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Oxidative rearrangement of 2-alkoxy-3,4-dihydro-2*H*-pyrans: stereocontrolled synthesis of 4,5-cis-disubstituted tetrahydrofuranones including whisky and cognac lactones and crobarbatic acid

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ABSTRACT

Oxidation of 2-alkoxy-3,4-dihydro-2*H*-pyrans **3** with dimethyldioxirane or MTO/urea–H_2O_2 followed by Jones oxidation leads to rearrangement and stereocontrolled formation of 4,5-cis-disubstituted tetrahydrofuranones. The method is applied to the synthesis of the whisky lactone **9**, cognac lactone **10** and crobarbatic acid **17**.

1. Introduction

Tetrahydrofurans (THFs) are key motifs of several classes of biologically important natural product,[1] and methods for their stereocontrolled synthesis are therefore important and actively sought.[2] In 1970, Hall and co-workers reported that oxidation of some simple 2-alkoxy-3,4-dihydro-2*H*-pyrans **3** (R^2–R^4=H) with *m*-CPBA afforded the THFs **4**, presumably via the intermediate epoxide **5** (Scheme 1).[3] Since then, this rearrangement has been exploited in the specific case of spiroketal synthesis, by Ireland[4] and Rizzacasa and McRae.[5] Because a wide range of the starting pyrans **3** may be readily accessed by Lewis-acid promoted hetero-Diels–Alder reaction between an enone and an enol ether, we wished to explore the generality of the oxidative rearrangement process, particularly with regard to diastereoselectivity issues, which had not previously been addressed. Our recent demonstration that diastereoselective aziridination of **3** leads to substituted pyrrolidines with a high level of stereocontrol provided encouragement in this regard.[6] In this paper, we report in full our studies on the oxidative rearrangement of pyrans **3**.

2. Results and discussion

2.1. Synthesis of dihydropyrans 3

We aimed to prepare a wide range of substrates **3** bearing a variety of substitution patterns. Initially, we employed thermal cycloaddition between enones **1** and enol ethers **2** under Yb(FOD) catalysis (Table 1, conditions A).[7] However, these conditions generally required long reaction times (1–10 days). Therefore, we investigated microwave conditions (conditions B), which allowed completion in much shorter times (2–3 h). Where applicable, the cycloadditions afforded predominantly one diastereomer. Literature precedent[7] suggests that the major diastereomer is the *endo*-cycloadduct, with the *C*2-alkoxy group and the *C*4-substituent R^3 in a cis-relationship. Analysis of ^1H NMR coupling constants for the major product supported by molecular mechanics analysis (MMFF, Spartan) suggested that H2 is pseudoaxial (J_{H2-H3} 7.0–9.5 Hz) and thus both the *C*2-alkoxy substituent and the *C*4-substituent R^3 are likely to be pseudoequatorial. On standing in $CDCl_3$, the major *endo*-diastereomer underwent epimerisation to the minor *exo*-isomer, having a pseudoaxial alkoxy group (J_{H2-H3} 2.5–3.0 Hz), preferred due to the anomeric effect.

2.2. Oxidative rearrangement of 6-substituted pyrans

With a convenient synthesis of substrates **3** in hand, we were now in a position to test their epoxidation/rearrangement. Initially, we employed the least substituted substrate **3a** to screen several common epoxidation reagents (Table 2). Reaction of **3a** with commercial *m*-CPBA in CH_2Cl_2 (entry 1) afforded only a low yield (14%) of the desired THF **4a**, along with the lactol **6** (ca. 10%), presumably arising from hydrolysis of **4a**. Concerns that the low yield of **4a** may be partly due to its volatility led us also to test the ^{n}Bu-substrate **3b** under these conditions (entry 2). A higher yield of **4** (39%) was indeed obtained, and smaller quantities of hydrolysis product **6**. Next, we tested isolated solutions of dimethyldioxirane (DMDO)[8] (entries 3 and 4). Surprisingly, the major reaction product in this case was the lactol **6**, even when the acetone solutions of DMDO solutions were dried over K_2CO_3 prior to use. The combined product yield (yield of **4**+yield of **6**) was, however, better with DMDO than with *m*-CPBA. Potential difficulties in preparing DMDO solutions on large scale prompted us to

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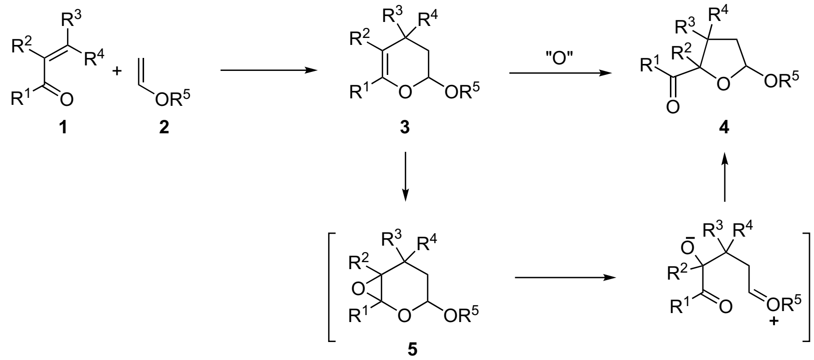
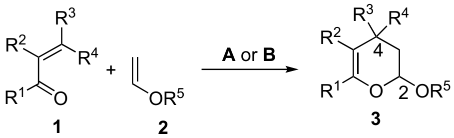


Scheme 1.

attempt in situ formation of DMDO[9] from acetone and Oxone (entries 5 and 6). The reaction with the less volatile substrate **3b** afforded a highly promising combined product yield (76%, entry 6), but the longer reaction times meant that we preferred to use isolated DMDO solutions in subsequent investigations. An attempt at using the more reactive trifluoroacetone/Oxone system[10] with **3b** did not provide any of the desired product.

In order to simplify product analysis and purification, and also to facilitate eventual stereochemical analysis, we wished to convert the mixture of lactol ethers **4** and lactols **6** into a common product.

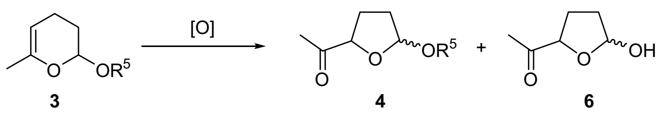
Table 1
Enone/enol ether hetero Diels–Alder reaction



Entry	R^1	R^2	R^3	R^4	**1**	R^5	**2**	**3**	Yield[i]	dr[j]
1[a]	Me	H	H	H	**1a**	Et	**2a**[c]	**3a**	70	N/A
2[a]	Me	H	H	H	**1a**	^{n}Bu	**2b**[d]	**3b**	55	N/A
3[a]	Me	H	Me	H	**1b**	^{n}Bu	**2b**[d]	**3c**	40	6:1
4[a]	Me	H	^{i}Pr	H	**1c**	^{n}Bu	**2b**[d]	**3d**	75	6:1
5[a]	Me	H	Me	Me	**1d**	^{n}Bu	**2b**[e]	**3e**	54	N/A
6[a]	Me	H	Ph	H	**1e**	Et	**2a**[e]	**3f**	50	≥99:1
7[a]	Me	H	CH_2OBn	H	**1f**	Et	**2a**[f]	**3g**	67	≥99:1
8[a]	Me	H	$(CH_2)_4CH{=}CHEt$	H	**1g**	Et	**2a**[f]	**3h**	56	4:1
9[a]	H	H	Ph	H	**1h**	Et	**2a**[g]	**3i**	100	≥99:1
10[b]	H	H	Ph	H	**1h**	Et	**2a**[h]	**3i**	89	≥99:1
11[a]	H	H	Me	H	**1i**	Et	**2a**[e]	**3j**	88	≥99:1
12[b]	H	H	Me	H	**1i**	Et	**2a**[e]	**3j**	66	≥99:1
13[a]	H	H	CH_2OBn	H	**1j**	Et	**2a**[e]	**3k**	99	≥99:1
14[b]	H	H	^{i}Pr	H	**1k**	Et	**2a**[e]	**3l**	58	≥99:1
15[b]	H	H	*p*-MeO C_6H_4	H	**1l**	Et	**2a**[e]	**3m**	98	≥99:1
16[a]	H	H	Et	H	**1m**	Et	**2a**[e]	**3n**	98	≥99:1
17[a]	H	Me	H	H	**1n**	Et	**2a**[e]	**3o**	91	N/A
18[a]	H	Me	Me	H	**1o**	Et	**2a**[e]	**3p**	90	≥99:1
19[a]	H	Me	Et	H	**1p**	Et	**2a**[e]	**3q**	93	≥99:1
20[a]	H	Me	Ph	H	**1q**	Et	**2a**[e]	**3r**	85	≥99:1
21[b]	H	Me	Furyl	H	**1r**	Et	**2a**[e]	**3s**	13	≥99:1
22[b]	H	Me	OEt	H	**1s**	Et	**2a**[e]	**3t**	26	≥99:1
23[b]	H	^{n}Bu	H	H	**1t**	Et	**2a**[e]	**3u**	85	N/A
24[b]	H	Ph	Me	H	**1u**	Et	**2a**[e]	**3v**	91	3:1
25[b]	Ph	H	H	H	**1v**	Et	**2a**[e]	**3w**	48	N/A
26[b]	Ph	H	Me	Me	**1w**	Et	**2a**[e]	**3x**	41	N/A
27[b]	Ph	H	Et	Et	**1x**	Et	**2a**[e]	**3y**	12	N/A
28[b]	Ph	H	CyHex		**1y**	Et	**2a**[e]	**3z**	30	N/A
29[b]	*p*-MeO C_6H_4	H	Me	Me	**1z**	Et	**2a**[e]	**3aa**	27	N/A
30[b]	*p*-Me C_6H_4	H	Me	Me	**1aa**	Et	**2a**[e]	**3ab**	40	N/A
31[b]	*p*-Cl C_6H_4	H	Me	Me	**1ab**	Et	**2a**[e]	**3ac**	44	N/A
32[b]	*p*-NO_2 C_6H_4	H	Me	Me	**1ac**	Et	**2a**[e]	**3ad**	58	N/A
33[b]	2-Naphthyl	H	Me	Me	**1ad**	Et	**2a**[e]	**3ae**	41	N/A

[a] Conditions A: pressure tube, 45–100 °C, YbFOD catalyst (2–5 mol %), 1–10 days.
[b] Conditions B: microwave, 55–80 °C, YbFOD catalyst (5 mol %), 2–6 h.
[c] 7 equiv of **2** to **1**.
[d] 2 equiv of **2** to **1**.
[e] 5 equiv of **2** to **1**.
[f] 10 equiv of **2** to **1**.
[g] 12 equiv of **2** to **1**.
[h] 6 equiv of **2** to **1**.
[i] Combined yield of diastereoisomers (%).
[j] The ratio of *endo* to *exo* determined by ^1H NMR.

Table 2
Preliminary screen of oxidants

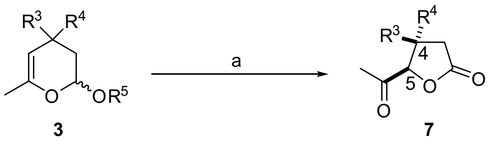


Entry	R^5	**3**	Reagent	Time	**4**	Yield **4**[d]	dr **4**[e]	Yield **6**[h]	dr **6**[i]
1	Et	**3a**	*m*-CPBA[a]	2 h	**4a**	14	2:1[f]	10	1:1
2	^{n}Bu	**3b**	*m*-CPBA[a]	3 h	**4b**	39	2:1[g]	<5	1:1
3	Et	**3a**	DMDO[b]	3 h	—	—	—	53	1:1
4	^{n}Bu	**3b**	DMDO[b]	3 h	**4b**	9	2:1[g]	64	1:1
5	Et	**3a**	Acetone/Oxone®[c]	24 h	**4a**	13	2:1[f]	—	1:1
6	^{n}Bu	**3b**	Acetone/Oxone®[c]	24 h	**4b**	46	2:1[g]	30	1:1

[a] *m*-CPBA (1.0 equiv), CH_2Cl_2, 0 °C to rt.
[b] DMDO (1.0 equiv), CH_2Cl_2, 0 °C to rt.
[c] Acetone/Oxone®, $NaHCO_3$, Na_2EDTA (pH=7.5), CH_2Cl_2, 0 °C to rt.
[d] Combined yield of diastereoisomers (%).
[e] The ratio determined by ^1H NMR.
[f] Inseparable diastereoisomers.
[g] Separable diastereoisomers.
[h] Combined yield of inseparable diastereoisomers (%).
[i] The ratio determined by ^1H NMR.

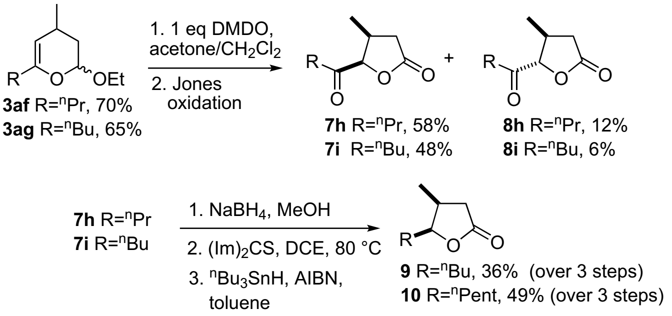
Reduction was considered for this purpose, but initial attempts (Et_3SiH, $BF_3 \cdot Et_2O$) led to reduction of the ketone as well as the lactol ether/lactol, thus further complicating the product mixture. Turning instead to oxidation, we discovered that Jones oxidation would convert the mixture of **4** and **6** cleanly into a common lactone product **7**. The DMDO/Jones procedure was applied to several pyrans **3** and the results are displayed in Table 3. The substrate **3c** bearing a CH_3-substituent at *C*4 provided the first evidence for diastereoselective THF formation (3:1 diastereoselectivity, entry 2). The major isomer was shown to have the cis-relative configuration **7** by NOE studies (notably, NOE between H4 and H5), while the minor, trans-isomer showed NOE interactions between H5 and the *C*4-methyl group. This stereochemical outcome is consistent with predominant epoxidation on the less hindered face of **3c**, trans- to the *C*4-methyl substituent. With larger *C*4-substituents, the levels of diastereoselectivity were higher (entries 3–6), with NOE studies again indicating the cis-configuration in the major product. As in our earlier aziridination studies on **3**, we found that this oxidative rearrangement chemistry tolerated the presence of an oxygen functionality (entry 3), an isolated alkene (entry 6), and a quaternary centre in the substrate (entry 7).

Table 3
Conversion of pyrans **3** to lactones **7**; (a) DMDO (1.0 equiv), CH_2Cl_2, 0 °C to rt/Jones reagent (3.0 equiv), acetone, 0 °C to rt



Entry	**3**	R^3	R^4	R^5	**7**	Yield **7**[a]	dr[b]
1	**3b**	H	H	^{n}Bu	**7a**	69	—
2	**3c**	Me	H	^{n}Bu	**7b**	53	3:1[c]
3	**3g**	CH_2OBn	H	Et	**7c**	48	95:5
4	**3d**	^{i}Pr	H	^{n}Bu	**7d**	63	9:1
5	**3f**	Ph	H	Et	**7e**	65	>95:5[d]
6	**3h**	$(CH_2)_4CH{=}CHEt$	H	Et	**7f**	64	>95:5[d]
7	**3e**	Me	Me	^{n}Bu	**7g**	50	—

[a] Isolated yield of **7** over two steps from **3** (%).
[b] The ratio of cis to trans determined by ^1H NMR spectrum of the crude reaction mixture.
[c] Isomers separable by column chromatography: *cis*-lactone 32%, *trans*-lactone 10%.
[d] Only the cis product observed by ^1H NMR.



Scheme 2.

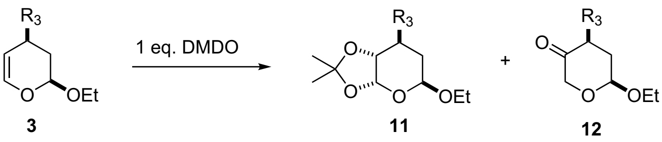
In order to demonstrate the application of the oxidative rearrangement chemistry to natural product synthesis, we were attracted to the *Quercus* lactones, in particular the lactones **9** and **10** (Scheme 2) partly responsible for aroma and flavour in whisky and cabernet sauvignon wine.[11] Oxidative rearrangement of the appropriate substrates with DMDO followed by Jones oxidation proceeded to give a mixture of diastereomers (5:1 for **7h**/**8h**; 8:1 for **7i**/**8i** by ^1H NMR analysis), from which the desired cis-isomers could be separated (58% for **7h**; 48% for **7i**). The superfluous ketone moiety was removed by reduction ($NaBH_4$) followed by Barton–McCombie deoxygenation, providing the *cis*-lactones **9** and **10**, the spectroscopic data of which matched those reported for the natural products.[12,13]

2.3. Oxidative rearrangement of 6-unsubstituted pyrans

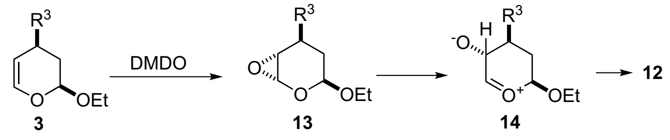
The chemistry described above successfully accomplished the stereoselective synthesis of lactones **7** containing a ketone functionality in the product ($R^1 \neq H$). We were keen to extend the method to substrates **3** with $R^1{=}H$, because an effective catalytic enantioselective hetero-Diels–Alder reaction has been reported[14] for the synthesis of these specific substrates. This would allow us to prepare our lactone products in enantiomerically pure form. Disappointingly, we were not able to effect DMDO-mediated epoxidation/rearrangement on these substrates. Reaction of **3** ($R^1{=}H$) with DMDO instead afforded the acetonide **11** as the major identified product (Table 4). A similar outcome has been reported in the reaction of glycals with DMDO.[15] In one case (entry 3), a further product, ketone **12**, was also isolated. Both **11** and **12** could conceivably arise from the desired intermediate epoxide **13** (Scheme 3). Opening of epoxide **13** with acetone solvent would lead to **11**. Unimolecular ring opening to **14** and hydride shift would convert **13** into ketone **12**.

Experiments using *m*-CPBA with 6-unsubstituted substrates **3** ($R^1{=}H$) also failed to provide the desired oxidation/rearrangement, with ring opening of the intermediate epoxide by solvent or carboxylic acid co-product again being suspected. Seeking epoxidation

Table 4

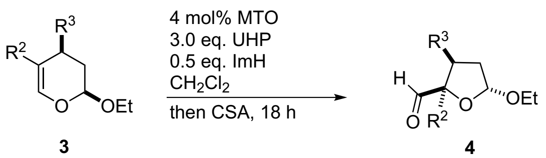


Entry	**3**	R^3	**11**	Yield **11**	**12**	Yield **12**
1	**3i**	Ph	**11a**	30		—
2	**3l**	^{i}Pr	**11b**	25		—
3	**3m**	*p*-MeO Ph	**11c**	31	**12a**	14



Scheme 3.

