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ARTICLE

Stereoselective synthesis of *trans*-THF rings using oxidative cyclisation–radical deoxygenation sequence: Application to the formal synthesis of *trans*-(2*R*,5*R*)-linalool oxide

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An efficient stereoselective synthesis of *cis*-2,5-disubtituted tetrahydrofuran (THF) diols has been achieved using permanganate-mediated oxidative cyclisation of 1,5-diene precursors. The facial selectivity during the course of cyclisation was induced by incorporating conveniently accessible chiral auxiliaries such as (2*R*)-10,2-camphorsultam, (*S*)-4-benzyloxazolidin-2-one and (–)-8-phenylmenthol. The use of (2*R*)-10,2-camphorsultam furnished the desired THF product as a single isolated diastereoisomer. Conformational analyses are presented to rationalize the origin of facial selectivity and synthetic investigation towards successfully accomplished transformation of *cis*-2,5-disubstituted THF diols into corresponding *trans*-THF compounds is also described, leading to a stereoselective formal synthesis of *trans*-(2*R*,5*R*)-linalool oxide.

Introduction

From cytotoxic natural products to industrial synthetic analogues, 2,5-disubstituted tetrahydrofurans (THFs) are common motifs present in bioactive molecules.[1] WHI-261 (**1**)[2] also named as COBRA-0, and COBRA-1 (**2**)[3] are synthetic anti-cancer drug molecules which are effective against human tumour cell lines; *trans*-linalool oxide (**3**)[4] is a monoterpenoid present in essential oils and one of the most commonly used compounds in beverages, foods, and perfumery, whilst 14-deacetyl eurylene (**4**) contains both *cis*- and *trans*-2,5-disubstituted THF units and exhibits a significant cytotoxicity against KB cells[5] (IC_{50}: 0.52 μg/mL, Fig. 1). The most widely recognised biosynthetic route to 2,5-disubstituted THF units involves sophisticated enzyme-catalysed epoxidation–ring-opening cascades applied to acyclic polyene precursors,[6] and their intrinsic ionophoric nature provides a metal binding tendency with physiologically important metallic cations.[7] This ability of polyethers to bind metal ions is recognised as one mechanism of action leading to their notable bioactivity.

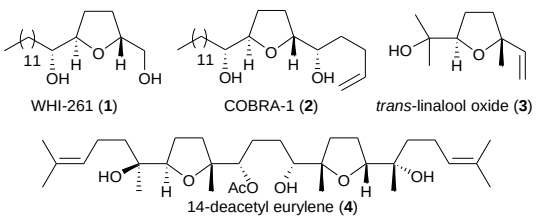

Fig. 1 Structures of representative molecules containing *trans*-2,5-disubstituted THF rings

Given their distinctive structural features combined with remarkable cytotoxicity, 2,5-disubstituted THFs have attracted an unusually high level of interest from the synthetic community, and much time and efforts to establish new synthetic protocols to obtain adequate quantities for expediting their biological evaluations. Among various established methodologies towards the synthesis of THFs, oxidative cyclisation involving metal–oxo-promoted processes is prevalent and these have been effectively applied to 5-hydroxyalkenes, 1,5-dienes and 5,6-dihydroxyalkenes (Fig. 2). Oxorhenium $[Re^{(VII)}]$[8] and $Co^{(II)}$ (ref. 9) oxidants have been reported to induce *trans*-selectivity in the incipient THF rings from 5-hdroxyalkenes (Fig. 2a); $Mn^{(VII)}$ (ref. 10), $Os^{(VIII)}$ (ref. 11) and $Ru^{(VIII)}$ (ref. 12) based oxidising agents

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promote the formation of *cis*-THF adducts when applied to 1,5-dienes (Fig. 2b), whereas $Os^{(VI)}$ (ref. 13), $Cr^{(VI)}$ (ref. 14) and $Ru^{(VIII)}$ (ref. 15) species provide a convenient access to *cis*-selective THF rings from 5,6-dihydroxyalkenes (Fig. 2c). Furthermore, $Os^{(VI)}$ chemistry has been extended to 5-hydroxy-6-protected aminoalkenes, 5,7- and 5,8-dihydroxyalkenes to synthesize *cis*-2,5-disubstituted THF motifs.[16] Mechanistically, $Co^{(II)}$ catalysed cyclisation follows a radical pathway,[9] whereas other metal-based transformations are believed to involve sequential [3+2] cycloadditions.[10b] However, a Sharpless–type [2+2] cycloadditions sequence was also proposed.[10c] Kinetic isotopic investigations[17a] and spectroscopic determination of the intermediate species[17b] reveal that operational mechanism follows [3+2] pathway, which was later supported by DFT calculations and labeling studies, confirming that concerted [3+2] cycloaddition is favoured by about 40 kcal/mol relative to the stepwise [2+2] counterpart.[17c,d]

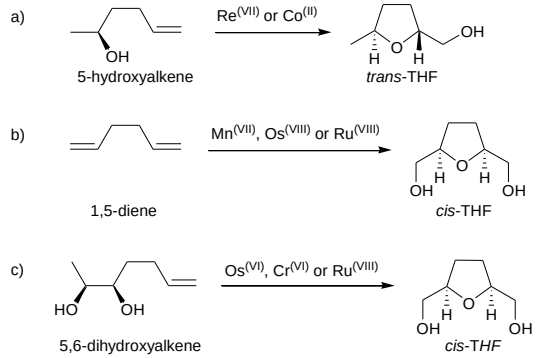
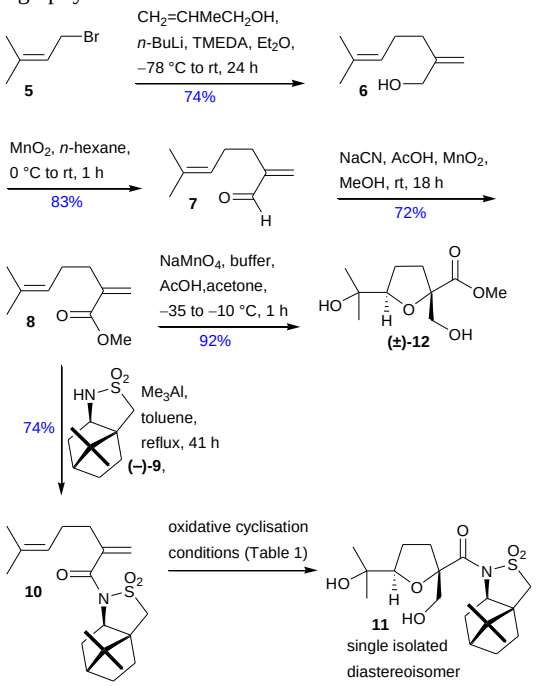


Fig. 2 Synthesis of 2,5-disubstituted THF rings by metal–oxo-promoted cyclisations.

During research studies in the domain of oxidative cyclisation of 1,5-dienes and 1,5,9-trienes, it was observed that a direct stereoselective route for the *trans*-selective permanganate-mediated oxidative cyclisation of 1,5-diene motif is lacking, though the conversion of *cis*-THF diol into *trans*-THF product *via* oxa-carbenium ion intermediate is described.[18] A conceptually different methodology involves the formation of a *cis*-THF diol by oxomanganese [$Mn^{(VII)}$] promoted cyclisation of 1,5-diene substrate and subsequent conversion into desired *trans*-THF product *via* Barton–McCombie radical deoxygenation.[19] Herein, a detailed synthetic investigation towards the stereoselective synthesis of *cis*-THF diols and their conversion into *trans*-THF motifs is reported.

Results and Discussion

Commercially available prenyl bromide (**5**) was alkylated with the dianion generated from methallyl alcohol to yield allylic alcohol **6** in good yield (Scheme 1).[20] Oxidation of allylic alcohol **6** was carried out using Mn-based oxidising agents such as MnO_2 and $BaMnO_4$ to furnish the aldehyde **7**.[21] However, after optimization of experimental procedures, MnO_2 was found superior compared to $BaMnO_4$, in terms of yield and shorter reaction time. Treatment of crude aldehyde **7** with NaCN/AcOH in MeOH offered an *in situ* generation of cyanohydrin, which was readily oxidised by MnO_2 to acyl cyanide and subsequent nucleophilic attack of MeOH afforded the diene methyl ester **8**.[22] For a stereoselective oxidative cyclisation, a chiral auxiliary would be required to direct the metal oxidant to one face of the enoyl alkene. For this purpose, (2*R*)-10,2-camphorsultam (**(–)-9**) was selected and synthesized on multi-gram scale (36 g, 54% yield over 4 steps) according to the literature reports.[23,24] Coupling of diene ester **8** with a pre-formed aluminium complex of chiral auxiliary **(–)-9** provided 1,5-dienoate **10** in good yield,[25] which was ready to test for the key oxidative cyclisation. Permanganate oxidative cyclisation of dienoate **10** gave the *cis*-THF diol **11** as a single diastereoisomer along with recovery of the starting dienoate **10** (up to 45%).[19,26] Relative stereochemistry of the *cis*-THF diol **11** was assigned unequivocally by X-ray crystallography.[19b]



Scheme 1 Permanganate-mediated oxidative cyclisation to prepare *cis*-THF diols **11** and **12**.

entry	Oxidative cyclisation conditions	**10** yield (%)	**11** yield (%)
1	$NaMnO_4$ (1.5 eq., 0.4 M aq.), AcOH (3.0 eq.), buffer, acetone, –35 to –10 °C, 1 h.	45	33 (60)[a]
2	$NaMnO_4$ (1.7 eq., 0.4 M aq.), AcOH (3.0 eq.), buffer, acetone, –40 to 0 °C, 1 h.	30	32 (46)[a]
3	$KMnO_4$ (2.0 eq., 0.4 M aq.), AcOH (4.0 eq.), Adogen 464 (0.5 eq.), ether, rt, 30 min.	41	38 (65)[a]

Table 1 Optimisation studies towards oxidative cyclisation of dienoate **10**. [a]numbers in the brackets indicate % yield of *cis*-THF diol **11** on the basis of recovered starting material **10**.

