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Diastereo- and enantioselective bond activation of alkanols by gaseous metal ions

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Dedicated to Professor Jean-Claude Tabet on the occasion of this 60th birthday

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Abstract

The loss of water from metastable 2-butanol/Mn^+ cations is examined by means of mass spectrometry in conjunction with isotopic labeling. Dehydration of 2-butanol by bare Mn^+ is associated with a significant diasteroselectivity which can be traced back to 1,2-interactions. In extending the approach towards the interaction of stereocenters in two different ligands attached to a metal center, collision-induced dissociation (CID) of mass-selected V(IV) complexes (BINOLate)V(OH)($CH_3CH(OH)R$)$^+$ are investigated, where BINOLate stands for the diolate derived from 1,1′-bi-2-naphthol. For the corresponding complexes of 2-octanol (R = n-C_6H_{13}) and 1-phenylethanol (R = c-C_6H_5), significant differences are found between the fragmentation patterns of the corresponding homochiral *R*,*R*- (or *S*,*S*) and heterochiral *R*,*S*-complexes. In the case of 2-butanol (R = C_2H_5), however, the differential steric demands of the alkyl substitutents of the alkanol are too small such that the CID patterns are identical for the corresponding *R*,*R*- and *R*,*S*-complexes.

Keywords: BINOL; C–H bond activation; Diastereoselectivity; Enantioselectivity; Manganese complexes; Mass spectrometry; Vanadium complexes

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1. Introduction

Over the last decades, mass spectrometric research has demonstrated that many bare and ligated transition metal ions are capable of activating a broad variety of substrates including numerous examples of C–H and C–C bond activations [1]. Even though coordination of a metal cation M^+ by additional ligands L often decreases the reactivity of the corresponding ML^+ complexes in comparison to bare M^+, bond activations can still be accomplished and often display enhanced selectivities [2–5]. As far as stereochemistry is concerned, however, mass spectrometric reports about stereospecific reactions of gaseous ions were mostly limited to relatively rigid systems or polyfunctional molecules [6]. While some approaches using diastereoselective isotopic labeling have revealed significant steric effects in the gas phase [7] and several attempts using chiral reagent gases in chemical ionization have been pursued [8–10], a breakthrough was realized with the application of the kinetic method to stereochemical questions [11–15].

Here, we report an attempt to create a system in which a transition metal ion bearing a chiral ligand reacts with chiral substrates; secondary alkanols are chosen as the latter. To this end, the dehydration of 2-butanol/Mn^+ is probed first by means of regio- and diastereoselective deuterium labeling. Secondly, a cationic vanadium complex with a ligand derived from 1,1′-bi-2-naphthol is used to probe the potential of ligand-induced chiral differentiation between *R*- and *S*-2-alkanols.

2. Experimental details

The reactivity of 2-butanol/Mn^+ was investigated using a modified VG ZAB/HF/AMD four-sector mass spectrometer of BEBE configuration (B stands for magnetic and E for electric sector) which has been previously described [16]. Briefly, the metal complexes were generated by chemical ionization (CI, repeller voltage ca. 0 V) of a mixture of Cp′Mn(CO)$_3$ (Cp′ = methyl cyclopentadienyl) and the 2-butanol of interest. The ions were accelerated to 8 keV

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kinetic energy and mass-selected by means of B(1)/E(1) at a resolution of $m/\Delta m = 2000–3000$. Unimolecular fragmentations of metastable ions (MI) occurring in the field-free region preceding B(2) were recorded by scanning this sector; the last sector E(2) was not used in this study. The H_2O/HDO ratios given below are averages of several independent measurements with a standard deviation of ±1 for the intensities normalized to $\Sigma = 100$.

