# The (Schiff base)vanadium(V) Complex Catalyzed Oxidation of Bromide − A New Method for the in situ Generation of Bromine and Its Application in the Synthesis of Functionalized Cyclic Ethers

**Marco Greb,[a] Jens Hartung,*[a][‡] Franz Köhler,[a] Kristina Špehar,[a][‡] Ralph Kluge,[b] and René Csuk[b]**

**Keywords:** Bromide / *tert*-Butyl hydroperoxide / Catalysis / Oxidation / Peroxy complexes / Tetrahydrofuran / Vanadium

(Schiff base)vanadium(V) complexes **5** with tridentate imine auxiliaries served as catalysts for the oxidation of $Br^-$ with *tert*-butyl hydroperoxide (TBHP) in nonaqueous solvents. This reaction has been applied for the conversion of substituted 4-penten-1-ols into 5-*exo*-bromo-cyclized products, including a diastereomerically pure heterocyclic precursor used in a synthesis of the all-*trans*-configured 2,3,4,5-substituted tetrahydrofuran 2-*epi*-magnosalicin. Treatment of ω-substituted bis(homoallylic) alcohols with the reagent combination of pyHBr, TBHP, and a vanadium(V) catalyst **5** afforded 6-*endo*-cyclized products, i.e. brominated tetrahydropyrans, as major compounds. The results from $^{51}V$ NMR, ESI-MS, and supporting reactivity-selectivity studies indicated that the mechanism of the new bromination reaction consists of vanadium-dependent and vanadium-independent steps. A (Schiff base)vanadium(V) compound **5** is required for activation of TBHP via in situ formation of the corresponding *tert*-butylperoxy complex. This reagent oxidizes $Br^-$, which under the reaction conditions provides $Br_2$ as the active brominating reagent. The molecular bromine generated thus is released into the solution at a steady rate and serves as a reagent for the synthesis of β-brominated cyclic ethers from bis(homoallylic) alcohols in a second, vanadium-independent step.


## Introduction

The on-site generation of molecular bromine,[1] either in a separate ex situ free halogen reactor[2] or in solution (i.e. in situ),[3] avoids the necessity to store $Br_2$ in larger quantities in a laboratory or at a production site. This strategy also circumvents the need to dispose of the waste HBr formed in the course of most substitution-based electrophilic brominations of organic substrates, because the hydrobromic acid is almost instantly oxidized to $Br_2$ in a succeeding step of the reaction cycle (Figure 1).[4] This concept has been successfully applied in, for example, the CAB/$H_2O_2$ process (i.e. the side-chain oxidation of toluenes)[5] and in the formation of aryl halide based disinfectants from electron-rich aromatic compounds.[6]

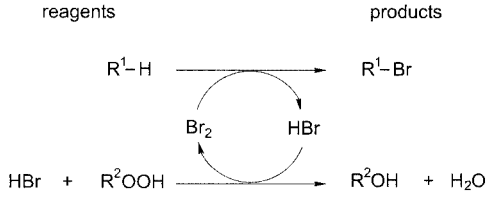



Figure 1. Principle for the in situ generation of $Br_2$ and its application in the synthesis of organobromine compounds;[1−4,7] $R^1$ = e.g. aryl; $R^2$ = H, alkyl

The generation of $Br_2$ from HBr and $H_2O_2$ was discovered and investigated in depth by Maas and Hiebert in 1924.[8] The fact that this reaction requires a comparatively low pH in order to proceed with a satisfactory rate has precluded its application in the synthesis of acid-labile fine chemicals for a long time.[9] This situation changed considerably in the last decades because vanadium(V)-dependent haloperoxidases have been isolated from various algae[10] and fungi.[11] These enzymes are able to catalyze the oxidation of, for example, $Br^-$ with $H_2O_2$ under physiological conditions.[12] In particular, a vanadium(V)-dependent bromoperoxidase (VBPO) from the brown algae *Ascophyllum nodosum* has attracted attention,[10a] since its turnover of $Br^-$ at pH = 6.5 in the presence of the primary oxidant $H_2O_2$ exceeds that of the powerful reagent $VO(O_2)_2^-$ at

[a] Institut für Organische Chemie, Universität Würzburg, Am Hubland, 97074 Würzburg, Germany
[b] Institut für Organische Chemie, Universität Halle-Wittenberg, Kurt-Mothes-Straße 2, 06120 Halle (Saale), Germany
Fax: (internat.) + 49-345-5527030
E-mail: kluge@chemie.uni-halle.de
csuk@chemie.uni-halle.de
[‡] New address: Fachbereich Chemie, Organische Chemie, Technische Universität Kaiserslautern, Erwin-Schrödinger-Straße, 67663 Kaiserslautern, Germany
Fax: (internat.) + 49-631-205-3921
E-mail: hartung@chemie.uni-kl.de
Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.

pH = 1.[13] Although the exact nature of the electrophilic halogenating reagent in such transformations remains the subject of ongoing discussions,[14] the fundamentals of this chemistry are of notable synthetic interest, since they combine the benefits of on-site generation of $Br_2$ with that of transition metal based catalysis. In view of this background, we have started to explore the vanadium(V)-catalyzed oxidation of $Br^-$ with the aim of developing a method that is applicable for the conversion of a given bis(homoallylic) alcohol **1** into β-brominated cyclic ethers, i.e. a tetrahydrofuran **2** or a tetrahydropyran **3**, (Figure 2).[7] A major objective of this study was associated with the search for an adequate combination of bromide source and primary oxidant that would reduce the inherent propensity of (Schiff base)vanadium(V) complexes in the presence of *tert*-butyl hydroperoxide (TBHP) to convert alkenols **1** directly into hydroxy-functionalized tetrahydrofurans.[15,16] Thus, reactivity-selectivity studies on the vanadium(V)-catalyzed oxidation of bromide were conducted. The results were supplemented by information obtained from spectroscopic and spectrometric investigations in order to interpret crucial steps in the process such as peroxide activation and the generation of an active brominating reagent.[17,18]

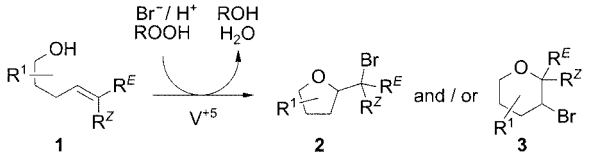



Figure 2. Strategy for the conversion of alkenols **1** in the presence of $Br^-$, ROOH, and $V^{5+}$ into bromo-cyclized target products **2** and/or **3**; R = H, $C(CH_3)_3$; $R^1$ = $CH_3$, $C_6H_5$, aryl; $R^E$ = H, $CH_3$, $C_6H_5$; $R^Z$ = H, $CH_3$; $V^{+5}$ = (Schiff base)vanadium(V) complex, e.g. **5** (see Table 1)

## Results

### 1. Preparation and Characterization of (Schiff base)vanadium(V) Complexes

Tridentate Schiff base auxiliaries, which differ in solubility (**4a**, **4b**), in the heteroatom functionalities on the amino alcohol side chain (**4c**−**4e**), or in the steric demand of the hydrocarbon substituent (**4f**, **4g**) (Figure 3), were chosen in order to screen for selectivity and catalytic reactivity of the derived vanadium(V) reagents **5** for the oxidation of bromide under different conditions.[16,19] Auxiliaries $H_2L^1$−$H_2L^7$ (**4a**−**g**) were prepared from appropriate *o*-hydroxyarenecarbaldehydes and selected amino alcohols in EtOH at reflux. Chiral amino alcohols were obtained through $NaBH_4/I_2$-mediated reductions of the corresponding amino acids.[20] Treatment of methylsulfanyl-functionalized ligand **4c** with TBHP furnished sulfoxide **4d** in 47% yield as a mixture of *like*/*unlike*-configured diastereomers.

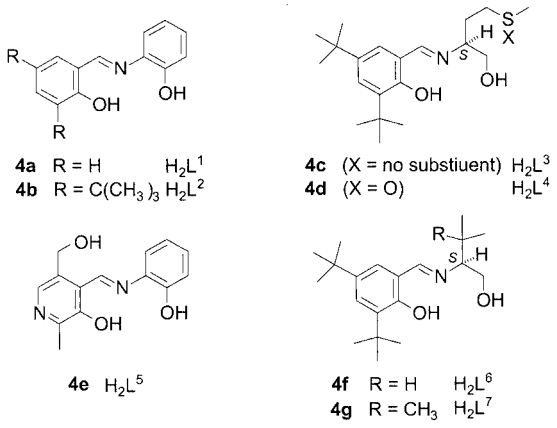



Figure 3. Structures of Schiff bases $H_2L^1$−$H_2L^7$ (**4a**−**g**) intended to serve as ligands for the syntheses of vandium(V) complexes **5a**−**g** (see Table 1)[16,19]

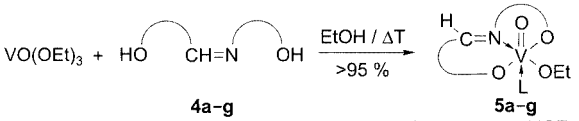
Dark brown to black (Schiff base)vanadium(V) complexes **5** were prepared in excellent yields (> 95%) by mixing of equimolar amounts of $VO(OEt)_3$ and one of the auxiliaries **4a**−**g** in hot EtOH (Table 1).[21] Compounds **5a**−**g** are soluble in $CH_3CN$, $CHCl_3$, $CH_2Cl_2$, or EtOH. Dilute solutions of, for example, methioninol-derived vanadium(V) compound **5c** in $CHCl_3$ typically exhibit a reddish color, which darkens to brown with increasing concentration. If dissolved in EtOH, complexes **5** show $^{51}V$ NMR signals that are located in the spectral range between δ = −529 ppm (**5a**) and −551 ppm (**5f**). Single $^{51}V$ NMR resonances were observed for complexes **5a**, **5b**, **5d**, and **5e**, whereas compounds **5c**, **5f**, and **5g** were each characterized by two slightly separated signals (Δδ = 3 for **5c**, 8 for **5f**, and 16 for **5g**). IR spectra (KBr) of all complexes **5** were recorded. The spectral information given in Table 1 is restricted to the diagnostic V=O stretching mode because the ligands had been characterized independently. Except for the sulfoxide-derived complex **5d** ($\tilde{\nu}$ = 961 $cm^{-1}$) and the pyridoxal-based compound **5e** ($\tilde{\nu}$ = 945 $cm^{-1}$), all absorptions are grouped around 989 ± 10 $cm^{-1}$. Solutions of vanadium(V) complexes **5** displayed featureless UV/Vis spectra consisting of up to three bands. The energetically lowest band for each compound was located in the λ = 625 (**5b**) and 673 nm (**5d**) range. Except for the pyridoxal-derived coordination compound **5e**, each vanadium(V) complex displayed a second electronic transition in the near UV region [361 (**5a**) to 318 nm (**5g**)]. A third band was present in the spectra of the methioninol-derived complex **5c** (437 nm), the valinol derivative **5f** (444 nm), and the *tert*-leucinol-based vanadium(V) compound **5g** (423 nm).

### 2. The Oxidation of Bromide in the Presence of 1-Phenyl-4-penten-1-ol (6)

Suitable reaction conditions for the synthesis of brominated cyclic ethers (Figure 1) were identified by varying: (i) the primary oxidant, (ii) the bromide source, (iii) the solvent, and (iv) the vanadium(V) reagent **5**. In all instances, the conversion of 1-phenyl-4-penten-1-ol (**6**)[22] into 2-(bromomethyl)-5-phenyltetrahydrofuran (**7**) served as reporter reaction. Initial efforts were directed towards an application of $H_2O_2$ as reactive oxygen source (Supporting Information, see also the footnote on the first page of this article).[23] For this purpose, solutions of $Bu_4NBr$ ($c_0$ = 0.1 M) and alkenol **6** ($c_0$ = 2 × $10^{-2}$ M) in DMF were treated

Table 1. Preparation of vanadium(v) complexes **5a−g** from $VO(OEt)_3$ and auxiliaries **4a−g** (see Figure 3)




**4a−g** **5a−g**

L = vacant or HOEt

| entry | 4,5 | $\delta^{51}$V [ppm][a] | $\nu_{V=O}$[cm$^{-1}$][b] | $\lambda_{max}$[nm][c] (lg$\varepsilon$ [lmol$^{-1}$s$^{-1}$]) |
|---|---|---|---|---|
| 1 | **a** | −529 | 990 | 361 (3.80) 659 (2.40) |
| 2 | **b** | −539 | 999 | 349 (3.90) 625 (2.34) |
| 3 | **c** | −534 / −537[d] | 987 | 350 (3.69) 652 (2.06) 437 (1.91) |
| 4 | **d** | −544 | 961 | 334 (3.76) 673 (2.88) |
| 5 | **e** | −531 | 945 | 556 (2.81) 652 (2.66) |
| 6 | **f** | −543 / −551 | 994 | 321 (3.78) 652 (2.50) 444 (2.53) |
| 7 | **g** | −533 / −549 | 978 | 318 (3.80) 658 (1.94) 423 (2.33) |

[a] In EtOH, referenced versus $VOCl_3$ as internal standard ($\delta$ = 0 ppm). [b] In KBr pellets. [c] In EtOH. [d] Broad.

with different concentrations of $H_2O_2$ ($c_0 = 4 \times 10^{-3}$ M to $2 \times 10^{-2}$ M) and VOL$^1$(OEt)(EtOH) (**5a**) ($c_0 = 4 \times 10^{-3}$ M to $2 \times 10^{-2}$ M). Since the oxidation of $Br^-$ consumes 1 equiv. of $H^+$ per equiv. of $H_2O_2$ (see Figure 1 for $R^2$ = H), aqueous HCl ($c_0 = 1 \times 10^{-3}$ M to $2 \times 10^{-2}$ M) was added to the reaction mixture in order not to limit the oxidation in acid.[23] These experiments, however, provided only traces (< 2%, GC) of 2-(bromomethyl)-5-phenyltetrahydrofuran (**7**).[22] No target compound **7** was obtained if the reactions were conducted in the absence of aqueous HCl, or if equimolar ratios of $H_2O_2$ *and* **5a** were added to the reaction mixture. In additional experiments, the HCl concentration was increased to $2.2 \times 10^{-2}$ M, which was associated with an improvement in the yield of product **7** (26%, at 20 °C for 48 h). Addition of 5 mol % of complex **5a** to a similarly prepared solution of $H_2O_2$, aq. HCl, and substrate **6** did not raise the yield of heterocycle **7** (27%). The use of 100 mol % of complex **5a** under such conditions completely inhibited the formation of tetrahydrofuran **7** (Supporting Information).

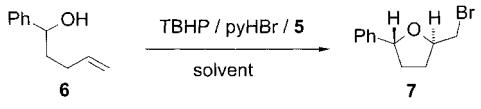
In view of the observed complications, the primary oxidant $H_2O_2$ was replaced by *tert*-butyl hydroperoxide (TBHP). Attempts to apply aqueous TBHP for the synthesis of bromomethyl-substituted tetrahydrofuran **7** followed the same trends that had been noted in (Schiff base)-vanadium(v) complex catalyzed oxidations of $Br^-$ in the presence of aqueous $H_2O_2$. We therefore restricted ourselves to the use of anhydrous TBHP and dry solvents. Further, $Bu_4NBr$ was replaced by pyridinium hydrobromide (pyHBr). This reagent is adequately soluble in $CH_3CN$, $CHCl_3$, and $CH_2Cl_2$, media that are commonly applied in preparative-scale bromocyclizations.[24] Further, this modification helped to maintain the ratio of $H^+$ to oxidizable $Br^-$ constant throughout the reaction.

