Accepted Manuscript

Formation of 3-Acyloxy-γ-butyrolactones from 4-Pentenols in Vanadium-Catalyzed Oxidations

Matthias Amberg , Maike Dönges , Georg Stapf , Jens Hartung

PII: S0040-4020(14)00671-1

DOI: 10.1016/j.tet.2014.05.011

Reference: TET 25560

To appear in: *Tetrahedron*

Received Date: 14 November 2013

Revised Date: 2 May 2014

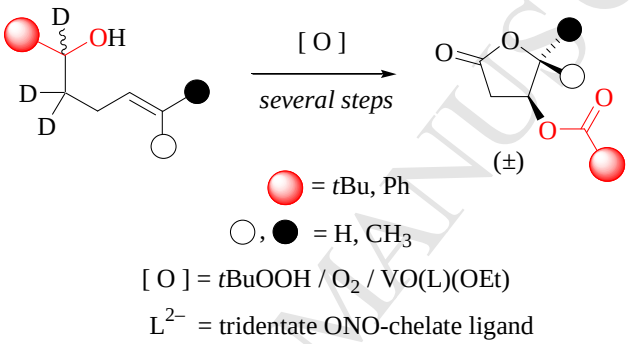
Accepted Date: 3 May 2014

Please cite this article as: Amberg M, Dönges M, Stapf G, Hartung J, Formation of 3-Acyloxy-γ-butyrolactones from 4-Pentenols in Vanadium-Catalyzed Oxidations, *Tetrahedron* (2014), doi: 10.1016/j.tet.2014.05.011.

Formation of 3-Acyloxy-γ-butyrolactones from 4-Pentenols in Vanadium-Catalyzed Oxidations

Matthias Amberg, Maike Dönges, Georg Stapf, and Jens Hartung*

Fachbereich Chemie, Organische Chemie, Technische Universität Kaiserslautern, Erwin-Schrödinger-Straße, D-67663 Kaiserslautern, Germany



Formation of 3-Acyloxy-γ-butyrolactones from 4-Pentenols in Vanadium-Catalyzed Oxidations

Matthias Amberg, Maike Dönges, Georg Stapf, and Jens Hartung*

Fachbereich Chemie, Organische Chemie, Technische Universität Kaiserslautern, Erwin-Schrödinger-Straße, D-67663 Kaiserslautern, Germany

* Corresponding author. Tel.: +49-631-205-2431, Fax: +49-631-205-3921, e-mail: hartung@chemie.uni-kl.de

Keywords: Deuterium labeling; Dioxygen; Oxidation catalysis; Radicals; Tetrahydrofuran; Vanadium.

Abstract: *O*-Acyl derivatives of 3-hydroxy-γ-butyrolactone are formed in up to 20 % yield as by-products from 1-alkyl- and 1-phenyl-substituted 4-pentenols and *tert*-butyl hydroperoxide (TBHP) in vanadium-catalyzed synthesis of (tetrahydrofuran-2-yl)-methanols. The lactones are secondary products formed from (tetrahydrofuran-2-yl)-methanols via hydrogen atom abstraction in positions 4 and 5, as derived from experiments starting from deuterium-labeled alkenols. Stereocenters at tetrahydrofuran carbon 2 and the proximate hydroxyl carbon of the alkanol side chain retain configuration in the course of oxidative tetrahydrofuran conversion. In an atmosphere of nitrogen or argon, no γ-butyrolactone formation occurs, pointing to dioxygen as terminal oxidant for the secondary oxidation. Adding cyclohexa-1,4-diene or γ-terpinene to a solution of a 4-pentenol, TBHP, and a vanadium-catalyst exposed to air inhibits formation of γ-butyrolactones. A third approach to prevent γ-butyrolactones to be formed in oxidative 4-pentenol cyclization uses *cis*-2,6-bis-(methanolate)-piperidine instead of *N*-salicylidene-*ortho*-aminophenol as tridentate auxiliary for the vanadium catalyst.

1. Introduction

Vanadium(V) compounds have a long and successful history in oxidation catalysis for activating peroxides.[1] One of the most prominent reagents for oxidizing carbon-carbon double bonds is *tert*-butyl hydroperoxide (TBHP).[2] The peroxide dissolves in most organic solvents and binds at room temperature to esters of orthovanadic acid to furnish *tert*-butyl peresters (*tert*-butyl peroxy vanadates).[3,4] Like other d^0 transition metal peroxy complexes, peresters of orthovanadic acid are strong oxidants, able to convert alkenes into epoxides,[5] allylic alcohols (2-propenols) into epoxy alcohols,[6] oximes and nitrones into nitro compounds,[7,8] thioethers

into sulfoxides,[9] and bromide into bromine.[10] The principal co-product formed from oxidations with TBHP is *tert*-butanol, a volatile liquid (bp 83 °C), which evaporates from reaction mixtures at room temperature under reduced pressure and can be recovered via fractional distillation for producing *tert*-butyl ethers or carboxylic esters as additives, reagents, or solvents.[11]

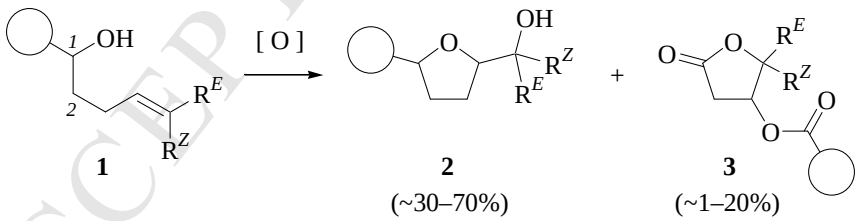
Almost all vanadium compounds for activating TBHP in use today are *O*-esters of orthovanadic acid, having one or two alkoxy groups replaced by a chelate ligand.[12] The auxiliary modifies selectivity of vanadium(V) compounds for stereoselectively epoxidizing 2-propenols (allylic alcohols), 3-butenols (homoallylic alcohols), and oxidatively cyclizing 4-pentenols (dihomoallylic alcohols). The most effective auxiliaries for controlling stereoselectivity in alkenol oxidation by TBHP catalyzed by vanadium(V) complexes are bishydroxamic acids,[6] Schiff-base-derived iminodiols,[13] and *N*-heterocyclic aminodiols.[14]

Apart from stereocontrol, aspects of chemoselectivity increasingly attract attention in vanadium-catalyzed oxidations.[1] As alkenol- and peroxide consumption progresses, many vanadium(V) compounds undergo chemical changes, gradually favoring homolytic side reactions. Chemo-, stereo-, and regioselectivity in oxygen atom transfer from *tert*-butyl peroxy vanadate(V) to nucleophilic acceptors differs from oxidative radical reactions, diversifying the product manifold as substrate conversion approaches synthetically attractive levels.[10,15]

In a project dealing with synthesis of chiral terpene- and acetogenin-derived natural products we started to face the problem that 4-pentenols, such as **1**, required up to three equivalents of TBHP for being quantitatively oxidized.[14] An excess of TBHP in least instances raised yields of (tetrahydrofuran-2-yl)-isopropan-2-ols, for example **2**. Instead, 3-acyloxy-γ-

butyrolactones of the type **3** appeared as unwanted by-products in up to 20 % yield (Scheme 1). At a stage where yields of a tetrahydrofuranylmethanol in a benchmark reaction remained below 40 %, we addressed the origin of oxidative γ-butyrolactone formation from 4-pentenols in a mechanistic study. In the following paragraphs we summarize the major findings from this project and show details how to modify the original experimental procedure for improving yields of tetrahydrofuranylmethanols (e.g. **2**).

The most important results of the study shows that type **3** γ-butyrolactones are secondary oxidation products, formed from (tetrahydrofuran-2-yl)-methanol **2**, an alkyl hydroperoxide, a vanadium complex, *and* dioxygen. Conducting alkenol oxidation by TBHP in an atmosphere of nitrogen or argon, adding a 1,4-dihydroarene as reactive hydrogen atom donor, or using a new *cis*-2,6-bis-(hydroxymethyl)-piperidine-derived vanadium complex in lower concentration for a shorter reaction time almost entirely prevents γ-butyrolactone formation, thus raising yields of (tetrahydrofuran-2-yl)-methanol **2**.

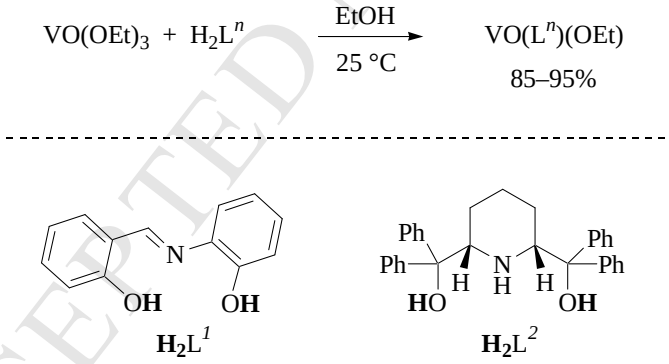


Scheme 1. Products of 4-pentenol oxidation ([O] = *tert*-butyl hydroperoxide in combination with a vanadium complex (vide infra); the open circle stands for an alkyl and an aryl group; R^E, R^Z = hydrogen or methyl).

2. Results and Interpretation

2.1 Vanadium(V) complexes

The compounds we use in natural product synthesis for catalyzing stereoselective oxidative 4-pentenol cyclization by *tert*-butyl hydroperoxide (TBHP) are vanadium(V) complexes of the general formula VO(L^n)(OEt), whereby $(L^n)^{2-}$ denotes a dibasic tridentate iminodiolate prepared from 2-hydroxybenzaldehyde and 2-aminophenol (n = 1),[5] or, more recently, the dianion of *cis*-2,6-bis-(hydroxymethyl)-piperidine (n = 2; Scheme 2).[16] Schiff-base complex VO(L^1)(OEt) is a dark brown, almost black crystalline solid,[5,17] separating from a solution of ethanol as ethanol solvate. 2,6-Bis-(diphenylhydroxymethyl)-piperidine-derived vanadium(V) complex VO(L^2)(OEt) is a pale yellow crystalline compound, adopting a greenish color when exposed for some days to air.[10,18,19,20]



Scheme 2. Synthesis of vanadium(V) compounds VO(L^n)(OEt) (95 % for n = 1, 85 % for n = 2) from auxiliaries H_2L^n [acidic protons being removed in the course of vanadium complexation are printed in bold; VO(L^1)(OEt) crystallizes as EtOH adduct[21] from a solution of ethanol, referred to in the Experimental part as VO(L^1)(OEt)(EtOH)].

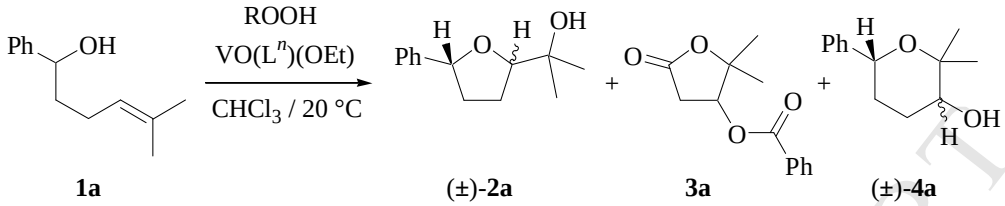
2.2 Oxidation of 4-pentenols by *tert*-butyl hydroperoxide

According to a standard experimental set up developed for oxidizing alkenol **1** by *tert*-butyl hydroperoxide (TBHP), a 0.16-molar solution of 1-phenyl-5-methylhex-4-en-1-ol (**1a**) in chloroform, the most practical solvent for this purpose,[13] is treated with 1.5 equivalents of TBHP, commercially obtained as 5.5-molar solution in nonane, and 10 mol% of Schiff-base complex VO(L^1)(OEt), or alternatively, 10 mol% of *cis*-2,6-bis-(hydroxymethyl)-piperidine complex VO(L^2)(OEt). Alkenol **1a** is quantitatively consumed within 72 hours at a temperature of 20–24 °C, providing 2-(5-phenyltetrahydrofuran-2-yl)-propan-2-ol (**2a**) as major product, with a strong stereochemical preference for the cis-isomer. The reaction yields in addition 13 % of 6-phenyl-2,2-dimethyltetrahydropyran-3-ol (**4a**) as approximately equimolar mixture of cis/trans-stereoisomers, and 4–11 % of γ-butyrolactone **3a** (Table 1, entries 1 and 3).[17,22]

Without externally added Lewis-acids VO($L^{1–2}$)(OEt), no oxidative alkenol turnover occurs. Changing the terminal oxidant to cumene hydroperoxide (CHP) affords (tetrahydrofuran-2-yl)-isopropanol **2a**, γ-butyrolactone **3a**, and tetrahydropyranol **4a** in similar distribution of stereoisomers, as oxidation of alkenol **1a** by TBHP (Table 1, entries 2 and 4). From this information we concluded that γ-butyrolactone **3a** forms independently from the chemical nature of the alkyl hydroperoxide and from the type of vanadium(V) complex used for activating the terminal oxidant.

Table 1. Products formed from alkyl hydroperoxide-mediated oxidation of prenyl-type alkenol

1a, catalyzed by two different oxovanadium complexes



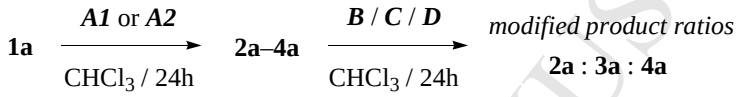
1a (±)-**2a** **3a** (±)-**4a**

entry	VO(L^n)(OEt) [a]	ROOH	**2a** / % (*cis*:*trans*)	**3a** / %	**4a** / % (*cis*:*trans*)
1	VO(L^1)(OEt)	TBHP[b]	60 (96:4)	5	13 (57:43)
2	VO(L^1)(OEt)	CHP[c]	74 (95:5)	7	12 (56:44)
3	VO(L^2)(OEt)	TBHP	26 (>96:4)	11	13 (45:55)
4	VO(L^2)(OEt)	CHP	35 (96:4)	4	12 (53:47)

[a] General conditions: $c_0^{\mathbf{2a}}$ = 0.16 M; c_0^{ROOH} = 0.23 M; 72 h reaction time; 10 mol% of VO(L^1)(OEt) or VO(L^2)(OEt). [b] 5.5 molar solution in nonane. [c] 80 % by weight.

In a screening for parameters promoting γ-butyrolactone formation we found that larger surface areas of reaction solutions improve yields of cyclic ester **3a**. The chosen standard flask gave rise to a rather large contact area between the liquid and the gas phase above the solution. Charging this glassware with chloroform, alkenol **1a**, 1.5 equivalents of TBHP, and 10 mol% of VO(L^1)(OEt), and allowing the solution to stir for 24 hours at 20 °C, provides 80 % of tetrahydrofuranylisopropanol **2a**, 15 % of tetrahydropyranol **4a**, and 5 % of γ-butyrolactone **3a** (Scheme 3, procedure ***A1***). Exposing this mixture for 24 hours to air does not change the ratio of products **2a**–**4a** (procedure ***B***). Treating the solution obtained from procedure ***A1*** for 24 hours with 1.5 equivalents of TBHP in an atmosphere of argon (procedure ***C***) causes the fraction of tetrahydrofuran **2a** to decrease by approximately a quarter, while the percentage of

lactone **3a** increases by almost the same amount. The fraction of tetrahydropyranol **4a** remains unchanged. Adding TBHP to the solution obtained from procedure ***A1***, and exposing this reaction mixture to air (procedure ***D***), reduces the fraction of tetrahydrofuran **2a**, increases the amount of lactone **3a**, and leaves the ratio of tetrahydropyranol **4a** approximately unaffected. From these results we concluded that TBHP in combination with air modifies VO(L^1)(OEt) to a vanadium compound, hereafter referred to as $[V]_{mod}$ (Scheme 4), which induces in a second step oxidative conversion of one of the products into γ-butyrolactone **3a**.



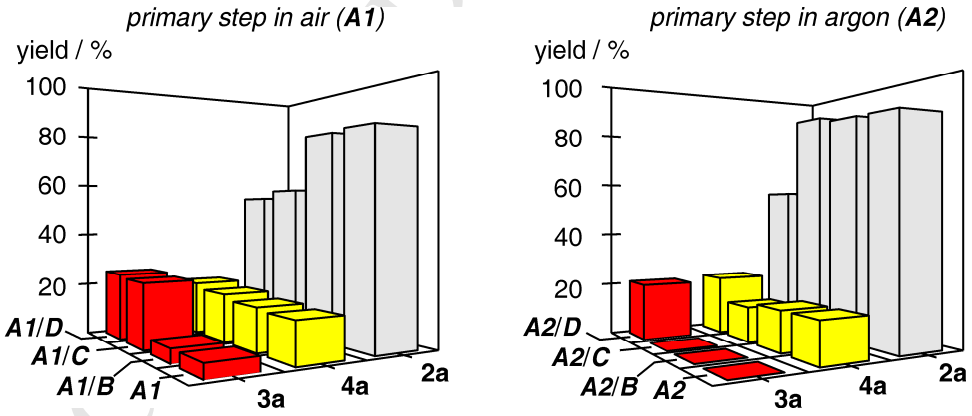
A1 = TBHP / air / VO(L^1)(OEt)

A2 = TBHP / argon / VO(L^1)(OEt)

B = air / [V]

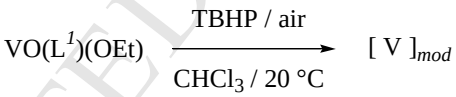
C = TBHP / argon / [V]

D = TBHP / air / [V]



Scheme 3. Effect of oxovanadium(V) complex preconditioning on γ-butyrolactone formation (all reactions were performed in chloroform at 20 °C; Ar = argon; TBHP = *tert*-butyl hydroperoxide; air = laboratory atmosphere; [V] denotes a vanadium compound formed from VO(L^1)(OEt) in runs ***A1*** or ***A2***; relative product ratios determined via GC).

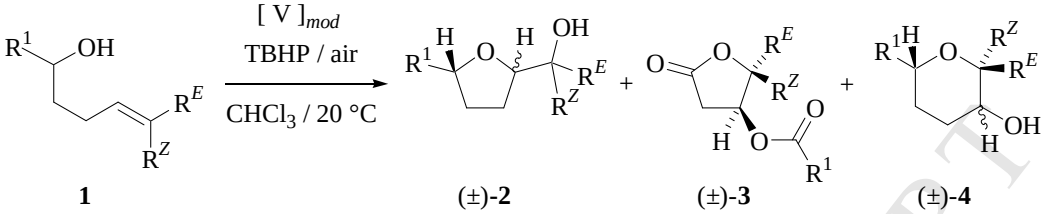
To address the role of dioxygen in oxidative γ-butyrolactone formation, we stirred in a second set of experiments alkenol **1a**, VO(L^1)(OEt), and TBHP for 24 hours in an atmosphere of argon (Scheme 3, procedure ***A2***). The reaction provides an 85/15-mixture of tetrahydrofuranylmethanol **2a** and tetrahydropyranol **4a** as sole identifiable products (GC-MS-analysis). Allowing this solution to rest for 24 hours in an atmosphere of air (procedure ***B***), or adding 1.5 equivalents of TBHP in an atmosphere of argon (procedure ***C***), induces no obvious chemical changes. Exposing the solution obtained from experiment ***A2*** to air *and* TBHP (procedure ***D***) furnishes γ-butyrolactone **3a** by lowering the fraction of tetrahydrofuran **2a** by almost the same degree, leaving the fraction of tetrahydropyranol **4a** almost unchanged. From these results we concluded that dioxygen *and* TBHP are essential for obtaining γ-butyrolactone **3a** from cyclic ethers **2a** and/or **4a**.



Scheme 4. Oxidative preconditioning of Schiff-base complex VO(L^1)(OEt) (used as EtOH-solvate) for improving efficiency in γ-butyrolactone formation from 4-pentenols (cf. Table 2).

Using $[V]_{mod}$ as catalyst for oxidation of alkenols **1b**–**d** by TBHP furnishes γ-butyrolactones differing in substitution at position 4 and the hydroxyl oxygen (Scheme 4; Table 2, entries 2–4). These results show that γ-butyrolactones are generally by-products in vanadium-catalyzed oxidations of 1-substituted 4-pentenols by TBHP.