Table 5



Entry	**3**	R₂	R₃	**4**	Yield **4**
1	**3o**	Me	H	**4c**	13
2	**3p**	Me	Me	**4d**	28
3	**3q**	Me	Et	**4e**	35
4[a]	**3r**	Me	Ph	**4f**	10[b]
5	**3t**	Me	OEt	**4g**	54
6	**3u**	^{n}Bu	H	**4h**	63

[a] MTO (8 mol %) and 6 equiv UHP used.
[b] 4-Oxo-3-phenylpentenal (5%) also isolated.

processes that could be performed in the absence of nucleophilic solvents or additives, we were attracted to reports[16] of glycal epoxidations using urea/H_2O_2 under methyltrioxorhenium catalysis in the presence of imidazole ligands. Early attempts using these conditions with a range of substrates **3** suggested that the desired aldehyde products **4** were not formed in more than trace amounts. For some substrates **3** (R^1=H; $R^2 \neq$H), resonances were observed in the ^{1}H NMR spectrum of the crude product at ca. 4.0–4.5 ppm, which were tentatively assigned to the epoxide intermediate **13**. Addition of CSA to the reaction mixture to promote rearrangement of **13**, following consumption of **3** in the epoxidation step, pleasingly led to isolable quantities of the desired product **4** (Table 5, entries 1–5), albeit in low-to-moderate yields. The products **4** prepared under the stated conditions were isolated after column chromatography as single diastereomers. When longer reaction times were employed, the isolated products were in some cases obtained in higher yields but lower diastereoselectivity. While the reasons for this were not examined in detail, we believe that this is due partly to epimerisation at the acetal centre and partly to slower rearrangement of the minor diastereomer of the intermediate epoxide. The shorter reaction times provided products, which could be isolated as essentially single diastereomers, which greatly facilitated product characterisation.

NOESY experiments suggested the depicted configuration for the isolated isomers, which is again in accord with epoxidation trans- to R^3. Specifically, for **4e**, we observed NOESY correlations between the C-2 methyl and H3, and between the aldehyde proton and the *C*3–Et substituent. The acetal centre was tentatively assigned due to the absence of a NOESY interaction between the 2-Me and the acetal proton. Despite these encouraging results, the method appeared to be rather substrate-specific. Attempted oxidative rearrangement (not shown in Table 5) of substrates **1k** and **1m** (R^2=H; R^3=^{i}Pr or Et) was not successful.

While our earlier studies with DMDO epoxidations suggested that at least partial hydrolysis of the lactol ether products to the corresponding lactols was likely, we were unable to isolate any lactols from these MTO reactions. In order to converge any alternative diastereomers and lactols to a common product, we subjected the crude product of the epoxidation/rearrangement step to Jones oxidation, as in our earlier studies. Since the resultant mixture of carboxylic acids was not readily separable, we transformed the resulting product mixture into the corresponding PMB-esters.

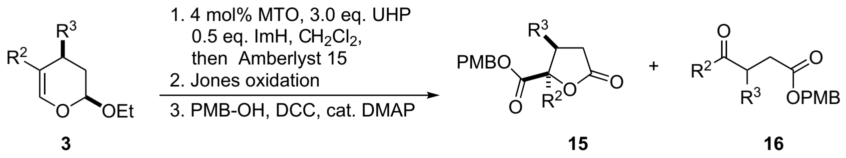
The yields of the desired lactone products **15** were disappointing (Table 6), with the moderate diastereoselectivities suggesting that the earlier isolation of single diastereomers of **4** was indeed due to incomplete rearrangement of the minor epoxide diastereomer and/or the chromatographic purification. The low yield of **15** was explained partly by the formation of the ketoester **16**, the result of oxidative decarboxylation,[17] as a significant by-product. To probe the origin of **16**, a sample of **15** was hydrolysed to the corresponding carboxylic acid, which when submitted to Jones conditions indeed underwent oxidative decarboxylation. Attempts to minimise this side-reaction by reducing the time period of exposure to Jones reagent after the epoxidation rearrangement, were not successful in improving the yield of **15**.

Although the low yields, moderate diastereoselectivities and narrow substrate scope were disappointing, we aimed to prove the relative configuration of the major diastereomer of **15** by conversion to crobarbatic acid, a component of a natural product.[18] Cleavage of the PMB-ester of **15a**, derived from oxidative rearrangement/Jones oxidation of **3p**, gave (±)-crobarbatic acid **17** as an inseparable 2:1 mixture of diastereoisomers (Scheme 4). The major isomer had the depicted configuration as indicated by comparison to ^{1}H NMR data for the two diastereomers reported by Donohoe.[18]

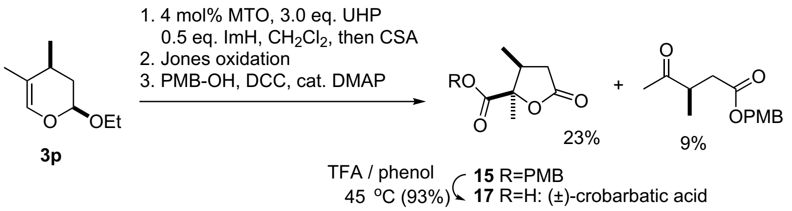
2.4. Enantioselective THF synthesis

We next turned to the synthesis of enantiomerically enriched products. The disappointing oxidative rearrangement results with 6-unsubstituted substrates (R^1=H), required for Jacobsen's catalytic asymmetric hetero-Diels–Alder reaction,[14] led us to focus instead on enantioselective epoxidation. Since there is as yet no effective enantioselective MTO-catalysed epoxidation, we concentrated first on the use of chiral dioxiranes.[19] In view of the low enantioselectivities observed for enol ether epoxidation using chiral ketone

Table 6



Entry	**3**	R₂	R₃	**15**	Yield **15**	dr **15**	Yield **16**
1	**3p**	Me	Me	**15a**	23	2:1	9
2	**3t**	Me	OEt	**15b**	21	9:1	48
3	**3v**	Ph	Me	**15c**	0	—	21



Scheme 4.

Table 7

Epoxidation of DHPs with Jacobsen's catalyst **19**; (a) 4-phenyl pyridine *N*-oxide (0.2 equiv), (*R*,*R*)-Jacobsen's cat **19** (0.05 equiv), NaOCl (1.5 equiv), CH_2Cl_2, 0 °C to rt, (b) Jones reagent (3.0 equiv), acetone, 0 °C to rt

Entry	Substrate	R^1	R^3 (=R^4)	R^5	7	Yield[a] (%)	ee (%)
1	**3a**	Me	H	Et	**7j**	40	0[b]
2	**3e**	Me	Me	^{n}Bu	**7k**	16	0[b]
3	**3w**	Ph	H	Et	(*S*)-**7l**	55	38[c]
4	**3x**	Ph	Me	Et	(*S*)-**7m**	49	58[c]
5	**3y**	Ph	Et	Et	(*S*)-**7n**	45	69[c]
6	**3z**	Ph	CyHex	Et	(*S*)-**7o**	40	80[c]
7	**3aa**	*p*-MeO ph	Me	Et	(*S*)-**7p**	35	79[c]
8	**3ab**	*p*-Me ph	Me	Et	(*S*)-**7q**	43	70[c]
9	**3ac**	*p*-Cl ph	Me	Et	(*S*)-**7r**	40	76[c]
10	**3ad**	*p*-NO_2 ph	Me	Et	(*S*)-**7s**	64	46[c]
11	**3ae**	2-Naph	Me	Et	(*S*)-**7t**	41	71[c]

[a] Yield over two steps.
[b] Based on the optical rotation.
[c] By chiral HPLC analysis.

catalysts developed in our own laboratories,[20] we chose to test Shi's fructose-derived chiral ketone **18**.[21] Disappointingly, **18**/Oxone did not afford any of the desired product from substrates **3a**, **3d**, or **3w**, even under higher reaction pH conditions (pH 10). Next, we explored Jacobsen's Mn(salen) catalyst (*R*,*R*)-**19**, in conjunction with 1.5 equiv of NaOCl as co-oxidant and 0.2 equiv of pyridine oxide as additive (Table 7, Fig. 1). Pleasingly, Jacobsen epoxidation of **3a** indeed afforded the desired rearrangement product **7j** (entry 1). However, optical rotation analysis suggested that this material was racemic. In order to provide greater steric differentiation of the two sides of the alkene, we studied the *C*4-disubstituted substrate **3e**, but again racemic product was obtained (entry 2). Since aromatic alkenes are generally superior substrates in Jacobsen epoxidation, we examined substrate **3w**. Pleasingly, this led to the first observation of significant asymmetric induction (38% ee, entry 3). The absolute configuration of the major enantiomer of product **7l** was found to be *S* by chiral HPLC comparison to an authentic sample prepared by a literature route.[22] This outcome is also in accord with that observed by Jacobsen for enantioselective epoxidation of trisubstituted alkenes.[23] Addition of *C*4-substituents led to higher enantioselectivity (entries 4–6) with larger substituents affording higher levels of enantiocontrol. Next, we explored the electronic effect of *para*-substituents on the aromatic ring (entries 7–10). Electron donating substituents led to increased ee (compare entries 4, 7 and 8) while the electron-withdrawing nitro group gave lower enantioselectivity (entry 10). The *p*-Cl-substituent also led to improved ee (entry 9), as did replacement of the phenyl group with napthyl group (entry 11). In order to check whether differing levels of background epoxidation could be responsible for the substituent effects on enantioselectivity, we subjected substrates **3x**, **3aa** and **3ad** to the Jacobsen conditions in the absence of the Mn(salen) catalyst. No reaction was observed for the latter. While disappearance of the former two substrates was noted, none of the product **7** was observed. Thus differing levels of background reaction is not likely to explain the enantioselectivity trends. Electronic effects in Jacobsen epoxidations have been observed previously, and have been quantified using Hammett correlations. Jacobsen studied the effect on epoxide ee of tuning the effect of substituents in the catalyst.[24] Additionally, there are reports of Hammett studies of substituent effects in the substrate on the ratio of *cis*/*trans* epoxides obtained from cinnamates and stilbenes.[25] However, we were not aware of any study of Hammett correlation of substituent effects in the substrate to product enantiomeric excess. A Hammett plot using log (% *S* product/% *R* product) based on the enantiomeric excesses in Table 7 (entries 4, 7–10) was found to give poor correlation to the substituent σ_{para} values (r^2=0.563) or σ^+_{para} (r^2=0.796). As noted in the qualitative analysis of the results in Table 7, the data point for the *p*-Cl substituent was noticeably off the best-fit line for the Hammett correlation: omission of this data point gave a good correlation to σ^+_{para} (r^2=0.967, slope −0.32). The σ^+_{para} parameter is derived from a study of the rates of S_N1 hydrolysis of substituted aryl halides, which proceed via a benzylic carbocation.[26] A good correlation of ee to this parameter suggests that the transition state leading to the major enantiomer has a larger degree of benzylic cation character than the transition state leading to the minor enantiomer.

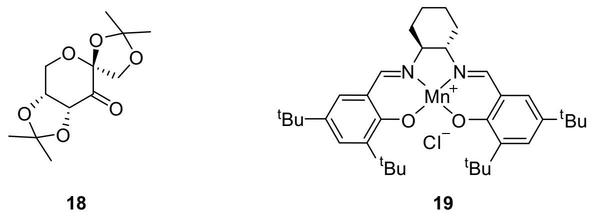


Figure 1. Shi's fructose-derived chiral ketone **18** and Jacobsen's Mn(salen) catalyst (*R*,*R*)-**19**.

3. Conclusions

We have investigated the oxidative rearrangement of a wide range of 2-alkoxypyrans **3** using several common epoxidation reagent systems. Substrates with 6-substitution generally react effectively: they undergo oxidative rearrangement using DMDO, and this process proceeds with good to excellent levels of stereocontrol when a 4-substituent is present. The high cis-selectivity of this process has been exploited in the synthesis of whisky and cognac lactones. Substrates lacking 6-substitution generally gave poorer results: a narrow range of these were found to undergo oxidative rearrangement using MTO/urea–H_2O_2, but yields and diastereoselectivities were generally moderate-to-poor. This chemistry allowed synthesis of crobarbatic acid as a diastereomeric mixture. Finally, 6-phenyl-substituted substrates were found to undergo Jacobsen epoxidation with enantioselectivities of up to 79% ee, with highest ee values for electron-rich aromatic substrates.

4. Experimental

4.1. General experimental

Reactions were run under a positive pressure of nitrogen. Unless otherwise stated, organic layers were dried using $MgSO_4$. Flash column chromatography was performed using BDH F_{254} silica gel. Analytical thin layer chromatography was performed on pre-coated Merck silica gel 60 F_{254} glass backed plates and visualised by either UV light (254 nm) or reactive stain reagents as appropriate. NMR analyses were performed on Bruker AC 250 MHz, AV 400 MHz or DX 400 MHz instruments; Chemical shifts are quoted in parts per million relative to TMS (as referenced to residual $CHCl_3$ δ_H=7.26 or $CDCl_3$ δ_C=77.0). Infrared analyses were recorded on NaCl plates. A Mattson Satellite FTIR spectrometer was employed in the absorption range of 4000–600 cm^{-1}. Microwave reactions were carried out using a CEM Discover instrument. Chemical Ionisation Mass Spectrometry was carried out with ammonia reagent gas using a Micromass Autospec-Q spectrometer. Melting points were determined using a Reichert hot stage microscope apparatus. Optical rotations were recorded on an Optical-Activity AA-5 Polarimeter, with a path length of 10 cm in chloroform unless stated otherwise. $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Concentrations (c) are given in grams per 100 cm^3. Chiral HPLC was performed on Hewlett Packard Series 1100 HPLC system with Chiralcel columns using ^{i}PrOH/hexane as eluent. For HPLC, retention times are quoted in minutes.

4.2. Preparation of enones 1

4.2.1. *(E)-5-Benzyloxy-pent-3-en-2-one* ***1f***[27]

Compound **1f** was prepared by literature procedure.[27]

4.2.2. *(3E,9Z)-Dodecadien-2-one* ***1g***

To a solution of LiCl (0.50 g, 12.0 mmol) in MeCN (90 mL) at room temperature under N_2 was added diethyl(2-oxopropyl)-phosphonate (2.70 g, 12.0 mmol) in MeCN (20 mL). To the reaction mixture was added DBU (1.50 g, 10.0 mmol) dropwise and then a solution of *cis*-6-nonenal (1.40 g, 10.0 mmol) in THF/MeCN (1:1, 40 mL) was added. After stirring overnight, the reaction mixture was quenched with water/brine (1:1, total volume 200 mL). The phases were separated and extracted with EtOAc (2×50 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$ and concentrated to afford the crude product. Column chromatography eluting with EtOAc/petrol (3:7) gave **1g** (1.20 g, 66%) as a colourless oil. ν_{max}/cm^{-1} 2932, 1677, 1360, 1254, 980; δ_H (250 MHz, $CDCl_3$) 6.79 (1H, dt, J 16.0, 7.0, $CH{=}CHC(O)CH_3$), 6.05 (1H, dt, J 16.0, 1.5, $CH{=}CHC(O)CH_3$), 5.42–5.22 (2H, m, $CH_2CH{=}CHCH_2$), 2.26–2.16 (2H, m, CH_2), 2.22 (3H, s, $COCH_3$), 2.08–1.95 (4H, m, 2×CH_2), 1.54–1.29 (4H, m, 2×CH_2), 0.94 (3H, t, J 7.5, CH_2CH_3); δ_C (63 MHz, $CDCl_3$) 198.7 (C), 148.4 (CH), 132.0 (CH), 131.3 (CH), 128.6 (CH), 32.3 (CH_2), 29.2 (CH_2), 27.6 (CH_2), 26.8 (CH_3), 26.7 (CH_2), 20.5 (CH_2), 14.3 (CH_3); m/z (CI) 198 $(M+NH_4)^+$, 181 $(M+H)^+$; m/z calcd for $C_{12}H_{21}O$ $(M+H)^+$, 181.1592; found: 181.1594.

4.2.3. *1-Phenylprop-2-en-1-one* ***1v***[28]

Compound **1v** was prepared according to literature procedure.

4.2.4. *3-Methyl-1-phenylbut-2-en-1-one* ***1w***,[29] *3-ethyl-1-phenylpent-2-en-1-one* ***1x***[30] *and 2-cyclohexylidene-1-phenylethanone* ***1y***[31]

Compounds **1w**, **1x** and **1y** were prepared according to a literature procedure.[32]

4.2.5. *1-(4-Methoxyphenyl)-3-methylbut-2-en-1-one* ***1z***[33]

Compound **1z** was prepared according to a literature procedure.[34]

4.3. General procedure for the preparation of enones (1ab–1ad) by Grignard reaction/MnO_2 oxidation

To a 0.05 M solution of aryl aldehyde (1.0 equiv) in dried Et_2O at room temperature under N_2 was added 0.5 M (2-methylprop-1-enyl)magnesium bromide (in THF, 1.2 equiv). After stirring for 5 h, the reaction was quenched with NH_4Cl (aq). It was then extracted with Et_2O and $NaHCO_3$ (aq) followed by brine. The organic layer was dried by $MgSO_4$ and the solvent was evaporated under reduced pressure. The crude product was dissolved in acetone and MnO_2 (20.0 equiv) was added to the mixture. After stirring at room temperature overnight, Mn residues were removed by filtration and the resulting product was concentrated to give the crude product. Column chromatography, eluting with Et_2O/petrol (1:9) gave the corresponding pure product.

4.3.1. *1-(4-Chlorophenyl)-3-methylbut-2-en-1-one* ***1ab***

Prepared by the general procedure (34 mL of Grignard reagent, 2.00 g of aldehyde and 30.00 g of MnO_2) to give a corresponding product **1ab** as a yellow oil (1.45 g, 53%). ν_{max} ($CHCl_3$)/cm^{-1} 2976–2913 (CH), 1662 (α, β-unsaturated C=O); δ_H (400 MHz, $CDCl_3$) 7.89 (2H, d, J 8.5, 2×CH in Ph), 7.43 (2H, d, J 8.5, 2×CH in Ph), 6.72 (1H, s, CH), 2.23 (3H, s, CH_3), 2.04 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 190.1 (C), 157.7 (CH), 138.6 (C), 137.6 (C), 129.6 (2×CH), 128.7 (2×CH), 120.7 (C), 28.1 (CH_3), 21.3 (CH_3); m/z (CI) 195 (MH^+,100%). Found: MH^+, 195.0577; $C_{11}H_{11}OCl$ requires: MH^+, 195.0577.

4.3.2. *1-(4-Nitrophenyl)-3-methylbut-2-en-1-one* ***1ac***

Prepared by the general procedure (31 mL of Grignard reagent, 2.00 g of aldehyde and 29.00 g of MnO_2) to give a corresponding product **1ac** as a yellow solid (0.35 g, 13%). Mp 114–116 °C; ν_{max} ($CHCl_3$)/cm^{-1} 2947–2903 (CH), 2853, 1656 (α, β-unsaturated C=O), 1613 (NO_2); δ_H (400 MHz, $CDCl_3$) 8.32 (2H, d, J 9.0, 2×CH in Ph), 8.08 (2H, d, J 9.0, 2×CH in Ph), 6.78 (1H, s, CH), 2.30 (3H, s, CH_3), 2.10 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 189.3 (C), 160.4 (CH), 149.8 (C), 144.1 (C), 129.1 (2×CH), 123.7 (2×CH), 120.4 (C), 28.3 (CH_3), 21.6 (CH_3); m/z (CI) 206 (MH^+,100%). Found: MH^+, 206.0816; $C_{11}H_{11}NO_3$ requires: MH^+, 206.0817.

4.3.3. *3-Methyl-1-(naphthalen-2-yl)but-2-en-1-one* ***1ad***[35]

Prepared by the general procedure (40 mL of Grignard reagent, 2.00 g of aldehyde and 32.00 g of MnO_2) to give the corresponding product **1ad** as a yellow solid (1.38 g, 69%).

4.4. Typical procedure for hetero Diels–Alder reaction

4.4.1. *Conditions A*

To vinyl ether **2** (2.0–10.0 equiv) at room temperature in a pressure tube was added enone **1** (1.0 equiv) and YbFOD (0.02–0.05 equiv). The tube was sealed and the solution was then stirred at the appropriate temperature (45–100 °C) for 1–10 days. After allowing the mixture to cool to room temperature, column chromatography, eluting with diethyl ether/petrol, gave the alkoxydihydropyran product.

4.4.2. *Conditions B*

To vinyl ether **2** (5.0 equiv) was added enone **1** (1.0 equiv) and YbFOD (0.05 equiv). After reaction under microwave conditions (300 W, 24 psi) at 65 °C for 2-3 h, column chromatography, eluting with diethyl ether/petrol (5:95 to 1:9), gave the product 2-alkoxydihydropyrans.

