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Supporting Information (7 pages)

Chiral Hydroperoxides as Oxygen Source in the Catalytic Stereoselective Epoxidation of Allylic Alcohols by Sandwich-Type Polyoxometalates: Control of Enantioselectivity through a Metal-Coordinated Template

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Experimental Section

General Aspects. Melting points are uncorrected. The enantiomeric ratios (*er*) of the epoxides **2g-l** were measured, after isolation of the product, by high-performance liquid chromatography (HPLC) on a chiral column [Daicel Chiralcel OD column (250 x 4.6 mm), UV detection at 220 nm, flow rate of 0.8 mL/min, 9:1 mixture of *n*-hexane : isopropanol as eluent]. The absolute configurations of the known epoxides **2g-l** were assigned by direct comparison of the specific rotations, determined on a polarimetric Chiralyser or on a polarimeter with the literature value.^{8,13c} The enantiomeric ratio of the geraniol epoxide **2m**^{13c} was determined by GC-MS with a β -TG chiral column (25 m). The conversions and material balances were determined by ¹H-NMR spectroscopy with dimethyl isophthalate as internal standard. TLC analysis was conducted on precoated silica-gel foils 60 F₂₅₄ (20 x 20 cm) from Merck, Darmstadt. Spots were visualized by treatment with the polymolybdic acid (5% solution in ethanol) test spray. Silica gel (32 – 63 μ m) from Woelm, Erlangen was used for flash chromatography. For peroxide tests, potassium iodide/starch indicator paper from Merck was utilized. Solvents were dried by standard methods and purified by distillation before use. Commercially available chemicals were employed without further purification, unless otherwise stated.

Starting Materials. The sandwich-type oxovanadium(IV)-substituted polyoxometalates, K₁₂{ZnW(VO)₂(ZnW₉O₃₄)₂}·30H₂O, and the other transition-metal [Mn(II), Fe(III), Zn(II), Pd(II) and Pt(II)] derivatives were synthesized by the literature procedure.¹⁸ The ruthenium(III) analog, Na₁₁{ZnW[Ru₂(H₂O)(OH)](ZnW₉O₃₄)₂}·42H₂O, was made according to the procedure reported earlier.⁵ The vanadium-containing α -Keggin PV₂Mo₁₀O₄₀⁵⁻ was obtained according to a procedure as reported.²⁷ The allylic alcohols **1e**, *trans*-**1j**, and **1m** are commercially available; the derivatives **1a**,²⁸ **1b**,²⁹ **1c**,²⁸ **1d**,²² **1f**,³⁰ and **1g**,³¹ **1h**,³² **1i**,³² **1k**,³³ *cis*-**1j**,³⁵ **1l**,³⁵ **1n**,³⁶ **1o**,³⁶ **1p**³⁷ were synthesized and fully characterized according to literature procedures. The racemic (1-phenyl)ethyl hydroperoxide (**4a**) and [(1-(4-chlorophenyl)]ethyl hydroperoxide (**4b**) were synthesized according to the known methods.³⁸ *tert*-Butyl hydroperoxide (*t*-BuOOH) was employed as a 4.0 M solution in 1,2-dichloroethane, prepared by extraction of aqueous 70% *t*-BuOOH with 1,2-dichloroethane (3 x 20 mL); its concentration was determined by iodometric titration. The enantiopure (> 99%) (*S*)-(-)-(1-phenyl)ethyl hydroperoxide was obtained by enzymatic kinetic resolution³⁹ and (4*R*,5*R*)-TADOOH and (4*R*,5*R*)-Me-TADOOH were prepared according to the known procedure.^{13f,14}

Caution! Organic hydroperoxides are potentially dangerous and should be handled with care. To avoid accidents, the preparation and use of such hydroperoxides should always run on a small scale.