Table 2. Products of 4-pentenol oxidation by TBHP under aerobic conditions [a]



1 (±)-**2** (±)-**3** (±)-**4**

entry	**1**–**4**	R^1	R^E	R^Z	**2** / % (*cis*:*trans*)	**3** / %	**4** / % (*cis*:*trans*)
1	**a**	Ph	CH_3	CH_3	59 (96:4)	11	17 (51:49)
2	**b**	Ph	CH_3	H	54 (40:60)	11	8 (<5:95)
3	**c**	Ph	H	H	38 (40:60)	5	– [b]
4	**d**	*t*Bu	CH_3	CH_3	56 (>95:5)	16	11 (<5:95)

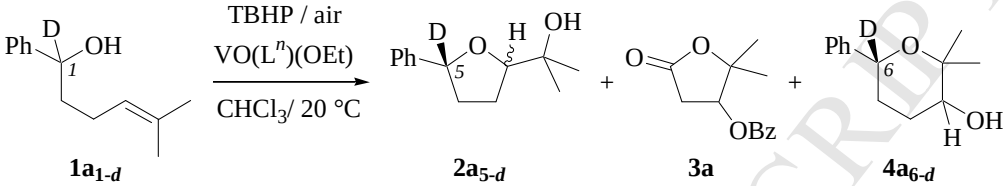
[a] For [V]$_{mod}$ refer to Scheme 4 and the Experimental; TBHP = *tert*-butyl hydroperoxide. [b] Not detected (GC, ^{1}H-NMR).

2.3 Oxidation of deuterated alkenols

γ-Butyrolactone **3a** ($C_{13}H_{14}O_4$) comprises three additional oxygen atoms and four fewer hydrogen atoms compared to alkenol **1a** ($C_{13}H_{18}O$). To identify carbon-hydrogen bonds being broken in oxidative γ-butyrolactone formation, we prepared deuterated 5-methyl-1-phenylhexen-1-ols **1a**$_{1\text{-}d}$, **1a**$_{2,2\text{-}d_2}$ and **1a**$_{3,3\text{-}d_2}$ and treated the compounds with TBHP, VO(L$^{1-2}$)(OEt) in solutions of chloroform exposed to air (Tables 3–5). For synthetic reasons we extended reaction times and successively added further aliquots of TBHP. From such reaction mixtures we isolated by chromatography tetrahydrofurans **2a**$_{5\text{-}d}$, **2a**$_{4,4\text{-}d_2}$, and **2a**$_{3,3\text{-}d_2}$ and tetrahydropyrans **4a**$_{6\text{-}d}$, **4a**$_{5,5\text{-}d_2}$, and **4a**$_{4,4\text{-}d_2}$, showing deuterium labeling at positions expected according to the general mechanism describing oxygen atom transfer to the π-bond of substrate

1a in vanadium(V)-catalyzed reactions.[17]

Table 3. Products formed from vanadium(V)-catalyzed oxidation of alkenol $\mathbf{1a_{1\text{-}d}}$ [a,b]

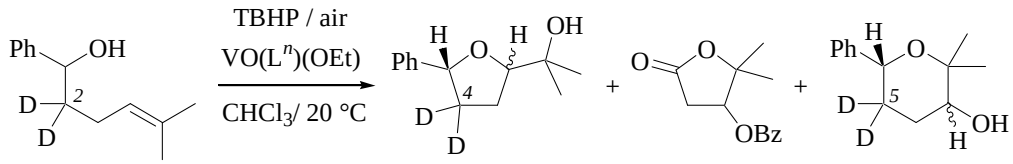


$\mathbf{1a_{1\text{-}d}}$ $\mathbf{2a_{5\text{-}d}}$ **3a** $\mathbf{4a_{6\text{-}d}}$

entry	*n*	*t* / h	$\mathbf{2a_{5\text{-}d}}$ / % (*cis*:*trans*)	**3a** / %	$\mathbf{4a_{6\text{-}d}}$ / % (*cis*:*trans*)
1	1	48	71 (93:7)	3	14 (46:54)
2	1	72	64 (94:6)	4	9 (46:54)
3	1	168 [c]	47 (98:2)	12	12 (50:50)
4	2	48	47 (95:5)	2	8 (49:51)
5	2	72	40 (95:5)	2	7 (42:58)
6	2	168 [c]	21 (>99:1)	6	8 (44:56)

[a] Systematic for indexing of deuterated compounds: $\mathbf{n_{x,x\text{-}d_m}}$ **n** refers to compound number, **x** to location of a deuterium atom (***d***), and **m** the number of deuterium atoms present in the molecule. [b] general conditions: c_0 ($\mathbf{1a_{1\text{-}d}}$) = 0.12 M, 10 mol% of VO(L^n)(OEt); VO(L^1)(OEt) was used as ethanol adduct; c_0^{TBHP} = 0.18 M. [c] Addition of additional 1.5 equiv. of TBHP after 72 hours, otherwise identical conditions as in footnote [b].

Table 4. Products of vanadium(V)-catalyzed oxidation of alkenol $\mathbf{1a_{2,2\text{-}d_2}}$ [a,b]



1a$_{2,2\text{-}d_2}$ (±)-**2a**$_{4,4\text{-}d_2}$ **3a** (±)-**4a**$_{5,5\text{-}d_2}$

entry	*n*	*t* / h	**2a**$_{4,4\text{-}d_2}$ / % (*cis*:*trans*)	**3a** / %	**4a**$_{5,5\text{-}d_2}$ / % (*cis*:*trans*)
1	1	48	56 (93:7)	9	13 (41:59)
2	1	72	44 (94:6)	6	8 (46:54)
3	1	168 [c]	24 (96:4)	21	13 (45:55)
4	2	48	17 (97:3)	2	6 (34:66)
5	2	72	36 (96:4)	– [d]	8 (38:62)
6	2	168 [c]	8 (98:2)	15	9 (39:61)

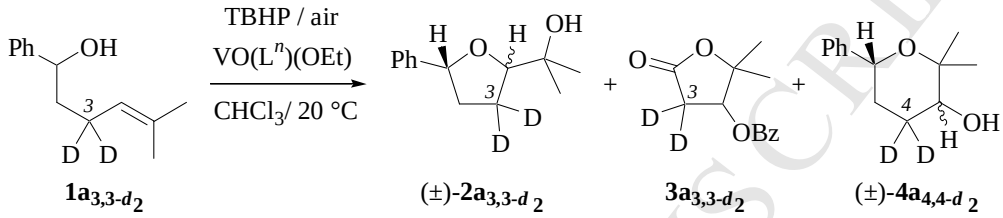
[a] Systematic for indexing of deuterated compounds, see Table 3. [b] General conditions: c_0 (**1a**$_{2,2\text{-}d_2}$) = 0.12 M, 10 mol% of VO(L^n)(OEt); VO(L^1)(OEt) was used as ethanol adduct; c_0^{TBHP} = 0.18 M. [c] Addition of additional 1.5 equiv. of TBHP after 72 hours, otherwise identical conditions as in footnote [b]. [d] Not detected.

Proton-NMR and carbon-13 NMR-data of the γ-butyrolactones show that deuterated alkenols **1a**$_{1\text{-}d}$ and **1a**$_{2,2\text{-}d_2}$ exclusively furnish the non-deuterated product **3a**. Simplified proton-NMR fine structures and a quintet-splitting of 21.4 Hz of the resonance of carbon 3 showed that the γ-butyrolactone obtained from alkenol **1a**$_{3,3\text{-}d_2}$ is the twofold deuterated product **3a**$_{3,3\text{-}d_2}$ (Table 5).

The results obtained from oxidation of deuterated derivatives of prenyl-type substrate **1a**, in reactions catalyzed by Schiff-base complex VO(L^1)(OEt) and *cis*-2,6-bis-(hydroxymethyl)-piperidine complex VO(L^2)(OEt) in summary show that two hydrogens from C2 and one

hydrogen from C1 are removed in the course of oxidative γ-butyrolactone formation, leaving to the hydroxyl group as putative fourth position for hydrogen atom abstraction (vide infra).

Table 5. Products of vanadium(V)-catalyzed oxidation of alkenol **1a**$_{3,3\text{-}d_2}$ [a,b]



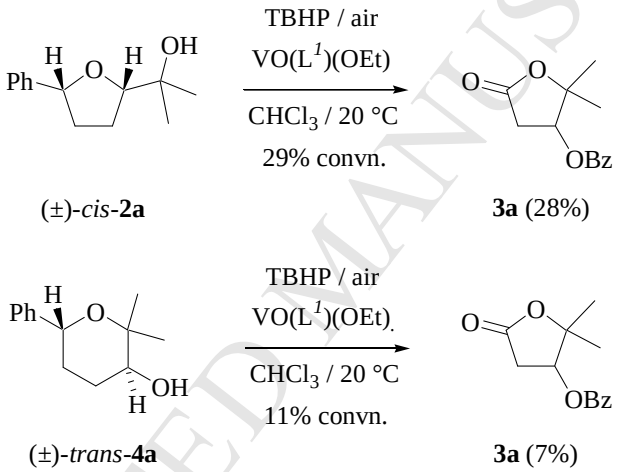
entry	*n*	*t* / h	**2a**$_{3,3\text{-}d_2}$ / % (*cis*:*trans*)	**3a**$_{3,3\text{-}d_2}$ / %	**4a**$_{4,4\text{-}d_2}$ / % (*cis*:*trans*)
1	1	48	30 (97:3)	1	7 (44:56)
2	1	72	52 (96:4)	4	9 (36:64)
3	1	168 [c]	27 (97:3)	13	8 (47:53)

[a] Systematic for indexing of deuterated compounds, see Table 3. [b] General conditions: c_0 (**1a**$_{3,3\text{-}d_2}$) = 0.12 M, 10 mol% of VO(L^n)(OEt); VO(L^1)(OEt) was used as ethanol solvate complex; c_0^{TBHP} = 0.18 M. [c] Addition of additional 1.5 equiv. of TBHP after 72 hours, otherwise identical conditions as in footnote [b].

2.4 Oxidation of primary products

The results summarized in sections 2.2 and 2.3 point to (tetrahydrofuran-2-yl)-propanol **2a** as progenitor of 3-acyloxy-γ-butyrolactone **3a**. To test this hypothesis, we treated the cis-isomer of 5-phenyl-(tetrahydrofuran-2-yl)-2-isopropanol **2a** with TBHP and oxovanadium(V) Schiff-base complex VO(L^1)(OEt), and exposed this solution for 72 hours to air. Under such

conditions, 29 % of tetrahydrofuran **2a** are oxidatively converted into 28 % of γ-butyrolactone **3a** (Scheme 5, top). The configuration of recovered starting material **2a** is exclusively cis. In a second experiment, we treated the trans-isomer of tetrahydropyranol **4a** accordingly, providing 7 % of γ-butyrolactone **3a** and 89 % of recovered starting material showing exclusively trans-configuration (Scheme 5, bottom). No γ-butyrolactone **3a** forms when cyclic ethers *cis*-**2a** and *trans*-**4a** are stirred without externally added VO(L[1])(OEt) in solutions of TBHP exposed to air.



Scheme 5. γ-Butyrolactone formation from cyclic ethers *cis*-**2a** and *trans*-**4a**.

For testing the idea that the γ-butyrolactone forming reaction involves autoxidation, we exposed solutions of cyclic ethers *cis*-**2a** and *trans*-**4a** and azobisisobutyronitrile (AIBN) in α,α,α-trifluorotoluene (TFT) at a temperature of 80 °C to air. The experiments afforded cyclic ester **3a** in 21 % yield from *cis*-**2a**, and in 7 % yield starting from *trans*-**4a**.

The results obtained from oxidative conversion of cyclic ethers in summary show that

tetrahydrofuranylmethanol *cis*-**2a** *and* tetrahydropyranol *trans*-**4a** are progenitors of γ-butyrolactone **3a**.

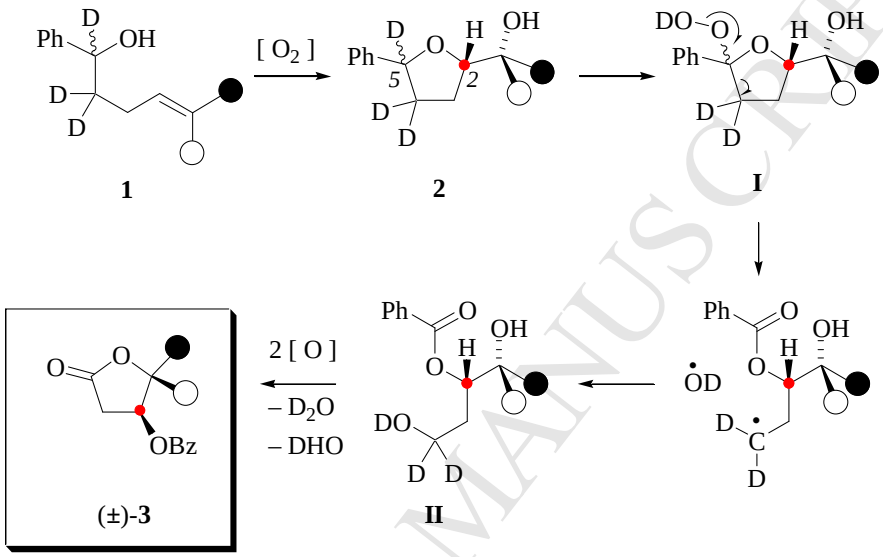
2.5 Mechanistic proposal

From the information summarized in the preceding paragraphs we derived a mechanism for describing transformation of alkenol **1** into γ-butyrolactone **3** (Schemes 6 and 7). In the first step, alkenol **1** is stereoselectively oxidized by a *tert*-butylperoxy vanadium(V) complex into substituted (tetrahydrofuran-2-yl)-methanol *cis*-**2** as major product and a cis/trans-mixture of tetrahydropyranol **4** as minor product.[13,17]

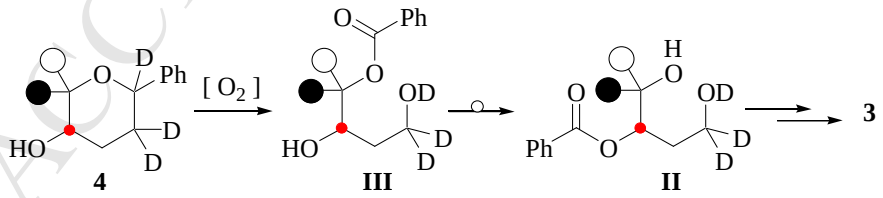
(5-Phenyltetrahydrofuran-2-yl)-methanols insert dioxygen preferentially at the benzylic carbon-hydrogen bond, to afford tertiary ether hydroperoxide **I** (Scheme 6).[23] Homolytically breaking the oxygen-oxygen bond in hydroperoxide **I** gives an tetrahydrofuranyl-5-oxyl radical, which induces fragmentation of the tetrahydrofuran ring. The β-fragmentation is thermochemically driven by relief of the tetrahydrofuran strain and electron delocalization in the ester group and gives rise to a vicinal radical pair. Combining the radical pair furnishes acyloxydiol **II**. For explaining quantitative loss of deuterium atoms bound to positions 1 and 2 of alkenol **1a** (vide supra), the primary alcohol **II** is successively dehydrogenated to furnish γ-butyrolactone **3** as terminal product. The mechanism of autoxidative γ-butyrolactone **3a** formation extends to conversion of tetrahydropyranol *trans*-**4a**, by introducing a 1,2-benzoyl group migration, converting tertiary ester **III** into primary ester **II** (Scheme 7).

An alternatively possible scenario leading from tetrahydrofuranylmethanol **2** via an

intermediate 4,5-dihydrofuran in a singlet-oxygen-mediated oxidation to a progenitor of g-butyrolactone **3** cannot be entirely excluded at this point.[24] If this reaction occurs, the dihydrofuran concentration remains small, since we did not detect intermediates of this kind via GC-MS.



Scheme 6. Proposed pathway for γ-butyrolactone formation from 2-(5-phenyltetrahydrofuran-2-yl)-methanols **2** {roman numbers refer to hypothetical intermediates, ○ and ● = H or CH_3; the red spot at C2 marks the stereocenter that remains unchanged (vide infra); [O] = TBHP/VO(L^n)(OR), *n* = 1, 2; R = e.g. Et or *t*Bu}.



Scheme 7. Proposed pathway for γ-butyrolactone formation from 6-phenyltetrahydropyran-3-ols **4** (roman numbers refer to hypothetical intermediates, ○ and ● = H or CH_3).

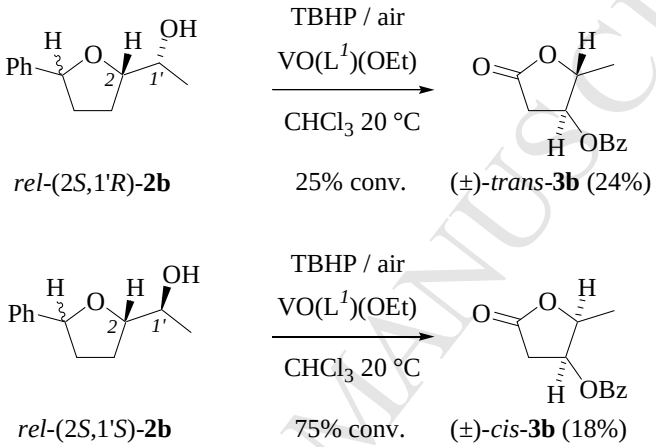
For investigating the role of vanadium(V) complexes as autoxidation initiators, we analyzed products of cumene hydroperoxide decomposition by VO(L^1)(OEt), vanadium(IV) analogue VO(HL^1)$_2$[25] as putative model for [V]$_{mod}$.[26,27] Such controls clarified that cumene hydroperoxide quantitatively decomposes in solutions of VO(L^1)(OEt) or VO(HL^1)$_2$ in chloroform, leading to (2-hydroxy-2-propyl)-benzene, acetophenone, styrene, and isopropylbenzene. Acetophenone forms by homolytically breaking the oxygen-oxygen bond of cumene hydroperoxide to afford the cumyloxyl radical.[28,29] Alkoxyl radicals, such as the cumyloxyl radical, abstract a hydrogen atom preferentially from the weakest carbon-hydrogen bond, which is the benzylic position in 5-phenyltetrahydrofuranylisopropanol **2a**. The controls in summary provide an explanation for the role of vanadium complexes in oxidative γ-butyrolactone formation.[30]

2.6 Mechanistic implications

2.6.1 Retention of configuration at tetrahydrofuran carbon 2 and the center of chirality in the alkanol side chain

The proposed mechanism of γ-butyrolactone formation implies that stereocenters at tetrahydrofuran carbon 2 and the proximate exocyclic hydroxyl carbon of type **2b**-(tetrahydrofuran-2-yl)-ethan-1-ols retain configuration. To test this prediction, we treated the diastereomer of 1-(5-phenyltetrahydrofuran-2-yl)-ethan-1-ol (**2b**) showing relative (2*S*,1'*R*)-configuration, abbreviated hereafter as *unlike*-stereoisomer, with TBHP and VO(L^1)(OEt) in a solution exposed to air. This experiment furnishes diastereomerically pure γ-butyrolactone

trans-**3b**, whereas the *like*-stereoisomer of **2b** affords cis-configured lactone *cis*-**3b** (Scheme 8). From this information we concluded that substrates *rel*-(2*S*,1'*R*)-**2b** and *rel*-(2*S*,1'*S*)-**2b** retain configuration at carbons 2 and 1', as tetrahydrofuran rings are oxidatively broken and intermediates converted into γ-butyrolactones *cis*/*trans*-**3b** (cf. Scheme 6).



Scheme 8. Oxidation of side chain stereoisomers of 5-phenyl-(tetrahydrofuran-2-yl)ethanol **2b**.

