Alcohol-Activated Vanadium-Containing Polyoxometalate Complexes in Homogeneous Glucose Oxidation Identified with $^{51}$V-NMR and EPR Spectroscopy

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Alcoholic solvents, especially methanol, show an activating effect for heteropolyacids in homogenously catalysed glucose transformation reactions. In detail, they manipulate the polyoxometalate-based catalyst in a way that thermodynamically favoured total oxidation to CO$_2$ can be completely suppressed. This allows a nearly 100% carbon efficiency in the transformation reaction of glucose to methyl formate in methanolic solution at mild reaction conditions of 90 °C and 20 bar oxygen pressure. By using powerful spectroscopic tools like $^{51}$V-NMR and continuous wave EPR we could unambiguously prove that the vanadate-methanol-complex($\text{VO(OMe)}_n$) is responsible for the selectivity shift in methanolic solution compared to the aqueous reference system.

Introduction

Biomass is a promising feedstock for the production of high-value chemicals with high oxygen content.$^{[1]}$ Consequently, the interest in cost-effective biomass conversion is growing in recent years.$^{[2,3]}$ Lignocellulosic biomass as the most abundant class of biogenic materials typically contains more than 50 wt% sugars that can be upgraded to valuable platform chemicals. Lignocellulosic biomass consists of three main components: lignin, hemicellulose and cellulose.$^{[4,5]}$ The aromatic lignin has been traditionally used for heat and power purposes through combustion in the pulp and paper industry.$^{[6]}$ Hemicellulose mainly contains C$_6$ sugars like xylose or arabinose having important applications for biofuel production (e.g. bioethanol) and for the generation of valuable chemical intermediates (e.g. furfural).$^{[7]}$ Cellulose is considered as one of the most abundant biopolymers on earth comprising linear β(1,4) glucose C$_6$-chain links. Therefore, glucose is often used as a model substrate for cellulose.$^{[8]}$ Furthermore, the latter can be converted into valuable products such as biofuels and platform chemicals like 5-Hydroxymethylfurfural (5-HMF), levulinic acid (LevA) or formic acid (FA).$^{[9,10]}$

The reaction sequence for valorisation of lignocellulose starts with the fractionation of the main components followed by acid-catalysed hydrolysis of cellulose and hemicellulose into water-soluble monosaccharides such as glucose, fructose, or xylose and the subsequent oxidative cleavage of C–C bonds in monosaccharides into low-molecular carboxylic acids like formic acid,$^{[10]}$ acetic acid$^{[11]}$ or lactic acid.$^{[12]}$ Over-oxidation of the monosaccharides and intermediates results in the thermodynamically favoured complete combustion to carbon dioxide and water.$^{[13]}$

In general, it is a big challenge to convert organic carbon present in biomass into valuable compounds with good selectivity and high yields.$^{[14]}$

The required oxidative carbon-carbon bond cleavage by using molecular oxygen (O$_2$) in polar media can be accomplished by several metal catalysts.$^{[15]}$ In particular, V-containing catalysts such as polyoxometalates (POMs)$^{[16,17,10]}$ and simple vanadium precursors such as NaVO$_3$ from or VO$_2$ can effectively catalyse this transformation in aqueous solution. POMs provide strong Bronsted acidity, high proton mobility, fast multi-electron transfer, high solubility in various solvents, and excellent resistance against hydrolytic or oxidative degradations.$^{[17,18,20,21]}$ We could demonstrate, for example, that the Keggin-type POM ($\text{H}_3\text{PV}_7\text{Mo}_7\text{O}_{40}$ (HPA-5)) converts watersoluble carbohydrates to formic acid as the sole product in the liquid phase at 90 °C using 20 bar oxygen.$^{[18]}$ This process is named OxFA process$^{[9,22,23,24]}$ However, the classical OxFA process in aqueous solution suffers from a maximum formic acid yield of 60% in a monophasic reaction system.$^{[3,25]}$ To overcome the limitations of the aqueous reaction system, the investigation of catalytic pathways and catalytic species is of major importance.
In a previous paper, we could explain the effect of different vanadium species occurring in aqueous solution with nuclear magnetic resonance (NMR) and electron paramagnetic resonance (EPR) spectroscopy. In detail, we could show that under aerobic conditions (20 bar oxygen atmosphere) substituted \( \text{V}^{4+} \) species are the predominantly active species in the oxidation of glucose to formic acid. Moreover, under anaerobic conditions (20 bar \( \text{N}_2 \) atmosphere), paramagnetic acid-bound vanadyl species catalyse the transformation of glucose to lactic acid.\(^{[24]}\)

Very recently, some of us found that using different alcoholic solvents like methanol and ethanol can manipulate the reaction mechanism of HPA-5 in liquid phase biomass oxidation. The outstanding result of a nearly perfect yield of methyl formate (\( > 99 \% \)) from glucose using methanol as a solvent instead of water lead to the question which specific influence the solvent exerts on the catalyst. We could unambiguously prove that the reaction mechanism in methanol differs from the common one in aqueous media. Especially the total oxidation to \( \text{CO}_2 \) can be completely suppressed in methanol.\(^{[24]}\) The impressive solvent effects were also recognized by Deng et al.\(^{[27]}\) and Lu et al.\(^{[14]}\) for similar reaction systems but not further investigated.