In an initial run, TBHP (1.1 equiv.), pyHBr (1.5 equiv.), and 1-phenyl-4-penten-1-ol (**6**) were stirred at 20 °C for 48 h in the absence of vanadium(v) complex **5a** to furnish a 29% yield (GC) of 2-(bromomethyl)-5-phenyltetrahydrofuran (**7**). This reactivity is referred to from now on as *background bromination*. The molar ratio of reagents used in this transformation was established in a separate series of experiments. The formation of target product **7** was improved to 72% (GC) upon addition of 1 mol % of VOL$^1$(EtO)(EtOH) (**5a**) (Table 2, Entry 4). An increase in the molar ratio of catalyst **5a** under otherwise identical conditions provided 73% (GC; 5 and 10 mol % of **5a**, Supporting Information and Table 2, Entries 1 and 3), 45% (GC, 50 mol % of **5a**, Supporting Information), and 44% yields (GC) of product **7** (100 mol % of **5a**, Supporting Information). A change of the solvent from $CH_3CN$ to $CHCl_3$ (10 mol % of **5a**) was associated with a slight decrease in the diastereoselectivity for formation of disubstituted tetrahydrofuran **7**, from *cis*/*trans* = 28:72 ($CH_3CN$) to 34:66 (Table 2, Entries 1 and 2). Application of di-*tert*-butyl-substituted vanadium(v) complex VOL$^2$(OEt) (**5b**) in this reaction indicated comparable reactivity but improved solubility in $CH_3CN$ *and* $CHCl_3$ relative to compound **5a** (Table 2, Entry 5). The use of 1 mol % of methylsulfanyl-substituted catalyst **5c** in $CHCl_3$ was sufficient to convert substrate **6** into product **7** in 61% yield in 8 h (GC, *cis*/*trans* = 34:66). If this reaction is performed on a larger scale, it is advisable to increase the amount of catalyst VOL$^3$(OEt) (**5c**) to 5 mol % (66% yield of **7** after 10 h, Table 2, Entry 7). The synthesis of tetrahydrofuran **7** from alkenol **6** took considerably longer to reach completion if vanadium(v) complex VOL$^4$(OEt) (**5d**) with the sulfoxide-functionalized chelate ligand was used as catalyst (73%, *cis*/*trans* = 34:66, Table 2, Entry 9). The use of either the pyridoxal-derived complex VOL$^5$(OEt) (**5e**), the leucinol-based coordination compound VOL$^6$(OEt) (**5f**), or the *tert*-butylaminoethanol derivative VOL$^7$(OEt) (**5g**) provided 70−71% yields of product **7** (*cis*/*trans* = 28:72, Table 2, Entries 10−12) after 48 h. Pursuit of further optimization studies was refrained from in the latter three instances, since catalysts **5e−g** offered a similar selectivity profile to that of *o*-aminophenol-derived vanadium(v) complex **5a**.

Additional information concerning the rate of product formation from bis(homoallylic) alcohol **6**, TBHP, pyHBr, and selected (Schiff base)vanadium(v) complexes **5** was obtained by monitoring of the yield of bromocyclization product **7** as a function of the reaction time. The information outlined in Figure 4 indicates that the rate of (bromomethyl)phenyltetrahydrofuran formation in $CHCl_3$ increased over the sequence of catalysts **5c** (10 mol %) > **5d** (10 mol %) > **5c** (1 mol %) > **5a** (10 mol %) > **5a** (1 mol %) > no catalyst (Supporting Information). In detail, the use of 1 mol % of methioninol-derived vanadium(v) complex **5c** led to a 3.8-fold increase in the rate of product formation, which was improved to a factor of 4.5 in relation to the uncatalyzed reaction if 10 mol % of **5c** was used as catalyst. It is worth mentioning that 1 mol % of $VO(acac)_2$, if applied as catalyst under such conditions, led to the formation of a

Table 2. Screening for reactivity: application of vanadium(v) catalysts **5a**−**g** for the oxidation of bromide in the presence of 1-phenyl-4-penten-1-ol (**6**)




6 7

| entry | 5 | (mol %) | solvent | t [h] | 7 [%] | (*cis* : *trans*) |
|---|---|---|---|---|---|---|
| 1 | **5a** | 10 | $CH_3CN$ | 48 | 73 | (28 : 72) |
| 2 | **5a** | 10 | $CHCl_3$ | 48 | 72 | (34 : 66) |
| 3 | **5a** | 5 | $CH_3CN$ | 48 | 73 | (28 : 72) |
| 4 | **5a** | 1 | $CH_3CN$ | 48 | 72 | (28 : 72) |
| 5 | **5b** | 1 | $CH_3CN$ | 48 | 72 | (28 : 72) |
| 6 | **5c** | 1 | $CHCl_3$ | 8 | 61 | (34 : 66) |
| 7 | **5c** | 5 | $CHCl_3$ | 10 | 66[a] | (34 : 66) |
| 8 | **5c** | 10 | $CHCl_3$ | 8 | 73 | (34 : 66) |
| 9 | **5d** | 10 | $CHCl_3$ | 48 | 73 | (34 : 66) |
| 10 | **5e** | 1 | $CH_3CN$ | 48 | 70 | (28 : 72) |
| 11 | **5f** | 1 | $CH_3CN$ | 48 | 71 | (28 : 72) |
| 12 | **5g** | 1 | $CH_3CN$ | 48 | 71 | (28 : 72) |

[a] Preparative scale (0.5 mmol). All other yields were determined by GC with *n*-$C_{14}H_{30}$ as internal standard. An experimental error of ±5% was estimated for similarly determined yields.

31% yield of product **7** after 5 h and a 61% yield after 48 h from alkenol **6**, TBHP, and pyHBr (Supporting Information).

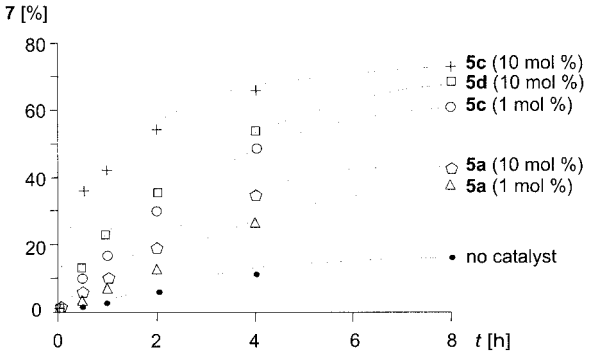



Figure 4. Time dependence of 2-(bromomethyl)-5-phenyltetrahydrofuran formation from 1-phenyl-4-penten-1-ol (**6**), TBHP, and pyHBr in the presence of vanadium(v) catalysts **5a**, **5c**, and **5d** ($CHCl_3$, 20 °C, GC)

In addition to the reactivity studies, the conversion of 1-phenyl-4-penten-1-ol (**6**) into bromocyclized product **7** was monitored by $^1$H NMR spectroscopy with the aim of detecting additional products that had escaped the chromatographic workup procedure, thus improving the mass balance of this reaction (Figure 5). Spectra were recorded prior to addition of pyHBr and catalyst **5c** (≡ 0 min), after 15, 30, 60, 240, and 360 min, and after 6 d ($CDCl_3$, 20 °C). The stacking plot of two selected spectral regions, at δ = 4.0−5.2 and 5.7−6.0 ppm, illustrates that alkenol **6** is transformed into heterocycle **7** and a new product that has been identified as 4,5-dibromo-1-phenylpentan-1-ol (**8**) (50:50 mixture of *like*/*unlike* isomers). The ratio of products *cis*-**7**/*trans*-**7** to the two diastereomers of **8** remained constant during the course of this reaction. In a separate experiment, diastereomerically pure heterocycles *cis*-**7** and *trans*-**7**[22] were each treated with 1 equiv. of pyHBr in $CDCl_3$ at 20 °C for 48 h. In both instances, resonances of the opposite diastereomer or of the dibromide **8** were not observed.

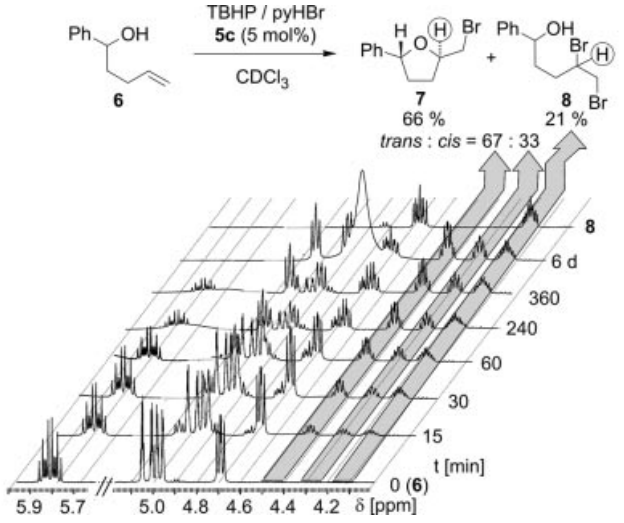



Figure 5. Stacking plot: time-dependent $^1$H NMR study on the conversion of 1-phenyl-4-penten-1-ol (**6**) in the presence of TBHP (1.1 equiv.), pyHBr (1.5 equiv.), and methioninol-derived vanadium(v)-catalyst **5c** (20 °C, $CDCl_3$); the selected spectral region depicts the resonances of olefinic protons, benzylic protons, and protons located in the vicinity of oxy or bromo substituents; for illustrative purposes the spectra of neat alkenol **6** and of purified dibromide **8** (equimolar mixture of *like*/*unlike* isomers) have been added to this plot

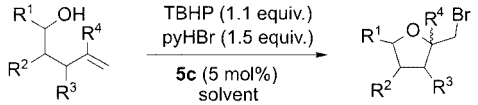
### 3. The Formation of Bromocyclization Products from Bis(homoallylic) Alcohols

The scope of the (Schiff base)vanadium(v)-catalyzed oxidation of bromide in the synthesis of bromocyclization products was explored in bromination reactions of 1-, 2-, 3-, and 4-substituted bis(homoallylic) alcohols **9**−**13**.[22] All transformations were conducted under previously optimized conditions (Table 2) on a preparative scale with 5 mol % of methioninol-derived (Schiff base)vanadium(v) complex **5c** as catalyst, TBHP as primary oxidant, and pyHBr as bromide source (Table 3). This setup is referred to from now on as the *standard conditions*. Treatment of 1-(*p*-methoxyphenyl)-4-penten-1-ol (**9**) in $CH_2Cl_2$ under these conditions afforded a 69% yield of 5-(*p*-anisyl)-2-(bromomethyl)tetrahydrofuran (**14**) (*cis*/*trans* = 33:67). Bromocyclization of 4-methyl-1-phenyl-4-penten-1-ol (**10**) in $CH_2Cl_2$ furnished a 64% yield of 2,2,5-substituted oxolane **15** (*cis*/*trans* = 26:74). An 82% yield of 2-(bromomethyl)-4-phenyltetrahydropyran (**16**) (*cis*/*trans* = 74:26) was obtained from 2-phenylpentenol (**11**) in $CH_3CN$[25] and an 88% yield (*cis*/*trans* = 72:28) in $CH_2Cl_2$. 3-Phenyl-4-pentenol (**12**) was converted under standard conditions into 2-(bromomethyl)-3-phenyltetrahydrofuran (**17**) in 55% yield (*cis*/*trans* = 21:79, in $CH_3CN$) and in 56% yield (*cis*/*trans* =

30:70, in $CH_2Cl_2$).[25] A 66% yield of 2-(bromomethyl)-2-phenyltetrahydrofuran (**18**) was obtained upon treatment of 4-phenylpentenol (**13**) with TBHP, pyHBr, and 5 mol % of **5c** in $CH_2Cl_2$.[26]

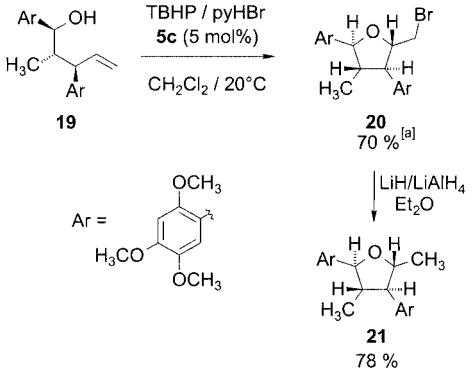
Table 3. Application of the vanadium(v)-catalyzed oxidation of $Br^-$: bromocyclizations of substituted bis(homoallylic) alcohols **9**–**13**




**9–13** **14–18**

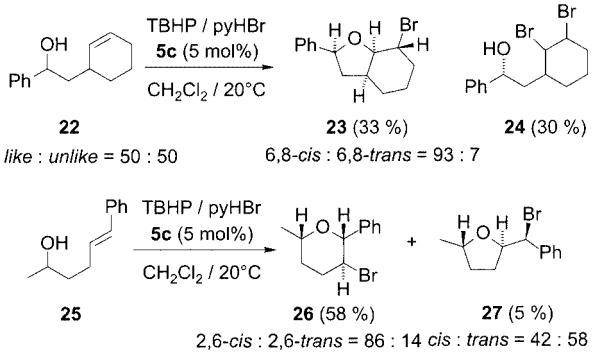
| entry | 9–13 | $R^1$ | $R^2$ | $R^3$ | $R^4$ | solvent | 14–18 | yield [%] (*cis* : *trans*) |
|---|---|---|---|---|---|---|---|---|
| 1 | **9** | *p*-$H_3COC_6H_4$ | H | H | H | $CH_2Cl_2$ | **14** | 69 (33 : 67) |
| 2 | **10** | $C_6H_5$ | H | H | $CH_3$ | $CH_2Cl_2$ | **15** | 64 (26 : 74) |
| 3 | **11** | H | $C_6H_5$ | H | H | $CH_3CN$ | **16** | 82 (74 : 26) |
| 4 | **11** | H | $C_6H_5$ | H | H | $CH_2Cl_2$ | **16** | 88 (72 : 28) |
| 5 | **12** | H | H | $C_6H_5$ | H | $CH_3CN$ | **17** | 55 (21 : 79) |
| 7 | **12** | H | H | $C_6H_5$ | H | $CH_2Cl_2$ | **17** | 56 (30 : 70) |
| 8 | **13** | H | H | H | $C_6H_5$ | $CH_2Cl_2$ | **18** | 66 |

The conversion of (1*S**,2*S**,3*R**)-2-methyl-1,3-bis(2,4,5-trimethoxyphenyl)-4-penten-1-ol (**19**)[27] in the presence of pyHBr, TBHP, and catalyst **5c** provided diastereomerically pure ($^1$H NMR) all-*trans*-configured tetrasubstituted tetrahydrofuran **20** (70%, Scheme 1). Side products originating either from arene bromination[28] or from methyl ether cleavage were not detected ($^1$H NMR spectroscopy).[29] Reduction ($LiAlH_4$/LiH)[30] of the bromocyclization product **20** provided tetrahydrofuran **21**, the 2-epimer of the neolignan-derived natural product (±)-magnosalicin.[31]




Scheme 1. Formation of 2-*epi*-magnosalicin (**21**) from 2-methyl-1,3-bis(2,4,5-trimethoxyphenyl)-4-penten-1-ol (**19**)
[a] The 2-*cis*-configured diastereomer of bromocyclization product **20** was not detected ($^1$H NMR spectroscopy)

Treatment of 2-(cyclohex-2-en-1-yl)-1-phenylethanol (**22**, 50:50 mixture of *like*/*unlike* stereoisomers)[32] with the reagent combination of TBHP, pyHBr, and vanadium(v) catalyst **5c** (5 mol %) furnished a 33% yield of bicyclic tetrahydrofuran **23**[33] and a 30% yield of a 77:23 diastereomeric mixture of two dibromohydrins **24** of hitherto unknown relative configuration (Scheme 2). Product **23** is predominantly formed from the diastereomer *like*-**22** (6,8-*cis*/6,8-*trans* = 93:7),[33] whereas dibromide **24**, for reasons of mass balance, is considered to originate mainly from *unlike*-**22**.




