A Highly Efficient Procedure for Ruthenium Tetroxide Catalyzed Oxidative Cyclizations of 1,5-Dienes

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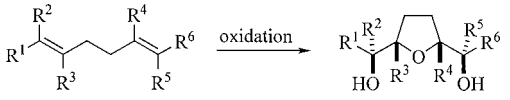
Dedicated to Professor H. M. R. Hoffmann on the occasion of his 70th birthday

Keywords: Oxidative cyclization / Tetrahydrofurans / Ruthenium / Oxidation / Catalysis

We report a highly efficient procedure for the oxidative cyclization of 1,5-dienes, which generally allows for high yields and selectivities. A solid-supported terminal oxidant and a finely tuned solvent mixture have both been identified as critical factors for this high efficiency. As little as 0.2 mol-% ruthenium(III) chloride as a pre-catalyst for the ruthenium tetroxide generated in situ is required to accomplish oxidative cyclization. This exceptionally low catalyst loading, high diastereoselectivity, mild reaction conditions, and a simple workup procedure are key features of this process.

Introduction

2,5-Disubstituted tetrahydrofurans (THFs) are common structural features in a variety of biologically important classes of natural products. Among these are the polyether ionophore antibiotics[1,2] and the annonaceous acetogenins.[3,4] A number of methods for the synthesis of 2,5-disubstituted THFs have been reported;[5] in principle, the single-step formation of THF derivatives by oxidative cyclization of 1,5-dienes can be regarded as the most efficient approach (Scheme 1).[6] Such unique and mechanistically intriguing oxidative cyclizations have been reported with the use of stoichiometric amounts of permanganate,[7,8] or in a catalytic fashion with osmium tetroxide[9] or ruthenium tetroxide.[10]



Scheme 1. Oxidative cyclization of 1,5-dienes.

Yields and selectivities are often low, however, due to unwanted overoxidation processes (including C–C-bond cleavage) and also presumably due to isolation problems attributable to the high water solubility of the diol products. Donohoe and co-workers recently presented a procedure affording high yields (generally in the 72–95% range) for an oxidative cyclization of 1,5-dienes.[9c] In their work, 5 mol-% osmium tetroxide was used as a catalyst. High yields were possible through the addition of a Brønsted acid, such as an excess of trifluoroacetic acid.

As part of our interest in polyether compounds, our research is focused on ruthenium tetroxide as a catalyst for oxidative cyclization. Ruthenium tetroxide is a powerful oxidizing agent classically used for oxidative C–C-bond cleavage.[11,12] More recently, it has also been applied for selective C–H oxidations,[13] dihydroxylations,[14] and keto hydroxylations.[15]

In 1981 Sharpless et al. reported on the unexpected finding of an oxidative cyclization of geranyl acetate under conditions usually applied for the Sharpless oxidation (the ruthenium tetroxide mediated oxidative scission of olefins to furnish carboxylic acids).[10a] This result – which parallels that of the previously known permanganate promoted process – was surprising, since the high oxidative power of ruthenium(VIII) [and ruthenium(VI)] usually results in a quick C–C-bond cleavage. Sica et al.[10b] and Piccialli et al.,[10c,10d] building on this seminal finding by Sharpless' group, recently investigated this transformation in more detail, and found that a simple change of solvents resulted in improved yields and product distribution. Representative results from these previous studies are summarized in Scheme 2.

Here we report on a greatly improved procedure, generally affording high yields and selectivities, for ruthenium tetroxide-mediated oxidative cyclizations. Key features of this process are unprecedentedly low catalyst loading and a simple workup procedure.

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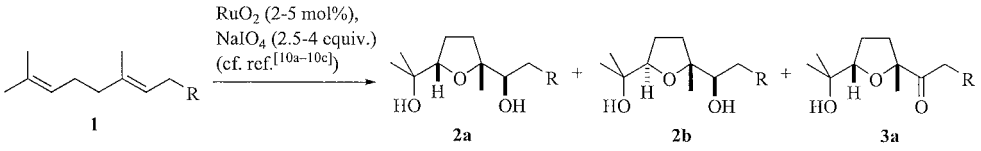


Isolated yields of **2a**, **2b** and **3a**:

Sharpless conditions (ref.[10a]):	39%	12%	12%
Sica conditions (ref.[10b]):	50%	19%	18%
Piccialli conditions (ref.[10c]):	62%	9%	5%

Scheme 2. Representative results of previous procedures for the ruthenium tetroxide mediated oxidative cyclization of geraniol derivatives.

Results and Discussion

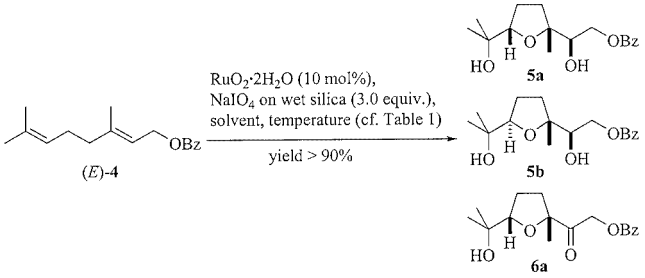
Initial Experiments and Investigations into Reaction Medium

Our initial experiments focused on avoiding water as a cosolvent. Water usually has to be added to solubilize sodium periodate, the terminal oxidizing agent, and we reasoned that product isolation should be significantly facilitated – and yields were expected to be improved at the same time – by avoiding this cosolvent. We therefore decided to look for a solid-supported terminal oxidant.[16] In our initial experiments, ruthenium dioxide (10 mol-%) was chosen as a source for ruthenium tetroxide and geranyl benzoate [(*E*)-**4**] (Scheme 3) as a substrate. We eventually found that use of sodium periodate on wet silica[17] as a solid-supported terminal oxidant resulted in a smooth conversion of the diene substrate. The starting material was almost quantitatively converted into the desired cyclization product (yield >90%). This product, however, was isolated as a mixture of diastereoisomers accompanied by some overoxidation product (Entry 1, Table 1).

We next investigated the influence of solvent and temperature on diastereoselectivity and amount of unwanted overoxidation product (ketone **6a**), and the results are summarized in Table 1. Whereas the reaction temperature had little effect on diastereoselectivity and product distribution, a profound solvent effect was observed. Nonpolar chlorinated solvents such as dichloromethane (DCM) or chloroform yielded only small quantities of overoxidation product (ketone **6a**) but suffered from low diastereoselectivity (Entries 1 and 2, Table 1). On the other hand, more polar, weakly coordinating solvents such as acetone or tetrahydrofuran gave high diastereoselection but slightly diminished selectivity with regard to the overoxidation process (Entries 8–10, Table 1). Irrespective of solvent, yields were generally high (>90%). Both the product distribution and the diastereoselectivity were slightly improved on lowering the reaction temperature from room temperature to 0 °C.

On examining solvent mixtures, we were pleased to find that the use of a mixture of THF and DCM gave high selectivities, in terms both of the ratio between the desired diol product and ketone (ratio **5/6** = 20:1) and of the diastereoselectivity (ratio **5a/5b** > 95:5). The best results were obtained with the use of 10 vol-% DCM in THF at 0 °C (Entry 15, Table 1).

Table 1. Effect of solvent and temperature on RuO_4-mediated oxidative cyclization of geranyl benzoate [(*E*)-**4**].



Entry	Solvent	Temperature [°C]	Ratio[a] **5/6**	*dr*[a]
1	DCM	0	19:1	60:40
2	$CHCl_3$	25	16:1	63:37
3	pentane	25	5.5:1	56:44
4	EtOAc	25	3:1	77:23
5	MeCN	25	7:1	81:19
6	MeCN	0	9:1	83:17
7	EtCN	0	4:1	75:25
8	acetone	0	4:1	93:7
9	THF	25	3:1	95:5
10	THF	0	6:1	>95:5
11	Et_2O	25	9:1	54:46
12	*t*BuOH	25	3:1	78:22
13	acetone/$CHCl_3$[b]	25	9:1	80:20
14	THF/DCM[b]	0	8:1	52:48
15	THF/DCM[c]	0	20:1	>95:5

[a] Product ratio and diastereoselectivity were determined by ^{1}H NMR or GC (*dr* diastereomeric ratio; i.e. ratio of **5a/5b**). [b] A 1:1 mixture of solvents was used. [c] 10 vol-% of DCM in THF were used.