The aim of this study is to explain the solvent effect on the oxidation of glucose with vanadium containing heteropolyacids in more detail. For this purpose, we investigated different alcohol-water mixtures via NMR and EPR spectroscopy and identified the predominant species being responsible for catalysing different glucose transformation pathways.

### Results and Discussion

#### Catalytic Glucose Oxidation using Various Solvents

In a previous study, some of our group investigated the effect of different solvents on the HPA-5 catalysed reaction of glucose to formic acid.\(^{[25]}\) Interestingly, significant differences in product selectivity were observed (see Table 1). Hereby, besides water as a standard solvent for glucose oxidation also alcoholic solvents like methanol, ethanol, n-propanol and n-butanol were tested. The experiments were performed in a tenfold screening plant with a batch mode reactor setup consisting of ten 20 mL autoclaves. Each reactor was filled with 1 mmol glucose as substrate, 0.1 mmol HPA-5 catalyst dissolved in 10 g solvent. Each catalytic oxidation reaction was conducted at 90 °C and 20 bar oxygen for 24 h. The conversion of glucose was around 100% in every tested solvent. However, depending on the solvent the product composition varied. Using water as a solvent lead to formic acid as the main product (Y = 56%) and \( \text{CO}_2 \) (43%) as the only by-product at full glucose conversion. In pure methanol there is only one product, which is methyl formate, the product of the esterification of formic acid and the solvent methanol. Formic acid, however, undergoes further esterification in all alcoholic solvents. Using ethanol as a solvent, ethyl formate (ester of formic acid in ethanol) occurs as the main product with a yield of 49%. A significant amount \( (Y = 18\%) \) of ethyl acetate (ester of acetic acid in ethanol) was formed as a by-product. In the gas phase, \( \text{CO}_2 \) as well as CO are found in a combined yield of 33%. In n-propanol as well as in n-butanol the same product compositions like using ethanol were detected. The combined yield of \( \text{CO}_2 \) and CO in both solvents are higher \( (45\% \text{ and } 43\%) \) than in ethanol and nearly as high as in water.\(^{[24]}\)

Depending on the solvent, the different product compositions and the reaction mechanisms strongly differ. In water (Scheme 1) the main product is formic acid with the side product \( \text{CO}_2 \).\(^{[24,28]}\)

Heteropolyacids (HPAs) are well-known redox catalysts based on the fast and reversible multielectron transfer.\(^{[21,28]}\) The reduction of the vanadium-oxygen (\( V-O \)) species catalyses the oxidative \( C-C \) bond cleavage under water elimination (Scheme 1). After every \( C-C \) bond cleavage the vanadium-oxygen species are oxidized by oxygen from the aerobic atmosphere to complete the catalytic cycle or activate an oxidant to form an intermediate that oxidizes the reactants.\(^{[10]}\) To get deeper insight into the catalytic active vanadium-oxygen species, a former study of some of our group analysed the HPA-5 catalyst in water before and after the reaction with \( ^{31}\text{V-NMR} \) and EPR spectroscopy.\(^{[24]}\) The \( ^{31}\text{V-NMR-spectra} \) show an isomerization reaction of the HPA-5 catalyst. It is well known in literature that aqueous HPA-5 solution contains a complex mixture of different species and isomers due to different pH-dependent equilibrium reactions of \( V-Mo-P \)-substituted HPAs in aqueous solution (for further description see\(^{[31]}\)). Therefore, the vanadium-NMR spectra of HPA-5 \( (\text{H}_2\text{PV}_4\text{Mo}_5\text{O}_{26}) \) in aqueous solution shows lower and higher vanadium-substituted Keggin species such as: \( \text{H}_2\text{PV}_4\text{Mo}_5\text{O}_{26} \) (HPA-6), \( \text{H}_2\text{PV}_4\text{Mo}_5\text{O}_{26} \) (HPA-4),

### Table 1. Yield and conversion of the oxidation of glucose using different solvents.\(^{[26]}\)

| Entry | Solvent | Conversion [%] | Yield formic acid/corresponding ester [%] | Yield formic acid/corresponding ester [%] | Yield \( \text{CO}_2 \) [%] | Yield CO [%] |
|-------|---------|----------------|------------------------------------------|------------------------------------------|----------------------|----------------|
| 1     | Water   | 100            | 56                                       | 0                                        | 43                   | 1              |
| 2     | Methanol| 100            | 100                                      | 0                                        | 0                    | 0              |
| 3     | Ethanol | 100            | 49                                       | 18                                       | 21                   | 12             |
| 4     | n-propanol | 100          | 47                                       | 9                                        | 24                   | 21             |
| 5     | n-butanol| 100            | 37                                       | 20                                       | 27                   | 16             |

