20); HRMS (ESI) $C_7H_9O_4Br$+Na requires 258.9582, found 258.9568. *(±) (3R,4S,4aR,7aS)-4-Bromo-3-methyl-tetrahydro-furo[3,2-c][1,2]dioxin -6-one* (**14a**): ν_{max} (film)/cm^{-1} 1789, 1149, 1023, 849; δ_H (600 MHz; $CDCl_3$) 1.45 (3H, d, *J*=6.6 Hz), 2.81 (2H, dd, *J*=6.6, 18 Hz), 4.18 (1H, dd, *J*=3.0 Hz), 4.49 (1H, dq, *J*=3.0, 6.6 Hz), 4.69 (1H, dd, *J*=3.6 Hz), 5.12 (1H, dd, *J*=4.2, 6.0 Hz); δ_C (150 MHz; $CDCl_3$) 172.8, 80.6, 77.6, 75.2, 54.0, 33.7, 17.7; *m*/*z* (EI) (M^+ 237, 1%), 195(15), 139(17), 115 (50), 71(100), 55 (20); HRMS (ESI) $C_7H_9O_4Br$+Na requires 258.9582, found 258.9568.

*4.6.8. (±) (3R,4S,4aR,7aS)-4-Iodo-3-methyl-tetrahydro-furo[3,2-c][1,2]dioxin-6-one (**14b**).* Yield: 137 mg, 76% as a colourless solid; R_f 0.51 (2:3 ethyl acetate/hexane); Mp 105–107 °C, ν_{max} (Nujol)/cm^{-1} 1780, 1198, 1166, 1005, 925; δ_H (600 MHz; $CDCl_3$) 1.44 (3H, d, *J*=6.6 Hz), 2.80 (2H, dd, *J*=5.3, 4.2 Hz), 4.33 (1H, dd, *J*=3.6 Hz), 4.71 (1H, dq, *J*=3.6, 6.6 Hz), 4.93 (1H, t, *J*=4.2 Hz) 5.15 (1H, q, *J*=4.2 Hz); δ_C (150 MHz; $CDCl_3$) 173.1, 81.9, 79.8, 75.5, 33.9, 22.2, 19.44; *m*/*z* (EI) (M^+ 284, 14%), 254(22), 157(70), 128,(26) 71(100); HRMS (ESI) $C_7H_9O_4I$+Na requires 306.9443, found 306.9446.

The crystallographic data (excluding structure factors) for 14b has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 689285. Copies of the data can be obtained free of charge, on application to CCDC,12 Union Road, Cambridge CB2, 1EZ, UK (fax: +44 1223 336033 or email: deposit@ccdc.ac.uk).

*4.6.9. Crystallographic data for **14b**.* *M*=284.04, *T*=173(2) K, triclinic, *P*-1, *a*=5.5421(13), *b*=8.731(2), *c*=9.3074(14) Å, α=77.610(12), β=82.565(15), γ=87.999(15)°, *V*=436.16(16) $Å^3$, *Z*=2, D_x=2.163 g cm^{-3}, *F*(000)=272, μ=3.644 mm^{-1}, no. of unique data (AFC12κ/SATURN724 using Mo Kα radiation so that θ_{max}=25.0°)=1454, no. of parameters=109, *R* (1440 data with $I \geq 2\sigma(I)$)=0.029, *wR* (all data)=0.075. The structure was solved by direct-methods (SHELXS-97) and refined (anisotropic displacement parameters, H atoms in the riding model approximation and a weighting scheme $w=1/[\sigma^2(F_o^2)+0.046P^2+0.053P]$ where $P=(F_o^2+2F_c^2)/3$) with SHELXL-97 on F^2. The maximum residual electron density peak of 1.17 e $Å^{-3}$ was located 0.94 Å from the I atom. CCDC deposition number: 689285.