Sodium permanganate as an oxidising agent in the absence of phase-transfer catalyst (PTC) offered comparatively lower yields of

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the resultant *cis*-THF diol **11** (Table 1, entries 1 and 2). However, the best yield was found when cyclisation was performed using potassium permanganate in the presence of PTC, Adogen 464 (Table 1, entry 3).[10d] Despite of all efforts to increase the conversion proved unsuccessful. Notably, a single diastereoisomeric *cis*-THF diol **11** was obtained in each reaction, which provides striking evidence for an effective facial selectivity induced by the chiral auxiliary **(–)-9** during the course of sequential [3+2] permanganate-catalysed cycloadditions. Low reactivity of the dienoate **10** and appearance of single diasteromeric product can be attributed to the effective shielding by the attached chiral auxiliary. This proposal was tested by performing permanganate-mediated oxidative cyclisation for the methyl ester diene **8** under the same reaction conditions, which resulted an highly efficient formation of the racemic *cis*-THF diol **12** in 92% yield.[19b]

As the stereoselectivity of the reaction is controlled by a chiral auxiliary **(–)-9**, the sense of diastereofacial preference observed in the oxidative cyclisation of 1,5-dienoate **10** can be explained by the preferred orientation of enoyl olefin and the relevant arrangement of C=O and NSO_2 moieties. It is proposed that based on steric and electronic reasons, *s-trans* orientation of enoyl olefin[27] and an *anti*-position of C=O and NSO_2 groups are favoured,[28] as demonstrated by two conformational models **A** and **B** (Fig. 3). If the metal atom (M) coordinates with the equatorial oxygen of the sulfonyl moiety and enoyl oxygen atom as shown in the case of conformer **B**, the *Si*-face of the electron–deficient alkene is effectively blocked by the camphor structure and the initial attack of permanganate ion (MnO_4^-) takes place from the *Re*-face followed by cyclisation. However, if metal-chelation is absent as reflected in the conformation **A**, the *Si*-face of enoyl olefin is also blocked; this time by the axial oxygen atom of the camphorsultam auxiliary **(–)-9** and approach of MnO_4^- would take place from the *Re*-face. Both conformation models favour a *Re*-face attack of MnO_4^-, which is consistent with the obtained diastereoselective outcome and proceed *via* transition state **13** as a result of double [3+2] cycloadditions followed by hydrolysis to afford the *cis*-THF diol **11** as a single diastereoisomer. Low reaction yield and recovery of the unreacted starting material indicate that the *Re*-face in both conformations also experiences some sterics, which hinders initial attack of MnO_4^- on the electron-poor enoate alkene.

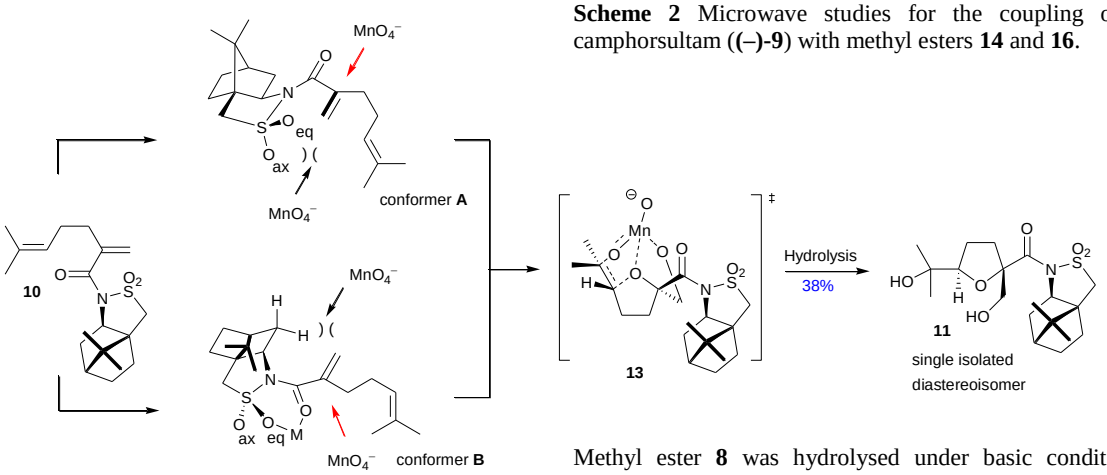
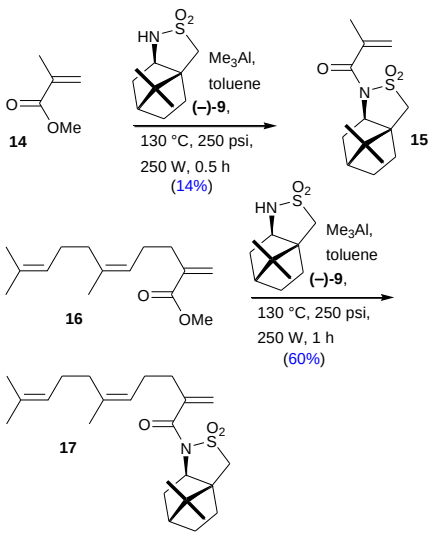


Fig. 3 Rationalization of the diastereoinduction obtained by incorporating (2*R*)-10,2-camphorsultam (**(–)-9**) for the oxidative cyclisation of 1,5-dienoate **10**.

At this juncture, an attempt was made to shorten the synthetic route towards dienoate **10** by subjecting allylic alcohol **6** to one-step MnO_2-mediated oxidation approach.[29] The desired diene methyl ester **8** was obtained, albeit in poor yield (15%) along with 70% recovery of the starting allylic alcohol **6**. Also, efforts were carried out to shorten the reaction time (originally 41 hours) for the coupling reaction of methyl ester **8** with the chiral auxiliary **(–)-9**. In this context, a model study was performed using microwave irradiation for a commercially available ester **14**, which was added to a pre-formed aluminium complex of (2*R*)-10,2-camphorsultam (**(–)-9**) in a microwave tube and the reaction mixture was irradiated (Scheme 2). The desired product **15** was isolated in poor yield along with 58% recovery of the auxiliary **(–)-9**. The starting material **14** could not be recovered, probably because of its high volatility. The same reaction was attempted with another available triene ester **16**, which provided the desired trienoate **17** and unreacted chiral auxiliary **(–)-9** in 60 and 23% yields respectively. Due to associated difficulties in improving the yield under microwave conditions, it was decided to investigate the effect of other readily available chiral auxiliaries, (*S*)-4-benzyloxazolidin-2-one (**(–)-21**)[30] and 8-phenylmenthol (**(–)-24**)[31] in the oxidative cyclisation.



Scheme 2 Microwave studies for the coupling of (2*R*)-10,2-camphorsultam (**(–)-9**) with methyl esters **14** and **16**.

Methyl ester **8** was hydrolysed under basic conditions and the resultant carboxylic acid **18** was converted to its activated ester **19** by treating with pentaflourophenol and DCC (Scheme 3).[32] As anticipated, oxidative cyclisation of PFP ester **19** provided *cis*-THF diol **20** in good yield, though lower in comparison with the oxidative cyclisation of methyl ester **8**. Treatment of lithiated salt of

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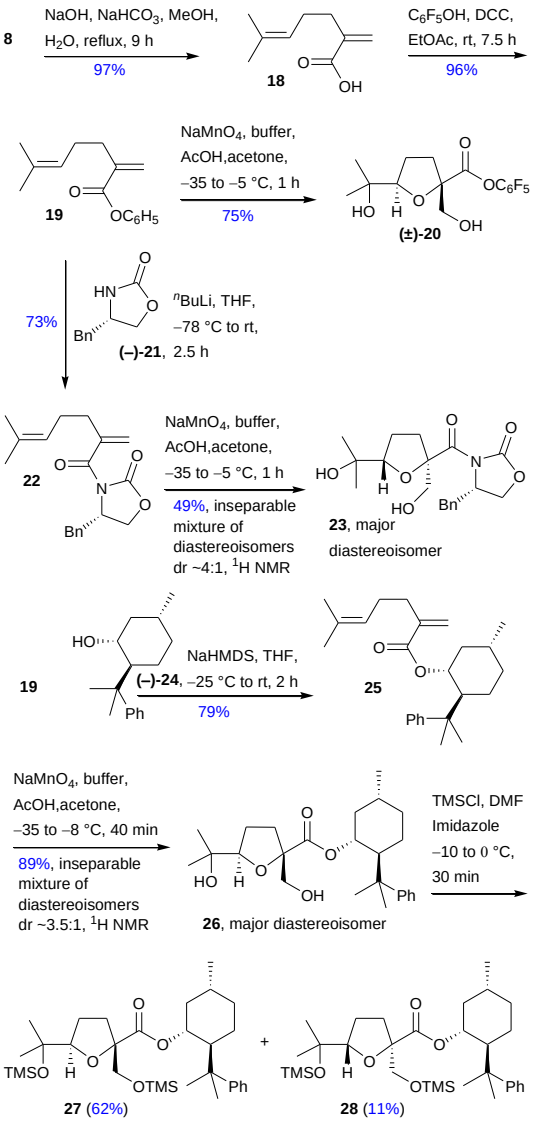
oxazolidinone based chiral auxiliary **(–)-21** with the ester **19** gave the diene **22**, which on oxidative cyclisation afforded the *cis*-THF diol **23** as a major diastereoisomer (dr ~4:1, ^{1}H NMR) in moderate yield.[33] Both diastereoisomers were not separable by flash column chromatography. With this moderate levels of yield and diastereoselectivity for the oxidative cyclisation of dienoate **22**, application of another commercially available chiral auxiliary was investigated. Coupling of diene ester **19** with sodium salt of cyclohexyl based auxiliary **(–)-24** furnished the desired 1,5-dienoate **25**, which was subjected to permanganate-mediated oxidative cyclisation to provide *cis*-THF diol **26** as a major diastereoisomer in an excellent yield and acceptable level of diastereoinduction (dr ~3.5:1, ^{1}H NMR).[34] Pleasingly, separation of the diastereoisomers was successfully achieved chromatographically by protecting inseparable mixture of diastereomeric oxidative cyclisation products as their bis-TMS ethers **27** and **28**, and rest of the investigation was carried out with diastereomerically pure *cis*-THF adduct **27**.



Scheme 3 Oxidative cyclisation of 1,5-dienoates **19**, **22** and **25**; stereoselective synthesis of bis-protected *cis*-THF diol **27**.

It is proposed that the observed stereochemical outcome during the oxidative cyclisation of 1,5-dienoate **22** may be accounted for by the preferential blockage of the rear face of the electron-poor enoate alkene by the phenyl ring present in the chiral auxiliary, as indicated in the *s-trans* enoate conformer **C** (Fig. 4). Due to this shielding, attack of MnO_4^- would take place preferentially from the front face, affording the *cis*-THF diol **23** as the major diastereoisomer *via* the transition state **29**. The major product **26** from the oxidative cyclisation of dienoate **25** is formed through the transition state **30**, which results by the blockage of the front face of the more electron deficient alkene by the phenyl ring as shown in the *s-trans* enoate conformer **D**.