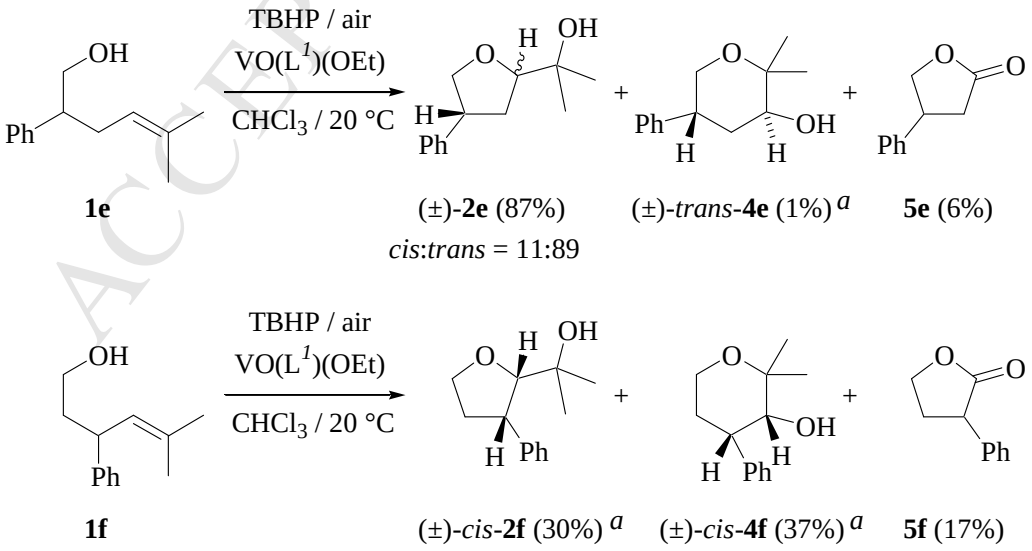
2.6.2 Oxidation of prenyl-type 4-pentenols bearing phenyl groups in positions 2 and 3

The proposed mechanism of oxidative (tetrahydrofuran-2-yl)-methanol conversion into γ-butyrolactones of the type **3** implies that ether hydroperoxides selectively form by inserting dioxygen into the carbon-hydrogen bond at position 5. The radical stabilizing effect of the phenyl group in **2a** and the *tert*-butyl group in **2d** is larger than the stabilizing effect of the 2-hydroxy-2-propyl group, given electron withdrawing contribution of the β-hydroxyl group.

Isomers of **2a** bearing a phenyl group at carbons 3 or 4, according to this interpretation, should provide other secondary oxidation products than type **3**-γ-butyrolactones.

In order to assess selectivity in γ-butyrolactone formation from other substrates than 1-substituted 4-pentenols, we stirred a solution of 2-phenyl-5-methylhex-4-en-1-ol (**1e**), TBHP, and 10 mol% of VO(L[1])(OEt) in chloroform, while being exposed to air (Scheme 9). From this mixture we isolated 2-(4-phenyltetrahydrofuran-2-yl)-propan-2-ol (**2e**) in a yield of 87 % as 11/89-mixture of cis/trans-isomers, traces of tetrahydropyranol *trans*-**4e**, and 6 % of 3-phenyl-γ-butyrolactone **5e**. Oxidation of 3-phenyl-5-methylhex-4-en-1-ol (**1f**) performed under similar conditions furnished 30 % of *cis*-2-(3-phenyltetrahydrofuran-2-yl)-propan-2-ol *cis*-(**2f**) and 37 % *trans*-3-phenyl-2,2-dimethyltetrahydropyran-3-ol *cis*-(**4f**), besides 17 % of 2-phenyl-γ-butyrolactone **5f**.

The results from oxidations of 1-, 2- and 3-substituted 4-pentenols **1a**, **1e** and **1f** in summary show that selectivity in oxidative γ-butyrolactone formation is guided by strengths of α-carbon-hydrogen bonds in **2a**, **2e**, and **2f**, which is in line with an autoxidation mechanism.



Scheme 9. Oxovanadium(V)-catalyzed oxidation of 2- and 3-phenyl-substituted prenyl-type 4-pentenols **1e**–**f**. [a] Diastereomerically pure (proton-NMR).

2.6.3 Preventing γ-butyrolactone formation in 2-(tetrahydrofuran-2-yl)-isopropanol synthesis from prenyl-type 4-pentenols

For preventing γ-butyrolactones to be oxidatively formed, we devised three modifications of the original experimental set up.

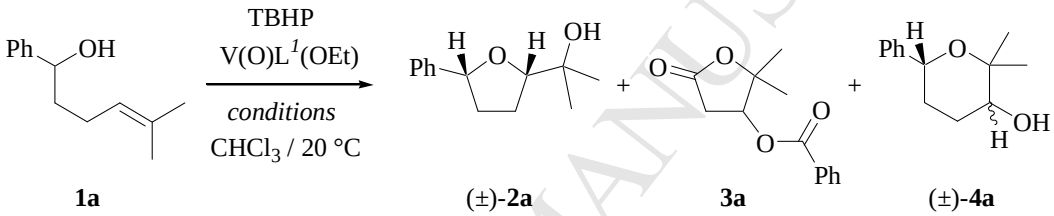
In the first modification we excluded air. Oxidizing alkenol **1a** by TBHP in an atmosphere of nitrogen, under otherwise standard conditions, raised the yield of (tetrahydrofuran-2-yl)-propanol **2a** by 5 % to 65 %, without providing γ-butyrolactone **3a** (Table 6, entry 1).

The second modification addressed the proposed free radical-type hydroperoxidation in α-position to the tetrahydrofuran oxygen of **2a**. For disrupting radical chain reactions, we added hydrogen atom donors, such as cyclohexa-1,4-diene (CHD) or naturally occurring derivative γ-terpinene (γ-Ter),[31] to solutions of alkenol **1a**, TBHP, and VO(L^1)(OEt) kept in an atmosphere of air. From such solutions we isolated 70–74 % of (5-phenyltetrahydrofuran-2-yl)-2-propanol **2a** and 1–2 % of γ-butyrolactone **3a** (Table 7, entries 2–3).

The third modification related to a change of the catalyst, from Schiff-base complex VO(L^1)(OEt) to piperidine-derived complex VO(L^2)(OEt).[16] The latter reagent is a stronger Lewis-acid, able to more selectively activate TBHP when used in lower concentration, and applied for shorter reaction times, compared to vanadium complex VO(L^1)(OEt). Oxidation of

1-phenyl-5-methylhex-4-en-1-ol (**1a**) by TBHP catalyzed by VO(L^2)(OEt) is complete at room temperature within six hours, leading to a product mixture composed of 80 % of *cis*-(5-phenyltetrahydrofuran-2-yl)-2-propanol *cis*-**2a**, 19 % of tetrahydropyranol **4a** as 37/63-mixture of cis/trans-stereoisomers, and only 0.8 % γ-butyrolactone **3a**, as exemplified in a GC-screening (Supplementary data).

Table 6. Products formed from phenylmethylhexenol **1a** in anaerobic or reductive conditions.[a]



1a (±)-**2a** **3a** (±)-**4a**

entry	conditions	**2a** / % (*cis*:*trans*)	**3a**/ %	**4a** / % (*cis*:*trans*)
1	N_2	65 (94:6)	– [b]	13 (45:55)
2	CHD / air	74 (94:6)	2	12 (35:65)
3	γ-Ter / air	70 (94:6)	1	17 (32:68)

[a] VO(L^1)(OEt) was used as ethanol-solvate complex; 72 h reaction time; 5 mol% of vanadium compound. [b] Not detected.

3. Concluding remarks

3-Acyloxy-γ-butyrolactones are secondary products, formed from (tetrahydrofuran-2-yl)-methanols, the primary products of oxidative 4-pentenol cyclization by TBHP, and dioxygen in vanadium-catalyzed reactions. Excluding air prevents oxidative consumption of

(tetrahydrofuran-2-yl)-methanols, similar to adding reactive hydrogen atom donors, such as cyclohexa-1,4-diene or γ-terpinene. The third approach to prevent oxidative γ-butyrolactone formation uses *cis*-2,6-bis-(methanolate)-piperidine instead of *N*-salicylidene-*ortho*-aminophenol as tridentate auxiliary for the vanadium catalyst. This modification furnishes a stronger Lewis-acidic vanadium(V) reagent, able to catalyze (tetrahydrofuran-2-yl)-methanol formation from a 4-pentenol and TBHP at lower concentration in shorter time. Using one of the three modifications allows peroxide decomposition to adhere more effectively to the oxygen atom transfer pathway, preventing oxidative radical reactions to become significant.

Apart from addressing a significant chemoselectivity problem in vanadium-catalyzed oxidation we noticed that elementary reactions used for describing oxidative degradation of 5-substituted tetrahydrofuranyl-2-methanols (e.g. **2**) allow rationalizing stereoselectivity in a method used for some time to determine absolute configuration of natural products. Ozonolyzing chiral dihydrofurans, furanocoumarins, and isoprenoids furnishes enantiomerically pure 3-acyloxy- or 3-hydroxyl-substituted 4,4-dimethyl-γ-butyrolactones. The configuration of the aliphatic α-carbon, for example, of a chiral furanocoumarin, in this approach, is correlated to the absolute configuration of the lactone formed by ozonolysis.[32,33,34] The intermediate justifying this stereochemical correlation is the hydroxyaldehyde derived from **II**, relating configuration of carbon 2 in tetrahydrofuran **2a** to the stereocenter of the dihydrofuran-natural product.

A second stereochemical aspect deserving comment by the end of this article refers to configuration of the product obtained from 3-phenyl-5-methylhex-4-en-1-ol (**1f**) and TBHP, catalyzed by VO(L^1)(OEt). In an earlier study we described this product erroneously as 2,3-

trans due to a flaw in the chosen analytic method.[13] Originally, we used a sample as reference for GC-analysis prepared from alkenol **1f** and *meta*-chloroperoxybenzoic acid, leading to the 2,3-trans-stereoisomer of **2f**. The 2,3-trans- and the 2,3-cis-stereoisiomer of **2f** unfortunately show similar retention times under conditions used for GC-analysis. In the present study we isolated and spectroscopically characterized products obtained from oxidation of alkenol **1f** and TBHP, catalyzed by VO(L^1)(OEt), showing that the correct configuration of the products is *cis*-**2f** and *cis*-**4f** (Scheme 9).

4. Experimental

4.1. General

For general laboratory practice and instrumentation see ref.[35] and the Supplementary Data.

4.2 Oxidations catalyzed by vanadium(V) Schiff-base complex and TBHP as terminal oxidant

4.2.1 General method. A solution of TBHP (136 µL, 5.5 M in nonane) was added to a solution of VO(L^1)(OEt) (18.5 mg, 50 µmol; used as ethanol solvate as obtained from synthesis; H_2L^1 = *N*-salicylidene 2-aminophenol) in chloroform (1.5 mL). The resulting mixture was heated for 1 minute at 60 °C and treated at a temperature of 20 °C with a solution of alkenol **1** in chloroform (1.5 mL). The reaction mixture was stirred for 72 hours at a temperature of 20 °C and filtrated afterwards through a pad of neutral aluminium oxide. Organic products adsorbed were washed with ethyl acetate (5 mL) from the pad of aluminium oxide. Combined filtrate and washings were concentrated at a bath temperature of 40 °C in an aspirator vacuum to leave an oily residue, which was purified by flash-chromatography using

the eluent specified in sections 4.2.2–4.2.4.

*4.2.2. Oxidation of 5-methyl-1-phenylhex-4-en-1-ol (**1a**).* 5-Methyl-1-phenylhex-4-en-1-ol (**1a**): 95.2 mg (500 µmol). Eluent used for chromatographic purification: petroleum ether/ethyl acetate = 8:2 (*v*/*v*). *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol (**2a**).* Yield: 61.6 mg (299 µmol, 60 %), 96/4-mixture of cis/trans isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol (**4a**).* Yield: 13.6 mg (66.1 µmol, 13 %), 57/43-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**).* Yield: 6.06 mg, (25.9 µmol, 5 %).

*4.2.3. Oxidation of 5-methyl-2-phenylhex-4-en-1-ol (**1e**).* 5-Methyl-2-phenylhex-4-en-1-ol (**1e**): 94.5 mg (497 µmol). Eluent used for chromatographic purification: petroleum ether/ethyl acetate = 2:1 (*v*/*v*). *2-(4-Phenyltetrahydrofuran-2-yl)-propan-2-ol (**2e**).* Yield: 89 mg (431 µmol, 87 %), 11/89-mixture of cis/trans-isomers). *trans-2,2-Dimethyl-5-phenyltetrahydropyran-3-ol trans-(**4e**).* Yield: 1 mg (4.8 µmol, 1 %). *4-Phenyl-2(3H)-dihydrofuranone (**5e**).* Yield: 5 mg, (30.8 µmol, 6 %).

*4.2.4. Oxidation of 5-methyl-3-phenylhex-4-en-1-ol (**1f**).* 5-Methyl-3-phenylhex-4-en-1-ol (**1f**): 96.0 mg (504 µmol). Eluent used for chromatographic purification: petroleum ether/ethyl acetate = 2:1 (*v*/*v*). *cis-2-(3-phenyltetrahydrofuran-2-yl)-propan-2-ol cis-(**2f**).* Yield: 31 mg (150 µmol, 30 %). *cis-2,2-Dimethyl-4-phenyltetrahydropyran-3-ol cis-(**4f**).* Yield: 39 mg (189 µmol, 38 %). *3-Phenyl-2(3H)-dihydrofuranone (**5f**).* Yield: 14 mg, (86.3 µmol, 17 %).

4.3 Oxidations catalyzed by Piperidine-Derived Oxovanadium(V) Complex VO(L^2)(OEt) and TBHP as terminal oxidant

*4.3.1 Oxidation of 5-methyl-1-phenylhex-4-en-1-ol (**1a**) – 72 hours.* To a solution of VOL^2(OEt) [H_2L^2 = *cis*-2,6-bis(diphenylmethanol)piperidine] (28.0 mg, 50 µmol) in chloroform (3 mL) was added a solution of TBHP (5.5 M in nonane) (273 µL, 1.50 mmol). The mixture was stirred for 3 minutes at 60 °C and was treated at 20 °C with a solution of 5-methyl-1-phenylhex-4-en-1-ol (**1a**) (190 mg, 1.00 mmol) in chloroform (3 mL). The reaction mixture was stirred at a temperature of 20 °C for 72 hours and filtrated through a pad of neutral aluminium oxide. Organic products were washed from the aluminium oxide with ethyl acetate (15 mL). Combined filtrate and washings were concentrated at a bath temperature of 40 °C in an aspirator vacuum to leave an oily residue, which was purified by flash-chromatography [diethyl ether/pentane = 1:1 (*v*/*v*)]. *2-(5-phenyltetrahydrofuran-2-yl)-propan-2-ol (**2a**).* Yield: 53.6 mg (260 µmol, 26 %), 96/4 mixture of cis/trans-isomers. *2,2-dimethyl-6-phenyltetrahydropyran-3-ol (**4a**).* Yield: 33.8 mg (130 µmol, 13 %), 45/55-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**).* Yield: 26.1 mg, (110 µmol, 11 %).

*4.3.2 Oxidation of 5-methyl-1-phenylhex-4-en-1-ol (**1a**) – 6 hours.* To a solution of VOL^2(OEt) [H_2L^2 = *cis*-2,6-bis(diphenylmethanol)piperidine] (27.3 mg, 50 µmol) in chloroform (3 mL) was added a solution of TBHP (5.5 M in nonane) (273 µL, 1.50 mmol). The mixture was stirred for 5 minutes and was treated at 20 °C with a solution of 5-methyl-1-phenylhex-4-en-1-ol (**1a**) (190 mg, 1.00 mmol) in chloroform (3.3 mL). The reaction mixture

was stirred at 20 °C for 6 hours and filtrated through a pad of neutral aluminium oxide. Lipophilic products were washed from the aluminium oxide with ethyl acetate (15 mL). Combined filtrate and washings were concentrated at 40 °C in an aspirator vacuum to leave an oily residue, which was analyzed by GC-MS. Relative yield: 80 % *cis*-(5-phenyltetrahydrofuran-2-yl)-2-propanol *(cis*-**2*a*)**, 19 % *2,2-dimethyl-6-phenyltetrahydropyran-3-ol (**4a**)*, 37/63-mixture of cis/trans-isomers, 0.8 % *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (***3a***).*

4.4 Cumene hydroperoxide as terminal oxidant

4.4.1 Oxidation catalyzed by Schiff-base Complex VO(L^1)(OEt). To a solution of VO(L^1)(OEt), used as ethanol solvate VO(L^1)(OEt)(EtOH) (H_2L = *N*-salicylidene 2-aminophenol) (18.5 mg, 50 µmol) in chloroform (1.5 mL) was added neat cumene hydroperoxide (135 µL, 752 µmol). The resulting mixture was heated for 1 minute at 60 °C and treated at 20 °C with a solution 5-methyl-1-phenylhex-4-en-1-ol (**1a**) (95.2 mg, 500 µmol) in chloroform (1.5 mL). The reaction mixture was stirred for 72 hours at 20 °C and filtrated through a pad of neutral aluminium oxide. Organic products adsorbed were washed with ethyl acetate (5 mL) from the pad of aluminium oxide. Combined filtrate and washings were concentrated at 40 °C in an aspirator vacuum to leave an oily residue, which was purified by flash-chromatography using petroleum ether/ethyl acetate = 8:2 (*v*/*v*) as eluent. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol (**2a**).* Yield: 75.9 mg (368 µmol, 74 %) as 95/5-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol (**4a**).* Yield: 12.4 mg (60.1 µmol, 12 %) as 56/44-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-*

*dihydrofuranone (**3a**)*. Yield: 8.4 mg, (35.9 µmol, 7 %).

4.4.2 Oxidation catalyzed by Piperidine-Derived Complex VO(L^2)(OEt). To a solution of VO(L^2)(OEt) [H_2L^2 = 2,6-bis-(1-hydroxy-1,1-diphenyl-methyl)pyridine] (28.0 mg, 50 µmol) in chloroform (3 mL) was added a neat cumene hydroperoxide (286 mg , 1.50 mmol). The mixture was stirred for 5 min at 20 °C and was treated with a solution of 5-methyl-1-phenylhex-4-en-1-ol (**1a**) (192 mg, 1 mmol) in chloroform (3 mL). The reaction mixture was stirred 72 hours at 20 °C and filtrated through a pad of neutral aluminium oxide. Organic products adsorbed were washed with ethyl acetate (15 mL) from the pad of aluminium oxide. Combined filtrate and washings were concentrated at 40 °C in an aspirator vacuum to leave an oily residue, which was purified by flash-chromatography using diethyl ether/pentane = 1:1 (*v*/*v*) as eluent. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol (**2a**)*. Yield: 70.1 mg (340 µmol, 35 %) as 96/4-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol (**4a**)*. Yield: 24.6 mg (119 µmol, 12 %) as 53/47-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**)*. Yield: 8.4 mg, (35.6 µmol, 4 %).

4.5. Oxidations catalyzed by preconditioned vanadium(V) Schiff-base complex

4.5.1 General method. To a solution of VO(L^1)(OEt) (18.5 mg, 50 µmol; used as ethanol solvate as obtained from synthesis; H_2L^1 = *N*-salicylidene 2-aminophenol) in chloroform (1.5 mL) was added a solution of *tert*-butyl hydroperoxide (TBHP) (136 µl, 5.5 M in nonane). The mixture was heated for 1 minute at 60 °C and further chloroform (1.5 mL) was added and the mixture was allowed cooling to room temperature. Stirring was continued for 72 hours at a

temperature of 20 °C and the mixture was concentrated afterwards in an aspirator vacuum at a bath temperature of 40 °C to leave a dark residue, which was dissolved in chloroform (1.5 mL). To this solution was added a solution of TBHP in nonane (136 µl, 5.5 M solution of TBHP). The resulting mixture was heated for 1 minute at 60 °C and treated at 20 °C with a solution of the alkenol in chloroform (1.5 mL). The reaction mixture was stirred for 72 hours at a temperature of 20 °C and filtrated through a pad of neutral aluminium oxide. Organic products adsorbed were washed with ethyl acetate (5 mL) from the pad of aluminium oxide. Combined filtrate and washings were concentrated at 40 °C in an aspirator vacuum to leave an oily residue, which was purified by flash-chromatography using the eluent specified in sections 4.5.2–4.5.5.

*4.5.2. Oxidation of 5-methyl-1-phenylhex-4-en-1-ol (**1a**).* 5-Methyl-1-phenylhex-4-en-1-ol (**1a**): 95.2 mg (500 µmol). Eluent used for chromatographic purification: petroleum ether/ethyl acetate = 8:2 (*v*/*v*). *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol (**2a**).* Yield: 60.3 mg (292 µmol, 59 %), 96/4-mixture of cis/trans-isomers. *2,2-dimethyl-6-phenyltetrahydropyran-3-ol (**4a**).* Yield: 17.2 mg (83.3 µmol, 17 %), 51/49-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone* (**3a**). Yield: 12.7 mg, (54.2 µmol, 11 %).