The fragmentation behavior of chiral vanadium complexes with 2-alkanols was investigated with a commercial VG BIO-Q mass spectrometer as described elsewhere [17]. In brief, the VG BIO-Q consists of an electrospray ionization (ESI) source combined with a tandem mass spectrometer of QHQ configuration (Q stands for quadrupole and H for hexapole). For the present experiments, approximately 0.1 ml of the chiral alcohol was added to approximately 1 ml of a millimolar solution of BINOL and either $OVSO_4$ or VCl_3 in methanol/water (1:1); the VCl_3 sample was partially hydrolyzed and might contain some V(IV). These solutions were introduced through a stainless steel capillary into the ESI source via a syringe pump (5 μl/min). Nitrogen was used as nebulizer and drying gas at a source temperature of 90 °C. Optimal yields of the desired complexes were achieved by adjusting the cone voltage (U_c) to about 40 V. For collision-induced dissociation (CID) at low collision energies, the ions of interest were mass-selected using Q1, interacted with xenon as a collision gas in the hexapole H under single-collision conditions at variable collision energies ($E_{lab} = 0–10$ eV), while Q2 was scanned to monitor the ionic products. As pointed out previously, the VG-BIO-Q does not allow one to directly extract quantitative threshold information from CID experiments due to several limitations of the commercial instrument [17]. Even at $E_{lab} = 0$ eV, for example, non-negligible ion decay is observed which is attributed to collision gas being present not only in the hexapole, but also in the focusing regions between the mass analyzers. Nevertheless, the energy dependence of the CID fragments can be approximated by sigmoid functions of the type $I_i(E_{CM}) = (BR_i/(1 + e^{(E_{1/2}-E_{CM})b})$ using a least-square criterion [18]; for the parent ion M: $I_M(E_{CM}) = [1 - \Sigma(BR_i/(1 + e^{(E_{1/2,i}-E_{CM})b_i})]$ Here, BR_i stands for the branching ratio of a particular product ion ($\Sigma BR_i = 1$), $E_{1/2}$ is the energy at which the sigmoid function has reached half of its maximum, E_{CM} is the collision energy in the center-of-mass frame ($E_{CM} = (m_T/(m_T + m_I))E_{lab}$, where m_T and m_I stand for the masses of the collision gas and the ion, respectively), and b describes the rise of the sigmoid curve. In consecutive dissociations, all secondary product ions were summed to the primary fragment. Further, non-negligible ion decay at $E_{lab} = 0$ eV as well as some fraction of non-fragmenting parent ions at large collision energies were acknowledged by means of scaling and normalization. This empirical, yet physically reasonable approach is able to reproduce the measured ion yields quite well. It is obvious, however, that the term $E_{1/2}$ used in the exponent does not correspond to the intrinsic appearance energies of the fragmentation of interest, not to speak of the corresponding thermochemical thresholds at 0 K. The phenomenological threshold energies given below were derived from linear extrapolations of the rise of the sigmoid curves at $E_{1/2}$ to the base line. In the present case, our focus is whether or not any differences for enantiomeric complexes occur. Therefore, we refrain from a detailed analysis of most threshold behaviors and treat the observed ion abundances in a more pragmatic manner aimed at unraveling the occurrence of any stereochemical effects.

The isotopologs of 2-butanols were prepared as racemic mixtures using standard labeling procedures. Briefly, **1a** was made by reaction of CD_3MgI with propanal followed by hydrolysis with concentrated Na_2SO_4 solution, **1b** and **1c** accordingly from the corresponding ethyl magnesium bromides and acetaldehyde, **1d** and **1e** by reduction of *Z*- and *E*-2-butene oxide with $LiAlD_4$, and **1f** by treatment of $CH_3CH(OLi)CH_2CH_3$ with D_2O. The chiral 2-pentanols were prepared by Cu(I) catalyzed addition of the corresponding ethyl Grignard compounds to *R*- and *S*-propene oxide. All other compounds were used as purchased.

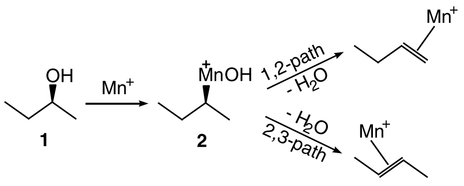
3. Unimolecular decay of 2-butanol/Mn^+ complexes

Before addressing the reactions of chiral metal complexes with 2-alkanols, let us consider the dehydration of 2-butanol (**1**) by the bare Mn^+ cation for illustrating our mass spectrometric approach to the investigation of stereochemical effects [19]. 2-Butanol is chosen as a model because it allows for a stereochemical distinction at a minimal size of the system. The choice of manganese as the metal is due to its relatively poor reactivity in particular with respect to C–H and C–C bond activations when compared to other transition metal cations [1,20]. Therefore, a selective activation of the C–OH bond appears likely to occur, followed by hydrogen transfer from the remaining alkyl backbone and subsequent loss of neutral water concomitant with formation of a butene/Mn^+ complex (reaction 1). Metal ions for which C–H and C–C bond activations are more facile might instead give rise to extensive H/D exchange processes as well as skeletal rearrangements, thereby complicating the analysis of the labeling data with respect to stereochemical effects.

$$Mn^+ + CH_3CH(OH)CH_2CH_3 \rightarrow Mn(C_4H_8)^+ + H_2O \quad (1)$$

An obvious initial aspect concerns the regioselectivity of reaction (1). Thus, 1,2-elimination of water leads to 1-butene/Mn^+, 2,3-elimination affords *E*- or Z-2-butene/Mn^+ (Scheme 1), and more complex reactions might occur as well. Next, possible stereochemical effects in the course of reaction (1) are investigated. To this end, the fragmentation patterns of complexes of Mn^+ with several labeled 2-butanols are probed by mass spectrometric means.

Metastable **1**/Mn^+ undergoes three unimolecular dissociations leading to loss of water as the major pathway along with minor routes associated with the eliminations of butene



Scheme 1.

