Synthesis of 2,5-Diformylfuran and Furan-2,5-Dicarboxylic Acid by Catalytic Air-Oxidation of 5-Hydroxymethylfurfural. Unexpectedly Selective Aerobic Oxidation of Benzyl Alcohol to Benzaldehyde with Metal/Bromide Catalysts**

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Abstract: The alcohol group of hydroxymethylfurfural (compound 1, HMF) is preferentially oxidized by dioxygen and metal/bromide catalysts [Co/Mn/Br, Co/Mn/Zr/Br; Co/Mn=Br/(Co+Mn) = 1.0 mol/mol] to form the dialdehyde, 2,5-diformylfuran (compound 2, DFF) in 57% isolated yield. HMF can be also oxidized, via a network of identified intermediates, to the highly insoluble 2,5-furandicarboxylic acid (compound 5, FDA) in 60% yield. For comparison, benzyl alcohol gives benzaldehyde in 80% using the same catalyst system. Over-oxidation (to CO_2) of HMF is much higher than that of the benzyl alcohol but can be greatly reduced by increasing catalyst concentration.

Introduction

At the current rate of consumption, proven crude oil reserves are estimated to last for less than four decades.[1] Therefore, in recent years serious consideration has been given, in both academia and industry, to alternative feedstocks for the chemical industry of the future. The use of renewable resources, i.e., naturally occurring carbohydrates and oils produced by various plants, would result in the development of benign, environmentally friendly processes, the so-called green chemistry.[2]

5-Hydroxymethylfurfural (HMF; compound 1) is one of the few individual organic compounds that can be prepared directly from various carbohydrates in up to 98% yield. While the best yields of HMF have been obtained from fructose, other abundant, low-cost mono-, di-, and polysaccharides can be used, such as glucose, sucrose, and starch.[3]

Selective oxidation reactions of HMF are presently viewed as attractive routes to 2,5-furandicarboxylic acid (FDA) and/or 2,5-diformylfuran (DFF; compound 2), monomers for furan-containing polymers and materials with special properties.[4] While a variety of oxidants have been used for oxidation of HMF to 2,5-furandicarboxylic acid and DFF, only few reports describe catalytic oxidations of HMF with oxygen or air, the most economical oxidants. Thus, HMF has been oxidized with O_2 to 2,5-furandicarboxylic acid in the presence of heterogeneous Pt catalysts with stoichiometric amounts of alkali[5,6] and to DFF with TEMPO radicals[7,8] or supported vanadium catalysts.[9,10] Although homogeneously catalyzed oxidation reactions of alcohols have received much attention in recent years,[11–18] no reports have appeared in the literature, describing the oxidation of HMF with O_2 and soluble metal complex catalysts.

In this paper, we report the first examples of aerobic HMF oxidation reactions, catalyzed with homogeneous metal/bromide systems. The easily prepared, low-cost metal/bromide catalysts, the most common being a mixture of Co/Mn/Br, are widely used for the selective and efficient autoxidation reactions of hydrocarbons,[19] e.g., the large scale industrial synthesis of terephthalic, isophthalic, and trimellitic acids

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from *p*-xylene, *m*-xylene, and pseudocumene respectively.[1,19] Surprisingly little is known, however, about oxidation of alcohols using the metal/bromide catalysts.[19] In this work, we found that, depending on reaction conditions, hydromethylfurfural can be oxidized to DFF or 2,5-furandicarboxylic acid with unexpectedly high selectivity. Furthermore, the selective formation of DFF in the metal bromide-catalyzed oxidation of HMF prompted us to study the oxidation of benzyl alcohol under similar conditions. Remarkably, it was found that under controlled conditions this oxidation can afford benzaldehyde in high yield.