*4.5.3. Oxidation of (E)-1-phenylhex-4-en-1-ol (**1b**).* (*E*)-1-Phenylhex-4-en-1-ol (**1b**): 88.1 mg (500 µmol). Eluent used for chromatographic purification: petroleum ether/ethyl acetate = 8:2 (*v*/*v*). *rel-(2S,1'S)-1-(5-Phenyltetrahydrofuran-2-yl)-ethanol rel-(2S,1'S)-(**2b**).* Yield: 52.1 mg (271 µmol, 54 %), 40/60-mixture of cis/trans-isomers. *rel-(2S,3R,6S)-2-Methyl-6-*

*phenyltetrahydropyran-3-ol (**4b**)*. Yield: 9.28 mg, (42.1 µmol, 8 %). *trans-4-Benzoyloxy-5-methyl-2(3H)-dihydrofuranone (**3b**)*. Yield : 10.3 mg (53.6 µmol, 11 %).

*4.5.4. Oxidation of 1-phenylpent-4-en-1-ol (**1c**)*. 1-Phenylpent-4-en-1-ol (**1c**): 81.1 mg (499 µmol). Eluent used for chromatographic purification: petroleum ether/ethyl acetate = 8:2 (*v*/*v*). *5-Phenyltetrahydrofuran-2-yl)-methanol (**2c**)*. Yield: 33.5 mg (188 µmol, 38 %), 40/60-mixture of cis/trans-isomers. *4-Benzoyloxy-2(3H)-dihydrofuranone (**3c**)*. Yield: 5.0 mg, (24.1 µmol, 5 %). *1-Phenylpent-4-en-1-one*. Yield: 4.2 mg (26.0 µmol, 5 %). *1-Phenylethanol*. Yield: 3.9 mg (31.6 µmol, 6 %). Recovered 1-phenylpent-4-en-1-ol (**1c**): 28.6 mg (176 µmol, 35 %).

*4.5.5. Oxidation of 2,2,7-trimethyloct-6-en-3-ol (**1d**)*. 2,2,7-Trimethyloct-6-en-3-ol (**1d**): 84.2 mg (494 µmol). Eluent used for chromatographic purification: diethyl ether/pentane = 1:2 (*v*/*v*). *cis-2-(5-tert-butyl-tetrahydrofuran-2-yl)-propan-2-ol cis-(**2d**)*. Yield: 51.5 mg (276 µmol, 56 %). *trans-2,2-Dimethyl-6-tert-butyl-tetrahydropyran-3-ol trans-(**4d**)*. Yield: 10.3 mg (55.3 µmol, 11 %). *4-Pivaloyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3d**)*. Yield: 16.9 mg, (78.9 µmol, 16 %).

4.6 Variation of Additives and Oxidants

4.6.1 Dihydroarenes as additives – general method. To a solution of VO(L^1)(OEt)(EtOH) (H_2L^1 = *N*-salicylidene 2-aminophenol) (18.5 mg, 50 µmol) in chloroform (1.5 mL) was added a solution of TBHP (136 µL, 5.5 M) in nonane. The resulting mixture was heated for 1 minute

at 60 °C and treated at a temperature of 20 °C with a solution alkenol **1** in chloroform (1.5 mL). The reaction mixture was stirred for 72 hours at a temperature of 20 °C and filtrated through a pad of neutral aluminium oxide. Organic products adsorbed were washed with ethyl acetate (5 mL) from the pad of aluminium oxide. Combined filtrate and washings were concentrated at a bath temperature of 40 °C in an aspirator vacuum to leave an oily residue, which was purified by flash-chromatography using the eluent specified below.

4.6.2 Cyclohexadiene as additive. Reactants: 5-methyl-1-phenylhex-4-en-1-ol (**1a**) (95.2 mg, 500 µmol), cyclohexa-1,4-diene (60.1 mg, 750 µmol), TBHP, and VO(L^1)(OEt)(EtOH) in chloroform according to general method 14.1. Eluent used for chromatographic purification: petroleum ether/ethyl acetate = 8:2 (*v*/*v*). *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol (**2a**).* Yield: 76.1 mg (369 µmol, 74 %) as 94/6-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol (**4a**).* Yield: 12.7 mg (61.8 µmol, 12 %) as 35/65-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**).* Yield: 2.0 mg, (8.6 µmol, 2 %).

4.6.3 γ-Terpinene as additive. Reactants: 5-methyl-1-phenylhex-4-en-1-ol (**1a**) (95.2 mg, 500 µmol), γ-terpinene (102 mg, 750 µmol), TBHP, and VO(L^1)(OEt)(EtOH) in chloroform according to general method 14.1. Eluent used for chromatographic purification: petroleum ether/ethyl acetate = 8:2 (*v*/*v*). *2-(5-phenyltetrahydrofuran-2-yl)-propan-2-ol (**2a**).* Yield: 71.8 mg (348 µmol, 70 %) as 94/6-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol (**4a**).* Yield: 17.7 mg (85.7 µmol, 17 %) as 32/68-mixture of

cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**)*. Yield: 1.3 mg, (6.32 µmol, 1 %).

4.6.4 Oxidation of alkenols by TBHP in an atmosphere of nitrogen. In an atmosphere of nitrogen, a solution of VO(L^1)(OEt)(EtOH) (H_2L = *N*-salicylidene 2-aminophenol) (19 mg, 63 µmol) in chloroform (1.5 mL) was treated with a solution of TBHP in nonane (136 µL, 5.5 M solution of TBHP). The resulting mixture was heated for 1 minute at 60 °C and treated at 20 °C with a solution 5-methyl-1-phenylhex-4-en-1-ol (**1a**) (102 mg, 536 µmol) in chloroform (1.5 mL). The reaction mixture was stirred for 72 hours at 20 °C and filtrated through a pad of neutral aluminium oxide. Organic products adsorbed were washed with ethyl acetate (5 mL) from the pad of aluminium oxide. Combined filtrate and washings were concentrated at 40 °C in an aspirator vacuum to leave an oily residue, which was purified by flash-chromatography using petroleum ether/ethyl acetate = 2:1 (*v*/*v*) as eluent. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol (**2a**)*. Yield: 71.9 mg (349 µmol, 65 %) as 94/6-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol (**4a**)*. Yield: 14.4 mg (69.8 µmol, 13 %) as 45/55-mixture of cis/trans-isomers.

4.7 Oxidation of Cyclic Ethers

4.7.1 General method for oxidation by TBHP. To a solution of VO(L^1)(OEt)(EtOH) (H_2L = *N*-salicylidene aminophenol) in chloroform was added a solution of TBHP (5.5 M) in nonane. The mixture was heated for one minute to 60 °C and treated at a temperature of 20 °C with a solution of tetrahydrofuran **2** or tetrahydropyran **4** dissolved in chloroform. The reaction

mixture was stirred 72 hours at 20 °C and filtrated through a pad of neutral aluminium oxide. Organic products were washed with ethyl acetate (5 mL) from the pad of aluminium oxide. Combined filtrate and washings were concentrated at a bath temperature of 40 °C in an aspirator vacuum to leave an oily residue, which was analyzed by GC-MS and ^{1}H-NMR.

*4.7.2 Oxidation of trans-2-(5-phenyltetrahydrofuran-2-yl)-propan-2-ol trans-(**2a**).* Reactants: tetrahydropyranol *trans*-**4a** (103 mg, 499 µmol) (>96/4-ratio of cis/trans-isomers, according to proton-NMR spectroscopy), TBHP (136 µL, 5.5 M solution in nonane), chloroform (2 × 1.5 mL), VO(L[1])(OEt)(EtOH) (18.5 mg, 50 µmol). *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**)*. Yield: 32.7 mg, (140 µmol, 28 %). Recovered trans-*2,2-dimethyl-6-phenyltetrahydropyran-3-ol (**4a**)*: 73.1 mg (354 µmol, 71 %). Stereochemical analysis based on proton-NMR spectroscopy.

*4.7.3 Oxidation of rel-(2S,1'S)-1-(5-phenyltetrahydrofuran-2-yl)-ethanol rel-(2S,1'S)-**2b**.* Reactants: *rel*-(2*S*,1'*S*)-1-(5-phenyltetrahydrofuran-2-yl)-ethanol *rel*-(2*S*,1'*S*)-(**2b**) as 75/25-mixture of cis/trans-isomers (194 mg 1.01 mmol), TBHP (273 µL, 5.5 M solution in nonane), 2 × 3 mL of chloroform, 36.9 mg of VO(L[1])(OEt)(EtOH) (H_2L = *N*-salicylidene 2-aminophenol) (100 µmol). cis-*4-Benzoyloxy-5-methyl-2(3H)-dihydrofuranone (**3b**)*. Yield: 39.8 mg, (181 µmol, 18 %). Recovered rel-*(2*S,*1'*S*)-1-(5-phenyltetrahydrofuran-2-yl)-ethanol rel-(2*S,*1'*S*)-(**2b**)*: 51.5 mg (249 µmol, 25 %), as 78/22-mixture of cis/trans-isomers.

*4.7.4 Oxidation of rel-(2S,1'R)-1-(5-phenyltetrahydrofuran-2-yl)-ethanol rel-(2S,1'R)-**2b**.*

Reactants: *rel*-(2*S*,1'*R*)-1-(5-phenyltetrahydrofuran-2-yl)-ethanol *rel*-(2*S*,1'*R*)-(**2b**) as 40/60-mixture of cis/trans-isomers (61.5 mg, 320 µmol), TBHP (90 µL, 5.5 M solution in nonane), chloroform (2 × 2 mL), VO(L^1)(OEt)(EtOH) (11.7 mg, 34 µmol). *trans-4-Benzoyloxy-5-methyl-2(3H)-dihydrofuranone (**3b**)*. Yield: 16.7 mg, (75.8 µmol, 24 %). Recovered rel-*(2*S,*1*'R*)-1-(5-phenyltetrahydrofuran-2-yl)-ethanol* rel-*(2*S,*1*'R*)-(**2b**)*: 46.3 mg (241 µmol, 75 %) as 39/61-mixture of cis/trans-isomers.

*4.7.5 Oxidation of trans-2,2-dimethyl-6-phenyltetrahydropyran-3-ol trans-(**4a**).* Reactants: *trans*-2-(5-phenyltetrahydrofuran-2-yl)-propan-2-ol (**2a**) (70.1 mg, 340 µmol), TBHP (93 µL, 5.5 M solution in nonane), chloroform (2 × 2 mL), VO(L^1)(OEt)(EtOH) (12.5 mg, 34 µmol). *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**).* Yield: 5.7 mg, (24.3 µmol, 7 %). Recovered trans-*2-(5-phenyltetrahydrofuran-2-yl)-propan-2-ol (**2a**)*: 62.4 mg (302 µmol, 89 %).

*4.7.6 Aerobic oxidation of trans-2-(5-phenyltetrahydrofuran-2-yl)-propan-2-ol trans-(**2a**).* A solution of *trans*-2-(5-phenyltetrahydrofuran-2-yl)-propan-2-ol (**2a**) (69.0 mg, 334 µmol), in α,α,α-trifluorotoluene (6 mL) was treated with azoisobutyronitrile (12.5 mg, 76.1 µmol). The resulting mixture was stirred 48 hours at 80 °C. The solution was concentrated at 40 °C in an aspirator vacuum to leave an oily residue which was purified by flash-chromatography using petroleum ether/ethyl acetate = 2:1 (*v*/*v*) as eluent. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**).* Yield: 16.5 mg (70.4 µmol, 21 %). Recovered trans-*2-(5-phenyltetrahydrofuran-2-yl)-propan-2-ol (**2a**)*: 51.6 mg, (250 µmol, 75 %).

*4.7.7 Aerobic oxidation trans-2,2-dimethyl-6-phenyltetrahydropyran-3-ol trans-(**4a**).* A solution of *trans*-2,2-dimethyl-6-phenyltetrahydropyran-3-ol *trans*-(**4a**) (81.0 mg, 393 µmol) in α,α,α-trifluorotoluene (6 mL) was treated with azoisobutyronitrile (12.3 mg, 74.9 µmol). The resulting mixture was stirred 48 hours at 80 °C. The solution was concentrated at 40 °C in an aspirator vacuum to leave an oily residue, which was analyzed by GC-MS and ^{1}H-NMR. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**)*. Yield: 6.4 mg, (27.5 µmol, 7 %). Recovered trans-*2,2-dimethyl-6-phenyltetrahydropyran-3-ol (**4a**)*: 71.8 mg (348 µmol, 89 %).

4.8 Decomposition of Cumene Hydroperoxide

4.8.1 General method. To a solution of vanadium catalyst in chloroform (1.5 mL) was added cumene hydroperoxide (80 percent by weight). The mixture was heated for one minute to 60 °C and treated at a temperature of 20 °C with chloroform (1.5 mL). The reaction mixture was stirred 72 hours at 20 °C and filtrated through a pad of neutral aluminium oxide. Lipophilic products were washed with ethyl acetate (5 mL) from the pad of aluminium oxide. The eluate was treated with triphenylphosphine and the solution stirred for 5 minutes.

4.8.2 VOL^{1}(OEt) as catalyst. Reactants: VO(L^{1})(OEt)(EtOH) (H_2L = *N*-salicylidene 2-aminophenol) (18.5 mg, 50 µmol), cumene hydroperoxide (142 mg, 933 µmol) and triphenylphosphine (131 mg, 499 µmol) according to general method 15.1. GC-MS analysis showed formation of cumene, styrene, acetophenone and (2-hydroxy-2-propyl)benzene; no triphenylphosphine oxide was found in GC-MS.

4.8.3 VOL^1(OEt) as stoichiometric reagent. Reactants: VO(L^1)(OEt)(EtOH) (H_2L = *N*-salicylidene 2-aminophenol) (138 mg, 373 µmol), cumene hydroperoxide (71,1 mg, 467 µmol) and triphenylphosphine (66 mg, 252 µmol) according to general method 15.1. GC-MS analysis showed formation of cumene, styrene, acetophenone and (2-hydroxy-2-propyl)benzene; no triphenylphosphine oxide was found in GC-MS.

4.8.4 VO(HL^1)$_2$ as catalyst. Reactants: VO(HL^1)$_2$ (H_2L = *N*-salicylidene 2-aminophenol) (28.5 mg, 54,8 µmol), cumene hydroperoxide (142 mg, 933 µmol) and triphenylphosphine (131 mg, 499 µmol) according to general method 15.1. GC-MS analysis showed formation of cumene, styrene, acetophenone and (2-hydroxy-2-propyl)benzene; no triphenylphosphine oxide was found in GC-MS.

4.8.5 VO(HL^1)$_2$ as stoichiometric reagent. Reactants: VO(HL^1)$_2$ (H_2L = *N*-salicylidene 2-aminophenol) (238 mg, 458 µmol), cumene hydroperoxide (71.1 mg, 467 µmol) and triphenylphosphine (66 mg, 252 µmol) according to general method 15.1. GC-MS analysis showed formation of cumene, styrene, acetophenone and (2-hydroxy-2-propyl)benzene; no triphenylphosphine oxide was found in GC-MS.

4.9. Synthesis of Deuterated Alkenols

*4.9.1 5-Methyl-1-phenylhex-4-en-1-d-1-ol (**1a$_{1\text{-}d}$**).* In an atmosphere of dry nitrogen, $LiAlD_4$ (236 mg, 5.62 mmol) was suspended in dry diethyl ether (10 mL) and treated in a drop wise

manner at a temperature of 0 °C with a solution of 5-methyl-1-phenylhex-4-en-1-one (2.13 g, 11.3 mmol) in dry diethyl ether (10 mL). The resulting reaction mixture is boiled under reflux while being stirred for 2 hours and cooled afterwards in an ice-bath to 0 °C. At this temperature, an aqueous saturated solution of NH_4Cl is added (20 mL) to afford a liquid two-phase system, which is acidified by 2 M-hydrochloric acid to pH 3−4 in the aqueous phase. The organic phase was separated and the aqueous phase extracted with diethyl ether (3 × 30 mL). Combined organic phases were successively washed with brine (100 mL) and H_2O (100 mL). The resulting clear solution was dried ($MgSO_4$) and concentrated under reduced pressure (700 mbar / 40 °C) to leave an oily residue, which was purified by chromatography [dichloromethane/petroleum ether = 3:1 (*v*/*v*)]. Yield: 1.51 g (7.89 mmol, 70 %), colorless oil. R_f = 0.23 [dichloromethane/petroleum ether = 3:1 (*v*/*v*)].^{1}H-NMR ($CDCl_3$, 600Mz) δ 1.59 (s, 3 H, CH_3), 1.70 (s, 3 H, CH_3), 1.72−1.77 (m, 1 H, 2-H), 1.82−1.86 (m, 1 H, 2-H), 1.88 (s, 1 H, OH), 2.01−2.12 (m, 2 H, 3-H), 5.15 (tt, J = 7.1, 1.3 Hz, 1 H, 4-H), 7.26−7.29 (m, 1 H, Ar−H), 7.34−7.35 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 17.9 (CH_3), 24.6 (C3), 25.9 (CH_3), 39.0 (C2), 74.0 (t, $J_{C,D}$ = 22.2 Hz, C1), 123.9 (C4), 126.0 (Ar−C), 127.6 (Ar−C), 128.6 (Ar−C), 132.5 (C5), 144.8 (Ar−C). Anal. calcd. for $C_{13}H_{17}DO$ (191.29): C, 81.63; H/$D_{eff,}$ 9.48; Found.: C, 81.31; H/D_{eff} 9.32.[36]

*4.9.2 5-Methyl-1-phenylhex-4-en-2,2-d_2-1-ol (**1a**$_{2,2\text{-}d_2}$).* A slurry of 5-methyl-1-phenylhex-4-en-1-one (3.08 g, 16.4 mmol) in D_2O (30 mL) was treated with KO*t*Bu (3.87 g, 34.5 mmol) and stirred for 140 h at a temperature 24 °C. The resulting mixture was extracted with *tert*-butyl methyl ether (3 × 30 mL). Combined organic washings were dried ($MgSO_4$) and

concentrated at a bath temperature of 40 °C and a pressure of 700 mbar. The residue was taken up in D_2O (30 mL) and treated again with KO*t*Bu (3.87 g, 34.5 mmol) for 140 h at 24 °C. The resulting mixture was extracted with *tert*-butyl methyl ether (3 × 30 mL), dried ($MgSO_4$) and concentrated at a bath temperature of 40 °C and a pressure of 700 mbar to leave an oil, which was taken up in dry diethyl ether (10 mL) and added in a drop wise manner to a suspension of $LiAlH_4$ (0.22 g, 5.79 mmol) in dry diethyl ether (10 mL) being stirred at 0 °C in an atmosphere of dry nitrogen. The reaction mixture is boiled under reflux for 2 hours while being stirred and cooled afterwards to 0 °C. After carefully hydrolyzing the reaction mixture at 0 °C with an aqueous saturated solution of NH_4Cl (20 mL), 2 M-hydrochloric acid is added to adjust the pH of the aqueous phase to 3−4. The organic phase is separated and the aqueous phase extracted with *tert*-butyl methyl ether (3 × 20 mL). Combined organic phases and washings are sequentially washed with brine (100 mL) and H_2O (100 mL) to afford a clear solution which was dried ($MgSO_4$). Removing the solvent at a pressure of 700 mbar and a bath temperature of 40 °C furnished an oily residue, which was purified by chromatography [dichloromethane/petroleum ether = 3:1 (*v*/*v*)]. Yield: 970 mg (5.05 mmol, 31 %), R_f = 0.22 [dichloromethane/petroleum ether = 3:1 (*v*/*v*)], colorless oil. ^{1}H-NMR ($CDCl_3$, 600Mz) δ 1.59 (s, 3 H, CH_3), 1.69 (s, 3 H, CH_3), 1.86 (s, 1 H, OH), 1.95−2.09 (m, 2 H, 3-H), 4.67 (s, 1 H, 1-H), 5.14 (tt, J = 12.0, 6 Hz, 1 H, 4-H), 7.25−7.28 (m, 1 H, Ar−H), 7.33−7.35 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 17.9 (CH_3), 24.4 (C3), 25.9 (CH_3), 38.5 (quin, $J_{C,D}$ = 19.4 Hz, C2), 74.3 (C1), 123.9 (C4), 126.0 (Ar−H), 127.6 (Ar−H), 128.6 (Ar−H), 132.4 (C5), 144.9 (Ar−H). Anal. Calcd for $C_{13}H_{16}D_2O$ (192.29): C, 81.20; H/$D_{eff,}$ 9.43; Found.: C, 80.87; H/D_{eff} 9.29.[36]