*4.6.10. (±) (3R,4S,4aR,7aS)-3-Methyl-4-phenylselanyl-tetrahydro-furo[3,2-c][1,2]dioxin-6-one (**14c**).* Yield: 167 mg, 57% as a yellow oil; R_f 0.29 (dichloromethane); ν_{max} (film)/cm^{-1} 1789, 1478, 1156, 1020, 692; δ_H (600 MHz; $CDCl_3$) 1.47 (3H, d, *J*=6.6 Hz), 2.75 (1H, dd, *J*=1.8, 18.6 Hz), 2.80 (1H, dd, *J*=6.6, 18.6 Hz), 3.59 (1H, dd, *J*=3 Hz), 4.62 (1H, dq, *J*=2.4, 6.6 Hz) 4.75 (1H, dd, *J*=3.0, 4.2 Hz), 5.13 (1H, dt, *J*=3.3, 6.6 Hz), 7.24–7.28 (1H, m), 7.32–7.37 (2H, m), 7.58–7.62 (2H, m); δ_C (75 MHz; $CDCl_3$) 173.9, 134.4, 129.7, 129.2, 128.7, 79.9, 78.3, 75.7, 41.6, 34.6, 19.8; *m*/*z* (EI) (M^+ 314, 100%), 234(24), 157(90), 77 (61), 51(11); HRMS (ESI) $C_{13}H_{14}O_4Se$+Na requires 336.9954, found 336.9951.

*4.6.11. (±) (3R,4S,4aR,7aS)-4-Bromo-3-phenyl-tetrahydro-furo[3,2-c][1,2]dioxin-6-one (**14d**).* Yield 76 mg, 56% as colourless needles; R_f 0.47 (dichloromethane); Mp 124–126 °C; ν_{max} (Nujol)/cm^{-1} 1792, 1164, 1124, 1079, 1033; δ_H (300 MHz; $CDCl_3$) 2.85–3.00 (2H, m), 4.62 (1H, t, *J*=4.5 Hz), 5.07 (1H, dd, *J*=4.5, 6.0 Hz), 5.21 (1H, ddd, *J*=3.9, 6.3, 6.3 Hz), 5.63 (1H, d, *J*=4.5 Hz), 7.35–7.42 (5H, m); δ_C (75 MHz; $CDCl_3$) 172.9, 135.1, 129.6, 128.9, 127.7, 87.6, 78.7, 76.3, 44.6, 33.7; *m*/*z* (EI) (M^+ 297, 1%), 280(75), 235(100), 128(75), 77(25); HRMS (ESI) $C_{12}H_{11}O_4Br$+Na requires 320.9738, found 320.9736.

*4.6.12. (±) (3R,4S,4aR,7aS)-4-Iodo-3-phenyl-tetrahydro-furo[3,2-c][1,2]dioxin-6-one (**14e**).* Yield: 88 mg, 56% as colourless needles; R_f 0.38 (dichloromethane); Mp 154–155 °C; ν_{max} (Nujol)/cm^{-1} 1789, 1165, 1073, 1022; δ_H (300 MHz; $CDCl_3$) 2.92–2.99 (1H, m), 3.09 (1H, dd, *J*=18, 3.0 Hz), 4.71 (1H, dd, *J*=3.3, 5.4 Hz), 5.21–5.28 (2H, m), 5.81 (1H, d, *J*=5.4 Hz), 7.41–7.46 (5H, m); δ_C (75 MHz; $CDCl_3$) 172.9, 135.6, 129.7, 128.9, 127.7, 88.8, 80.6, 77.2, 33.6, 21.6; *m*/*z* (EI) (M^+ 346, 1%), 220(64), 158(73), 107(100), 91(55), 70(37); HRMS (ESI) $C_{12}H_{11}O_4I$+Na requires 368.9599, found 368.9594.

*4.6.13. (±) (3R,4S,4aR,7aS)-3-Phenyl-4-phenylselanyl-tetrahydro-furo[3,2-c][1,2]dioxin-6-one (**14f**).* Yield: 93 mg, 55% as a yellow oil; R_f 0.50 (dichloromethane); ν_{max} (film)/cm^{-1} 3060, 2995, 1789, 1578, 1154, 1022; δ_H (600 MHz; $CDCl_3$) 2.87–2.95 (2H, m), 4.02 (1H, t, *J*=3.6 Hz), 4.98 (1H, dd, *J*=3.6, 6.0 Hz), 5.21 (1H, ddd, *J*=3.0, 6.9, 6.9 Hz), 5.51 (1H, d, *J*=3.6 Hz), 7.28–7.40 (8H, m), 7.54–7.57 (2H, m); δ_C (75 MHz; $CDCl_3$) 173.8, 136.7, 134.8, 129.6, 129.2, 128.9, 128.9, 128.8, 127.9, 86.6, 78.6, 76.4, 41.9, 34.7; *m*/*z* (EI) (M^+ 375, 1%), 282(6), 203(100), 157(63), 105(50), 77(38); HRMS (ESI) $C_{18}H_{16}O_4Se$+Na requires 399.0112, found 399.0118.