Results

Products Formed

GC/MS studies were performed on two selected samples during HMF autoxidation at 70 bar, which are consistent with the products and pathways given on Figure 1. In addition, the usual products from the autoxidation of acetic acid were observed, i. e., formic acid, acetoxyacetic acid, glycolic acid, maleic acid, fumaric acid, succinic acid, and bromosuccinic acid in trace amounts. A side reaction is the esterification of the alcohols to form the more oxidatively stable acetate, see compounds **6** and **7** in Figure 1 and benzyl acetate in Figure 2. DFF and FDA have been isolated and characterized by elemental analysis and NMR spectra. The 2-carboxy-5-formylfuran was identified and quantified by ^{1}H NMR spectroscopy of isolated solid samples that were either 2,5-furandicarboxylic acid or 2,5-furandicarboxylic acid/2-carboxy-5-formylfuran mixtures. The oxidation of benzyl alcohol gives the expected benzaldehyde, benzyl acetate, and benzoic acid products (see Figure 2).
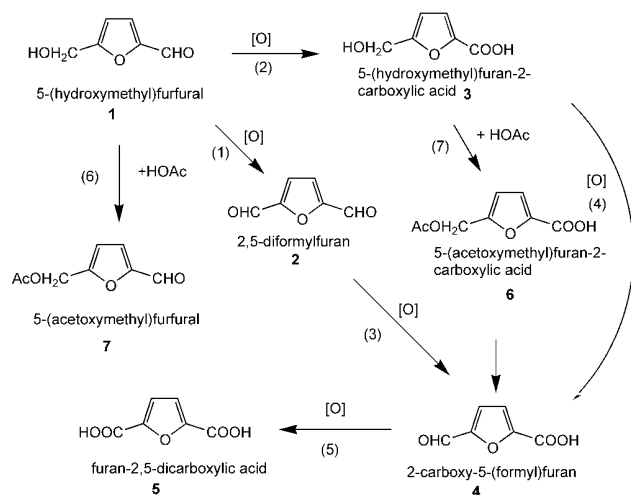

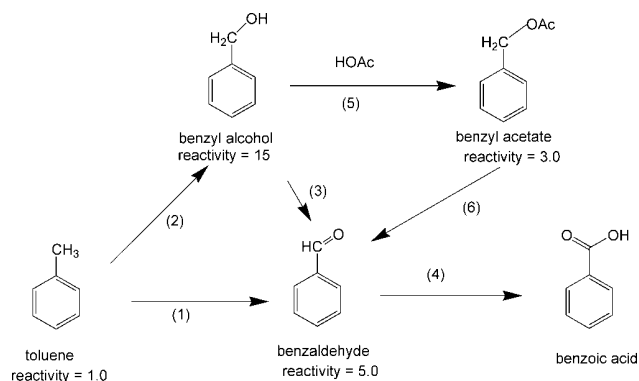**Figure 1.** Products from the autoxidation of hydroxymethyl-furfural

Figure 2. Products during autoxidation of benzyl alcohol

Formation of Diformylfuran from Hydromethyl-furfural and Benzaldehyde from Benzyl Alcohol at Atmospheric Pressure (Table 1)

In experiments 1 and 5, the attempt to initiate the reaction at the lower temperature failed, hence the temperature was raised to the higher given value. The formation of the reaction products, as determined by GC and LC, from HMF and benzyl alcohol is illustrated in Figures 3 and 4. Maximum observed yield of the aldehydes is 57% for DFF and 80% for benzaldehyde. Maximum aldehyde yields occur as the conversion of the alcohol approaches 100%. The selectivity decreases as the conversion of the alcohol increases with the values for HMF (51–90%) being lower than for benzyl alcohol (80–93%), see Figure 5. Doubling the catalyst concentration during the oxygenation of HMF (i) increases the reaction rate by a factor of 2.1, (ii) increases the yield and selectivity to DFF by 5 and 10%, respectively, and (iii) decreases the 'overoxidation' to CO and CO_2 by a factor of 4 (see experiments 2, 3, and 4 in Table 1 and Figure 6). Further increase in catalyst concentration does not further improve DFF yield (see experiments 4, 5, and 6). For benzyl alcohol, the maximum benzaldehyde yield of 80% occurs at a conversion of 85% with only 4.6% benzoic acid and 3.8% benzyl acetate formed (Table 1, experiment 7). Based on their rates of disappearance, benzyl alcohol is 2.0 times more reactive than HMF (see examples 4, 7, and 8 in Table 8).