Table 1
Losses of H_2O and HDO from metastable complexes of labeled 2-butanols with Mn^+ cations[a,b]

Substrate		H_2O	HDO
$CH_3CH(OH)CH_2CH_3$	**1**	100	
$CD_3CH(OH)CH_2CH_3$	**1a**	85	15
$CH_3CH(OH)CD_2CH_3$	**1b**	32	68
$CH_3CH(OH)CH_2CD_3$	**1c**	98	2
syn-$CH_3CH(OH)CHDCH_3$	**1d**	67	33
anti-$CH_3CH(OH)CHDCH_3$	**1e**	75	25
$CH_3CH(OD)CH_2CH_3$	**1f**	<2[c]	>98[c]

[a] Normalized to $\Sigma = 100$ for the dehydration channels; loss of D_2O is <1 in all cases.

[b] Other reactions are losses of butene and loss of the entire butanol ligand. For the unlabeled ion the branching ratio for the eliminations of H_2O, C_4H_8, and C_4H_9OH is 65:25:10.

[c] Limits derived from interference of **1f**/Mn^+ by ^{13}C-**1**/Mn^+ due to H/D exchange of **1f** with residual protons present in the inlet system of the mass spectrometer.

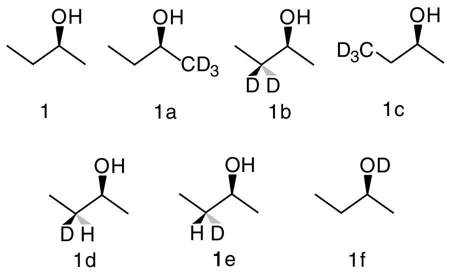


Chart 1.

and the entire alkanol ligand, thereby affording $Mn(H_2O)^+$ and Mn^+, respectively. Here, we restrict the analysis to dehydration according to reaction (1). Table 1 lists the branching of H_2O and HDO losses from various labeled derivatives (Chart 1)[1] from which the following conclusions can be drawn. (i) Almost exclusive loss of HDO from **1f**/Mn^+ and the absence of D_2O loss for all complexes demonstrate that the hydroxy group of the alkanol remains intact during the reaction. Thus, only the origin of the second hydrogen atom in the water molecule lost remains to be clarified. (ii) As shown by the significant amount of HDO from **1a**/Mn^+ and **1b**/Mn^+, this second hydrogen atom is preferentially delivered from the 1- and 3-positions. (iii) The contribution from the 4-position can almost be neglected. In comparison with other transition metal cations with alkanols [21–24], the dehydration of **1**/Mn^+ proceeds quite selectively whereas most other metals induce extensive H/D exchange reactions.

In order to probe the operation of a stereochemical effect (SE) in the dehydration of **1**/Mn^+ by mass spectrometric means, diastereoselective isotopic labeling is applied, which allows the translation of stereochemical properties into mass differences [7,25–31]. As a consequence of deuteration, however, the experimental branching ratios will not only depend on SE, but also on the kinetic isotope effects (KIEs) associated with dehydration. Moreover, inspection of the data in Table 1 indicates a competition between 1,2- and 2,3-elimination of water in **1**/Mn^+. A quantitative analysis needs to acknowledge these effects also including their couplings because the competing routes may affect the H_2O/HDO ratios due to the operation of isotopically sensitive branching [32–34]. Specifically, any channel associated with a significant KIE due to deuteration of a certain position will be diminished by the competing channels. This is qualitatively reflected in the experimental data, in that the loss of HDO from **1a**/Mn^+ implies 15% of 1,2-elimination, whereas the elimination of H_2O from **1b**/Mn^+ amounts to more than twice that figure. Provided a sufficient set of labeled substrates is available, a phenomenological kinetic approach can resolve the situation. Here, a simple kinetic modeling with three basic assumptions is applied [35]: (i) the regioselectivity of dehydration is described by the rate constants $k_1 - k_4$ with $\Sigma k_i = 1$, where the subscripts stand for the position in the alkyl backbone from which the H(D) atom is delivered, (ii) a common KIE is attributed to all HDO losses which appears as a reasonable approximation based on the results obtained for metastable propanol/Fe^+ complexes [23,24], and finally, (iii) 2,3-dehydration of the diastereomeric complexes **1d**/Mn^+ and **1e**/Mn^+ is allowed to bear an SE. Accordingly, Eqs. (2a)–(2e) are obtained.

$$I_{H_2O} : I_{HDO}(\mathbf{1a}/Mn^+) = (k_2 + k_3 + k_4) : (k_1/\mathrm{KIE}) \tag{2a}$$

$$I_{H_2O} : I_{HDO}(\mathbf{1b}/Mn^+) = (k_1 + k_2 + k_4) : (k_3/\mathrm{KIE}) \tag{2b}$$

$$I_{H_2O} : I_{HDO}(\mathbf{1c}/Mn^+) = (k_1 + k_2 + k_3) : (k_4/\mathrm{KIE}) \tag{2c}$$

$$I_{H_2O} : I_{HDO}(\mathbf{1d}/Mn^+) = \left(k_1 + k_2 + \tfrac{1}{2}k_3/\mathrm{SE} + k_4\right) : \left(\tfrac{1}{2}k_3/\mathrm{KIE}\right) \tag{2d}$$

$$I_{H_2O} : I_{HDO}(\mathbf{1e}/Mn^+) = \left(k_1 + k_2 + \tfrac{1}{2}k_3 + k_4\right) : \left(\tfrac{1}{2}k_3/\mathrm{KIE}/\mathrm{SE}\right) \tag{2e}$$