\( ^{[a]} \) Corresponding ester of formic acid in the different solvents: methanol: methyl formate, ethanol: ethyl formate, n-propanol: propyl formate, n-butanol: butyl formate. \( ^{[b]} \) Corresponding esters of acetic acid in the different solvents: methanol: methyl acetate, ethanol: ethyl acetate, n-propanol: propyl acetate, n-butanol: butyl acetate. Reaction conditions: 1 mmol glucose, 0.1 mmol catalyst dissolved in 10 g solvent, 20 bar \( \text{O}_2 \), 90 °C, 24 h, 1000 rpm; Conversion and product yields determined as described in the corresponding section of the experimental part.
The occurrence of the other diamagnetic species found before and after the reaction does not change at all (see Supporting Information, Figure S4). Before the reaction, the amount of paramagnetic vanadium species measured by EPR spectroscopy were comparably large with 29% relative to the amount of $V^4+$-species measured by EPR spectroscopy were comparably large with 29% relative to the amount of $V^4+$-species. The only vanadium(IV)-species before the reaction before the reaction show two peaks. One sharp peak at $-486$ ppm and a broad peak between $-500$ ppm and $-540$ ppm (Figure 1). According to Lee et al. the broad peak was identified as vanadate ester$(VO(OMe))_2$. The sharp peak at $-486$ ppm could be assigned to an octahedral vanadium species. After reaction, the diamagnetic vanadium species change: A higher broad peak shows more vanadate-ester-species than before the reaction at around $-520$ ppm. The octahedral vanadium species changed into a vanadate-methanol-complex$(VO(OH))_2$ at $-477$ ppm. This behaviour could very well explain the different reaction mechanisms of the same HPA-5 catalyst precursor in aqueous vs. methanolic solution. In detail, the methanolic solvent inhibits the isomerization of the HPA-5 catalyst and forms some complexes with methanol. In advance, complexation with methanol increases the stability

$\left[PV^4_5Mo_{10}O_{38}\right]^{13-} + H^+ \rightleftharpoons \left[HPV^4_5Mo_{10}O_{38}\right]^{5-} + VO_4^{3-}$ (1)

Analysing Different Catalytic Vanadium Species with NMR and EPR in Methanolic Solution

Based on mechanistic investigations using $^{13}$C-labelled glucose as a substrate, we could show that HPA-5 catalysed glucose oxidation in methanolic solution leads to formic acid and further esterification to methyl formate as shown in Scheme 2.

Since the choice of the solvent has such a dramatic influence on the product selectivity, we had a closer look into the effects the solvents exhibit on the catalytic species by using $^{51}$V-NMR and EPR spectroscopy.

Furthermore, the former study revealed that the oxidation reaction of glucose to methyl formate in methanol needs lower partial pressures of oxygen and has faster reaction kinetics than the glucose oxidation reaction in aqueous solution. Therefore, the samples for the $^{51}$V-NMR measurements for the analysis of the reaction species before the reaction were prepared without substrate to avoid an inadvertent reaction. The NMR spectra before the reaction show two peaks. One sharp peak at $-486$ ppm and a broad peak between $-500$ ppm and $-540$ ppm (Figure 1). According to Lee et al. the broad peak was identified as vanadate ester$(VO(OMe))_2$. The sharp peak at $-486$ ppm could be assigned to an octahedral vanadium species. After reaction, the diamagnetic vanadium species change: A higher broad peak shows more vanadate-ester-species than before the reaction at around $-520$ ppm. The octahedral vanadium species changed into a vanadate-methanol-complex$(VO(OH))_2$ at $-477$ ppm. This behaviour could very well explain the different reaction mechanisms of the same HPA-5 catalyst precursor in aqueous vs. methanolic solution. In detail, the methanolic solvent inhibits the isomerization of the HPA-5 catalyst and forms some complexes with methanol. In advance, complexation with methanol increases the stability.

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of the HPA-5 catalyst and therefore the amount of $\text{VO}_2^+$ decreases[Eq. (1)]. As stated by Lu et. al.,\cite{35} this leads to a lower oxidation capacity of methanolic media relative to the pure aqueous media.\cite{14,36} These vanadium-methanol complexes suppress CO$_2$ and CO formation according to the results in Table 1.

For the HPA-5 catalyst in methanol before the reaction, combined room temperature and low temperature frozen solution EPR measurements show that three different $\text{V}^{4+}$ species are present (see Figure 2 and Figure S7). According to EPR measurements of a VOSO$_4$ sample solvated in methanol (see Figure S2), one species, called A$_{\text{MeOH}}$ ($g_{\text{iso}} = 1.963(4)$, $A_{\text{iso}} = 318(4)$ MHz), can be assigned to vanadyl ions solvated in methanol. We tentatively assign the other two species, namely VO$^{2+}$ @Keggin species 1 ($g_{\text{iso}} = 1.965(40)$, $A_{\text{iso}} = 232 (60)$ MHz) and VO$^{2+}$ @Keggin species 2 ($g_{\text{iso}} = 1.961(1)$, $A_{\text{iso}} = 265 (9)$ MHz) to VO$^{2+}$ coordinated at the surface of the Keggin molecule according to Gutjahr et al.\cite{37} and Pöppel et al.\cite{38} After reaction, only the signal of species A$_{\text{MeOH}}$ (see Figure 2 and Figure S7) could be observed. Interestingly, the amount of this species has increased by almost a factor of four from 11 % to 39 % (relative to the amount of $\text{V}^{4+}$) in a comparing VOSO$_4$ sample in water before the reaction as shown in Figure S1 and Table S2) after glucose oxidation in methanolic solution. After reaction, 4.4 wt.% water was measured by Karl-Fischer Titration. Water is formed due to the separation of 6 mol water at the final esterification step of formic acid with methanol. This low amount of water might lead to the presence of vanadyl-pentaqua complexes. However, we have to note that vanadyl solvated in methanol and water cannot be clearly distinguished by the applied EPR methodology due to the similar spin Hamiltonian parameters (see Figure S1 and S2 as well as Table S1).