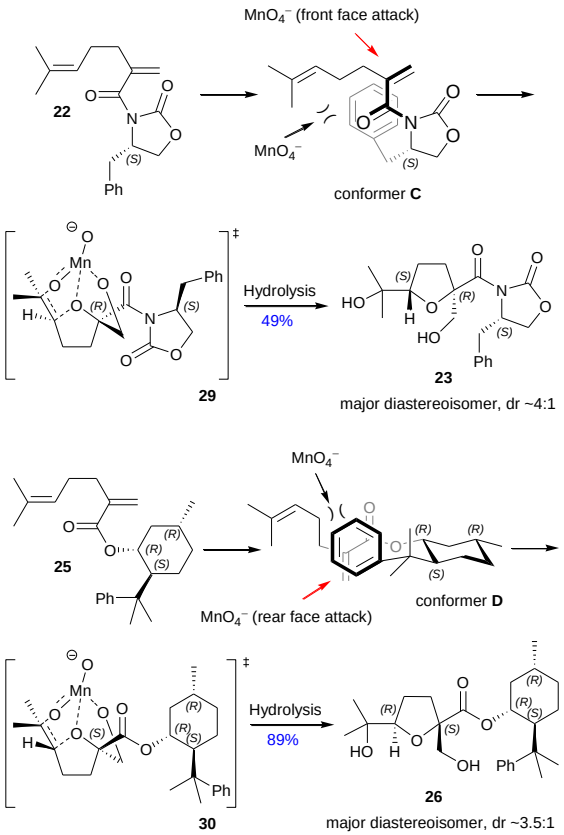


Fig. 4 Origin of facial selectivity during the oxidative cyclisation of 1,5-dienoates **22** and **25** bearing chiral auxiliaries.

To provide substrates for the radical deoxygenation, conversion of primary carbinol present in the *cis*-THF diols **11** and **12** into corresponding thionoformate was envisaged. Treatment of *cis*-THF precursors **11** and **12** with chlorothionoformate in the presence of DMAP afforded the desired thionoformates **31** and **32** respectively (Scheme 4).[35] In case of diastereomerically pure *cis*-THF diol **11**, degradation of the starting material was noticed and the desired product was obtained in 33% yield. Efforts to improve the reaction yield by altering the reaction conditions such as temperature, time and stoichiometric amounts of the reagents made a very little impact. This low yield can be ascribed to the impediment caused by the steric bulk of the attached sultam auxiliary **(–)-9** as it was observed during the oxidative cyclisation step. The degradation of the starting material might be triggered by the presence of free tertiary hydroxyl group, especially in a situation when primary hydroxyl group is experiencing steric hindrance. Alternatively, xanthate formation

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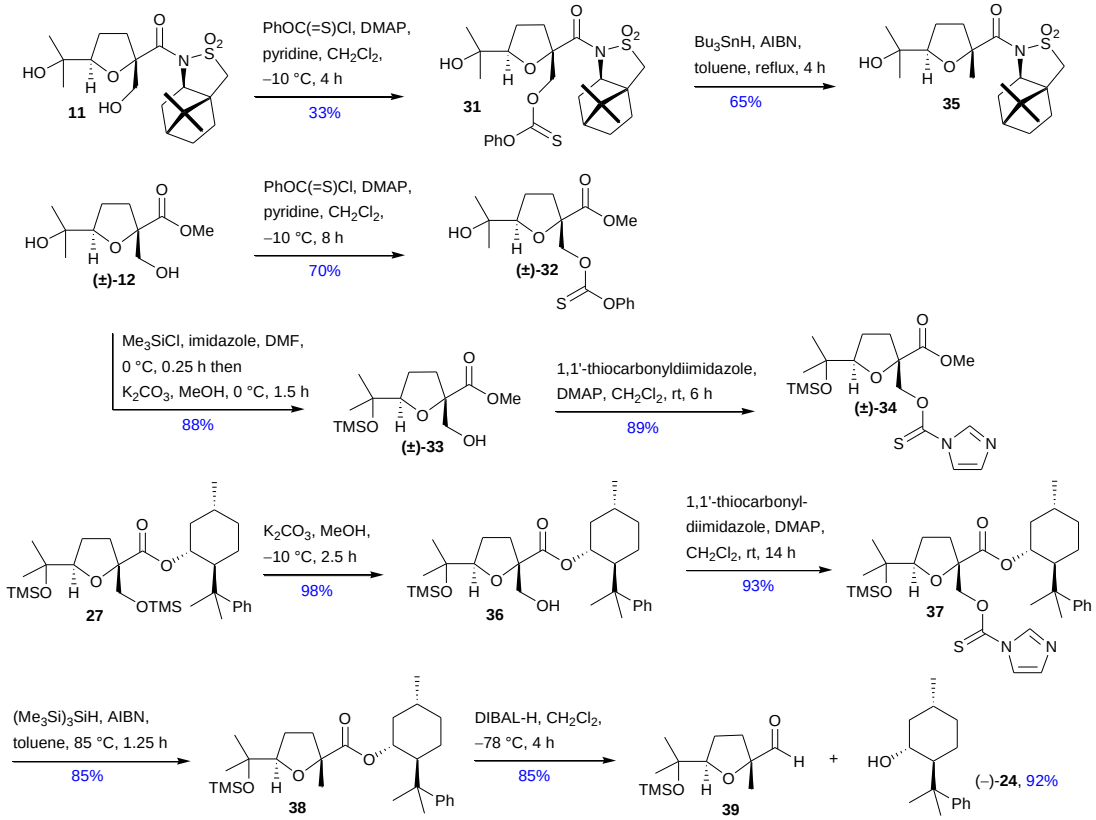

Scheme 4 Synthetic investigations towards the transformation of *cis*-THF diols into *trans*-THF adducts *via* radical deoxygenation.

using CS_2 and MeI in the presence of NaH and imidazole also proved unsuccessful to provide the desired product when applied to racemic *cis*-THF diol **12** and the starting material was recovered in 55% yield after flash chromatographic purification.[36]

Moving to another approach to provide substrates for the radical deoxygenation, the tertiary hydroxyl group of the racemic *cis*-THF diol **12** was protected as TMS ether **33** and the product was treated with 1,1′-thiocarbonyldiimidazole in the presence of imidazole to afford the racemic thionocarbamate **34** in an excellent yield (Scheme 4).[37] A survey of conditions for the radical deoxygenation revealed that $(Bu_4N)_2S_2O_8$ was a suitable reagent.[38] Initial attempts towards the radical cleavage of the substrates **31**, **32** and **34** failed to afford the desired *trans*-THF products on treatment with $(Bu_4N)_2S_2O_8$ and degradation of the starting material to afford intricate reaction mixture was noticed by TLC and crude ^{1}H NMR. Additives such as Na_2CO_3 and Et_3N have also been reported to facilitate the reaction, which also proved ineffective for this particular transformation. Gratifyingly, treatment of the thionoformate **31** with conventional hydride source, Bu_3SnH afforded the required *trans*-THF product **35** in good yield,[39] achieving a formal conversion of *cis*-THF diol **11** into *trans*-THF **35**. Encouraged by successful accomplishment of radical deoxygenation, selective removal of primary TMS ether from bis-TMS protected THF adduct **27** provided mono-protected THF **36**, which was subsequently converted to thionocarbamate **37** in an excellent yield. An alternate radical source, tris-trimethylsilyl silane (TTMSS) was also used for radical deoxygenation.[40] Pleasingly, an end-game was achieved by treating thionocarbamate **37** with TTMSS/AIBN in hot toluene to afford the desired *trans*-THF compound **38** in good yield. Finally, reductive cleavage of the chiral auxiliary from the *trans*-THF compound **38** furnished the THF aldehyde **39** in excellent yield and pure 8-phenylmenthol (**(–)-24**, 92%), demonstrating the potential to recycle the chiral auxiliary. Stereoselective total synthesis of *trans*-(2*R*,5*R*)-linalool oxide (**3**), a commercially useful monoterpenoid can easily be achieved by deprotection of the tertiary silyl ether and subsequent methylenation of the aldehyde **39**, which highlights the effectiveness of this protocol.

Conclusions

In summary, an efficient route to prepare *trans*-2,5-disubstituted THF rings, a common motif present in numerous bioactive natural products, from *cis*-2,5-disubstituted diols is described. This route employs permanganate-mediated oxidative cyclisation applied to 1,5-dienoate followed by radical deoxygenation of the resultant primary carbinol. Facial selectivity during the course of oxidative cyclisation was controlled by incorporating readily available external chiral auxiliaries and obtained diastereoinduction is explained by the conformational models. Reductive cleavage of the chiral auxiliary was efficiently carried out using facile conditions to promote functional group transformation for further synthetic manipulations and to demonstrate the potential of recycling chiral auxiliary. Work is ongoing in the area of stereoselective oxidative cyclisation followed by specific transformations and the process can provide a useful route to the synthesis of *trans*-THF rings containing natural products and synthetic analogues of pivotal importance.

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Experimental

Experimental, characterization data and NMR spectra for the compounds **6-8, 10-12, 18** and **19** are reported.[19b]

General: All air/moisture sensitive reactions were carried out under an inert atmosphere, in an oven dried glassware. The solvents Et_2O (from Na/benzophenone), toluene and CH_2Cl_2 (from CaH_2) were distilled before use, and where appropriate, other reagents and solvents were purified by standard techniques.[41] TLC was performed on aluminium–pre-coated plates with silica gel 60 with an F_{254} indicator; visualised under UV light (254 nm) and/or by staining with $KMnO_4$ (10% aq.). Flash column chromatography was performed with Merck Kieselgel 60 silica gel. Fourier-transform infrared (FT-IR) spectra are reported in wavenumbers (cm^{-1}) and were collected on a Nicolet 380 fitted with a Diamond platform, as solids or neat liquids. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solution using a Bruker AC300 or and AV300 (300 and 75 MHz respectively) or on a Bruker DPX400 (400 and 100 MHz respectively). Chemical shifts are reported in δ units using $CHCl_3$ as an internal standard (δ 7.27 ppm ^1H and δ 77.00 ppm ^{13}C). Coupling constants (*J*) were recorded in Hz. The following abbreviations for the multiplicity of the peaks are s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), sxt (sextet), br (broad), and m (multiplet). Optical rotations were measured using PolAAr 2001 polarimeter with 589 nm light source. Melting points were obtained in an open capilliary and are uncorrected. Electron impact and chemical ionisation mass spectra were obtained using a Fisons VG platform single quadrapole mass spectrometer. Electrospray mass spectra were obtained using a Micromass platform mass analyser with an electrospray ion source. The buffer solution used in the aq. permanganate-promoted oxidative cyclisation was an aq. 8:2 mixture of 1/15 M KH_2PO_4 and 1/15 M NaH_2PO_4 at pH 6.5.

General procedure for the microwave conditions of coupling of (2*R*)-10,2-camphorsultam ((–)-9) with methyl esters: To the solution of (2*R*)-10,2-camphorsultam (**(–)-9**, 1.25 mmol) in distilled toluene (0.25 M, on the basis of mmol of methyl ester) was added dropwise $(Me)_3Al$ (1.25 mmol) at room temperature. After stirring for 15 min, a solution of methyl ester (1.0 mmol) in distilled toluene (0.5 mL) was added and the resulting mixture was placed in microwave at 130 ˚C, 250 psi and 250 W for 30–60 min. At this stage, the mixture was taken out from microwave and diluted with CH_2Cl_2 (5 mL), water (2 mL) and Rochelle salt (2 mL) and stirred for 1 hour at room temperature. The organic phase was separated, dried (Na_2SO_4), filtered and concentrated *in vacuo* to afford the crude product.