Scheme 2. Formation of bromination products from 5-substituted bis(homoallylic) alcohols **22** and **25**

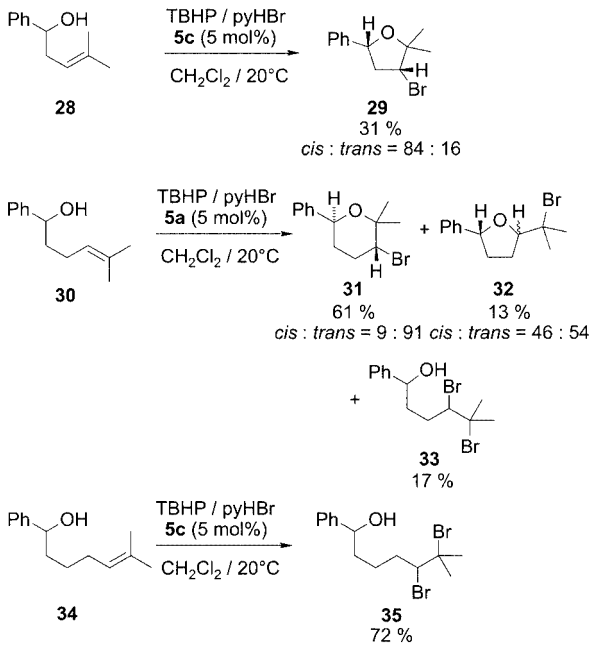
The reaction between pyHBr, TBHP, and $VOL^3(OEt)$ (**5c**) (5 mol %) in the presence of (*E*)-6-phenyl-5-hexen-2-ol (**25**)[22] provided brominated tetrahydropyran **26** as the major (58%, 2,6-*cis*/2,6-*trans* = 86:14) and 2-[bromo(phenyl)methyl]-5-methyltetrahydrofuran (**27**) as a minor product (5%, *cis*/*trans* = 42:58).[26]

Bromocyclization of 4-methyl-1-phenyl-4-penten-1-ol (**28**) under standard conditions exclusively afforded 5-*endo*-cyclized product **29** (31%, *cis*/*trans* = 84:16) after chromatographic workup.[16] The higher homologue, 5-methyl-1-phenyl-5-hexen-1-ol (**30**), was converted into a mixture of tetrahydropyran **31** (61%, *cis*/*trans* = 9:91),[25] disubstituted tetrahydrofuran **32** (13%, *cis*/*trans* = 46:54),[25] and dibromo alcohol **33** (17%, 50:50 mixture of *like*/*unlike* diastereomers), if treated similarly.[34] Treatment of 6-methyl-1-phenyl-5-hepten-1-ol (**34**) with the reagent combination of TBHP, pyHBr, and catalyst **5c** (5 mol %) afforded 5,6-dibromo-6-methyl-1-phenylheptan-1-ol (**35**) (72%, 50:50 mixture of diastereomers) as sole product (Scheme 3).

## 4. Mechanistic Studies: The Search for Intermediates

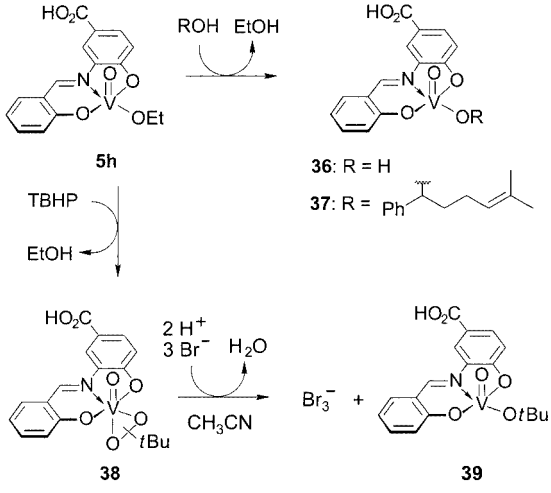
In order to clarify the role of (Schiff base)vanadium(v) complexes **5** in the bromination reaction of organic substrates starting from $Br^-$, TBHP, and an alkenol, $^{51}$V NMR spectroscopic, ESI mass spectrometric, and reactivity-selectivity studies were conducted. In all instances the properties and the reactivity of *o*-aminophenol-derived vanadium(v) complex **5a** served as benchmark, because its chemistry has previously been explored in some detail.[15,16,35] Upon addition of TBHP to a sample of **5a** in $CDCl_3$ ($\delta = -529$ ppm, referenced to $VOCl_3$), a new sharp signal appeared at $\delta = -569$ ppm, which was assigned, on the basis of reference data from the literature, to the corresponding *tert*-butylperoxy complex (not shown).[35–37] Further, an intense resonance at $\delta = -434$ ppm appeared 1 min after mixing of the reagents. A spectrum that was recorded 10 min after addition of 1-phenyl-4-penten-1-ol (**6**) and pyHBr to this solution showed resonances at $\delta = -434$, $-529$, $-539$,




Scheme 3. The conversion of ω,ω-dimethyl-1-phenyl-substituted alkenols **28**, **30**, and **34** into brominated compounds

−543, and −569 ppm. After 24 h, the $^{51}V$ NMR spectrum of this reaction mixture was characterized by a strong sharp resonance at δ = −569 ppm. The remaining signals had either faded completely (δ = −434 ppm) or had become very small (δ = −542, −539 ppm). In order to further verify formation of (peroxy)(Schiff base)vanadium(v) complexes from the reaction between coordination compounds **5** and TBHP, solutions containing both reagents were analyzed by ESI-MS.[38−41] Attempts to detect neutral vanadium(v) complex **5a** by ESI-MS failed in both negative- and positive-ion polarity modes. In order to overcome this problem, carboxy-substituted coordination compound VOL$^8$(OEt) (**5h**) was prepared. This compound allows more facile anion formation under ESI-MS conditions through deprotonation of its carboxylic acid functionality. Vanadium complex **5h**, dissolved in $CDCl_3$, exhibited a single sharp $^{51}V$ NMR resonance at δ = −538 ppm. Addition of TBHP to a solution of **5h** led to the appearance of two new resonances: a stronger one at δ = −438 ppm and a weaker one at δ = −578 ppm. In combination with the information obtained from previous investigations,[15,16,35−37] the signal at δ = −578 ppm was assigned to (peroxy)(Schiff base)vanadium(v) complex **38** (Scheme 4). Subsequently, a solution of **5h** in $CH_2Cl_2$/$CH_3CN$ was injected into an ESI mass spectrometer operating in the negative ion polarity mode. An intense signal at *m*/*z* = 366 (zoom scan 366.0, calcd. 366.02) was recorded that originated from the molecular ion [VOL$^8$(OEt) − H]$^-$ (Figure 6, inset a). The observed isotopic envelope of this ion was in good agreement with the calculated values. Further, signals originating from the complex [VOL$^8$(OH) − H]$^-$ (*m*/*z* = 338) and clusters of the type [M[M − H]]$^-$ (*m*/*z* = 733) and [M$_2$[M − H]]$^-$ (*m*/*z* = 1100) were also detected. The fragmentation process (collision-induced dissociation, CID) of the isolated parent ion at *m*/*z* = 366 (MS$^3$ experiment) pointed to the formation of one main product ion at *m*/*z* = 322 that probably originated from the loss of $H_3CCHO$ (Δ*m* = 44 amu). In a second experiment, a 10-fold excess of TBHP was added to a solution of (Schiff base)vanadium(v) complex **5h** in $CH_2Cl_2$. The reaction mixture was allowed to stand for 30 min and was afterwards diluted with $CH_3CN$. The ESI mass spectrum of this sample exhibited a molecular ion peak at *m*/*z* = 410, which was assigned to the signal [VOL$^8$(*t*BuOO) − H]$^-$, relating to peroxy complex **38** (Figure 6). The zoom scan spectrum of this ion showed an *m*/*z* value of 409.9 (calcd. 410.04) and the expected isotopic envelope (Figure 6, insets b and c). In addition to the latter signal, other peaks were present in this spectrum, which were interpreted as decomposition products of peroxy complex **38** {e.g. [VOL$^8$(OH) − H]$^-$ (*m*/*z* = 338), [VOL$^8$(OCH$_3$) − H]$^-$ (*m*/*z* = 352), [VOL$^8$(O*t*Bu) (**39**) − H]$^-$ (*m*/*z* = 394)} and the corresponding mixed clusters of the type [M$_A$(M$_B$ − H)]$^-$ at *m*/*z* = 691, 705, 733, 749, and 763. The identity of peroxy complex **38** was confirmed by investigating its fragmentation pattern (CID). The CID spectrum of the isolated parent ion showed two main product ions at *m*/*z* = 354 (Δ*m* = 56 amu) and *m*/*z* = 336 (Δ*m* = 74 amu), probably formed by the loss of isobutene in the former case and a $C_3H_6O_2$ or $C_4H_{10}O$ fragment in the latter (Figure 6, inset d). In succeeding experiments, a marked propensity of (Schiff base)vanadium(v) complex **5h** to undergo ligand exchange reactions through replacement of the $C_2H_5O^-$ with an $OH^-$ ligand (e.g. from the reaction of **5h** with water, formation of complex **36**) was noted. Similarly, treatment of **5h** with a 10-fold excess of 5-methyl-1-phenyl-4-hexen-1-ol (**30**) furnished vanadium complex **37**, which was identified by the molecular ion peak at *m*/*z* = 510 [VOL$^8$(-OC$_{13}$H$_{17}$) − H]$^-$ (zoom scan *m*/*z* = 510.2, calcd. 510.11).




Scheme 4. Ligand exchange in the (Schiff base)vanadium(v) complex **5h**: (i) formation of *tert*-butylperoxy complex **38** ($^{51}V$ NMR spectroscopy and ESI-MS) and its reactivity towards bromide, and (ii) generation of complexes **36** and **37**

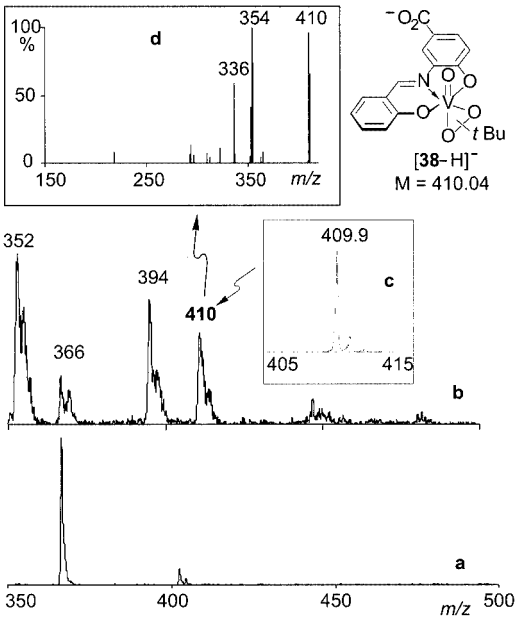
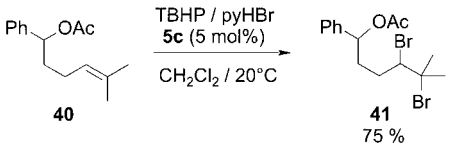



Figure 6. Identification of (Schiff base)vanadium(v) peroxy complex [**38** − H]$^{-}$ by ESI-MS; insets: (a) full-scan spectrum of complex **5h** (negative ions; solvent: $CH_2Cl_2/CH_3CN$); (b) full-scan spectrum 30 min after treatment of complex **5h** with TBHP; (c) zoom-scan spectrum showing the molecular ion [M − H]$^{-}$ of peroxy complex **38**; (d) fragmentation (CID spectrum) of the isolated parent ion at $m/z$ = 410

The reactivity of *tert*-butylperoxy complex **38** was explored by ESI-MS analysis of solutions that were obtained by mixing (Schiff base)vanadium(v) complex **5h** in $CH_2Cl_2/CH_3CN$ with TBHP *and* pyHBr. An intense signal at $m/z$ = 237 was observed in this case (negative ion polarity mode). Due to its fingerprint isotopic envelope of $m/z$ = 237, 239, 241 and 243 in an intensity ratio of 1:3:3:1, this signal was assigned to the $Br_3^-$ ion. Further ions detected in this experiments originated from [VOL$^8$(OH) − H]$^-$ ($m/z$ = 338), [VOL$^8$(Br)$_2$]$^-$ ($m/z$ = 480), and [$V_2O_3$(L$^8$)$_2$Br]$^-$ ($m/z$ = 739). A positive-ion polarity mode ESI spectrum of this sample pointed to the formation of the following cations: [$Py_2H_2Br$]$^+$ ($m/z$ = 239), [VOL$^8$py]$^+$ ($m/z$ = 401), [$V_2O_3$(L$^8$)$_2$H]$^+$ ($m/z$ = 661), and [$V_2O_3$(L$^8$)$_2$pyH]$^+$ ($m/z$ = 740). It should, however, be noted that these cations were also detected from a solution of **5h** and pyHBr in $CH_2Cl_2/CH_3CN$ without TBHP.

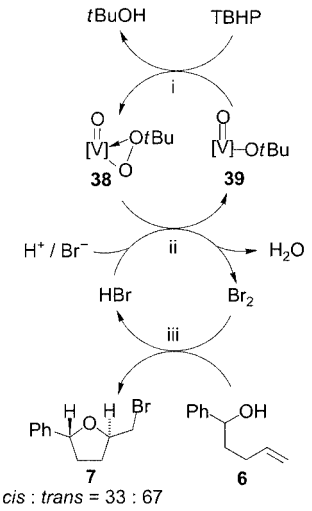
The formation of $Br_2$ and hence $Br_3^-$, which exists in equilibrium with $Br_2$ and $Br^-$ under the reaction conditions,[42] has been confirmed in further experiments, such as in the formation of a 75% yield of dibromide **41** upon treatment of *O*-acetyl-protected alkenol **40** with TBHP, pyHBr, and catalyst **5c** under standard conditions (Scheme 5).




Scheme 5. Formation of dibromide **41** from olefin **40**

## Discussion

The oxidation of bromide in nonaqueous solvents is a synthetically useful transformation for the in situ generation of $Br_2$. This reagent is in turn applicable for selectively converting unsaturated alcohols into bromocyclized products with an *N*-bromosuccinimide (NBS)-[25,43] or 2,4,4,6-tetrabromocyclohexa-2,5-dienone (TBCD)-like selectivity,[43,44] but with improved efficiency in selected instances (Scheme 6).[7a] This new alkenol bromination reaction applies the principles of transition metal catalyzed oxidations for the activation of an environmentally benign and powerful but safe to handle primary oxidant.[15] In this study, coordination compounds of the type VOL(OEt) **5** (L = dibasic tridentate imine auxiliary) in combination with *tert*-butyl hydroperoxide have been applied for this purpose. The choice of this system originated from the experimentally determined Adam parameter of $x_{SO}$ = 0.2 for the reagent combination of VOL$^1$(OEt)(EtOH) (**5a**) and TBHP, which points to electrophilic properties of the active oxidant generated in situ, such as required for the oxidation of $Br^-$ (reference values: $x_{SO}$ = 1.0 for $NaOH/H_2O_2$; $x_{SO}$ = 0.0 for $TBHP/HClO_4$).[45–47]




Scheme 6. Schematic presentation of reaction cycles leading to the formation of 2-(bromomethyl)-5-phenyltetrahydrofuran (**7**) from TBHP, pyHBr, 1-phenyl-4-penten-1-ol (**6**), and vanadium(v) compounds **38** and **39** (data refer to reaction in $CHCl_3$); O=[V]$^+$ refers to the fragment VOL$^+$, where $H_2L$ represents a tridentate dibasic Schiff base auxiliary such as **4**

In earlier work, (Schiff base)vanadium(v) complexes **5** have been reported to catalyze the diastereoselective oxygenation of substituted bis(homoallylic) alcohols **1** with TBHP as primary oxidant.[16,35] The fact that addition of pyHBr changes the reactivity of this system entirely from direct π-bond oxygenation towards electrophilic bromination is one of the major results of the present study. The overall sequence proceeds through: (i) TBHP activation [i.e. formation of (peroxy)(Schiff base)vanadium(v) complexes, e.g. **38** from **39**], (ii) $Br_2$ generation in situ, and (iii) bromocyclization of alkenols in a non-vanadium-dependent step (Scheme 6).