Preparation of Stock Solutions of Hydrophobic M-POM Catalysts. The catalytic reactions with the polyoxometalates were performed by transferring the polyoxoanion into the organic solvents with a quaternary ammonium cation. For this purpose, the alkali metal of all transition-metal-substituted POMs were exchanged with hydrophobic quaternary ammonium salts (Aliquot 336) analogous to the literature protocol.⁴ Thus, stock solutions of M-POM (0.1 mM) were prepared by dissolving 0.01 mmol of $\text{K}_{12}\{\text{ZnWV}_2\text{O}_2(\text{ZnW}_9\text{O}_{34})_2\} \cdot 30\text{H}_2\text{O}$ [O=V(IV)-POM], $\text{Na}_{12}\{\text{ZnW}[\text{Mn}(\text{H}_2\text{O})]_2(\text{ZnW}_9\text{O}_{34})_2\} \cdot 46\text{H}_2\text{O}$, [Mn(II)-POM], $\text{Na}_{12}\{\text{ZnW}[\text{Zn}(\text{H}_2\text{O})]_2(\text{ZnW}_9\text{O}_{34})_2\} \cdot 46\text{H}_2\text{O}$ (Zn(II)-POM), $\text{Na}_{11}\{\text{ZnW}[\text{Ru}_2(\text{H}_2\text{O})(\text{OH})](\text{ZnW}_9\text{O}_{34})_2\} \cdot 42\text{H}_2\text{O}$ [Ru(III)-POM], $\text{Na}_{10}\{\text{ZnW}[\text{Fe}(\text{H}_2\text{O})]_2(\text{ZnW}_9\text{O}_{34})_2\} \cdot 46\text{H}_2\text{O}$ [Fe(III)-POM], $\text{K}_{12}\{\text{ZnW}[\text{Pd}(\text{H}_2\text{O})]_2(\text{ZnW}_9\text{O}_{34})_2\} \cdot 38\text{H}_2\text{O}$ [Pd(II)-POM], or $\text{K}_{12}\{\text{ZnW}[\text{Pt}(\text{H}_2\text{O})]_2(\text{ZnW}_9\text{O}_{34})_2\} \cdot 36\text{H}_2\text{O}$ [Pt(II)-POM] and methyltricaprylammonium chloride (0.125 mmol) in a 1:1 mixture of water/1,2-dichloroethane (200 mL). Under gentle heating at 40 °C and magnetic stirring, the color of the organic phase turned yellow (except for the Zn(II)-POM), whereas the aqueous phase was decolorized. The organic solution layer was separated, dried over anhydrous Na_2SO_4 , and used as such.

G1: General Procedure for the Epoxidation of the Allylic Alcohols 1 by O=V(IV)-POM with Racemic Hydroperoxide 4. In a 5-mL, round-bottomed flask were placed the particular allylic alcohol **1** (0.50 mmol) and dimethyl isophthalate (0.20 mmol) as internal standard, in 0.5 mL of a stock solution (0.1 mM) of the oxovanadium(IV) POM catalyst. The reaction was initiated by addition of 1.1 equiv. (0.55 mmol) of the racemic (1-phenyl)ethyl hydroperoxide (**4a**) at the desired temperature, the mixture was stirred magnetically for 24 h and the solvent was removed (20 °C/50 mbar). The conversions, material balances, product ratios and the diastereomer ratios of the epoxide **2** were determined by ¹H-NMR analysis directly on the crude mixture. The epoxides **2a-f** were then purified by silica-gel chromatography with a mixture of ethyl ether and petroleum ether (30-50 °C) as eluent, and characterized based on literature reported NMR data.^{22,30,40-43} **The POM catalysts may**

be readily removed from the product by silica-gel chromatography and, thus, the purified products are not contaminated by metals.

The results are given in Table 1 (see main text) and Table S1.

Table S1. Catalytic Oxidation of Mesitylol (**1a**) by a Variety of Transition-Metal-Substituted Polyoxometalates with the Racemic Hydroperoxide **4b** as Oxygen Source

$[\text{ZnWM}_2(\text{ZnW}_9\text{O}_{34})_2]^{9-}$ (0.01 mol%)

entry	M	temp. ^b (°C)	convn ^a (%)	mb ^a (%)	selectivity ^a	
					chemo (2a:3a)	diastereo (<i>threo</i> : <i>erythro</i>)
1	OV(IV)	20	> 95	> 95	> 95: 5	91: 9
2	OV(IV)	50 ^c	> 95	> 95	> 95: 5	91: 9
3	Mn(II)	50	85	85	90:10	90:10
4	Ru(III)	50	94	70	70:30	90:10
5	Fe(III)	50	18	95	90:10	94: 6
6	Zn(II)	50	8	90	85:15	95: 5
7	Pd(II)	50	18	92	93: 7	92: 8
8	Pt(II)	50	12	95	88:12	95: 5

^a Conversions (allylic alcohol), material balances and product ratios were determined by ¹H-NMR analysis of the crude reaction mixture, *ca.* 5% error of the stated value.

^b For entries 3-8, 0.02 mol% catalyst was employed; no conversion was observed at 20 °C. ^c Reaction time was 6 h.

For mechanistic comparison, the same set of chiral allylic alcohols **1** was also oxidized by Mn(II)-POM according to the **G1** procedure, with hydroperoxides as oxygen source. The results are given in Table S2.