***N*-(3-Methyl-2-methylene-propylate)-(2*R*)-camphor-10,2-sultam (15):** Following the general procedure for the coupling (2*R*)-10,2-camphorsultam (**(–)-9**) with methyl esters under microwave conditions, methyl ester **14** (100 mg, 1.0 mmol) provided the crude (267 mg) after 30 min as a yellowish white solid. Purification by column chromatography (SiO_2 eluting with 20% EtOAc/hexane) afforded the title product **15** as a yellow oil (45 mg, 0.16 mmol, 14%). The pure chiral auxiliary **(–)-9** was also recovered as a white solid (156 mg, 0.72 mmol, 58%). $[\alpha]_D$ = –37.0 (*c* 0.45, $CHCl_3$, 26 ˚C); FT-IR ν_{max} (neat) 2961, 2919, 2882, 1679, 1334, 1194, 1132, 1063, 976 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.70 (1H, br, C=C*H*H), 5.66 (1H, d, *J* = 1.5 Hz, C=CH*H*), 4.05 (1H, dd, *J* = 7.5, 5.0 Hz, C*H*N), 3.52 (1H, d, *J* = 13.8 Hz, C*H*HSO$_2$), 3.40 (1H, d, *J* = 13.5 Hz, CH*H*SO$_2$), 2.06-1.90 (5H, m, C*H*H and 2 x CH_2), 2.01 (3H, s, CH_3), 1.44-1.38 (2H, m, CH_2), 1.24 (3H, s, CH_3), 1.01 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.25 (*C*ON), 138.98 (*C*=CH_2), 124.31 (*C*=CH_2), 65.44 (*C*HN), 53.56 (CH_2SO_2), 48.02 (*C*CH_2), 47.71 (*C*$(CH_3)_2$), 45.26 (*C*HC$(CH_3)_2$), 38.35 (CH_2CHN), 33.28 (CH_2CH), 26.47 (CH_2C), 21.32 (CH_3), 19.89 (CH_3), 18.71 (CH_3) ppm; LRMS (ES^+) m/z 306 (100%, $[M+Na]^+$)]$^+$); HRMS (ES^+) m/z Calculated: 306.1134; Found: 306.1132 ($[M+H]^+$).

***N*-((*Z*)-Methyl 6,10-dimethyl-2-methyleneundeca-5,9-dienoyl)-(2*R*)-camphor-10,2-sultam (17):** Following the general procedure for the coupling (2*R*)-10,2-camphorsultam (**(–)-9**) with methyl ester under microwave conditions, methyl ester **16** (100 mg, 0.42 mmol) afforded a yellow oil after 60 min as a crude product (177 mg). Purification by column chromatography (SiO_2 eluting with 20% EtOAc/hexane) afforded the title trieneoate **17** as a yellow oil (106 mg, 0.25 mmol, 60%). Physical and spectroscopic data were in accordance with the literature.[19a] The pure chiral auxiliary **(–)-9** was also recovered as a white solid (26 mg, 0.12 mmol, 23%). $[\alpha]_D$ = –41.8 (*c* 0.33, $CHCl_3$, 25 ˚C); FT-IR ν_{max} (neat) 2960, 2914, 1680, 1336, 1196, 1132, 1063, 976 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.76 (1H, s, =C*H*H), 5.63 (1H, s, =CH*H*), 5.15 (2H, t, *J* = 7.0 Hz, 2 x C=C*H*CH_2), 4.05 (1H, dd, *J* = 7.3, 4.8 Hz, C*H*N), 3.51 (1H, d, *J* = 13.6 Hz, C*H*HSO$_2$), 3.40 (1H, d, *J* = 13.6 Hz, CH*H*SO$_2$), 2.39-2.19 (4H, m, 2 x CH_2), 2.06 (4H, s, 2 x CH_2), 2.05-1.90 (5H, m, C*H* and 2 x CH_2), 1.69 (6H, s, 2 x CH_3), 1.61 (3H, s, CH_3), 1.44-1.38 (2H, m, CH_2), 1.24 (3H, s, CH_3), 1.00 (3H, s, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.10 (*C*ON), 143.15 (*C*=CH_2), 135.94 (CH_3*C*), 131.50 ($(CH_3)_2$*C*), 124.34 (C=*C*H_2), 124.12 (C=*C*HCH_2), 123.49 (C=*C*HCH_2), 65.53 (*C*HN), 53.60 (*C*CH_2), 47.92 (*C*H_2SO_2), 47.70 (*C*$(CH_3)_2$), 45.20 (*C*HC$(CH_3)_2$), 38.38 (CH_2CHN), 33.21 (CH_2C), 32.76 (CH_2C=CH_2), 31.94 (CH_2C=CH), 26.55 (CH_2CH_2C), 26.48 (CH_2CH_2), 26.04 (CH_2CH_2), 25.69 (CH_3), 23.33 (CH_3), 21.25 (CH_3), 19.87 (CH_3), 17.63 (CH_3) ppm; LRMS 442 (100%, $[M+Na]^+$), 420 (20%, $[M+H]^+$); HRMS (ES^+) m/z Calculated: 442.2386; Found: 442.2380 ($[M+Na]^+$).

General procedure for the permanganate-mediated oxidative cyclization of 1,5-dienoates: To a vigorously stirred mixture of 1,5-dienoate (1 mmol) and phosphate buffer (0.5 M, on the basis of mmol of 1,5-dienoate) in acetone (0.05 M, on the basis of mmol of 1,5-dienoate) at –35 ˚C was added a solution of $NaMnO_4$ (1.5 mmol) containing AcOH (3 mmol). The purple mixture was stirred rapidly for 40–60 min, during which time the temperature of the acetone cooling bath had raised to –8 to –5˚C and the reaction mixture had turned dark brown. At this, the reaction was quenched with sat. aq. $Na_2S_2O_5$ (30 mL) to dissolve all of the precipitated manganese salt and then repeatedly extracted using CH_2Cl_2 (4 x 60mL). The organic extracts were combined, dried (Na_2SO_4), filtered and concentrated *in vacuo* to give the crude product.

***Rac.* (2*S*,5*R*)-Perfluorophenyl tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (20):** Following the general procedure for the permanganate-mediated oxidative cyclization of 1,5-dienoate, diene ester **19** (735 mg, 2.30 mmol) afforded the crude as a viscous oil (765 mg). Purification by column chromatography (SiO_2 eluting with EtOAc/hexane (5 to 40%)) afforded racemic THF diols **20** as a white solid (638 mg, 1.72 mmol, 75%). mp = 73–75 ˚C; FT-IR ν_{max} (neat) 3337, 2977, 2933, 2877, 1781, 1519, 1471, 1102, 1055, 996 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.14 (1H, t, *J* = 7.5 Hz, C*H*, THF), 4.08 (1H, d, *J* = 11.3 Hz, C*H*HOH), 3.90 (1H, d, *J* = 11.3 Hz, CH*H*OH), 2.82 (1H, br, O*H*), 2.35 (2H, t, *J* = 7.5 Hz, CH_2, THF), 2.10-1.96 (2H, m, CH_2, THF), 1.35 (3H, s, CH_3), 1.26 (1H, s, O*H*), 1.19 (3H, s, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.01 (*C*OO), 87.97 (*C*H, THF), 86.26 (*C*CH_2OH, THF), 71.60 ($(CH_3)_2$*C*), 65.97 (*C*H_2OH), 32.40 (*C*H_2, THF), 27.42 (*C*H_2, THF), 25.94 (CH_3), 25.28 (CH_3) ppm (aromatic carbons were not observed); LRMS 393 (100%,

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$[M+Na]^+$); HRMS (ES^+) m/z Calculated: 393.0737; Found: 393.0736 ($[M+Na]^+$).

(*S*)-3-(6-Methyl-2-methylenehept-5-enoyl)-4-benzyloxazolidin-2-one (22): To a solution of (*S*)-benzyloxazolidinone (**(–)-21**, 75.5 mg, 0.43 mmol) in dry THF (5 mL) was added *n*-BuLi (0.2 mL of 2.5 M in hexane, 0.49 mmol) at –78 ˚C. The solution was allowed to warm to –60 ˚C over 1 hour whereupon a solution of the diene ester **19** (130 mg, 0.41 mmol) in dry THF (5 mL) was added dropwise. The solution was then allowed to warm to room temperature. After 1 hour stirring at room temperature, the reaction was diluted in Et_2O (20 mL) and quenched with NH_4Cl (sat. aq. sol., 25 mL). The organic phase was washed with $NaHCO_3$ (sat. aq. sol., 2 x 20 mL), dried (Na_2SO_4) and concentrated *in vacuo* to give yellow oil (147 mg). Purification by column chromatography (SiO_2 eluting with EtOAc/hexane (5 to 20%)) afforded the title product **22** as a yellow oil (93 mg, 0.23 mmol, 73%). $[\alpha]_D$ = 56.8 (*c* 1.25, $CHCl_3$, 25 ˚C); FT-IR ν_{max} (neat) 2954, 2920, 2862, 1785, 1694, 1517, 1176, 1129, 763, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.22 (5H, m, 5 x C*H*, Ar), 5.45 (1H, s, C=C*H*H), 5.42 (1H, s, C=C*H*H), 5.15 (1H, tt, *J* = 7.0, 1.5 Hz, =C*H*CH_2), 4.79-4.72 (1H, m, C*H*N), 4.29 (1H, t, *J* = 8.5 Hz, CH_2O), 4.21 (1H, dd, *J* = 8.5, 4.5 Hz, CH_2O), 3.42 (1H, dd, *J* = 13.6, 3.5, Hz, CC*H*Ph), 2.85 (1H, dd, J = 13.6, 9.5 Hz, CC*H*Ph), 2.46 (2H, t, *J* = 7.5 Hz, CH_2), 2.45 (2H, q, *J* = 7.5 Hz, CH_2), 1.73 (3H, s, CH_3), 1.66 (3H, s, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.03 (*C*ONCO), 152.85 (*C*OOCH_2), 143.93 (*C*CH_2), 135.06 (*C*, Ar), 132.61 (*C*CHCH_2), 129.39 (2 x *C*H, $Ar_{(meta)}$), 128.96 (2 x *C*H, $Ar_{(ortho)}$), 127.40 (*C*H, $Ar_{(para)}$), 123.08 (*C*HCH_2), 119.45 (*C*H_2), 66.43 (O*C*H_2), 55.30 (N*C*HCH_2), 37.70 (*C*H_2C), 33.05 (*C*H_2CCH_2), 26.53 (*C*H_2CH_2), 25.65 (*C*H_3), 17.72 (*C*H_3) ppm; LRMS (ES^+) m/z 336 (100%, $[M+Na]^+$); HRMS (ES^+) m/z Calculated: 336.1570; Found: 336.1565 ($[M+Na]^+$).