With respect to the pair of diastereomers **1d** and **1e**, it is important to note that the KIE and the SE accumulate for one of the two diastereomers while they attenuate each other for the second one. A differentiation of the KIEs associated with the transfer of the diastereotopic H(D) atoms is not required in Eqs. (2d) and (2e) because any difference of these KIEs would itself be caused by a stereochemical effect and is thus already included in the parameter SE.

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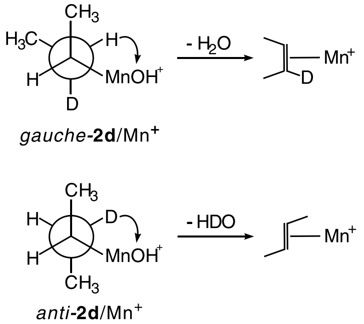
[1] Because the metal center is achiral, only diastereoselectivity can be probed. Accordingly, racemic mixtures were used. For the sake of simplicity, however, only one set of enantiomers is shown in Chart 1.



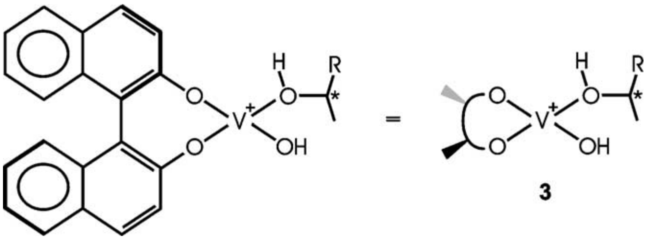
Scheme 2.

Eqs. (2a)–(2c) provide information about the branching ratios and the KIE whereas only (2d) and (2e) also comprise the SE. Within the experimental error margins, an excellent match of experimental and modeled data is obtained for $k_1 = 0.21 \pm 0.02$, $k_2 = 0.00 \pm 0.01$, $k_3 = 0.76 \pm 0.02$, and $k_4 = 0.03 \pm 0.01$, SE $= 1.13 \pm 0.04$, and KIE $= 1.51 \pm 0.07$. Hence, the 2,3-dehydration of 2-butanol/Mn^+ is associated with a small, but clearly significant diastereoselectivity. The observed diastereoselectivity can be explained by a consideration of the corresponding Newman projections of the putative insertion intermediate 2 (Scheme 2). Thus, *syn*-elimination of H_2O from *gauche*-**2d** is disfavored by both *gauche* interactions and formation of the less stable *Z*-butene/Mn^+. Instead, loss of HDO from *anti*-**2d** involves a KIE, but lacks *gauche* interactions and can lead to *E*-butene/Mn^+.

A key aspect of this kind of analysis is that the explicit inclusion of various reaction pathways which proceed in competition is essential for the evaluation of an accurate SE. Neglect of the competing reactions would instead cause an overestimation of the SE. A mere comparison of the H_2O/HDO ratios of **1d**/Mn^+ and **1e**/Mn^+, for example, might be used to extract SE $= (75:25)/(67:33) \approx 1.5$)[2], whereas the modeling reveals a significantly smaller effect. We note in passing that significant SEs have also been observed in the metal-mediated C–H bond activations of some alkanediols with larger backbones [33,34].

4. Collision-induced dissociation of chiral alkanol/V(IV) complexes

In the above example, the diastereoselectivity of a metal-induced reaction is probed which involves adjacent stereocenters within the substrate. Next, we consider reactions in which a stereochemical constraint in one ligand affects the activation of another ligand. Thus, in addition to a primary process (e.g., a bond activation), a secondary interaction giving rise to a stereodiscrimination is searched



Scheme 3.

for in the case of metal-mediated reactions of 2-alkanols. As a chiral precursor, we have chosen 1,1′-bi-2-naphthol (BINOL). In addition, the metal is changed from manganese to vanadium because this early transition metal is more oxophilic and may therefore enable a more rigid coordination to the chiral ligand.