It is noteworthy that ether solvents such as THF or diethyl ether are uncommon solvents for ruthenium tetroxide mediated reactions. In fact, ethers are known to be oxidized to the corresponding esters by ruthenium tetroxide,[11,12] so diethyl ether has even been used to quench such oxidation reactions. Various control experiments revealed that such unwanted C–H oxidations do not occur with the procedure presented here (vide infra). A recent study by Sheldon et al. shows that ruthenium tetroxide catalyzed ether oxidations are highly pH-dependent and only occur in basic media, with an optimal pH of 9–9.5.[18] It can therefore be concluded that the stability of ethers under our reaction conditions is attributable to the slightly acidic reaction medium.[19]

Investigations into Pre-catalyst and Catalyst Loading

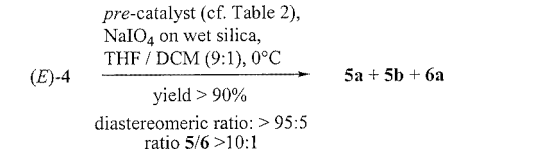
For catalytic oxidative cyclizations, 2–5 mol-% of catalyst are usually used. Unlike in osmium tetroxide mediated transformations, where osmium tetroxide itself is used as the source of catalyst, in ruthenium tetroxide catalyzed oxidative cyclizations the choice of pre-catalyst may play a crucial role. A range of ruthenium compounds are insoluble in organic solvents, so the formation of the catalytically active ruthenium tetroxide from these derivatives is slow and often incomplete. When, for instance, ruthenium dioxide is used, there is usually a solid black residue visible throughout the whole course of the reaction, clearly indicating only partial conversion of ruthenium dioxide into ruthenium tetroxide. With soluble ruthenium pre-catalysts, on the other hand, tight binding ligands may inhibit or at least decelerate the oxidation to ruthenium tetroxide.[20] Both effects – low solubility and tight binding ligands – may result in a reduced amount of active catalyst (i.e., ruthenium tetroxide). In view of these considerations and driven by the search for a more reactive catalyst, we investigated a set of pre-catalysts. As a substrate we chose diene (*E*)-**4**, whilst 2.2 equiv. of sodium periodate on wet silica were used as terminal oxidizing agent.

Interestingly, all pre-catalysts investigated gave the cyclized product in good yield (generally >90%). We observed, however, a considerable influence on reaction rates. After screening of various pre-catalysts it became clear that ruthenium(III) chloride and TPAP[21] (tetrapropylammonium perruthenate) represent the most reactive catalyst precursors (Table 2). Pleasingly, it proved possible to reduce the catalyst loading to a remarkable 0.2 mol-% with these ruthenium sources, without loss in selectivity or yield and with short reaction times (Entries 2–4 and 8, Table 2). Other pre-catalysts were less effective (Table 2). As would be expected, strong binding ligands such as phosphane ligands or the acetylacetonato (acac) ligand gave significantly reduced reaction rates (Entries 5 and 6, Table 2). In the latter case, unaltered $Ru(acac)_3$ could be detected throughout the course of the experiment. It is worth mentioning that the reaction with TPAP as a pre-catalyst (Entry 8, Table 2) was not catalyzed, or at least not as efficiently catalyzed, by the perruthenate ion under these conditions.[22] No conversion was detectable when stoichiometric amounts of TPAP were employed in the absence of any cooxidant (Entry 9, Table 2).

Taken together, the best results were achieved with use of either ruthenium(III) chloride or TPAP as pre-catalyst. Amazingly, both these precursors are as active as the unpleasant to handle ruthenium tetroxide itself (Entry 10, Table 2). Both of these pre-catalysts are commercially available, easy to handle, and soluble in a range of solvents, including organic solvents. The preparation of stock solutions is facile and such solutions can conveniently be kept for months at room temperature without any loss of activity.[23] No special precautions to avoid moisture or air have to be taken.

Under optimized conditions, use of as little as 0.2 mol-% ruthenium(III) chloride (added as a 0.01 M stock solution in THF or water[23]) in the presence of 2.2 equiv of sodium periodate on wet silica was sufficient to achieve complete conversion of geranyl benzoate [(*E*)-**4**] at 0 °C within 90 min.

Table 2. Study on the effect of pre-catalyst.



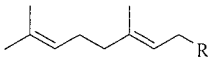
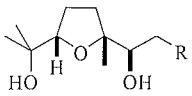
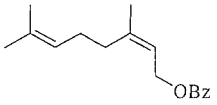
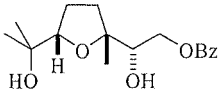
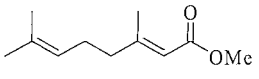
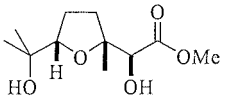
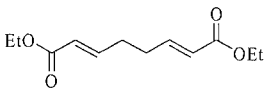
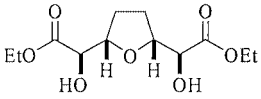
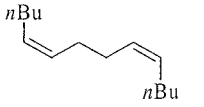
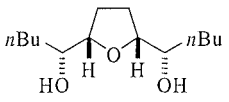
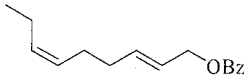
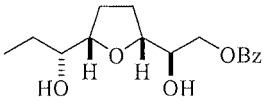
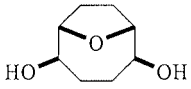
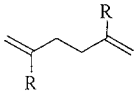
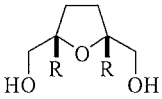
Entry	Pre-catalyst	Catalyst loading [mol-%]	Temp. [°C]	Reaction time[g] [min]
1	$RuO_2 \cdot 2H_2O$[a]	10	0	90
2	$RuCl_3$[b]	10	0	30
3	$RuCl_3$[b]	1.0	0	45
4	$RuCl_3$[b]	0.2	0	90
5	$Ru(acac)_3$[a,c]	10	25	480
6	$Ru(PPh_3)_2Cl_2$[b]	0.2	0	240
7	Ru/C[a]	0.2	25	2880
8	TPAP[d]	0.2	0	80
9	TPAP[a,e]	100	0	n.r.
10	RuO_4[f]	0.2	0	95

[a] Added as a solid. [b] 0.01 M stock solution in THF was used. [c] Reaction carried out in DCM. [d] 0.01 M stock solution in acetone was used. [e] No other oxidant added. [f] 0.042 M stock solution in water was used. [g] Reactions were run until complete consumption of the starting material was detected (as judged by TLC). (n.r. no reaction).

Substrate Scope

We next applied the optimized procedure to a set of differently substituted 1,5-dienes. As summarized in Table 3, a broad range of substrates were smoothly converted into the corresponding 2,5-hydroxymethyl-THFs in high yields and with good selectivity. A wide range of functional groups such as esters, amides, and ethers are stable under these mild reaction conditions (Table 3). Moreover, typical protecting groups, including ester, ether, and silyl ether protecting groups, are compatible. It is worth noting that even a benzyl ether remains intact (Entry 4, Table 3). No indication of the formation of the corresponding C–H-oxidation product (i.e., the corresponding benzoate) or products derived from aromatic degradation was found (vide supra). Irrespective of the double bond substitution pattern, good to excellent yields of THF product were obtained. Mono-, di-, and trisubstituted double bonds reacted equally well. Moreover, the electronic properties of the participating double bonds could be varied, ranging from simple alkyl-substituted to electron-deficient alkenes. Generally none, or only a trace amount, of the undesired overoxidation product was detected. Only in the case of (*Z*)-configured olefins was a significant amount of ketone formed (Entries 7, 10, and 12, Table 3). The relative stereochemistry between the ether oxygen and the flanking hydroxy groups is simply

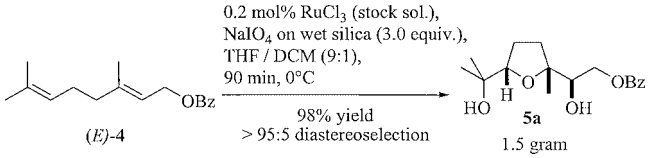
Table 3. Oxidative cyclization of 1,5-dienes under optimized conditions.

Entry	Substrate	Product		Yield [%][a]	d.r.[b]
1			**5a**; R = OBz	95	> 95:5
2			**7**, R = OTBDPS	92	> 95:5
3			**8**; R = OTBDMS	60	> 95:5
4			**9**; R = OBn	98	90:10
5			**10**; R = NHBz	99	80:20
6			**11**; R = NHTs	75	> 95:5
7			**5c** (**6a**)	74 (98)[a]	> 95:5
8			**12**	75	> 95:5
9			**13**	72	> 95:5
10			**14** (**15**)	23 (75)[a]	> 95:5
11			**16**	89	> 95:5
12			**17** (**18**)	55 (72)[a]	> 95:5
13			**19**; R = Me	74	> 95:5
14			**20**; R = H	93	> 95:5

[a] Yields refer to isolated yields of diol product after chromatography; yields in parenthesis include the overoxidation product, obtained as a byproduct in these cases. In all other cases the amount of overoxidation product formed was less than 5%. [b] Ratio determined by ^{1}H NMR or GC of crude reaction mixtures (*dr* diastereomeric ratio).

determined by the geometry of the corresponding double bonds. The diastereoselectivity of *cis*-THF formation was high; in most cases, in fact, the corresponding *trans* product could not be detected, except in Entries 4 and 5. In both these cases, however, the diastereoselectivity could be improved by a simple change of protecting group. Thus, up to four stereogenic centers could be generated with essentially complete stereocontrol (Entries 9–12, Table 3). As no aqueous workup is required, even highly water-soluble products could be isolated in good yields (e.g., Entry 14, Table 3, see also Exp. Sect.).