*4.9.3 5-Methyl-1-phenylhex-4-en-3,3-d_2-1-ol (**1a**$_{3,3\text{-}d_2}$).* A solution of ethyl-3-methylbut-2-enoate (8.50 g, 66.3 mmol) in dry diethyl ether (45 mL) is added to a suspension of $LiAlD_4$ (1.86 g, 44.3 mmol) in dry diethyl ether (20 mL) being stirred at 0 °C in an atmosphere of dry nitrogen. The reaction mixture is boiled under reflux for 2 hours while being stirred and cooled afterwards to 0 °C. After carefully hydrolyzing the reaction mixture at 0 °C with an aqueous saturated solution of NH_4Cl (40 mL), 2 M-hydrochloric acid is added to adjust the pH of the aqueous phase to 3−4. The organic phase is separated and the aqueous phase extracted with *tert*-butyl methyl ether (3 × 30 mL). Combined organic phases are sequentially washed with brine (100 mL) and H_2O (100 mL) to afford a clear solution, which was dried ($MgSO_4$).[37] Removing the solvent at a pressure of 700 mbar and a bath temperature of 40 °C furnishes a residue, which is dissolved in dry pentane (20 mL) and added at −40 °C in a drop wise manner to a solution of PBr_3 (6.80 g, 25.0 mmol) in dry pentane (100 mL). Additional PBr_3 (2.80 g, 10.3 mmol) is added and the resulting mixture stirred for one hour at −4 °C and for two hours at 0 °C. Afterwards, methanol (15 mL) is added in a drop wise manner at 0 °C, while stirring is being continued for further 30 minutes. The organic phase (upper layer) is separated and filtrated through a pad of celite. The filtrate is concentrated under reduced pressure (300 mbar / 40 °C) to leave a residue, which is dissolved in acetone (150 mL) and treated with ethyl benzoylacetate (8.38 g, 43.6 mmol) and K_2CO_3 (6.67 g, 48.3 mmol). The resulting slurry is boiled for 24 h under reflux, while being stirred. The solids are filtrated off at room temperature and the filtrate concentrated under reduced pressure (550 mbar) and a bath temperature of 40 °C to leave an oily residue, which is dissolved in ethanol (60 mL). The clear

solution is treated with an aqueous 2 N-solution of NaOH (150 mL) and heated for 24 h under reflux, while being stirred. The resulting mixture is extracted at room temperature with dichloromethane (3 × 100 mL). Combined organic phases are washed with brine (100 mL), dried ($MgSO_4$), and concentrated at a pressure of 700 mbar and a bath temperature of 40 °C. The remaining colorless oil is dissolved in dry diethyl ether (7 mL) and added in a drop wise manner to a suspension of $LiAlH_4$ in dry diethyl ether (15 mL), which is stirred at 4 °C in an atmosphere of dry nitrogen. The reaction mixture is boiled under reflux for 1.5 hours, while being stirred. Water (10 mL) and a 10-percent by weight aqueous solution of $NaHCO_3$ (5 mL) are successively and carefully added. The resulting precipitate is filtrated off. The organic phase from the filtrate is separated and the aqueous layer extracted with diethyl ether (2 × 70 mL). Combined organic phase and washings are dried ($MgSO_4$) and concentrated at a pressure of 700 mbar and a bath temperature of 40 °C to leave an oil, which was distilled (3×10^{-4} mbar, 122 °C) and purified by chromatography [dichloromethane/petroleum ether = 3:2 (*v*/*v*)]. Yield: 2.66 g (14.0 mmol, 20 %), R_f = 0.31 [dichloromethane$_2$/petroleum ether = 3:2 (*v*/*v*)], colorless oil. Bp 122 °C (3.4×10^{-1} mbar). ^{1}H-NMR ($CDCl_3$, 400Mz) δ 1.51 (s, 3 H, CH_3), 1.62 (s, 3 H, CH_3), 1.66−1.67 (m, 1 H, 2-H), 1.72−1.78 (m, 1 H, 2-H), 1.83−1.89 (m, 1 H, OH), 4.60 (m, 1 H, 1-H), 5.06 (s, 1 H, 4-H), 7.17−7.26 (m, 5 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 101 MHz) δ 17.7 (CH_3), 23.7 (quin, $J_{C,D}$ = 19.5 Hz, C3), 25.7 (CH_3), 38.9 (C2) 74.2 (C1), 123.6 (C4), 125.8 (Ar−C), 127.4 (Ar−C), 128.3 (Ar−C), 132.3 (C5), 144.7 (Ar−C). Anal. Calcd for $C_{13}H_{16}D_2O$ (192.29): C, 81.20; H/$D_{eff,}$ 9.43; Found.: C, 80.90; H/D_{eff} 9.80.[36]

4.10 Vanadium-Catalyzed Oxidation of Deuterated Alkenols

4.10.1 General method. To a solution of VO(L^n)(OEt) [H_2L^1 = *N*-salicylidene aminophenol, derived vanadium complex used as ethanol solvate, as obtained from synthesis] in chloroform was added a solution of TBHP (3.5 M in toluene). The mixture was stirred for 3 minutes and was treated at a temperature of 20 °C with a solution of a deuterated alkenol (**1a**$_{1\text{-}d}$, **1a**$_{2,2\text{-}d_2}$, **1a**$_{3,3\text{-}d_2}$) in chloroform. The reaction mixture was stirred for the time specified in sections 4.10.2–4.10.4. Additional TBHP is added were indicated and stirring continued at a temperature of 20 °C for up to a maximum of 168 hours. The reaction mixture is filtrated through a pad of neutral aluminium oxide. Organic products adsorbed are washed with ethyl acetate (15 mL) from the pad of aluminium oxide. Combined filtrate and washings were concentrated at a temperature of 40 °C in an aspirator vacuum to leave an oily residue, which was purified by flash-chromatography [petroleum ether/*tert*-butyl methyl ether = 3:2 (*v*/*v*)]. Deuterated tetrahydrofuranmethanols, tetrahydropyranols and γ-butyrolactones were characterized using authentic samples from syntheses described in the Supplementary data.

*4.10.2 Oxidation of 5-methyl-1-phenylhex-4-en-d-1-ol (**1a**$_{1\text{-}d}$) (48 hours reaction time).* Reactants: alkenol **1a**$_{1\text{-}d}$ (191 mg, 1.00 mmol) in chloroform (4 mL), VO(L^1)(OEt)(EtOH) (36.9 mg, 10 mol%), TBHP (430 µL, 3.5 M solution in toluene, 1.50 mmol) in chloroform (3.6 mL). Reaction time 48 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-5-d (**2a**$_{5\text{-}d}$).* Yield: 147 mg (709 µmol, 71 %, 93/7-mixture of cis/trans-isomers. R_f = 0.67 [ethyl acetate/diethyl ether/pentane = 1:1:2 (*v*/*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 1.23 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 1.79−1.84 (m, 1 H, 4-H), 1.96−1.99 (m, 2 H, 3-H), 2.11 (s, 1 H, OH), 2.28−2.33 (m, 1 H, 4-H), 3.87 (t, *J* = 7.4 Hz, 1 H, 2-H), 7.27−7.29 (m, 1 H, Ar−H),

7.33−7.38 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 24.7 (CH_3), 26.6 (C3), 27.4 (CH_3), 34.3 (C4), 71.6 (C1'), 80.8 (t, $J_{C,D}$ = 22.2 Hz, C5), 86.3 (C2), 126.1 (Ar−C), 127.6 (Ar−C), 128.6 (Ar−C), 142.5 (Ar−C). GC-MS (t_r = 17.21; 70 eV, EI): *m*/*z* (%) = 148 (26), 130 (17), 118 (23), 105 (100), 92 (26), 77 (9), 59 (61). HRMS (EI$^+$) *m*/*z* 192.1138 [M^+ –CH_3]; calculated mass for $C_{12}H_{14}DO_2^+$: 192.1135. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-6-d (**4a$_{6\text{-}d}$**).* Yield: 28.1 mg (136 µmol, 14 %), 46/54-mixture of cis/trans-isomers. Data for *trans*-(**4a$_{6\text{-}d}$**): R_f = 0.24 [petroleum ether/ethyl acetate = 4:1 (*v*/*v*)], colorless crystals. Mp 135 °C. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 1.21 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3), 1.39 (d, *J* = 4.9 Hz, 1 H, OH), 1.53−1.58 (m, 1 H, 5-H), 1.63−1.70 (m, 1 H, 5-H), 1.82−1.87 (m, 2 H, 4-H), 3.48 (dd, *J* = 11.5, 4.4 Hz, 1 H, 3-H), 7.14−7.17 (m, 1 H, Ar−H), 7.22−7.27 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 16.5 (CH_3), 28.5 (CH_3), 29.0 (C4), 34.2 (C5), 71.7 (t, $J_{C,D}$ = 20.8 MHz, C6), 74.4 (C3), 75.8 (C2), 126.1 (Ar−C), 127.5 (Ar−C), 128.5 (Ar−C), 143.0 (Ar−C). GC-MS (t_r = 17.90/EI) *m*/*z* 149 (11), 131 (7), 118 (5), 105 (100), 92 (8), 78 (9), 59 (11). *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**).* Yield: 6.93 mg (30.0 µmol, 3 %).

*4.10.3 Oxidation of 5-methyl-1-phenylhex-4-en-2,2-d$_2$-1-ol (**1a$_{2,2\text{-}d_2}$**) (48 hours reaction time)*

Reactants: alkenol **1a$_{2,2\text{-}d_2}$** (193 mg, 1.00 mmol) in chloroform (4 mL), VO(L[1])(OEt)(EtOH) (36.9 mg, 10 mol%), TBHP (430 µL, 3.5 M solution in toluene, 1.50 mmol) in chloroform (3.6 mL). Reaction time: 48 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-4,4-d$_2$ (**2a$_{4,4\text{-}d_2}$**).* Yield: 117 mg (562 µmol, 56 %), 93/7-mixture of cis/trans-isomers. R_f = 0.68 [ethyl acetate/diethyl ether/pentane = 1:1:2 (*v*/*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.23 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 1.96 (dd, 2 H, *J* = 7.4 Hz, 3-H), 2.12 (s, 1 H, OH), 3.88 (t, *J* = 7.8

Hz, 1 H, 2-H), 4.87 (s, 1 H, 5-H), 7.27−7.30 (m, 1 H, Ar−H), 7.33−7.38 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 24.7 (CH_3), 26.4 (C3), 27.4 (CH_3), 33.7 (quin, $J_{C,D}$ = 20.8 Hz, C4), 71.7 (C1'), 81.1 (C5), 86.3 (C2), 126.1 (Ar−C), 127.6 (Ar−C), 128.6 (Ar−C), 142.6 (Ar−C). GC-MS (t_r = 17.20; 70 eV, EI) : *m*/*z* (%) = 149 (27), 132 (12), 118 (12), 106 (100), 92 (18), 59 (52). HRMS (EI$^+$) *m*/*z* 193.1191 [M^+ –CH_3]; calculated mass for $C_{12}H_{13}D_2O_2^+$: 193.1198. *2,2-Dimethyl-6*-phenyltetrahydropyran-*3-ol-5,5-d*$_2$ (***4a*$_{5,5\text{-}d_2}$**). Yield: 27.2 mg (131 µmol, 13 %), 41/59-mixture of cis/trans-isomers. Data for *trans*-(**4a**$_{5,5\text{-}d_2}$): R_f = 0.20 [petroleum ether/ethyl acetate = 4:1 (*v*/*v*)], colorless crystals. Mp 134 °C. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 1.31 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.68 (s, 1 H, OH), 1.73−1.77 (m, 1 H, 4-H), 1.92 (dd, *J* = 12.8, 4.9 MHz, 1 H, 4-H), 3.56 (dd, *J* = 11.8, 4.6 Hz, 1 H, 3-H), 4.57 (s, 1 H, 6-H), 7.25−7.27 (m, 1 H, Ar−H), 7.32−7.38 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 16.5 (CH_3), 28.5 (CH_3), 28.8 (C4), 33.5 (quin, $J_{C,D}$ = 19.4 Hz, C5), 72.0 (C6), 74.2 (C3), 75.9 (C2), 126.1 (Ar−C), 127.4 (Ar−C), 128.4 (Ar−C), 143.1 (Ar−C). GC-MS (t_r = 17.93/EI) *m*/*z* 150 (12), 132 (7), 106 (100), 79 (7), 59 (12). Anal. Calcd. for $C_{13}H_{16}D_2O_2$ (208.29): C, 74.96; H/D_{eff}, 8.71; Found: C, 74.90; H/D_{eff}, 8.56.[36] *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**)*. Yield: 19.8 mg (84.5 µmol, 9 %).

4.10.4 Oxidation of 5-methyl-1-phenylhex-4-en-3,3-d$_2$*-1-ol (**1a*$_{3,3\text{-}d_2}$**) (48 hours reaction time)*

Reactants: alkenol **1a**$_{3,3\text{-}d_2}$ (194 mg, 1.01 mmol) in chloroform (4 mL), VO(L^1)(OEt)(EtOH) (37.4 mg, 10 mol%), TBHP (430 µl, 3.5 M solution in toluene, 1.50 mmol) in chloroform (3.6 mL). Reaction time: 48 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-3,3-d*$_2$ (***2a*$_{3,3\text{-}d_2}$**). Yield: 62.1 mg (298 µmol, 30 %) 97/3-mixture of cis/trans-isomers, brown oil. R_f =

0.25 [diethyl ether/pentane = 1:1 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.26 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.82−1.85 (m, 1 H, 4-H), 2.16 (s, 1 H, OH), 2.31−2.35 (m, 1 H, 4-H), 3.90 (s, 1 H, 2-H), 4.89−4.92 (m, 1 H, 5-H), 7.29−7.32 (m, 1 H, Ar−H), 7.36−7.41 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 24.7 (CH_3), 26.0 (quin, $J_{C,D}$ = 19.4 Hz, C3), 27.3 (CH_3), 34.2 (C4), 71.6 (C1'), 81.2 (C5), 86.1 (C2), 126.1 (Ar−C), 127.6 (Ar−C), 128.6 (Ar−C), 142.5 (Ar−C). GC-MS (t_r = 17.20; 70 eV, EI): *m*/*z* (%) = 149 (24), 132 (13), 119 (18), 104 (100), 91 (15), 77 (9), 59 (48). *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-4,4-d$_2$* (**4a$_{4,4\text{-}d_2}$**). Yield: 13.9 mg (66.7 µmol, 7 %) 44/56-mixture of cis/trans-isomers, brown oil. Data for *trans*-(**4a$_{4,4\text{-}d_2}$**): R_f = 0.36 [petroleum ether/ethyl acetate = 4:1 (*v*/*v*)], colorless crystals. Mp 136 °C. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 1.32 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.45 (d, *J* = 5.5 Hz, 1 H, OH), 1.63−1.67 (m, 1 H, 5-H), 1.94 (dd, *J* = 13.6, 2.5, 1 H, 5-H), 3.58 (d, *J* = 5.2 Hz, 1 H, 3-H), 4.59 (dd, 1 H, *J* = 11.7, 2.4 Hz, 6-H), 7.25−7.28 (m, 1 H, Ar−H), 7.33−7.38 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 16.5 (CH_3), 28.1−28.4 (m, C4), 28.5 (CH_3), 34.1 (C5), 72.1 (C6), 74.3 (C3), 75.8 (C2), 126.1 (Ar−C), 127.5 (Ar−C), 128.5 (Ar−C), 143.1 (Ar−C). GC-MS (t_r = 17.84/EI) *m*/*z* 150 (11), 132 (8), 106 (100), 91 (6), 78 (11), 59 (12). *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone-3,3-d$_2$ (**3a$_{3,3\text{-}d_2}$**).* Yield: 2.55 mg (10.8 µmol, 1 %). R_f = 0.36 [ethyl acetate/hexane = 4:1 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 1.41 (s, 6 H, CH_3), 5.34 (s, 1 H, 4-H), 7.36−7.39 (m, 2 H, Ar−H), 7.49−7.53 (m, 1 H, Ar−H), 7.93−7.95 (m, 2 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz): δ = 22.0 (CH_3), 26.5 (CH_3), 35.7 (quin, $J_{C,D}$ = 21.4 Hz, C4), 75.1 (C3), 86.6 (C2), 128.8 (Ar−C), 129.1 (Ar−C), 129.9 (Ar-C), 133.9 (Ar−C), 165.6 (CO), 173.7 (CO).

Acknowledgements. This work was supported by the Deutsche Forschungsgemeinschaft (grant Ha1705/8–2), the state Rheinland Pfalz (scholarships for G.S. and M.A.), and NanoKat. This work is part of Ph.D. theses of M.A. and G.S, and the Diploma thesis of M.D.

Supplementary data. Supplementary data associated with this article containing instrumentation, solvent purification, reagent specification, experimental details for alkenol oxidation, synthesis of deuterated tetrahydrofuranyl-2-methanols and deuterated tetrahydropyran-3-ols, proton- and carbon-13 NMR-data of oxidation products can be found in the online version of the article at doi:.....

1. Sheldon R. A. In *Aspects of Homogeneous Catalysis*; Ugo, R. Ed.; Reidel Publishing: Dordrecht, **1981**, vol. 4, pp. 3–69.
2. (a) Milas, N. A.; Harris, S. A. *J. Am. Chem. Soc.* **1938**, *60*, 2434–2436. (b) Sharpless, K. B.; Verhoeven, T. R. *Aldrichim. Acta* **1979**, *12*, 63–74. (c) Hill, J. G.; Rossiter, B. E.; Sharpless, K. B. *J. Org. Chem.* **1983**, *48*, 3607–3608.
3. Wischang D.; Brücher O.; Hartung J. *Coord. Chem. Rev.* **2011,** *255***,** 2204–2217.
4. Conte V.; Di Furia F.; Modena G. *J. Org. Chem.*, **1988**, *53*, 1665–1669.
5. Mimoun, H.; Mignard, M.; Brechot, P.; Saussine, L. *J. Am. Chem. Soc*. **1986**, *108*, 3711–3718.
6. Zhang W.; Basak A.; Kosugi Y.; Hoshino Y.; Yamamoto H. *Angew. Chem.* **2005**, *117*, 4463–4465.
7. Aebischer B.; Vasella A. *Helv. Chim. Act.* **1982**, *65*, 621–634.

8. Dupuis J.; Giese B.; Hartung J.; Leisung M. *J. Am. Chem. Soc*. **1985**, *107*, 4332–4333.

9. (a) Holland H. L. *Chem. Rev*. **1988**, *88*, 473–485. (b) Wojaczyński J.; Wojaczyńska E. *Chem. Rev*. **2010**, *110*, 4303–4356.

10. Brücher, O.; Hartung, J. *ACS Catal*. **2011**, *1*, 1448–1454.

11. Wright S. W.; Haagemann D. L.; Wright A. S.; McClure L. D. *Tetrahedron Lett*. **1997**, *42*, 7345–7348.

12. (a) Crans, D. C.; Smee, J. J.; Gaidamauskas E.; Yang L. *Chem. Rev*. **2004**, *104*, 849–902. (b) Hirao T. *Chem. Rev*. **1997**, *97*, 2707–2724.

13. Hartung J.; Drees S.; Greb M.; Schmidt P.; Svoboda I.; Fuess H.; Murso A.; Stalke D. *Eur. J. Org. Chem*. **2003**, 2388–2408.

14. Hartung, J.; Ludwig, A.; Demary, M.; Stapf G. In *Vanadium the Versatile Metal, ACS-Symposium Series 974*; Kustin, K., Pessoa, J.C., Crans D.C., Eds.; American Chemical Society: Washington DC, **2007**, ch 4., pp. 38–50.

15. Sheldon, R.A.; van Doorn, J.A. *J. Catal*. **1973**, *31*, 427–437.

16. Dönges M.; Amberg M.; Stapf G.; Kelm H.; Bergsträßer U.; Hartung J. accepted, http://dx.doi.org/10.1016/j.ica.2014.02.007.