The following dihydropyrans gave spectroscopic data in accord with those in the literature, **3a**,[36] **3c**,[6] **3d**,[37] **3f**,[38] **3i**,[14] **3j**,[14] **3k**,[14] **3l**,[14] **3m**,[14] **3n**,[14] **3p**.[14]

4.4.3. *2-Butoxy-6-methyl-3,4-dihydro-2H-pyran* ***3b***

Prepared by the general procedure (conditions A, 1.0 equiv of diene **1a**, 2.0 equiv of vinyl ether **2b**, 0.05 equiv of Yb catalyst, 90 °C, 6 days) to give **3ac** (2.80 g, 55%) as a pale yellow oil. ν_{max} (CHCl$_3$)/cm^{-1} 2958–2936 (CH), 1721, 1687 (C=C); δ_H (250 MHz, CDCl$_3$) 4.97 (1H, t, *J* 3.5, OCHO), 4.52 (1H, t, *J* 3.5, C=CH), 3.78 (1H, dt, *J* 9.5, 6.5, OCH$_2$), 3.50 (1H, dt, *J* 9.5, 6.5, OCH$_2$), 2.20–1.69 (4H, m, CH$_2$CH$_2$), 1.68–1.48 (2H, m, CH$_2$), 1.42–1.24 (2H, m, CH$_2$), 1.71 (3H, s, CCH$_3$), 0.90 (3H, t, *J* 7.5, CH$_2$C*H*$_3$); δ_C (125 MHz, CDCl$_3$) 147.4 (C), 97.4 (CH), 96.1 (CH), 67.9 (CH$_2$), 31.8 (CH$_2$), 26.4 (CH$_2$), 19.9 (CH$_3$), 19.3 (CH$_2$), 17.0 (CH$_2$), 13.8 (CH$_3$); *m*/*z* (CI) 140, 171 (MH$^+$), 197. Found: MH$^+$, 171.1387; C$_{10}$H$_{18}$O$_2$ requires: MH$^+$, 171.1385.

4.4.4. *2-Butoxy-4,4,6-trimethyl-3,4-dihydro-2H-pyran* ***3e***

Prepared by the general procedure (conditions A, 1.0 equiv of diene **1d**, 5.0 equiv of vinyl ether **2b**, 0.05 equiv of Yb catalyst, 100 °C, 5 days) to give **3e** (1.60 g, 54%) as a pale yellow oil. ν_{max} (CHCl$_3$)/cm^{-1} 2958–2872 (CH), 1676 (C=C); δ_H (250 MHz, CDCl$_3$) 4.88 (1H, dd, *J* 7.5, 3.0, OCHO), 4.32 (1H, s, C=CH), 3.88 (1H, dt, *J* 9.5, 6.5, OCH$_2$), 3.48 (1H, dt, *J* 9.5, 6.5, OCH$_2$), 1.76–1.25 (6H, m, CH$_2$, CH$_2$CH$_2$), 1.71 (3H, s, C=CCH$_3$), 1.02, 1.00 (6H, s, C(CH$_3$)$_2$), 0.92 (3H, t, *J* 7.5, CH$_2$C*H*$_3$); δ_C (63 MHz, CDCl$_3$) 145.9 (C), 107.4 (CH), 98.4 (CH), 68.6 (CH$_2$), 41.7 (CH$_2$), 31.8 (CH$_2$), 31.4 (CH$_3$), 30.5 (CH$_3$), 29.6 (C), 19.7 (CH$_3$), 19.3 (CH$_2$), 13.8 (CH$_3$); *m*/*z* (CI) 199 (MH$^+$, 100%). Found: MH$^+$, 199.1695; C$_{12}$H$_{22}$O$_2$ requires: MH$^+$, 199.1698.

4.4.5. *(2S*,4S*)-2-Benzyloxymethyl-2-ethoxy-6-methyl-3,4-dihydro-2H-pyran* ***3g***

Prepared by the general procedure (conditions A, 1.0 equiv of diene **1f**, 10.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 55 °C, 1 day) to give **3g** (0.60 g, 67%) as a pale yellow oil. ν_{max} (CHCl$_3$)/cm^{-1} 2976–2857 (CH), 1714, 1643 (C=C); δ_H (250 MHz, CDCl$_3$) 7.38–7.23 (5H, m, Ph), 5.01 (1H, dd, *J* 7.5, 1.0, OCHO), 4.55–4.51 (3H, CH$_3$C=C*H*, PhCH$_2$), 4.00 (1H, dq, *J* 9.5, 7.0, OC*H*$_2$CH$_3$), 3.60 (1H, dq, *J* 9.5, 7.0, OC*H*$_2$CH$_3$), 3.43 (2H, d, *J* 7.0, BnOCH$_2$), 2.73–2.55 (1H, m, BnOCH$_2$C*H*), 2.09 (1H, ddd, *J* 13.0, 6.5, 2.0, CHC*H*$_2$CH), 1.77 (3H, s, CCH$_3$), 1.67 (1H, ddd, *J* 13.0, 6.5, 2.0, CHC*H*$_2$CH), 1.26 (3H, t, *J* 7.0, CH$_2$C*H*$_3$); *m*/*z* (CI) 263 (MH$^+$, 100%), 280 (MNH$_4^+$). Found: MH$^+$, 263.1652; C$_{16}$H$_{22}$O$_3$ requires: MH$^+$, 263.1647.

4.4.6. *(2S*,4S*)-2-Ethoxy-6-methyl-4-(Z-octen-5-yl)-3,4-dihydro-2H-pyran* ***3h***

Prepared by the general procedure (conditions A, 1.0 equiv of diene **1g**, 10.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 55 °C, 5 days) to give **3h** (0.55 g, 56%) in a 4:1 inseparable mixture as a pale yellow oil. Data in accordance with the literature.[6] ν_{max} (CHCl$_3$)/cm^{-1} 3002–2855 (CH), 1719, 1652 (C=C); δ_H (250 MHz, CDCl$_3$) 5.40–5.24 (2H$_{both}$, m, CH=CH), 5.01 (1H$_{minor}$, t, *J* 3.0, OCHO), 4.88 (1H$_{major}$, dd, *J* 9.0, 2.0, OCHO), 4.51–4.48 (1H$_{minor}$, m, C=CH), 4.49–4.36 (1H$_{major}$, m, C=CH), 4.01–3.77 (1H$_{both}$, dt, *J* 9.5, 7.0, OCH$_2$), 3.63–3.50 (1H$_{both}$, m, OCH$_2$), 2.32–1.80 (5H$_{both}$, m, C=CHC*H*CH$_2$, CH$_2$, CH$_2$), 1.72 (3H$_{both}$, s, CH=CC*H*$_3$), 1.52–1.12 (11H$_{both}$, m, 4×CH$_2$ and OCH$_2$C*H*$_3$), 0.94 (3H$_{both}$, t, *J* 7.5, CH$_2$C*H*$_3$); *m*/*z* (CI) 253 (MH$^+$, 100%), 270 (MNH$_4^+$, 100%). Found: MH$^+$, 253.2172; C$_{16}$H$_{28}$O$_2$ requires: MH$^+$, 253.2168.

4.4.7. *2-Ethoxy-5-methyl-3,4-dihydro-2H-pyran* ***3o***

Prepared by the general procedure (conditions B, 5.0 mmol, 1.0 equiv of methacrolein **1n**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 65 °C, 2 h) to afford the title compound **3o** (646 mg, 91%) as a colourless oil. ν_{max} (CH$_2$Cl$_2$)/cm^{-1} 3210, 1384, 1106, 1034; δ_H (400 MHz, CDCl$_3$) 6.05 (1H, s, OC*H*=C), 4.93–4.90 (1H, m, OC*H*CH$_2$), 3.82 (1H, dq, *J* 9.7, 7.0, OC*H*HCH$_3$), 3.55 (1H, dq, *J* 9.8, 7.0, OCH*H*CH$_3$), 2.15–2.03 (1H, m, OC*H*HCH$_2$), 1.89–1.79 (3H, m, CCH$_2$C*H*$_2$ and OCH*H*CH$_2$), 1.56 (3H, s, HC=CC*H*$_3$), 1.22 (3H, t, *J* 7.1, OCH$_2$C*H*$_3$); δ_C (63 MHz, CDCl$_3$) 134.9 (CH), 109.3 (C), 96.2 (CH), 63.5 (CH$_2$), 26.7 (CH$_2$), 21.9 (CH$_2$), 18.4 (CH$_3$), 15.1 (CH$_3$); *m*/*z* (CI) 143 (M+H)$^+$, 160 (M+NH$_4$)$^+$. Found: 143.1067 (M+H)$^+$; C$_8$H$_{15}$O$_2$ requires: 143.1072.

4.4.8. *(2S*,4S*)-2-Ethoxy-4-ethyl-5-methyl-3,4-dihydro-2H-pyran* ***3q***

Prepared by the general procedure (conditions A, 20.0 mmol, 1.0 equiv *trans*-2-methyl-2-pentenal **1p**, 5.0 equiv of vinyl ether **2a**, 0.02 equiv of Yb catalyst, 55 °C, 10 days) to afford the title compound **3q** (3.17 g, 93%) as a colourless oil. ν_{max} (CH$_2$Cl$_2$)/cm^{-1} 2964, 1664, 1458, 1378, 1140, 1082, 1059; δ_H (400 MHz, CDCl$_3$) 6.08 (1H, s, OC*H*=C), 4.83 (1H, dd, *J* 8.3, 2.1, OC*H*CH$_2$), 3.90 (1H, dq, *J* 9.5, 7.1, OC*H*HCH$_3$), 3.54 (1H, dq, *J* 9.5, 7.1, OCH*H*CH$_3$), 2.18–2.11 (1H, m, CC*H*CH$_2$), 1.98 (1H, ddd, 13.2, 6.7, 2.1, CHC*H*HCH), 1.71–1.61 (2H, m, CHC*H*$_2$CH$_3$), 1.36–1.24 (1H, m, CHCH*H*CH), 1.23 (3H, t, *J* 7.1, OCH$_2$C*H*$_3$), 0.87 (3H, t, *J* 7.1, CHCH$_2$C*H*$_3$); δ_C (100 MHz, CDCl$_3$) 136.3 (CH), 112.5 (C), 99.2 (CH), 64.1 (CH$_2$), 35.8 (CH), 33.1 (CH$_2$), 24.7 (CH$_2$), 15.6 (CH$_3$), 15.2 (CH$_3$), 10.5 (CH$_3$); *m*/*z* (CI) 171 (M+H)$^+$, 188 (M+NH$_4$)$^+$. Found: 171.1385 (M+H)$^+$; C$_{10}$H$_{19}$O$_2$ requires: 171.1385.

4.4.9. *(2S*,4R*)-2-Ethoxy-5-methyl-4-phenyl-3,4-dihydro-2H-pyran* ***3r***

Prepared by the general procedure (conditions A, 8.0 mmol, 1.0 equiv *trans*-2-methyl-cinnamaldehyde **1q**, 5.0 equiv of vinyl ether **2a**, 0.04 equiv of Yb catalyst, 65 °C, 10 days) to afford the title compound **3r** (1.57 g, 90%) as a colourless oil. ν_{max} (CH$_2$Cl$_2$)/cm^{-1} 3201, 1384, 1348, 1107, 1034; δ_H (250 MHz, CDCl$_3$) 7.16–7.33 (5H, m, Ar*H*), 6.28 (1H, s, OC*H*=C), 4.95 (1H, dd, *J* 8.5, 2.1, OC*H*CH$_2$), 3.92 (1H, dq, *J* 9.5, 7.1, OC*H*HCH$_3$), 3.56 (1H, dq, *J* 9.5, 7.1, OCH*H*CH$_3$), 3.42 (1H, br t, *J* 8.4, CC*H*CH$_2$), 2.26 (1H, ddd, 13.5, 7.5, 2.1, CHC*H*HCH), 1.97 (1H, ddd, 13.5, 9.7, 8.5, CHCH*H*CH), 1.32 (3H, s, HC=CC*H*$_3$), 1.22 (3H, t, *J* 7.1, OCH$_2$C*H*$_3$); δ_C (63 MHz, CDCl$_3$) 143.2 (C), 137.8 (CH), 128.4 (CH), 128.1 (CH), 126.4 (CH), 111.4 (C), 98.8 (CH), 64.1 (CH$_2$), 42.5 (CH), 38.1 (CH$_2$), 16.1 (CH$_3$), 15.2 (CH$_3$); *m*/*z* (CI) 219 (M+H)$^+$, 236 (M+NH$_4$)$^+$. Found: 219.1389 (M+H)$^+$; C$_{14}$H$_{19}$O$_2$ requires: 219.1385.

4.4.10. *(2S*,4S*)-2-Ethoxy-4-(furan-2-yl)-5-methyl-3,4-dihydro-2H-pyran* ***3s***

Prepared by the general procedure (conditions B, 5.0 mmol, 1.0 equiv 2-methyl-3-(2-furyl)-propenal **1r**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 65 °C, 4 h) to give **3s** (137 mg, 13%) as a pale yellow oil. ν_{max} (CH$_2$Cl$_2$)/cm^{-1} 2975, 1666, 1379, 1134, 1004, 934, 731; δ_H (250 MHz, CDCl$_3$) 7.31 (1H, dd, *J* 1.8, 0.8, Ar*H*), 6.29 (1H, *J* 3.2, 1.8, Ar*H*), 6.18 (1H, s, OC*H*=C), 6.08 (d, *J* 3.0, Ar*H*), 4.94 (1H, dd, *J* 5.8, 4.2, OC*H*CH$_2$), 3.89 (1H, dq, *J* 9.8, 7.1, OC*H*HCH$_3$), 3.61–3.47 (2H, m, OCH*H*CH$_3$ and CC*H*CH$_2$), 2.21–2.14 (2H, m, CHC*H*$_2$CH), 1.42 (3H, s, HC=CCH$_3$), 1.20 (3H, t, *J* 7.1, OCH$_2$C*H*$_3$); δ_C (100 MHz, CDCl$_3$) 155.9 (C), 141.0 (CH), 137.0 (CH), 110.1 (CH), 109.5 (C), 105.9 (CH), 98.2 (CH), 64.0 (CH$_2$), 35.1 (CH), 33.5 (CH$_2$), 16.1 (CH$_3$), 15.1 (CH$_3$); *m*/*z* (CI) 209 (M+H)$^+$, 226 (M+NH$_4$)$^+$. Found: 209.1182 (M+H)$^+$; C$_{12}$H$_{17}$O$_3$ requires: 209.1178.

4.4.11. *(2S*,4S*)-2,4-Diethoxy-5-methyl-3,4-dihydro-2H-pyran* ***3t***

Prepared by the general procedure (conditions B, 5.0 mmol, 1.0 equiv 2-methyl-3-(2-furyl)-propenal **1s**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 65 °C, 3 h) to afford the title compound **3t** (248 mg, 26%) as a colourless oil. ν_{max} (CH$_2$Cl$_2$)/cm^{-1} 2975, 1668, 1456, 1379, 1139, 1096; δ_H (400 MHz, CDCl$_3$) 6.10 (1H, s, OC*H*=C), 4.90 (1H, dd, *J* 7.1, 2.7, OC*H*CH$_2$), 3.92–1.94 (7H, br m, 2×OC*H*$_2$CH$_3$, CHC*H*$_2$CH, and CC*H*CH$_2$), 1.59 (3H, s, HC=CCH$_3$), 1.21 (3H, t, *J* 7.1, OCH$_2$C*H*$_3$), 1.10 (3H, d, *J* 7.0, OCH$_2$C*H*$_3$); δ_C (63 MHz, CDCl$_3$) 138.0 (CH), 110.7 (C), 97.7 (CH), 71.4 (CH), 64.4 (CH$_2$), 63.3 (CH$_2$), 33.6 (CH$_2$), 15.5 (CH$_3$), 15.0 (CH$_3$), 14.6 (CH$_3$); *m*/*z* (CI) 204 (M+NH$_4$)$^+$. Found: 204.1600 (M+NH$_4$)$^+$; C$_{10}$H$_{22}$NO$_3$ requires: 204.1600.

*4.4.12. 5-Butyl-2-ethoxy-3,4-dihydro-2H-pyran **3u***

Prepared by the general procedure (conditions B, 5.0 mmol, 1.0 equiv 2-methylenehexanal **1t**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 65 °C, 2 h) to afford the title compound **3u** (743 mg, 81%) as a colourless oil. $\nu_{\max}$ (CH_2Cl_2)/cm^{-1} 2962, 1671, 1456, 1376, 1144, 1074; δ_H (250 MHz, $CDCl_3$) 6.05 (1H, s, OC*H*=C), 4.92 (1H, t, *J* 3.3, OC*H*CH$_2$), 3.82 (1H, dq, *J* 9.7, 7.1, OC*H*HCH$_3$), 3.55 (1H, dq, *J* 9.7, 7.0, OCH*H*CH$_3$), 1.98–1.40 (10H, br m, 5×C*H*$_2$), 1.21 (3H, t, *J* 7.1, OCH$_2$C*H*$_3$), 0.89 (3H, t, *J* 7.0, OCH$_2$C*H*$_3$); δ_C (63 MHz, $CDCl_3$) 135.0 (CH), 113.4 (C), 96.3 (CH), 63.4 (CH$_2$), 32.5 (CH$_2$), 29.9 (CH$_2$), 26.8 (CH$_2$), 22.1 (CH$_2$), 19.9 (CH$_2$), 15.2 (CH$_3$), 13.9 (CH$_3$); *m*/*z* (CI) 185 $(M+H)^+$, 202 $(M+NH_4)^+$. Found: 185.1539 $(M+H)^+$; $C_{11}H_{21}O_2$ requires: 185.1542.

4.4.13. (2S,4S*)-2-Ethoxyethoxy-4-methyl-5-phenyl-3,4-dihydro-2H-pyran **3v***

Prepared by the general procedure (conditions B, 5.0 mmol, 1.0 equiv 2-phenyl-2-butenal **1u**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 65 °C, 2 h) to afford the title compound **3v** (995 mg, 91%, 3:1 dr) as a pale yellow oil. $\nu_{\max}$ (CH_2Cl_2)/cm^{-1} 2976, 2929, 1639, 1445, 1156, 1137, 1097, 976, 851, 760, 698; δ_H (250 MHz, $CDCl_3$) 7.35–7.16 (5H, m, Ar*H*), 6.53 (1H, s, OC*H*=C), 5.08 (1H$_{\text{major}}$, dd, *J* 5.9, 2.6, OC*H*CH$_2$), 5.02 (1H$_{\text{minor}}$, dd, *J* 6.6, 2.3, OC*H*CH$_2$), 3.92 (1H, dq, *J* 9.5, 7.1, OC*H*HCH$_3$), 3.64 (1H$_{\text{minor}}$, dq, *J* 9.6, 7.1, OCH*H*CH$_3$), 3.59 (1H$_{\text{major}}$, dq, *J* 9.5, 7.0, OCH*H*CH$_3$), 3.06–2.83 (1H, m, CC*H*CH$_2$), 2.17 (1H$_{\text{major}}$, ddd, *J* 13.6, 6.9, 2.6, CHC*H*HCH), 2.05 (1H$_{\text{minor}}$, dd, *J* 13.2, 6.6, CHCH*H*CH), 1.88–1.75 (1H, m, CHCH*H*CH), 1.27 (3H$_{\text{minor}}$, t, *J* 7.1, OCH$_2$C*H*$_3$), 1.26 (3H$_{\text{major}}$, t, *J* 7.1, OCH$_2$C*H*$_3$), 1.05 (3H$_{\text{major}}$, d, *J* 7.1, CHC*H*$_3$), 1.02 (3H$_{\text{minor}}$, d, *J* 7.1, CHC*H*$_3$); δ_C (63 MHz, $CDCl_3$) 138.5 (C)$_{\text{minor}}$, 138.3 (C)$_{\text{major}}$, 128.3 (CH), 126.2 (CH), 126.0 (CH), 119.7 (C), 98.1 (CH)$_{\text{major}}$, 96.6 (CH)$_{\text{minor}}$, 64.1 (CH$_2$), 35.4 (CH$_2$), 26.4 (CH$_2$)$_{\text{major}}$, 25.3 (CH$_2$)$_{\text{minor}}$, 20.4 (CH$_3$)$_{\text{minor}}$, 19.9 (CH$_3$)$_{\text{major}}$, 15.2 (CH$_3$); *m*/*z* (CI) 219 $(M+H)^+$, 236 $(M+NH_4)^+$. Found: 219.1377 $(M+H)^+$; $C_{14}H_{19}O_2$ requires: 219.1385.

