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Iron catalyzed oxidation of benzylic alcohols to benzoic acids

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The bidentate *N*,*O*-ligands phenol-pyrazole (**HL1**), naphthol-pyrazole (**HL2**) and the commercially available ligand 5methylphenol-benzotriazole (**HL3**) were used for the synthesis of novel iron(III) complexes. The mononuclear iron complexes [FeCl(**L1**)₂] (**1**), [FeCl(**L2**)₂] (**2**) and [FeCl(**L3**)₂] (**3**) are stable to air and moisture, both in the solid state as well as in solution, while the dinuclear, μ -oxido bridged complex [{Fe(**L1**)₂}₂(μ -O)] (**1a**) is air sensitive. All four complexes **1**, **2**, **3** and **1a** were investigated for their catalytic activity in the direct one-pot oxidation of primary alcohols to carbonic acids with 30% aq. hydrogen peroxide (H₂O₂) as the oxidation agent. The activity in oxidation reactions of the isolated, mononuclear complexes **1-3** was further compared to their *in situ* prepared analogues **IS1-3**. Experimentally obtained results indicate a tendency of higher activity for the oxidation of primary alcohols for the *in situ* prepared complexes. In conclusion, the oxidation of aromatic primary alcohols to carboxylic acids using isolated iron(III) complexes and *in situ* generated complexes in the presence of H₂O₂ results in good to high yields. The reaction is straight-forward, clean and generates water as the only by-product.

Introduction

Iron is one of the most versatile metal centers in the arsenal of transition metals, possesses several stable oxidation states and allows various coordination geometries by ligands that make it an interesting target for chemical applications. An excellent review article summarizing the development of iron catalysis written by Bolm et al. in 2004 triggered an enormous surge in research.¹ Today, iron catalysis has reached applications in virtual all fields of homogeneous catalysis. Such catalysts are particularly interesting considering that iron is cheap, nontoxic, readily available and rich in oxidation states.² Since 2004 significant improvements were made in the field of iron catalysis, which is evident by the recent publication of a 218 page review article in *Chemical Reviews*.³ One important reaction in chemistry is the oxidation of chemical compounds that is widely used in the laboratory as well as on industrial scale.^{4,5} Especially the selective oxidation of alcohols into their carbonyl derivatives (Scheme 1) is a fundamental reaction in the pool of oxidation reactions.⁶ Specifically the selective cascade oxidation of alcohols to carbonyl compounds is attractive because the desired molecules can be directly synthesized in one-pot sequences (e.g. primary alcohols \rightarrow aldehydes \rightarrow carboxylic acids; secondary alcohols ketones \rightarrow esters; cycloalkanols \rightarrow cycloalkanones \rightarrow lactones or α , β -enones, etc).^{7,8}



Scheme 1. Cascade oxidation of alcohols

The direct conversion of primary alcohols to carboxylic acid is still a challenging task to achieve.⁸ Traditionally, alcohol oxidation methods require stoichiometric amounts of chromium- or manganese-based compounds and chlorinated solvents, that are hazardous materials requiring special disposal procedures.⁹ Efficient methods to achieve this transformation are the Jones oxidation (CrO₃/H₂SO₄), the RuCl₃/H₅IO₆ protocol, TEMPO-catalyzed reactions based oxidation conditions (e.g. with sodium hypochlorite NaOCl, or bleach) or other chromium- or ruthenium-based methods like CrO₃/H₅IO₆.¹⁰ Using the Jones reagent is the least favorable protocol to catalyze this transformation, because CrO₃ is generally known to be very toxic and carcinogenic. Compared to the Jones oxidation, the Swern oxidation is a good alternative, although it involves a two-step process followed by the oxidation of the resulting aldehyde to the carboxylic acid.

Several metal catalysts including palladium, copper, ruthenium, and cobalt have been developed for the oxidation of alcohols using environmental friendly oxidants like H_2O_2 and O_2 .^{9,11} While alcohol oxidations catalyzed by iron complexes have also been investigated in detail, there is no generally applicable protocol available and therefore research in this field is still ongoing. Nevertheless, the one-pot cascade transformation of alcohols directly to carboxylic acids is still a relatively uninvestigated field of chemistry.^{5,12,13,14} In 1969 Welch *et al.* published the oxidation of primary alcohols to

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carboxylic acids (based on the previous developed procedure of Pappo and Becker)¹⁵ by using a catalytic amount of RuO₄ in presence of NaIO₄ as secondary oxidant during the preparation of the mold metabolite culmorin.¹⁶ Sharpless *et al.* reported in 1981 a single example of the oxidation of a primary alcohol to the corresponding carboxylic acid. The so called "Sharpless modification" of the method by Pappo and Becker very quickly found widespread use in the transformation of primary alcohols to carboxylic acids.¹⁷ A more recent example for an improvement of the "Sharpless modification" is found in the work of Prashad et al. A simple substitution of CCl₄ with EtOAc allows the isolation of the carboxylic acid in higher yield (80% to 93% yield), with the advantage of using less toxic solvent.¹⁸ The group of Grützmacher published several examples of coupling reactions of primary alcohols with water giving carboxylic acids.¹⁹ In 2013 the group of Milstein reported a Ru(III) complex that was able to catalytically oxidize alcohols to carboxylic acids in water under basic conditions without the need of an oxidant (Scheme 2).