(2*R*,5*S*)-((*S*)-4-benzyloxazolidin-2-one)tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (23, major diastereoisomer);(2*S*,5*R*)-((*S*)-4-benzyloxazolidin-2-one)tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (minor diastereoisomer): Following the general procedure for the permanganate-mediated oxidative cyclization of 1,5-dienoate, diene ester **22** (81 mg, 0.26 mmol) afforded the crude as a yellow oil (80 mg, dr ~4:1, ^1H NMR). Purification by column chromatography (SiO_2 eluting with EtOAc/hexane (5 to 40%)) afforded an inseparable diasteromeric mixture of THF diols **23** along with the minor diastereoisomer as a colorless oil (46 mg, 0.126 mmol, 49%). $[\alpha]_D$ = 11.6 (*c* 3.1, $CHCl_3$, 25 ˚C); FT-IR ν_{max} (neat) 3436, 2972, 2923, 2871, 1779, 1694, 1457, 1089, 1051, 765, 732, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30-7.12 (5H, m, 5 x C*H*, Ar), 4.70-4.64 (1H, m, C*H*N), 4.24 (1H, d, *J* = 11.6 Hz, C*H*HOCO), 4.16 (1H, d, *J* = 11.6 Hz, C*H*HOCO), 4.13 (1H, dd, *J* = 9.0, 3.0 Hz Hz, C*H*, THF), 3.96_{maj} and 3.91_{min} (1H, dd *J* = 9.0, 7.0 Hz, C*H*HOH), 3.86_{maj} and 3.76_{min} (1H, d, *J* = 11.6 Hz, CH_2O), 3.23 (1H, dd, *J* = 13.5, 3.0 Hz, C*H*HC), 2.74 (1H, dd, *J* = 13.5, 9.0 Hz, C*H*HC), 2.33-2.21 (2H, m, C*HH*, THF), 1.90-1.78 (3H, m, O*H* and C*HH*, THF), 1.28_{maj} and 1.25_{min} (3H, s, CH_3), 1.11_{maj} and 1.10_{min} (3H, s, CH_3) ppm (an OH was not observed); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.47 (*C*ON), 152.30 (*C*OO), 135.13 (*C*, Ar), 129.43 (2 x *C*H, $Ar_{(meta)}$), 128.94 (2 x *C*H, $Ar_{(ortho)}$), 127.35 (*C*H, $Ar_{(para)}$), 90.23_{min} and 89.91_{maj} (*C*CH_2OH, THF), 87.24_{maj} and 87.05_{min} (*C*H, THF), 71.20 (*C*CH), 66.76_{min} and 66.55_{maj} (O*C*H_2), 56.98_{min} and 56.70_{maj} (*C*H_2OH), 37.75 (*C*HCH_2), 31.93_{min} and 31.62_{maj} (*C*H_2), 27.51_{maj} and 27.36_{min} (*C*H_2, THF), 26.40_{maj} and 26.21_{min} (*C*H_2, THF), 24.82_{maj} and 24.54_{min} (2 x *C*H_3) ppm; LRMS (ES^+) m/z 386 (100%, $[M+Na]^+$); HRMS (ES^+) m/z Calculated: 386.1574; Found: 386.1578 ($[M+Na]^+$).

(1*R*,2*S*,5*R*)-5-Methyl-2-(2-phenylpropan-2-yl)cyclohexyl-6-methyl-2-methylenehept-5-enoate (25): To a solution of 8-phenylmenthol (**(–)-24**, 303 mg, 1.30 mmol) in dry THF (40 mL) was added NaHMDS (1,03 mL, 1.0 M in THF, 1.03 mmol) at –25 ˚C. The solution was allowed to warm to –25 ˚C over 1.5 hours whereupon a solution of the diene ester **19** (418 mg, 1.30 mmol) in dry THF (2 mL) was added dropwise. The solution was then allowed to warm to room temperature. After stirring at room temperature for 30 min, the reaction was diluted in Et_2O (25 mL) and quenched with sat. aq. NH_4Cl (15 mL). The organic phase was separated, washed with sat. aq. $NaHCO_3$ (2 x 20 mL), dried (Na_2SO_4) and concentrated *in vacuo* to give a yellow oil as the crude product as a yellow oil (425 mg). Purification by column chromatography (SiO_2 eluting with 5 % EtOAc/hexane) afforded the title diene **25**, bearing chiral auxiliary 8-phenylmenthol (**(–)-24**), as a yellow oil (380 mg, 1.03 mmol, 79%). $[\alpha]_D$ = –31.1 (*c* 1.13, $CHCl_3$, 30 ˚C); FT-IR ν_{max} (neat) 2954, 2920, 2862, 1706, 1176, 1129, 763 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28-7.10 (5H, m, 5 x C*H*, Ar), 5.69 (1H, d, *J* = 1.5 Hz, C=C*H*H), 5.30 (1H, d, *J* = 1.5 Hz, C=CH*H*), 5.11-5.06 (1H, m, =C*H*CH_2), 4.92 (1H, td, *J* = 10.8, 4.3 Hz, OC*H*), 2.11-2.05 (6H, m, 3 x CH_2), 1.70 (3H, s, CH_3), 1.70-1.32 (2H, m, CH_2), 1.62 (3H, s, CH_3), 1.33 (3H, s, CH_3), 1.27 (3H, s, CH_3), 1.17-0.91 (4H, m, 2 x CH_2), 0.90 (3H, d, *J* = 6.5 Hz, CH_3CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.26 (*C*OO), 151.43 (*C*CH, Ar), 140.57 (*C*=CH_2), 131.95 ($(CH_3)_2$*C*), 127.97 (2 x *C*H, $Ar_{(meta)}$), 125.43 (2 x *C*H, $Ar_{(ortho)}$), 125.03 (*C*H, $Ar_{(para)}$), 124.38 (=*C*H_2), 123.60 (C=*C*HCH_2), 74.61 (O*C*H), 50.55 (*C*HCPh), 41.78 (*C*Ph), 39.83 (*C*H_2CH(CH_3)), 34.62 (*C*H_2C=CH_2), 31.65 (*C*HCH_3), 31.33 (*C*H_2CH_2CH), 26.93 (*C*H_2CH_2), 26.85 (2 x *C*H_3), 26.44 (*C*H_2CH), 25.65 (*C*H_3), 21.78 (*C*H_3), 17.71 (*C*H_3) ppm; LRMS (ES^+) m/z 391 (100%, $[M+Na]^+$); HRMS (ES^+) m/z Calculated: 391.2608; Found: 391.2605 ($[M+Na]^+$).

(2*S*,5*R*)-((1*R*,2*S*,5*R*)-5-Methyl-2-(2-phenylpropan-2-yl)cyclohexyl) tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (26, major diastereoisomer); (2*R*,5*S*)-((1*R*,2*S*,5*R*)-5-Methyl-2-(2-phenylpropan-2-yl)cyclohexyl) tetrahydro-2-(hydroxymethyl)-5-(2-hydroxypropan-2-yl)furan-2-carboxylate (minor diastereoisomer): Following the general procedure for the permanganate-mediated oxidative cyclization of 1,5-dienoate, diene ester **25** (375 mg, 1.02 mmol) afforded the crude as a yellow oil (411 mg, dr ~3.5:1, ^1H NMR). Purification by column chromatography (SiO_2 eluting with EtOAc/hexane (5 to 40%)) afforded an inseparable diasteromeric mixture of THF diols **26** along with the minor diastereoisomer as a yellow oil (378 mg, 0.90 mmol, 89%). $[\alpha]_D$ = –15.4 (*c* 0.915, $CHCl_3$, 28 ˚C); FT-IR ν_{max} (neat) 3390, 2957, 2923, 2871, 1721, 1457, 1089, 1051, 765, 732, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31-7.16 (5H, m, 5 x C*H*, Ar), 4.92_{min} and 4.80_{maj} (1H, td, *J* = 10.7, 4.4 Hz, OC*H*), 4.05_{maj} and 3.93_{min} (1H, t, *J* = 7.1 Hz, C*H*, THF), 3.74-3.47 (2H, m, CH_2OH), 2.73 (1H, br, O*H*), 2.34 (1H, br, O*H*), 2.05-1.88 (5H, m, C*H* and 2 x CH_2, THF), 1.49-1.26 (5H, m, C*H* and 2 x CH_2), 1.37 (3H, s, CH_3), 1.29 (3H, s, CH_3), 1.27 (3H, s, CH_3), 1.25 (3H, s, CH_3), 1.15-0.75 (2H, m, CH_2), 0.86 (3H, d, *J* = 6.5 Hz, CH_3CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.59_{maj} and 173.09_{min} (*C*OO), 150.76_{maj} and 150.51_{min} (*C*CH, Ar), 128.03 (2 x *C*H, $Ar_{(meta)}$), 125.66_{maj} and 125.58_{min} (2 x *C*H, $Ar_{(ortho)}$), 125.34 (*C*H, $Ar_{(para)}$), 87.67_{maj} and 87.35_{min} (*C*H, THF), 86.46_{maj} and 85.06_{min} (*C*CH_2OH, THF), 76.18 (O*C*H), 71.41_{maj} and 71.30_{min} (*C*OH), 65.96_{maj} and 65.59_{min} (*C*H_2OH), 50.33_{maj} and 49.96_{min} (*C*HCPh), 41.59_{maj} and 41.42_{min} (*C*Ph), 40.12_{maj} and 38.17_{min} (*C*H_2CH(CH_3)), 34.50_{maj} and 34.43_{min} (*C*H_2CH_2CH), 32.11_{maj} and 31.30_{min} (*C*H_2, THF), 28.75 (*C*HCH_3), 27.54_{maj} and 27.42_{min} (*C*H_2, THF), 27.50 (*C*H_3), 27.16 (*C*H_3), 26.09 (*C*H_2C), 25.66_{maj} and 25.47_{min} (*C*H_3), 25.17 (*C*H_3), 21.72_{maj} and 14.19_{min} (*C*H_3) ppm;

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LRMS (ES^+) m/z 441 (40%, $[M+Na]^+$), 859 (100%, $[2M+Na]^+$); HRMS (ES^+) m/z Calculated: 441.2611; Found: 441.2607 ($[M+Na]^+$).