*4.4.14. 2-Ethoxy-6-phenyl-3,4-dihydro-2H-pyran **3w***

Prepared by the general procedure (conditions B, 3.1 mmol, 1.0 equiv of diene **1v**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 55 °C, 2 h) to give alkoxydihydropyran **3w** (0.30 g, 48%) as a pale yellow oil. $\nu_{\max}$ ($CHCl_3$)/cm^{-1} 2974 (CH), 1722, 1684 (C=C); δ_H (400 MHz, $CDCl_3$) 7.60 (2H, d, *J* 8.0, 2×CH in Ph), 7.37–7.27 (3H, m, 3×CH in Ph), 5.45 (1H, dd, *J* 3.5, 4.5, OCHO), 5.26 (1H, t, *J* 3.5, C=CH), 4.01 (1H, dq, *J* 9.5, 7.0, OC*H*H), 3.72 (1H, dq, *J* 9.5, 7.0, OCH*H*), 2.44–2.15 (2H, m, CH$_2$), 1.97–1.90 (2H, m, CH$_2$), 1.28 (3H, t, *J* 7.0, CH$_3$); δ_C (125 MHz, $CDCl_3$) 148.1 (C), 136.0 (C), 128.1, 127.7, 124.3 (5×CH), 98.0 (CH), 97.6 (CH), 63.8 (CH$_2$), 26.5 (CH$_2$), 17.6 (CH$_2$), 15.3 (CH$_3$); *m*/*z* (CI) 205 (MH$^+$,100%). Found: MH$^+$, 205.1225; $C_{13}H_{16}O_2$ requires: MH$^+$, 205.1228.

*4.4.15. 2-Ethoxy-4,4-dimethyl-6-phenyl-3,4-dihydro-2H-pyran **3x***

Prepared by the general procedure (conditions B, 6.2 mmol, 1.0 equiv of diene **1w**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 55 °C, 4 h) to give alkoxydihydropyran **3x** (0.60 g, 41%) as a yellow oil. $\nu_{\max}$ ($CHCl_3$)/cm^{-1} 3058–2957 (CH), 2250, 1649 (C=C); δ_H (500 MHz, $CDCl_3$) 7.62–7.65 (2H, m, 2×CH in Ph), 7.28–7.39 (3H, m, 3×CH in Ph), 5.26 (1H, s, CCHC), 5.14 (1H, dd, *J* 2.5, 8.0, OCHO), 4.15 (1H, dt, *J* 9.5, 7.0, OC*H*H), 3.74 (1H, dt, *J* 9.5, 7.0, OCH*H*), 1.85–1.89 (1H, m, CH$_2$), 1.77–1.81 (1H, m, CH$_2$), 1.35 (3H, t, *J* 7.0, CH$_2$C*H*$_3$), 1.21 (3H, s, CH$_3$), 1.19 (3H, s, CH$_3$); δ_C (125 MHz, $CDCl_3$) 146.6 (C), 135.7 (C), 128.1, 127.8, 124.6 (5×CH), 108.6 (CH), 98.7 (CH), 64.6 (CH$_2$), 42.0 (CH$_2$), 31.5 (CH$_3$), 30.6 (CH$_3$), 30.5 (C), 15.4 (CH$_3$); *m*/*z* (CI) 233 (MH$^+$,100%). Found: MH$^+$, 233.1537; $C_{15}H_{20}O_2$ requires: MH$^+$, 233.1542.

*4.4.16. 2-Ethoxy-4,4-diethyl-6-phenyl-3,4-dihydro-2H-pyran **3y***

Prepared by the general procedure (conditions B, 6.4 mmol, 1.0 equiv of diene **1x**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 70–80 °C, 4 h) to give alkoxydihydropyran **3y** (0.20 g, 12%) as a pale yellow oil. $\nu_{\max}$ ($CHCl_3$)/cm^{-1} 2968 (CH), 2254, 1713, 1650 (C=C); δ_H (400 MHz, $CDCl_3$) 7.58–7.61 (2H, m, 2×CH in Ph), 7.24–7.35 (3H, m, 3×CH in Ph), 5.20 (1H, s, CCHC), 5.06 (1H, dd, *J* 2.5, 8.5, OCHO), 4.14 (1H, dt, *J* 9.5, 7.0, OC*H*H), 3.70 (1H, dt, *J* 9.5, 7.0, OCH*H*), 1.68–1.80 (2H, m, CH$_2$), 1.39–1.54 (4H, 2×CC*H*$_2$CH$_3$), 1.32 (3H, t, *J* 7.0, OCH$_2$C*H*$_3$), 0.88 (3H, t, *J* 7.5, CH$_3$), 0.85 (3H, t, *J* 7.5, CH$_3$); δ_C (125 MHz, $CDCl_3$) 147.9 (C), 135.8 (C), 128.1, 127.9, 124.6 (5×CH), 106.1 (CH), 98.9 (CH), 64.6 (CH$_2$), 37.5 (CH$_2$), 36.7 (C), 33.6 (CH$_2$), 31.5 (CH$_2$), 15.4 (CH$_3$), 8.3 (2×CH$_3$); *m*/*z* (CI) 261 (MH$^+$, 100%). Found: MH$^+$, 261.1851; $C_{17}H_{24}O_2$ requires: MH$^+$, 261.1854.

*4.4.17. 4-Ethoxy-2-phenyl-3-oxa-spiro[5,5]undec-1-ene **3z***

Prepared by the general procedure (conditions B, 9.2 mmol, 1.0 equiv of diene **1y**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 65 °C, 6 h) to give alkoxydihydropyran **3z** (0.75 g, 30%) as a pale yellow oil. $\nu_{\max}$ ($CHCl_3$)/cm^{-1} 2927 (CH), 2251, 1648 (C=C); δ_H (400 MHz, $CDCl_3$) 7.58–7.62 (2H, m, CH in Ph), 7.24–7.34 (3H, m, CH in Ph), 5.38 (1H, s, CCHC), 5.07 (1H, dd, *J* 8.5, 2.5, OCHO), 4.12 (1H, dt, *J* 9.5, 7.0, OC*H*H), 3.69 (1H, dt, *J* 9.5, 7.0, OCH*H*), 2.00 (1H, d, *J* 13.0, 1H in CH$_2$), 1.38–1.68 (11H, m, 1H in CH$_2$, 5×CH$_2$ in CyHex), 1.31 (3H, t, *J* 7.0, CH$_2$C*H*$_3$); δ_C (100 MHz, $CDCl_3$) 146.8 (C), 135.8 (C), 128.6, 128.0, 124.6 (5×CH), 107.1 (CH), 98.5 (CH), 64.5 (CH$_2$), 39.4 (CH$_2$), 39.3 (CH$_2$), 36.6 (C), 33.6 (CH$_2$), 26.0 (CH$_2$), 22.0 (CH$_2$), 21.5 (CH$_2$), 15.3 (CH$_3$); *m*/*z* (CI) 273 (MH$^+$,100%). Found: MH$^+$, 273.1849; $C_{18}H_{24}O_2$ requires: MH$^+$, 273.1854.

*4.4.18. 2-Ethoxy-6-(4-methoxyphenyl)-4,4-dimethyl-3,4-dihydro-2H-pyran **3aa***

Prepared by the general procedure (conditions B, 5.3 mmol, 1.0 equiv of diene **1z**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 60 °C, 5 h) to give alkoxydihydropyran **3aa** (0.38 g, 27%) as a yellow oil. $\nu_{\max}$ ($CHCl_3$)/cm^{-1} 3380, 2960 (CH), 2360, 2054, 1646 (C=C), 1622; δ_H (400 MHz, $CDCl_3$) 7.55 (2H, d, *J* 8.5, 2×CH in Ph), 6.89 (2H, d, *J* 8.5, 2×CH in Ph), 5.11–5.13 (2H, m, CCHC, OCHO), 4.14 (1H, dt, *J* 15.0, 7.5, 1H in OC*H*H), 3.84 (3H s, OCH$_3$), 3.73 (1H, dt, *J* 15.0, 7.5, 1H in OCH*H*), 1.89–1.70 (2H, m, CH$_2$), 1.34 (3H, t, *J* 7.0, CH$_2$CH$_3$), 1.18 (3H, s, CCH$_3$), 1.16 (3H, s, CCH$_3$); δ_C (100 MHz, $CDCl_3$) 159.4 (C), 146.4 (C), 128.4 (C), 125.9 (2×CH), 113.5 (2×CH), 107.0 (CH), 98.7 (CH), 64.5 (CH$_2$), 55.3 (CH$_3$), 42.1 (CH$_2$), 31.6 (CH$_3$), 30.7 (CH$_3$), 30.4 (C), 15.4 (CH$_3$); *m*/*z* (CI) 263 (MH$^+$,100%). Found: MH$^+$, 263.1642; $C_{16}H_{22}O_3$ requires: MH$^+$, 263.1647.

*4.4.19. 2-Ethoxy-4,4-dimethyl-6-p-tolyl-3,4-dihydro-2H-pyran **3ab***

Prepared by the general procedure (conditions B, 11.5 mmol, 1.0 equiv of diene **1aa**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 65 °C, 3 h) to give alkoxydihydropyran **3ab** (1.13 g, 40%) as a yellow oil. $\nu_{\max}$ ($CHCl_3$)/cm^{-1} 2956–2926 (CH), 2867, 1649 (C=C); δ_H (400 MHz, $CDCl_3$) 7.50 (2H, d, *J* 8.0, 2×CH in Ph), 7.15 (2H, d, *J* 8.0, 2×CH in Ph), 5.19 (1H, s, C=CH), 5.11 (1H, dd, *J* 8.0, 2.5, OCHO), 4.13 (1H, dt, *J* 9.5, 7.0, OC*H*H), 3.72 (1H, dt, *J* 9.5, 7.0, OCH*H*), 2.37 (3H, s, CH$_3$Ph), 1.73–1.86 (2H, m, CH$_2$), 1.33 (3H, t, *J* 7.0, CH$_2$C*H*$_3$), 1.18 (3H, s, CH$_3$), 1.16 (3H, s, CH$_3$); δ_C (100 MHz, $CDCl_3$) 146.6 (C), 137.6 (C), 132.9 (C), 128.8 (2×CH), 124.4 (2×CH), 107.8 (CH), 98.6 (CH), 64.5 (CH$_2$), 42.0 (CH$_2$), 31.5, 30.6 (2×CH$_3$), 30.5 (C), 21.2 (CH$_3$), 15.4 (CH$_3$); *m*/*z* (CI) 247 (MH$^+$,100%). Found: MH$^+$, 247.1689; $C_{16}H_{22}O_2$ requires: MH$^+$, 247.1685.

*4.4.20. 6-(4-Chlorophenyl)-2-ethoxy-4,4-dimethyl-3,4-dihydro-2H-pyran **3ac***

Prepared by the general procedure (conditions B, 5.2 mmol, 1.0 equiv of diene **1ab**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 65 °C, 5 h) to give alkoxydihydropyran **3ac** (0.60 g, 44%) as a yellow oil. $\nu_{\max}$ ($CHCl_3$)/cm^{-1} 2958–2926 (CH), 2867, 1648 (C=C); δ_H (400 MHz, $CDCl_3$) 7.54 (2H, d, *J* 8.5, 2×CH in Ph), 7.31 (2H, d, *J* 8.5, 2×CH in Ph), 5.23 (1H, s, CCHC), 5.12 (1H, dd, *J* 8.0, 2.5, OCHO), 4.11

(1H, dt, *J* 9.5, 7.0, OC*H*H), 3.71 (1H, dt, *J* 9.5, 7.0, OCH*H*), 1.72–1.87 (2H, m, CH_2), 1.33 (3H, t, *J* 7.0, CH_2CH_3), 1.19 (3H, s, CCH_3), 1.17 (3H, s, CCH_3); δ_C (100 MHz, $CDCl_3$) 145.7 (C), 134.2 (C), 133.5 (C), 128.2 (2×CH), 125.8 (2×CH), 109.0 (CH), 98.8 (CH), 64.6 (CH_2), 41.8 (CH_2), 31.4 (CH_3), 30.5 (C, CH_3), 15.4 (CH_3); *m*/*z* (CI) 267 (MH^+,100%). Found: MH^+, 267.1149; $C_{15}H_{19}O_2Cl$ requires: MH^+, 267.1152.

4.4.21. *6-(4-Nitrophenyl)-2-ethoxy-4,4-dimethyl-3,4-dihydro-2H-pyran* ***3ad***

Prepared by the general procedure (conditions B, 1.6 mmol, 1.0 equiv of diene **1ac**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 65 °C, 5 h) to give alkoxydihydropyran **3ad** (0.25 g, 58%) as a yellow oil. ν_{max} ($CHCl_3$)/cm^{-1} 3466, 2254, 1640 (C=C), 1518 (NO_2); δ_H (400 MHz, $CDCl_3$) 8.20 (2H, d, *J* 9.0, 2×CH in Ph), 7.74 (2H, d, *J* 9.0, 2×CH in Ph), 5.46 (1H, s, CCHC), 5.16 (1H, dd, *J* 7.5, 2.5, OCHO), 4.05–4.15 (1H, m, OC*H*H), 3.68–3.77 (1H, m, OCH*H*), 1.90–1.77 (2H, m, CH_2), 1.32 (3H, t, *J* 7.0, CH_2CH_3), 1.22 (3H, s, CH_3), 1.19 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 147.1 (C), 145.0 (C), 141.8 (C), 125.0 (2×CH), 123.5 (2×CH), 112.8 (CH), 98.9 (CH), 64.8 (CH_2), 41.5 (CH_2), 31.2 (CH_3), 30.6 (C), 30.2 (CH_3), 15.3 (CH_3); *m*/*z* (CI) 278 (MH^+,100%). Found: MH^+, 278.1405; $C_{15}H_{19}NO_4$ requires: MH^+, 278.1392.

4.4.22. *2-Ethoxy-4,4-dimethyl-6-(naphthalen-2-yl)-3,4-dihydro-2H-pyran* ***3ae***

Prepared by the general procedure (conditions B, 4.8 mmol, 1.0 equiv of diene **1ad**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 65 °C, 5 h) to give alkoxydihydropyran **3ae** (0.55 g, 41%) as a yellow oil. ν_{max} ($CHCl_3$)/cm^{-1} 3057–2926 (CH), 2868, 1643 (C=C), 1626; δ_H (400 MHz, $CDCl_3$) 8.09 (1H, s, CH in Naph), 7.79–7.90 (3H, m, 3×CH in Naph), 7.71 (1H, dd, *J* 8.5, 1.5, CH in Naph), 7.45–7.51 (2H, m, 2×CH in Naph), 5.41 (1H, s, CCHC), 5.21 (1H, dd, *J* 2.5, 8.0, OCHO), 4.22 (1H, dt, *J* 9.5, 7.0, OC*H*H), 3.79 (1H, dt, *J* 9.5, 7.0, OCH*H*), 1.82–1.94 (2H, m, CH_2), 1.38 (3H, t, *J* 7.0, CH_2CH_3), 1.24 (3H, s, CH_3), 1.21 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 146.6 (C), 133.3 (C), 133.0 (C), 132.9 (C), 128.4 (CH), 127.63 (CH), 127.55 (CH), 126.1 (CH), 125.9 (CH), 123.3 (CH), 122.8 (CH), 109.4 (CH), 98.8 (CH), 64.7 (CH_2), 42.0 (CH_2), 31.5 (CH_3), 30.65 (CH_3), 30.63 (C), 15.4 (CH_3); *m*/*z* (CI) 283 (MH^+,100%). Found: MH^+, 283.1691; $C_{19}H_{22}O_2$ requires: MH^+, 283.1698.

4.4.23. *(2S*,4S*)-2-Ethoxy-4-methyl-6-propyl-3,4-dihydro-2H-pyran* ***3af***

Prepared by the general procedure (conditions B, 4.3 mmol, 1.0 equiv of diene **1**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 55 °C, 5 days) to give **3af** (0.55 g, 70%) in a 4:1 inseparable mixture as a colourless oil. ν_{max} ($CHCl_3$)/cm^{-1} 2961–2873 (CH), 1675 (C=C); δ_H (250 MHz, $CDCl_3$) 5.00 ($1H_{minor}$, t, *J* 3.0, OCHO), 4.88 ($1H_{major}$, dd, *J* 8.5, 2.0, OCHO), 4.44 ($1H_{minor}$, d, *J* 1.0, C=CH), 4.33 ($1H_{major}$, d, *J* 1.0, C=CH), 3.93 ($1H_{major}$, dq, *J* 9.5, 7.0, OC*H*H), 3.56 ($1H_{major}$, dq, *J* 9.5, 7.0, OCH*H*), 2.48–2.28 ($2H_{both}$, m, 2×C*H*CH_3), 2.03–1.90 ($4H_{both}$, m, 2×CH_2), 1.55–1.14 ($8H_{both}$, 2×CH_2, 2×CH_2), 1.23 ($3H_{major}$, t, *J* 7.0, OCH_2CH_3), 0.99 ($3H_{major}$, d, *J* 7.0, CHCH_3), 0.89 ($3H_{major}$, t, *J* 7.5, $CH_2CH_2CH_3$); ^{13}C could not be obtained due to the rapid decomposition of the sample in $CDCl_3$; *m*/*z* (CI) 185 (MH^+,100%). Found: MH^+, 185.1550; $C_{11}H_{20}O_2$ requires: MH^+, 185.1542.

4.4.24. *(2S*,4S*)-6-Butyl-2-ethoxy-4-methyl-3,4-dihydro-2H-pyran* ***3ag***

Prepared by the general procedure (conditions B, 7.8 mmol, 1.0 equiv of diene **1**, 5.0 equiv of vinyl ether **2a**, 0.05 equiv of Yb catalyst, 55 °C, 3 h, microwave) to give **3ag** (1.01 g, 65%) in a 4:1 inseparable mixture as a colourless oil. ν_{max} ($CHCl_3$)/cm^{-1} 2957–2872 (CH), 1673 (C=C); δ_H (250 MHz, $CDCl_3$) 5.02 ($1H_{major}$, t, *J* 3.0, OCHO), 4.90 ($1H_{minor}$, dd, *J* 8.5, 2.0, OCHO), 4.45 ($1H_{major}$, d, *J* 0.5, C=CH), 4.35 ($1H_{minor}$, d, *J* 1.0, C=CH), 3.85 ($1H_{major}$, dq, *J* 9.5, 7.0, OC*H*H), 3.58 ($1H_{major}$, dq, *J* 9.5, 7.0, OCH*H*), 2.48–2.33 ($1H_{major}$, m C*H*CH_3), 2.09–1.95 ($2H_{major}$, m, CH_2), 1.51–1.18 ($18H_{both}$, m, 2×CH_2, 2×CH_2, 2×CH_2, 2×OCH_2CH_3), 1.01 ($3H_{minor}$, d, *J* 7.0, CHCH_3), 1.00 ($3H_{major}$, d, *J* 7.0, CHCH_3), 0.92 ($3H_{major}$, t, *J* 7.0, CHCH_3); δ_C (125 MHz, $CDCl_3$) 151.2 $(C)_{minor}$, 149.8 $(C)_{major}$, 102.7 $(CH)_{major}$, 102.0 $(CH)_{minor}$, 96.7 $(CH)_{major}$, 99.8 $(CH)_{minor}$, 64.1 $(CH_2)_{minor}$, 63.5 $(CH_2)_{major}$, 36.7 $(CH_2)_{minor}$, 35.2 $(CH2)_{major}$, 33.7 $(CH_2)_{minor}$, 33.4 $(CH_2)_{major}$, 29.2 $(CH_2)_{major}$, 29.1 $(CH_2)_{minor}$, 26.4 $(CH)_{minor}$, 22.1 $(CH)_{major}$, 21.7 $(CH_2)_{major}$, 21.6 $(CH_2)_{minor}$, 15.3 $(CH_3)_{major}$, 15.2 $(CH_3)_{major}$, 13.9 $(CH_3)_{major}$, 13.9 $(CH_3)_{minor}$ [22 out of 24 carbons observed]; *m*/*z* (CI) 199 (MH^+,100%). Found: MH^+, 199.1697; $C_{12}H_{22}O_2$ requires: MH^+, 199.1698.