As an essential prerequisite for synthetic applications we also studied the scaling up of this transformation. Pleasingly, the reaction could be carried out on a gram scale without any reduction in yield or selectivity. Thus, 5.0 mmol of geranyl benzoate was converted into the corresponding THF derivative at 0 °C in 90 min. After quenching (2-propanol), simple filtration, and solvent evaporation, 1.5 g of essentially pure product[24] was obtained (Scheme 3).



Scheme 3. Gram scale oxidative cyclization of geranyl benzoate [(*E*)-**4**] under optimized conditions.

Assignment of Relative Configuration and Stereochemical Correlation

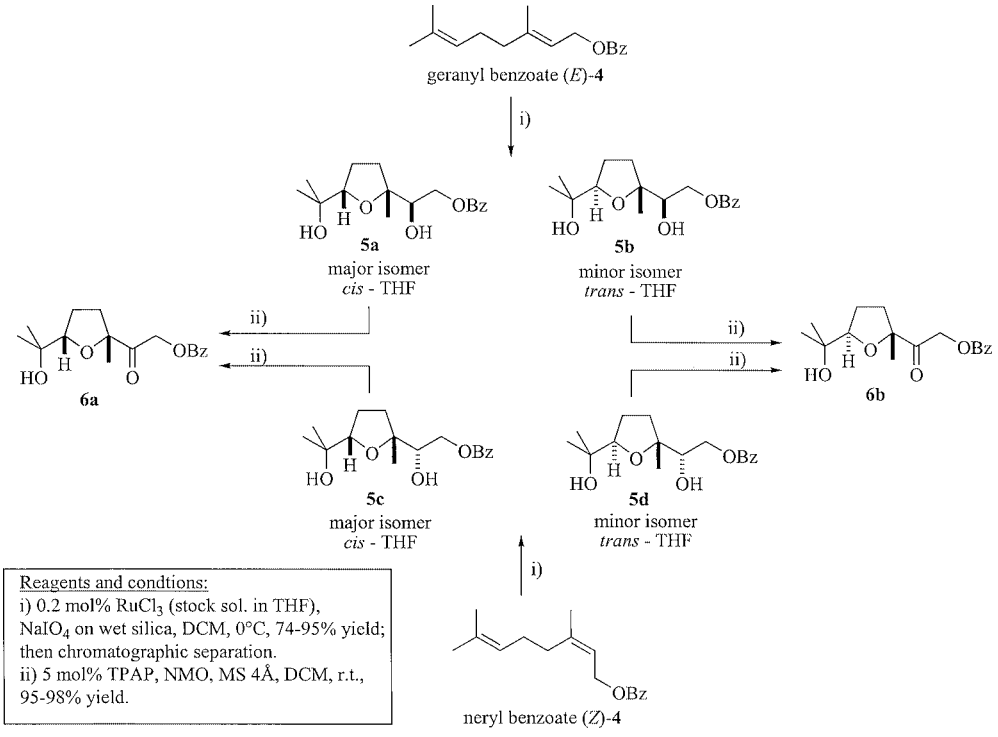
To put the mechanistic interpretation on a solid basis, an extensive investigation of relative stereochemistry and stereochemical correlation of products obtained from the oxidative cyclization was carried out (cf. Scheme 4). Since the minor isomers were not available by the optimized route, reaction conditions were chosen to provide this material as well. The reactions were thus carried out in DCM as a solvent (cf. Table 1). The major and minor diastereoisomers from the oxidative cyclization both of geranyl benzoate [(*E*)-**4**] and its (*Z*)-isomer, neryl benzoate [(*Z*)-**4**], were chromatographically separated, yielding all four possible hydroxy-THF diastereoisomers **5a**–**d** (Scheme 4). These compounds were independently subjected to TPAP-catalyzed alcohol oxidation.[21] Close inspection of analytical data revealed the identities of the two ketones derived from the two major oxidative cyclization products **5a** and **5c**. Likewise, oxidation of the two alcohols **5b** and **5d** yielded ketone **6b**, a diastereoisomer of compound **6a**. NOESY investigation of both diol and ketone compounds **5a**–**d** and **6a**–**b** clearly showed the major products to be *cis*-THF derivatives, whereas the minor ones were the corresponding *trans* derivatives. In addition, crystallization and X-ray diffraction of the major diol product from oxidative cyclization of geranyl acetate unambiguously confirmed the assigned relative stereochemistry (see Exp. Section).

Clearly, as with other oxidative cyclization methods, the *cis*-THF isomers are obtained as the major products. With the reported procedure this stereoisomer can be obtained almost exclusively by using the crucial solvent mixture composed of 10 vol-% of DCM in THF.

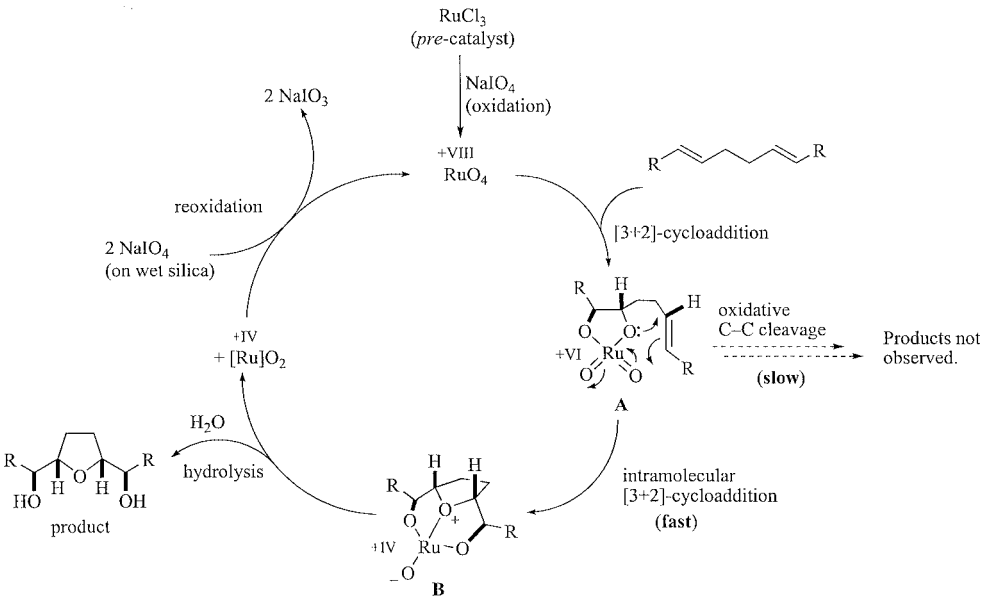
Proposed Mechanism

In analogy to the known permanganate[7b,7d] and osmium tetroxide mediated[9c] reactions and on the basis of recent DFT (density functional theory) calculations,[25] we propose the following mechanism for the ruthenium tetroxide mediated oxidative cyclization (Scheme 5). Oxidation of the pre-catalyst is followed by an initial [3+2] cycloaddition[26] between ruthenium tetroxide and one of the olefinic double bonds, giving rise to a cyclic ruthenium(VI) ester intermediate (**A**). This initial step is followed by a presumably fast intramolecular [3+2] cycloaddition to the distal double bond. The cyclic ruthenium(IV) diester **B**[27] is then hydrolyzed to liberate the tetrahydrofuran product and a ruthenium(IV) species, which is finally reoxidized to ruthenium tetroxide. It should be noted that the timing of reoxidation of ruthenium may be different from that depicted in Scheme 5; it may occur at an earlier stage of the catalytic cycle. The competing C–C-bond cleavage (cf. Scheme 5) appears to be slow under these reaction conditions.

The proposed mechanistic model accounts for the relative stereochemistry of all four stereocenters introduced. As both [3+2] cycloadditions occur stereospecifically *syn*, the relative stereochemistry between the ether oxygen atom and the flanking hydroxy groups is simply determined by the starting geometry of the C–C-double bonds. The relative stereochemistry across the THF ring is established in the



Scheme 4. Stereochemical correlation of oxidative cyclization products.



Scheme 5. Proposed mechanism for the ruthenium tetroxide catalyzed oxidative cyclization of 1,5-dienes.

crucial second [3+2] cycloaddition. It is therefore the conformation of intermediate **A** that determines the formation of either *cis*- of *trans*-THF. We believe that the solvent composition is decisive in favoring the depicted conformation and thus the preferred or exclusive formation of *cis*-THF products.

Conclusions

In conclusion, we have presented a highly efficient procedure for the ruthenium tetroxide mediated oxidative cyclization of 1,5-dienes. This method combines high efficiency with high practicability. Key features of this process are: *i*) an exceptional low catalyst loading, *ii*) high yields, *iii*) high stereoselectivity, and *iv*) a simple workup procedure (no aqueous workup necessary). As little as 0.2 mol-% ruthenium(III) chloride (as a source for ruthenium tetroxide) is required for this highly efficient process. Up to four stereogenic centers are introduced into a simple achiral starting material with high diastereoselectivity in a single-step transformation.

Our current research is focused on more detailed understanding of the reaction mechanism, the development of an asymmetric variant[28] of this oxidative cyclization method, and also on synthetic applications.