(2*S*,5*R*)-((1*R*,2*S*,5*R*)-5-Methyl-2-(2-phenylpropan-2-yl)cyclohexyl)tetrahydro-2-(methoxytrimethylsilyl)-5-(2-trimethylsiloxy-propan-2-yl)furan-2-carboxylate (27); (2*R*,5*S*)-((1*R*,2*S*,5*R*)-5-Methyl-2-(2-phenylpropan-2-yl)cyclohexyl) tetrahydro-2- (methoxytrimethylsilyl)-5-(2-trimethylsiloxy-propan-2-yl)furan-2-carboxylate (28): To a solution of inseparable diastereomeric mixture of *cis*-THF diol **26** and it's minor diastereoisomer (378 mg, 0.90 mmol) in DMF (10 mL) was added imidazole (735 mg, 10.8 mmol), followed by the addition of Me_3SiCl (1.14 mL, 9.0 mmol) at –5 ˚C. The reaction mixture was stirred for 1 hour, during which the temperature raised to 0 ˚C. The reaction was quenched with sat. aq. NH_4Cl (3 mL) and H_2O (5 mL). The aqueous phase was extracted with Et_2O (2 x 20 mL) and combined organic phases were dried (Na_2SO_4), filtered and concentrated *in vacuo* to give the crude as a yellow oil (412 mg). Purification by column chromatography (SiO_2 eluting with CH_2Cl_2/hexane (10 to 30%)) afforded the title bis-protected THF **27** (single major diastereoisomer by ^1H NMR) as a yellow oil (315 mg, 0.56 mmol, 62%). The more polar minor diastereoisomer **28** was also isolated as a yellow oil (54 mg, 0.10 mmol, 11%). **27, major diastereoisomer**: $[\alpha]_D$ = –16.1 (*c* 1.01, $CHCl_3$, 30 ˚C); FT-IR ν_{max} (neat) 2954, 2915, 2865, 1726, 1249, 1094, 1039, 872, 836, 751, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32-7.16 (5H, m, 5 x C*H*, Ar), 4.85 (1H, td, *J* = 10.6, 4.3 Hz, OC*H*), 4.00 (1H, m, C*H*, THF), 3.83 (1H, d, *J* = 10.1 Hz, C*H*HOSi(CH_3)$_3$), 3.57 (1H, d, *J* = 10.1 Hz, CH*H*OSi(CH_3)$_3$), 2.05-1.79 (5H, m, C*H* and 2 x CH_2, THF), 1.70-1.24 (5H, m, C*H* and 2 x CH_2), 1.41 (3H, s, CH_3), 1.28 (3H, s, CH_3), 1.23 (6H, s, 2 x CH_3), 1.15-0.79 (2H, m, CH_2), 0.85 (3H, s, d, *J* = 6.5 Hz, CH_3CH), 2.59 (9H, s, COSi(CH_3)$_3$), –0.48 (9H, s, $CH_2OSi(CH_3)_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.50 (*C*OO), 150.85 (*C*CH, Ar), 127.96 (2 x *C*H, $Ar_{(meta)}$), 125.73 (2 x *C*H, $Ar_{(ortho)}$), 125.22 (*C*H, $Ar_{(para)}$), 87.80 (*C*CH_2O, THF), 87.58 (*C*H, THF), 75.87 (O*C*H), 75.00 (*C*OSi(CH_3)$_3$), 66.73 (*C*H_2OSi(CH_3)$_3$), 50.41 (*C*HCPh), 41.61 (*C*Ph), 40.31 (*C*H_2CH(CH_3)), 34.59 (*C*H_2CH_2CH), 31.50 (*C*H_2, THF), 31.29 (*C*HCH_3), 29.77 (*C*H_3), 27.94 (*C*H_3), 27.34 (*C*H_2, THF), 25.52 (*C*H_2C), 25.14 (*C*H_3), 24.27 (*C*H_3), 21.77 (*C*H_3), 2.59 (3C, COSi(*C*H_3)$_3$), –0.48 (3C, $CH_2OSi(CH_3)_3$) ppm; LRMS (ES^+) m/z 585 (65%, $[M+Na]^+$), 1148 (100%, $[2M+Na]^+$); HRMS (ES^+) m/z Calculated: 585.3407; Found: 585.3405 ($[M+Na]^+$). **28, minor diastereoisomer**: $[\alpha]_D$ = –15.5 (*c* 1.405, $CHCl_3$, 27 ˚C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.32-7.16 (5H, m, 5 x C*H*, Ar), 4.86 (1H, td, *J* = 10.6, 4.3 Hz, OC*H*), 3.89 (1H, m, C*H*, THF), 3.75 (1H, d, *J* = 10.1 Hz, C*H*HOSi(CH_3)$_3$), 3.69 (1H, d, *J* = 10.1 Hz, CH*H*OSi(CH_3)$_3$), 2.17-1.79 (5H, m, C*H* and 2 x CH_2, THF), 1.52-1.1.21 (3H, m, C*H* and CH_2), 1.44 (3H, s, CH_3), 1.31 (3H, s, CH_3), 1.23 (3H, s, CH_3), 1.21 (3H, s, CH_3), 1.03-0.79 (4H, m, CH_2), 0.84 (3H, d, *J* = 6.3 Hz, CH_3CH), 0.12 (9H, s, COSi(CH_3)$_3$), 0.10 (9H, s, $CH_2OSi(CH_3)_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.80 (*C*OO), 150.41 (*C*CH, Ar), 127.94 (2 x *C*H, $Ar_{(meta)}$), 125.92 (2 x *C*H, $Ar_{(ortho)}$), 125.29 (*C*H, $Ar_{(para)}$), 87.74 (*C*CH_2O, THF), 87.54 (*C*H, THF), 75.97 (O*C*H), 74.92 (*C*OSi(CH_3)$_3$), 66.38 (*C*H_2OSi(CH_3)$_3$), 50.60 (*C*HCPh), 41.63 (*C*Ph), 40.51 (*C*H_2CH(CH_3)), 34.55 (*C*H_2CH_2CH), 31.34 (*C*HCH_3), 31.29 (*C*H_2, THF), 30.73 ((*C*H_3), 27.82 (*C*H_3), 27.49 (*C*H_3), 25.59 (*C*H_2, THF), 25.42 (*C*H_2C), 23.34 (*C*H_3), 21.75 (*C*H_3), 2.57 (3C, COSi(*C*H_3)$_3$), –0.54 (3C, $CH_2OSi(CH_3)_3$) ppm.

General procedure for the preparation of thionoformate from *cis*-THF diols: To a solution of *cis*-THF diol (1 mmol), pyridine (10 mmol) and catalytic DMAP (0.2 mmol) in CH_2Cl_2 (0.02 M) was added phenyl chlorothionoformate (10 mmol) at 0 ˚C. The bright yellow mixture was stirred for 4 hours at room temperature, diluted with CH_2Cl_2 (50 mL) and washed with HCl (2N, 20 mL) and water (2 x 20 mL). The organic phase was dried (Na_2SO_4), filtered and concentrated *in vacuo* to afford the crude product as a bright yellow oil.

***N*-[*O*-((2*S*,5*R*)-2-Methyl *O*-phenylcarbonothioatyl) tetrahydro-5-(2-hydroxypropan-2-yl)furan-2-yl]-2-(2*R*)-camphor-10,2-sultam (31):** Following the general procedure to prepare thionoformate, diastereomerically pure *cis*-THF diol **11** (235 mg, 0.59 mmol) afforded the crude product as a yellow oil (220 mg). Purification by column chromatography (SiO_2 eluting with EtOAc/hexane (10 to 25%)) afforded the thionoformate **31** as a yellow oil (104 mg, 0.19 mmol, 33%). $[\alpha]_D$ = –37.0 (*c* 0.7, $CHCl_3$, 24 ˚C); FT-IR ν_{max} (neat) 3535, 2967, 2950, 2870, 1677, 1340, 1287, 1200, 1051 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (2H, t, *J* = 8.0 Hz, 2 x C*H*, $Ar_{(meta)}$), 7.29 (1H, m, C*H*, $Ar_{(para)}$), 7.11 (2H, t, *J* = 8.0 Hz, 2 x C*H*, $Ar_{(orth)}$), 4.98 (1H, d, *J* = 11.0 Hz, C*H*HO), 4.85 (1H, d, *J* = 11.0 Hz, CH*H*O), 4.16 (1H, t, *J* = 7.0 Hz, C*H*N), 4.10 (1H, dd, *J* = 7.5, 4.5 Hz, C*H*, THF), 3.55 (1H, d, *J* = 13.4 Hz, C*H*HSO_2), 3.46 (1H, d, *J* = 13.4 Hz, CH*H*SO_2), 2.84 (1H, br, O*H*), 2.50-1.87 (8H, m, 2 x CH_2 and 2 x CH_2, THF), 1.45-1.28 (3H, m, C*H* and CH_2), 1.28 (3H, s, CH_3), 1.23 (3H, s, CH_3), 1.18 (3H, s, CH_3), 1.01 (3H, s, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.08 (*C*=S), 175.27 (*C*ON), 153.49 (*C*CH, Ar), 129.47 (2 x *C*H, $Ar_{(meta)}$), 126.53 (*C*H, $Ar_{(para)}$), 121.93 (2 x *C*H, $Ar_{(ortho)}$), 88.89 (*C*CH_2, THF), 87.46 (*C*H, THF), 75.42 (*C*H_2O), 71.29 ((CH_3)$_2$*C*), 67.62 (*C*HN), 54.59 (*C*H_2S), 47.92 (*C*CH_2S), 47.57 (*C*(CH_3)$_2$), 45.48 (*C*HC(CH_3)$_2$), 39.24 (*C*H_2CHN), 35.30 (*C*H_2C), 33.69 (*C*H_2, THF), 27.31 (*C*H_2CH_2C), 26.16 (*C*H_2, THF), 25.98 (*C*H_3), 23.98 (*C*H_3), 21.77 (*C*H_3), 19.91 (*C*H_3) ppm; LRMS (ES^+) m/z 560 (100%, $[M+Na]^+$); HRMS (ES^+) m/z Calculated: 560.1747; Found: 560.1749 ($[M+Na]^+$).