### 1. The Reactivity of (Schiff base)vanadium(v) Complexes 5 towards TBHP

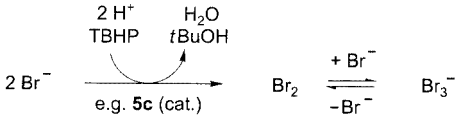
(Schiff base)vanadium(v) complexes **5** have been prepared and characterized according to previously disclosed guidelines.[16,21,47] The reaction of coordination compounds **5a** and **5h** with TBHP provides at least two new vanadium(v) complexes, one of them is characterized by an about 40 ppm high-field shift in relation to the resonance of the starting vanadium(v) reagent ($^{51}$V NMR spectroscopy). The magnitude and the sign of the shift is consistent with the formation of the corresponding $\eta^2$-*tert*-butylperoxy complex (Scheme 4).[35−37] It should be noted that additional $^{51}$V NMR resonances at $\delta = -434$ ppm (from **5a**) and $\delta = -438$ ppm (from **5h**) were observed after TBHP addition. These signals of yet unidentified vanadium(v) complexes were conserved upon addition of 1 equiv. of pyHBr, but faded within 24 h. Treatment of coordination compounds **5a** or **5h** with TBHP and pyHBr provided two additional signals in both instances. On the basis of reference values from the literature, one of these resonances was assigned in both cases to the corresponding (hydroxo)vanadium(v) complex (e.g. $\delta = -543$ ppm from **5a**).[23]

Support for the interpretation that (*tert*-butylperoxy)vanadium(v) complexes (e.g. **38**) are formed from the reaction between a vanadium(v) compound VOL(EtO) (**5**) and TBHP was obtained from the results of ESI-MS investigations (Scheme 4 and Figure 6). The choice of a carboxy-substituted ligand in complex **5h** for this purpose was guided by the necessity to allow facile anion generation under ESI conditions in order to record spectra in the negative ion mode. This technique has been applied to identify (Schiff base)vanadium(v) complex **5h** and its *tert*-butylperoxy derivative **38** by their molecular ions $[M - H]^-$ and subsequent CID fragmentations of the trapped ions.

### 2. Evidence for the Formation of Molecular Bromine

The oxidation of $Br^-$ with TBHP in anhydrous media requires peroxide activation through coordination to (Schiff base)vanadium(v) complex **5** (fast reaction) or protonation (e.g. from $pyH^+$, slow reaction).[49] Both processes are considered to afford $Br_2$ as active bromination reagent for the following reasons:

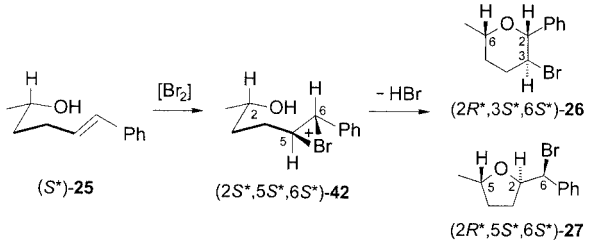
(i) The oxidation potential of TBHP ($E° = 1.20$ V versus NHE in $CH_3OH/C_6H_6$)[50] exceeds the value required for the conversion of $Br^-$ into $Br_2$ or into the tribromide anion [$E°(Br_2/Br^-) = 0.73$ V, $E°(Br_3^-/Br^-) = 1.13$ V, both versus NHE in $CH_3CN$].[42] The latter intermediate has been identified in ESI-MS studies of authentic reaction mixtures {$K = ([Br_2][Br^-])/[Br_3^-] = 6.8-7.0$ in $CH_3CN$ at 25 °C}.[42] On the basis of additional experiments that have not been disclosed in this report, the conversion of $Br^-$ into $Br_2$ with the peroxidic reagent TBHP is the rate-determining step in the synthesis of heterocycle **7** from alkenol **6**. This reaction consumes 1 equiv. of $H^+$ per equiv. of oxidized $Br^-$ (Scheme 7).[23] It is therefore limited in acid, as noted in transformations of substrate **6** with TBHP, catalyst **5a**, and $Bu_4NBr$ in the absence of an additional proton source (e.g. the formation of an 11% yield of bromocyclization product **7** from substrate **6**).




Scheme 7. Intermediates from the (Schiff base)vanadium(v) complex catalyzed oxidation of pyHBr with TBHP

(ii) The product of bromide oxidation was trapped with 1-phenyl-4-penten-1-ol (**6**) to afford 2-(bromomethyl)-5-phenyltetrahydrofuran (**7**) as the major product and 4,5-dibromo-1-phenylpentan-1-ol (**8**) as a minor compound (Figures 4 and 5). Products of identical chemo-, regio-, and diastereoselectivities have been obtained upon treatment of a solution of 1-phenyl-4-penten-1-ol (**6**) in $Et_2O$ with $Br_2$. An application of TBCD in $CH_2Cl_2$ for this purpose afforded an 88% yield of bromocyclized product **7** (*cis*/*trans* = 31:69), without providing dibromide **8**.

(iii) A stereochemical analysis of compounds obtained from the (Schiff base)vanadium(v)-catalyzed oxidation of $Br^-$ with TBHP points to products that are characteristic of a bromonium ion pathway, for example, the formation of *trans*-1,2-dibromocyclohexane (74%, Supporting Information) from cyclohexene and 5,6-*like*-configured bromocyclization products **26** and **27** from (*E*)-6-phenyl-5-hexen-2-ol (**25**) (Scheme 8). The latter observation points to a diastereoselective conversion of, for example, the arbitrarily selected enantiomer (*S**)-**25** into bromonium ion (2*S**,5*S**,6*S**)-**42**, which for stereoelectronic reasons rearranges through a backside approach of the oxygen nucleophile onto the positively polarized carbon−bromine bonds (i.e., C5−Br or C6−Br) to furnish 5,6-*like*-configured tetrahydropyran **26** as the major product and 5,6-*like*-arranged tetrahydrofuran **27** as a minor product (Scheme 8).




Scheme 8. Stereochemical model for the selective conversion of alkenol (*S**)-**25** into products (2*R**,3*S**,6*S**)-**26** and (2*R**,5*S**,6*S**)-**27**; [$Br_2$] = TBHP, pyHBr, **5c**

Application of (Schiff base)vanadium(v) catalyst **5a** for initiation of bromocylizations was not compatible with the use of aqueous solvents or of $H_2O_2$ as primary oxidant. The conversion of 1-phenyl-4-penten-1-ol (**6**) into 2-(bromomethyl)-5-phenyltetrahydrofuran (**7**) with the reagent combination of TBHP and pyHBr in anhydrous media was complete (GC) after 8−48 h in the case of vanadium(v)-catalyzed reactions, whereas 14−21 d were re-

quired for the same transformation in the absence of a catalyst **5**. The most active catalyst in the present study was the methioninol-derived complex **5c**, if applied in chlorinated solvents. Since the marked reactivity of reagent **5c** could, in principle, have been associated with its conversion into the sulfoxide derivative **5d** in an early phase of the reaction, the latter reagent was independently prepared and its catalytic activity checked.[51] Comparison of rates for formation from alkenol **6** points to differences in the catalytic activity of vanadium reagents **5c** and **5d** (Figure 4).

The diastereoselectivity of product formation from substrate **6** was independent of the auxiliary $L^{2-}$ in VOL(OEt) (**5**) but was improved slightly upon an increase in solvent polarity. The catalytic activity of reagents **5** was most pronounced within the first 120 min and leveled off after approximately 4 h. Thereafter, the rate of product formation in the presence of either of the selected complexes **5a−g** was similar to that of the background bromination. It was not possible to resume effective catalysis in this late phase by adding further amounts of catalyst **5**.

### 3. Application of the (Schiff base)vanadium(v)-Catalyzed Oxidation of Bromide − Bromocyclization of Alkenols

Bromocyclizations of 1-, 2-, and 3-substituted bis(homoallylic) alcohols provided 2,5-*trans*-, 2,4-*cis*-, and 2,3-*trans*-disubstituted tetrahydrofurans (i.e. 5-*exo*-bromocyclized compounds) as major products (Table 3, Schemes 1−3). The magnitudes and the degrees of stereochemical preferences for product formation in such ring-closure reactions resembled those observed in $I_2$- or NBS-mediated halocyclizations with these or structurally related substrates.[22,25,30] This information has been applied in the present study in order to develop a concise synthesis of the 2-epimer **21** of the naturally occurring tetrasubstituted tetrahydrofuran (±)-magnosalicin − an antiallergic compound that has been isolated from the buds of the far eastern plant *Magnolia salicifolia*.[31] The ease and the efficiency of this transformation are noteworthy. In spite of the potential of pyHBr to cleave aromatic methyl ether entities[31] or to furnish products of arene bromination if treated with **5c** and TBHP (Supporting Information), no such side products were identified ($^1$H NMR spectroscopy).

Products of 5-*endo*- or 6-*endo*-selective ring closures were prepared from bis(homoallylic) alcohols with ω-substituted π-bonds. In those instances, polar contributions in transition states of C−O bond formation are more important than stereoelectronic effects.[7] The fact that the attempted bromocyclization of 6-methyl-1-phenyl-5-hepten-1-ol (**34**) by the new procedure exclusively furnished dibromide **35** ($^1$H NMR) points to a comparatively slow 7-*endo* ring closure, which obviously is not able to compete with a direct π-bond bromination of this substrate in terms of the associated rate.

## Conclusion

(Schiff base)vanadium(v) complexes catalyze the oxidation of $Br^-$ in nonaqueous solvents with TBHP as primary oxidant. This transformation leads to an efficient in situ generation of $Br_2$, which is applicable for selectively converting bis(homoallylic) alcohols into bromocyclized products with an NBS- or TBCD-like selectivity under mild conditions. The reaction profits from the phenomenon of catalysis, which is desirable for larger scale state-of-the-art applications and provides products of notable synthetic utility, as in the synthesis of the 2-epimer **21** of natural product (±)-magnosalicin.

The mechanism of the new method for bromocyclization of alkenols proceeds in three decisive steps. In the first step, TBHP binds to a vanadium(v)-based catalyst to furnish the corresponding (*tert*-butylperoxy)(Schiff base)vanadium(v) complex (e.g. **38**). The activated peroxide is considered to be the oxidant for the conversion of $Br^-$ into $Br_2$, which then serves as a brominating reagent for the subsequent bromocyclization of alkenols in a third, vanadium(v)-independent step. The results from transformations of monosubstituted bis(homoallylic) alcohols [e.g. 1-phenyl-4-penten-1-ol (**6**)] suggest that the efficiency of TBCD, which is the reagent most frequently applied today for conducting bromocyclizations in multistep natural product syntheses, is competitive with, to slightly superior to, the new method. The fact, however, that the oxidative procedure has been successfully applied in instances in which TBCD failed to provide useful yields, such as in the synthesis of the strained hexasubstituted core of the marine natural product aplysiapyranoid A and its 5-*epi* isomer, shows that it is worth consideration, especially in nontrivial cases in which slow but steady release of the electrophilic brominating reagent is required.[7a]

## Experimental Section

**1. General Remarks:** $^1$H, $^{13}$C and $^{51}$V NMR spectra were recorded with Bruker AC 250 and WM 400 instruments (20 °C) in $CDCl_3$ solution unless otherwise noted. Residual protons of deuterated solvents [$\delta_H$ = 7.26 ($CDCl_3$)] and the corresponding carbon resonances in $^{13}$C NMR spectra [$\delta_C$ = 77.0 ppm ($CDCl_3$)] were taken as internal standards. $^{51}$V NMR resonances were referenced against $VOCl_3$ as external standard ($VOCl_3$; δ = 0 ppm). IR spectra were recorded as KBr pellets with a Perkin−Elmer 1600 FT-IR spectrometer. UV/Vis: EtOH solutions in 1-cm quartz cuvettes with a Perkin−Elmer 330 spectrophotometer. MS: Varian MATCH 7 spectrometer [EI 70 eV]. ESI-MS: mass spectra were obtained with an ESI mass spectrometer LCQ (Finnigan Mat) under the following conditions: solvent flow, 8 μL/min, ESI spray voltage 3.3 kV, capillary temperature 150 °C, capillary voltage −34 or +34 V, tube lens-offset −10 or +10 V, sheath gas $N_2$, damping gas He. The CID experiments were carried out in the mass analyzer region with use of He as the collision gas and by applying a resonance excitation RF voltage (varying from 0 to 5 V, peak-to-peak). The masses, charge states, and isotopic envelopes of the parent ions and the fragment ions (CID) were established by applying the zoom-scan mode (high-resolution scan, resolution < 0.2 amu, 10 amu width). The solutions for the ESI measurements were prepared in $CH_2Cl_2$, simulating the typical oxidation conditions. Immediately before the measurements, the solutions were diluted with $CH_3CN$ to a final concentration of approx. $10^{-3}$ M. After filtration through

a 0.2-μm filter, the solutions were directly injected into the API source of the mass spectrometer by syringe pump. GC: Carlo Erba GC 6000 (Vega Series 2), FID, Spectra Physics Integrator 4290, DB-5 column (30 m × 0.32 mm, 0.25 μm film, J&W Scientific), split 10:1, helium as carrier gas with a flow of 3 mL/min (80 kPa), 220 °C injector and detector temperature, temperature program: 70 °C (5 min), 10 °C $min^{-1}$ to 150 °C, 25 °C $min^{-1}$ to 220 °C, 220 °C (15 min), reference values for retention times: 2-(bromomethyl)-5-phenyltetrahydrofuran (**7**): $R_t$ = 11.90 min for *cis*-**7** and 12.10 min for *trans*-**7**. C,H,N,S analyses: Microanalytical Laboratory, Universität Würzburg and Technische Universität Kaiserslautern, Carlo Erba 1106 or LECO CHNS-932. Solvents were purified according to standard procedures.[52] *tert*-Butyl hydroperoxide (5.5 M in nonane) and triethyl vanadate(V) were obtained from Fluka and Aldrich and were used as received. Pyridinium hydrobromide was obtained from Aldrich and was dried with $P_2O_5$ and stored under nitrogen. Petroleum ether was distilled prior to use (b.p. 35−45 °C).

### 2. Preparation of Schiff-Base Ligands $H_2L$ (4)

**3,5-Di-*tert*-butyl-*N*-(2-hydroxyphenyl)salicylidenimine (4b) ($H_2L^2$):** 3,5-Di-(*tert*-butyl)-2-hydroxybenzaldehyde (469 mg, 2 mmol) and *o*-aminophenol (218 mg, 2 mmol) were dissolved in dry EtOH (15 mL) and heated under reflux for 3−4 h. The solvent was removed in vacuo and the residue was dried at 5 × $10^{-2}$ mbar (20 °C) to afford Schiff base **4b** (645 mg, 99%) as a pale yellow solid; m.p. 128 °C. $^1$H NMR ($CDCl_3$, 250 MHz): δ = 1.40 [s, 9 H, $C(CH_3)_3$], 1.53 [s, 9 H, $C(CH_3)_3$], 6.98−7.10 (m, 2 H, Ar−H), 7.19−7.30 (m, 2 H, Ar−H), 7.32 ($m_c$, 1 H, Ar−H), 7.55 ($m_c$, 1 H, Ar−H), 8.76 (s, 1 H, CH) ppm. $^{13}$C NMR ($CDCl_3$, 63 MHz): δ = 29.4, 31.4, 34.1, 35.1, 115.7, 118.2, 118.5, 121.0, 127.3, 128.4, 128.7, 136.0, 137.1, 141.2, 149.9, 157.7, 165.2 ppm. MS (70 eV, EI): *m*/*z* (%) = 325 (48) [$M^+$], 310 (100) [$M^+ - CH_3$], 268 (24) [$M^+ - C(CH_3)_3$], 282 (43) [$C_{18}H_{20}NO_2^+$], 254 (13) [$C_{16}H_{16}NO_2^+$], 120 (31) [$C_7H_6NO_2^+$], 57 (61) [$C_4H_9^+$]. IR (KBr): $\tilde{\nu}$ = 3544 $cm^{-1}$, 3484, 2953, 2903, 2870, 1615, 1583, 1489, 1168, 756. HRMS ($C_{21}H_{27}NO_2$, 325.5): calcd. 325.2042, found 325.2038.