Experimental Section

General Remarks: All reagents were used as purchased from commercial suppliers. Solvents were purified by conventional methods prior to use. Column chromatography: Merck silica gel 60, 0.040–0.063 mm (230–400 mesh). TLC: precoated aluminium sheets, Merck silica gel 60, F_{254}; detection by UV or by cerium/molybdenum solution [phosphomolybdic acid (25 g), $Ce(SO_4)_2 \cdot H_2O$ (10 g), concd. H_2SO_4 (60 mL), H_2O (940 mL)]. ^1H and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ with a Bruker AC 500 instrument. Chemical shifts δ are given relative to TMS as internal standard or relative to the resonance of the solvent (^1H: $CDCl_3$, δ = 7.24 ppm; ^{13}C: $CDCl_3$, δ = 77.0 ppm). Mass spectra were recorded with Varian MAT 771 or MAT 112 S instruments. FT-IR spectra were recorded with a Nicolet 5 SXC instrument with DTGS detector. All substrates were prepared by standard procedures. The starting material for THF **13** was prepared by a procedure by Montgomery et al.[29] Compounds **17**,[30] **18**,[30] **19**,[10b] and **20**[31] have been prepared previously and full data have been provided. Analytical data for these compounds were identical to published data and are not given.

Preparation of Sodium Periodate on Wet Silica:[17] Sodium periodate (5.14 g, 24.0 mmol) was suspended in water (12 mL) and the mixture was heated to 70 °C with magnetic stirring in a 100 mL flask. Silica gel (20 g, 230–400 mesh) was added to this slightly cloudy solution in one go (at 70 °C). The flask was removed from the heating bath, stoppered, and vigorously shaken until a fine, homogeneous powder had developed. The final concentration of solid-supported periodate was 0.64 mmol g^{-1}. This reagent can be kept for month at room temperature without any detectable loss of activity.

General Procedure for the Ruthenium Tetroxide Catalyzed Oxidative Cyclization of 1,5-Dienes (0.5 mmol Scale): The 1,5-diene (0.5 mmol, 1 equiv.) was added to a suspension of sodium periodate on wet silica (1.72 g, 1.1 mmol, 2.2 equiv.) in distilled tetrahydrofuran (9 mL) and distilled dichloromethane (1 mL). The mixture was cooled to 0 °C. A stock solution of ruthenium trichloride in tetrahydrofuran or water (0.01 M, 0.1 mL, 0.001 mmol; 0.002 equiv.) was added dropwise to this suspension, the reaction mixture was stirred at 0 °C, and the reaction progress was monitored by TLC. After complete conversion of the starting material the reaction was quenched by addition of 2-propanol (2 mL, excess). The mixture was stirred for another 10 min and was then filtered through a sintered glass funnel, followed by careful washing with ethyl acetate. The solvent was removed under reduced pressure to yield the essentially pure product. Additionally, it may be found advantageous to separate from inorganic contaminants by filtration through a plug of silica. In cases in which byproducts were obtained, chromatographic separation was carried out. This pro-

cedure is easily scalable and can be used without any modification to prepare gram quantities of THF products.

General Procedure for the TPAP Oxidation of THF-diols: A solution of a THF-diol (0.5 mmol) and *N*-methylmorpholine *N*-oxide (2.0 mmol, 4.0 equiv.) in dry dichloromethane (10 mL) containing molecular sieves (4 Å, 500 mg) was stirred at room temperature for 15 min. After addition of TPAP (tetrapropylammonium perruthenate, 0.025 mmol, 5 mol-%), the reaction mixture was stirred until complete conversion was detected (TLC). The mixture was filtered through a short pad of silica and washed with ethyl acetate. After removal of solvents, pure products were obtained without the necessity for further purification.

Crystal Data for the Oxidative Cyclization Product of Geranyl Acetate: $C_{12}H_{22}O_5$, $MW = 246.3$, orthorhombic, space group *Pbca*, $a = 9.284(5)$ Å, $b = 14.571(5)$ Å, $c = 19.296(5)$ Å, $\alpha = 90.000(5)°$, $\beta = 90.000(5)°$, $\gamma = 90.000(5)°$, $V = 2610.3(18)$ Å^3, $Z = 8$, $T = 293(2)$ K, radiation wavelength Mo-$K\alpha = 0.71069$ Å, 9225 reflections measured, 1027 unique ($R_{int} = 0.0919$), $R_1 = 0.0643$, w$R_2 = 0.1149$.
CCDC-278925 contains the supplementary crystallographic data and can be obtained free of charge from the Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

2-Hydroxy-2-[5-(1-hydroxy-1-methylethyl)-2-methyl-tetrahydrofuran-2-yl]ethyl Benzoates 5

***cis*-THF 5a:** ^{1}H NMR (500 MHz): δ = 1.08 [s, 3 H, C(2)–CH_3], 1.23 [s, 6 H, C(5)–COH(CH_3)$_2$], 1.65 [ddd, ^3J = 7.4, 8.4, ^2J = 12.4 Hz, 1 H, C(3)–Ha], 1.88 [m, 1 H, C(4)–Ha], 1.93 [m, 1 H, C(4)–Hb], 2.20 [ddd, ^3J = 5.4, 9.2, ^2J = 12.4 Hz, 1 H, C(3)–Hb], 3.33 (s, 1 H, OH), 3.80 [dd, ^3J = 3.3, 8.0 Hz, 1 H, C(2)–C(OH)*H*–R], 3.84 [t, ^3J = 7.3 Hz, 1 H, C(5)–H], 4.34 [dd, ^3J = 8.0, ^2J = 11.6 Hz, 1 H, C(2)–CHOH–CH_2–OBz], 4.50 [dd, ^3J = 3.3, ^2J = 11.6 Hz, 1 H, C(2)–CHOH–CH_2–OBz], 7.39 (ddd, ^4J = 1.4, ^3J = 7.8, 8.3 Hz, 2 H, Ar), 7.51 (tt, ^4J = 1.4, ^3J = 7.8 Hz, 1 H, Ar), 8.02 (ddd, ^4J = 1.4, 1.4, ^3J = 8.4 Hz, 2 H, Ar) ppm. ^{13}C NMR (125 MHz): δ = 23.1 (C-4), 25.3 [C(2)–*C*H$_3$], 26.6 [C(5)–COH(*C*H$_3$)$_2$], 27.7 [C(5)–COH(*C*H$_3$)$_2$], 35.6 (C-3), 66.6 [C(2)–CHOH–*C*H$_2$–OBz], 71.9 [C(5)–*C*OH(CH$_3$)$_2$], 75.4 (C-2), 84.3 [C(2)–*C*HOH], 85.7 (C-5), 128.4 (Ar), 129.8 (Ar), 130.1 (Ar), 133.1 (Ar), 167.0 (C=O) ppm. FT-IR (KBr): $\tilde{\nu}$ = 708, 1036, 1082, 1179, 1128, 1287, 1453, 1709, 2935, 2971, 3323 cm^{-1}. MS (pos. FAB): *m*/*z* = 59 (18%, [C$_3$H$_7$O]$^+$), 77 (45%, [Ph]$^+$), 105 (100%, [PhCO]$^+$), 125 (27%, [C$_8$H$_{15}$O$_2$ – H$_2$O]$^+$), 143 (86%, [C$_8$H$_{15}$O$_2$]$^+$), 275 (6%, [*M* – H$_2$O – CH$_3$]$^+$), 291 (0.2%, [*M* – H$_2$O]$^+$), 293 (0.05%, [*M* – CH$_3$]$^+$), 309 (0.02%, [*M* + H]$^+$). HRMS: calcd. *m*/*z* for C$_{16}$H$_{21}$O$_5$ ([*M* – CH$_3$]$^+$) 293.139; found *m*/*z* 293.139.

***trans*-THF 5b:** ^{1}H NMR (500 MHz): δ = 1.09 [s, 3 H, C(5)–COH(CH_3)$_2$], 1.16 [s, 3 H, C(5)–COH(CH_3)$_2$], 1.20 [s, 3 H, C(2)–CH_3], 1.72 [ddd, ^3J = 3.0, 7.3, ^2J = 12.0 Hz, 1 H, C(3)–Ha], 1.84 [m, 2 H, C(4)–H$_2$], 2.06 [m, 1 H, C(3)–Hb], 3.76 [dd, ^3J = 6.5, 9.2 Hz, 1 H, C(5)–H], 3.84 [dd, ^3J = 3.0, 7.7 Hz, 1 H, C(2)–C(OH)*H*–R], 4.24 [dd, ^3J = 7.7, ^2J = 11.6 Hz, 1 H, C(2)–CHOH–CH_2–OBz], 4.42 [dd, ^3J = 3.0, ^2J = 11.6 Hz, 1 H, C(2)–CHOH–CH_2–OBz], 7.39 (t, ^3J = 8.0 Hz, 2 H, Ar), 7.51 (t, ^3J = 8.0 Hz, 2 H, Ar), 8.02 (d, ^3J = 8.0 Hz, Ar) ppm. ^{13}C NMR (125 MHz): δ = 22.2 (C-4), 24.1 [C(2)–*C*H$_3$], 26.6 [C(5)–COH(*C*H$_3$)$_2$], 27.5 [C(5)–COH(*C*H$_3$)$_2$], 34.9 (C-3), 66.0 [C(2)–CHOH–*C*H$_2$–OBz], 70.7 [C(5)–*C*OH(CH$_3$)$_2$], 75.2 (C-2), 84.2 [C(2)–*C*HOH], 86.8 (C-5), 128.4 (Ar), 129.8 (Ar), 130.4 (Ar), 133.2 (Ar), 166.9 (C=O) ppm. FT-IR (KBr): $\tilde{\nu}$ = 713, 913, 1120, 1276, 1383, 1451, 1602, 1718, 2874, 2932, 2973, 3442 cm^{-1}. MS (pos. FAB): *m*/*z* = 71 (27%, [THF – 2 H]$^+$), 105 (100%, [PhCO]$^+$), 143 (15%, [C$_8$H$_{15}$O$_2$]$^+$), 291 (13%, [*M* – H$_2$O]$^+$), 309 (3%, [*M* + H]$^+$), 331 (21%, [*M* + Na]$^+$). HRMS: calcd. *m*/*z* for C$_{17}$H$_{23}$O$_4$ ([*M* – OH]$^+$) 291.160; found *m*/*z* 291.160.