The rate of disappearance of the alcohol and the rate of disappearance of the aromatic aldehyde are consistent with first order kinetics and the rate constants are given on Table 1. The rate of disappearance of HMF is 8.1 times faster than the rate of disappearance of 2-carboxy-5-formylfuran, suggesting that the dialdehyde is quite stable, as seen from the kinetic data on Table 1. This is consistent with the subsequent work-up of the reaction mixture and isolation of DFF in a yield close to that previously determined by GC. The benzyl alcohol, however, reacts to form benzaldehyde faster by only a factor of 1.1 than benzaldehyde reacting to benzoic acid (Table 1). Re-

Table 1. Oxygenation of hydroxymethylfurfural and benzyl alcohol at ambient atmospheric pressure

Exp.	1	2	3	4	5	6	7
	HMF	HMF	HMF	HMF	HMF	HMF	benzyl alcohol
Temp, °C	50 then 95	75	75	75	50 then 75	75	75
Reagent, M	0.725	0.794	0.804	0.797	0.796	0.806	0.793
Co, mM	2.6	6.6	6.6	13.5	26.8	27.3	13.4
Zr, mM	0.0	0.15	0.15	0.15	0.15	0.15	0.15
Rate, s^{-1} [a]	–	9.68(0.18) [0.997]	8.12(0.61) [0.972]	16.6(1.4) [0.999]	10.8(0.5) [0.992]	15.1(0.5) [0.994]	40.4(3.9) [0.988]
Alcohol, half-life, min	–	119	142	69	106	76.5	28.5
Rate, s^{-1} [b]	–	1.22(0.34) [0.862]	–	–	–	–	30(3) [0.943]
Time,min [c]	414	450	642	310	550	430	100
Yield [c]	41	51	50	57	51	52	80
Conv.,% [c]	98	92	95	91	95	97	85
Select.,% [c]	42	55	53	63	54	54	93
Acetate,% [c]	8.4	5.9	7.5	7.2	6.1	5.7	5.6
Alcohol to CO_x [d]	–	7.4	8.5	2.1	1.8	2.6	0.05

[a] Rate of disappearance of aromatic alcohol $\times 10^5$. Standard deviation in parenthesis ( ), correlation coefficient in brackets [ ].
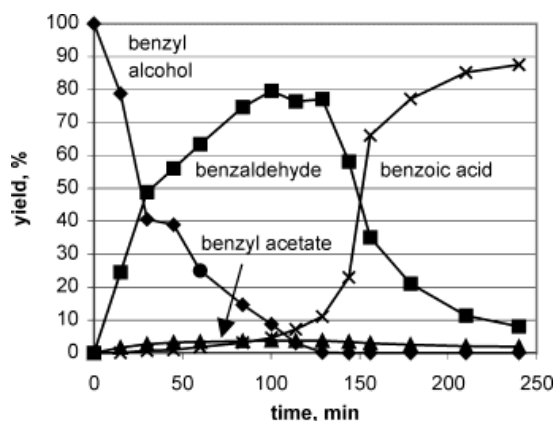[b] Rate of disappearance of aromatic aldehyde.
[c] When maximum alkylaromatic aldehyde is observed.
[d] Loss of alcohol due to carbon monoxide and carbon dioxide formation. Assumes no CO_x formation from the solvent.
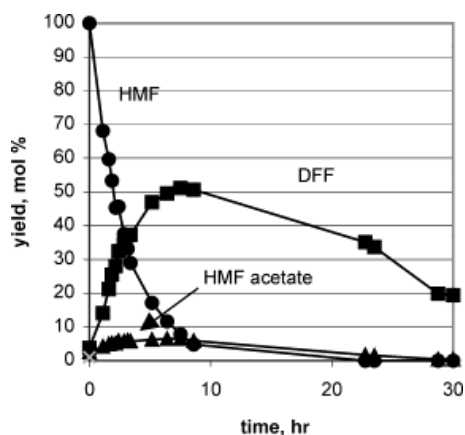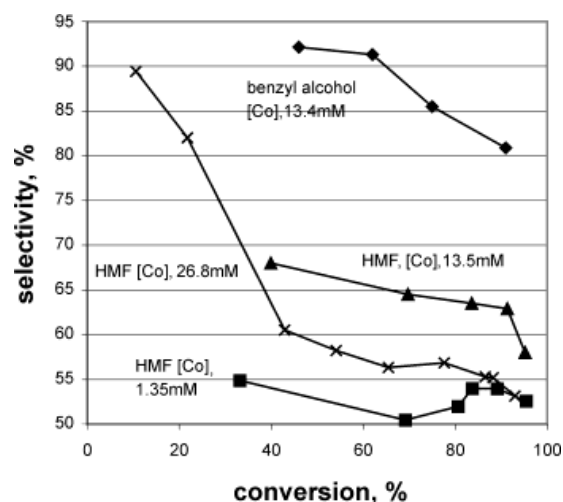