Table S2. Reactivity, Chemoselectivity and Diastereoselectivity of the Catalytic Epoxidation of Allylic Alcohols **1** by the 'Sandwich'-Type Polyoxometalate Mn(II)-POM with Hydroperoxide (ROOH) as oxygen source

entry	substrate	ROOH	convn [%] ^a	mb	selectivity	
					chemo ^a (2 : 3)	diastereo ^a (<i>threo</i> : <i>erythro</i>)
1		<i>t</i> BuOOH	82	89	72:28	82:18
2	1a	(4a)	50	80	92:08	89:11
3		(4b)	85	85	90:10	90:10
4	1b	4b	35	70	55:45	25:75
7	1c	4b	50	80	90:10	78:22
5	1n	4b	62	88	91:09	55:45
6	1o	4b	46	78	95:05 ^b	65:35
8	1p	4b	40	95	50:50	60:40

^a Conversions (allylic alcohol), material balances and product ratios were determined by ¹H-NMR analysis of the crude reaction mixture, ca. 5% error of stated value; ^b 40% of isomerized epoxide observed in a *threo* : *erythro* ratio of 55:45.

G2: General Procedure for the Catalytic Enantioselective Epoxidation of Allylic Alcohols 1d-i by O=V(IV)-POM with the Chiral Hydroperoxide TADOOH. A Schlenk tube was charged with dimethyl isophthalate (0.2 mmol) as internal standard and a stock solution of O=V(IV)-POM (0.5 mL, 0.1 mM). The particular allylic alcohol **1** (0.50 mmol) was added, and prior to the addition of the oxygen donor, the molar ratio of substrate to internal standard was determined by ¹H-NMR analysis. Subsequently, 1.1 equiv. of the enantiomerically pure hydroperoxide TADOOH (280 mg, 0.55 mmol) was added at the desired temperature. The resulting mixture was stirred magnetically for the time specified in Table 2 (see main text). After removal of the solvent (20 °C/20 mbar), the conversion and material balance were determined by ¹H-NMR analysis directly on the crude

reaction mixture. The residue was then purified by silica-gel chromatography, with a mixture of ethyl ether and petroleum ether (30-50 °C) as eluent; first the TADDOL was obtained in > 95% yield as a white solid without loss of the enantiopurity (determined by HPLC analysis on a chiral OD column), and subsequently the literature known epoxides **2g-m**^{8,13c,35} were isolated in good yields.

For comparison, additional primary allylic alcohols were also oxidized by Ru(III)-POM with the hydroperoxides (*S*)-(-)-**4a** and TADOOH according to the **G2** procedure. The results are given in Table S3.

Table S3. Asymmetric Epoxidation of the Primary Allylic Alcohols **1** by the Ru(III)-POM with the Chiral Hydroperoxide R*OOH

entry	substrate	R*OOH	solvent	convn ^a [%]	mb ^a [%]	product distribution [%] ^b			er ^c 2 [%]
						2	3	PhCHO	
1		(<i>S</i>)-(-)- 4a	C ₆ D ₅ CD ₃	78	90	47	33	20	60 : 40 (<i>2S,3S</i>)
2	1g	TADOOH	ClCH ₂ CH ₂ Cl	14	90	15	70	15	n.d. ^d
3		(<i>S</i>)-(-)- 4a	C ₆ D ₅ CD ₃	56	78	60	28	12	53 : 47 (<i>2S,3S</i>)
4	1h	TADOOH	ClCH ₂ CH ₂ Cl	38	90	70	28	<2	60 : 40 (<i>2S,3S</i>)
5		(<i>S</i>)-(-)- 4a	C ₆ D ₅ CD ₃	55	90	40 ^e	47 ^f	13	57 : 43 (<i>2R,3R</i>)
6	cis-1j	TADOOH	ClCH ₂ CH ₂ Cl	43	95	74 ^g	25 ^h	<1	57 : 43 (<i>2R,3R</i>)
7		(<i>S</i>)-(-)- 4a	C ₆ D ₅ CD ₃	40	75	60	40	-	63 : 37 (<i>2R,3R</i>)
8	1k	TADOOH	ClCH ₂ CH ₂ Cl	36	78	70	30	-	55 : 45 (<i>2R,3R</i>)

^aDetermined by ¹H-NMR analysis directly on the crude reaction mixture, ca. 5% error of the stated value; mb is material balance. ^bNormalized to 100%. ^cEnantiomeric ratio (er) determined by HPLC analysis on a chiral OD column; in parentheses, configuration of major enantiomer. ^dNot determined due to the low amount of epoxide obtained. ^e60% isomerized *trans* epoxide (er 53:47). ^f25% *trans* aldehyde. ^g35% isomerized *trans* epoxide (er 52:48). ^h45% *trans* aldehyde.

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