***cis*-THF 5c:** ^{1}H NMR (500 MHz): δ = 1.04 [s, 3 H, C(5)–C(CH_3)(CH$_3$)OH], 1.19 [s, 3 H, C(2)–CH$_3$], 1.23 [s, 3 H, C(5)–C(CH$_3$)(CH_3)OH], 1.49 [ddd, ^3J = 8.3, 8.3, ^2J = 12.5 Hz, 1 H, C(3)–Ha], 1.80 [m, 1 H, C(4)–Ha], 1.93 [m, 1 H, C(4)–Hb], 2.20 [m, 1 H, C(3)–Hb], 3.76 [t, 1 H, ^3J = 7.4 Hz, C(5)–H], 3.87 [dd, ^3J = 2.5, 7.7 Hz, 1 H, C(2)–C*H*(OH)CH$_2$OBz], 4.12 [dd, ^3J = 7.7, ^2J = 11.6 Hz, 1 H, C(2)–CH(OH)C*Ha*HbOBz], 4.59 [dd, ^3J = 2.5, ^2J = 11.6 Hz, 1 H, C(2)–CH(OH)CHa*Hb*OBz], 7.38 (m, 2 H, Ar), 7.51 (m, 2 H, Ar), 8.02 (Ar) ppm. ^{13}C NMR (125 MHz): δ = 23.3 (C-4), 23.9 [C(2)–CH$_3$], 26.6 [C(5)–C(*C*H$_3$)(CH$_3$)OH], 27.4 [C(5)–C(CH$_3$)(*C*H$_3$)OH], 33.5 (C-3), 66.3 [C(2)–CH(OH)CH_2OBz], 70.8 [C(5)–*C*(CH$_3$)(CH$_3$)OH], 75.1 (C-2), 84.2 [C(2)–*C*H(OH)CH$_2$OBz], 87.4 (C-5), 128.4 (Ar), 129.7 (Ar), 130.0 (Ar), 133.1 (Ar), 166.9 (CO) ppm. FT-IR (KBr): $\tilde{\nu}$ = 712, 1086, 1277, 1706, 2871, 2929, 2974, 3418, 3470 cm^{-1}. MS (pos. FAB): *m*/*z* = 71 (51%, [THF – 2 H]$^+$), 77 (25%, [Ph]$^+$), 105 (100%, [C$_7$H$_5$O]$^+$), 143 (20%, [C$_8$H$_{15}$O$_2$]$^+$), 291 (21%, [*M* – OH]$^+$), 309 (9%, [*M* + H]$^+$), 331 (25%, [*M* + Na]$^+$). HRMS: calcd. *m*/*z* for C$_{16}$H$_{21}$O$_5$ ([*M* – CH$_3$]$^+$) 293.139; found *m*/*z* 293.139.

***trans*-THF 5d:** ^{1}H NMR (500 MHz): δ = 1.09 [s, 3 H, C(5)–C(CH_3)(CH$_3$)OH], 1.16 [s, 3 H, C(5)–C(CH$_3$)(CH_3)OH], 1.20 [s, 3 H, C(2)–CH$_3$], 1.64 [m, 1 H, C(3)–Ha], 1.81 [m, 2 H, C(4)–Ha, C(4)–Hb], 2.15 [m, 1 H, C(3)–Hb], 3.77 [t, ^3J = 2.8, 7.6 Hz, 1 H, C(5)–H], 3.88 [dd, ^3J = 2.8, 7.6 Hz, 1 H, C(2)–C*H*(OH)CH$_2$OBz], 4.28 [dd, ^3J = 7.7, ^2J = 11.7 Hz, 1 H, C(2)–CH(OH)C*Ha*HbOBz], 4.47 [dd, ^3J = 7.6, ^2J = 2.8 Hz, 1 H, C(2)–CH(OH)CHa*Hb*OBz], 7.38 (m, 2 H, Ar), 7.51 (m, 1 H, Ar), 8.02 (m, 2 H, Ar) ppm. ^{13}C NMR (125 MHz): δ = 23.3 (C-4), 23.9 (2-CH$_3$), 26.6 [C(5)–C(*C*H$_3$)(CH$_3$)OH], 27.4 [C(5)–C(CH$_3$)(*C*H$_3$)OH], 33.5 (C-3), 66.3 [C(2)–CH(OH)CH_2OBz], 70.8 [C(5)–*C*(CH$_3$)(CH$_3$)OH], 75.1 (C-2), 84.2 [C(2)–*C*H(OH)CH$_2$OBz], 87.4 (C-5), 128.4 (Ar), 129.7 (Ar), 130.0 (Ar) 133.1 (Ar), 166.9 (CO) ppm. FT-IR (KBr): $\tilde{\nu}$ = 713, 1070, 1277, 1719, 2875, 2934, 2947, 3442 cm^{-1}. MS (pos. FAB): *m*/*z* = 71 (33%, [THF – 2 H]$^+$), 77 (95%, [Ph]$^+$), 105 (100%, [C$_7$H$_5$O]$^+$), 143 (10%, [C$_8$H$_{15}$O$_2$]$^+$), 291 (11%, [*M* – OH]$^+$), 309 (3%, [*M* + H]$^+$), 331 (28%, [*M* + Na]$^+$). HRMS: calcd. *m*/*z* for C$_{16}$H$_{21}$O$_5$ [*M* – CH$_3$]$^+$ 293.139; found *m*/*z*, 293.139.

2-[5-(1-Hydroxy-1-methylethyl)-2-methyl-tetrahydrofuran-2-yl]-2-oxoethyl Benzoates 6

***cis*-THF 6a:** ^{1}H NMR (500 MHz): δ = 1.12 [s, 3 H, C(2)–CH_3], 1.27 [s, 3 H, C(5)–COH(CH_3)$_2$], 1.40 [s, 3 H, C(5)–COH(CH_3)$_2$], 1.81 [m, 3 H, C(4)–H$_2$, C(3)–Hb], 2.42 [m, 1 H, C(3)–Ha], 2.50 (s, OH), 3.88 [dd, ^3J = 6.3, 8.5 Hz, 1 H, C(5)–H], 5.16 [d, ^2J = 17.5 Hz, 1 H, C(2)–CO–CH_2–OBz], 5.35 [dd, ^2J = 17.5 Hz, 1 H, C(2)–CO–CH_2–OBz], 7.39 (t, ^3J = 8.0 Hz, 2 H, Ar), 7.52 (t, ^3J = 8.0 Hz, 2 H, Ar), 8.03 (d, ^3J = 8.0 Hz, Ar) ppm. ^{13}C NMR (125 MHz): δ = 24.0 (C-4), 25.6 [C(5)–COH(*C*H$_3$)$_2$], 26.0 [C(2)–*C*H$_3$], 27.4 [C(5)–COH(*C*H$_3$)$_2$], 36.2 (C-3), 66.2 [C(2)–CO–*C*H$_2$–OBz], 71.0 [C(5)–*C*OH(CH$_3$)$_2$], 87.0 (C-2), 88.1 (C-5), 128.4 (Ar), 129.0 (Ar), 129.9 (Ar), 133.3 (Ar), 166.9 [RO–*C*(=O)Ph], 206.3 [C(2)–*C*=O–R] ppm. FT-IR (KBr): $\tilde{\nu}$ = 712, 1119, 1279, 1451, 1723, 1740, 2876, 2933, 2976, 3456, 3518 cm^{-1}. MS (pos. FAB): *m*/*z* = 71 (23%, [THF – 2 H]$^+$), 105 (100%, [Ph–CO]$^+$), 143 (28%, [C$_8$H$_{15}$O$_2$]$^+$), 289 (32%, [*M* – OH]$^+$), 307 (2%, [*M* + H]$^+$), 329 (9%, [*M* + Na]$^+$). HRMS: calcd. *m*/*z* for C$_{16}$H$_{19}$O$_5$ ([*M* – CH$_3$]$^+$) 291.123; found *m*/*z* 291.123.