To further reveal the dominating effect in water/methanol mixtures, a full series of different compositions between pure water (Table 2, entry 1) and pure methanol (Table 2, entry 8) were prepared. Nearly full glucose conversion was achieved in all experiments. In pure water 56 % of the carbon ends up in formic acid and 43 % in CO$_2$. In contrast, in pure methanol 100 % of the carbon yields in methyl formate. Two general trends could be observed: An increasing amount of water from 10 to 90 % leads to a small increase of CO$_2$ formation significantly due to the formation of the aforementioned vanadate-methanol-complex ($\text{IVO(OMe)O}_4$)$^{2-}$). This phenomenon could be explained by the faster reaction kinetics of the methanolic reaction pathway compared to the aqueous one.\cite{39} The yield of CO nearly stays constant and is negligible < 1 %. Depending on the methanol content in the mixture, a different equilibrium of formic acid and methyl formate was observed.

![Figure 2. Experimental (black) and simulated (coloured) room temperature EPR-spectra of HPA-5 dissolved in pure methanol a) before and b) after the reaction. In a) the simulated signal in red is the sum of the simulated signals assigned to species A$_{\text{MeOH}}$ (blue) and to two different VO$^{2+}$ complexes at the surface of some Keggin molecule (species 1 – green and species 2 – purple). Those room temperature simulations were determined by least square fits assuming spin Hamilton parameters determined by EPR of the frozen solution spectrum for all three species determined at $T = 60$ K (see Figure S7). In b), the simulated signal is assigned to species A$_{\text{MeOH}}$. See Tables S2 and S3 for spin Hamiltonian parameters.](image)

| Entry | Water | Methanol | Glucose conversion [%] | Yield Formic acid [%] | Yield Methyl formate [%] | Yield CO$_2$ [%] | Yield CO [%] |
|-------|-------|----------|------------------------|----------------------|-------------------------|-----------------|-------------|
| 1     | 100   | 0        | 100                    | 56                   | 0                       | 43              | 1           |
| 2     | 90    | 10       | 91                     | 72.4                 | 17.0                    | 3.3             | 0.3         |
| 3     | 70    | 30       | 97                     | 57.5                 | 36.7                    | 2.5             | 0.3         |
| 4     | 50    | 50       | 98                     | 44.3                 | 51.9                    | 1.6             | 0.2         |
| 5     | 30    | 70       | 99                     | 34.2                 | 63.6                    | 1.0             | 0.2         |
| 6     | 10    | 90       | 100                    | 19.9                 | 79.6                    | 0.5             | 0           |
| 7     | 0     | 100      | 100                    | 0                    | 100                     | 0               | 0           |

[a] Reaction conditions: 1 mmol glucose, 0.1 mmol catalyst HPA-5 dissolved in 10 g solvent, 20 bar O$_2$, 90 °C, 24 h, 1000 rpm; Conversion and product yields determined as described in the corresponding section of the experimental part.
Analysing the $^{51}$V-NMR spectra of the different water/methanol mixtures, different diamagnetic V$^{4+}$-species overlap (see Figure 3 and Figures S5 and S6). The water content leads to an isomerization of the diamagnetic vanadium species. Even at low water content of 30 wt.%, an isomerization of the HPA-5 species occurs (see Figure S6). The transition between the different diamagnetic vanadium-(V)-species cannot be clearly identified according to the $^{51}$V-NMR-spectra of the solutions. Exemplary, the $^{51}$V-NMR spectra are displayed in Figure 3 for a 50/50 mixture of water and methanol.

The $^{51}$V-NMR spectrum before the reaction shows three significant peaks between $-520$ ppm and $-560$ ppm which correspond to the HPA-1, HPA-2 and HPA-3/VO$_2^+$ species, respectively. These species can, however, be subordinated by the broad[VO(OMe)O]$_2$$^{2-}$ peak (see Figure 3). It can be assumed that the isomerization superimposes the methanol complex ([VO(OMe)O]$_2$$^{2-}$). After reaction, the peaks of the three lower substituted HPA-species are sharpened. Also, in both spectra there is a spread of HPA-4 to HPA-6 (between $-570$ ppm and $-600$ ppm). Due to the isomerization, no[VO(OMe)$_2$]$_n$ after the reaction nor octahedral vanadium before the reaction could be detected. The results of the EPR spectroscopy for the 50/50 mixture of methanol and water show the same amount of species A$_{MeOH}$ (ca 50%) before and after reaction (see Tables S2 and S3, Figures S8 and S9). This amount is significantly larger than observed for the sample in pure methanol, indicating that significant amounts of vanadyl-water complexes contribute to the signal of A$_{MeOH}$ in addition to vanadyl-methanol complexes. The fact that the amount of species A$_{MeOH}$ has not changed after the reaction indicates that no additional V$^{4+}$ species are formed during the reaction. This strongly indicates that the increase of species A$_{MeOH}$ in the 100% methanol sample after the reaction originates from the formation of vanadyl-water complexes. Furthermore, in the water-methanol mixture, no signals of coordinated VO$_2^+$ @Keggin species were observed before the reaction in contrast to the 100% methanol sample. This indicates that the presence of water suppresses the formation of such complexes which might also explain their absence in the 100% methanol sample after the reaction.