**(2*S*)-3,5-Di-*tert*-butyl-*N*-[1-hydroxy-4-(methylsulfinyl)butyl]-salicylidenimine (4d) ($H_2L^4$):** A solution of Schiff base **4c**[16] (100 mg, 0.29 mmol) in dry $CH_2Cl_2$ (4 mL) was treated with TBHP (56 μL of a 5.5 M solution in nonane, 0.31 mmol). The reaction mixture was stirred at 20 °C for 5 d. The solution was filtered through a short pad of $SiO_2$, and the yellow band of starting material **4c** was eluted with petroleum ether/$Et_2O$ (1:1, v/v). The sulfoxide **4d** was then eluted from this column with $CH_3OH$ to provide a yellow solution, which was concentrated in vacuo to furnish after drying 50.1 mg (47%) of ligand **4d**: viscous yellow oil, mixture of *like*/*unlike* diastereomers. $^1$H NMR ($CDCl_3$, 250 MHz): δ = 1.31 [s, 9 H, $C(CH_3)_3$], 1.43 [s, 9 H, $C(CH_3)_3$], 1.60−2.30 (br. s, OH), 2.09−2.29 (m, 2 H, $CH_2$), 2.58 (s, 3 H, $CH_3$), 2.67−2.81 (m, 2 H, $CH_2$), 3.43−3.63 (m, 1 H, CH), 3.69−3.96 (m, 2 H, $CH_2$), 7.17 ($m_c$, 1 H, Ar−H), 7.43 ($m_c$, 1 H, Ar−H), 8.48 (s, 1 H, CH) ppm. $^{13}$C NMR ($CDCl_3$, 101 MHz): δ = 24.8, 25.9, 29.3, 29.4, 31.3, 31.5, 34.2, 35.0, 38.4, 38.8, 50.5, 51.2, 65.8, 65.9, 70.1, 70.8, 117.5, 126.4 (2C), 127.6, 136.8, 136.9, 140.6, 157.9, 168.0, 168.1 (2 C's not detected) ppm. IR (KBr): $\tilde{\nu}$ = 3387 $cm^{-1}$, 3318, 2956, 2910, 2866, 1630, 1467, 1440, 1032. MS (70 eV, EI): *m*/*z* (%) = 367 (100) [$M^+$], 351 (11) [$M^+ - O$], 336 (10) [$C_{19}H_{30}NO_2S^+$], 303 (61) [$C_{19}H_{30}NO_2^+$], 288 (93) [$C_{19}H_{29}NO^+$], 272 (23) [$C_{18}H_{29}NO^+$], 232 (29) [$C_{15}H_{22}NO^+$], 71 (13) [$C_4H_8O^+$], 57 (50) [$C_4H_9^+$], 41 (18) [$C_3H_5^+$]. HRMS ($C_{20}H_{33}NO_3S$, 367.6): calcd. 367.2181, found 367.2182.

### 3. Preparation of (Schiff base)vanadium(V) Complexes

**General Procedure:** A solution of a Schiff base **4** (1 mmol) in dry EtOH (10 mL) was added under nitrogen to a solution of $VO(OEt)_3$ (202 mg, 1 mmol) in dry EtOH (5 mL). The reaction mixture was stirred at 20 °C for 1 h to furnish a dark brown solution. The solvent was removed under reduced pressure to provide, after drying at 5 × $10^{-2}$ mbar (20 °C), the corresponding (Schiff base)vanadium(V) complex **5** in quantitative yield.

**VOL$^1$(OEt)(EtOH) (5a):** Yield: 360 mg (quant.) from 213 mg **4a**; dark brown, microcrystalline solid. $^{51}$V NMR (105 MHz): δ = −529 ppm (EtOH); −529 ($CD_3OD$); −529 ($CDCl_3$). IR (KBr): $\tilde{\nu}$ = 990 $cm^{-1}$ (V=O). UV/Vis (EtOH): $\lambda_{max.}$ (lg ε) = 242 nm (4.16), 341 (3.78), 361 (3.80), 659 (2.40).

**VOL$^2$(OEt) (5b):** Yield: 440 mg (quant.) from 325 mg **4b**; dark brown to black solid. $^{51}$V NMR (105 MHz): δ = −539 ppm (EtOH). IR (KBr): $\tilde{\nu}$ = 999 $cm^{-1}$ (V=O). UV/Vis (EtOH): $\lambda_{max.}$ (lg ε) = 257 nm (4.15), 349 (3.90), 485 (2.98), 526 (2.53), 625 (2.34). $C_{23}H_{30}NO_4V$ (435.4): calcd. C 63.44, H 6.94, N 3.22; found C 63.48, H 6.89, N 3.18.

**VOL$^3$(OEt) (5c):** Yield: 466 mg (quant.) from 352 mg **4c**; black, microcrystalline solid. $^{51}$V NMR (105 MHz): δ = −534, −557 ppm (EtOH); −562 /−573 (br.) ppm, ($CDCl_3$). IR (KBr): $\tilde{\nu}$ = 987 $cm^{-1}$ (V=O). UV/Vis (EtOH): $\lambda_{max.}$ (lg ε) = 251 nm (4.25), 350 (3.69), 437 (1.91), 652 (2.06). $C_{22}H_{36}NO_4SV$ (461.5): calcd. C 57.25, H 7.86, N 3.03, S 6.95; found C 56.13, H 7.22, N 3.24, S 7.00.

**VOL$^4$(OH)($H_2O$) (5d):** Yield: 471 mg (quant.) from 368 mg **4d**; dark brown solid. $^{51}$V NMR (105 MHz): δ = −544 ppm (EtOH); −439, −433, −558 ppm (in $CDCl_3$). IR (KBr): $\tilde{\nu}$ = 961 $cm^{-1}$. UV/Vis (EtOH): $\lambda_{max.}$ (lg ε) = 260 (4.33), 334 (3.76), 518 (3.01), 673 (2.88). $C_{22}H_{32}NO_5SV{\cdot}H_2O$ (467.5): calcd. C 51.38, H 7.33, N 3.00, S 6.86; found C 49.56, H 7.33, N 2.04, S 5.06.

**VOL$^5$(OEt) (5e):** Yield: 360 mg (quant.) from 258 mg **4e**; black, microcrystalline solid. $^{51}$V NMR (105 MHz): δ = −531 ppm (in EtOH). IR (KBr): $\tilde{\nu}$ = 945 $cm^{-1}$ (V=O). UV/Vis (EtOH): $\lambda_{max.}$ (lg ε) = 549 nm (2.87), 556 (2.81), 652 (2.66).

**VOL$^8$(OEt) (5h):** A solution of 3-amino-4-hydroxybenzoic acid (306 mg, 2.0 mmol) and 2-hydroxybenzaldehyde (244 mg, 2.0 mmol) in dry EtOH (15 mL) was heated at reflux for 4 h. The solvent was removed under reduced pressure to furnish a yellow residue, which was recrystallized twice from $CH_3OH$ to afford a crude product (412 mg). A fraction of this material (206 mg) was treated with $VO[OCH(CH_3)_2]_3$ (286 mg) in dry EtOH (10 mL).The reaction mixture was heated at reflux for 30 min. Afterwards, the amount of solvent was concentrated to half of its volume to provide a dark solution that was allowed to stand at 20 °C for 24 h. (Schiff base)vanadium(V) complex **5h** separated as a black, microcrystalline solid from this solution to provide pure **5h** (120 mg, 33%) after filtration and drying. $^{51}$V NMR (105 MHz): δ = −534 ppm (in EtOH); −538 ppm (in $CDCl_3$). IR (KBr): $\tilde{\nu}$ = 991 $cm^{-1}$ (V=O). UV/Vis (EtOH): $\lambda_{max.}$ (lg ε) = 267 (4.51), 363 (4.26), 564 (4.18), 661 (4.38). $C_{16}H_{14}NO_6V$ (367.2): calcd. C 52.33, H 3.84, N 3.81; found C 52.40, H 3.87, N 4.01.

### 4. Vanadium(V)-Catalyzed Oxidation of Bromide in the Presence of Alkenols

**General Procedure:** In a typical run, catalyst VOL$^3$(OEt) (**5c**, 11.5 mg, 25.0 μmol, 5 mol%) was dissolved in a dry solvent [$CH_3CN$, $CHCl_3$ or $CH_2Cl_2$ (2 mL)]. TBHP (100 μL of a 5.5 M solution in nonane, 0.55 mmol) was added, and the solution was

heated at 40 °C for 2 min. Stirring was continued at 20 °C for 5 min. Afterwards, this solution was added portionwise to a solution of alkenol (0.50 mmol) and pyHBr (120 mg, 0.75 mmol) in a dry solvent ($CH_3CN$, $CHCl_3$ or $CH_2Cl_2$, 3 mL). The reaction mixture was stirred at 20 °C for 48 h. Afterwards, the solvent was removed under reduced pressure to provide a brown, viscous, oily residue that was purified by column chromatography [$SiO_2$; typical eluent: petroleum ether/$Et_2O$ (10:1, v/v)].

**Bromocyclization of 1-Phenyl-4-penten-1-ol (6)**

**2-(Bromomethyl)-5-phenyltetrahydrofuran (7):**[25] Yield: 79.6 mg (66%), *cis*/*trans* = 34:66, colorless liquid. ***cis*-7:** $R_f$ = 0.73 [$SiO_2$; petroleum ether/$Et_2O$ (10:1, v/v)]. $^1H$ NMR ($CDCl_3$, 250 MHz): δ = 1.86−2.01 (m, 2 H, $CH_2$), 2.17−2.35 (m, 2 H, $CH_2$), 3.50 (dd, *J* = 10.1, 5.4 Hz, 1 H, $CH_2$), 3.58 (dd, *J* = 10.1, 5.4 Hz, 1 H, $CH_2$), 4.35 ($m_c$, 1 H, CH), 4.95 (dd, *J* = 8.1, 5.9 Hz,,1 H, CH), 7.23−7.41 (m, 5 H, Ph−H) ppm. $^{13}C$ NMR ($CDCl_3$, 63 MHz): δ = 30.4, 34.3, 35.8, 78.5, 82.1, 125.8, 127.5, 128.7, 142.2 ppm. ***trans*-7:** $R_f$ = 0.80 [$SiO_2$; petroleum ether/$Et_2O$ (10:1, v/v)]. $^1H$ NMR ($CDCl_3$, 250 MHz): δ = 1.86−2.01 (m, 2 H, $CH_2$), 2.17−2.35 (m, 1 H, $CH_2$), 2.38− 2.56 (m, 1 H, $CH_2$), 3.46 (dd, *J* = 10.1, 7.2 Hz, 1 H, $CH_2$), 3.55 (dd, *J* = 10.1, 3.8 Hz, 1 H, $CH_2$), 4.48 ($m_c$, 1 H, CH), 5.10 (dd, *J* = 8.3, 6.1 Hz, 1 H, CH), 7.23− 7.41 (m, 5 H, Ph−H) ppm. $^{13}C$ NMR ($CDCl_3$, 63 MHz): δ = 31.1, 35.2, 36.0, 78.7, 81.5, 125.6, 127.4, 128.6, 142.6 ppm.

**4,5-Dibromo-1-phenylpentan-1-ol (8):** Yield 33.8 mg (21%), 50:50 mixture of diastereomers, colorless liquid. $R_f$ = 0.26 [$SiO_2$; petroleum ether/$Et_2O$ (10:1, v/v)]. $^1H$ NMR ($CDCl_3$, 400 MHz): δ = 1.58−1.72 (br. s, 2 H, OH), 1.75−2.10 (m, 6 H, $CH_2$), 2.18−2.28 (m, 1 H, $CH_2$), 2.33−2.42 (m, 1 H, $CH_2$), 3.61 (dd, *J* = 9.9, 4.4 Hz, 2 H, $CH_2$), 3.84 (2 t, *J* = 9.9 Hz, 2 H, $CH_2$), 4.20 ($m_c$, 2 H, CH), 4.74 ($m_c$, 2 H, CH), 7.28−7.39 (m, 10 H, Ar−H) ppm. $^{13}C$ NMR ($CDCl_3$, 101 MHz): δ = 32.4, 32.8, 36.0, 36.1, 36.2 (2 C), 52.5, 52.9, 73.6, 74.2, 125.7, 125.8, 127.8, 127.9, 128.6, 128.7, 144.1, 144.2 ppm. MS (70 eV, EI): *m*/*z* (%) = 304 (12) [$M^+$ − OH], 242/240 (12) [$M^+$ − Br], 147 (29) [$C_{10}H_{11}O^+$], 129/128 (29) [$C_{10}H_9^+$], 117 (100) [$C_9H_9^+$], 104 (22) [$C_8H_9^+$], 91 (22) [$C_7H_7^+$], 77 (13) [$C_6H_5^+$], 41 (13) [$C_2H_2^+$]. $C_{11}H_{14}Br_2O$ (322.0): calcd. C 41.03, H 4.38; found C 41.07, H 4.08.

**Bromocyclization of 1-(4-Methoxyphenyl)-4-penten-1-ol (9)**

**2-(Bromomethyl)-5-(4-methoxyphenyl)tetrahydrofuran (14):** Yield: 93.5 mg (69%), *cis*/*trans* = 33:67, colorless liquid. $C_{12}H_{15}BrO_2$ (271.2): calcd. C 53.16, H 5.58; found C 52.25, H 5.49. MS (70 eV, EI): *m*/*z* (%) = 270/272 (23) [$M^+$], 239/241 (15) [$M^+$ − $OCH_3$], 191 (21) [$M^+$ − Br], 135 (100) [$C_9H_{10}O^+$], 83 (21) [$C_5H_8^+$], 55 (36) [$C_3H_3O^+$]. ***cis*-14:** $R_f$ = 0.44 [$SiO_2$; petroleum ether/$Et_2O$ (6:1, v/v)]. $^1H$ NMR ($CDCl_3$, 250 MHz): δ = 1.83−2.05 (m, 2 H, $CH_2$), 2.14−2.35 (m, 2 H, $CH_2$), 3.47 (dd, *J* = 10.1, 6.1 Hz, 1 H, $CH_2$), 3.56 (dd, *J* = 10.1, 2.7 Hz, 1 H, $CH_2$), 3.80 (s, 3 H, $OCH_3$), 4.31 ($m_c$, 1 H, CH), 4.89 (dd, *J* = 8.2, 5.8 Hz, 1 H, CH), 6.88 ($m_c$, 2 H, Ar−H), 7.30 ($m_c$, 2 H, Ar−H) ppm. $^{13}C$ NMR ($CDCl_3$, 63 MHz): δ = 30.5, 34.2, 35.9, 55.3, 78.3, 81.8, 113.8, 127.2, 134.2, 159.1 ppm. ***trans*-14:** $R_f$ = 0.45 [$SiO_2$; petroleum ether/$Et_2O$ (6:1, v/v)]. $^1H$ NMR ($CDCl_3$, 250 MHz): δ = 1.82−2.10 (m, 2 H, $CH_2$), 2.20−2.40 (m, 2 H, $CH_2$), 3.44 (dd, *J* = 10.1, 6.7 Hz, 1 H, $CH_2$), 3.54 (dd, *J* = 10.1, 4.9 Hz, 1 H, $CH_2$), 3.80 (s, 3 H, $OCH_3$), 4.46 ($m_c$, 1 H, CH), 5.03 (dd, *J* = 7.9, 5.4 Hz, 1 H, CH), 6.87 ($m_c$, 2 H, Ar−H), 7.25 ($m_c$, 2 H, Ar−H) ppm. $^{13}C$ NMR ($CDCl_3$, 63 MHz): δ = 31.3, 35.1, 36.1, 55.3, 78.5, 81.3, 113.8, 127.0, 134.5, 159.0 ppm.