***trans*-THF 6b:** ^{1}H NMR (500 MHz): δ = 1.13 [s, 3 H, C(5)–C(CH_3)(CH$_3$)OH], 1.24 [s, 3 H, C(5)–C(CH$_3$)(CH_3)OH], 1.39 [s, 3 H, C(2)–CH$_3$], 1.84 [m, 3 H, C(3)–Ha, C(4)–Ha, C(4)–Hb], 2.29 [m, 1 H, C(3)–Hb], 3.88 [m, 1 H, C(5)–H], 5.22 [s, 2 H, C(2)–COCH_2OBz], 7.41 (m, 2 H, Ar), 7.51 (m, 1 H, Ar), 8.05 (m, 2 H,

Ar) ppm. ^{13}C NMR (125 MHz): δ = 24.3 (C-4), 24.4 [C(2)–CH_3], 25.9 [C(5)–C(CH_3)(CH_3)OH], 27.2 [C(5)–C(CH_3)(CH_3)OH], 35.4 (C-3), 65.9 [C(2)–C(O)CH_2OBz], 70.7 [C(5)–C(CH_3)(CH_3)OH], 88.1 (C-2), 88.4 (C-5), 128.4 (Ar), 129.8 (Ar), 130.0 (Ar), 133.3 (Ar), 166.1 [ArC(O)OCH$_2$], 207.5 [2-C(O)CH$_2$OBz] ppm. FT-IR (KBr): $\tilde{\nu}$ = 711, 1061, 1078, 1278, 1723, 1740, 2875, 2877, 2935, 3349, 3525 cm^{-1}. MS (pos. FAB): *m*/*z* = 71 (20%, [THF – 2 H]$^+$), 77 (27%, [Ph]$^+$), 105 (100%, [C_7H_5O]$^+$), 143 (33%, [$C_8H_{15}O_2$]), 289 (35%, [*M* – OH]$^+$), 307 (8%, [*M* + H]$^+$), 329 (21%, [*M* + Na]$^+$). HRMS: calcd. *m*/*z* for $C_{16}H_{22}O_5$ [*M* – CH_3]$^+$ 291.123, found *m*/*z* 293.123.

2-{5-[2-(*tert*-Butyldiphenylsilanyloxy)-1-hydroxyethyl]-5-methyl-tetrahydrofuran-2-yl}propan-2-ol (7): ^{1}H NMR (500 MHz): δ = 1.03 [s, 3 H, C(2)–CH_3], 1.07 (s, 12 H, Si-*t*Bu), 1.19 [s, 6 H, C(5)–COH(CH_3)$_2$], 1.55 [ddd, ^3J = 6.3, 8.5, ^2J = 12.2 Hz, 1 H, C(3)–Ha], 1.87 [m, 1 H, C(4)–Ha], 1.98 [m, 1 H, C(4)–Hb], 2.22 [ddd, ^3J = 6.6, 8.9, ^2J = 12.2 Hz, 1 H, C(3)–Hb], 3.67 [dd, ^3J = 8.5, ^2J = 4.2 Hz, 1 H, C(2)–CHOH–CH_2–OTBDPS], 3.78 [m, 3 H, C(5)–H, C(2)–C(OH)*H*–R, C(2)–CHOH–CH_2–OTBDPS], 7.40 (m, 6 H, Ar), 7.66 (dd, ^4J = 1.5, ^3J = 7.8 Hz, 4 H, Ar) ppm. ^{13}C NMR (125 MHz): δ = 19.3 (Si-*t*Bu), 23.2 [s, C(2)–CH$_3$], 25.1 [C(5)–COH(*C*H$_3$)$_2$], 26.1 [C(5)–COH(*C*H$_3$)$_2$], 27.0 (Si-*t*Bu), 27.8 (C-4), 35.2 (C-3), 64.8 [C(5)–*C*OH(CH$_3$)$_2$], 71.8 (C-2), 76.8 (C-5), 83.6 [C(2)–*C*HOH], 85.8 [C(2)–CHOH–*C*H$_2$–OTBDMS], 127.9 (Ar), 129.9 (Ar), 133.2 (Ar), 135.6 (Ar) ppm. FT-IR (KBr): $\tilde{\nu}$ = 505, 702, 740, 825, 1064, 1113, 1428, 1472, 2857, 2885, 2931, 2963, 3397 cm^{-1}. MS (EI, 90 °C): *m*/*z* = 43 (17%, [CH_3CO]$^+$), 143 (6%, [C_3H_7O–THF–CH_3]$^+$), 199 (5%, [$SiPh_2OH$]$^+$), 285 (2%, [TBDPS–O–CH_2]$^+$), 349 (1%, [*M* – H_2O – H_2O – C_4H_9]$^+$), 367 (2%, [*M* – H_2O – C_4H_9]$^+$). HRMS: calcd. *m*/*z* for $C_{22}H_{27}O_3Si$ ([*M* – H_2O – C_4H_9]$^+$) 367.173; found *m*/*z* 367.174.

2-{5-[2-(*tert*-Butyldimethylsilanyloxy)-1-hydroxyethyl]-5-methyl-tetrahydrofuran-2-yl}propan-2-ol (8): ^{1}H NMR (500 MHz): δ = 0.07 (s, 6 H, Si–Me), 0.89 (s, 9 H, Si-*t*Bu), 1.08 [s, 3 H, C(2)–CH_3], 1.14 [s, 3 H, C(5)–COH(CH_3)$_2$], 1.23 [s, 3 H, C(5)–COH(CH_3)$_2$], 1.59 [ddd, ^3J = 6.5, 8.7, ^2J = 12.4 Hz, 1 H, C(3)–Ha], 1.90 [m, 1 H, C(4)–Ha], 2.02 [m, 1 H, C(4)–Hb], 2.28 [ddd, ^3J = 6.7, 9.1, ^2J = 12.4 Hz, 1 H, C(3)–Hb], 2.98 (s, 1 H, OH), 3.33 (s, 1 H, OH), 3.58 [dd, ^3J = 8.7, ^2J = 3.9 Hz, 1 H, C(2)–CHOH–CH_2–OTBDMS], 3.67 [dd, ^3J = 9.9, 8.7 Hz, 1 H, C(2)–C(OH)*H*–R], 3.77 [dd, ^3J = 9.9, ^2J = 3.9 Hz, 1 H, C(2)–CHOH–CH_2–OTBDMS], 3.84 [t, ^3J = 7.1 Hz, 1 H, C(5)–H] ppm. ^{13}C NMR (125 MHz): δ = –5.3 (Si–Me), 18.3 (Si-*t*Bu), 23.4 [C(2)–CH$_3$], 25.1 (C-4)) , 26.0 (Si-*t*Bu), 26.1 [C(5)–COH(*C*H$_3$)$_2$], 27.9 [C(5)–COH(*C*H$_3$)$_2$], 35.2 (C-3), 63.7 [C(5)–*C*OH(CH$_3$)$_2$], 71.8 (C-2), 76.6 (C-5), 83.6 [C(2)–*C*HOH], 86.9 [C(2)–CHOH–*C*H$_2$–OTBDMS] ppm. FT-IR (KBr): $\tilde{\nu}$ = 778, 838, 1068, 1116, 1254, 1464, 1472, 2930, 2957, 3405 cm^{-1}. MS (pos. FAB): *m*/*z* = 43 (69%, [CH_3CO]$^+$), 143 (21%, [C_3H_7O–THF–CH_3]$^+$), 283 (10%, [*M* – OH – H_2O]$^+$), 301 (18%, [*M* – OH]$^+$), 318 (8%, [*M* + H]$^+$), 341 (44%, [*M* + Na]$^+$). HRMS: calcd. *m*/*z* for $C_{15}H_{31}O_4Si$ ([*M* – CH_3]$^+$) 303.199, found *m*/*z* 303.198.