4.5. Oxidation methods

4.5.1. *Conditions A*

To a 0.02 M solution of 2-alkoxydihydropyrans **3** (1.0 equiv) in CH_2Cl_2, 55% *m*-CPBA (1.0 equiv) in CH_2Cl_2 (0.16–0.30 M) at 0 °C under N_2 was added dropwise. After stirring at room temperature, the white precipitate was filtered off from the reaction mixture and then phosphate buffer solution was added to the filtered solution. The CH_2Cl_2 layer was separated off from the aqueous layer. The organic layer was washed with aqueous saturated $NaHCO_3$ solution, dried with $MgSO_4$ and filtered. Column chromatography, eluting with EtOAc/petrol, gave (major product) the lactol ether as a colourless oil and as a mixture of diastereoisomers, along with (minor product) the volatile lactol, also as a colourless oil and as an inseparable mixture (1:1) of diastereomers.

4.5.2. *Conditions B*

To a 0.02 M solution of 2-alkoxydihydropyran **3** in CH_2Cl_2 (10 mL) at 0 °C was added a DMDO/acetone solution (1.0 equiv, 0.01–0.04 M).[9] The reaction mixture was kept in the ice-bath for 30 min and then allowed to stir at rt. After the solution was concentrated, column chromatography, eluting with diethyl ether/petrol, gave lactols as major products and lactol ethers as minor products.

4.5.3. *Conditions C*

To a degassed, oven dried vessel was added dry pre-heated 4 Å molecular sieves (1 g), urea hydrogen peroxide (3.0–6.0 equiv), imidazole (0.5 equiv) and distilled CH_2Cl_2 (10 mL). The mixture was cooled to 0–5 °C under an inert atmosphere of Ar and MTO (4–8 mol %) was then added to give a deep yellow colour. The dihydropyran **3** (1.0 equiv) was added dropwise and the reaction warmed to rt. On consumption of the starting material (TLC analysis), CSA (0.2 equiv) was added and the reaction mixture stirred for 18 h. On completion, the mixture was filtered, washed with CH_2Cl_2, concentrated under reduced pressure and then purified via flash column chromatography to give the required epoxidation-rearrangement product.

4.5.4. *Conditions D (in situ DMDO formation)*

To a 0.02 M solution of acetone (20.0 equiv) and 2-alkoxydihydropyran **3** (1.0 equiv) in CH_2Cl_2 at 0 °C was added 0.4 mM Na_2EDTA (aq, adjusting to pH ~ 7.5). A mixture of Oxone® (2.5 equiv) and $NaHCO_3$ (4.0 equiv) was ground together before being added to the reaction mixture over 30 min. After stirring vigorously at room temperature overnight, the organic layer was washed with aqueous saturated $NaHCO_3$ solution, dried with $MgSO_4$, filtered and concentrated. Column chromatography, eluting with diethyl ether/petrol (3:2), gave lactol ethers as the major products and lactols as minor products.

4.5.5. *(2R*,5R*)-1-(5-Hydroxy-tetrahydro-furan-2-yl)-ethanone and (2R*,5S*)-1-(5-hydroxy-tetrahydro-furan-2-yl)-ethanone* ***6***[39]

Prepared by the oxidation method (conditions B, 3 h) to give **6** (263 mg, dr 1:1, 53%). ν_{max} ($CHCl_3$)/cm^{-1} 2959 (CH), 1716 (C=O), 1649; δ_H (250 MHz, CDCl$_3$) 5.60 (1H$_a$, t, *J* 2.5, C*H*OH), 5.53 (1H$_b$, t, *J* 2.5, C*H*OH), 5.11 (2H$_{both}$, s, 2×OH), 4.53 (1H$_a$, dd, *J* 9.0, 5.0, C(O)CH), 4.36 (1H$_b$, t, *J* 8.0, C(O)CH), 2.53–1.72 (8H$_{both}$, m, 4×CH$_2$), 2.15 (3H$_a$, s, CH$_3$), 2.08 (3H$_b$, s, CH$_3$); δ_C (125 MHz, CDCl$_3$) 210.5, 209.2 (C), 99.4, 99.2 (CH), 84.0, 82.5 (CH), 33.3, 32.2 (CH$_2$), 26.5, 25.9 (CH$_3$), 25.5, 25.1 (CH$_2$); *m*/*z* (CI) 148 (MNH$_4^+$, 100%). Found: MNH$_4^+$, 148.0975; $C_6H_{10}O_3$ requires: MNH$_4^+$, 148.0974.

4.5.6. (2R,5R*)-1-(5-Ethoxy-tetrahydro-furan-2-yl)-ethanone and (2R*,5S*)-1-(5-ethoxy-tetrahydro-furan-2-yl)-ethanone* ***4a***[3]

Prepared using oxidation method A, on **3a** (1.0 equiv, 1.6 mmol) for 2 h to give **4a** (32 mg, 14%) in an inseparable mixture (2:1) as a colourless oil. ν_{max} (CHCl$_3$)/cm^{-1} 2979 (CH), 2254, 1716 (C=O); δ_H (250 MHz, CDCl$_3$) 5.25 (1H$_{minor}$, t, *J* 3.5, OCHO), 5.18 (1H$_{major}$, t, *J* 3.5, OCHO), 4.45 (1H$_{minor}$, dd, *J* 9.0, 5.5, C(O)CH), 4.32 (1H$_{major}$, t, *J* 8.0, C(O)CH), 3.85 (2H$_{both}$, dq, *J* 9.5, 7.0, 2×OC*H*H), 3.46 (2H$_{both}$, dq, *J* 9.5, 7.0, 2×OCH*H*), 2.42–1.80 (8H$_{both}$, m, 4×CH$_2$), 2.22 (3H$_{major}$, s, C(O)CH$_3$), 2.18 (3H$_{minor}$, s, C(O)CH$_3$), 1.17 (3H$_{minor}$, t, *J* 7.0, CH$_2$C*H*$_3$), 1.20 (3H$_{major}$, t, *J* 7.0, CH$_2$CH$_3$); δ_C (125 MHz, CDCl$_3$) 105.0, 104.6 (CH), 84.7, 82.4 (CH), 63.2, 61.2 (CH$_2$), 32.9, 31.6 (CH$_3$), 26.9, 26.7 (CH$_2$), 25.5, 19.1 (CH$_2$), 15.0, 15.2 (CH$_3$).

4.5.7. (2R,5R*)-1-(5-Butoxy-tetrahydro-furan-2-yl)-ethanone and (2R*,5S*)-1-(5-butoxy-tetrahydro-furan-2-yl)-ethanone* ***4b***

Prepared using oxidation method A, on **3b** (1.0 equiv, 3.0 mmol) for 3 h to give major compounds **4b**$_{minor}$ (13%) and **4b**$_{major}$ (26%) as a separable mixture (2:1) in a colourless oil (220 mg, **4b**$_{minor}$+**4b**$_{major}$=39%), **4b**$_{major}$: ν_{max} (CHCl$_3$)/cm^{-1} 2962–2876 (CH), 1722 (C=O), 1644; δ_H (250 MHz, CDCl$_3$) 5.28 (1H, t, *J* 2.0, OCHO), 4.49 (1H, dd, *J* 9.0, 6.0, C(O)CH), 3.70 (1H, dt, *J* 9.5, 6.5, OC*H*H), 3.42 (1H, dt, *J* 9.5, 6.5, OCH*H*), 2.40–1.79 (4H, m, CH$_2$, CH$_2$), 2.19 (3H, s, CCH$_3$), 1.62–1.42 (2H, m, CH$_2$), 1.42–1.25 (2H, m, CH$_2$), 0.91 (3H, t, *J* 7.5, CH$_2$C*H*$_3$); δ_C (125 MHz, CDCl$_3$), 209.0 (C), 104.8 (CH), 82.4 (CH), 67.4 (CH$_2$), 31.7 (CH$_2$), 31.6 (CH$_2$), 26.9 (CH$_2$), 26.1 (CH$_3$), 19.3 (CH$_2$), 13.8 (CH$_3$); *m*/*z* (CI) 171 (MH$^+$). Found: MNH$_4^+$, 204.1595; $C_{10}H_{18}O_3$ requires: MNH$_4^+$, 204.1560; **4b**$_{\mathbf{minor}}$: ν_{max} (CHCl$_3$)/cm^{-1} 2962–2876 (CH), 1721 (C=O), 1642; δ_H (250 MHz, CDCl$_3$) 5.19 (1H, dd, *J* 4.5, 1.5, OCHO), 4.34 (1H, t, *J* 8.0, C(O)CH), 3.80 (1H, dt, *J* 9.5, 6.5, OC*H*H), 3.43 (1H, dt, *J* 9.5, 6.5, OCH*H*), 2.25 (3H, s, CH$_3$), 2.22–1.87 (4H, m, CH$_2$, CH$_2$), 1.62–1.43 (2H, m, CH$_2$), 1.42–1.22 (2H, m, CH$_2$), 0.92 (3H, t, *J* 6.5, CH$_2$C*H*$_3$); δ_C (125 MHz, CDCl$_3$), 211.0 (C), 105.3 (CH), 84.7 (CH), 67.7 (CH$_2$), 32.8 (CH$_2$), 31.7 (CH$_2$), 26.7 (CH$_2$), 25.5 (CH$_3$), 19.4 (CH$_2$), 13.9 (CH$_3$); *m*/*z* (CI) 171 (MH$^+$). Found: MNH$_4^+$, 204.1595; $C_{10}H_{18}O_3$ requires: MNH$_4^+$, 204.1560.

4.5.8. (3aR,5S*,7R*,7aR*)-5-Ethoxy-2,2-dimethyl-7-phenyl-tetrahydro-3aH-[1,3]dioxolo[4,5-b]pyran* ***11a***

Prepared using oxidation method B (0.5 mmol, 1.0 equiv **3i**, 1.0 equiv DMDO, rt, 18 h) to afford the title compound **11a** (42 mg, 30%) as a colourless oil. ν_{max} (CH$_2$Cl$_2$)/cm^{-1} 2977, 1371, 1117, 1043, 1009, 699; δ_H (400 MHz, CDCl$_3$) 7.39–7.19 (5H, m, Ar*H*), 5.57 (1H, d, *J* 4.1, OCHO), 5.10 (1H, dd, *J* 7.8, 6.6, OC*H*CH$_2$), 4.21 (1H, dd, *J* 8.0, 4.1, OC*H*CH), 3.97 (1H, dq, *J* 9.6, 7.1, OC*H*HCH$_3$), 3.57 (1H, dq, *J* 9.6, 7.1, OCH*H*CH$_3$), 2.96 (1H, ddd, *J* 13.7, 7.9, 3.7, OC*H*CH$_2$), 2.20 (1H, ddd, *J* 14.2, 6.4, 3.7, CHC*H*HCH), 1.71 (1H, dt, *J* 7.9, 14.0, CHCH*H*CH), 1.61 (3H, s, OCC*H*$_3$), 1.35 (3H, s, OCC*H*$_3$), 1.24 (3H, t, *J* 7.0, OCH$_2$C*H*$_3$); δ_C (100 MHz, CDCl$_3$) 141.9 (C), 128.7 (CH), 127.4 (CH), 126.9 (CH), 111.3 (C), 97.3 (CH), 95.2 (CH), 82.7 (CH), 63.5 (CH$_2$), 42.0 (CH), 32.8 (CH$_2$), 28.1 (CH$_3$), 26.5 (CH$_3$), 15.2 (CH$_3$); *m*/*z* (CI) 279 (M+H)$^+$, 296 (M+NH$_4$)$^+$. Found: 296.1864, (M+NH$_4$)$^+$; $C_{16}H_{26}NO_4$ requires: 296.1862.

4.5.9. (3aR,5S*,7R*,7aR*)-5-Ethoxy-7-isopropyl-2,2-dimethyl-tetrahydro-3aH-[1,3]dioxolo[4,5-b]pyran* ***11b***

Prepared using oxidation method B (0.5 mmol, 1.0 equiv **3l**, 1.0 equiv DMDO, rt, 18 h) to afford the title compound **11b** (31 mg, 25%) as a colourless oil. ν_{max} (CH$_2$Cl$_2$)/cm^{-1} 2975, 1379, 1131; δ_H (500 MHz, CDCl$_3$) 5.38 (1H, d, *J* 3.9, OCHO), 4.94 (1H, dd, *J* 8.2, 6.3, OC*H*CH$_2$), 3.97 (1H, dd, *J* 7.4, 3.9, OC*H*CH), 3.92 (1H, dq, *J* 9.7, 7.1, OCH*H*CH$_3$), 3.52 (1H, dq, *J* 9.7, 7.1, OCH*H*CH$_3$), 1.94 (1H, ddd, *J* 14.1, 6.2, 3.6, CHC*H*HCH), 1.81–1.73 (1H, m, CHC*H*CH$_2$), 1.64–1.61–1.54 (1H, m, CHC*H*CH$_3$), 1.54 (3H, s, OCC*H*$_3$), 1.37 (3H, s, OCC*H*$_3$), 1.20 (3H, t, *J* 7.1, OCH$_2$C*H*$_3$), 1.13 (1H, ddd, *J* 13.9, 8.3, 8.3, CHCH*H*CH), 0.98 (3H, d, *J* 6.8, CHC*H*$_3$), 0.91 (3H, d, *J* 6.7, CHC*H*$_3$); δ_C (125 MHz, CDCl$_3$) 110.8 (C), 97.8 (CH), 95.3 (CH), 79.5 (CH), 63.3 (CH$_2$), 41.9 (CH), 29.9 (CH), 28.6 (CH$_2$), 28.1 (CH$_3$), 26.4 (CH$_3$), 20.5 (CH$_3$), 19.1 (CH$_3$), 15.2 (CH$_3$); *m*/*z* (CI) 245 (M+H)$^+$, 262 (M+NH$_4$)$^+$. Found: 262.2024, (M+NH$_4$)$^+$; $C_{13}H_{28}NO_4$ requires: 262.2018.

4.5.10. (3aR,5S*,7R*,7aR*)-5-Ethoxy-7-(4-methoxyphenyl)-2,2-dimethyl-tetrahydro-3aH-[1,3]dioxolo[4,5-b]pyran* ***11c*** *and (4R*,6S*)-6-ethoxy-4-(4-methoxyphenyl)-dihydro-2H-pyran-3(4H)-one* ***12a***

Prepared using oxidation method B (0.5 mmol, 1.0 equiv **3m**, 1.0 equiv DMDO, rt, 18 h) to afford the title compounds **11c** (48 mg, 31%) and **12a** (16 mg, 14%) as colourless oils. Compound (**11c**); ν_{max} (CH$_2$Cl$_2$)/cm^{-1} 2973, 1379, 1131; δ_H (400 MHz, CDCl$_3$) 7.21 (2H, d, *J* 8.6, Ar*H*), 6.88 (2H, d, *J* 8.6, Ar*H*), 5.55 (1H, d, *J* 4.1, OCHO), 5.09 (1H, dd, *J* 7.8, 6.6, OC*H*CH$_2$), 4.16 (1H, dd, *J* 8.0, 4.1, OC*H*CH), 3.96 (1H, dq, *J* 9.6, 7.1, OC*H*HCH$_3$), 3.79 (3H, s, OC*H*$_3$), 3.57 (1H, dq, *J* 9.6, 7.1, OCH*H*CH$_3$), 2.91 (1H, ddd, *J* 13.8, 8.0, 3.7, CHC*H*CH$_2$), 2.17 (1H, ddd, *J* 14.1, 6.4, 3.7, CHC*H*HCH), 1.67 (1H, dt, *J* 14.0, 7.9, CHCH*H*CH), 1.60 (3H, s, OCCH$_3$), 1.34 (3H, s, OCCH$_3$), 1.24 (3H, t, *J* 7.1, OCH$_2$C*H*$_3$); δ_C (100 MHz, CDCl$_3$) 158.5 (C), 134.0 (C), 128.3 (CH), 114.0 (CH), 111.2 (C), 97.3 (CH), 95.2 (CH), 63.4 (CH$_2$), 55.2 (CH$_3$), 41.2 (CH), 32.9 (CH$_2$), 28.1 (CH$_3$), 26.5 (CH$_3$), 15.5 (CH$_3$); *m*/*z* (CI) 326 (M+NH$_4$)$^+$. Found: 326.1976 (M+NH$_4$)$^+$; $C_{17}H_{28}NO_5$ requires: 326.1967.

Compound (**12a**); ν_{max} (CH$_2$Cl$_2$)/cm^{-1} 1735 (C=O), 1379, 1131; δ_H (250 MHz, CDCl$_3$) 7.05 (2H, d, *J* 8.7, Ar*H*), 6.89 (2H, d, *J* 8.8, Ar*H*), 5.22 (1H, t, *J* 6.6, OCHO), 4.37 (1H, d, *J* 17.6, OC*H*H(O)), 4.06 (1H, d, *J* 17.6, OCH*H*(O)), 3.92–3.78 (5H, OC*H*HCH$_3$, CC*H*CH$_2$ and OC*H*$_3$), 3.57 (1H, dq, *J* 9.6, 7.1, OCH*H*CH$_3$), 2.64 (1H, td, *J* 6.3, 14.3, CHC*H*HCH), 2.13 (1H, dt, *J* 6.4, 14.2, CHCH*H*CH), 1.26 (3H, t, *J* 7.1, OCH$_2$C*H*$_3$); δ_C (100 MHz, CDCl$_3$) 210.5 (C), 158.8 (C), 129.6 (CH), 128.3 (C), 114.0 (CH), 97.5 (CH), 66.6 (CH$_2$), 63.4 (CH$_2$), 55.2 (CH$_3$), 48.6 (CH), 34.9 (CH$_2$), 15.1 (CH$_3$); *m*/*z* (CI) 251 (M+H)$^+$, 268 (M+NH$_4$)$^+$. Found: 268.1548, (M+NH$_4$)$^+$; $C_{14}H_{22}NO_4$ requires: 268.1549.