In summary, even a small amount of methanol contributes to a significant reduction of CO$_2$ production. An isomerization and superposition of the different vanadium species can be deduced from a water content of 30 wt.%-. Nevertheless, the reaction kinetics of the methanol species is so fast that even with a low methanol content, the largest amount of formic acid is produced via the methanolic reaction path (Scheme 2), as shown by the low CO$_2$ yields. The EPR results show that mainly water-vanadium and presumably additional methanol-vanadium complexes appear in the methanol and methanol/water samples before and after reaction. In addition, coordinated VO$_2^+$ @ Keggin species appear in the pure methanol sample before reaction. Since the latter were not observed for the 50/50 mixture of methanol and water, we conclude that the reaction mechanism is mainly catalysed by the complexion of the diamagnetic vanadium-(V)-species. The $^{51}$V-NMR spectra of the mixtures do not show any octahedral or[VO(OMe)$_2$]$_n$ complexes, suggesting that the ([VO(OMe)O]$_2$$^{2-}$) complex is the catalytically active V$^{4+}$-complex in methanolic solution.

Analyzing Different Catalytic Vanadium Species in Ethanolic Solution using NMR and EPR Spectroscopy

Using ethanolic solution, however, the reaction of glucose to ethyl formate and even to acetic acid and therefore ethyl acetate were observed (see Table 1). Figure 4 shows the $^{51}$V-NMR spectra in pure ethanol before and after reaction. Before reaction, similar to methanolic solution, HPA-5 forms a complex with ethanol VO(OEt)$_2$ (peak at $-592$ ppm). Again, in order to prevent isomerization of the different HPA-species due to the fast reaction in ethanol, we prepared the sample without glucose as a substrate. After reaction, again VO(OEt)$_2$ remains the predominant species. Moreover, small new peaks between $-475$ ppm and $-550$ ppm occur. However, no references for these species can be found in literature. Again, some water (around 3.5 wt%) is formed due to the final esterification step. Therefore, we assume that analogous to methanolic solution different vanadate-ester-species (here[VO(OEt)O]$_2$$^{2-}$ as well as a complex with the formed ethyl acetate) are formed.
Figure 4. $^{51}$V-NMR spectrum of HPA-5 before (top) and after (bottom) a reaction with 1 mmol glucose, 20 bar O$_2$ at 90 °C and 1000 rpm for 24 h in pure ethanol. The measurement before the reaction was carried out without substrate.

Additional EPR measurements in pure ethanolic solution show the presence of a paramagnetic vanadium species A$_{\text{EtOH}}$ (g$_{\text{iso}}$ = 1.965(5), A$_{\text{iso}}$ = 316(4) MHz) before and after reaction (see Tables S4 and S5 as well as Figures S10 and S11). These EPR parameters are typical for vanadyl-ethanol complexes: For VOSO$_4$ in pure ethanol, we determined for vanadyl-ethanol complexes the following parameters: g$_{\text{iso}}$ = 1.965(4), A$_{\text{iso}}$ = 317(3) MHz (see Figure S3 and Table S1). However, these parameters also coincide with those of vanadyl-pentaaqua complexes so that we cannot clearly distinguish by EPR between vanadyl solvated in ethanol and water (compare data in Table S1).[24] In this context, it is interesting to note that we observed for the VOSO$_4$ sample in pure ethanol also a signal of the solid salt of vanadyl sulfate (Figure S3).[24] This is in good agreement with the observation that vanadyl is less soluble in ethanol than in water. Furthermore, before reaction the water content in the pure ethanol sample was only 0.03 wt% and increased to 3.5 wt% after reaction due to esterification in the last reaction step. The corresponding EPR derived amount of species A$_{\text{EtOH}}$ increased from 9% before to 44% after reaction (Table S4). Therefore, it is most likely that before reaction, only a small amount of species A$_{\text{EtOH}}$ was present due to the small fraction of present water and the low solubility of vanadyl in ethanol. After reaction, the EPR derived amount of species A$_{\text{EtOH}}$ increased by always a factor of five due to the larger fraction of present water which leads to the formation of vanadyl-pentaaqua complexes, similar to the sample in pure methanol. To further analyse the behaviour of different ethanol-water-mixtures, an additional 50/50 mixture of water and ethanol was also investigated. Table 3 shows the results and the effect of the mixture on the product selectivity of formic acid respectively ethyl formate as well as acetic acid and ethyl acetate.