4.7. General procedure for the synthesis of 1,2-dioxines 12a,b and 15a,b

To a solution of 1,2-dioxines (1 equiv) in dry benzene (10 mL/100 mg 1,2-dioxine) was added AIBN (2 equiv) and tri-*n*-BuSnH (3 equiv) at room temperature. The mixture was then heated under reflux for 2 h, following this potassium fluoride (3.3 equiv) in acetonitrile (10 mL) was added to the mixture and stirring continued overnight. The volatiles were removed in vacuo and the crude residue was purified by column chromatography to give the desired 1,2-dioxines **12a**,**b** and **15a**,**b**.

*4.7.1. (±) (3R,4aS,7aS)-3-Methyl-hexahydro-furo[3,2-c][1,2]dioxine (**12a**).* Yield: 38 mg, 66% as a colourless oil; R_f 0.55 (dichloromethane); ν_{max} (film)/cm^{-1} 2930, 2873, 1464, 1377, 1064; δ_H (600 MHz; $CDCl_3$) 1.46 (3H, d, *J*=6.6 Hz), 1.90 (1H, ddd, *J*=2.4, 2.4, 14.4 Hz), 1.93–1.96(1H, m), 2.11–2.15 (1H, m), 2.18 (1H, ddd, *J*=4.8, 6.6, 14.4 Hz), 3.77 (1H, ddd, *J*=4.8, 8.4, 8.4 Hz), 3.83 (1H, dt, *J*=3, 4.8 Hz), 4.03 (1H, ddd, *J*=8.4 Hz), 4.23 (1H, ddq, *J*=1.8, 6.6, 6.6 Hz), 4.67 (1H, ddd, *J*=1.2, 3, 6 Hz); δ_C (75 MHz; $CDCl_3$) 80.8, 73.3, 72.9, 65.8, 30.9, 29.9, 19.6; *m*/*z* (EI) (M^+ 167, 1%), 143(38), 95(100), 87(46), 71(28), 55(15); HRMS (ESI) $C_7H_{12}O_3$+Na requires 167.0684, found 167.0680.

*4.7.2. (±) (3S,4aS,7aS)-3-Phenyl-hexahydro-furo[3,2-c][1,2]dioxine (**12b**).* Yield: 40 mg, 67% as colourless oil; R_f 0.44 (dichloromethane); ν_{max} (film)/cm^{-1} 2936, 2881, 1731, 1456, 1071, 1024; δ_H (600 MHz; $CDCl_3$) 1.96–2.01 (1H, m), 2.13–2.19 (1H, sextet, *J*=6.9 Hz), 2.40–2.47 (2H, m), 3.75 (1H, ddd, *J*=5.4, 8.4, 8.4 Hz), 3.84 (1H, q, *J*=8.4 Hz), 4.15 (1H, q, *J*=4.8 Hz), 4.85 (1H, ddd, *J*=3.0, 4.5, 6.9 Hz), 5.17 (1H, dd, *J*=6 Hz), 7.27–7.37 (3H, m), 7.5–7.52 (2H, m); δ_C (75 MHz; $CDCl_3$) 140.2, 128.2, 127.7, 127.2, 81.8, 78.4, 72.9, 65.8, 30.7, 29.4; *m*/*z* (EI) (M^+ 206, 1%), 188(14), 157(32), 105(100), 77(64), 55(21); HRMS (ESI) $C_{12}H_{14}O_3$+Na requires 229.0841, found 229.0838.

*4.7.3. (±) (3R,4aS,7aS)-3-Methyl-tetrahydro-furo[3,2-c][1,2]dioxin-6-one (**15a**).* Yield: 21 mg, 81% as colourless oil; R_f 0.19 (dichloromethane); ν_{max} (film)/cm^{-1} 2937, 1779, 1159, 1025; δ_H (300 MHz; $CDCl_3$) 1.58 (3H, d, *J*=6.6 Hz), 2.11 (1H, ddd, *J*=15.0, 2.4 Hz), 2.26 (1H, ddd, *J*=15.0, 7.2, 4.2 Hz), 2.69 (1H, dd, *J*=18.3, 1.2 Hz), 2.8 (1H, dd, *J*=18.3, 6.6 Hz), 4.47 (1H, ddq, *J*=13.6, 2.4, 6.9 Hz), 4.72 (1H, ddd, *J*=3.0, 4.2, 4.2 Hz), 4.85 (1H, ddd, *J*=1.2, 4.8, 4.8 Hz); δ_C (75 MHz; $CDCl_3$) 98.8, 86.5, 85.2, 80.9, 79.3, 66.4, 65.8, 56.7, 52.5, 28.6, 28.2, 17.9, 13.4; *m*/*z* (EI) (M^+ 158, 9%), 143(7), 95(7), 87(12), 71(100), 45(9); HRMS (ESI) $C_7H_{10}O_4$+Na requires 181.0477, found 181.0471.