4.5.11. (2R,5R*)-5-Ethoxy-2-methyl-tetrahydrofuran-2-carbaldehyde* ***4c***

Prepared using oxidation method C (1.0 mmol, 1.0 equiv **3o**) to afford the title compound **4c** (21 mg, 13%) as a colourless oil. ν_{max} (CH$_2$Cl$_2$)/cm^{-1} 2977, 2932, 2801, 1735 (C=O), 1451, 1375, 1339, 1209, 1109, 1083, 1042, 1008, 976, 877; δ_H (400 MHz, CDCl$_3$) 9.54 (1H, s, CC*H*(O)), 5.21 (1H, d, *J* 4.8, OC*H*O), 3.80 (1H, dq, *J* 9.5, 7.1, OC*H*HCH$_3$), 3.47 (1H, dq, *J* 9.5, 7.1, OCH*H*CH$_3$), 2.33 (1H, app td, *J* 9.0, 12.6, CC*H*HCH$_2$), 2.09–1.99 (1H, m, CCH*H*CH$_2$), 1.91 (1H, dddd, *J* 12.8, 8.8, 3.3, 0.7, CH$_2$C*H*HCH), 1.67 (1H, ddd, *J* 12.8, 9.7, 3.3, CH$_2$CH*H*CH), 1.27 (3H, s, CC*H*$_3$), 1.16 (3H, t, *J* 7.1, OCH$_2$C*H*$_3$); δ_C (100 MHz, CDCl$_3$) 203.2 (CH), 104.7 (CH), 87.0 (C), 63.0 (CH$_2$), 32.3 (CH$_2$), 30.7 (CH$_2$), 20.8 (CH$_3$), 15.0 (CH$_3$); *m*/*z* (CI) 176 (M+NH$_4$)$^+$. Found: 176.1286 (M+NH$_4$)$^+$; $C_8H_{18}NO_3$ requires: 176.1287.

4.5.12. (2R,3S*,5R*)-5-Ethoxy-2,3-dimethyl-tetrahydrofuran-2-carbaldehyde* ***4d***

Prepared using oxidation method C (1.0 mmol, 1.0 equiv **3p**) to afford the title compound **4d** (48 mg, 28%) as a colourless oil. ν_{max} (CH$_2$Cl$_2$)/cm^{-1} 1730, 1662, 1548, 1444, 1379, 1132, 922; δ_H (400 MHz, CDCl$_3$) 9.85 (1H, s, CC*H*(O)), 5.31 (1H, dd, *J* 5.7, 3.7, OC*H*O), 3.89 (1H, dq, *J* 9.5, 7.1, OC*H*HCH$_3$), 3.52 (1H, dq, *J* 9.6, 7.1, OCH*H*CH$_3$), 2.47 (1H, ddd, *J* 13.3, 8.2, 5.7, CHC*H*HCH), 2.24–2.06 (1H, m, CC*H*CH$_2$), 1.73–1.60 (1H, m, CHCH*H*CH), 1.26 (3H, s CC*H*$_3$), 1.22

(3H, t, *J* 7.1, OCH_2CH_3), 1.06 (3H, d, *J* 7.2, $CHCH_3$); δ_C (100 MHz, $CDCl_3$) 205.6 (CH), 104.8 (CH), 89.6 (C), 63.8 (CH_2), 43.3 (CH), 41.2 (CH_2), 20.7 (CH_3), 15.2 (CH_3), 14.5 (CH_3); *m*/*z* (CI) 173 $(M+H)^+$, 190 $(M+NH_4)^+$. Found: 190.1441 $(M+NH_4)^+$; $C_9H_{20}NO_3$ requires: 190.1443.

4.5.13. (2R*,3S*,5R*)-5-Ethoxy-3-ethyl-2-methyl-tetrahydrofuran-2-carbaldehyde **4e**

Prepared using oxidation method C (1.0 mmol, 1.0 equiv **3q**) to afford the title compound **4e** (65 mg, 35%) as a colourless oil. ν_{max} (CH_2Cl_2)/cm^{-1} 3055, 1728 (C=O), 1384, 1260, 1142, 1015; δ_H (400 MHz, $CDCl_3$) 9.83 (1H, s, CC*H*(O)), 5.31 (1H, dd, *J* 5.7, 4.0, OC*H*O), 3.86 (1H, dq, *J* 9.5, 7.1, OC*H*HCH_3), 3.51 (1H, dq, *J* 9.5, 7.1, OCH*H*CH_3), 2.48 (1H, ddd, *J* 13.5, 8.9, 5.8, CHC*H*HCH), 1.97–1.87 (1H, m, CC*H*CH_2), 1.66 (1H, ddd, *J* 13.5, 9.5, 3.9, CHCH*H*CH), 1.56–1.46 (1H, m, CHCH*H*CH_3), 1.34–1.27 (1H, m, CHC*H*HCH_3), 1.27 (3H, s, CCH_3), 1.20 (3H, t, *J* 7.1, OCH_2CH_3), 0.90 (3H, t, *J* 7.4, CCH_2CH_3); δ_C (63 MHz, $CDCl_3$) 205.0 (CH), 104.8 (CH), 89.4 (C), 63.7 (CH_2), 51.1 (CH), 39.2 (CH_2), 22.6 (CH_3), 20.9 (CH), 15.2 (CH_3), 13.3 (CH_3); *m*/*z* (CI) 204 $(M+NH_4)^+$. Found: 204.1603 $(M+NH_4)^+$; $C_{10}H_{22}NO_3$ requires: 204.1600.

4.5.14. (2R*,3R*,5R*)-5-Ethoxy-2-methyl-3-phenyl-tetrahydrofuran-2-carbaldehyde **4f** and 4-oxo-3-phenylpentanal[40]

Prepared using oxidation method C (1.5 mmol, 1.0 equiv **3r**) to afford the title compounds **4f** (35 mg, 10%) and 4-oxo-3-phenylpentanal, (10 mg, 4%) as colourless oils. ν_{max} (CH_2Cl_2)/cm^{-1} 2979, 1731 (C=O), 1620, 1496, 1376, 1087, 992, 769, 701; δ_H (250 MHz, $CDCl_3$) 9.65 (1H, s, CC*H*(O)), 7.34–7.16 (5H, m, Ar*H*), 5.47 (1H, dd, *J* 5.7, 3.7, OCHO), 3.95 (1H, dq, *J* 9.4, 7.1, OC*H*HCH_3), 3.61 (1H, dq, *J* 9.4, 7.1, OCH*H*CH_3), 3.36 (1H, br t, *J* 9.5, CC*H*CH_2), 2.74 (1H, ddd, *J* 14.0, 9.7, 5.7, CHC*H*HCH), 2.44 (1H, ddd, *J* 14.0, 9.2, 3.6, CHCH*H*CH), 1.39 (3H, s, CCH_3), 1.28 (3H, t, *J* 7.1, OCH_2CH_3); δ_C (63 MHz, $CDCl_3$) 202.6 (CH), 136.3 (C), 128.6 (CH), 128.6 (CH), 127.5 (CH), 104.8 (CH), 89.6 (C), 63.9 (CH_2), 54.5 (CH), 39.2 (CH_2), 21.1 (CH_3), 15.2 (CH_3); *m*/*z* (CI) 252 $(M+NH_4)^+$. Found: 252.1589 $(M+NH_4)^+$; $C_{14}H_{22}NO_3$ requires: 252.1600.

4.5.15. 4-Oxo-3-phenylpentanal[40]

ν_{max} (CH_2Cl_2)/cm^{-1} 2922, 2852, 1714 (C=O), 1659, 1632, 1357; δ_H (250 MHz, $CDCl_3$) 9.77 (1H, s, CH_2C*H*(O)), 7.39–7.18 (5H, m, Ar*H*), 4.24 (1H, dd, *J* 9.8, 4.1, CC*H*CH_2), 3.45 (1H, dd, *J* 18.6, 9.8, CHC*H*HCH), 2.65 (1H, dd, *J* 18.5, 4.1, CHCH*H*CH), 2.13 (3H, s, CCH_3); δ_C (63 MHz, $CDCl_3$) 206.4 (C), 199.9 (CH), 137.5 (C), 129.2 (CH), 128.2 (CH), 127.8 (CH), 52.8 (CH), 46.6 (CH_2), 28.7 (CH_3); *m*/*z* (CI) 194 $(M+NH_4)^+$, 177 $(M+H)^+$.

4.5.16. (2R*,3S*,5R*)-3,5-Diethoxy-2-methyl-tetrahydrofuran-2-carbaldehyde **4g**

Prepared using oxidation method C (1.0 mmol, 1.0 equiv **3t**) to afford the title compound **4g** (105 mg, 54%) as a colourless oil. ν_{max} (CH_2Cl_2)/cm^{-1} 2979, 1735 (C=O), 1442, 1376, 1182, 1086, 1047; δ_H (400 MHz, $CDCl_3$) 9.73 (1H, s, CC*H*(O)), 5.31 (1H, dd, *J* 5.7, 1.8, OCHO), 3.91–3.83 (2H, m, OC*H*HCH_3 and CC*H*CH_2), 3.53 (1H, dq, *J* 9.6, 7.1, OC*H*HCH_3), 3.47 (1H, dq, *J* 9.2, 6.9, OCH*H*CH_3), 3.36 (1H, dq, *J* 9.6, 6.9, OCH*H*CH_3), 2.35 (1H, ddd, *J* 14.1, 7.5, 5.6, CHC*H*HCH), 2.13 (1H, ddd, *J* 14.2, 2.9, 1.8, CHCH*H*CH), 1.29 (3H, s CCH_3), 1.22 (3H, t, *J* 7.1, OCH_2CH_3), 1.11 (3H, t, *J* 7.0, OCH_2CH_3); δ_C (100 MHz, $CDCl_3$) 202.3 (CH), 105.0 (CH), 88.9 (C), 86.7 (CH), 66.0 (CH_2), 63.4 (CH_2), 39.0 (CH_2), 20.3 (CH_3), 15.0 (CH_3), 14.9 (CH_3); *m*/*z* (CI) 203 $(M+H)^+$, 220 $(M+NH_4)^+$. Found: 203.1276 $(M+H)^+$; $C_{10}H_{19}O_4$ requires: 203.1283.

4.5.17. (2R*,5R*)-2-Butyl-5-ethoxy-tetrahydrofuran-2-carbaldehyde **4h**

Prepared using oxidation method C (1.0 mmol, 1.0 equiv **3u**) to afford the title compound **4h** (126 mg, 63%, 2:1 dr) as a colourless oil. (63%). ν_{max} (CH_2Cl_2)/cm^{-1} 2958, 1735 (C=O), 1460, 1373, 1112, 1043; δ_H (400 MHz, $CDCl_3$) 9.56 (1H_{major}, s, CC(O)H), 9.54 (1H_{minor}, s, CC(O)H), 5.21–5.19 (1H, m, OCHO), 3.79 (1H, dq, *J* 9.4, 7.1, OCH*H*CH_3), 3.46 (1H, dq, *J* 9.4, 7.1, OC*H*HCH_3), 2.32–1.18 (10H, m, 5×C*H*$_2$), 1.19 (3H_{minor}, t, *J* 7.1, OCH_2CH_3), 1.15 (3H_{major}, t, *J* 7.1, OCH_2CH_3), 0.89–86 (3H, m, CH_2CH_3); δ_C (100 MHz, $CDCl_3$) 204.4 $(CH)_{major}$, 203.4 $(CH)_{minor}$, 104.6 $(CH)_{major}$, 104.3 $(CH)_{minor}$, 90.7 $(C)_{minor}$, 89.7 $(C)_{major}$, 63.0 $(CH_2)_{major}$, 62.7 $(CH_2)_{minor}$, 36.2 $(CH_2)_{minor}$, 34.6 $(CH_2)_{major}$, 32.5 $(CH_2)_{minor}$, 32.4 $(CH_2)_{major}$, 29.8 $(CH_2)_{minor}$, 28.8 $(CH_2)_{major}$, 25.9 $(CH_2)_{minor}$, 25.3 $(CH_2)_{major}$, 23.0 (CH_2), 15.1 $(CH_3)_{minor}$, 14.9 $(CH_3)_{major}$, 13.9 (CH_3); *m*/*z* (CI) 218 $(M+NH_4)^+$. Found: 218.1755, $(M+NH_4)^+$; $C_{11}H_{24}NO_3$ requires: 218.1756.

4.6. General procedure for rearrangement/Jones oxidation of alkoxydihydropyrans

To a 0.02 M solution of the 2-alkoxydihydropyran **3** in CH_2Cl_2 at 0 °C was added DMDO/acetone (1 equiv of a 0.02–0.045 M solution). The reaction mixture was kept in the ice-bath for 30 min and then allowed to stir at rt. After the acetone was evaporated, the crude material was washed with saturated aqueous $NaHCO_3$ solution and concentrated to give a mixture of lactol and lactol ether. This mixture was dissolved in acetone (4.0 M) at 0 °C and 3.0 M Jones reagent (3.0 equiv relative to initial 2-alkoxydihydropyran) was added dropwise. After the reaction mixture was allowed to stir at rt, the excess of oxidants was quenched by the addition of 2-propanol until the brown colour of the mixture turned to green. The reaction mixture was diluted with diethyl ether and the precipitated chromium salts were dissolved by the addition of saturated aqueous NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with diethyl ether, dried and concentrated. Column chromatography gave 4,5-*cis*-lactones as major products and 4,5-*trans*-lactones as minor products. Configurations of 4,5-*cis*-isomers and 4,5-*trans*-isomers were assigned by NOESY experiments. The following dihydrofuranones gave spectroscopic data in accord with those in the literature: **7a**,[41] **7b**,[42] **7d**,[37] **7g**.[43]

4.6.1. (4R*,5R*)-5-Acetyl-4-(benzyloxymethyl)-dihydrofuran-2(3H)-one **7c**

Prepared by the general procedure (0.8 mmol of 2-alkoxydihydropyran, 0.02 M DMDO 40 mL, 3.0 M Jones reagent 2.4 mL, 3 h for DMDO oxidation, 30 min for Jones oxidation) to give **7c** (>95:5) as a colourless oil (96 mg, 48% over two steps). ν_{max} ($CHCl_3$)/cm^{-1} 2874 (CH), 2089, 1780 (lactone), 1645; δ_H (250 MHz, $CDCl_3$), 7.39–7.19 (5H, m, Ph), 4.80 (1H, d, *J* 8.0, C(O)CH), 4.40 (1H, d, *J* 21.5, PhCH_2), 4.36 (1H, d, *J* 21.5, PhCH_2), 3.53 (1H, dd, *J* 9.5, 3.0, BnOCH_2), 3.38 (1H, dd, *J* 9.5, 3.0, BnOCH_2), 3.03 (1H, dtt, *J* 8.0, 9.5, 3.0, BnOCH_2C*H*), 2.72 (1H, dd, *J* 17.5, 9.5, C(O)CH_2), 2.55 (1H, dd, *J* 17.5, 4.0, C(O)CH_2), 2.23 (3H, s, C(O)CH_3); δ_C (125 MHz, $CDCl_3$) 206.5 (C), 175.5 (C), 136.9 (C), 128.4 (2×CH), 127.9 (CH), 127.6 (2×CH), 83.1 (CH), 73.1, 68.0 (2×CH_2), 38.1 (CH_2), 32.2 (CH), 28.1 (CH_3); *m*/*z* (CI) 266 (MNH_4^+, 100%). Found: MNH_4^+, 266.1395; $C_{14}H_{16}O_4$ requires: MNH_4^+, 266.1392.

4.6.2. (4R*,5R*)-5-Acetyl-4-phenyl-dihydro-furan-2-one **7e**

Prepared by the general procedure (0.9 mmol of 2-alkoxydihydropyran, 0.045 M DMDO 20 mL, 3.0 M Jones reagent 2.7 mL, 3 h for DMDO oxidation, 30 min for Jones oxidation) to give **7e** as a white solid (120 mg, 65% over two steps). Mp 92–93 °C; ν_{max} ($CHCl_3$)/cm^{-1} 3035–2877 (CH), 1772 (lactone), 1721 (C=O), 1650; δ_H (250 MHz, $CDCl_3$) 7.35–7.13 (5H, m, Ph), 5.09 (1H, d, *J* 8.0, OCH), 4.05 (1H, dt, *J* 8.0, 6.0, CH), 2.96 (1H, dd, *J* 17.5, 8.5, C*H*H), 2.88 (1H, dd, *J* 17.5, 6.0, CH*H*), 1.64 (3H, s, CH_3); δ_C (125 MHz, $CDCl_3$), 205.0 (C), 175.6 (C), 135.8 (C), 129.2 (2×CH), 128.4 (CH), 127.6 (2×CH), 85.6

(CH), 44.0 (CH), 34.5 (CH_2), 28.0 (CH_3); _m/z_ (CI) 222 (MNH_4^+, 100%). Found: MNH_4^+, 222.1127; $C_{12}H_{12}O_3$ requires: MNH_4^+, 222.1130.

4.6.3. (4S*,5R*,Z)-5-Acetyl-4-(oct-5-enyl)-dihydrofuran-2(3H)-one **7f**

Prepared by the general procedure (1.2 mmol of 2-alkoxydihydropyran, 0.03 M DMDO 40 mL, 3.0 M Jones reagent 2.5 mL, 3 h for DMDO oxidation, 30 min for Jones oxidation) to give **7f** as a colourless oil (130 mg, 64% over two steps). ν_{max} ($CHCl_3$)/cm^{-1} 3007–2858 (CH), 2358, 2330, 1790 (lactone), 1717 (C═O); δ_H (250 MHz, $CDCl_3$) 5.47–5.14 (2H, m, CH═CH), 4.82 (1H, d, _J_ 7.5, C(O)CH), 2.86–2.65 (1H, m, C(O)CHC_H_), 2.65 (1H, dd, _J_ 17.0, 8.0, C(O)CH_2CH), 2.37 (1H, dd, _J_ 17.0, 6.0, C(O)CH_2CH), 2.26 (3H, s, C(O)CH_3), 2.07–1.96 (2H, m, C$H_2$$CH_3$), 1.52–1.02 (8H, m, 4×$CH_2$), 0.94 (3H, t, _J_ 7.5, CH_2CH_3); δ_C (125 MHz, $CDCl_3$) 205.8 (C), 175.5 (C), 132.2, 128.3 (2×CH), 84.9 (CH), 38.7 (CH_2), 33.6 (CH), 29.3, 28.8, 28.7, 27.1, 26.7 (5×CH_2), 20.5 (CH_3), 14.3 (CH_3); _m/z_ (CI) 256 (MNH_4^+, 100%). Found: MNH_4^+, 256.1907; $C_{14}H_{22}O_3$ requires: MNH_4^+, 256.1913.

4.6.4. (4S*,5R*)-4-Methyl-5-pentanoyl-dihydrofuran-2(3H)-one **7h** _and (4R*,5R*)-4-methyl-5-pentanoyl-dihydrofuran-2(3H)-one_ **8h**

Prepared by the general procedure (2.6 mmol of 2-alkoxydihydropyran, 0.03 M DMDO 90 mL, 3.0 M Jones reagent 3.0 mL, 3 h for DMDO oxidation, 30 min for Jones oxidation) to give a 5:1 mixture; **7h** (290 mg, 58%) and **8h** (60 mg, 12%) as a pale yellow oil.

4.6.4.1. (4S*,5R*)-4-Methyl-5-pentanoyl-dihydrofuran-2(3H)-one **_7h_**. ν_{max} ($CHCl_3$)/cm^{-1} 2255, 1788 (lactone), 1719 (C═O); δ_H (250 MHz, $CDCl_3$), 4.80 (1H, d, _J_ 7.0, OCH), 3.08–2.82 (1H, m, CH_3C_H_), 2.73 (1H, dd, _J_ 17.0, 8.0, C(O)CH_2CH), 2.29 (1H, dd, _J_ 17.0, 4.5, C(O)CH_2CH), 2.78–2.32 (2H, m, CH_2C$H_2$$CH_3$), 1.71–1.56 (2H, m, C$H_2$$CH_2$$CH_3$), 1.00 (3H, d, _J_ 7.0, CHCH_3), 0.94 (3H, t, _J_ 7.5, CH_2CH_3); δ_C (125 MHz, $CDCl_3$), 207.8 (C), 175.6 (C), 84.9 (CH), 42.9 (CH_2), 36.4 (CH), 33.1, 16.0 (2×CH_2), 14.8, 13.6 (2×CH_3); _m/z_ (CI) 188 (MNH_4^+, 100%). Found: MNH_4^+, 188.1289; $C_9H_{14}O_3$ requires: MNH_4^+, 188.1286.