Starting from millimolar solutions of *R*- or *S*-BINOL and $OVSO_4$ or VCl_3 in methanol/water (1:1), complexes having a (BINOLate)V^+ core (denoted as $[V^*]^+$ further below) can be generated by means of electrospray ionization (ESI); here, BINOLate stands for the diolate derived from 1,1′-bi-2-naphthol. Under relatively mild conditions of ionization, the complex $[V^*](OH)(CH_3OH)^+$ is obtained in reasonable yield. Addition of a secondary alkanol, $CH_3CH(OH)R$, to the methanol/water mixture then also leads to the corresponding $[V^*](OH)(CH_3CH(OH)R)^+$ ions simplified as structure **3** in Scheme 3. The ions of interest are then mass selected by means of Q1, subjected to CID with xenon in the hexapole at variable collision energies (E_{lab}), and the products are analyzed using Q2. Note further that only one of both partners needs to be varied, e.g., reaction of a chiral metal complex with the *R*- and *S*-enantiomers of the substrate or vice versa, because mass spectrometric experiments are not sensitive to the absolute configuration [15].

$$[V^*](OH)(CH_3OH)^+ \rightarrow [V^*](OCH_3)^+ + H_2O \qquad (3a)$$

$$[V^*](OH)(CH_3OH)^+ \rightarrow [V^*](OH)^+ + CH_3OH \qquad (3b)$$

Before addressing the complexes of some chiral 2-alkanols, the CID spectra of the corresponding complexes of methanol and 2-propanol are discussed. CID of mass-selected $[V^*](OH)(CH_3OH)^+$ at variable collision energies between $E_{lab} = 0$ and 10 eV leads to loss of neutral water (reaction 3a) as a minor route and expulsion of the entire methanol ligand (reaction 3b) as the major one. A closer inspection of the branching between reactions (3a) and (3b) is quite instructive as far as ion structure is concerned. Loss of water already occurs at low collision energies and even at E_{lab} formally set to zero. However, this channel does not gain much in abundance at elevated collision energies and even depletes at $E_{CM} > 2$ eV. In marked contrast, collision-induced loss of methanol according to reaction (3b) shows a behavior typical for an endothermic ligand loss with an apparent threshold of about 0.7 eV in the center-of-mass frame (Fig. 1). Accordingly,

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[2] More correctly, the square root should be considered, i.e., SE $= [(75:25)/(67:33)]^{0.5} = 1.22$; however, this value also exceeds the one derived from the kinetic modeling because competition is not taken into account.

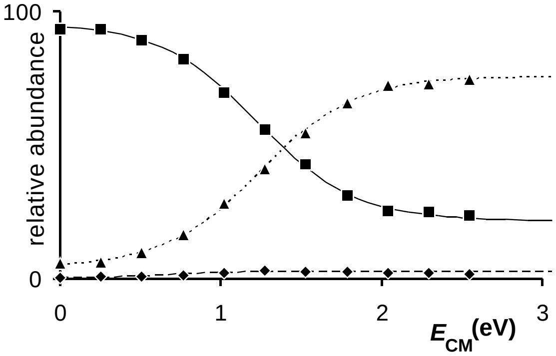
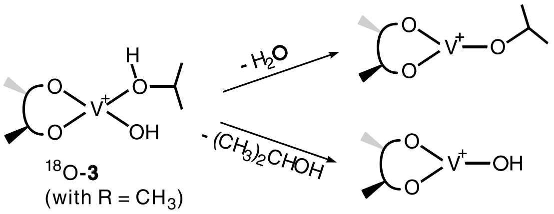


Fig. 1. CID of mass-selected $[(BINOLate)V(OH)(CH_3OH)]^+$ at variable collision energies $E_{lab} = 0–10\,eV$ given in the center-of-mass frame ($E_{CM} \approx 0.25E_{lab}$): Parent ion (■), loss of CH_3OH (▲) and loss of H_2O (◆). The lines connecting the experimental data points represent a modeling of the ion yields by sigmoid functions with the parameters BR $= 0.974$, $E_{1/2} = 1.25\,eV$, and $b = 3.4\,eV^{-1}$ for loss of CH_3OH and BR $= 0.024$, $E_{1/2} = 0.74\,eV$, and $b = 9.4\,eV^{-1}$ for loss of H_2O, respectively. Note that the sigmoid function is unable to describe the depletion of the H_2O loss channel for $E_{CM} > 2\,eV$.

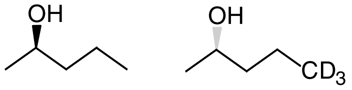
it is concluded that reaction (3a) is thermochemically favored, but kinetically hindered compared to reaction (3b). This reasoning is fully consistent with the suggested structure $[V^*](OH)(CH_3OH)^+$, whereas the opposite behavior is expected for the tautomeric complex $[V^*](OCH_3)(H_2O)^+$. Further, the anticipated structure $[V^*](OCH_3)^+$ for the ionic product of reaction (3a) is supported by the loss of formaldehyde inter alia observed upon CID of this ion which is considered characteristic for transition metal methoxides [36].