2-[5-(2-Benzyloxy-1-hydroxyethyl)-5-methyl-tetrahydrofuran-2-yl]-propan-2-ol (9): ^{1}H NMR (500 MHz): δ = 1.08 [s, 3 H, C(2)–CH$_3$], 1.14 [s, 3 H, C(5)–COH(CH_3)$_2$], 1.21 [s, 3 H, C(5)–COH(CH_3)$_2$], 1.60 [ddd, ^3J = 7.0, 8.5, ^2J = 12.4 Hz, 1 H, C(3)–Ha], 1.89 [m, 1 H, C(4)–Ha], 1.98 [m, 1 H, C(4)–Hb], 2.21 [ddd, ^3J = 6.2, 9.1, ^2J = 12.4 Hz, 1 H, C(3)–Hb], 3.07 (s, 1 H, OH), 3.14 (s, 1 H, OH), 3.56 [dd, ^3J = 8.4, 9.5 Hz, 1 H, C(2)–C(OH)*H*–R], 3.65 [dd, ^3J = 9.5, ^2J = 3.3 Hz, 1 H, C(2)–CHOH–CH_2–OBn], 3,72 [dd, ^3J = 8.4, ^2J = 3.3 Hz, 1 H, C(2)–CHOH–CH_2–OBn], 3.83 [t, ^3J = 7.1 Hz, 1 H, C(5)–H], 4.56 (d, ^2J = 7.6 Hz, 2 H, Ph-CH_2–OR), 7.30 (m, 5 H, Ar) ppm. ^{13}C NMR (125 MHz): δ = 23.3 (C-4), 25.1 [C(2)–CH$_3$], 26.4 [C(5)–COH(*C*H$_3$)$_2$], 27.8 [C(5)–COH(*C*H$_3$)$_2$], 35.2 (C-3), 71.2 [C(2)–CHOH–*C*H$_2$–OBn], 71.8 [C(5)–*C*OH(CH$_3$)$_2$], 73.5 (Ph-*C*H$_2$–OR), 84.0 [C(2)–*C*HOH], 75.5 (C-2), 85.8 (s, C-5), 127.8 (Ar), 128.5 (Ar), 138.0 (Ar) ppm. FT-IR (KBr): $\tilde{\nu}$ = 698, 737, 1028, 1071, 1117, 1384, 1454, 1718, 2871, 2926, 2969, 3438 cm^{-1}. MS (pos. FAB): *m*/*z* = 43 (14%, [CH_3CO]$^+$), 91 (22%, [C_7H_7]$^+$), 204 (2%, [*M* – C_3H_7O – CH_3O]$^+$), 235 (1%, [*M* – C_3H_7O]$^+$), 277 (6%, [*M* + H – H_2O]$^+$), 295 (4%, [*M* + H]$^+$). HRMS: calcd. *m*/*z* for $C_8H_{15}O_2$ ([C_3H_7O–THF–CH_3]$^+$) 143.107; found *m*/*z* 143.108.

***N*-{2-Hydroxy-2-[5-(1-hydroxy-1-methylethyl)-2-methyl-tetrahydrofuran-2-yl]ethyl}benzamide (10):** ^{1}H NMR (500 MHz): δ = 0.96 [s, 3 H, C(2)–CH_3], 1.08 [s, 3 H, C(5)–COH(CH_3)$_2$], 1.11 [s, 3 H, C(5)–COH(CH_3)$_2$], 1.51 [m, 1 H, C(3)–Hb], 1.75 [m, 1 H, C(4)–Hb], 1.87 [m, 1 H, C(4)–Ha], 2.06 [ddd, ^3J = 5.5, 9.2, ^2J = 14.2 Hz, 1 H, C(3)–Ha], 3.20 [m, 1 H, C(5)–H], 3.53 [m, 1 H, C(2)–C*H*OH–CH$_2$–NHBz], 3.72 [m, 2 H, C(2)–CHOH–CH_2–NHBz], 7.23 (t, ^3J = 7.3 Hz, 2 H, Ar), 7.31 (t, ^3J = 7.3 Hz, 1 H, Ar), 7.66 (t, ^3J = 7.3 Hz, 2 H, Ar) ppm. ^{13}C NMR (125 MHz): δ = 23.3 (C-4), 25.4 [C(2)–*C*H$_3$], 26.3 [C(5)–COH(*C*H$_3$)$_2$], 27.8 [C(5)–COH(*C*H$_3$)$_2$], 35.5 (C-3), 42.7 [C(2)–CHOH–*C*H$_2$NHBz], 71.9 [C(5)–*C*OH(CH$_3$)$_2$], 75.2 (C-2), 85.0 [C(2)–*C*HOH], 85.8 (C-5), 127.2 (Ar), 128.4 (Ar), 131.4 (Ar), 134.3 (Ar), 168.4 (Ph-*C*ONHR) ppm. FT-IR (KBr): $\tilde{\nu}$ = 951, 1084, 1311, 1541, 1641, 1140, 2875, 2934, 2972, 3370 cm^{-1}. MS (pos. FAB): *m*/*z* = 71 (28%, [THF – 2 H]$^+$), 105 (100%, [PhCO]$^+$), 143 (11%, [C_3H_7O–THF–CH_3]$^+$), 308 (24%, [*M* + H]$^+$), 330 (13%, [*M* + Na]$^+$). HRMS: calcd. *m*/*z* for $C_{16}H_{22}NO_4$ ([*M* – CH_3]$^+$) 292.145; found *m*/*z* 292.144.

***N*-{2-Hydroxy-2-[5-(1-hydroxy-1-methylethyl)-2-methyl-tetrahydrofuran-2-yl]ethyl}-4-methylbenzenesulfonamide (11):** ^{1}H NMR (500 MHz): δ = 1.05 [s, 6 H, C(5)–COH(CH_3)$_2$], 1.19 [s, 3 H, C(2)–CH_3], 1.11 [s, 3 H, C(5)–COH(CH_3)$_2$], 1.59 [ddd, ^3J = 8.4, 8.4, ^2J = 14.2 Hz,1 H, C(3)–Hb], 1.84 [m, 1 H, C(4)–Hb], 1.91 [m, 1 H, C(4)–Ha], 2.08 [ddd, ^3J = 5.1, 9.2, ^2J = 14.2 Hz, 1 H, C(3)–Ha], 2.38 (s, 3 H, Ar-CH_3), 2.90 [dd, ^3J = 8.1, 12.7 Hz, 1 H, C(5)–H], 3.17 [m, 1 H, C(2)–C*H*OH–CH$_2$–NHTos], 3.46 [dd, ^3J = 3.0, ^2J = 8.1 Hz, 1 H, C(2)–CHOH–CH_2–NHTos], 3.78 [dd, ^3J = 7.4, ^2J = 8.1 Hz, 1 H, C(2)–CHOH–CH_2–NHTos], 5.81 (s, 1 H, NH), 7.26 (d, ^3J = 8.0 Hz, 2 H, Ar), 7.72 (d, ^3J = 8.0 Hz, 2 H, Ar) ppm. ^{13}C NMR (125 MHz): δ = 21.4 (C-4), 23.3 [C(2)–*C*H$_3$], 25.4 (Ar-*C*H$_3$), 26.3 [C(5)–COH(*C*H$_3$)$_2$], 27.6 [C(5)–COH(*C*H$_3$)$_2$], 35.6 (C-3), 45.2 [C(2)–CHOH–*C*H$_2$–NHTos], 72.0 [C(5)–*C*OH(CH$_3$)$_2$], 75.0 (C-2), 84.7 [C(2)–*C*HOH–CH$_2$–NHTos], 85.7 (C-5), 127.1 (Ar), 129.6 (Ar), 136.8 (Ar), 143.2 (Ar) ppm. FT-IR [KBr]: $\tilde{\nu}$ = 552, 662, 815, 1090, 1160, 1328, 1451, 1598, 2877, 2931, 2974, 3287 cm^{-1}. MS (EI, 160 °C): *m*/*z* = 43 (39%, [CH_3CO]$^+$), 59 (12%, [C_3H_7O]$^+$), 71 (26%, [THF – 2 H]$^+$), 91 (35%, [C_7H_7]$^+$), 143 (100%, [C_3H_7O–THF–CH_3]$^+$), 155 (38%, [$C_7H_7SO_2$]$^+$), 324 (2%, [*M* – CH_3 – H_2O]$^+$), 357 (0.3%, [*M*]$^+$). HRMS: calcd. *m*/*z* for $C_{17}H_{27}NO_5S$ ([*M*]$^+$) 357.161; found *m*/*z* 357.161.

Methyl Hydroxy[5-(1-hydroxy-1-methylethyl)-2-methyl-tetrahydrofuran-2-yl]acetate (12): ^{1}H NMR (500 MHz): δ = 1.09 [s, 3 H, C(2)–CH$_3$], 1.26 [s, 3 H, C(5)–COH(CH_3)$_2$], 1.31 [s, 3 H, C(5)–COH(CH_3)$_2$], 1.70 [m, 1 H, C(3)–Ha], 1.85 [m, 1 H, C(4)–Ha], 2.02 [m, 1 H, C(4)–Hb], 2.34 [ddd, ^3J = 2.6, 8.7, ^2J = 12.1 Hz, 1 H, C(3)–Hb], 3.80 (s, 3 H, CO_2CH_3), 3.83 [dd, ^3J = 6.5, 9.2 Hz, 1 H, C(5)–H], 4.03 [s, 1 H, C(2)–C(OH)*H*–CO_2Me] ppm. ^{13}C NMR (125 MHz): δ = 16.1 (C-4), 18.7 [C(2)–*C*H$_3$], 25.6 [C(5)–*C*OH-(CH$_3$)$_2$], 26.1 [C(5)–*C*OH(CH$_3$)$_2$], 40.9 (C-3), 50.6 (CO_2CH_3), 115.3 [C(5)–*C*OH(CH$_3$)$_2$], 123.0 (C-2), 132.4 (C-5), 160.0 [C(2)–*C*(OH) H–CO_2Me], 167.1 (C=O) ppm. FT-IR (KBr): $\tilde{\nu}$ = 1094, 1212, 1379, 1440, 1737, 2878, 2936, 2975, 3439 cm^{-1}. MS (EI, 160 °C): *m*/*z* = 43 (100%, [CH_3CO]$^+$), 59 (32%, [C_3H_7O]$^+$), 71 (45%, [THF –

2 H]$^+$), 143 (47%, [C_3H_7O–THF–CH_3]$^+$), 173 (11%, [M – C_3H_7O]$^+$), 199 (2%, [M – CH_3 – H_2O]$^+$), 217 (5%, [M – CH_3]$^+$). HRMS: calcd. m/z for $C_{10}H_{17}O_5$ ([M – CH_3]$^+$) 217.108; found m/z 217.109.