Figure 3. Autoxidation of hydroxymethylfurfural at 75 °C

Figure 4. Autoxidation of benzyl alcohol at 75 °C

Figure 5. Benzaldehyde selectivity as function of catalyst concentration and type of alkylaromatic alcohol

benzyl alcohol is close to completion, despite the fact that $PhCH_2OH$ and PhCHO exhibit very similar measured reactivities in the same experiment.

Formation of DFF from HMF at 70 Bar Air (Table 2)
Experimental error, as determined by 5 replicate experiments, is given in entry 7 of Table 2. As can be seen, 50 and 75 °C for 2 h are sufficient conditions for obtaining good yields of DFF, up to 63%. By comparing experiments 1 and 2, 3 and 4, 5 and 6, and 8 and 9, one finds that increasing catalyst concentration leads to (i) increased activity as evidenced by higher conversions, (ii) higher selectivity for DFF (except for experiments 5 and 6), and (iii) higher yield. Comparing experiments 1 and 3, 2 and 4, 5 and 8, and 6 and 9, one finds that the Co/Mn/Zr/Br catalyst is
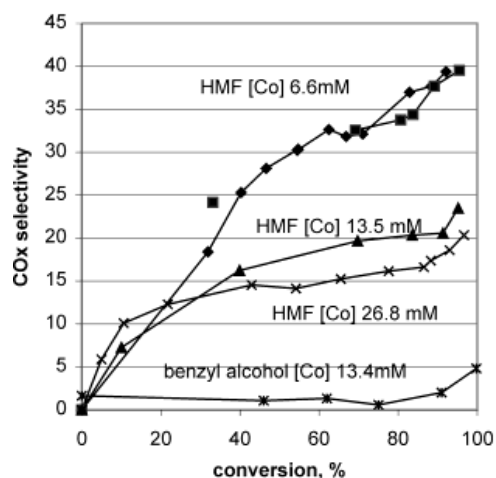
markably, the oxidation is catalyzed in such a way that essentially all the benzyl alcohol reacts *first*. The benzaldehyde formed starts to undergo further oxidation to benzoic acid only after the oxidation of the

Figure 6. Carbon oxide selectivity as function of catalyst concentration and type of alkylaromatic alcohol

more active, giving higher conversion, than Co/Mn/Br, with the only exception being experiments 2 and 3 where the conversions are similar. The addition of zirconium not only affects conversion, but can also profoundly increase the selectivity (Table 2). This point is illustrated by experiments 1 and 3 where the addition of Zr results in a much higher yield of DFF (67 vs. 38%) at the same conversion of ca. 60%. Experiments 6 and 8, for which the conversions vary significantly, represent the only exception. Under comparable conditions, the conversion increases with temperature, as expected.

Formation of 2-Carboxy-5-formylfuran and 2,5-Furandicarboxylic Acid at 70 Bar (Table 3)

The initial amount of HMF used was only 0.2–0.75 g and the yields are based on isolated and washed solids which were analyzed by NMR. When the temperature is increased from 75 to 100–125 °C, precipitation of poorly soluble 2,5-furandicarboxylic acid commences. 2-Carboxy-5-formylfuran is also either fairly insoluble or is prone to co-crystallization with 2,5-furandicarboxlic acid, which results in their co-precipitation. The yield increases with catalyst concentration (Figure 7), with temperature (entries 1 and 2 and 3 and 4 of Table 3), but not with the addition of Zr to the Co/Mn/Br catalyst (entries 1 and 3 and 2 and 4). Extrapolation from Figure 7 suggests that the maximum obtainable 2,5-furandicarboxylic acid yield is about 70% using the Co/Mn/Zr/Br catalyst at the specified molar ratios of these elements. It is believed that variation of the molar amounts of the Co, Mn, Zr, and Br could well improve the yield of 2,5-furandicarboxylic acid. Since the oxidation proceeds through three steps from HMF to 2,5-furandicarboxylic acid (steps 1, 3, and 5 in Figure 1) and the reactivity of the HMF is probably higher than 2-carboxy-5-formylfuran one would expect that staging the temperature would increase yield.[19] This was not observed however, since staging the temperature from an initial value of 50 °C for 1 h and then 125 °C for 2 h gave no better results than the oxygenation at 125 °C for 3 h (Figure 7).