4.6.4.2. (4R*,5R*)-4-Methyl-5-pentanoyl-dihydrofuran-2(3H)-one **_8h_**. ν_{max} ($CHCl_3$)/cm^{-1} 2255, 1788 (lactone), 1719 (C═O); δ_H (250 MHz, $CDCl_3$), 4.32 (1H, d, _J_ 7.0, OCH), 2.68 (1H, dd, _J_ 17.0, 8.5, C(O)CH_2), 2.19 (1H, dd, _J_ 17.0, 7.5, C(O)CH_2), 2.60–2.43 (3H, m, C$H_2$$CH_2$$CH_3$,$CH_3$C_H_), 1.61 (2H, tq, _J_ 11.0, 6.5, CH_2C$H_2$$CH_3$), 1.26 (3H, d, _J_ 6.5, CHCH_3), 0.91 (3H, t, _J_ 6.5, CH_2CH_3); δ_C (125 MHz, $CDCl_3$), 207.8 (C), 175.0 (C), 87.9 (CH), 40.4, 35.8 (2×CH_2), 33.6 (CH), 18.5 (CH_2), 16.2, 13.6 (2×CH_3); _m/z_ (CI) 188 (MNH_4^+, 100%). Found: MNH_4^+, 188.1284; $C_9H_{14}O_3$ requires: MNH_4^+, 188.1284.

4.6.5. (4S*,5R*)-4-Methyl-5-pentanoyl-dihydrofuran-2(3H)-one **7i** _and (4S*,5S*)-4-methyl-5-pentanoyl-dihydrofuran-2(3H)-one_ **8i**

Prepared by above general procedure (2.8 mmol of 2-alkoxydihydropyran, 0.07 M DMDO 40 mL, 3.0 M Jones reagent 3.0 mL, 3 h for DMDO oxidation, 30 min for Jones oxidation) to give an 8:1 mixture; **7i** (250 mg, 48%) and **8i** (31 mg, 6%) in an 8:1 ratio in a pale yellow oil.

4.6.5.1. (4S*,5R*)-4-Methyl-5-pentanoyl-dihydrofuran-2(3H)-one **_7i_**. ν_{max} ($CHCl_3$)/cm^{-1} 2254, 1789 (lactone), 1716 (C═O); δ_H (250 MHz, $CDCl_3$), 4.80 (1H, d, _J_ 10.0, OCH), 2.93–2.95 (1H, m, CH_3C_H_), 2.72 (1H, dd, _J_ 17.5, 8.0, C(O)CH_2CH), 2.73–2.40 (2H, m, CH_2 in ^{n}Bu), 2.28 (1H, dd, _J_ 17.5, 4.5, C(O)CH_2CH), 1.62–1.54 (2H, m, CH_2 in ^{n}Bu), 1.38–1.28 (2H, m, CH_2 in ^{n}Bu), 0.99 (3H, d, _J_ 7.0, CHCH_3), 0.91 (3H, t, _J_ 7.5, CH_2CH_3); δ_C (125 MHz, $CDCl_3$), 207.8 (C), 175.6 (C), 84.9 (CH), 40.7 (CH_2), 36.4 (CH_2), 36.4 (CH), 24.6, 22.2 (2×CH_2), 14.8, 13.8 (2×CH_3); _m/z_ (CI) 202 (MNH_4^+, 100%). Found: MNH_4^+, 202.1447; $C_{10}H_{16}O_3$ requires: MNH_4^+, 202.1443.

4.6.5.2. (4S*,5S*)-4-Methyl-5-pentanoyl-dihydrofuran-2(3H)-one **_8i_**. ν_{max} ($CHCl_3$)/cm^{-1} 2254, 1789 (lactone), 1716 (C═O); δ_H (250 MHz, $CDCl_3$), 4.33 (1H, d, _J_ 9.5, OCH), 2.69 (1H, dd, _J_ 17.5, 8.5, C(O)CH_2CH), 2.62–2.48 (3H, m, CH_3C_H_, CH_2 in ^{n}Bu), 2.20 (1H, dd, _J_ 17.5, 4.5, C(O)CH_2CH), 1.61–1.53 (2H, m, CH_2 in ^{n}Bu), 1.37–1.26 (2H, m, CH_2 in ^{n}Bu), 1.27 (3H, d, _J_ 6.5, CHCH_3), 0.90 (3H, t, _J_ 7.5, CH_2CH_3); δ_C (125 MHz, $CDCl_3$), 207.4 (C), 175.3 (C), 88.0 (CH), 38.3, 35.8 (2×CH_2), 33.6 (CH), 24.8, 22.2 (2×CH_2), 18.5, 13.8 (2×CH_3); _m/z_ (CI) 202 (MNH_4^+, 100%). Found: MNH_4^+, 202.1438; $C_{10}H_{16}O_3$ requires: MNH_4^+, 202.1443.

4.7. Synthesis of Quercus lactones

4.7.1. (4S*,5S*)-5-butyl-4-methyl-dihydrofuran-2(3H)-one **_9_**[13]

To a solution of ketone **7h** (0.87 mmol, 1.0 equiv) in MeOH (10 mL) was added a solution of $NaBH_4$ (0.87 mmol, 1.0 equiv) in EtOH (10 mL). After stirring at room temperature under N_2 overnight, the reaction mixture was concentrated, taken up in diethyl ether and washed with water. The ether layer was dried and concentrated to give a colourless oil (130 mg), which was diluted in DCE (10 mL). To the solution was added thiocarbonyldiimidazole (1.30 mmol, 1.5 equiv) under N_2. The reaction mixture was stirred and the temperature was gradually increased to 80 °C. After stirring overnight, the reaction mixture was concentrated, diluted with diethyl ether and washed with water. The ether layer was dried and concentrated to give a pale yellow oil (80 mg). To a refluxing solution of ^{n}BuSnH (0.96 mmol, 1.1 equiv) and AIBN (0.09 mmol, 0.1 equiv) in toluene (10 mL) under N_2 was added dropwise a solution of the crude oil above in toluene (10 mL). After stirring at reflux overnight, the organic layer was washed with water, which was re-extracted with ether. The combined organics were dried and concentrated. Column purification, eluting with EtOAc/petrol (1:1), gave _(4S*,5S*)-5-butyl-4-methyl-dihydrofuran-2(3H)-one_ **9** (37 mg, 36%). Data found in accordance with the literature.[13]

4.7.2. (4S*,5S*)-4-Methyl-5-pentyl-dihydrofuran-2(3H)-one **_10_**[12]

To a solution of ketone **7i** (0.66 mmol, 1.0 equiv) in MeOH (20 mL) was added a solution of $NaBH_4$ (0.66 mmol, 1.0 equiv) in EtOH (10 mL). After stirring at room temperature under N_2 overnight, the reaction mixture was concentrated, diluted with diethyl ether and washed with water. The ether layer was dried and concentrated to give a colourless oil (197 mg), which was diluted in DCE (20 mL). To the solution was added thiocarbonyldiimidazole (0.99 mmol, 1.5 equiv) under N_2. The reaction mixture was stirred and the temperature was gradually increased to 80 °C. After stirring overnight, the reaction mixture was concentrated, diluted with diethyl ether and washed with water. The ether layer was dried and concentrated to give a pale yellow oil (205 mg). To a refluxing solution of ^{n}BuSnH (0.73 mmol, 1.1 equiv) and AIBN (0.07 mmol, 0.1 equiv) in toluene (20 mL) under N_2 was added dropwise a solution of the crude oil above in toluene (20 mL). After stirring at reflux overnight, the organic layer was washed with water, which was re-extracted with ether. The combined organics were dried and concentrated. Column purification, eluting with EtOAc/petrol (1:1), gave _(4S*,5S*)-4-methyl-5-pentyl-dihydrofuran-2(3H)-one_ **10** (108 mg, 49%). Data found in accordance with the literature.[12]

4.8. General procedure for the synthesis of compounds 15a–15c and 16a–16c

4.8.1. Conditions E

To a degassed, dry vessel was added dry pre-heated 4 Å molecular sieves (1 g), urea hydrogen peroxide (3.0 equiv), imidazole (0.5 equiv) and distilled CH_2Cl_2 (10 mL). The mixture was stirred at rt in an inert atmosphere and MTO (4 mol %) was then added to give a deep yellow reaction mixture. 2-Alkoxydihydropyran (1.0 equiv) was subsequently added and the reaction was monitored via TLC. On consumption of the starting material, the product mixture was then passed through a small pad of Celite™. The filtrate was then diluted further in dry CH_2Cl_2 (10 mL) and Amberlyst 15® (30 mg) was added. The reaction mixture was left to stir under an inert atmosphere for 4 h and monitored via TLC analysis. The product mixture was subsequently concentrated under reduced pressure and the crude material diluted in acetone (3 mL) and reacted with 10.0 equiv of Jones reagent for 1.5 h. On completion, the reaction mixture was quenched with IPA and the inorganic chromium salts removed by filtration. $NaHCO_3$ was added to the filtrate until the pH was moderately basic. The unwanted organics were removed by extraction (2×30 mL) with EtOAc. The aqueous fractions were collected, acidified with 3 M HCl and re-extracted (2×20 mL) with EtOAc. The organic layers were subsequently collected, dried over $MgSO_4$ and then concentrated under reduced pressure. To a separate oven dried vessel was added 1.0 equiv of *p*-nitrobenzylalcohol, in dry CH_2Cl_2, (5–10 mL), 0.1 equiv of DMAP, 1.1 equiv of DCC and the reaction was stirred under an atmosphere of Ar for 15 min. The crude material from the Jones reaction was subsequently dissolved in CH_2Cl_2 (2 mL) and added dropwise to the DCC coupling mixture and left to stir for 18 h. On completion, the reaction mixture was filtered and washed with Et_2O. The filtrate was concentrated under reduced pressure and purified by column chromatography (start 90% PE/10% EtOAc, end 60% PE/ 40% EtOAc) to give the desired esters.

4.8.2. (2R,3S*)-4-Methoxybenzyl-2,3-dimethyl-5-oxo-tetrahydrofuran-2-carboxylateacid **15a** and 4-methoxybenzyl 3-methyl-4-oxopentanoate **16a***

Prepared by the general MTO oxidation method (conditions E, 1.0 mmol, 1.0 equiv **3p**) to afford the title compounds **15a** (64 mg, 23%, 2:1 dr) and **16a** (23 mg, 9%) as colourless oils. Compound (**15a**); ν_{max} (CH_2Cl_2)/cm^{-1} 2935, 2856, 1789 (C=O), 1739 (C=O), 1614, 1516, 1462, 1282, 1245, 1173, 1090, 960, 823; δ_H (400 MHz, $CDCl_3$) 7.29 ($2H_{both}$, d, *J* 8.6, Ar*H*), 6.89 ($2H_{minor}$, d, *J* 8.6, Ar*H*), 6.88 ($2H_{major}$, d, *J* 8.6, Ar*H*), 5.20 ($1H_{major}$, d, *J* 11.9, OCH_2Ph), 5.18 ($1H_{minor}$, d, *J* 11.8, OCH_2Ph), 5.11 ($1H_{minor}$, d, *J* 11.9, OC*H*HPh), 5.07 ($1H_{major}$, d, *J* 11.9, OCH*H*Ph), 3.83 ($3H_{both}$, s, OCH_3), 2.66 ($1H_{minor}$, dd, *J* 17.4, 8.3, CC*H*HCH), 2.61 ($1H_{major}$, dd, *J* 16.7, 8.1, CC*H*HCH), 2.52–2.42 ($1H_{minor}$, m, $CCHCH_2$), 2.38–2.28 ($1H_{minor}$, m, $CCHCH_2$), 2.31 ($1H_{minor}$, dd, *J* 16.7, 12.0, CCH*H*CH), 2.25 ($1H_{major}$, dd, *J* 17.5, 7.5, CCH*H*CH), 1.65 ($3H_{major}$, s, CCH_3), 1.61 ($3H_{minor}$, s, CCH_3), 0.91 ($3H_{major}$, t, *J* 7.5, CCH_3), 0.87 ($3H_{minor}$, t, *J* 7.5, $CHCH_3$); δ_C (100 MHz, $CDCl_3$) 177.2 $(C)_{minor}$, 175.5 $(C)_{major}$, 171.9 $(C)_{minor}$, 170.2 $(C)_{minor}$, 161.3 $(C)_{minor}$, 159.9 $(C)_{major}$, 130.5 $(CH)_{major}$, 130.1 $(CH)_{minor}$, 127.1 $(C)_{minor}$, 127.0 $(C)_{major}$, 114.0 (CH), 87.2 $(C)_{major}$, 86.1 $(C)_{minor}$, 67.4 $(CH_2)_{minor}$, 67.3 $(CH_2)_{major}$, 55.3 (CH_3), 41.0 $(CH)_{major}$, 36.7 $(CH)_{minor}$, 36.2 $(CH_2)_{minor}$, 35.8 $(CH_2)_{major}$, 21.9 $(CH_3)_{major}$, 18.2 $(CH_3)_{minor}$, 15.1 $(CH_3)_{minor}$, 14.0 $(CH_3)_{major}$; *m*/*z* (CI) 296 $(M+NH_4)^+$. Found: 296.1491 $(M+NH_4)^+$; $C_{15}H_{22}NO_5$ requires: 296.1498.

Compound (**16a**); ν_{max} (CH_2Cl_2)/cm^{-1} 1731 (C=O), 1713 (C=O), 1613, 1515, 1461, 1452, 1248, 1161, 1033; δ_H (400 MHz, $CDCl_3$) 7.27 (2H, d, *J* 8.2, Ar*H*), 6.88 (2H, d, *J* 8.7, Ar*H*), 5.05 (1H, d, *J* 12.0, OC*H*HPh), 5.00 (1H, d, *J* 12.0, OCH*H*Ph), 3.80 (3H, s, OCH_3), 3.06–2.96 (1H, m, $CCHCH_2$), 2.79 (1H, dd, *J* 16.8, 8.7, CHCH*H*C), 2.32 (1H, dd, *J* 16.8, 5.4, CHC*H*HC), 2.19 (3H, s, CCH_3), 1.14 (3H, t, *J* 7.3, $CHCH_3$); δ_C (100 MHz, $CDCl_3$) 210.7 (C), 172.2 (C), 159.6 (C), 130.0 (CH), 127.9 (C), 113.9 (CH), 66.2 (CH_2), 55.3 (CH_3), 42.7 (CH), 36.9 (CH_2), 28.4 (CH_3), 16.5 (CH_3); *m*/*z* (CI) 268 $(M+NH_4)^+$. Found: 268.1553 $(M+NH_4)^+$; $C_{14}H_{22}NO_4$ requires: 268.1549.

4.8.3. (2R,3S*)-4-Methoxybenzyl-4-ethoxy-5-methyl-2-oxo-tetrahydrofuran-5-carboxylate **15b** and 4-methoxybenzyl 3-ethoxy-4-oxopentanoate **16b***

Prepared by the general MTO oxidation method (conditions E, 0.75 mmol, 1.0 equiv **3t**) to afford the title compound **15b** (51 mg, 21%, 9:1 dr) and **16c** (97 mg, 48%). Compound (**15b**); ν_{max} (CH_2Cl_2)/cm^{-1} 2978, 1792 (C=O), 1746 (C=O), 1613, 1515, 1456, 1379, 1248, 1172, 1104, 1032, 957, 825; δ_H (400 MHz, $CDCl_3$) 7.33 (2H, d, *J* 8.7, Ar*H*), 6.92 (2H, d, *J* 8.6, Ar*H*), 5.24 (1H, d, *J* 11.9, OC*H*HPh), 5.14 (1H, d, *J* 11.9, OCH*H*Ph), 4.06 (1H, dd, *J* 7.2, 6.7, $CCHCH_2$), 3.83 (3H, s, OCH_3), 3.52–3.49 (2H, m, OCH_2CH_3), 2.82 (1H, dd, *J* 17.6, 7.3, CC*H*HCH), 2.73 (1H, dd, *J* 17.6, 6.7, CCH*H*CH), 1.69 (3H, s, CCH_3), 1.09 (3H, t, *J* 7.0, OCH_2CH_3); δ_C (100 MHz, $CDCl_3$) 173.3 (C), 169.1 (C), 159.7 (C), 130.2 (CH), 127.3 (C), 113.9 (CH), 86.9 (C), 81.5 (CH), 67.3 (CH_2), 66.5 (CH_2), 55.3 (CH_3), 34.9 (CH_2), 22.2 (CH_3), 15.0 (CH_3); *m*/*z* (CI) 326 $(M+NH_4)^+$. Found: 326.1601 $(M+NH_4)^+$; $C_{16}H_{24}NO_{\mathbf{6}}$ requires: 326.1604.

Compound (**16b**); ν_{max} (CH_2Cl_2)/cm^{-1} 2951, 2360, 1733, 1614, 1516, 1462, 1353, 1461, 1249, 1174, 1163, 1033, 823; δ_H (400 MHz, $CDCl_3$) 7.32 (2H, d, *J* 8.6, Ar*H*), 6.91 (2H, d, *J* 8.7, Ar*H*), 5.11 (2H, s, OCH_2Ph), 4.11 (1H, dd, *J* 7.3, 5.0, $CCHCH_2$), 3.84 (3H, s, OCH_3), 3.58 (2H, m, OCH_2CH_3), 2.77 (1H, dd, *J* 15.9, 5.0, CHC*H*HC), 2.71 (1H, dd, *J* 16.0, 7.3, CHCH*H*C), 2.54 (3H, s, CCH_3), 1.22 (3H, t, *J* 7.0, OCH_2CH_3); δ_C (100 MHz, $CDCl_3$) 209.0 (C), 170.3 (C), 159.7 (C), 130.1 (CH), 127.7 (C), 113.9 (CH), 81.5 (CH), 66.7 (CH_2), 66.5 (CH_2), 55.3 (CH_3), 37.0 (CH_2), 26.0 (CH_3), 15.3 (CH_3); *m*/*z* (CI) 298 $(M+NH_4)^+$. Found: 298.1657 $(M+NH_4)^+$; $C_{15}H_{24}NO_5$ requires: 298.1654.

*4.8.4. 4-Methoxybenzyl-3-methyl-4-oxo-4-phenylbutanoate **16c***

Prepared by the general MTO oxidation method (conditions E, 1.0 mmol, 1.0 equiv **3v**) to afford the title compound **16c** (66 mg, 21%) as a colourless oil. ν_{max} (CH_2Cl_2)/cm^{-1} 1730 (C=O), 1682, 1611, 1514, 1454, 1341, 1247, 1167, 1033, 976, 822, 705; δ_H (400 MHz, $CDCl_3$) 7.97 (2H, d, *J* 7.2, Ar*H*), 7.59–7.54 (1H, m, Ar*H*), 7.49–7.44 (2H, m, Ar*H*), 7.23 (2H, d, *J* 8.6, Ar*H*), 6.85 (2H, d, *J* 8.7, Ar*H*), 5.04 (1H, d, *J* 12.0, OC*H*HPh), 4.99 (1H, d, *J* 12.0, OCH*H*Ph), 4.00–3.90 (1H, m, $CCHCH_2$), 3.80 (3H, s, OCH_3), 3.00 (1H, dd, *J* 16.8, 8.5, CHC*H*HC), 2.48 (1H, dd, *J* 16.8, 5.7, CHCH*H*C), 1.21 (3H, d, *J* 7.2, CCH_3); δ_C (100 MHz, $CDCl_3$) 202.7 (C), 172.2 (C), 159.6 (C), 133.0 (CH), 130.0 (CH), 128.6 (CH), 128.4 (CH), 127.9 (C), 113.9 (CH), 66.2 (CH_2), 55.2 (CH_3), 37.5 (CH_2), 37.2 (CH), 17.8 (CH_3); *m*/*z* (CI) 330 $(M+NH_4)^+$. Found: 330.1712 $(M+NH_4)^+$; $C_{19}H_{24}NO_4$ requires: 330.1705.