When switching from methanol to larger alkanols, loss of water from complexes of structure **3** can either involve metal-alkoxide formation in analogy to reaction (3a) or arise from an internal dehydration of the alkanol ligand like in the 2-butanol/Mn^+ system described above. This aspect can be tackled by means of an ^{18}O labeling experiment. Thus, addition of 50 μl of $H_2{}^{18}O$ to a solution of BINOL and VCl_3 in methanol with 10% 2-propanol inter alia affords an ion with $m/z = 414$ upon ESI, formally corresponding to the putative complex $[V^*](^{18}OH)(CH_3CH(OH)CH_3)^+$. CID of mass-selected $m/z = 414$ leads to losses of water, propene, and propanol in proportions of 45:<1:55 and 10:<1:90 at $E_{lab} = 5$ and 10 eV, respectively. As far as the labeling distributions are concerned, loss of $H_2{}^{18}O$ prevails over that of $H_2{}^{16}O$ (ratios: ca. 10:1 at $E_{lab} = 5\,eV$ and ca. 12:1 at $E_{lab} = 10\,eV$), whereas elimination of $C_3H_7{}^{16}OH$ prevails over that of $C_3H_7{}^{18}OH$ (ratios: ca. 12:1 at $E_{lab} = 5\,eV$ and ca. 17:1 at $E_{lab} = 10\,eV$). Based on these results, it is concluded that dehydration preferentially involves the hydroxy group attached to the vanadium center and the hydrogen atom of the alkanol's hydroxy group, and loss of the propanol ligand occurs without substantial $^{16}O/^{18}O$ exchange (Scheme 4). Small fractions of formal $^{16}O/^{18}O$ exchanges can be attributed to more complex pathways (see below).

Next, the reactions of the enantiomers of some chiral 2-alkanols are considered (Table 2). In the case of 2-butanol, no significant differences between the homochiral *R*,*R*- and the heterochiral *R*,*S*-complexes (**3** with R = C_2H_5) are observed. Obviously, the differential steric demands of the alkyl substitutents in 2-butanol, i.e., methyl versus ethyl, are too small. Similarly, no significant SEs occur for the enantiomeric 2-pentanols (losses of H_2O and 2-pentanol, data not shown). In this specific case, the availability of some labeled enantiomers also allows to probe the SE associated with the binding of 2-pentanol to the $[V^*]^+$ core. Thus, ESI of *R*-BINOL with a mixture of *R*-**4** and *S*-**4a** (Chart 2) inter alia affords the complexes $[V^*]$(*R*-**4**-H)(*S*-**4a**)$^+$ and $[V^*]$(*R*-**4**)(*S*-**4a**-H)$^+$ (both $m/z = 513$), which formally correspond to complexes of type **3** in which the free hydroxy group is replaced by a (chiral) 2-pentoxy ligand. CID of mass-selected $m/z = 513$ at $E_{lab} = 5\,eV$ leads to losses of *R*-**4** and *S*-**4a** in a ratio of $k_{R\text{-}\mathbf{4}}/k_{S\text{-}\mathbf{4a}} = 1.22 \pm 0.02$.[3] It would be premature, however, to deduce a stereochemical effect from this observation because a KIE might operate as well. Considering that the labeled C(5) position presumably does not participate in the ligand loss (see above), only a small, secondary KIE is to be expected. However, the SE associated with differentiation of the two enantiomers may be of similar magnitude. In fact, control experiments with a racemic mixture of **4** and **4a** leads to a ratio of $k_{\mathbf{4}}/k_{\mathbf{4a}} = 1.42 \pm 0.02$ upon CID. Hence, the KIE even exceeds the SE in this case. Nevertheless, comparison of the ratios for the two enantiomers and the racemic mixture leads to a significant SE $= k_{R\text{-}\mathbf{4}}/k_{S\text{-}\mathbf{4}} = 0.86 \pm 0.03$ for 2-pentanol. Thus, formation of the homochiral complex (*R*-BINOLate)V(*R*-**4**-H)$^+$ is slightly preferred compared to the heterochiral complex (*R*-BINOLate)V(*S*-**4**-H)$^+$ [37]. To a first approximation, we may assume that the same preference for the homochiral complex holds true for the complexes having structure **3**.



Scheme 4.



R-**4** *S*-**4a**

Chart 2.

Further enlargement of the substituent R does indeed also lead to significant SEs in the CID spectra of

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[3] Chiral discrimination of the adduct formation occurring in solution can be neglected because it would in itself be due to an SE and is thus already included in this phenomenological parameter.

Table 2
Neutral fragments[a] lost upon CID of mass-selected (BINOLate)V(OH)(alkanol)$^+$ complexes at variable collision energies (E_{lab} in eV, collision gas: xenon)