17. Hartung, J. Pure & Appl. Chem. **2005**, 77, 1559–1574.

18. Mimoun, H.; Mignard, M.; Brechot, P.; Saussine, L. *J. Am. Chem. Soc*. **1986**, *108*, 3711–3718.

19. Greb, M.; Hartung, J.; Köhler, F.; Špehar, K.; Kluge, R.; Csuk, R. *Eur. J. Org. Chem*. **2004**, 3799–3813.

20. Bellemin-Laponnaz, S.; Coleman, K.S.; Dierkes, P.; Masson, J.-P.; Osborn, J.A. *Eur. J. Inorg. Chem.* **2000**, 1645–1649.

21. Clague, M.J.; Keder, N.L.; Butler, A. *Inorg. Chem.* **1993**, *32*, 4754–4761.

22. Hartung J.; Greb M. *J. Organomet. Chem.* **2002**, *661*, 67–84.

23. Luo Y.-R. In *Handbook of Bond Dissociation Energies in Organic Compounds*; CRC Press: Boca Raton, **2003**, pp. 57–61.

24. Gollnick, K.; Knutzen-Mies, K. *J. Org. Chem.* **1991**, *56*, 4017–4027.

25. Cornman C. R.; Kampf J.; Lah M. S.; Pecoraro V. L. *Inorg. Chem.* **1992**, *31*, 2035–2043.

26. Bonchio M.; Conte V.; Di Furia F.; Modena G.; Moro S. *Inorg. Chem.*. **1994**, *33*, 1631–1637.

27. Cenci S.; Di Furia F.; Modena G.; Curci R. *Chem. Soc., Perkin Trans. 2* **1978**, 979–984.

28. (a) Baciocchi A.; Bietti M.; Salamone M.; Steenken S. *J. Org. Chem.* **2002**, *67*, 2266–2270. (b) Avilla D. V.; Brown C. E.; Ingold K. U.; Lusztyk J. *J. Am. Chem. Soc*. **1993**, *115*, 466–470.

29. Bietti M.; Lanzalunga O.; Salamone M. *J. Org. Chem*. **2005**, *70*, 1417–1422.

30. Schur C.; Becker N.; Bergsträßer U.; Gottwald T.; Hartung J. *Tetrahedron* **2011**, *67*, 2338–2347.

31. (a) Fries P.; Halter D.; Kleinschek A.; Hartung J. *J. Am. Chem. Soc.* **2011**, *133*, 3906–3912. (b) Hawari J. A.; Engel P. S.; Griller D. *Int. J. Chem. Kinet.* **1985**, *17*, 1215–1219.

32. Ishii H.; Sfkiguchi F.; Ishikawa T. *Tetrahedron* **1981**, *37*, 285–290.

33. Ishii H.; Kobayashi J.; Sakurada A; Ishikawa T. *J. Chem. Soc. Perkin Trans. 1* **1992**, 1681–1684.

34. Grundon M. F.; McColl I. S. *Phytochemistry* **1975**, *14*, 143–150.

35. Hartung, J.; Bergsträsser, U.; Daniel, K.; Schneiders, N.; Svoboda, I.; Fuess, H.; *Tetrahedron* **2009**, DOI:10.1016/j.tet.2009.01.067.

36. Voss, G.; Schramm, W. *Helv. Chim. Acta*, **2000**, *83*, 2884–2892.

37. Vassilikogiannakis, G.; Chronakis, N.; Orfanopoulos, M. *J. Am. Chem. Soc.* **1998**, *120*, 9911–9920.

Supplementary Data for

Formation of 3-Acyloxy-γ-butyrolactones from 4-Pentenols in Vanadium-Catalyzed Oxidations

Matthias Amberg, Maike Dönges, Georg Stapf, and Jens Hartung

Fachbereich Chemie, Organische Chemie, Technische Universität Kaiserslautern, Erwin-Schrödinger-Straße, D-67663 Kaiserslautern, Germany

Contents

1 General Remarks

(i) Compound numbering in the Supplementary Data is consistent with the accompanying article.

(ii) Reference numbering refers exclusively to the Supplementary data.

2 Instrumentation

2.1 NMR-spectroscopy

^{1}H- and ^{13}C-NMR spectra were recorded with FT-NMR DPX 200, DPX 400 and DMX 600 instruments (*Bruker*). Chemical shifts refer to the δ-scale. Tetramethylsilane was used as internal standard.

2.3 Gas chromatography coupled to mass spectrometry

GC-MS Analysis was performed with a HP 6890 Series (*Hewlett Packard*) system and mass detector with a HP-5MS column (*Agilent*, 30 m × 0.25 mm, 0.25 µm). Temperature program: 40 °C (3 min), 10 °C min^{-1} → 280 °C, 280 °C (10 min).

2.3 High resolution mass spectra

High resolution mass spectra (EI, 70 eV) were detected on a GCT Premier Micromass (*Waters*).

2.4 Combustion analysis

Combustion analyses were performed with a vario Micro cube CHNS (*Elementar Analysentechnik / Hanau*).

2.5 Thin layer chromatography

Reaction progress was monitored via thin layer chromatography (tlc) on Polygram sheets coated with silica gel (60 F_{254}, *Merck*). Compounds on developed tlc-sheets were detected with the aid of the UV-VIS indicator commercially disposed on the sheets, becoming apparent by a lamp emitting 254-nm light. As alternative method for detecting compounds on developed tlc-sheets was staining by Ekkert´s reagent and subsequently heating, leading to colored spots for alcohols and ketones.

2.6 Melting points

Melting points were determined on a digital melting point apparatus 9100 (*Electrothermal*).

3 Chemicals

Petroleum ether refers to the fraction boiling between 40 °C and 60 °C. All solvents were used in analytical quality or purified according to standard procedures.[1]

tert-Butyl hydroperoxide (TBHP; 5.5 M solution in nonane), cyclohexa-1,4-diene, γ-terpinene and cumene hydroperoxide (80 percent by weight) were purchased from Aldrich Chemicals.

5-Methyl-1-phenylhex-4-en-1-ol (**1a**)[2], 5-Methyl-1-phenylhex-4-en-1-one[2] (*E*)-1-phenylhex-4-en-1-ol (**1b**)[3], 1-phenylpent-4-en-1-ol (**1c**)[4], 2,2,7-trimethyloct-6-en-3-ol (**1d**)[5], 5-methyl-2-phenylhex-4-en-1-ol (**1e**)[6], 5-methyl-3-phenylhex-4-en-1-ol (**1f**)[7], 3-hydroxy-2,2-dimethyl-tetrahydrodrofuran-5-one[8], VO(L)(OEt)(EtOH)[5] (H_2L = *N*-salicylidene 2-aminophenol), $VO(HL)_2$[9] (H_2L = *N*-salicylidene 2-aminophenol) and VO(L)(OEt)[10] H_2L = *cis*-2,6-bis(diphenylmethanol)-piperidine were synthesized according to published procedures. A 3.5 M solution of *tert*-butyl hydroperoxide (TBHP) in toluene was prepared according to Sharpless *et al*. and the concentration determined as described.[11] Chloroform used for oxidations was filtrated trough a pad of basic aluminium oxide.

4 Spectroscopic Data and Preparation of References

4.1 Deuterated Tetrahydrofuranmethanols

4.1.1 General remarks

Deuterated tetrahydrofurans **2a**$_{5\text{-}d}$, **2a**$_{4,4\text{-}d_2}$ and **2a**$_{3,3\text{-}d_2}$ were prepared from deuterated alkenols as described in the associated article. Compounds **2a**$_{5\text{-}d}$, **2a**$_{4,4\text{-}d_2}$ and **2a**$_{3,3\text{-}d_2}$ were purified by repetitive chromatographic separation [petroleum ether/*tert*-butyl methyl ether = 3:2 (*v*/*v*)].

4.1.2 *cis*-2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-5-*d* *cis*-(**2a**$_{5\text{-}d}$)

R_f = 0.67 [ethyl acetate/diethyl ether/pentane = 1:1:2 (*v*/*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 1.23 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 1.79−1.84 (m, 1 H, 4-H), 1.96−1.99 (m, 2 H, 3-H), 2.11 (s, 1 H, OH), 2.28−2.33 (m, 1 H, 4-H), 3.87 (t, J = 7.4 Hz, 1 H, 2-H), 7.27−7.29 (m, 1 H, Ar−H), 7.33−7.38 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 24.7 (CH_3), 26.6 (C3), 27.4 (CH_3), 34.3 (C4), 71.6 (C1'), 80.8 (t, $J_{C,D}$ = 22.2 Hz, C5), 86.3 (C2), 126.1 (Ar−C), 127.6 (Ar−C), 128.6 (Ar−C), 142.5 (Ar−C). GC-MS (t_r = 17.21; 70 eV, EI): *m*/*z* (%) = 148 (26), 130 (17), 118 (23), 105 (100), 92 (26), 77 (9), 59 (61). HRMS (EI$^+$) *m*/*z* 192.1138 [M^+ –CH_3]; calculated mass for $C_{12}H_{14}DO_2^+$: 192.1135.

4.1.3 *trans*-2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-5-*d* *trans*-(**2a**$_{5\text{-}d}$)

R_f = 0.67 [ethyl acetate/diethyl ether/pentane = 1:1:2 (*v*/*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 1.19 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.79−2.33 (m, 5 H, 3-H, 4-H, OH), 4.03−4.06 (m, 1 H, 2-H), 7.27−7.38 (m, 5 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 24.7 (CH_3), 26.6 (C3), 27.4 (CH_3), 34.3 (C4), 71.7 (C1'), 86.3 (C2), 126.1 (Ar−C), 127.6 (Ar−C), 128.6 (Ar−C), 142.5 (Ar−C).

4.1.4 *cis*-2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-4,4-d_2 *cis*-(**2a**$_{4,4\text{-}d_2}$)

R_f = 0.68 [ethyl acetate/diethyl ether/pentane = 1:1:2 (*v*/*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.23 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 1.96 (dd, 2 H, J = 7.4 Hz, 3-H), 2.12 (s, 1 H, OH), 3.88 (t, J = 7.8 Hz, 1 H, 2-H), 4.87 (s, 1 H, 5-H), 7.27−7.30 (m, 1 H, Ar−H), 7.33−7.38 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 24.7 (CH_3), 26.4 (C3), 27.4

(CH_3), 33.7 (quin, $J_{C,D}$ = 20.8 Hz, C4), 71.7 (C1'), 81.1 (C5), 86.3 (C2), 126.1 (Ar−C), 127.6 (Ar−C), 128.6 (Ar−C), 142.6 (Ar−C). GC-MS (t_r = 17.20; 70 eV, EI) : *m*/*z* (%) = 149 (27), 132 (12), 118 (12), 106 (100), 92 (18), 59 (52). HRMS (EI^+) *m*/*z* 193.1191 [$M^+ - CH_3$]; calculated mass for $C_{12}H_{13}D_2O_2^+$: 193.1198.

4.1.5 *trans*-2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-4,4-d_2 *trans*-($2a_{4,4\text{-}d_2}$)

R_f = 0.68 [ethyl acetate/diethyl ether/pentane = 1:1:2 (*v*/*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.19 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.96−2.13 (m, 3 H, 3-H, OH), 4.03−4.06 (m, 1 H, 2-H), 4.99 (s, 1 H, 5-H), 7.27−7.38 (m, 5 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 24.2 (CH_3), 26.5 (C3), 27.4 (CH_3), 66.5 (C1'), 81.6 (C5), 86.8 (C2), 125.7 (Ar−C), 127.10 (Ar−C), 128.44 (Ar−C), 141.04 (Ar−C).

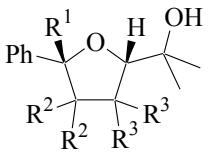
4.1.6 *cis*-2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-3,3-d_2 *cis*-($2a_{3,3\text{-}d_2}$)

R_f = 0.25 [diethyl ether/pentane = 1:1 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.26 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.82−1.85 (m, 1 H, 4-H), 2.16 (s, 1 H, OH), 2.31−2.35 (m, 1 H, 4-H), 3.90 (s, 1 H, 2-H), 4.89−4.92 (m, 1 H, 5-H), 7.29−7.32 (m, 1 H, Ar−H), 7.36−7.41 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 24.7 (CH_3), 26.0 (quin, $J_{C,D}$ = 19.4 Hz, C3), 27.3 (CH_3), 34.2 (C4), 71.6 (C1'), 81.2 (C5), 86.1 (C2), 126.1 (Ar−C), 127.6 (Ar−C), 128.6 (Ar−C), 142.5 (Ar−C). GC-MS (t_r = 17.20; 70 eV, EI): *m*/*z* (%) = 149 (24), 132 (13), 119 (18), 104 (100), 91 (15), 77 (9), 59 (48).

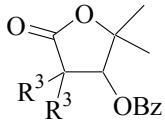
4.1.7 *trans*-2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-3,3-d_2 *trans*-($2a_{3,3\text{-}d_2}$)

R_f = 0.25 [diethyl ether/pentane = 1:1 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.22 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 1.93−1.96 (m, 1 H, 4-H), 2.16 (s, 1 H, OH), 2.39−2.42 (m, 1 H, 4-H), 4.07 (s, 1 H, 2-H), 5.01−5.04 (m, 1 H, 5-H), 7.29−7.32 (m, 1 H, Ar−H), 7.36−7.41 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 24.2 (CH_3), 26.0 (quin, $J_{C,D}$ = 19.4 Hz, C3), 28.5 (CH_3), 36.1 (C4), 71.9 (C1'), 81.7 (C5), 86.6 (C2), 125.7 (Ar−C), 127.1 (Ar−C), 128.7 (Ar−C), 143.1 (Ar−C).

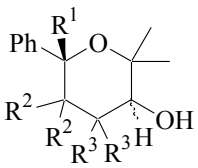
Table S1. Chemical shifts and multiplicity of diagnostic ^{1}H-NMR signals of deuterated and non deuterated heterocycles **2a**, **3a**, and **4a** [a]



***cis*-2a**



3a



4a

2a–4a	R^1	R^2	R^3	δ/ppm / multiplicity [b]				
				2–H	3–H	4–H	5–H	6–H
***cis*-2a**	H	H	H	3.87 / t	1.98 / q	2.31 / m 1.83 / m	4.86 / dd	
***cis*-2a$_{5\text{-}d}$**	D	H	H	3.87 / t	1.98 /m	2.30 / m 1.83 / m	– [c]	
***cis*-2a$_{4,4\text{-}d_2}$**	H	D	H	3.88 / t	1.93 / dd	–	4.87 / s	
***cis*-2a$_{3,3\text{-}d_2}$**	H	H	D	3.90 / s	– [c]	2.33 / m 1.83 / m	4.90 / m	
3a			H		3.16 / dd 2.71 / dd	5.44 / dd		
3a$_{3,3\text{-}d_2}$			D		– [c]	5.34 / s		
***cis*-4a**	H	H	H		3.48 / s	1.60–1.79 / m		4.70 / dd
***cis*-4a$_{6\text{-}d}$**	D	H	H		3.48 / m	1.60–1.97 / m		– [c]
***cis*-4a$_{5,5\text{-}d_2}$**	H	D	H		3.48 / m	1.72 / t 1.90 / m	– [c]	4.69 / s
***cis*-4a$_{4,4\text{-}d_2}$**	H	H	D		3.48 / s	– [c]	1.62 / t 1.80 / m	4.70 / dd
***trans*-4a**	H	H	H		3.55 / dd			4.56 / dd
***trans*-4a$_{6\text{-}d}$**	D	H	H		3.48 / dd	1.82–1.87 / m		– [c]
***trans*-4a$_{5,5\text{-}d_2}$**	H	D	H		3.56 / dd	1.75 / m 1.92 / dd	– [c]	4.57 / s
***trans*-4a$_{4,4\text{-}d_2}$**	H	H	D		3.58 / d	– [c]	1.65 / m 1.94 /dd	4.59 / dd

[a] Shaded fields refer to positions not available in **2a**, **3a**, and **4a**. [b] Chemical shift information for multiplets refer to center position of the signal. [c] Position of deuteration (see text of the associated article).

4.2 Non-Deuterated Tetrahydrofuranmethanols

4.2.1 *cis*-2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol *cis*-(2a)[5]

R_f = 0.25 [petroleum ether/ethyl acetate = 8:2 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.22 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3), 1.75–1.85 (m, 1 H, CH_2), 1.93–1.99 (m, 2 H, CH_2), 2.19 (br. s, 1 H, OH), 2.27–2.34 (m, 1 H, CH_2) 3.87 (t, *J* = 7.4 Hz, 1 H, CH), 4.86 (dd, *J* = 8.3, 6.9 Hz, 1 H, CH) 7.25–7.38 (m, 5 H, Ar–H).

4.2.2 *trans*-2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol *trans*-(2a)[5]

R_f = 0.25 [petroleum ether/ethyl acetate = 8:2 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.28 (s, 3 H, CH_3), 1.19 (s, 3 H, CH_3), 1.78–1.99 (m, 3 H, CH_2), 2.19 (br. s, 1 H, OH), 2.30–2.42 (m, 1 H, CH_2) 4.03 (dd, *J* = 8.9, 6.3 Hz, 1 H, CH), 4.98 (dd, *J* = 8.8, 5.9 Hz, 1 H, CH) 7.25–7.38 (m, 5 H, Ar–H).

4.2.3 *rel*-(2*S*,1'*S*)-1-(5-phenyltetrahydrofuran-2-yl)-ethanol *rel*-(2*S*,1'*S*)-(2b)

R_f = 0.17 [petroleum ether/ethyl acetate = 8:2 (*v*/*v*)]. *trans*-**3b**: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.18 (d, *J* = 6.44 Hz, 3 H, CH_3),1.80−1.92 (m, 1 H, CH_2), 1.94−2.09 (m, 2 H, CH_2), 2.18 (s, 1 H, OH), 2.35−2.42 (m, 1 H, CH_2), 4.03− 4.10 (m, 1 H, CH), 4.12−4.16 (m, 1 H, CH), 5.02 (dd, *J* = 8.49, 5.95 Hz, 1 H, CH) 7.24− 7.36 (m, 5 H, Ar-H). ^{13}C-NMR ($CDCl_3$, 101 MHz) δ 18.1 (*C*H_3), 25.7 (*C*H_2), 35.7 (*C*H_2), 68.2 (HO-*C*H), 81.7 (O-*C*H), 83.9 (O-*C*H), 126 (Ar−C), 127 (Ar−C), 129 (Ar−C), 143 (Ar−C). *cis*-**3b**: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.22 (d, *J* = 6.44 Hz, 3 H, CH_3),1.79−1.84 (m, 1 H, CH_2), 1.94−2.09 (m, 2 H, CH_2), 2.18 (s, 1 H, OH), 2.27−2.34 (m, 1 H, CH_2), 3.94−3.98 (m, 1 H, CH), 4.03−4.10 (m, 1 H, CH), 4.88 (dd, *J* = 8.29, 6.73 Hz, 1 H, CH), 7.24−7.36 (m, 5 H, Ar-H). ^{13}C-NMR ($CDCl_3$, 101 MHz) δ 18.6 (*C*H_3), 25.1 (*C*H_2), 34.1 (*C*H_2), 68.3 (HO–*C*H), 81.3 (O–*C*H), 83.5 (O-*C*H), 126 (Ar−C), 128 (Ar−C), 129 (Ar−C), 142 (Ar−C). HRMS (EI$^+$) *m*/*z* 192.1149 [M$^+$]; calculated mass for $C_{12}H_{16}O_2^+$: 192.1150.

4.2.4 *cis*-(5-Phenyltetrahydrofuran-2-yl)-methanol *cis*-(2c)[5]

R_f = 0.09 [petroleum ether/ethyl acetate = 8:2 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.81–1.92 (m, 2 H, CH_2), 2.02–2.11 (m, 1 H, CH_2), 2.04 (s, 1 H, OH), 2.28–2.40 (m, 1

H, CH_2) 3.65 (dd, J = 11.6, 6.1 Hz, 1 H, CH_2), 3.79 (dd, J = 11.5, 3.3 Hz, 1 H, CH_2), 4.18–4.23 (m, 1 H, CH), 4.91 (dd, J = 7.6, 6.7 Hz, 1 H, CH) 7.24–7.37 (m, 5 H, Ar–H).

4.2.5 *trans*-(5-Phenyltetrahydrofuran-2-yl)-methanol *trans*-(2c)[5]

R_f = 0.09 [petroleum ether/ethyl acetate = 8:2 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.81–1.92 (m, 2 H, CH_2), 2.02–2.11 (m, 1 H, CH_2), 2.04 (s, 1 H, OH), 2.28–2.40 (m, 1 H, CH_2) 3.60 (dd, J = 11.6, 6.1 Hz, 1 H, CH_2), 3.74 (dd, J = 11.7, 3.3 Hz, 1 H, CH_2), 4.34–4.40 (m, 1 H, CH), 5.00(dd, J = 8.2, 5.9 Hz, 1 H, CH) 7.24–7.37 (m, 5 H, Ar–H).