*4.7.4. (±) (3S,4aS,7aS)-3-Phenyl-tetrahydro-furo[3,2-c][1,2]dioxin-6-one (**15b**).* Yield: 34 mg, 73% as colourless oil; R_f 0.29 (dichloromethane); ν_{max} (film)/cm^{-1} 3064, 2941, 1789, 1179, 1039; δ_H (600 MHz; $CDCl_3$) 2.56 (1H, ddd, *J*=4.8, 7.8, 15 Hz), 2.64 (1H, ddd, *J*=4.2, 4.2, 15 Hz), 2.79 (1H, dd, *J*=3.0, 18.6 Hz), 2.86 (1H, dd, *J*=6.6, 18.6 Hz), 4.92–4.95 (1H, m), 4.99–5.01 (1H, m), 5.44 (1H, dd, *J*=4.2, 7.8 Hz), 7.31–7.44 (5H, m); δ_C (75 MHz; $CDCl_3$) 174.1, 137.9, 128.7, 128.7, 127.6, 79.3, 77.1, 74.6, 34.1, 29.1; *m*/*z* (EI) (M^+ 220, 1%), 176(33), 133(28), 105(100), 77(33), 51(14); HRMS (ESI) $C_{12}H_{12}O_4$+Na requires 243.0633, found 243.0639.

4.8. General procedure for the synthesis of 1,4-diols 16a and 17a

To a solution of 1,2-dioxine (1 equiv) in methanol (5 mL/500 mg of 1,2-dioxine) was added 5% Pd/C (10% by weight) under a hydrogen atmosphere and stirred until complete by TLC. The volatiles were removed in vacuo and crude residue was purified by column chromatography to give the desired 1,4-diols **16a** and **17a**.

*4.8.1. (±) (2S,3S)-2-((R)-2-Hydroxy-propyl)-tetrahydrofuran-3-ol (**16a**).* Yield: 40 mg, 69% as colourless oil; R_f 0.14 (ethyl acetate); ν_{max} (film)/cm^{-1} 3400, 2967, 1374, 1119, 1061; δ_H (600 MHz; $CDCl_3$) 1.28 (3H, d, *J*=6.6 Hz), 1.81–1.90 (2H, m), 1.95–1.99 (1H, m), 2.16–2.23 (1H, m), 2.48 (2H, br s), 3.71 (1H, ddd, *J*=4.8, 8.4, 8.4 Hz), 3.80 (1H, ddd, *J*=4.1, 6, 8.1 Hz), 3.99–4.09 (2H, m), 4.34 (1H, ddd, *J*=1.8, 3.6, 5.7 Hz); δ_C (75 MHz; $CDCl_3$) 81.7, 72.4, 65.9, 65.9, 37.4, 34.9, 24.8; *m*/*z* (EI) (M^+ 146, 1%), 128(16), 89(53), 71(68), 57(100), 45(68); HRMS (ESI) $C_7H_{14}O_3$+Na requires 169.0841, found 169.0836.

*4.8.2. (±) (4S,5S)-4-Hydroxy-5-((R)-2-hydroxy-propyl)-dihydrofuran-2-one (**17a**).* Yield: 21 mg, 62% as colourless oil; R_f 0.49 (ethyl acetate); ν_{max} (film)/cm^{-1} 3401, 2932, 1769, 1168, 1054; δ_H (600 MHz; $CDCl_3$) 1.34 (3H, d, *J*=6.0 Hz), 2.04 (2H, m), 2.55 (1H, d, *J*=18.0 Hz), 2.67 (2H, br s), 2.78 (1H, dd, *J*=6.0, 18.0 Hz), 4.05 (1H, sextet, *J*=6.0 Hz), 4.51 (1H, ddd, *J*=3.6, 7.2, 7.2 Hz), 4.54 (1H, dd, *J*=3.6, 6 Hz); δ_C (75 MHz; $CDCl_3$) 175.7, 83.6, 68.7, 65.3, 37.9, 36.4, 25.1; *m*/*z* (EI) (M^+ 160, 1%), 127(8), 98(66), 89(92), 71(83), 45(100); HRMS (ESI) $C_7H_{12}O_4$+Na requires 183.06332, found 183.0630.

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Supplementary data

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