Alkanol		E_{lab}	x_{frag}[b]	H_2O	Alkene	Alkanol	$[V^*](OH)_2$
R-$CH_3CH(OH)C_2H_5$[c]	*R*-BINOL	0	19	54		46	
		2	24	61		39	
		5	40	43		57	
		7	66	35		65	
		10	86	16		84	
S-$CH_3CH(OH)C_2H_5$[c]	*R*-BINOL	0	16	55		45	
		2	20	61		39	
		5	41	42		58	
		7	62	38		62	
		10	84	18		82	
R-$CH_3CH(OH)C_6H_{13}$	*R*-BINOL	0	10	48	6	46	
		2	13	51	5	44	
		5	23	51	3	46	
		7	36	35	2	63	
		10	63	20	1	79	
S-$CH_3CH(OH)C_6H_{13}$	*R*-BINOL	0	13	43	18	39	
		2	16	42	14	44	
		5	26	46	7	47	
		7	35	38	6	56	
		10	67	21	3	76	
S-$CH_3CH(OH)C_6H_5$[d]	*S*-BINOL	0	16	46	16	26	5
		2	21	47	14	25	8
		5	52	39	13	30	13
		7	70	33	12	42	11
		10	79	15	7	63	12
	R-BINOL	0	14	48	12	24	10
		2	18	46	14	23	12
		5	49	38	13	24	21
		7	68	29	8	35	25
		10	76	14	6	55	22

[a] Normalized to $\Sigma = 100$.
[b] Fraction of dissociated ions given as $x_{frag} = \Sigma I_{frag}/\Sigma I_i$.
[c] Loss of alkene is observed, but <1 at all collision energies.
[d] Missing fraction to $\Sigma = 100$ is due to loss of two water molecules.

the corresponding complexes of 2-octanol (**3** with R $=$ *n*-C_6H_{13}) and 1-phenylethanol (**3** with R $=$ *c*-C_6H_5). The major difference between the two diastereomers in the case of 2-octanol is associated with the collision-induced loss of octene which is significantly more pronounced for the heterochiral *S*,*R*-complex (Table 2). The ratio for the loss of neutral alkene is 0.36 ± 0.05 as an average over all five collision energies examined ($E_{lab} = 0$–10 eV). As pointed out for the 2-butanol/Mn$^+$ system, a simple consideration of branching ratios is insufficient for a more concise analysis because any hindrance of a particular channel inevitably favors the competing ones. Hence, the branching ratios were modeled by a kinetic scheme in analogy to the analysis of 2-butanol/Mn$^+$ described above. To this end, the relative rate constants of the three competing channels of the 2-octanol complex 3 (R $=$ *n*-C_6H_{13}), losses of water, alkene, and alkanol, are described by the averages of the *R*,*R*- and *R*,*S*-complexes at each collision energy ($k_{i,\mathrm{rac}}$) while being weighted by additional steric effects operative in each channel as expressed in Eqs. (4a)–(4c) with $\mathrm{SE} = k_{RR}/k_{\mathrm{rac}} = k_{\mathrm{rac}}/k_{RS}$ and $\Sigma k_i = 1$.

$$k_{H_2O} = k_{H_2O,\mathrm{rac}}\mathrm{SE}_{H_2O} \tag{4a}$$

$$k_{\mathrm{alkene}} = k_{\mathrm{alkene,rac}}\mathrm{SE}_{\mathrm{alkene}} \tag{4b}$$

$$k_{\mathrm{alkanol}} = k_{\mathrm{alkanol,rac}}\mathrm{SE}_{\mathrm{alkanol}} \tag{4c}$$

In this approach, we deliberately apply energy-independent SEs in order to acknowledge the experimental circumstances. Thus, first principle considerations would on the one hand suggest that the SEs are largest at low collision energies which are therefore considered most sensitive to stereochemical effects. On the other hand, CID is less efficient at low energies such that the determination of the fragment ion abundances is associated with increased errors. Assumption of energy-independent SEs therefore arises as a first-order compromise between fundamental considerations and experimental performance.

Within the experimental error margins, the analysis of the 2-octanol system leads to $SE_{H_2O} = 1.00 \pm 0.15$, $SE_{alkene} = 0.6 \pm 0.3$, and $SE_{alkanol} = 1.01 \pm 0.15$ for the data given in Table 2, where the relatively large error bar of SE_{alkene} arises from the weakness of this channel. It is important to point out that the kinetic analysis reveals that only loss of octene, which certainly involves activation of the chiral center of the alkanol ligand, bears a significant SE. Instead, inspection of the mere branching ratios might also imply SEs in the other channels (e.g., enhanced loss of H_2O from the *R*,*R* complex), but these turn out to be caused by mere competition.