**Bromocyclization of 4-Methyl-1-phenyl-4-penten-1-ol (10)**

**2-(Bromomethyl)-2-methyl-5-phenyltetrahydrofuran (15):** Yield: 81.7 mg (64%), *cis*/*trans* = 26:74, colorless liquid. $C_{12}H_{15}BrO$ (255.2): calcd. C 56.45, H 5.93; found C 56.47, H 5.81. MS (70 eV, EI): *m*/*z* (%) = 256/254 (3) [$M^+$], 161 (50) [$M^+$ − Br], 105 (100) [$C_8H_9^+$], 77 (49) [$C_6H_5^+$], 43 (56) [$C_2H_3O^+$]. ***cis*-15**: $R_f$ = 0.77 [$SiO_2$; petroleum ether/$Et_2O$ (13:1, v/v)]. $^1H$ NMR ($CDCl_3$, 250 MHz): δ = 1.50 (s, 3 H, $CH_3$), 1.86−2.02 (m, 2 H, $CH_2$), 2.16−2.41 (m, 2 H, $CH_2$), 3.50 ($m_c$, 2 H, $CH_2$), 5.04 ($m_c$, 1 H, CH), 7.23−7.46 (m, 5 H, Ph−H) ppm. $^{13}C$ NMR ($CDCl_3$, 63 MHz): δ = 25.2, 35.5, 36.4, 41.1, 81.3, 82.4, 125.9, 127.4, 128.3, 142.1 ppm. ***trans*-15:** $R_f$ = 0.77 [$SiO_2$; petroleum ether/$Et_2O$ (13:1, v/v)]. $^1H$ NMR ($CDCl_3$, 250 MHz): δ = 1.53 (s, 3 H, $CH_3$), 1.86−2.02 (m, 2 H, $CH_2$), 2.16−2.41 (m, 2 H, $CH_2$), 3.51 ($m_c$, 2 H, $CH_2$), 5.05 (dd, *J* = 9.0, 5.7 Hz, 1 H, CH), 7.23−7.42 (m, 5 H, Ph−H) ppm. $^{13}C$ NMR ($CDCl_3$, 63 MHz): δ = 25.9, 35.5, 36.4, 41.6, 82.0, 82.6, 125.7, 127.4, 128.3, 142.2 ppm.

**Bromocyclization of 2-Phenyl-4-penten-1-ol (11)**

**2-(Bromomethyl)-4-phenyltetrahydrofuran (16):** Yield: 106 mg (88%), *cis*/*trans* = 72:28, colorless liquid.[25]

**Bromocyclization of 3-phenyl-4-penten-1-ol (12)**

**2-(Bromomethyl)-3-phenyltetrahydrofuran (17):** Yield: 67.5 mg (56%), *cis*/*trans* = 30:70, colorless liquid.[25]

**Bromocyclization of 4-Phenyl-4-penten-1-ol (13)**

**2-(Bromomethyl)-2-phenyltetrahydrofuran (18):** Yield: 79.6 mg (66%), colorless liquid. $R_f$ = 0.52 [$SiO_2$; petroleum ether/$Et_2O$ (10:1, v/v)]. $^1H$ NMR ($CDCl_3$, 250 MHz): δ = 1.79−1.93 (m, 1 H, $CH_2$), 1.98−2.14 (m, 1 H, $CH_2$), 2.26 (ddd, *J* = 12.3, 7.9, 5.2 Hz, 1 H, $CH_2$), 2.43 (dt, *J* = 12.3, 8.2 Hz, 1 H), 3.65 (s, 2 H, $CH_2$), 3.94 (dt, *J* = 8.2, 5.8 Hz, 1 H, $CH_2$), 4.09 (dt, *J* = 8.2, 7.0 Hz, 1 H, $CH_2$), 7.24−7.44 (m, 5 H, Ph−H) ppm. $^{13}C$ NMR ($CDCl_3$, 63 MHz): δ = 26.1, 36.4, 42.2, 68.6, 85.3, 125.6, 127.4, 128.3, 144.0 ppm. MS (70 eV, EI): *m*/*z* (%) = 160 (78) [$M^+$ − HBr], 147 (100) [$C_{10}H_{11}O^+$], 118 (42) [$C_8H_7O^+$], 105 (57) [$C_7H_5O^+$], 91 (29) [$C_7H_7^+$], 77 (24) [$C_6H_5^+$], 51 (12) [$C_4H_3^+$]. $C_{11}H_{13}BrO$ (241.1): calcd. C 54.79, H 5.43; found C 54.03, H 5.45.

**Bromocyclization of (1*S**,2*S**,3*R**)-2-Methyl-1,3-bis(2′,4′,5′-trimethoxyphenyl)-4-penten-1-ol (19)**

**(2*R**,3*R**,4*S**,5*S**)-2-(Bromomethyl)-4-methyl-1,3-bis(2′,4′,5′-trimethoxyphenyl)-tetrahydrofuran (20):** A solution of $VOL^3(OEt)$ (**5c**; 11.6 mg, 5 mol %) in $CH_2Cl_2$ (2 mL) was treated with TBHP (100 μL of a 5.5 M solution in nonane, 0.55 mmol) as outlined in the General Procedure. This mixture was added dropwise to a solution of 2-methyl-1,3-bis(2′,4′,5′-trimethoxyphenyl)-4-penten-1-ol (**19**; 216 mg, 0.50 mmol) and pyHBr (120 mg, 0.75 mmol) in $CH_2Cl_2$ (3 mL). The reaction mixture was stirred at 20 °C for 48 h. The solvent was removed under reduced pressure to provide a residue, which was purified by column chromatography [$SiO_2$; petroleum ether/$Et_2O$ (1:1, v/v)]. Yield: 178 mg (70%), colorless solid. m.p. 44−46 °C. $R_f$ = 0.30 [$SiO_2$; petroleum ether/$Et_2O$ (1:1, v/v)]. $^1H$ NMR ($CDCl_3$, 400 MHz): δ = 0.90 (d, *J* = 6.4 Hz, 3 H, $CH_3$), 2.52 (ddq, *J* = 11.2, 9.6, 6.4 Hz, 1 H, CH), 3.36 (dd, *J* = 11.2, 8.8 Hz, 1 H, CH), 3.48 (dd, *J* = 10.6, 5.2 Hz, 1 H, $CH_2Br$), 3.62 (dd, *J* = 10.6, 3.9 Hz, 1 H, $CH_2Br$), 3.82 (s, 3 H, $OCH_3$), 3.83 (s, 3 H, $OCH_3$), 3.84 (s, 3 H, $OCH_3$), 3.89 (s, 9 H, 3×$OCH_3$), 4.46 (ddd, *J* = 8.9, 5.2, 3.9 Hz, 1 H, CH), 5.03 (d, *J* = 9.6 Hz, 1 H, CH), 6.53 (s, 1 H, Ar−H), 6.54 (s, 1 H, Ar−H), 6.76 (s, 1 H, Ar−H), 7.06 (s, 1 H, Ar−H) ppm. $^{13}C$ NMR (101 MHz): δ = 14.6,

36.8, 49.4, 52.2, 56.3, 56.5 (2C), 57.0, 57.2, 57.3, 82.6, 83.4, 98.3, 98.5, 112.0, 113.2, 118.8, 121.6, 143.7, 143.8, 149.1, 149.5, 152.2, 152.9 ppm. MS (70 eV, EI): *m*/*z* (%) = 510/512 (36) [$M^+$], 430 (2) [$M^+$ − Br], 223 (100) [$C_{12}H_{13}O_4^+$]. $C_{24}H_{31}BrO_7$ (511.4): calcd. C 56.37, H 6.11; found C 55.94, H 6.13.

**(2*R**,3*R**,4*S**,5*S**)-2,4-Dimethyl-1,3-bis(2′,4′,5′-trimethoxyphenyl)tetrahydrofuran (21):** A solution of 2-(bromomethyl)-4-methyl-1,3-bis(2′,4′,5′-trimethoxyphenyl)tetrahydrofuran (**20**; 124 mg, 240 μmol) in dry $Et_2O$ (5 mL) was added dropwise to a stirred mixture of LiH (10.1 mg, 1.44 mmol) and $LiAlH_4$ (29.0 mg, 720 μmol) in dry $Et_2O$ (10 mL), under argon. The mixture was stirred at 20 °C for 12 h and cooled to 0 °C, and $H_2O$ was added until no further hydrogen was evolved. The salts were dissolved with aq. HCl (10%, w/w), the organic phase was separated, and the aqueous phase was extracted with $Et_2O$ (2 × 10 mL). The combined organic phases were concentrated in vacuo to afford crude product (126 mg), which was purified by column chromatography [$SiO_2$; petroleum ether/$Et_2O$ (1:1, v/v)]. Yield: 81.0 mg (78%), colorless solid. $R_f$ = 0.35 [$SiO_2$; petroleum ether/$Et_2O$ (1:1, v/v)]. $^1$H NMR (400 MHz): δ = 0.90 (d, *J* = 6.6 Hz, 3 H, $CH_3$), 1.26 (d, *J* = 6.1 Hz, 3 H, $CH_3$), 2.44 (ddq, *J* = 10.9, 9.1, 6.4 Hz, 1 H, CH), 3.11 (dd, *J* = 10.9, 9.3 Hz, 1 H, CH), 3.80 (s, 3 H, $OCH_3$), 3.82 (s, 3 H, $OCH_3$), 3.83 (s, 3 H, $OCH_3$), 3.88 (s, 3 H, $OCH_3$), 3.89 (s, 6 H, 2 × $OCH_3$), 4.34 (dq, *J* = 9.3, 6.1 Hz, 1 H, CH), 5.01 (d, *J* = 9.3 Hz, 1 H, CH), 6.53 (s, 1 H, Ar−H), 6.55 (s, 1 H, Ar−H), 6.75 (s, 1 H, Ar−H), 7.07 (s, 1 H, Ar−H) ppm.

**Bromocyclization of 2-Cyclohex-2-en-1-yl-1-phenylethanol (22)**

**6,8-*trans*-5-Bromo-8-phenyl-7-oxabicyclo[4.3.0]nonane (23):** Yield: 46.6 mg (33%), 6,8-*cis*/6,8-*trans* = 7:93. $R_f$ = 0.82 [$SiO_2$; petroleum ether/$Et_2O$ (10:1, v/v)]. $^1$H NMR ($CDCl_3$, 250 MHz): δ = 1.23−1.81 (m, 4 H, $CH_2$), 1.82−1.88 (m, 1 H, $CH_2$), 1.94 (ddd, *J* = 12.5, 7.6, 6.4 Hz, 1 H, $CH_2$), 2.10 ($m_c$, 1 H, $CH_2$), 2.21 (ddd, *J* = 12.4, 7.3, 6, 5 Hz, 1 H, $CH_2$), 2.53−2.65 (m, 1 H, CH), 4.40 (t, *J* = 4.3 Hz, 1 H, CH), 4.44 ($m_c$, 1 H, CH), 5.22 (dd, *J* = 7.6, 7.3 Hz, 1 H, CH), 7.22−7.37 (m, 5 H, Ph−H) ppm. $^{13}$C NMR ($CDCl_3$, 63 MHz): δ = 19.8, 26.3, 30.5, 36.2, 40.5, 52.1, 79.6, 82.6, 125.3, 127.2, 128.4, 144.2 ppm. MS (70 eV): *m*/*z* (%) = 282/280 (43) [$M^+$], 211 (1) [$M^+$ − Br], 189 (4) [$C_{12}H_{14}O_2^+$], 129 (80), 120 (15) [$C_3H_6Br^+$], 105 (86) [$C_7H_5O^+$], 59 (1) [$C_2H_3O^+$], 43 (100) [$C_2H_3O^+$]. HRMS ($C_{14}H_{17}BrO$, 281.2): calcd. 280.0463; found 280.0462.

**2-(2,3-Dibromocyclohexyl)-1-phenylethanol (24):** Yield: 53.9 mg (30%), diastereomer I/diastereomer II = 23:77, colorless oil. $C_{14}H_{18}Br_2O$ (362.1): calcd. C 46.44, H 5.01; found C 46.82, H 5.08. MS (70 eV, EI): *m*/*z* (%) = 364/362 (1) [$M^+$], 280 (1) [$M^+$ − HBr], 205 (4) [$C_8H_{12}OBr^+$], 184 (26) [$C_2H_2Br_2^+$], 107 (100) [$C_7H_7O^+$], 81 (18) [$HBr^+$], 79 (57) [$Br^+$], 77 (25) [$C_6H_5^+$], 41 (13) [$C_3H_5^+$]. **Diastereomer I:** $R_f$ = 0.21 [$SiO_2$; petroleum ether/$Et_2O$ (10:1, v/v)]. $^1$H NMR ($CDCl_3$, 400 MHz): δ = 1.50 ($m_c$, 2 H) 1.58−1.79 (m, 3 H), 1.83−1.97 (m, 2 H), 2.37−2.51 (m, 2 H), 4.75−4.82 (m, 3 H), 7.27−7.37 (m, 5 H, Ph−H) ppm. $^{13}$C NMR ($CDCl_3$, 63 MHz): δ = 20.2, 26.0, 28.0, 32.5, 44.9, 54.2, 62.0, 71.8, 125.7, 127.7, 128.6, 144.5 ppm. **Diastereomer II:** $R_f$ = 0.28 [$SiO_2$; petroleum ether/$Et_2O$ (10:1, v/v)]. $^1$H NMR ($CDCl_3$, 400 MHz): δ = 1.43−1.54 (m, 1 H) 1.60−1.70 (m, 3 H), 1.82−1.93 (m, 3 H), 2.38−2.48 (m, 2 H), 4.70−4.79 (m, 3 H), 7.27−7.37 (m, 5 H, Ph−H) ppm. $^{13}$C NMR ($CDCl_3$, 63 MHz): δ = 20.4, 27.3, 28.2, 31.9, 44.4, 54.0, 60.3, 71.1, 125.5, 127.7, 128.6, 144.8 ppm.

**Bromocyclization of (*E*)-6-Phenyl-5-hexen-2-ol (25)**

**2,3-*trans*-3-Bromo-6-methyl-2-phenyltetrahydropyran (26):** Yield: 73.9 mg (58%), 2,6-*cis*/2,6-*trans* = 86:14, colorless liquid. $C_{12}H_{15}BrO$ (255.2): calcd. C 56.49, H 5.93; found C 56.19, H 5.87. MS (70 eV): *m*/*z* (%) = 256/254 (1) [$M^+$], 174 (95) [$M^+$ − Br], 118 (100) [$C_8H_6O^+$], 90 (49) [$C_7H_6^+$], 55 (14) [$C_4H_8^+$], 43 (10) [$C_3H_6^+$]. **2,6-*cis*-26:** $R_f$ = 0.64 [$SiO_2$; petroleum ether/$Et_2O$ (10:1, v/v)]. $^1$H NMR ($CDCl_3$, 250 MHz): δ = 1.23 (d, *J* = 6.4 Hz, 3 H, $CH_3$), 1.60 (ddt, *J* = 10.7, 4.0, 13.1 Hz, 1 H, $CH_2$), 1.79 ($m_c$, 1 H, $CH_2$), 2.16 (ddt, *J* =, 11.9, 4.5, 13.1 Hz, 1 H, $CH_2$), 2.55 (m, 1 H, $CH_2$), 3.74 (ddq, *J* = 13.1, 2.1, 6.4 Hz, 1 H, CH), 4.00 (ddd, *J* = 11.9, 10.1, 4.5 Hz, 1 H, CH), 4.39 (d, *J* = 10.1 Hz, 1 H, CH), 7.29−7.43 (m, 5 H, Ph−H) ppm. $^{13}$C NMR ($CDCl_3$, 63 MHz): δ = 21.6, 35.5, 36.2, 52.6, 74.6, 85.2, 127.8, 128.2, 128.4, 139.8 ppm. **2,6-*trans*-26:** $R_f$ = 0.45 [$SiO_2$; petroleum ether/$Et_2O$ (10:1, v/v)]. $^1$H NMR ($CDCl_3$, 250 MHz): δ = 1.38 (d, *J* = 6.7 Hz, 3 H, $CH_3$), 1.72 ($m_c$, 2 H, $CH_2$), 2.25−2.36 (m, 2 H, $CH_2$), 4.22 ($m_c$, 1 H, CH), 4.28 (dt, *J* = 5.8, 8.3 Hz, 1 H, CH), 4.79 (d, *J* = 8.3 Hz, 1 H, CH) 7.26−7.43 (m, 5 H, Ph−H) ppm. $^{13}$C NMR ($CDCl_3$, 63 MHz): δ = 17.5, 30.1, 30.8, 52.6, 68.8, 81.6, 127.3, 128.2, 128.4, 139.4 ppm.