***Rac.* *O*-((2*S*,5*R*)-2-(Methoxycarbonyl) tetrahydro-5-(2-hydroxypropan-2-yl)furan-2-yl)methyl *O*-phenyl carbonothioate (32):** Following the general procedure for the preparation of thionoformate, racemic *cis*-THF diol **12** (145 mg, 0.66 mmol) afforded the crude product as a yellow oil (215 mg). Purification by column chromatography (SiO_2 eluting with CH_2Cl_2/hexane (40 to 90%)) afforded the thionoformate **32** as a yellow oil (164 mg, 0.46 mmol, 70%). FT-IR ν_{max} (neat) 3383, 2971, 2877,1728, 1295, 1201, 1042, 772, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45-7.35 (2H, m, 2 x C*H*, $Ar_{(meta)}$), 7.27 (1H, m, C*H*, $Ar_{(para)}$), 7.10-7.06 (2H, m, 2 x C*H*, $Ar_{(ortho)}$), 4.84 (1H, d, *J* = 11.3 Hz, C*H*HO), 4.79 (1H, d, *J* = 11.3 Hz, CH*H*O), 4.12 (1H, t, *J* = 7.3 Hz, C*H*, THF), 3.78 (3H, s, OCH_3), 2.29-2.12 (3H, m, O*H* and CH_2, THF), 2.07-1.89 (2H, m, CH_2, THF), 1.29 (3H, s, CH_3), 1.15 (3H, s, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.98 (*C*=S), 172.73 (*C*OO), 153.31 (*C*CH, Ar), 129.45 (2 x *C*H, $Ar_{(meta)}$), 126.55 (*C*H, $Ar_{(para)}$), 121.75 (2 x *C*H, $Ar_{(ortho)}$), 88.23 (*C*H, THF), 84.53 (*C*CH_2O, THF), 75.29 (*C*H_2O), 71.04 ((CH_3)$_2$*C*), 52.57 (OCH_3), 32.84 (*C*H_2, THF), 27.31 (*C*H_2, THF), 25.61 (*C*H_3), 24.66 (**C**H_3) ppm; LRMS (ES^+) m/z 377 (100%, $[M+Na]^+$); HRMS (ES^+) m/z Calculated: 377.1029; Found: 377.1026 ($[M+Na]^+$).

***Rac.*(2*S*,5*R*)-Methyl tetrahydro-2-(hydroxymethyl)-5-(2-trimethylsiloxy-2-yl)furan-2-carboxylate (33):** To a stirred solution of racemic THF diol **12** (397 mg, 1.68 mmol) and imidazole (1.14 g, 16.8 mmol) in DMF (3 mL) was added Me_3SiCl (0.65 mL, 5.04 mmol) at 0 ˚C. The mixture was stirred at this temperature for 15 min. After this, anhydrous MeOH (2 mL) was added in the reaction mixture followed by the addition of K_2CO_3 (2 mg in 1 mL of anhydrous MeOH). The reaction mixture was stirred at 0 ˚C for 1.5 hours, whereupon it was quenched by acetic acid (5% aq., 5 mL). The organic phase was separated and the aqueous phase was re-

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extracted with Et_2O (2 x 20 mL). The combined organic phases were dried (Na_2SO_4), concentrated *in vacuo* to afford the crude as a pale yellow oil (443 mg). Purification by column chromatography (SiO_2 eluting with with EtOAc/hexane (10 to 20%)) afforded the title racemic carbinol **33** as a pale yellow oil (428 mg, 1.47 mmol, 88%). FT-IR ν_{max} (neat) 3465, 2950, 2890, 2868, 1732, 1242, 1169, 1037, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.96 (1H, t, *J* = 7.3 Hz, C*H*, THF), 3.84 (1H, dd, *J* = 11.3, 4.0 Hz, C*H*HOH), 3.74 (3H, s, OCH_3), 3.71 (1H, dd, *J* = 11.3, 9.0 Hz, CH*H*OH), 2.91 (1H, dd, *J* = 9.0, 4.0 Hz, O*H*), 2.27-1.86 (4H, m, 2 x CH_2), 1.37 (3H, s, CH_3), 1.18 (3H, s, CH_3), 0.15 (9H, s, Si,(CH_3)$_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.48 (*C*OO), 88.56 (*C*CH_2OH, THF), 86.81 (*C*H, THF), 75.18 ((CH$_3$)$_2$*C*), 66.14 (*C*H_2OH), 52.16 (OCH_3), 32.41 (*C*H_2, THF), 27.37 (*C*H_2, THF), 26.97 (*C*H_3), 26.30 (*C*H_3), 2.33 (3C, Si(*C*H_3)$_3$) ppm; LRMS (ES^+) m/z 313 (100%, $[M+Na]^+$); HRMS (ES^+) m/z Calculated: 313.1442; Found: 313.1442 ($[M+Na]^+$).

General procedure for the preparation of thionocarbamate: To a solution of mono-protected THF carbinol (1.0 mmol) in CH_2Cl_2 (0.05 M) was added DMAP (0.30 mmol) and thiocarbonyl diimidazole (3.0 mmol). The resultant bright yellow solution was stirred at room temperature for 8 hours. The reaction was concentrated *in vacuo* to give the crude product.

***Rac.*(2*S*,5*R*)-Methyl tetrahydro-2-(*O*-methoxy-1*H*-imidazol-1-carbothioyl)-5- (2-trimethylsiloxy-2-yl) furan-2-carboxylate (34):** Following the general method for the preparation of thionocarbamate, racemic mono-protected THF carbinol **33** (320 mg, 1.10 mmol) afforded crude as a yellow oil (445 mg). Purification by column chromatography (SiO_2 eluting with EtOAc/hexane (10 to 20%)) afforded the title racemic thionocarbamate **34** as a yellow oil (409 mg, 1.02 mmol, 89%). FT-IR ν_{max} (neat) 2965, 2953, 2840, 1737, 1390, 1330, 1286, 1246, 1173, 1037, 955, 839 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.30 (1H, s, NC*H*N), 7.60 (1H, t, *J* = 1.4 Hz, C*H*N), 7.03 (1H, dd, *J* = 1.4, 0.8 Hz, NC*H*CH), 4.91 (1H, d, *J* = 10.8 Hz, C*H*HO), 4.73 (1H, d, *J* = 10.8 Hz, CH*H*O), 4.04 (1H, m, C*H*, THF), 3.79 (3H, s, OCH_3), 2.28-1.93 (4H, m, 2 x CH_2, THF), 1.27 (3H, s, CH_3), 1.19 (3H, s, CH_3), 0.12 (9H, s, Si,(CH_3)$_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.69 (*C*=S), 173.01 (*C*OO), 136.87 (N*C*HN), 130.86 (N*C*HCH), 117.88 (*C*HN), 89.14 (*C*H, THF), 84.76 (*C*CH_2O, THF), 75.84 (*C*H_2OCS), 74.80 ((CH$_3$)$_2$*C*), 52.68 (OCH_3), 33.12 (CH_2, THF), 27.26 (CH_2, THF), 26.18 (CH_3), 25.47 (CH_3), 2.48 (3C, Si(CH_3)$_3$) ppm; LRMS (ES^+) m/z 423 (100%, $[M+Na]^+$); HRMS (ES^+) m/z Calculated: 423.1386; Found: 423.1392 ($[M+Na]^+$).

***N*-[(2*S*,5*R*)-Tetrahydro-5-(2-hydroxypropan-2-yl)-2-methylfuranoyl]-2-(2*R*)-camphor-10,2-sultam (35):** To a solution of thionoformate **31** (45 mg, 0.08 mmol) in toluene (2.0 mL) was added AIBN (7 mg, 0.04 mmol), followed by dropwise addition of Bu_3SnH (67 μL, 0.24 mmol). The resultant solution was heated to reflux for 4 hours. The reaction was concentrated in *vacuo* to afford crude product as a yellow oil (25 mg). Purification by column chromatography (SiO_2 eluting with CH_2Cl_2/hexane (10 to 30%)) afforded the *trans*-THF product **35** as a yellow oil (19 mg, 0.05 mmol, 65%). $[\alpha]_D$ = –32.97 (*c* 0.37, $CHCl_3$, 26 ˚C); FT-IR ν_{max} (neat) 3516, 2962, 2960, 2879, 1677, 1456, 1335, 1163, 1134, 1062, 912, 728 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.08 (1H, m, C*H*N), 4.00 (1H, t, *J* = 7.0 Hz, C*H*, THF), 3.51 (1H, d, *J* = 13.4 Hz, C*H*HSO$_2$), 3.40 (1H, d, *J* = 13.4 Hz, CH*H*SO$_2$), 2.75 (1H, br, O*H*), 2.32 (1H, dd, *J* = 12.6, 8.0 Hz, C*H*H, THF), 2.10-1.69 (7H, m, 2 x CH_2, C*H*H and CH_2, THF), 1.53 (3H, s, CH_3), 1.42-1.25 (3H, m, C*H*H and CH_2), 1.19 (3H, s, CH_3), 1.21 (3H, s, CH_3), 1.13 (3H, s, CH_3), 0.99 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.45 (*C*ON), 87.77 (*C*H, THF), 87.46 (*C*CH_3, THF), 71.29 ((CH$_3$)$_2$*C*), 67.68 (NC*H*), 54.59 (*C*H_2S), 47.80 (*C*(CH$_3$)$_2$), 47.48 (*C*CH_2S), 45.58 (*C*HC(CH$_3$)$_2$), 39.47 (*C*H_2CHN), 39.34 (*C*H_2C), 33.82 (*C*H_2, THF), 26.80 (*C*H_3), 26.13 (*C*H_2, THF), 25.86 (*C*H_2CH$_2$C), 24.46 (*C*H_3), 23.51 (*C*H_3), 21.88 (*C*H_3), 19.90 (*C*H_3) ppm; LRMS (ES^+) m/z 408 (100%, $[M+Na]^+$); HRMS (ES^+) m/z Calculated: 408.1815; Found: 408.1808 ($[M+Na]^+$).

(2*S*,5*R*)-((1*R*,2*S*,5*R*)-5-Methyl-2-(2-phenylpropan-2-yl)cyclohexyl)tetrahydro-2-(hydroxymethyl)-5-(2-trimethylsiloxy-propan-2-yl)furan-2-carboxylate (36): To a solution of bis-protected THF **27** (307 mg, 0.55 mmol) in MeOH (10 mL) was added dried powdered K_2CO_3 (83 mg) at –10 ˚C. The resultant milky mixture was stirred for 2.5 hours, while maintaining the temperature. The reaction was quenched by adding H_2O (2 mL) and MeOH was evaporated. The resultant residue was partitioned between Et_2O (30 mL) and H_2O (15 mL), and the organic phase was separated. The aqueous phase was re-extracted with Et_2O (2 x 30 mL), and the combined organic phases were dried (Na_2SO_4), filtered and concentrated *in vacuo* to give the crude as a yellow oil (270 mg). Purification by column chromatography (SiO_2 eluting with CH_2Cl_2/hexane (60 to 100%)) afforded the title mono-TMS protected THF carbinol **36** as a pale yellow oil (262 mg, 0.53 mmol, 98%). **[**α$]_D$ = –7.34 (*c* 1.07, $CHCl_3$, 26 ˚C); FT-IR ν_{max} (neat) 3478, 2955, 2922, 2871, 1725, 1251, 1172, 1050, 841, 761, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28-7.13 (5H, m, 5 x C*H*, Ar), 4.75 (1H, td, *J* = 10.6, 4.3 Hz, OC*H*), 3.94 (1H, m, C*H*, THF), 3.68 (1H, dd, *J* = 11.3, 3.7 Hz, C*H*HOH), 3.53 (1H, dd, *J* = 11.3, 9.4 Hz, CH*H*OH), 2.89 (1H, dd, *J* = 9.4, 3.7 Hz, O*H*), 2.15-1.84 (5H, m, C*H* and 2 x CH_2, THF), 1.56-1.20 (5H, m, C*H* and 2 x CH_2), 1.36 (3H, s, CH_3), 1.33 (3H, s, CH_3), 1.27 (3H, s, CH_3), 1.17 (3H, s, CH_3), 1.00-0.74 (2H, m, CH_2), 0.84 (3H, s, d, *J* = 6.4 Hz, CH_3CH), 0.14 (9H, s, COSi(CH_3)$_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.49 (*C*OO), 150.39 (*C*CH, Ar), 128.01 (2 x *C*H, Ar$_{(meta)}$), 125.68 (2 x *C*H, Ar$_{(ortho)}$), 125.37 (*C*H, Ar$_{(para)}$), 88.59 (*C*CH_2OH, THF), 86.13 (*C*H, THF), 75.91 (O*C*H), 75.02 (*C*OSi(CH$_3$)$_3$), 65.92 (*C*H_2OH), 50.42 (*C*HCPh), 41.41 (*C*Ph), 40.19 (*C*H_2CH(CH$_3$)), 34.53 (*C*H_2CH$_2$CH), 32.55 (*C*H_2, THF), 31.28 (*C*HCH$_3$), 29.32 (*C*H_3), 27.37 (*C*H_3), 27.23 (*C*H_2, THF), 27.07 (*C*H_2C), 26.45 (*C*H_3), 24.93 (*C*H_3), 21.73 (*C*H_3), 2.35 (3C, COSi(*C*H_3)$_3$) ppm; LRMS (ES^+) m/z 513 (100%, $[M+Na]^+$); HRMS (ES^+) m/z Calculated: 513.3007; Found: 513.3020 ($[M+Na]^+$).