4.2.6 *cis*-2-(5-*tert*-Butyl-tetrahydrofuran-2-yl)-propan-2-ol *cis*-(2d)[5]

R_f = 0.35 [diethyl ether : pentane = 1:2 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.91 (s, 9 H, $C(CH_3)_3$), 1.14 (s, 3 H, CH_3), 1.23 (s, 3 H, CH_3), 1.56–1.82 (m, 4 H, CH_2), 2.11 (br. s, 1 H, OH), 3.54 (dd, J = 8.3, 6.5 Hz, 1 H, CH), 6.64 (t, J = 7.2 Hz, 1 H, CH).

4.2.7 *cis*-2-(4-Phenyltetrahydrofuran-2-yl)-propan-2-ol *cis*-(2e)[5]

R_f = 0.29 [petroleum ether/ethyl acetate = 2:1 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.19 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 1.80–1.95 (m, 1 H, CH_2), 2.05 (br. s, 1 H, OH), 2.25–2.35 (m, 1 H, CH_2), 3.54 (t, J = 11.6 Hz, 1 H, CH_2), 3.77 (dd, J = 9.5, 8.1 Hz, 1 H, CH), 3.93 (dd, J = 9.8, 5.2 Hz, 1 H, CH), 4.22–4.28 (m, 1 H, CH_2) 7.21–7.34 (m, 5 H, Ar–H).

4.2.8 *trans*-2-(4-Phenyltetrahydrofuran-2-yl)-propan-2-ol *trans*-(2e)[5]

R_f = 0.29 [petroleum ether/ethyl acetate = 2:1 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.17 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3), 1.97 (ddd, J = 12.7, 7.8, 6.4 Hz, 1 H, CH_2), 2.05 (br. s, 1 H, OH), 2.22 (ddd, J = 12.7, 9.0, 7.3 Hz, 1 H, CH_2), 3.43 (ddd, J = 13.7, 9.0, 6.9 Hz, 1 H, CH_2), 3.84 (dd, J = 8.4, 7.2 Hz, 1 H, CH), 3.97 (t, J = 7.5 Hz, 1 H, CH), 4.25 (dd, J = 8.6, 6.8 Hz, 1 H, CH_2) 7.21–7.34 (m, 5 H, Ar–H).

4.2.9 *cis*-2-(3-Phenyltetrahydrofuran-2-yl)-propan-2-ol *cis*-(2f)[5]

R_f = 0.25 [petroleum ether/ethyl acetate = 2:1 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 0.88 (s, 3 H, C*H*$_3$), 1.06 (s, 3 H, C*H*$_3$), 1.72 (br. s 1 H, O*H*), 2.17 (dddd, J = 12.8, 9.1, 5.8, 3.7 Hz, 1 H C*H*$_2$), 2.45 (dddd, J = 12.8, 9.8, 8.2, 5.8 Hz, 1 H, C*H*$_2$), 3.40 (ddd, J = 8.5, 5.3, 3.8 Hz, 1 H, O-C*H*), 3.75 (d, J = 5.6 Hz, 1 H, Ar−C*H*), 3.97 (td, J_t = 9.2 Hz, J_d =

6.2 Hz, 1 H, O-CH_2), 4.27 (td, J_t = 8.7 Hz, J_d = 5.6 Hz, 1 H, CH_2), 7.20–7.36 (m, 5 H, Ar–H). δ25.8 (*C*H_3), 27.4 (*C*H_3), 34.4 (*C*H_2), 46.3 (Ar−*C*H) 66.8 (O-*C*H_2), 74.8 [*C*$(CH_3)_2$], 88.8 (O-*C*H), 127 (Ar−C), 128 (Ar−C), 129 (Ar−C), 142 (Ar−C).

3.3 Deuterated Tetrahydropyran-3-ols

4.3.1 General method

Neat $MoO_2(acac)_2$ is added to a solution of alkenols **1a**$_{1\text{-}d}$, **1a**$_{2,2\text{-}d_2}$ und **1a**$_{3,3\text{-}d_2}$ in benzene (35 mL). The solution is stirred in an atmosphere of dry nitrogen for 15 minutes at 40 °C and treated with a solution of TBHP in toluene (2.29 mL, 3.5 M solution of TBHP). The resulting mixture is stirred for 48 hours at a temperature of 40 °C and treated at room temperature with an aqueous saturated solution of NH_4Cl (100 mL). The organic phase is separated and the aqueous layer extracted with *tert*-butyl methyl ether (3 × 30 mL). Combined organic layer and washings are sequentially washed with an aqueous saturated solution of $NaHCO_3$ (100 mL), water (100 mL) and brine (100 mL) to afford a clear solution which is dried ($MgSO_4$) and concentrated at a pressure of 700 mbar and a bath temperature of 40 °C. The remaining residue was purified by chromatography [petroleum ether/ethyl acetate = 4:1 (*v*/*v*)] to afford a deuterated tetrahydropyranol as crystalline solid, which was crystallized from a 10/1-mixture of hexane/ethyl acetate.

4.3.1.1 *trans*-2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-6-*d* *trans*-(4a$_{6\text{-}d}$)

Reagents: 5-methyl-1-phenylhex-4-en-1-*d*-1-ol (**1a**$_d$) (772 mg, 4.03 mmol), $MoO_2(acac)_2$ (138 mg, 423 µmol), TBHP, and benzene. Yield: 139 mg (671µmol, 17 %), R_f = 0.24 [petroleum ether/ethyl acetate = 4:1 (*v*/*v*)], colorless crystals. Mp 135 °C. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 1.21 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3), 1.39 (d, J = 4.9 Hz, 1 H, OH), 1.53−1.58 (m, 1 H, 5-H), 1.63−1.70 (m, 1 H, 5-H), 1.82−1.87 (m, 2 H, 4-H), 3.48 (dd, J = 11.5, 4.4 Hz, 1 H, 3-H), 7.14−7.17 (m, 1 H, Ar−H), 7.22−7.27 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 16.5 (CH_3), 28.5 (CH_3), 29.0 (C4), 34.2 (C5), 71.7 (t, $J_{C,D}$ = 20.8 MHz, C6), 74.4 (C3), 75.8 (C2), 126.1 (Ar−C), 127.5 (Ar−C), 128.5 (Ar−C),

143.0 (Ar−C). GC-MS (t_r = 17.90/EI) *m*/*z* 149 (11), 131 (7), 118 (5), 105 (100), 92 (8), 78 (9), 59 (11).

4.3.1.2 *trans*-2,2-*Dimethyl*-6-phenyltetrahydropyran-3-ol-5,5-d_2 *trans*-(**4a**$_{5,5\text{-}d_2}$)

Reagents: 5-methyl-1-phenylhex-4-en-2,2-d_2-1-ol (**1a**$_{2,2\text{-}d_2}$) (717 mg, 3.75 mmol), $MoO_2(acac)_2$ (137 mg, 423 µmol), and TBHP and benzene. Yield: 83.5 mg (400 µmol, 11 %), R_f = 0.20 [petroleum ether/ethyl acetate = 4:1 (*v*/*v*)], colorless crystals. Mp 134 °C. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 1.31 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.68 (s, 1 H, OH), 1.73−1.77 (m, 1 H, 4-H), 1.92 (dd, *J* = 12.8, 4.9 MHz, 1 H, 4-H), 3.56 (dd, *J* = 11.8, 4.6 Hz, 1 H, 3-H), 4.57 (s, 1 H, 6-H), 7.25−7.27 (m, 1 H, Ar−H), 7.32−7.38 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 16.5 (CH_3), 28.5 (CH_3), 28.8 (C4), 33.5 (quin, $J_{C,D}$ = 19.4 Hz, C5), 72.0 (C6), 74.2 (C3), 75.9 (C2), 126.1 (Ar−C), 127.4 (Ar−C), 128.4 (Ar−C), 143.1 (Ar−C). GC-MS (t_r = 17.93/EI) *m*/*z* 150 (12), 132 (7), 106 (100), 79 (7), 59 (12). Anal. Calcd. for $C_{13}H_{16}D_2O_2$ (208.29): C, 74.96; H/D$_{eff}$, 8.71; Found: C, 74.90; H/D$_{eff}$, 8.56.[12]

4.3.1.3 *trans*-2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-4,4-d_2 *trans*-(**4a**$_{4,4\text{-}d_2}$)

Reagents: 5-methyl-1-phenylhex-4-en-3,3-d_2-1-ol (**1a**$_{3,3\text{-}d_2}$) (754 mg, 3.92 mmol), $MoO_2(acac)_2$ (136 mg, 417 µmol), TBHP and benzene. Yield: 102 mg (488 µmol, 13 %), R_f = 0.36 [petroleum ether/ethyl acetate = 4:1 (*v*/*v*)], colorless crystals. Mp 136 °C. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 1.32 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.45 (d, *J* = 5.5 Hz, 1 H, OH), 1.63−1.67 (m, 1 H, 5-H), 1.94 (dd, *J* = 13.6, 2.5, 1 H, 5-H), 3.58 (d, *J* = 5.2 Hz, 1 H, 3-H), 4.59 (dd, 1 H, *J* = 11.7, 2.4 Hz, 6-H), 7.25−7.28 (m, 1 H, Ar−H), 7.33−7.38 (m, 4 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 16.5 (CH_3), 28.1−28.4 (m, C4), 28.5 (CH_3), 34.1 (C5), 72.1 (C6), 74.3 (C3), 75.8 (C2), 126.1 (Ar−C), 127.5 (Ar−C), 128.5 (Ar−C), 143.1 (Ar−C). GC-MS (t_r = 17.84/EI) *m*/*z* 150 (11), 132 (8), 106 (100), 91 (6), 78 (11), 59 (12).

4.4 Non-Deuterated Tetrahydropyran-3-ols

4.4.1 *cis*-2,2-Dimethyl-6-phenyltetrahydropyran-3-ol *cis*-(4a)[5]

R_f = 0.22 [petroleum ether/ethyl acetate = 8:2 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.33 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.51 (s, 1 H, OH), 1.60–1.79 (m, 2 H, CH_2), 1.88–1.97 (m, 2 H, CH_2), 3.48 (br. s, 1 H, CH), 4.70 (dd, J = 11.7, 2.7 Hz, 1 H, CH) 7.21–7.39 (m, 5 H, Ar–H).

4.4.2 *trans*-2,2-Dimethyl-6-phenyltetrahydropyran-3-ol *trans*-(4a)

In an atmosphere of argon, a solution of 5-methyl-1-phenylhex-4-en-1-ol (**1a**) (766 mg, 4.03 mmol) and $MoO_2(acac)_2$ (134 mg, 411 µmol) in benzene (30 mL) was treated with a solution of TBHP in nonane (1.46 mL, 5.5 M solution of TBHP). The reaction mixture was stirred for 48 hours at 40 °C, treated at 20 °C with a saturated aqueous solution of NH_4Cl (100 mL), and extracted with *tert*-butyl methyl ether (3 × 100 mL). Combined organic extracts were sequentially washed with an aqueous saturated solution of $NaHCO_3$ (100 mL), water (100 mL), and brine (100 mL). The resulting clear solution was dried ($MgSO_4$) and concentrated under reduced pressure (10 mbar) at a bath temperature of 40 °C. The remaining yellow oil was purified by flash-chromatography [petroleum ether/ethyl acetate = 8:2 (*v*/*v*)]. The fraction having a ratio of fronts of R_f = 0.22 was collected, concentrated under reduced pressure and crystallized from a 10/1-mixture (*v*/*v*) of hexane/ethyl acetate (2.75 mL). Yield: 151 mg (732 µmol, 18 %), R_f = 0.22 [petroleum ether/ethyl acetate = 8:2 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.29 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.59 (br. s, 1 H, OH), 1.63–1.79 (m, 2 H, CH_2), 1.90–1.96 (m, 2 H, CH_2), 3.55 (dd, J = 11.4 , 4.3Hz, 1 H, CH), 4.56 (dd, J = 11.5, 2.0 Hz, 1 H, CH) 7.22–7.25 (m, 1 H, Ar–H) 7.30–7.37 (m, 4 H, Ar–H).

4.4.3 *rel*-(2*S*,3*R*,6*S*)-2-Methyl-6-phenyltetrahydropyran-3-ol *rel*-(2*S*,3*R*,6*S*)-(4b)

R_f = 0.17 [petroleum ether/ethyl acetate = 8:2 (*v*/*v*)]. ^{13}C NMR ($CDCl_3$, 101 MHz) δ 18.1 (*C*H_3), 25.7 (*C*H_2), 35.7 (*C*H_2), 68.2 (HO-*C*H), 81.7 (O-*C*H), 83.9 (O-*C*H), 126 (Ar−*C*), 127 (Ar−*C*), 129 (Ar−*C*), 143 (Ar−*C*). HRMS (EI$^+$) *m*/*z* 192.1149 [M$^+$]; calculated mass for $C_{12}H_{16}O_2^+$: 192.1150.

4.4.4 *trans*-2,2-Dimethyl-6-*tert*-butyl-tetrahydropyran-3-ol *trans*-(4d).[5]

R_f = 0.33 [diethyl ether/pentane = 1:2 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.85 (s, 9 H, $C(CH_3)_3$), 1.12 (s, 3 H, CH_3), 1.21 (s, 3 H, CH_3), 1.49–1.83 (m, 4 H, CH_2), 2.10 (br. s, 1 H, OH), 3.05 (dd, *J* = 11.6 , 2.2 Hz, 1 H, CH), 3.35 (dd, *J* = 11.5, 4.7 Hz, 1 H, CH).

4.4.5 *trans*-2,2-Dimethyl-5-phenyltetrahydropyran-3-ol *trans*-(4e)[5]

R_f = 0.24 [petroleum ether/ethyl acetate = 2:1 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.31 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3), 1.59 (br. s, 1 H, OH), 1.94–2.06 (m, 1 H, CH_2), 2.21 (ddd, J = 13.8, 12.3, 2.6 Hz, 1 H, CH_2), 3.20 (tt, *J* = 11.4 , 4.7 Hz, 1 H, CH), 3.61 (dd, *J* = 3.7, 3.4 Hz, 1 H, CH_2), 3.74 (dd, J = 11.9, 10.7 Hz, 1 H, CH_2), 3.80 (ddd, J = 11.7, 5.0, 1.8 Hz, 1 H, CH_2), 7.20–7.33 (m, 5 H, Ar–H).

4.4.6 *cis*-2,2-Dimethyl-4-phenyltetrahydropyran-3-ol *cis*-(4f)[5]

R_f = 0.25 [petroleum ether/ethyl acetate = 2:1 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 1.30 (s, 3 H, C*H*$_3$), 1.40 (s, 3 H, C*H*$_3$), 1.54 (dt, J_d = 13.2 Hz, J_t = 4.0 Hz, 1 H, eq. C*H*$_2$), 1.66 (br. s, 1 H, O*H*), 2.30 (qd, J_q = 13.0 Hz, J_d = 5.6 Hz, 1 H, ax. C*H*$_2$), 3.24 (dt, J_d = 13.1 Hz, J_t = 2.9 Hz, 1H, Ar−C*H*), 3.47 (s, 1 H, HO-C*H*), 3.85 (td, J_t = 12.2 Hz, J_d = 2.3 Hz, 1 H, O-C*H*$_2$), 3.90 (ddd, *J* = 11.7, 5.6, 1.5 Hz, 1 H, O-C*H*$_2$), 7.20–7.36 (m, 5 H, Ar–H). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 21.6 (*C*H$_3$), 24.1 (*C*H$_2$), 27.0 (*C*H$_3$), 41.1 (Ar−CH), 61.4 (O-*C*H$_2$), 74.5 (HO-*C*H), 71.9 (*C*(CH$_3$)$_2$), 127 (Ar−C), 128 (Ar−C), 129 (Ar−C), 142 (Ar−C).

4.5 γ-Butyrolactones

4.5.1 4-Benzoyloxy-5,5-dimethyl-2(3*H*)-dihydrofuranone-3,3-d_2 (**3a**$_{3,3\text{-}d_2}$)

To a solution of VO(L^1)(OEt)(EtOH) (60.0 mg, 162 µmol) in chloroform (4 mL) was added a solution of TBHP in toluene (600 µL, 3.5 M solution of TBHP) and stirred for three minutes at a temperature of 20 °C. To this mixture was added a solution of *cis*-2-(5-phenyltetrahydrofuran-2-yl)-propan-2-ol-3,3-d_2 (**2a**$_{3,3\text{-}d_2}$) (314 mg, 2.33 mmol) in chloroform (3.60 mL). The resulting solution was stirred for 7 days at a temperature of

20 °C and concentrated afterwards at a pressure of 700 mbar and a bath temperature of 40 °C. The remaining oil was purified by chromatography [ethyl acetate/hexane = 2:8 (*v*/*v*)]. R_f = 0.36 [ethyl acetate/hexane = 4:1 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 1.41 (s, 6 H, CH_3), 5.34 (s, 1 H, 4-H), 7.36−7.39 (m, 2 H, Ar−H), 7.49−7.53 (m, 1 H, Ar−H), 7.93−7.95 (m, 2 H, Ar−H). ^{13}C-NMR ($CDCl_3$, 151 MHz): δ = 22.0 (CH_3), 26.5 (CH_3), 35.7 (quin, $J_{C,D}$ = 21.4 Hz, C4), 75.1 (C3), 86.6 (C2), 128.8 (Ar−C), 129.1 (Ar−C), 129.9 (Ar-C), 133.9 (Ar−C), 165.6 (CO), 173.7 (CO).

4.5.2 4-Benzoyloxy-5,5-dimethyl-2(3*H*)-dihydrofuranone (3a)[5]

R_f = 0.18 [petroleum ether/ethyl acetate = 8:2 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.49 (s, 3 H, CH_3), 1.50 (s, 3 H, CH_3), 2.70 (dd, *J* = 18.5, 2.1 Hz, 1 H, CH_2), 3.16 (dd, *J* = 18.5, 6.6 Hz, 1 H, CH_2), 5.44 (dd, *J* = 6.6, 2.1 Hz, 1 H, CH), 7.45–7.48 (m, 2 H, Ar–H), 7.58–7.62 (m, 1 H, Ar–H), 8.02–8.04 (m, 2 H, Ar−H).

4.5.3 *cis*-4-Benzoyloxy-5-methyl-2(3*H*)-dihydrofuranone *cis*-(3b)[13]

R_f = 0.24 [petroleum ether/ethyl acetate = 8:2 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 1.47 (d, *J* = 6.6 Hz, 3 H, CH_3), 2.76 (dd, *J* = 18.2, 1.5 Hz, 1 H, CH_2), 3.02 (dd, *J* = 18.2, 6,5 Hz, 1 H, CH_2), 4.82 (qd, J_q = 6.5 Hz, J_d = 4.2 Hz, 1 H, CH), 5.71 (ddd, *J* = 6.0, 4.3, 1.4 Hz, 1 H, CH), 7.47 (d, *J*=7.5 Hz, 2 H, Ar–H), 7.61 (tt, *J* = 7.4, 1.4 Hz, 1 H, Ar–H), 8.04 (dd, *J* = 8.4, 1.4 Hz, 2 H, Ar–H).

4.5.4 *trans*-4-Benzoyloxy-5-methyl-2(3*H*)-dihydrofuranone *trans*-(3b)[14]

R_f = 0.24 [petroleum ether/ethyl acetate = 8:2 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.50 (d, *J* = 6.7 Hz, 3 H, CH_3), 2.75 (dd, *J* = 18.6, 2.2 Hz, 1 H, CH_2), 3.08 (dd, *J* = 18.7, 7.0 Hz, 1 H, CH_2), 4.78 (qd, J_q = 6.8, J_d = 1.7 Hz, 1 H, CH), 5.30 (dt, J_d = 6.9, J_t = 1.9 Hz, 1 H, CH), 7.45–7.49 (m, 2 H, Ar–H), 7.59–7.63 (m, 1 H, Ar–H), 8.03 (dd, J = 8.4, 1.3 Hz, 2 H, Ar–H).