**2,6-*unlike*-2-(6-Bromo-6-phenylmethyl)-5-methyltetrahydrofuran (27):** Yield: 6.5 mg (5%), *cis*/*trans* = 58:42, colorless liquid. **2,6-*unlike*-2,5-*cis*-27:** $^1$H NMR ($CDCl_3$, 600 MHz): δ = 1.27 (d, *J* = 6.1 Hz, $CH_3$), 1.45−1.53 (m, 1 H, $CH_2$), 2.00−2.08 (m, 2 H, $CH_2$), 2.18 ($m_c$, 1 H, $CH_2$), 4.10−4.18 (m, 1 H, CH), 4.41 (dt, *J* = 7.4, 6.2 Hz, 1 H, CH), 4.87 (d, *J* = 7.4 Hz, 1 H, CH), 7.26−7.35 (m, 3 H, Ph−H), 7.41−7.45 (m, 2 H, Ph−H) ppm. $^{13}$C NMR ($CDCl_3$, 151 M*Hz*): δ = 21.4, 30.8, 34.0, 57.8, 76.0, 81.9, 128.3, 128.4, 128.5, 139.5 ppm. **2,6-*unlike*-2,5-*trans*-27:** $^1$H NMR ($CDCl_3$, 600 MHz): δ = 1.18 (d, *J* = 6.1 Hz, $CH_3$), 1.45−1.55 (m, 1 H, $CH_2$), 2.02−2.10 (m, 2 H, $CH_2$), 2.26 ($m_c$, 1 H, $CH_2$), 4.17 ($m_c$, 1 H, CH), 4.53 (q, *J* = 7.0 Hz, 1 H, CH), 4.93 (d, *J* = 7.0 Hz, 1 H, CH), 7.26−7.35 (m, 3 H, Ph−H), 7.41−7.45 (m, 2 H, Ph−H) ppm. $^{13}$C NMR ($CDCl_3$, 151 MHz): δ = 21.1, 31.3, 33.9, 58.5, 76.3, 81.6, 128.3, 128.4, 128.5, 139.5 ppm.

**Bromocyclization of 4-Methyl-1-phenyl-3-penten-1-ol (28)**

**3-Bromo-2,2-dimethyl-5-phenyltetrahydrofuran (29):** Yield: 39.6 mg (31%, *cis*/*trans* = 84:16, colorless liquid. $C_{12}H_{15}BrO$ (255.2): calcd. C 56.49, H 5.93; found C 56.18, H 5.73. MS (70 eV): *m*/*z* (%) = 254/256 (1) [$M^+$], 174 [$M^+$ − HBr], 131 (96) [$C_9H_7O^+$], 69 (100) [$C_4H_5O^+$], 77 (30) [$C_6H_5^+$], 69 (44) [$C_5H_9^+$], 43 (69) [$C_2H_3O^+$]. ***cis*-29:** $R_f$ = 0.52 [$SiO_2$; petroleum ether/$Et_2O$ (10:1, v/v)]. $^1$H NMR ($CDCl_3$, 400 MHz): δ = 1.43 (s, 3 H, $CH_3$), 1.46 (s, 3 H, $CH_3$), 2.38 (dt, *J* = 13.0, 6.5 Hz, 1 H, $CH_2$), 2.90 (dt, *J* = 13.0, 9.8 Hz, 1 H, $CH_2$), 4.21 (dd, *J* = 9.8, 6.5 Hz, 1 H, CH), 4.98 (dd, *J* = 9.8, 6.5 Hz, 1 H, CH), 7.24−7.38 (m, 5 H, Ph−H) ppm. $^{13}$C NMR ($CDCl_3$, 101 MHz): δ = 26.3, 26.8, 44.8, 54.4, 77.9, 82.7, 125.7, 127.6, 128.4, 142.0 ppm. ***trans*-29:** $R_f$ = 0.67 [$SiO_2$; petroleum ether/$Et_2O$ (10:1, v/v)]. $^1$H NMR ($CDCl_3$, 400 MHz): δ = 1.48 (s, 3 H, $CH_3$), 1.49 (s, 3 H, $CH_3$), 2.54 (dt, *J* = 13.4, 7.0 Hz, 1 H, $CH_2$), 2.73 (dt, *J* = 13.4, 7.0 Hz, 1 H, $CH_2$), 4.21 (t, *J* = 7.0 Hz, 1 H, CH), 5.22 (t, *J* = 7.0 Hz, 1 H, CH), 7.24−7.37 (m, 5 H, Ph−H) ppm. $^{13}$C NMR ($CDCl_3$, 101 MHz): δ = 25.0, 27.3, 44.8, 55.6, 77.8, 83.4, 125.7, 127.5, 128.5, 142.6 ppm.

**Bromocyclization of 5-Methyl-1-phenyl-4-hexen-1-ol (30)**

**3-Bromo-2,2-dimethyl-6-phenyltetrahydropyran (31):** Yield: 164 mg (61%), *cis*/*trans* = 9:91 colorless liquid.

**2-(1-Bromo-1-methylethyl)-5-phenyltetrahydrofuran (32):** Yield: 35.1 mg (13%), *cis*/*trans* = 46:54, colorless liquid.

**4,5-Dibromo-5-methyl-1-phenylhexan-1-ol (33):** Yield: 59.5 mg (17%), *like*/*unlike* = 50:50, colorless liquid. $R_f$ = 0.26 [$SiO_2$; petroleum ether/$Et_2O$ (5:1, v/v)]. $C_{13}H_{18}Br_2O$ (350.1): calcd. C 44.60, H

5.18; found C 44.46, H 5.17. MS (70 eV, EI): *m/z* (%) = 269 (6) [$M^+$ − HBr], 251 (4) [$M^+$ − $H_2O$ − HBr], 189 (2) [$M^+$ − 2 HBr], 147 (5) [$C_{10}H_{11}O^+$], 107 (100) [$C_7H_7O^+$], 79 (22) [$Br^+$], 41 (8) [$C_3H_5^+$]. $^1$H NMR ($CDCl_3$, 600 MHz): δ = 1.79 (s, 3 H, $CH_3$), 1.81 (s, 3 H, $CH_3$), 1.80−1.95 (m, 3 H, 2 $CH_2$), 1.97 (s, 3 H, $CH_3$), 1.98 (s, 3 H, $CH_3$), 1.99−2.05 (m, 1 H, $CH_2$), 2.13−2.24 (m, 2 H, $CH_2$), 2.51−2.57 (m, 1 H, $CH_2$), 2.63−2.68 (m, 1 H, $CH_2$), 4.23 (dd, *J* = 11.1, 1.7 Hz, 1 H, CH), 4.25 (dd, *J* = 10.8, 1.7 Hz, 1 H, CH), 4.73 (dd, *J* = 7.9, 5.2 Hz, 1 H, CH), 4.77 (dd, *J* = 8.6, 4.5 Hz, 1 H, CH), 7.28−7.39 (m, 10 H, Ph−H) ppm. $^{13}$C NMR ($CDCl_3$, 151 MHz): δ = 28.3, 28.4, 32.2, 32.8, 35.2, 35.3, 37.6, 37.9, 66.4, 67.0, 68.5, 68.6, 73.3, 74.3, 125.7, 125.9, 127.7, 127.8, 128.5, 128.6, 144.3, 144.4 ppm.

**Bromocyclization of 6-Methyl-1-phenyl-5-hepten-1-ol (34)**

**5,6-Dibromo-6-methyl-1-phenylheptan-1-ol (35):** Yield: 131 mg (72%), *like/unlike* = 50:50. $R_f$ = 0.43 [$SiO_2$; petroleum ether/$Et_2O$ (5:1, v/v)]. $^1$H NMR ($CDCl_3$, 250 MHz): δ = 1.68−1.96 (m, 6 H, $CH_2$), 1.79 (s, 6 H, $CH_3$), 1.97 (s, 6 H, $CH_3$), 2.35−2.50 (m, 4 H, $CH_2$), 4.15 (dd, *J* = 6.1, 1.5 Hz, 1 H, CH), 4.19 (dd, *J* = 5.9, 1.4 Hz, 1 H, CH), 4.67−4.75 (m, 2 H, CH), 7.27−7.38 (m, 10 H, Ph−H) ppm. $^{13}$C NMR ($CDCl_3$, 63 MHz): δ = 24.6, 24.7, 25.2, 28.1 (2C), 35.3, 35.4, 35.5, 35.6, 38.0, 66.5, 66.6, 68.7, 70.4, 74.3, 74.5, 125.8, 125.9, 127.5, 127.6, 128.5, 128.6, 144.6, 144.7 ppm. IR (neat): $\tilde{\nu}$ = 3415 $cm^{-1}$, 3484, 3062, 3021, 2932, 2845, 1709, 1492, 1454, 1370, 1096, 760, 700. MS (70 eV): *m/z* (%) = 266/264 (4) [$M^+$ − HOBr], 202 (26) [$M^+$ − 2 HBr], 184 (46) [$M^+$ − HBr − HOBr], 128 (41) [$C_8H_{16}O^+$], 117 (100) [$C_9H_9^+$], 77 (28) [$C_6H_5^+$], 51 (15) [$C_4H_3^+$], 39 (15) [$C_3H_3^+$]. $C_{14}H_{20}Br_2O$ (364.1): calcd. C 46.18, H 5.54; found C 47.15, H 5.66.

**Bromination of 1-Phenylpent-4-en-1-yl Acetate (40)**

**1-Phenylpent-4-en-1-yl Acetate (40):**[34] 5-Methyl-1-phenyl-4-hexen-1-ol (4.00 g, 21.0 mmol) was dissolved in pyridine (16 mL). Acetic anhydride (254 mmol) was added portionwise, and the solution was stirred at 20 °C for 18 h. After removal of the volatiles under reduced pressure (80 °C, 10 mbar), the resulting residue was purified by distillation (110−140 °C/10 mbar), followed by column filtration ($SiO_2$; petroleum ether) to afford a colorless liquid (3.45 g, 71% yield). $^1$H NMR ($CDCl_3$, 250 MHz): δ = 1. 54 (s, 3 H, $CH_3$), 1.68 (s, 3 H, $CH_3$), 1.73−1.87 (m, 1 H, $CH_2$), 1.90−2.02 (m, 3 H, $CH_2$), 2.07 (s, 3 H, $CH_3$), 5.10 ($m_c$, 1 H, CH), 5.71 (dd, *J* = 7.3, 6.0 Hz, 1 H, CH), 7.23−7.38 (m, 5 H, Ph−H) ppm. $^{13}$C NMR ($CDCl_3$, 63 MHz): δ = 17.6, 21.2, 24.1, 25.7, 36.3, 75.6, 123.1, 126.5, 127.8, 128.4, 132.4, 140.7, 170.3 ppm.

**4,5-Dibromo-1-phenylpent-1-yl Acetate (41):** Yield: 147 mg (75%), *like/unlike* = 50:50, colorless liquid. $R_f$ = 0.67 [$SiO_2$; petroleum ether/$Et_2O$ (5:1, v/v)]. $^1$H NMR ($CDCl_3$, 250 MHz): δ = 1.73, 1.76 (2 s, 6 H, $CH_3$), 1.79−2.08 (m, 4 H, $CH_2$) 1.96 (2 s, 6 H, $CH_3$), 2.09, 2.10 (2 s, 6 H, $CH_3$), 2.19−2.38 (m, 2 H, $CH_2$), 2.43−2.57 (m, 2 H, $CH_2$), 4.21 (2 dd, *J* = 11.0, 1.8 Hz, 2 H, CH), 5.78 (dd, *J* = 7.6, 5.8 Hz, 1 H, CH), 5.84 (dd, *J* = 8.2, 3.9 Hz, 1 H, CH), 7.26−7.37 (m, 10 H, Ph−H) ppm. $^{13}$C NMR ($CDCl_3$, 63 MHz): δ = 21.3 (2 C), 28.0, 28.2, 31.7, 32.3, 35.0, 35.2, 35.3, 35.4, 65.6, 66.3, 68.3 (2 C), 74.3, 75.5, 126.3, 126.6, 128.0, 128.1, 128.5, 140.0, 140.3, 170.3 (2 C) (1 C not detected) ppm. MS (70 eV): *m/z* (%) = 394/390 (1) [$M^+$], 313/311 (1) [$M^+$ − Br], 122 (22) [$M^+$ − $C_3H_6Br$], 107 (68) [$C_7H_6O^+$], 79 (24) [$Br^+$], 51 (10) [$C_4H_3^+$], 43 (100) [$C_2H_3O^+$]. $C_{15}H_{20}Br_2O_2$ (392.1): calcd. C 45.95, H 5.54; found C 47.11, H 5.14.

## Acknowledgments

Financial support was provided by the Deutsche Forschungsgemeinschaft (Grant Ha 1705/8-1 and Schwerpunktprogramm: Peroxidchemie − Mechanistische und Präparative Aspekte des Sauerstofftransfers).

[1] The following abbreviations have been used: acac = acetylacetone monoanion, BPO = bromoperoxidase, CAB = cobalt(II) acetate/acetic acid/bromide, NBS = *N*-bromosuccinimide, TBCD = 2,4,4,6-tetrabromocyclohexa-2,5-dien-1-one, TBHP = *tert*-butyl hydroperoxide. Unless otherwise noted by an appropriate stereodescriptor, all graphics refer to racemic compounds.

[2] W. M. Weigert, W. Merck, H. Offermanns, G. Prescher, G. Schreyer, O. Weiberg, in *Wasserstoffperoxide und seine Derivate, Chemie und Anwendung* (Ed.: W. M. Weigert), Hüthig, Heidelberg, **1978**.

[3] C. W. Jones, *Applications of Hydrogen Peroxide and Derivatives* (Series Ed.: J. H. Clark), RSC Clean Technology Monographs, Cambridge, **1999**.

[4] [4a] B. M. Choudary, T. Someshwar, C. V. Reddy, M. L. Kantam, K. J. Ratnam, L. V. Sivaji, *Appl. Catal. A* **2003**, *251*, 397−409. [4b] I. M. Lazarev, N. A. Nedolya, *Russ. J. Org. Chem.* **2000**, *36*, 1758−1759. [4c] S. Mukhopadhyay, S. Anantha krishnan, S. B. Chandalia, *Org. Proc. Res. Dev.* **1999**, *3*, 451−454.

[5] [5a] W. Partenheimer, *J. Mol. Catal. A* **2003**, *206*, 105−119. [5b] W. Partenheimer, *J. Mol. Catal. A* **2001**, *174*, 29−33. [5c] W. Partenheimer, *Catal. Today* **1995**, *23*, 69−158.