Ethyl {5-[Ethoxycarbonyl(hydroxy)methyl]-tetrahydrofuran-2-yl}hydroxyacetate (13): ^{1}H NMR (500 MHz): δ = 1.22 (t, ^3J = 7.2 Hz, CH_3CH$_2$), 1.98 [m, 2 H, C(3)–Ha], 2.16 [m, 2 H, C(3)–Hb], 3.82 (s, 2 H, OH), 4.04 [d, ^3J = 1.9 Hz, 2 H, C(2)–CHOH–CO$_2$Et], 4.18 (q, ^3J = 7.2 Hz, 4 H, CH$_3$CH_2), 4.33 [m, 2 H, C(2)–H] ppm. ^{13}C NMR (125 MHz): δ = 14.1 (*C*H$_3$), 28.0 (C-3), 61.7 (CH$_3$*C*H$_2$), 73.4 (C-2), 80.6 (*C*HOH), 172.6 (*C*O$_2$Et) ppm. FT-IR (KBr): $\tilde{\nu}$ = 1029, 1130, 1201, 1271, 1369, 1640, 1742, 2939, 2983, 3440 cm^{-1}. MS (EI, 90 °C): m/z = 57 (24%, [C_4H_9]$^+$), 71 (27%, [THF – 2 H]$^+$), 99 (81%, [THF – CO – 2 H]$^+$), 155 (31%, [M – $C_4H_7O_3$ – H_2O]$^+$), 173 (100%, [M – $C_4H_7O_3$]$^+$), 203 (7%, [M – $C_3H_5O_2$]$^+$), 276 (0.3%, [M]$^+$). HRMS: calcd. m/z for $C_{12}H_{20}O_7$ ([M]$^+$) 276.121; found m/z 276.121.

1-[5-(1-Hydroxypentyl)-tetrahydrofuran-2-yl]pentan-1-ol (14): ^{1}H NMR (500 MHz): δ = 0.87 (t, ^3J = 7.3 Hz, 6 H, Me), 1.29 (m, 8 H, CH$_3$CH_2CH_2CH$_2$CHOH), 1.43 (m, 4 H, CH_2CHOH), 1.71 [m, 2 H, C(3)–Ha], 1.89 [m, 2 H, C(3)–Hb], 3.38 (m, 2 H, CHOH), 3.79 [m, 2 H, C(2)–H] ppm. ^{13}C NMR (125 MHz): δ = 14.1 (C-1), 22.8 (C-2), 27.9 (C-3), 28.1 (C-7), 33.8 (C-4), 74.4 (C-5), 82.8 (C-6) ppm. FT-IR (KBr): $\tilde{\nu}$ = 718, 907, 1122, 1279, 1466, 3350 cm^{-1}. MS (pos. FAB): m/z = 57 (100%, [C_4H_9]$^+$), 139 (9%, [M – $C_5H_{10}OH$ – H_2O]$^+$), 157 (14%, [M – $C_5H_{10}OH$]$^+$), 227 (12%, [M – OH]$^+$), 245 (7%, [M + H]$^+$), 267 (4%, [M + Na]$^+$). HRMS: calcd. m/z for $C_{14}H_{27}O_2$ ([M – OH]$^+$) 227.201; found m/z 227.201.

1-[5-(1-Hydroxypentyl)-tetrahydrofuran-2-yl]pentan-1-one (15): ^{1}H NMR (500 MHz): δ = 0.87 (m, 6 H, CH_3), 1.29 [m, 8 H, C(2)–CO–CH$_2$CH$_2$CH_2CH$_3$, C(5)–CHOH–CH_2CH_2CH_2CH$_3$], 1.54 [tt, ^3J = 7.2, 7.2 Hz, C(2)–CO–CH$_2$CH_2CH$_2$CH$_3$], 1.74 [m, 1 H, C(4)–Hb], 1.81 [m, 1 H, C(4)–Ha], 2.01 [m, 1 H, C(3)–Hb], 2.24 [m, 1 H, C(3)–Ha], 2.40 [m, 2 H, C(2)–CO–CH_2CH$_2$CH$_2$CH$_3$], 3.95 [m, 1 H, C(5)–CHOH-*n*Bu], 4.04 [ddd, 1 H, ^3J = 2.8, 6.3, 9.1 Hz, C(5)–H], 4.16 (s, 1 H, OH), 4.53 [dd, 1 H, ^3J = 3.3, 9.6 Hz, C(2)–H] ppm. ^{13}C NMR (125 MHz): δ = 13.9 [C(2)–CO–CH$_2$CH$_2$CH$_2$*C*H$_3$], 14.1 [C(5)–CHOH–CH$_2$CH$_2$CH$_2$*C*H$_3$], 22.3 [C(5)–CHOH–CH$_2$CH$_2$*C*H$_2$CH$_3$], 22.4 [C(5)–CHOH–CH$_2$*C*H$_2$CH$_2$CH$_3$], 22.8 (C-4), 25.6 [C(2)–CO–CH$_2$*C*H$_2$CH$_2$CH$_3$], 28.2 [C(2)–CO–CH$_2$CH$_2$*C*H$_2$CH$_3$], 29.7 (C-3), 32.6 [C(5)–CHOH–*C*H$_2$CH$_2$CH$_2$CH$_3$], 38.4 [C(2)–CO–*C*H$_2$CH$_2$CH$_2$CH$_3$], 71.1 [C(5)–*C*HOH-*n*Bu], 82.2 (C-2), 84.9 (C-5), 212.8 [C(2)–*C*O–*n*Bu] ppm.

2-Hydroxy-2-[5-(1-hydroxypropyl)-tetrahydrofuran-2-yl]ethyl Benzoate (16): ^{1}H NMR (500 MHz): δ = 0.96 [t, ^3J = 6.7 Hz, 3 H, C(5)–CHOH–CH$_2$CH_3], 1.40 [dq, ^3J = 6.7, 6.7 Hz, 2 H, C(5)–CHOH–CH_2CH$_3$], 1.80 [m, 1 H, C(3)–Ha], 2.02 [m, 3 H, C(3)–Hb, C(4)–H$_2$], 3.80 [m, 1 H, C(5)–CHOH–CH_2CH$_3$], 3.86 [m, 1 H, C(5)–H], 3.97 [td, ^3J = 2.9, 4.8 Hz, 1 H, C(2)–H], 4.11 [m, 1 H, C(2)–CHOH–CH$_2$–OBz], 4.39 [dd, ^3J = 5.0, ^2J = 11.4 Hz, 1 H, C(2)–CHOH–CH_2–OBz], 4.43 [dd, ^3J = 7.0, ^2J = 11.4 Hz, 1 H, C(2)–CHOH–CH_2–OBz], 7.41 (ddd, ^4J = 1.4, ^3J = 8.3, 7.0 Hz, 2 H, Ar), 7.54 (tt, ^4J = 1.4, ^3J = 7.0 Hz, 1 H, Ar), 8.03 (ddd, ^4J = 1.4, 1.4, ^3J = 8.3 Hz, 2 H, Ar) ppm. ^{13}C NMR (125 MHz): δ = 10.4 [C(5)–CHOH–CH$_2$*C*H$_3$], 24.2 (C-3), 26.3 (C-4), 28.6 [C(5)–CHOH–*C*H$_2$CH$_3$], 67.0 [C(2)–CHOH–*C*H$_2$–OBz], 72.3 [C(2)–*C*HOH–CH$_2$–OBz], 74.2 [C(5)–*C*HOH–CH$_2$CH$_3$], 78.9 (C-2), 88.9 (C-5), 128.4 (Ar), 129.8 (Ar), 130.0 (Ar), 133.1 (Ar), 166.8 (C=O) ppm. FT-IR (KBr): $\tilde{\nu}$ = 719, 906, 1124, 1277, 1452, 1714, 2883, 2927, 2961, 3323 cm^{-1}. MS (pos. FAB): m/z = 57 (81%, [C_3H_5O]$^+$), 59 (37%, [C_3H_7O]$^+$), 77 (70%, [Ph]$^+$), 105 (100%, [Ph-CO]$^+$), 277 (5%, [M + H – H_2O]$^+$), 295 (6%, [M + H]$^+$), 317 (8%, [M + Na]$^+$). HRMS: calcd. m/z for $C_{16}H_{21}O_4$ ([M – OH]$^+$) 277.144; found m/z 277.144. $C_{16}H_{22}O_5$: calcd. C 65.29, H 7.53; found C 65.15, H 7.41.

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