Table 2. Oxidation of hydroxymethylfurfural (HMF) to diformylfuran (DFF) at 70 bar air

Exp.	Catalyst	[Co], mM	HMF, M	Temp, °C	Time, h	HMF, conv. %	DFF select. %	DFF, yield %
1	Co/Mn/Br/Zr	3.44	0.375	50	2	60.4	66.6	40.2
2	Co/Mn/Br/Zr	6.82	0.372	50	2	69.2	65.3	45.2
3	Co/Mn/Br	3.44	0.375	50	2	60.6	38.4	23.3
4	Co/Mn/Br	6.82	0.377	50	2	61.7	54.6	33.7
5	Co/Mn/Br/Zr	3.44	0.375	75	2	82.5	73.2	60.4
6	Co/Mn/Br/Zr	6.82	0.375	75	2	99.7	61.6	61.4
7	Co/Mn/Br/Zr	6.82	1.12	75	2	74.1(1.0)	67.5(1.4)	49.9(0.6)
8	Co/Mn/Br	3.44	0.377	75	2	71	54.3	38.6
9	Co/Mn/Br	6.82	0.377	75	2	92.2	68.3	63.0

Table 3. Oxidation of hydromethylfurfural to 2-carboxy-4-formylfuran (CFF) and furan-2,5-dicarboxyfuran (FDA) at 70 bar air

| Exp.	catalyst	[Co], mM	[HMF], M	temp, C	time, h	CFF, mol %	FDA, mol %
1	Co/Mn/Br/Zr	3.44	0.377	100	2	3.1	18.7
2	Co/Mn/Br/Zr	3.44	0.371	125	2	2.1	36.5
3	Co/Mn/Br	3.44	0.377	100	2	4.1	29.7
4	Co/Mn/Br	3.44	0.374	125	2	1.8	35.2
5	Co/Mn/Br/Zr	3.44	0.758	50, 125	1, 2	1.6	28.3
6	Co/Mn/Br/Zr	6.82	0.753	50, 125	1, 2	2.5	28.1
7	Co/Mn/Br/Zr	13.7	0.749	50, 125	1, 2	0.0	55.4
8	Co/Mn/Br/Zr	20.5	0.755	50, 125	1, 2	0.0, 0.0	58.4, 63.1
9	Co/Mn/Br/Zr	3.41	0.781	125	3	1.7	27.7
10	Co/Mn/Br/Zr	6.82	0.774	125	3	0.0	41.6
11	Co/Mn/Br/Zr	13.7	0.0753	125	3	0.0	54.6
12	Co/Mn/Br/Zr	20.5	0.768	125	3	0.0, 0.0	60.9, 58.6
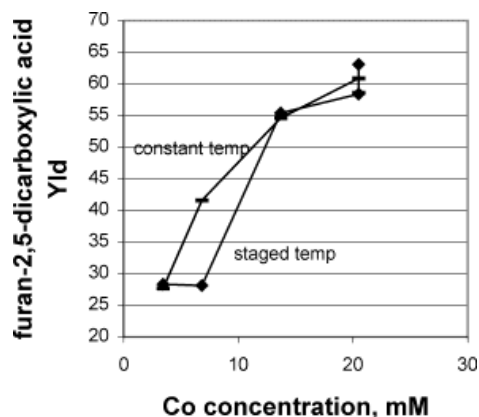
Figure 7. Effect of catalyst concentration and temperature staging on FDA yield. See details in Table 3.