$$[V^*](OH)(CH_3CH(OH)C_6H_5)^+ \rightarrow C_8H_9{}^+ + [V^*](OH)_2 \quad (5)$$

In the case of the corresponding complex of 1-phenylethanol (**3** with R = c-C_6H_5), a forth channel is observed which leads to the formation of a $C_8H_9{}^+$ cation, probably 1-phenylethylium [38], concomitant with loss of a neutral V(IV) fragment (reaction 5). The *S*,*S*/*S*,*R* ratio for the formation of $C_8H_9{}^+$ is 0.63 ± 0.04 at $E_{lab} = 5$ eV (average of three experiments) and 0.56 ± 0.1 as the average over all five collision energies ($E_{lab} = 0$–10 eV). The corresponding kinetic modeling of the experimental product distributions in analogy to Eqs. (4a)–(4c) yields $SE_{H_2O} = 0.95 \pm 0.25$, $SE_{alkene} = 1.01 \pm 0.25$, $SE_{alkanol} = 1.00 \pm 0.15$, and $SE_{C_8H_9{}^+} = 0.70 \pm 0.15$. Hence, only reaction (5) is associated with a significant SE, again with a preferential activation of the chiral center of the alkanol in the case of the heterochiral complex. With respect to the ^{18}O labeling study with 2-propanol (see above), we mention that the occurrence of reaction (5) also provides a rationale for the minor amount of $^{16}O/^{18}O$ exchange described above. Thus, even though liberation of a free carbocation does not occur in the case of 2-propanol (**3** with R = CH_3), an ion/neutral complex of the type $C_3H_7^+[V^*](OH)_2$ might serve as a transient and thus allow for an equilibration of both oxygen atoms.

Finally, we note that the experiments also reveal a limitation of the pursued ESI approach in that the yields of **3** are quite poor for R = c-C_6H_5, although still sufficient for CID. The simple reason is that the ESI mass spectrum is dominated by cationic species derived from 1-phenylethanol rather than vanadium-containing species. For similar reasons, attempts to generate complexes of the $[V^*]^+$ core with more promising chiral substrates such as amines, aminoalkanols, or alkane diols were so far unsuccessful.

5. Conclusion

The experimental findings demonstrate that the BINOLate ligand is able to induce differential reactivity of enantiomeric 2-alkanols attached to a cationic vanadium center at least when the difference between the substituents is large enough. Hence, the vanadium complexes accessible upon ESI show stereochemical effects across a coordinated transition metal with a considerable distance between the chiral centers. For several reasons, however, a clear-cut mechanistic rationale for the direction of the SE cannot be provided easily. Among others, a major obstacle is the lack of a reaction for which the operation of an SE can a priori be excluded and which could therefore serve as a reference. To a first approximation, however, the apparent threshold of about 0.7 eV for the loss of methanol from $[V^*](OH)(CH_3OH)^+$ in conjunction with the small SE for the binding of the enantiomeric 2-pentanols to the [V*] core (see above) implies that the difference of the binding energies of *R*- and *S*-enantiomers is much smaller than the total binding energy of the alkanol ligand. Accordingly, loss of ROH may be used as an approximate reference. On the basis of this assumption, it appears that the heterochiral complexes of 2-octanol and 1-phenylethanol are more easily activated at the chiral center than their homochiral counterparts.

In a more general perspective, there exist two extreme options for a stereoselective bond activation of a chiral substrate by a chiral metal complex, when the energy demand of the transition structure (TS) associated with bond activation is in the energetic vicinity of the bond dissociation energies (BDE) of the ligand. Either the BDEs of the hetero- and homochiral complexes differ more than the corresponding activation barriers (Fig. 2, case a) or the BDEs are similar whereas the diastereomeric TSs differ significantly (Fig. 2, case b). In the first case, the more weakly bound enantiomer shows less rearrangement via the TS than the more strongly bound one, while the opposite applies for the second case. Accordingly, in case (a) the directions of the SEs associated with ligand binding and bond activation are the same (more activation of the more strongly bound ligand) whereas these

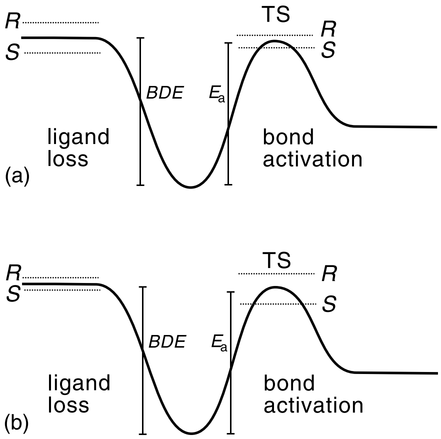

Fig. 2. Schematic potential-energy surface of a chiral metal complex ligated with either an *R*- or *S*-enantiomer of a substrate (*R* and *S* are chosen arbitrarily). The left hand side describes loss of the substrates, whereas the right hand side designates some kind of bond activation associated with a transition structure (TS). The full line stands for a hypothetical achiral complex (SE = 1), whereas the dotted lines show the changes of both channels due to stereochemical effects (SE ≠ 1). For a distinction between cases (a) and (b), see text.

directions differ in case (b) (more activation of the more weakly bound ligand).

Let us finally classify the reactions observed for the $[V^*]^+$ system according to these criteria. To a first approximation, the results for the enantiomeric 2-pentanol complexes suggest that the homochiral complexes are slightly more stable than the heterochiral ones. Instead, activation of the chiral centers in 2-octanol and 1-phenylethanol appears to be more pronounced for the heterochrial complexes. Accordingly, we may assign the complexes of type **3** belong to case b of Fig. 2 which is certainly the more interesting one in terms of asymmetric synthesis. Notwithstanding, it is quite obvious that the SEs observed in the present systems are quite small and further efforts are required.

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