4.5.5 4-Benzoyloxy-2(3*H*)-dihydrofuranone (3c)[15]

R_f = 0.04 [petroleum ether/ethyl acetate = 8:2 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.78 (d, *J* = 18.3 Hz, 1 H, CH_2), 2.97 (dd, *J* = 18.5, 6.6 Hz, 1 H, CH_2), 4.52 (d, *J* = 11.1 Hz,

1 H, CH_2), 4.61 (dd, J = 11.7, 4.7 Hz, 1 H, CH_2), 5.68 (dd, J_d = 6.6, 4.9 Hz, 1 H, CH), 7.43–7.48 (m, 2 H, Ar–H), 7.55–7.58 (m, 1 H, Ar–H), 8.02–8.04 (m, 2 H, Ar–H).

4.5.6 4-Pivaloyloxy-5,5-dimethyl-2(3*H*)-dihydrofuranone (3d)

To an ice-cooled solution of 4-hydroxy-5,5-dimethyl-2(3*H*)-dihydrofuranone (836 mg, 6.42 mmol), triethylamine (14.2 g, 141 mmol) and 4,4-dimethylaminopyridine (855 mg, 7.0 mmol) in dichloromethane (120 mL) was added in a dropwise manner neat pivaloyl chloride (10.1 mg, 83.8 mmol) while being stirred. Stirring was continued at 21 °C for sixty minutes. Water (100 mL) was subsequently added and the aqueous phase acidified to pH 1 by adding 6 M-hydrochloric acid. The organic phase was separated and washed with an aqueous saturated solution of $NaHCO_3$ (50 mL). The resulting solution was dried (Na_2SO_4) and concentrated at bath temperature of 40 °C in an aspirator vacuum. The residue was purified by flash-chromatography using a 1/2-mixture by volume of diethyl ether/pentane. Yield: 1.05 g (4.90 mmol, 76 %), colorless liquid, R_f = 0.21 [diethyl ether/pentane = 1:2 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.22 (s, 9 H, $C(CH_3)_3$), 1.41 (s, 3 H, CH_3), 1.45 (s, 3 H, CH_3), 2.51 (dd, J = 18.6, 2.1 Hz, 1 H, CH_2), 3.06 (dd, J = 18.6, 6.7, Hz, 1 H, CH_2), 5.16 (dd, J = 6.7, 2.2, Hz, 1 H, CH). ^{13}C-NMR ($CDCl_3$, 151 MHz) δ 21.6 (CH_3), 26.4 (CH_3), 27.0 [$C(CH_3)_3$], 36.0 (C3), 38.9 [$C(CH_3)_3$], 74.4 (C4), 86.4 (C5), 173.6 (C1'), 177.5 (C2). Anal. calcd. for $C_{11}H_{18}O_4$ (214.26): C, 61.66; H, 8.47; Found: C, 61.41; H, 8.55. GC-MS (EI): *m/z* (%) = 57 (100), 199 (15) [M^+-CH_3], 215 (5) [M^++H].

4.5.7 4-Phenyl-2(3*H*)-dihydrofuranone (5e)[16]

R_f = 0.36 [petroleum ether/ethyl acetate = 2:1 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.68 (dd, J = 17.5, 9.2 Hz, 1 H, CH_2), 2.93 (dd, J = 17.4, 8.8 Hz, 1 H, CH_2), 3.74–3.84 (m, 1 H, CH), 4.27 (dd, J = 9.0, 8.1 Hz, 1 H, CH_2), 4.67 (dd, J = 9.0, 7.8 Hz, 1 H, CH_2), 7.23–7.26 (m, 2 H, Ar–H), 7.29–7.32 (m, 1 H, Ar–H), 7.36–7.40 (m, 2 H, Ar–H).

4.5.8 3-Phenyl-2(3*H*)-dihydrofuranone (5f)[17]

R_f = 0.42 [petroleum ether/ethyl acetate = 2:1 (*v*/*v*)]. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.45 (dddd, J = 12.8, 10.2, 9.3, 8.3 Hz, 1 H, CH_2), 2.69–2.77 (m, 1 H, CH_2), 3.82 (dd, J =

10.1, 9.3 Hz, 1 H, CH), 4.36 (td, J_t = 9.2 Hz, J_d = 6.7 Hz, 1 H, CH_2), 4.49 (td, J_t = 8.6 Hz, J_d = 3.3 Hz, 1 H, CH_2), 7.28–7.40 (m, 5 H, Ar–H).

5 Oxidation of Deuterated Alkenols Catalyzed by Oxovanadium(V) Schiff-Base Complex VO(L^1)(OEt) – Different Reaction Times

5.1 General method

To a solution of VO(L^1)(OEt) (H_2L^1 = *N*-salicylidene 2-aminophenol; used as ethanol solvate as obtained from synthesis) in chloroform was added a solution of TBHP (3.5 M) in toluene. The mixture was stirred for 3 minutes at 20 °C and was treated at 20 °C with a solution of a deuterated alkenol (**1a**$_{1\text{-}d}$, **1a**$_{2,2\text{-}d_2}$, **2a**$_{3,3\text{-}d_2}$) in chloroform. The reaction mixture was stirred for the time specified in sections 5.1.1–5.1.6 at 20 °C and filtrated through a pad of neutral aluminium oxide. Organic products adsorbed were washed with ethyl acetate (15 mL) from the pad of aluminium oxide. Combined filtrate and washings were concentrated at a bath temperature of 40 °C in an aspirator vacuum to leave an oily residue, which was purified by flash-chromatography [petroleum ether/*tert*-butyl methyl ether = 3:2 (*v*/*v*)]. Deuterated tetrahydrofuranmethanols, tetrahydropyranols and γ-butyrolactones were characterized using authentic samples from syntheses described in the sections 5 and 7.

5.1.1 Oxidation of 5-methyl-1-phenylhex-4-en-d-1-ol (1a$_{1\text{-}d}$) – 72 hours

Reactants: alkenol **1a**$_{1\text{-}d}$ (192 mg, 1.00 mmol) in chloroform (4 mL), VO(L^1)(OEt)(EtOH) (37.0 mg, 10 mol%) and TBHP (430 µL, 3.5 M solution in toluene, 1.50 mmol) in chloroform (3.6 mL). Reaction time: 72 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-5-d (**2a**$_{5\text{-}d}$)*. Yield: 133 mg (642 µmol, 64 %), 94/6-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-6-d (**4a**$_{6\text{-}d}$)*. Yield: 17.7 mg (85.4 µmol, 9 %), 46/54-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**)*. Yield: 8.29 mg (35.4 µmol, 4 %).

5.1.2 Oxidation of 5-methyl-1-phenylhex-4-en-d-1-ol (1a$_{1\text{-}d}$) – 168 hours

Reactants: alkenol **1a**$_{1\text{-}d}$ (191 mg, 1.00 mmol) in chloroform (4 mL), VO(L^1)(OEt)(EtOH) (36.9 mg, 10 mol%), TBHP (2 × 430 µL, 3.5 M solution in toluene, 2 × 1.50 mmol; second aliquot added after 72 h) in chloroform (3.6 mL). Reaction time:

168 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-5-d (**2a**$_{5\text{-}d}$)*. Yield: 97.9 mg (470 µmol, 47 %), 98/2-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-6-d (**4a**$_{6\text{-}d}$)*. Yield: 24.4 mg (117 µmol, 12 %), 50/50-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**)*. Yield: 26.9 mg (115 µmol, 12 %).

5.1.3 Oxidation of 5-methyl-1-phenylhex-4-en-2,2-d$_2$-1-ol (**1a**$_{2,2\text{-}d_2}$) – 72 hours

Reactants: alkenol **1a**$_{2,2\text{-}d_2}$ (195 mg, 1.01 mmol) in chloroform (4 mL), VO(L^1)(OEt)(EtOH) (36.1 mg, 10 mol%), TBHP (430 µL, 3.5 M solution in toluene, 1.50 mmol) in chloroform (3.6 mL). Reaction time: 72 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-4,4-d$_2$ (**2a**$_{4,4\text{-}d_2}$)*. Yield: 92.1 mg (442 µmol, 44 %), 94/6-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-5,5-d$_2$* (**4a**$_{5,5\text{-}d_2}$). Yield: 17.1 mg (82.1 µmol, 8 %), 46/54-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone* (**3a**). Yield: 13.0 mg (55.5 µmol, 6 %).

5.1.4 Oxidation of 5-methyl-1-phenylhex-4-en-2,2-d$_2$-1-ol (**1a**$_{2,2\text{-}d_2}$) – 168 hours

Reactants: alkenol **1a**$_{2,2\text{-}d_2}$ (193 mg, 1.00 mmol) in chloroform (4 mL), VO(L^1)(OEt)(EtOH) (36.7 mg, 10 mol%), TBHP (2 × 430 µL, 3.5 M solution in toluene, 2 × 1.50 mmol; second aliquot added after 72 hours) in chloroform (3.6 mL). Reaction time: 168 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-4,4-d$_2$ (**2a**$_{4,4\text{-}d_2}$)*. Yield: 49.2 mg (236 µmol, 24 %), 96/4-mixture of cis/trans-isomers, brown oil. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-5,5-d$_2$ (**4a**$_{5,5\text{-}d_2}$)*. Yield: 26.7 mg (128 µmol, 13 %), 45/55-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**)*. Yield: 50.1 mg (214 µmol, 21 %).

5.1.5 Oxidation of 5-methyl-1-phenylhex-4-en-3,3-d$_2$-1-ol (**1a**$_{3,3\text{-}d_2}$) – 72 hours

Reactants: alkenol **1a**$_{3,3\text{-}d_2}$ (194 mg, 1.01 mmol) in chloroform (4 mL), VO(L^1)(OEt)(EtOH) (37.4 mg, 10 mol%), TBHP (430 µL, 3.5 M solution in toluene, 1.50 mmol) in chloroform (3.6 mL). Reaction time: 72 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-3,3-d$_2$ (**2a**$_{3,3\text{-}d_2}$)*. Yield: 108 mg (519 µmol, 52 %), 96/4-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-4,4-*

*d_2 (**$4a_{4,4\text{-}d_2}$**)*. Yield: 18.1 mg (86.9 µmol, 9 %, *cis*:*trans* = 36:64). *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone-3,3-d_2 (**$3a_{3,3\text{-}d_2}$**)*. Yield: 8.15 mg (34.5 µmol, 4 %).

5.1.6 Oxidation of 5-methyl-1-phenylhex-4-en-3,3-d_2-1-ol ($1a_{3,3\text{-}d_2}$) – 168 hours

Reactants: alkenol **$1a_{3,3\text{-}d_2}$** (193 mg, 1.01 mmol) in chloroform (4 mL), VO(L^1)(OEt)(EtOH) (37.2 mg, 10 mol%), TBHP (2 × 430 µl, 3.5 M solution in toluene, 2 × 1.50 mmol; second aliquot added after 72 hours) in chloroform (3.6 mL). Reaction time: 168 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-3,3-d_2 (**$2a_{3,3\text{-}d_2}$**)*. Yield: 55.2 mg (265 µmol, 27 %), 97/3-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-4,4-d_2 (**$4a_{4,4\text{-}d_2}$**)*. Yield: 15.9 mg (76.3 µmol, 8 %), 47/53-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone-3,3-d_2 (**$3a_{3,3\text{-}d_2}$**)*. Yield: 30.7 mg (130 µmol, 13 %).

6 Oxidation of Deuterated Alkenols Catalyzed by Piperidine-Derived Oxovanadium(V) Complex VO(L^2)(OEt) – Different Reaction Times

6.1 General method

To a solution of VO(L^2)(OEt) [H_2L^2 = *cis*-2,6-bis(diphenylmethanol)piperidine] in chloroform was added a solution of TBHP (3.5 M) in toluene. The mixture was stirred for 3 minutes at 20 °C and was treated at 20 °C with a solution of a deuterated alkenol (**1a**$_{1\text{-}d}$, **1a**$_{2,2\text{-}d_2}$) in chloroform. The reaction mixture was stirred for the time specified in sections 6.1.1–6.1.6 at a temperature of 20 °C and filtrated through a pad of neutral aluminium oxide. Organic products were washed from the aluminium oxide with ethyl acetate (15 mL). Combined filtrate and washings were concentrated at a bath temperature of 40 °C in an aspirator vacuum to leave an oily residue, which was purified by flash-chromatography [petroleum ether/*tert*-butyl methyl ether = 3:2 (*v*/*v*)]. Deuterated tetrahydrofuranmethanols, tetrahydropyranols and γ-butyrolactones were characterized using authentic samples from syntheses described in the sections 5 and 7.

6.1.1 Oxidation of 5-methyl-1-phenylhex-4-en-d-1-ol (1a1-d) – 48 hours.

Reactants: alkenol **1a**$_{1\text{-}d}$ (191 mg, 1.00 mmol) in chloroform (4 mL), VO(L^2)(OEt) (56.5 mg, 10 mol%), TBHP (430 µL, 3.5 M solution in toluene, 1.50 mmol) in chloroform (3.6 mL). Reaction time: 48 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-5-d (**2a**$_{5\text{-}d}$)*. Yield: 98.0 mg (473 µmol, 47 %), 95/5-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-6-d (**4a**$_{6\text{-}d}$)*. Yield: 15.9 mg (76.7 µmol, 8 %), 49/51-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone* (**3a**). Yield: 3.81 mg (16.3 µmol, 2 %).

6.1.2 Oxidation of 5-methyl-1-phenylhex-4-en-d-1-ol (1a$_{1\text{-}d}$) – 72 hours

Reactants: alkenol **1a**$_{1\text{-}d}$ (192 mg, 1.00 mmol) in chloroform (4 mL), VOL^2(OEt) (56.6 mg, 10 mol%), TBHP (430 µL, 3.5 M solution in toluene, 1.50 mmol) in chloroform (3.6

mL). Reaction time: 72 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-5-d (**2a**$_{5\text{-}d}$)*. Yield: 82.8 mg (399 µmol, 40 %), 95/5-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-6-d (**4a**$_{6\text{-}d}$)*. Yield: 15.1 mg (72.8 µmol, 7 %), 49/51-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**)*. Yield: 2.49 mg (10.6 µmol, 2 %).

6.1.3 Oxidation of 5-methyl-1-phenylhex-4-en-d-1-ol (1a$_{1\text{-}d}$) - 168 hours

Reactants: alkenol **1a**$_{1\text{-}d}$ (191 mg, 1.00 mmol) in chloroform (4 mL), VOL^2(OEt) (56.3 mg, 10 mol%), TBHP (2 × 430 µL, 3.5 M solution in toluene, 2 × 1.50 mmol; second aliquot added after 72 hours) in chloroform (3.6 mL). Reaction time: 168 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-5-d (**2a**$_{5\text{-}d}$)*. Yield: 42.5 mg (205 µmol, 47 %), >99/1-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-6-d (**4a**$_{6\text{-}d}$)*. Yield: 17.1 mg (82.5 µmol, 8 %), 44/56-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**)*. Yield: 12.9 mg (55.1 µmol, 6 %).

6.1.4 Oxidation of 5-methyl-1-phenylhex-4-en-2,2-d$_2$-1-ol (1a$_{2,2\text{-}d_2}$) – 48 hours

Reactants: alkenol **1a**$_{2,2\text{-}d_2}$ (193 mg, 1.00 mmol) in chloroform (4 mL), VO(L^2)(OEt) (57.0 mg, 10 mol%), TBHP (430 µL, 3.5 M solution in toluene, 1.50 mmol) in chloroform (3.6 mL). Reaction time: 48 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-4,4-d$_2$ (**2a**$_{4,4\text{-}d_2}$)*. Yield: 36.0 mg (173 µmol, 17 %), 97/3-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-5,5-d$_2$ (**4a**$_{5,5\text{-}d_2}$)*. Yield: 12.7 mg (61.0µmol, 6 %), 34/66-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone* (***3a***). Yield: 4.62 mg (19.6 µmol, 2 %).

6.1.5 Oxidation of 5-methyl-1-phenylhex-4-en-2,2-d$_2$-1-ol (1a$_{2,2\text{-}d_2}$) – 72 hours

Reactants: alkenol **1a**$_{2,2\text{-}d_2}$ (191 mg, 0.99 mmol) in chloroform (4 mL), VO(L^2)(OEt) (57.3 mg, 10 mol%), TBHP (430 µL, 3.5 M solution in toluene, 1.50 mmol) in chloroform (3.6 mL). Reaction time: 72 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-4,4-d$_2$ (**2a**$_{4,4\text{-}d_2}$)*. Yield: 74.8 mg (359 µmol, 36 %), 96/4-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-5,5-d$_2$ (**4a**$_{5,5\text{-}d_2}$)*. Yield: 17.5 mg (84.0 µmol, 8 %, *cis*:*trans* = 38:62).

6.1.6 Oxidation of 5-methyl-1-phenylhex-4-en-2,2-d_2-1-ol ($\mathbf{1a}_{2,2\text{-}d_2}$) – 168 hours Reactants: Alkenol $\mathbf{1a}_{2,2\text{-}d_2}$ (193 mg, 1.01 mmol) in chloroform (4 mL), VO(L^2)(OEt) (57.0 mg, 10 mol%), TBHP (2 × 430 μL, 3.5 M solution in toluene, 2 × 1.50 mmol; second aliquot added after 72 hours) in chloroform (3.6 mL). Reaction time: 168 hours at 20 °C. *2-(5-Phenyltetrahydrofuran-2-yl)-propan-2-ol-4,4-d_2 (**2a**$_{4,4\text{-}d_2}$)*. Yield: 15.7 mg (75.4 μmol, 8 %), 98/2-mixture of cis/trans-isomers. *2,2-Dimethyl-6-phenyltetrahydropyran-3-ol-5,5-d_2* ($\mathbf{4a}_{5,5\text{-}d_2}$). Yield: 18.0 mg (86.4 μmol, 9 %), 39/61-mixture of cis/trans-isomers. *4-Benzoyloxy-5,5-dimethyl-2(3H)-dihydrofuranone (**3a**)*. Yield: 36.3 mg (154 μmol, 15 %).

7 References

1. Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, Pergamon: Oxford, **1980**.
2. Michael, J. P.; Nkwelo, M. M. *Tetrahedron*, **1990**, *46*, 2549–2560.
3. Kimura, M.; Ezoe, A.; Mori, M.; Iwata, K.; Tamuro, Y. *J. Am. Chem. Soc.* **2006**, *128*, 8559–8568.
4. Lansbury, P. T.; Pattison, V. A. *J. Am. Chem. Soc.* **1962**, *84*, 4295–4298.
5. Hartung, J.; Drees, S.; Greb, M.; Schmidt, P.; Svoboda, I.; Fuess, H.; Murso, A.; Stalke, D. *Eur. J. Org. Chem.* **2003**, 2388–2408.
6. Paquette, L. A.; Gilday, J. P. *J. Org. Chem.* **1988**, *53*, 4972–4978.
7. Schmidt, V. A.; Alexanian, E. J. *Angew. Chem.* **2010**, *122*, 4593–4596.
8. Boyd, D. R.; Sharma, N. D.; Barr, S. A.; Carroll, J. G.; Mackerracher, D.; Malone, J. F. *J. Chem. Soc. Perkin Trans. 1*, **2000**, 3397–3405.
9. Akiyama, S.; Munakata, M. Polyhedron, 1994, 13, 2495–2499.
10. Dönges, M.; Amberg M.; Stapf G.; Kelm H.; Bergsträßer U.; Hartung J. submitted for publication.
11. (a) Sharpless K. B.; Verhoeven T. R.; *Aldrichim. Acta* **1979**, *12,* 63–74. (b) Hill J. G.; Rossiter B. E.; Sharpless K. B. *J. Org. Chem.* **1983**, *48*, 3607−3608.
12. Voss, G.; Schramm, W. *Helv. Chim. Acta*, **2000**, *83*, 2884–2892.
13. Afonso, C. A. M.; Barros, M. T.; Godinho, L. S.; Maycock, C. D. *Tetrahedron*, **1993**, 49, 4283–4292.
14. Chen, S.-Y.; Joullie, M. M. *J. Org. Chem*, **1984**, 49, 2168–2174.
15. Schmidt, J. A. R.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc*, **2005**, 127, 11426–11435.
16. Imada, Y.; Iida, H.; Murahashi, S.-I.; Naota, T. *Angew. Chem.* **2005**, 117, 1732–1734.
17. Ishii, Y.; Yoshida, T.; Yamawaki, K.; Ogawa, M.; *J. Org. Chem.* **1988**, 5549–5552.