Similar to the results in methanol-water mixtures (see Table 2), full glucose conversion was achieved in all samples. Moreover, significant differences in the product composition were observed. While in pure ethanol (Table 3, entry 3), 49% of the initial carbon yield in ethyl formate formation and 18% in ethyl acetate formation, 21% yield in CO$_2$ and 12% in CO. Interestingly, in the 50/50 water/ethanol-mixture (Table 3, entry 2), 56% FA-yield and 40% ethyl formate yields were detected. Neither ethyl acetate nor CO were found in the product mixture. Moreover, only 4% CO$_2$ yield was detected that is by far lower compared to pure water (Table 3, entry 3) were 43% CO$_2$ were formed and still 21% in pure ethanol.

To gain a deeper understanding of the different effects leading to such different product compositions in versatile liquid media and to reveal the influence of mixtures on the catalytically active vanadium species, the 50/50 ethanol/water mixture was also measured spectroscopically. As pointed out using the different methanol-water mixtures, the $^{51}$V-NMR spectra of the ethanol-water mixture also show a peak overlapping (see Figure 5). As in methanol, isomerization and superposition of different species is observed. Moreover, as detected by EPR, a correspondingly large amount of vanadium (about 40%, see Table S4) is present as the paramagnetic vanadium species A$_{\text{EtOH}}$ before and after reaction and therefore lead to line broadening and high background noise. The peaks at $-532$ ppm[VO(OEt)$_2$]$_2$ and $552$ ppm[VO$_2$(OEt)$_3$] are observed.

Table 3. Yield and conversion of the oxidation reaction of glucose using different ethanol/water mixtures.[a]

| Entry | Water | Ethanol | Glucose conversion [%] | Yield Formic acid [%] | Yield Ethyl formate [%] | Yield Acetic acid [%] | Yield Ethyl acetate [%] | Yield CO$_2$ [%] | Yield CO [%] |
|-------|-------|---------|------------------------|----------------------|------------------------|-----------------------|------------------------|----------------|-------------|
| 1     | 100   | 0       | 100                    | 56                   | 0                      | 0                     | 43                    | 1              |
| 2     | 50    | 50      | 98                     | 56                   | 40                     | 0                     | 0                     | 4              |
| 3     | 0     | 100     | 100                    | 0                    | 49                     | 0                     | 18                    | 21             | 12          |

[a] Reaction conditions: 1 mmol glucose, 0.1 mmol catalyst HPA-5 dissolved in 10 g solvent, 20 bar O$_2$, 90 °C, 24 h, 1000 rpm; Conversion and yields determined as described in the corresponding section of the experimental part.
Figure 5. $^{13}$C-NMR spectra of an ethanol/water mixture of 50/50 before (left) and after (right) reaction with 1 mmol glucose at 90 °C, 20 bar O$_2$, and 1000 rpm for 24 h. The measurement before the reaction was prepared without substrate.

$-555$ ppm[(HO)$_2$VO(OEt)$_2$]$^{2+}$, as well as $-605$ ppm[VO(OEt)$_4$]$^{4+}$ could be assigned to different vanadate-ester-species. The broad peak at $-600$ ppm could be some remnant of the ethanol-vanadium-complex. This leads to the assumption that the water isomerization is faster than the complexation of the vanadium with ethanol. After reaction, there is no more peak at $-600$ ppm.

As already mentioned, the EPR measurements show mainly species A EtOH before and after reaction (see Tables S4 and S5 as well as Figures S12 and S13). It is most reasonable that vanadium-pentaqua complexes contribute to most extent to this species, although they cannot be distinguished by EPR from vanadium-ethanol complexes.

Table 4 summarizes all identified vanadium species by EPR as well as NMR spectroscopy for the oxidation of glucose in the different tested solvents water, methanol and ethanol as well as mixtures thereof.