# Discussion

General Considerations

The reaction network in Figure 1 is consistent with the detailed studies of the oxidation reactions of many substituted methylaromatic species, aromatic alcohols, and benzaldehydes using metal/bromide catalysts.[19] The latter is thought to operate via a modified free radical chain mechanism (see below). The free radical chain mechanism gives the oxidizability of toluene, benzyl alcohol, and benzaldehyde as 0.05, 0.85, and 290 respectively.[22] It is clear from these values that the steady state concentration of benzaldehyde is *expected* to remain low in metal/bromide catalyzed systems. We find however that the oxygenation of HMF gives preferentially DFF rather than 5-(hydroxymethyl)furan-2-carboxylic acid (compare steps 1 and 2 on Figure 1). Extending this work to benzyl alcohol gave even higher yields and selectivity to aldehydes. The kinetics of the Co/Br catalyzed oxygenation of benzyl alcohol has been reported[23] albeit without a comment on potentially high selectivities and yields of benzaldehyde.

The advantages of the catalytic oxidation described herein is that the catalyst is composed of inexpensive, simple metal acetate salts and a source of ionic bromide (NaBr, HBr, etc.). The reaction times are within a few hours at easily accessible temperatures. The acetic acid solvent is inexpensive and nearly all alcohols are highly soluble in it. Although acetoxylation of the alcohols with the acetic acid solvent does occur, this side-reaction results in only a 5–8% yield loss. It is noteworthy that there are other solvents available for metal/bromide catalyzed systems, which could potentially eliminate this problem.[19] Due to the high activity of the metal/bromide catalysts the aldehyde formed in high yield can undergo further oxidation. To obtain high yields of aromatic benzaldehydes from

the corresponding aromatic alcohols the catalytic process should be carefully monitored, so that subsequent oxidation of the aldehyde formed can be avoided.

Structure of the Catalyst

Addition of the simple acetate salts into acetic acid results in a complex mixture which is only partially understood. A brief synopsis based on available information follows. The structures of Co(II) and Mn(II) in acetic acid/water mixtures can be summarized by the equation:

$$[M(HOAc)_4(OAc)_2]_n \xrightleftharpoons{+\ HOAc} \{[M(HOAc)_5(OAc)](OAc)\}_n$$
$$n = 1, 2$$
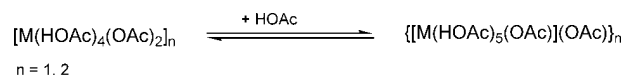
where the square brackets indicate the ligands in the inner coordination sphere. In acetic acid, the cationic metal species are largely associated, with the small quantities of the dissociated species existing as ion pairs[24] in both monomeric and dimeric forms (n = 1, 2).[25–27] Upon addition of water, equilibrium is established between various metal aquo acetic acid complexes. Using reported equilibrium constants[28] one can calculate the distribution of these complexes and demonstrate that these aquo/acetic acid metal species exist in 10% water/acetic acid mixtures.[29] The weakly bound AcOH ligand (5.9 kcal/mol) is labile, exchanging with water and acetic acid instantaneously at room temperature.[30] The addition of peracids, peroxy radicals, oxygenated intermediates, etc. to a mixture of Co(II)/Mn(II) in acetic acid may therefore result in fast ligand exchange to form the transient catalytic species. Addition of hydrogen bromide to Co(II) or Mn(II) or a Co(II)/Mn(II) mixture in anhydrous acetic acid results in the majority of the bromide being coordinated to the metal. However, addition of water (5% or greater) results in almost complete ionization of the M–Br bond.[29] In the presence of water the addition of bromide results in outer-sphere ligand exchange processes, as shown in the equation below.

$$\{[M(HOAc)_m(H_2O)_{m\ 5}(OAc)]_n(OAc)\}\ +\ \{H^+Br^-\} \longrightarrow$$

$$\{[M(HOAc)_m(H_2O)_{m-5}(OAc)]_n(Br)\}\ +\ HOAc$$
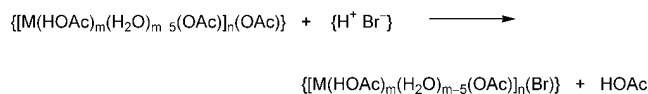
It is possible that the ion-paired bromide forms hydrogen bonds to the aquo ligands (Figure 8, structure b). The lability of the ligands, the known dimeric structure of Co(II) acetate, and polynuclearity of Zr(IV) in water suggests that polynuclear Co(II)–Mn(II) and Co(II)–Zr(IV)–Mn(II) may exist (Figure 8). Such mixed-metal polymeric species have been isolated from acetic acid.[51] Recent observations[32] suggest that acetic acid/water solutions may be more complex, containing water-rich microphases. It is proposed that Co(III) aquo

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