(2*S*,5*R*)-((1*R*,2*S*,5*R*)-5-Methyl-2-(2-phenylpropan-2-yl)cyclohexyl)tetrahydro-2-(*O*-methoxy-1*H*-imidazol-1-carbothioyl)-5-(2-trimethylsiloxypropan-2-yl)furan-2-carboxylate (37): Following the general procedure for the preparation of thionocarbamate, mono-protected THF carbinol **36** (260 mg, 0.53 mmol) afforded crude as a yellow oil (310 mg). Purification by column chromatography (SiO_2 eluting with EtOAc/hexane (5 to 25%)) afforded the title thiocarbonyl imidazolide **37** as a yellow oil (297 mg, 0.49 mmol, 93%). $[\alpha]_D$ = +7.85 (*c* 1.21, $CHCl_3$, 27 ˚C); FT-IR ν_{max} (neat) 2955, 2915, 2865, 1730, 1463, 1391, 1332, 1287, 1248, 1176, 1037, 955, 840, 764, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.31 (1H, t, *J* = 1.0 Hz, NC*H*N), 7.60 (1H, t, *J* = 1.0 Hz, C*H*N), 7.30-7.12 (5H, m, 5 x C*H*, Ar), 6.98 (1H, dd, *J* = 1.6, 1.0 Hz, NC*H*CH), 4.82 (1H, td, *J* = 10.6, 4.3 Hz, OC*H*), 4.71 (1H, d, *J* = 10.8 Hz, C*H*HO), 4.39 (1H, d, *J* = 10.8 Hz, CH*H*O), 4.04 (1H, t, *J* = 6.5 Hz, C*H*, THF), 2.04-1.73 (5H, m, C*H* and 2 x CH_2, THF), 1.55-1.36 (5H, m, C*H* and 2 x CH_2), 1.34 (3H, s, CH_3), 1.21 (3H, s, CH_3), 1.20 (3H, s, CH_3), 1.19 (3H, s, CH_3), 1.03-0.69 (2H, m, CH_2), 0.73 (3H, d, *J* = 6.4 Hz, CH_3CH), 0.07 (9H, s, COSi(CH_3)$_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.78 (*C*=S), 171.89 (*C*OO), 150.84 (*C*CH, Ar), 137.01 (N*C*HN), 130.72 (N*C*HCH), 128.14 (2 x *C*H, Ar$_{(meta)}$), 125.45 (2 x *C*H, Ar$_{(ortho)}$), 125.32 (*C*H, Ar$_{(para)}$), 117.88 (*C*HN), 89.17 (*C*H, THF),

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84.45 (CCH_2OH, THF), 76.61 (OCH), 75.87 (CH_2OCS), 74.64 ($COSi(CH_3)_3$), 49.88 (CHCPh), 41.40 (CPh), 39.99 ($CH_2CH(CH_3)$), 34.33 (CH_2CH_2CH), 32.77 (CH_2, THF), 31.17 ($CHCH_3$), 27.92 (CH_3), 27.40 (CH_3), 26.99 (CH_2, THF), 25.98 (CH_3), 25.92 (CH_2C), 25.59 (CH_3), 21.53 (CH_3), 2.46 (3C, $COSi(CH_3)_3$) ppm; LRMS (ES^+) m/z 623 (80%, $[M+Na]^+$), 601 (550%, $[M+H]^+$); HRMS (ES^+) m/z Calculated: 601.3126; Found: 601.3111 ($[M+H]^+$).

(2*R*,5*R*)-((1*R*,2*S*,5*R*)-5-Methyl-2-(2-phenylpropan-2-yl)cyclohexyl) tetrahydro-2-methyl-5-(2-trimethylsiloxypropan-2-yl)furan-2-carboxylate (38): To a solution of thionocarbamate **37** (292 mg, 0.49 mmol) in toluene (20 mL) was added AIBN (20.1 mg, 0.13 mmol), followed by dropwise addition of $(Me_3Si)_3SiH$ (0.6 mL, 1.96 mmol). The resultant solution was stirred at 85 ˚C for 75 min, then concentrated *in vacuo* to afford crude as a yellow oil (235 mg). Purification by column chromatography (SiO_2 eluting with EtOAc/hexane (5 to 15%)) afforded the title THF adduct **38** as a yellow oil (196 mg, 0.42 mmol, 85%). $[\alpha]_D = -18.03$ (*c* 1.37, $CHCl_3$, 28 ˚C); FT-IR ν_{max} (neat) 2954, 2918, 2865, 1725, 1456, 1371, 1248, 1169, 1092, 1041, 837, 762, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28-7.14 (5H, m, 5 x C*H*, Ar), 4.76 (1H, td, *J* = 10.7, 4.3 Hz, OC*H*), 3.90 (1H, dd, *J* = 7.5, 6.0 Hz, C*H*, THF), 1.99-1.79 (5H, m, C*H* and 2 x CH_2, THF), 1.69-1.36 (5H, m, C*H* and 2 x CH_2), 1.35 (3H, s, CH_3), 1.33 (3H, s, CH_3), 1.26 (3H, s, CH_3), 1.20 (3H, s, CH_3), 1.18 (3H, s, CH_3),1.00-0.70 (2H, m, CH_2), 0.83 (3H, d, *J* = 6.4 Hz, CH_3CH), 0.10 (9H, s, $COSi(CH_3)_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.10 (*C*OO), 150.59 (*C*CH, Ar), 127.98 (2 x *C*H, $Ar_{(meta)}$), 125.71 (2 x *C*H, $Ar_{(ortho)}$), 125.29 (*C*H, $Ar_{(para)}$), 87.45 (*C*H, THF), 83.96 (CCH_3 THF), 75.63 (OCH), 74.77 ($COSi(CH_3)_3$), 50.41 (CHCPh), 41.52 (CPh), 40.27 ($CH_2CH(CH_3)$), 36.56 (CH_2CH_2CH), 34.56 (CH_2, THF), 31.29 ($CHCH_3$), 29.65 (CH_3), 27.86 (CH_3), 27.31 (CH_2, THF), 26.11 (CH_2C), 25.28 (CH_3), 24.53 (CH_3), 23.96 (CH_3), 21.76 (CH_3), 2.57 (3C, $COSi(CH_3)_3$) ppm; LRMS (ES^+) m/z 497 (100%, $[M+Na]^+$); HRMS (ES^+) m/z Calculated: 497.3058; Found: 497.3058 ($[M+Na]^+$).

(2*R*,5*R*)-Tetrahydro-2-methyl-5-(2-trimethylsilyl-oxy-propan-2-yl)furan-2-carbaldehyde (39): To a solution of mono-protected THF compound **38** (189 mg, 0.40 mmol) in CH_2Cl_2 (6 mL) was added DIBAL-H (1.2 mL, 1.2 mmol) at –78 ˚C and the resultant solution was stirred for 4 hours, while keeping the temperature at –78 ˚C. The reaction was quenched at –78 ˚C by adding sat. aq. NH_4Cl (5 mL) and the temperature was allowed to rise to room temperature. Rochelle's salt (5 mL, aq. sat.) was added and the solution was stirred for 30 min at room temperature. The solution was diluted with CH_2Cl_2 (10 mL) and the organic phase was separated. The aqueous phase was re-extracted with CH_2Cl_2 (2 x 10 mL), and the combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give the crude as a yellow oil (175 mg). Purification by column chromatography (SiO_2 eluting with EtOAc/hexane (5 to 15%)) afforded the title aldehyde **39** as a pale yellow oil (83 mg, 0.34 mmol, 85%), followed by the commercially available pure chiral auxiliary (–)-**24** as a yellow oil (86 mg, 0.37 mmol, 92%). **39**: $[\alpha]_D = -1.46$ (*c* 1.265, $CHCl_3$, 29 ˚C); FT-IR ν_{max} (neat) 2975, 2888, 2786, 1736, 1249, 1174, 1061, 1041, 839, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.58 (1H, s, C*H*O), 3.81 (1H, t, *J* = 7.0 Hz, C*H*, THF), 2.09 (1H, ddd, *J* = 12.0, 8.0, 6.8 Hz, C*H*, THF), 1.96 (1H, ddt, *J* = 12.0, 8.0, 6.8 Hz, C*H*, THF), 1.83 (1H, m, C*H*, THF), 1.68 (1H, ddd, *J* = 12.0, 8.0, 6.8 Hz, C*H*, THF), 1.30 (3H, s, CH_3), 1.26 (3H, s, CH_3), 1.20 (3H, s, CH_3), 0.12 (9H, s, $COSi(CH_3)_3$) ppm; ^{13}C DEPT135 NMR (100 MHz, $CDCl_3$) δ 204.06 (*C*HO), 88.60 (*C*H, THF), 33.27 (CH_2, THF), 27.92 (CH_3), 26.58 (CH_2, THF), 26.18 (CH_3), 21.35 (CH_3), 2.95 (3C, $COSi(CH_3)_3$) ppm; LRMS (ES^+) m/z 267 (100%, $[M+Na]^+$); HRMS (ES^+) m/z Calculated: 267.1387; Found: 267.1385 ($[M+Na]^+$).

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