[6] [6a] S. Mukhopadhay, J. K. Mukhopadhyaya, D. E. Ponde, S. Cohen, B. G. S. Kurkalli, *Org. Proc. Res. Dev.* **2000**, *4*, 509−512. [6b] H. Bubbecke, P. Boldt, *Angew. Chem.* **1976**, *88*, 641−642; *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 608. [6c] A. Leulier, *Bull. Soc. Chim. Fr.* **1930**, *47*, 730−737.

[7] [7a] J. Hartung, M. Greb, *Tetrahedron Lett.* **2003**, *44*, 6091−6063. [7b] M. E. Jung, B. T. Fahr, D. C. D'Amico, *J. Org. Chem.* **1998**, *63*, 2982−2987. [7c] E. J. Corey, D.-C. Ha, *Tetrahedron Lett.* **1988**, *29*, 3171−3174. [7d] A. G. González, J. D. Martín, C. Pérez, M. A. Ramírez, F. Ravelo, *Tetrahedron Lett.* **1981**, *22*, 5071−5072.

[8] O. Maas, P. G. Hiebert, *J. Am. Chem. Soc.* **1924**, *46*, 290−308.

[9] M. Srebnik, R. Mechoulam, I. Yona, *J. Chem. Soc., Perkin Trans. 1* **1987**, 1423−1427.

[10] [10a] H. Vilter, *Phytochemistry* **1984**, *23*, 1387−1390. [10b] H. Vilter, *Bot. Mar.* **1983**, *26*, 451−455.

[11] [11a] E. G. M. Vollenbroek, L. H. Simons, J. W. M. P. van Schijndel, P. Barnett, M. Balzar, H. L. Dekker, C. van der Linden, R. Wever, *Biochem. Soc., Trans.* **1995**, *23*, 267−271. [11b] J. W. P. M. van Schijndel, E. G. M. Vollenbroek, R. Wever, *Biochim. Biophys. Acta* **1993**, *1161*, 249−256.

[12] H. Vilter, in *Metal Ions in Biological Systems* (Eds.: H. Siegel, A. Siegel), Marcel Dekker, New York, **1995**, vol. 31, p. 325−362.

[13] A. Butler, J. V. Walker, *Chem. Rev.* **1993**, *93*, 1937−1944.

[14] [14a] A. G. J. Ligtenbarg, R. Hage, B. L. Feringa, *Coord. Chem. Rev.* **2003**, *237*, 89−101. [14b] D. Rehder, *Coord. Chem. Rev.* **1999**, *182*, 297−322. [14c] A. Butler, *Coord. Chem. Rev.* **1999**, *187*, 17−35. [14d] M. Weynand, H.-J. Hecht, M. Kieß, M.-F. Liaud, H. Vilter, D. Schomburg, *J. Mol. Biol.* **1999**, *293*, 595−611. [14e] V. Conte, F. Di Furia, G. Licini, *J. Mol. Catal. A* **1997**, *157*, 335−361. [14f] A. T. Harrison, O. W. Howarth, *J. Chem. Soc., Dalton Trans.* **1985**, 1173−1177.

[15] J. Hartung, M. Greb, *J. Organomet. Chem.* **2002**, *661*, 67−84.

[16] J. Hartung, S. Drees, M. Greb, P. Schmidt, I. Svoboda, H. Fuess, A. Murso, D. Stalke, *Eur. J. Org. Chem.* **2003**, 2388−2408.

[17] [17a] O. Bortolini, C. Chiappe, V. Conte, M. Carraro, *Eur. J. Org. Chem.* **1999**, 3237−3239. [17b] B. J. Hamstra, G. J. Colpas, V. L. Pecoraro, *Inorg. Chem.* **1998**, *37*, 949−959. [17c] A. V. S. Rao, N. S. Islam, T. Ramasarma, *Arch. Biochem. Biophys.* **1997**, *342*, 289−297. [17d] G. J. Colpas, B. J. Hamstra, J. W. Kampf, V. L. Pecoraro, *J. Am. Chem. Soc.* **1994**, *116*, 3627−3628. [17e]

V. Conte, F. Di Furia, S. Moro, *Tetrahedron Lett.* **1994**, *35*, 7429−7432.

[18] [18a] O. Pestrovsky, R. van Eldik, P. Huston, J. H. Espenson, *J. Chem. Soc., Dalton Trans.* **1995**, 133−137. [18b] J. H. Espenson, O. Pestovsky, P. Huston, S. Staudt, *J. Am. Chem. Soc.* **1994**, *116*, 2869−2877. [18c] G. Meister, A. Butler, *Inorg. Chem.* **1994**, *33*, 3269−3275. [18d] M. S. Reynolds, S. J. Morandi, J. W. Raebiger, S. P. Melican, S. P. E. Smith, *Inorg. Chem.* **1994**, *33*, 4977−4984.

[19] Synthesis of Schiff-base ligands **4**. For **4c**, **4e**, **4f** see ref.[16][19a] **4a**: A. D. Westland, M. T. H. Tarafder, *Inorg. Chem.* **1981**, *20*, 3992−3995. [19b] **4e**: A. Saymal, M. R. Maurya, *Ind. J. Chem.* **1986**, *25A*, 1152−1155.

[20] M. J. McKennon, A. I. Meyers, K. Drauz, M. Schwarm, *J. Org. Chem.* **1993**, *58*, 3568−3571.

[21] Preparation of (Schiff base)vanadium(v) complexes. For **5c**, **5f**, **5g** see ref.[16], for **5e** see ref.[19b][21a] **5a**: H. Mimoun, M. Mignard, P. Brechot, L. Saussine, *J. Am. Chem. Soc.* **1986**, *108*, 3711−3718. [21b] M. J. Clague, N. L. Keder, A. Butler, *Inorg. Chem.* **1993**, *32*, 4754−4761.

[22] J. Hartung, M. Hiller, P. Schmidt, *Chem. Eur. J.* **1996**, *2*, 1014−1023.

[23] M. J. Clague, N. L. Keder, A. Butler, *Inorg. Chem.* **1993**, *32*, 4754−4761.

[24] [24a] J.-C. Harmange, B. Figadère, *Tetrahedron: Asymmetry* **1993**, *4*, 1711−1754. [24b] P. A. Bartlett, P. C. Ting, *J. Org. Chem.* **1986**, *51*, 2230−2240.

[25] J. Hartung, R. Kneuer, S. Laug, P. Schmidt, K. Špehar, I. Svoboda, H. Fuess, *Eur. J. Org. Chem.* **2003**, 4033−4052.

[26] T. Gottwald, M. Greb, J. Hartung, *Synlett* **2004**, 65−68.

[27] O. Muraoka, T. Sawada, E. Morimoto, G. Tanabe, *Chem. Pharm. Bull.* **1993**, *41*, 772−774.

[28] [28a] U. Bora, G. Bose, M. K. Chaudhuri, S. S. Dhar, R. Gopinath, A. T. Khan, B. K. Patel, *Org. Lett.* **2000**, *2*, 247−249. [28b] M. K. Chaudhuri, A. T. Khan, B. K. Patel, D. Dey, W. Kharmawophlang, T. R. Lakshmiprabha, G. C. Mandal, *Tetrahedron Lett.* **1998**, *39*, 8163−8166.

[29] K. M. Doxsee, M. Feigel, K. D. Stewart, J. W. Canary, C. B. Knobler, D. J. Cram, *J. Am. Chem. Soc.* **1987**, *109*, 3098−3107.

[30] J. Hartung, M. Hiller, P. Schmidt, *Liebigs Ann.* **1996**, 1425−1436.

[31] K. Mori, M. Komatsu, M. Kido, K. Nakagawa, *Tetrahedron* **1986**, *42*, 523−528.

[32] R. L. Snowden, K. H. Schulte-Elte, *Helv. Chim. Acta* **1981**, *64*, 2193−2202.

[33] J. Hartung, T. M. Kopf, R. Kneuer, P. Schmidt, *C. R. Acad. Sci., Ser. IIc: Chim.* **2001**, 649−666.

[34] J. P. Michael, M. M. Nkwelo, *Tetrahedron* **1990**, *46*, 2549−2560.

[35] J. Hartung, P. Schmidt, *Synlett* **2000**, 367−370.

[36] [36a] K. P. Bryliakov, N. N. Karpyshev, S. A. Fominsky, A. G. Tolstikov, E. P. Talsi, *J. Mol. Catal. A* **2001**, *171*, 73−80. [36b] D. Rehder, *Biological Applications of* $^{51}V$ *NMR Spectroscopy* in *Vanadium in Biological Systems* (Ed.: D. N. Chasteen), Kluwer Academic Publishers, Dordrecht, **1990**, pp. 173−197. [36c] A. T. Harrison, O. W. Howarth, *J. Chem. Soc., Dalton Trans.* **1985**, 1173−1177.

[37] [37a] J. S. Jaswal, A. S. Tracey, *J. Am. Chem. Soc.* **1993**, *115*, 5600−5607. [37b] J. S. Jaswal, A. S. Tracey, *J. Am. Chem. Soc.* **1992**, *114*, 3835−3840. [37c] J. S. Jaswal, A. S. Tracey, *Inorg. Chem.* **1991**, *30*, 3718−3722.

[38] [38a] R. B. Cole (Ed.) *Electrospray Ionisation Mass Spectrometry: Fundamentals, Instrumentation, and Applications*, John Wiley & Sons, New York, **1997**. [38b] M. G. Ikonomou, A. T. Blades, P. Kebarle, *Anal. Chem.* **1991**, *63*, 1989−1998. [38c] R. D. Smith, J. A. Loo, C. G. Edmonds, C. J. Barinaga, H. R. Udseth, *Anal. Chem.* **1990**, *62*, 882−899.

[39] [39a] W. J. Griffiths, A. P. Jonsson, S. Liu, D. K. Rai, Y. Wang, *Biochem. J.* **2001**, *355*, 545−561. [39b] M. Bonchio, O. Bortolini, V. Conte, S. Moro, *Eur. J. Inorg. Chem.* **2001**, 2913−2919. [39c] R. D. Smith, K. J. Light-Wahl, *Biol. Mass Spectrom.* **1993**, *22*, 493−501. [39d] J. B. Fenn, M. Mann, C. K. Meng, S. F. Wong, C. M. Whitehouse, *Science* **1989**, *246*, 64−71.

[40] [40a] B. F. G. Johnson, J. S. McIndoe, *Coord. Chem. Rev.* **2000**, *200−202*, 901−932. [40b] H. Junicke, R. Kluge, D. Steinborn, *J. Inorg. Biochem.* **2000**, *81*, 43−48. [40c] O. Bortolini, M. Carraro, V. Conte, S. Moro, *Eur. J. Inorg. Chem.* **1999**, 1489−1495. [40d] A. Wada, M. Harata, K. Hasegawa, K. Jitsukawa, H. Matsuda, M. Mukai, T. Kitagawa, H. Einaga, *Angew. Chem.* **1998**, *110*, 874−875; *Angew. Chem. Int. Ed.* **1998**, *37*, 798−799. [40e] O. Bortolini, V. Conte, F. DiFuria, S. Moro, *Eur. J. Inorg. Chem.* **1998**, 1193−1197. [40f] J. W. Sam, X.-J. Tang, J. Feisach, *J. Am. Chem. Soc.* **1994**, *116*, 5250−5256. [40g] R. Colton, B. D. James, I. D. Potter, J. C. Traeger, *Inorg. Chem.* **1993**, *32*, 2626−2629.

[41] [41a] D. A. Plattner, *Int. J. Mass Spectrom.* **2001**, *207*, 125−144. [41b] W. Adam, C. Mock-Knoblauch, C. R. Saha-Möller, M. Herderich, *J. Am. Chem. Soc.* **2000**, *122*, 9685−9691. [41c] A. O. Aliprantis, J. W. Canary, *J. Am. Chem. Soc.* **1994**, *116*, 6985−6986. [41d] S. R. Wilson, J. Perez, A. Pasternak, *J. Am. Chem. Soc.* **1993**, *115*, 1994−1997. [41e] S. R. Wilson, Y. Wu, *Organometallics* **1993**, *12*, 1478−1480.

[42] J. Datta, K. K. Kundu, *Ind. J. Chem.* **1990**, *29A*, 210−214.

[43] [43a] E. J. Corey, G. E. Keck, I. Székely, *J. Am. Chem. Soc.* **1977**, *99*, 2006−2008. [43b] E. Demol, P. Enggist, *Helv. Chim. Acta* **1971**, *54*, 456−463.

[44] [44a] I. C. González, C. J. Forsyth, *J. Am. Chem. Soc.* **2000**, *122*, 9099−9109. [44b] J. Suknewitsch, S. Budnitzky, *J. Prakt. Chem.* **1933**, *138*, 18−22. [44c] R. Benedikt, *Ber. Dtsch. Chem. Ges.* **1879**, *12*, 1006−1007.

[45] W. Adam, W. Haas, B. B. Lohray, *J. Am. Chem. Soc.* **1991**, *113*, 6202−6208.

[46] D. V. Deubel, *J. Org. Chem.* **2001**, *66*, 2686−2691.

[47] M. Greb, Diploma Thesis, University Würzburg, **2000**.

[48] [48a] S. Battacharya, T. Gosh, *Trans. Met. Chem.* **2002**, *27*, 89−94. [48b] C. P. Rao, A. Sreedhara, P. V. Rao, M. B. Verghese, K. Rissanen, E. Kolehmainen, N. K. Lokanath, M. A. Sridhar, J. S. Prasad, *J. Chem. Soc., Dalton Trans.* **1998**, 2383−2393. [48c] M. Bashirpoor, H. Schmidt, C. Schulzke, D. Rehder, *Chem. Ber./Receuil* **1997**, *130*, 651−657. [48d] G. Asgedom, A. Sreedhara, J. Kivikoski, J. Valkonen, E. Kolehmainen, C. P. Rao, *Inorg. Chem.* **1996**, *35*, 5674−5683. [48e] V. Vergopoulos, W. Priebsch, M. Fritzsche, D. Rehder, *Inorg. Chem.* **1993**, *32*, 1844−1849. [48f] U. Casellato, P. A. Vigato, R. Graziani, M. Vidali, F. Milani, M. M. Musiani, *Inorg. Chim. Acta* **1982**, *61*, 121−128. [48g] L. J. Theriot, G. O. Carlisle, H. J. Hu, *J. Inorg. Nucl. Chem.* **1969**, *31*, 2841−2844.

[49] N. B. Barhate, A. S. Gajare, R. D. Wakharkar, A. B. Bedekar, *Tetrahedron* **1999**, *55*, 11127−11142.

[50] C. O. Willits, C. Ricciuti, H. B. Knight, D. Swern, *Anal. Chem.* **1952**, *24*, 785−790.

[51] For vanadium(v)-catalyzed sulfoxidations see: [51a] T. S. Smith II, V. L. Pecoraro, *Inorg. Chem.* **2002**, *41*, 6754−6760. [51b] F. van der Felde, I. W. C. E. Arends, R. A. Sheldon, *Top. Catal.* **2000**, *13*, 259−265. [51c] A. H. Vetter, A. Berkessel, *Tetrahedron Lett.* **1998**, *39*, 1741−1744. [51d] C. Bolm, T. K. K. Luong, K. Harms, *Chem. Ber./Receuil* **1997**, *130*, 887−890. [51e] O. Bortolini, F. Di Furia, P. Scrimin, G. Modena, *J. Mol. Catal.* **1980**, *7*, 79−74. [51f] R. Curci, F. Di Furia, T. Testi, G. Modena, *J. Chem. Soc., Perkin Trans. 2* **1974**, 752−757.

[52] D. D. Perrin, W. L. F. Armarego, D. R. Perrin, *Purification of Laboratory Chemicals*, 2nd ed., Pergamon Press, Oxford, **1980**

Received February 3, 2004