4.8.5. (2R,3S*)-Crobarbatic acid **17**[18]*

To a degassed, dry vessel was added the tetrahydrofuranone ester **15a** (30 mg, 0.14 mmol), phenol (250 mg, 2.8 mmol, 20.0 equiv), TFA (10 μL, 0.14 mmol) and the mixture was stirred at 45 °C under an atmosphere of Ar for 1 h. The reaction was then quenched with $NaHCO_3$ and the organics were extracted with EtOAc (2×20 mL). The aqueous phase was acidified with 3 M HCl and re-extracted with EtOAc (2×20 mL). The organics were dried over $MgSO_4$, and concentrated under reduced pressure to afford the title compound **17** (22 mg, 93%, 2:1 dr) as an off-white crystalline solid. Data of both diastereoisomers in accordance with the literature.[18]

4.9. General procedure for enantioselective rearrangement/ Jones oxidation of alkoxydihydropyrans using Jacobsen's catalyst

A mixture of alkoxydihydropyran (0.32–1.35 mmol, 1.0 equiv) pre-dissolved in CH_2Cl_2 (0.07 M), Jacobsen catalyst **19** (0.1 equiv) and 4-phenyl pyridine *N*-oxide (0.2 equiv) was cooled down to 0 °C. Buffered bleach (1.5–3.0 equiv, pH ~ 11.5) pre-cooled to 0 °C was added to the mixture and the reaction was stirred at 0 °C. The reaction mixture was diluted with CH_2Cl_2, extracted with water and dried with Na_2SO_4. Short column purification was performed to remove Mn species with a solvent system of EtOAc/petrol (1:1). After the crude product was dissolved in acetone (0.07 M), Jones reagent (3.0 M; 3.0 equiv relative to initial 2-alkoxydihydropyran) was added dropwise. After stirring, the excess of oxidants was quenched by the addition of 2-propanol until the brown colour of the mixture turned to green. The reaction mixture was diluted with diethyl ether. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organics were dried, concentrated and column chromatography gave the lactone product.

4.9.1. *(S)-5-Benzoyl-dihydrofuran-2(3H)-one* ***7l***[44]

Prepared by the general procedure (1.35 mmol of 2-alkoxydihydropyran **3w**, 0.14 mmol of Jacobsen's catalyst, 0.28 mmol of pyridine *N*-oxide, 4.00 mmol of NaOCl, 4.00 mmol of 3.0 M Jones reagent, 6 h for epoxidation, 3 h for Jones oxidation) to give lactone (*S*)-**7l** as white crystals (140 mg, 55% over two steps). Mp 79–80 °C, ee 38% (HPLC analysis: OD-H column, 254 nm, flow 1.0 mL/min, ^{i}PrOH/hexane (5:95), t_{m}=37.90 min, t_{M}=46.15 min); $[\alpha]_D^{20}$ 0.0 (*c* 0.03, CHCl$_3$); δ_H (500 MHz, CDCl$_3$) 8.02–7.48 (5H, m, Ph), 5.82–5.76 (1H, m, CH$_2$C*H*), 2.65–2.44 (4H, m, 2×CH$_2$); *m*/*z* (CI) 208 (MNH$_4^+$, 100%), 398. Found: MNH$_4^+$, 208.0972; C$_{11}$H$_{10}$O$_3$ requires: MNH$_4^+$, 208.0974.

4.9.2. *(+)-(S)-5-Benzoyl-4,4-dimethyl-dihydrofuran-2(3H)-one* ***7m***

Prepared by the general procedure (1.29 mmol of 2-alkoxydihydropyran **3x**, 0.13 mmol of Jacobsen's catalyst, 0.26 mmol of pyridine *N*-oxide, 4.0 mmol of NaOCl, 4.0 mmol of 3.0 M Jones reagent, 6 h for epoxidation, 3 h for Jones oxidation) to give lactone (*S*)-**7m** as white crystals (140 mg, 49% over two steps). Mp 113–115 °C; ee 58% (HPLC analysis: OD column, 254 nm, flow 0.5 mL/min, 5% ^{i}PrOH/hexane (5:95), t_{M}=53.24 min, t_{m}=58.21 min); $[\alpha]_D^{20}$ +42.0 (*c* 0.01, CHCl$_3$); $\nu_{\max}$ (CHCl$_3$)/cm^{-1} 2969 (CH), 2343, 1789 (lactone), 1690 (C=O); δ_H (500 MHz, CDCl$_3$) 7.96 (2H, d, *J* 8.5, 2×CH in Ph), 7.67 (1H, dd, *J* 8.5, 7.5, CH in Ph), 7.55 (2H, d, *J* 7.5, 2×CH in Ph), 5.55 (1H, s, OCH), 2.60 (1H, d, *J* 17.0, CH$_2$), 2.36 (1H, d, *J* 17.0, CH$_2$), 1.40 (3H, s, CCH$_3$), 1.00 (3H, s, CCH$_3$); δ_C (100 MHz, CDCl$_3$) 195.7 (C), 175.7 (C), 135.8 (C), 134.3 (CH), 129.1 (2×CH), 128.6 (2×CH), 85.5 (CH), 41.8 (CH$_2$), 40.7 (C), 28.3, 23.5 (CH$_3$, CH$_3$); *m*/*z* (CI) 236 (MNH$_4^+$, 100%). Found: MNH$_4^+$, 236.1285; C$_{13}$H$_{14}$O$_3$ requires: MNH$_4^+$, 236.1287.

4.9.3. *(+)-(S)-5-Benzoyl-4,4-diethyl-dihydrofuran-2(3H)-one* ***7n***

Prepared by the general procedure (0.38 mmol of 2-alkoxydihydropyran **3y**, 0.04 mmol of Jacobsen's catalyst, 0.08 mmol of pyridine *N*-oxide, 1.14 mmol of NaOCl, 1.14 mmol of 3.0 M Jones reagent, 6 h for epoxidation, 3 h for Jones oxidation) to give lactone (*S*)-**7n** as a colourless oil (44 mg, 45% over two steps). ee 69% (HPLC analysis: OD-H column, 254 nm, flow 0.5 mL/min, ^{i}PrOH/hexane (2:98), t_{M}=49.18 min, t_{m}=60.11 min); $[\alpha]_D^{20}$ +47.0 (*c* 0.01, CHCl$_3$); $\nu_{\max}$ (CHCl$_3$)/cm^{-1} 3444, 2342, 1788 (lactone), 1649 (C=O); δ_H (500 MHz, CDCl$_3$) 7.96 (2H, d, *J* 8.5, 2×CH in Ph), 7.68 (1H, dd, *J* 8.5, 7.5, CH in Ph), 7.55 (2H, d, *J* 7.5, 2×CH in Ph), 5.71 (1H, s, OCH), 2.63 (1H, d, *J* 17.0, C(O)C*H*H), 2.30 (1H, d, *J* 17.0, C(O)CH*H*), 1.73–1.80 (1H, m, C*H*HCH$_3$), 1.60–1.68 (1H, m, CH*H*CH$_3$), 1.38–1.46 (1H, m, C*H*HCH$_3$), 1.12–1.22 (1H, m, CH*H*CH$_3$), 1.09 (3H, s, CH$_3$), 0.76 (3H, s, CH$_3$); δ_C (125 MHz, CDCl$_3$), 196.6 (C), 176.3 (C), 136.0 (C), 134.3 (CH), 129.1 (2×CH), 128.4 (2×CH), 82.2 (CH), 48.0 (C), 38.7 (CH$_2$), 28.8 (CH$_2$), 26.2 (CH$_2$), 9.1 (CH$_3$), 8.4 (CH$_3$); *m*/*z* (CI) 264 (MNH$_4^+$, 100%). Found: MNH$_4^+$, 264.1596; C$_{15}$H$_{18}$O$_3$ requires: MNH$_4^+$, 264.1600.

4.9.4. *(+)-(S)-1-Benzoyl-2-oxa-spiro[4,5]decan-3-one* ***7o***

Prepared by the general procedure (1.10 mmol of 2-alkoxydihydropyran **3z**, 0.11 mmol of Jacobsen's catalyst, 0.22 mmol of pyridine *N*-oxide, 3.30 mmol of NaOCl, 3.30 mmol of 3.0 M Jones reagent, 6 h for epoxidation, 3 h for Jones oxidation) to give lactone (*S*)-**7o** as a colourless oil (120 mg, 40% over two steps). ee 80% (HPLC analysis: OD column, 254 nm, flow 0.5 mL/min, ^{i}PrOH/hexane (5:95), t_{m}=57.82 min, t_{M}=79.09 min); $[\alpha]_D^{20}$ +29.2 (*c* 0.01, CHCl$_3$); $\nu_{\max}$ (CHCl$_3$)/cm^{-1} 3434, 2931 (CH), 2338, 1787 (lactone), 1685 (C=O); δ_H (400 MHz, CDCl$_3$) 7.94 (2H, d, *J* 9.0, 2×CH in Ph), 7.65 (1H, dd, *J* 9.0, 7.5, CH in Ph), 7.53 (2H, d, *J* 7.5, 2×CH in Ph), 5.53 (1H, s, OCH), 2.55 (2H, s, CH$_2$), 1.07–1.89 (10H, m, 5×CH$_2$ in CyHex); δ_C (100 MHz, CDCl$_3$), 196.2 (C), 175.9 (C), 136.2 (C), 134.2 (CH), 129.1 (2×CH), 128.5 (2×CH), 85.4 (CH), 45.0 (C), 37.3 (CH$_2$), 36.3, 32.9, 25.2, 23.1, 22.2 (5×CH$_2$); *m*/*z* (CI) 276 (MNH$_4^+$, 100%). Found: MNH$_4^+$, 276.1588; C$_{16}$H$_{18}$O$_3$ requires: MNH$_4^+$, 276.1600.

4.9.5. *(+)-(S)-5-(4-Methoxybenzoyl)-4,4-dimethyl-dihydrofuran-2(3H)-one* ***7p***

Prepared by the general procedure (0.53 mmol of 2-alkoxydihydropyran **3aa**, 0.05 mmol of Jacobsen's catalyst, 0.11 mmol of pyridine *N*-oxide, 1.59 mmol of NaOCl, 1.59 mmol of 3.0 M Jones reagent, 6 h for epoxidation, 3 h for Jones oxidation) to give lactone (*S*)-**7p** as a colourless oil (35 mg, 35% over two steps). ee 79% (HPLC analysis: OD column, 254 nm, flow 0.5 mL/min, ^{i}PrOH/hexane (5:95), t_{m}=104.08 min, t_{M}=119.72 min); $[\alpha]_D^{20}$ +56.0 (*c* 0.01, CHCl$_3$); $\nu_{\max}$ (CHCl$_3$)/cm^{-1} 2965–2931 (CH), 1788 (lactone), 1677 (C=O); δ_H (400 MHz, CDCl$_3$) 8.00 (2H, d, *J* 9.0, 2×CH in Ph), 7.01 (2H, d, *J* 9.0, 2×CH in Ph), 5.48 (1H, s, OC*H*), 3.92 (3H, s, CH$_3$), 2.62 (1H, d, *J* 17.0, CH$_2$), 2.33 (1H, d, *J* 17.0, CH$_2$), 1.40 (3H, s, CCH$_3$), 1.00 (3H, s, CCH$_3$); δ_C (100 MHz, CDCl$_3$), 193.8 (C), 175.9 (C), 164.4 (C), 131.0 (2×CH), 128.8 (C), 114.3 (2×CH), 85.3 (CH), 55.6 (CH$_3$), 41.8 (CH$_2$), 40.6 (C), 28.4 (CH$_3$), 23.5 (CH$_3$); *m*/*z* (CI) 266 (MNH$_4^+$, 100%). Found: MNH$_4^+$, 266.1403; C$_{14}$H$_{16}$O$_4$ requires: MNH$_4^+$, 266.1392.

4.9.6. *(+)-(S)-4,4-Dimethyl-5-(4-methylbenzoyl)-dihydrofuran-2(3H)-one* ***7q***

Prepared by the general procedure (0.64 mmol of 2-alkoxydihydropyran **3ab**, 0.06 mmol of Jacobsen's catalyst, 0.13 mmol of pyridine *N*-oxide, 1.92 mmol of NaOCl, 1.92 mmol of 3.0 M Jones reagent, 15 h for epoxidation, 1 h for Jones oxidation) to give lactone (*S*)-**7q** as a white solid (64 mg, 43% over two steps). Mp 157–160 °C; ee 70% (HPLC analysis: OJ column, 254 nm, flow 1.2 mL/min, ^{i}PrOH/hexane (2:98), t_{m}=33.14 min, t_{M}=45.97 min); $[\alpha]_D^{20}$ +37.0 (*c* 0.02, CHCl$_3$); $\nu_{\max}$ (CHCl$_3$)/cm^{-1} 2967–2931 (CH), 2874, 1788 (lactone), 1682 (C=O), 1606; δ_H (400 MHz, CDCl$_3$) 7.86 (2H, d, *J* 8.0, 2×CH in Ph), 7.34 (2H, d, *J* 8.0, 2×CH in Ph), 5.53 (1H, s, OCH), 2.61 (1H, d, *J* 17.0, CH$_2$), 2.46 (3H, s, CH$_3$Ph), 2.34 (1H, d, *J* 17.0, CH$_2$), 1.40 (3H, s, CCH$_3$), 0.99 (3H, s, CCH$_3$); δ_C (100 MHz, CDCl$_3$), 195.2 (C), 175.9 (C), 145.5 (C), 133.3 (C), 129.8 (2×CH), 128.7 (2×CH), 85.4 (CH), 41.8 (CH$_2$), 40.6 (C), 28.4, 23.5, 21.8 (3×CH$_3$); *m*/*z* (CI) 250 (MNH$_4^+$, 100%). Found: MNH$_4^+$, 250.1432; C$_{14}$H$_{16}$O$_3$ requires: MNH$_4^+$, 250.1443.

4.9.7. *(+)-(S)-5-(4-Chlorobenzoyl)-4,4-dimethyl-dihydrofuran-2(3H)-one* ***7r***

Prepared by the general procedure (0.75 mmol of 2-alkoxydihydropyran **3ac**, 0.08 mmol of Jacobsen's catalyst, 0.15 mmol of pyridine *N*-oxide, 2.25 mmol of NaOCl, 2.25 mmol of 3.0 M Jones reagent, 15 h for epoxidation, 1 h for Jones oxidation) to give lactone (*S*)-**7r** as white crystals (56 mg, 30% over two steps). Mp 155–158 °C; ee 76% (HPLC analysis: OD-H column, 254 nm, flow 0.5 mL/min, ^{i}PrOH/hexane (5:95), t_{m}=60.54 min, t_{M}=74.56 min); $[\alpha]_D^{20}$ +25.0 (*c* 0.01, CHCl$_3$); $\nu_{\max}$ (CHCl$_3$)/cm^{-1} 2963 (CH), 2874, 1789 (lactone), 1690 (C=O); δ_H (400 MHz, CDCl$_3$) 7.92 (2H, d, *J* 8.5, 2×CH in Ph), 7.53 (2H, d, *J* 8.5, 2×CH in Ph), 5.46 (1H, s, OCH), 2.59 (1H, d, *J* 17.0, CH$_2$), 2.38 (1H, d, *J* 17.0, CH$_2$), 1.45 (3H, s, CH$_3$), 1.00 (3H, s, CH$_3$); δ_C (100 MHz, CDCl$_3$), 194.7 (C), 175.4 (C), 141.0 (C), 134.1 (C), 130.0 (2×CH), 129.5 (2×CH), 85.6 (CH), 41.9 (CH$_2$), 40.8 (C), 28.2, 23.5 (2×CH$_3$); *m*/*z* (CI) 270 (MNH$_4^+$, 100%). Found: MNH$_4^+$, 270.0893; C$_{13}$H$_{13}$O$_3$Cl requires: MNH$_4^+$, 270.0897.

4.9.8. *(+)-(S)-4,4-Dimethyl-5-(4-nitrobenzoyl)-dihydrofuran-2(3H)-one* ***7s***

Prepared by the general procedure (0.32 mmol of 2-alkoxydihydropyran **3ad**, 0.03 mmol of Jacobsen's catalyst, 0.06 mmol of pyridine *N*-oxide, 1.00 mmol of NaOCl, 1.00 mmol of 3.0 M Jones reagent, 15 h for epoxidation, 3 h for Jones oxidation) to give lactone (*S*)-**7s** as a colourless oil (54 mg, 64% over two steps). ee 46% (HPLC analysis: OD-H column, 254 nm, flow 1.5 mL/min, ^{i}PrOH/hexane (10:90), t_m=35.79 min, t_M=43.31 min); $[\alpha]_D^{20}$ +14.0 (*c* 0.01, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2980 (CH), 2939, 1790 (lactone), 1698 (C=O), 1603; δ_H (400 MHz, $CDCl_3$) 8.39 (2H, d, *J* 9.0, 2×CH in Ph), 8.15 (2H, d, *J* 9.0, 2×CH in Ph), 5.44 (1H, s, OCH), 2.57 (1H, d, *J* 17.0, CH_2), 2.43 (1H, d, *J* 17.0, CH_2), 1.44 (3H, s, CCH_3), 1.02 (3H, s, CCH_3); δ_C (100 MHz, $CDCl_3$), 195.1 (C), 174.9 (C), 150.8 (C), 140.2 (C), 129.8 (2×CH), 124.2 (2×CH), 86.2 (CH), 42.0 (CH_2), 41.1 (C), 27.9, 23.4 (2×CH_3); *m*/*z* (CI) 250 (MNH_4^+, 100%). Found: MNH_4^+, 281.1141; $C_{13}H_{13}NO_5$ requires: MNH_4^+, 281.1137.

4.9.9. *(+)-(S)-5-(2-Naphthoyl)-4,4-dimethyl-dihydrofuran-2(3H)-one* ***7t***

Prepared by the general procedure (0.71 mmol of 2-alkoxy-dihydropyran **3ae**, 0.07 mmol of Jacobsen's catalyst, 0.14 mmol of pyridine *N*-oxide, 2.13 mmol of NaOCl, 2.13 mmol of 3.0 M Jones reagent, 15 h for epoxidation, 1 h for Jones oxidation) to give lactone (*S*)-**7t** as a colourless oil (78 mg, 41% over two steps). ee 71% (HPLC analysis: AD-H column, 254 nm, flow 1.8 mL/min, ^{i}PrOH/hexane (4:96), t_m=64.66 min, t_M=69.32 min); $[\alpha]_D^{20}$ +31.0 (*c* 0.01, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2962–2926 (CH), 1788 (lactone), 1681 (C=O), 1627; δ_H (400 MHz, $CDCl_3$) 8.48 (1H, s, CH in NapH), 7.93–8.04 (4H, m, 4×CH in Naph), 7.62–7.71 (2H, 2×CH in Naph), 5.71 (1H, s, OCH), 2.66 (1H, d, *J* 17.0, CH_2), 2.39 (1H, d, *J* 17.0, CH_2), 1.46 (3H, s, CH_3), 1.03 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$), 195.6 (C), 175.8 (C), 136.0 (C), 133.2 (C), 132.4 (C), 130.7 (CH), 129.8 (CH), 129.3 (CH), 129.2 (CH), 127.9 (CH), 127.3 (CH), 123.7 (CH), 85.5 (CH), 41.9 (CH_2), 40.8 (C), 28.4, 23.6 (2×CH_3); *m*/*z* (CI) 286 (MNH_4^+, 100%). Found: MNH_4^+, 286.1437; $C_{17}H_{16}O_3$ requires: MNH_4^+, 286.1443.

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