| Entry | Solvent | $V^{4+}$ Species before reaction$^{(c)}$ | $V^{4+}$ Species after reaction$^{(c)}$ | $V^{5+}$ Species before reaction$^{(c)}$ | $V^{5+}$ Species after reaction$^{(c)}$ | Reference |
|-------|---------|--------------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|-----------|
| 1     | Water   | [V$^{4+}$ O(H$_2$O)$_2$]$_2$$^{2+}$   | [V$^{4+}$ O(H$_2$O)$_2$]$_2$$^{2+}$   | [VO$_2$]$^{2+}$                     | [VO$_2$]$^{2+}$                     | This work |
|       |         | [V$^{4+}$ O(COOH)$_2$]$_2$$^{2+}$    | [V$^{4+}$ O(COOH)$_2$]$_2$$^{2+}$    |                                      |                                      |           |
| 2     | Methanol| [V$^{4+}$ O(OMe)$_2$]$_2$$^{2+}$     | [V$^{4+}$ O(OMe)$_2$]$_2$$^{2+}$     | [VO$_2$]$^{2+}$                     | [VO$_2$]$^{2+}$                     | This work |
|       |         | and presumably                       | and presumably                       |                                      |                                      |           |
|       |         | [V$^{4+}$ O(OMe)$_2$]$_2$$^{2+}$     | [V$^{4+}$ O(OMe)$_2$]$_2$$^{2+}$     | [VO(OMe)$_2$]$^{2-}$               | [VO(OMe)$_2$]$^{2-}$               |           |
| 3     | Water/  | [V$^{4+}$ O(OMe)$_2$]$_2$$^{2+}$     | [V$^{4+}$ O(OMe)$_2$]$_2$$^{2+}$     | [VO$_2$]$^{2+}$                     | [VO$_2$]$^{2+}$                     | This work |
| methanol|        | and presumably                       | and presumably                       |                                      |                                      |           |
|       |         | [V$^{4+}$ O(OMe)$_2$]$_2$$^{2+}$     | [V$^{4+}$ O(OMe)$_2$]$_2$$^{2+}$     | [VO(OMe)$_2$]$^{2-}$               | [VO(OMe)$_2$]$^{2-}$               |           |
| 4     | Ethanol | [V$^{4+}$ O(OEt)$_2$]$_2$$^{2+}$     | [V$^{4+}$ O(OEt)$_2$]$_2$$^{2+}$     | [VO(OEt)$_2$]$^{2-}$               | [VO(OEt)$_2$]$^{2-}$               | This work |
|       |         | and presumably                       | and presumably                       |                                      |                                      |           |
|       |         | [V$^{4+}$ O(OEt)$_2$]$_2$$^{2+}$     | [V$^{4+}$ O(OEt)$_2$]$_2$$^{2+}$     | [VO(OEt)$_2$]$^{2-}$               | [VO(OEt)$_2$]$^{2-}$               |           |
| 5     | Water/  | [V$^{4+}$ O(OEt)$_2$]$_2$$^{2+}$     | [V$^{4+}$ O(OEt)$_2$]$_2$$^{2+}$     | [VO(OEt)$_2$]$^{2-}$               | [VO(OEt)$_2$]$^{2-}$               | This work |
| ethanol|        | and presumably                       | and presumably                       |                                      |                                      |           |
|       |         | [V$^{4+}$ O(OEt)$_2$]$_2$$^{2+}$     | [V$^{4+}$ O(OEt)$_2$]$_2$$^{2+}$     | [VO(OEt)$_2$]$^{2-}$               | [VO(OEt)$_2$]$^{2-}$               |           |

[a] Reaction conditions: 1 mmol glucose, 0.1 mmol catalyst dissolved in 10 g solvent, 20 bar O$_2$, 90 °C, 24 h, 1000 rpm. [b] Determined by EPR spectroscopy. [c] Determined by $^{13}$C-NMR spectroscopy.
Conclusion
The HPA-5 catalysed oxidation reaction of glucose in various solvents results in different product selectivities. Especially methanol has a drastic effect as it leads to 100% carbon efficiency resulting in pure methyl formate at full glucose conversion. Hereby, competing total oxidation to carbon dioxide can be completely suppressed. However, this effect was by far less pronounced using ethanol as a solvent as it also leads to the formation of the corresponding acetic esters besides the desired ethyl formate. To shed light into this fascinating behaviour, we used $^{51}$V-NMR and EPR spectroscopy to investigate the different dia- and paramagnetic vanadium species in solution. Hereby, we could prove that besides the already known vanadyl pentaqua complex in aqueous solution, a new vanadyl-methanolate species occurs that is responsible for the high selectivity to methyl formate, $[\text{VO(O}Me\text{)}\text{O}]^{2-}$ is formed that is obviously the predominant catalytic active species in methanolic solution as well as in aqueous/methanolic solutions having a methanol content of at least 10%. Interestingly, a similar species could be also identified in ethanolic solution. However, here the vanadyl pentaqua complex is still the dominating catalytic species as the catalytic results especially in aqueous/ethanolic mixtures are similar to those in pure water. In the future, these results can be applied to the oxidation of real biomass in alcoholic solvents using vanadium substituted polyoxometalates. This represents an interesting area for further research.

Experimental Section
Materials
All reagents and substrates were commercially available and used as received. The model substrate glucose was supplied by Merck KGaA with a purity of 99.5%. The catalyst HPA-5 ($\text{H}_7\text{PV}_7\text{Mo}_7\text{O}_{40}$) was synthesized according to the literature.$^{[23,39]}$ The characterization of the catalyst has been carried out using a Perkin Elmer Plasma 400 ICP-OES device resulting in a P/V/Mo ratio of 1.48/60.93 for HPA-5. Oxygen (4.5 GA 201) was bought from Linde AG. Demineralized water, methanol (99.98%, VWR BDH Chemicals) and ethanol (absolute, VWR BDH Chemicals) were used as solvents for the experiments.

Catalytic Oxidation Reactions
The catalytic oxidation reactions were carried out in a tenfold screening plant with a batch mode reactor setup. It consists of ten 20 mL autoclaves made of Hastelloy C276. All pipes, valves and fittings were made of stainless steel 1.4571. The gaskets used were made of Teflon. The autoclaves were connected in parallel to a 20 mL autoclaves made of Hastelloy C276. All pipes, valves and fittings were made of stainless steel 1.4571. The gaskets used were made of Teflon. The autoclaves were connected in parallel to a heating plate equipped with magnetic stirrer bars. Additionally, each reactor was connected to a rupture disk with a burst pressure maximum of 90 bar.

Typical Work-up Procedure
For the catalytic oxidation reactions, each autoclave was filled with 1 mmol glucose (0.18 g), 0.1 mmol catalyst and 10 g of solvent. The system was purged with 10 bar pure oxygen in order to remove the residual air out of the reactors. Afterwards, the reactors were pre-pressurized with about 16 bar oxygen, the stirrer was set to 300 rpm and the heating was switched on. When the desired temperature of 90 °C was reached, the pressure was increased to the required pressure of 20 bar and the stirring speed was set to 1000 rpm in order to start the gas entrainment. This moment was set as starting time of the experiment.

Determination of Quantitative Reaction Parameters
After the reactions all products were quantitatively determined by HPLC-(High Performance Liquid Chromatography), NMR-(Nuclear Magnetic Resonance) and GC-(Gas Chromatography) analysis. Liquid phase analysis was carried out using either HPLC or $^{13}$C-NMR spectroscopy. The yields of all acids were determined by means of HPLC measurements using a HPLC from Jasco equipped with a 300 mm × 8 mm SH1011 Shodex column. The yields of the corresponding esters were quantified by $^{13}$C-NMR using a Jeol ECDX-400 MHz spectrometer (9.4 Tesla) at 293 K (1000 scans, 100.61 MHz) resulting in a resolution of 0.77 Hz. Both acid and ester yields were calculated as n(product)/n(C-atoms glucose). The determination of the gaseous by-products CO and CO$_2$ was done by means of GC-analysis using a Varian GC 450 equipped with a 2 m × 0.75 mm ID ShinCarbon ST column and calculated as n(CO)/n(C-atoms glucose). No other gaseous products could be detected by the used GC. Karl-Fischer Titration was used to determine the water content (759 KF Coulometer, Metrohm) of the respective aqueous solutions.

Identification of Catalytic Vanadium Species in Solution
All liquid samples were measured at room temperature by $^{51}$V-NMR. The $^{13}$C-NMR spectra were measured with 2024 scans in a range of −580 ppm to −460 ppm with an excitation frequency of 105.25 MHz and a resolution of 0.77 Hz. For the detection of $^{51}$V species, continuous wave (cw) EPR spectra of the liquid samples at room temperature were measured with a Bruker EMX micro spectrometer at X-band frequency (9.5 GHz) using a rectangular Varian resonator and special flat quartz glass tubes. Their shape avoids dielectric losses by the water molecules enabling the coupling of the microwave (mw) to the resonator even in the liquid state of the samples. The latter were prepared in the same way as reported previously.$^{[24]}$ In addition, the frozen samples were measured at $T=60 \text{ K}$ at the same spectrometer, but now fitted with an ER 4119 HS cylindrical cavity (9.4 GHz) equipped with an Oxford Instruments He cryostat ESR 900 for cooling. For those experiments the samples were pipetted into conventional X-band EPR tubes at room temperature which were sealed with thermoplastic film. All experimental room temperature spectra were conducted with a mw power of 20 mW and a modulation amplitude of 1 mT. Low temperature spectra were measured with the same modulation amplitude but with a mw power of 0.2 mW. All experimental EPR spectra were baseline corrected by polynomials up to third order and normalized by division with the quality factor measured by the spectrometer for each single sample. EPR signals of the $^{51}$V species were simulated using the MatLab toolbox EasySpin version 5.2.28.$^{[40]}$ Simulations of the room temperature spectra were proceeded almost in the same way as reported previously.$^{[24]}$ However, in the present paper we were able to determine experimentally the anisotropic parameters $\Delta g = \frac{g_{xx}}{g_{zz}} - \frac{2}{3}$ of the g-tensor and $\Delta V = \frac{1}{3} \frac{\Delta V_{zz}}{V_{zz}-V_{yy}}$ of the $^{51}$V hyperfine interaction (hfi) tensor for almost each single sample from the simulation of the
corresponding frozen solution spectrum at T = 60 K and obtained with that information experimentally justified rotational correlation times of the fast isotropic rotational motion of the various V⁴⁺ species at room temperature. The amount of the different V⁴⁺ species contributing to the room temperature EPR spectra were quantified by the double integration of the corresponding simulated signals. The corresponding unit of the amount was chosen such that the signal of VO₅SO₄ in water at room temperature as an amount equal to 100%. Different experimental parameters of different spectra like the number of scans were considered in a correct manner by appropriate normalization of the signals, if required. For reasons explained previously we have to admit that neither our NMR nor EPR methodology might be able to detect signals of distinct paramagnetic V⁴⁺ species with electron spin S = 1 which can be present in the samples, for example as V⁴⁺ hexaaqua cations.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: Keggin polyoxometalates · solvent effect · EPR spectroscopy · NMR spectroscopy · vanadium redox chemistry

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