$$R OH + OH = \frac{0.02 \text{ mol% [Ru]}}{H_2O, \text{ reflux}} = R OOO + 2H_2$$

Scheme 2. Milstein's one-pot oxidation of alcohols.¹⁴

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The oxygen atom being transferred originated from the solvent H_2O itself, under liberation of H_2 gas.^{14,20} Modified versions of Milstein's catalyst have since appeared.²¹ Very recently, a catalytic metal free oxidation of a homoserin residue to aspartaic acid was reported in a glycopeptide synthesis.²²

A selective iron-catalyzed one-pot oxidation of an alcohol to the respective carboxylic acid under mild conditions with H_2O_2 has not been published so far. However, other metals have shown to be able to convert benzyl alcohol to benzoic acid under mild, green conditions. In 2003 Punniyamurthy *et al.* reported on a cobalt(II)-catalyzed system for the oxidation of alcohols into carboxylic acids and ketones with hydrogen peroxide. After 6-9 hours of reaction time a yield of about 70 to 75% of carboxylic acid was obtained for the transformation of various primary alcohol substrates. To achieve these yields a relatively high amount of H_2O_2 (up to 20 equiv.) was needed. This complex was able to oxidize benzyl alcohol to benzoic acid with a yield of 76% as shown in Scheme 3.¹³



Scheme 3. Cobalt(II) catalyzed oxidation of alcohols.¹³

The ligands **HL1-3** were chosen based on the structure of an [Fe(III)-salen]Cl complex, that is a widely used iron complex in various fields of chemistry (Grignard-catalyzed cross-coupling, oxidation, enzyme models, magnetic materials etc.) (Figure 1).²³ We intended to synthesize new iron complexes with a similar *ONNO*-coordination sphere as in the [Fe(III)-salen]Cl complex, but using two bidentate ligands instead. We

reasoned that the coordination of two bidentate ligands instead of one rigid tetradentate ligand like salen could lead to a more flexible coordination sphere resulting in different, advantageous catalytic properties.



Figure 1. Bidenate N,O-ligands used in this study.

Results and discussion

Synthetic procedures

Aryloxide ligands with a pyrazol-3-yl-bonded moiety (HL1 and HL2) were prepared according to literature procedures.²⁴ The triazole-1-yl-bonded ligand HL3 is commercially available and was used as received (Figure 1). HL1 and HL2 were successfully used in our group for the synthesis of oxido-rhenium(V) and dioxido-molybdenum(VI) complexes and their application as catalysts for olefin epoxidation reactions.²⁵ Both metal complexes showed moderate to high yields with excellent selectivities towards to the epoxidation of cis-cyclooctene. The iron complexes [FeCl(L1-3)₂] (1, 2 and 3) were synthesized by the addition of the respective ligands HL1-HL3 to a solution of FeCl₃·6H₂O under the reaction condition shown in Scheme 4. Upon cooling complexes 1-3 precipitated from the reaction solution and were isolated by filtration. After washing with cold H₂O, EtOH and Et₂O they were isolated as dark blue to green powders in 58-71% yield. In the solid state the complexes can be stored under ambient conditions without any sign of decomposition for several months, whereas in CH₃CN solution after several days decomposition occurs. All complexes are nearly insoluble in apolar solvents (e.g. pentane, hexanes), poorly soluble in medium polar solvents (e.g. toluene) and sparingly soluble in polar solvents (e.g. MeOH, CH₃CN and CHCl₃). The elemental analyses of all three complexes were in good agreement with their predicted values. The molecular structure of 1 was confirmed by X-ray diffraction analysis (vide infra).



Scheme 4. Preparation of mononuclear iron complexes 1-3.

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In an attempt to obtain iron(II) complexes, the reaction of FeCl₂ with these ligands in absolute ethanol under inert atmosphere was investigated. With HL1 a light red precipitate could be isolated in 74% yield that analyzed in good agreement with the dinuclear complex [{Fe(L1)₂}₂(μ -O)] (1a) (Scheme 5). Recrystallization from DMSO led to single crystals suitable for X-ray diffraction analysis confirming the dinuclear nature of the complex 1a as displayed in Scheme 5 and Figure 3. Thus, under the employed reaction conditions oxidation occurred to an iron(III) complex. In the solid state 1a is far less stable compared to 1 as it decomposes after approx. 2 h under ambient conditions to unidentified products. Complex 1a is well soluble in strong polar solvents (e.g. MeOH, CH₃CN and CHCl₃) and can be stored in dry DMSO solution for several weeks if kept under nitrogen. The source of the oxygen atom is as yet unclear. The high yield hints towards residual water in the pre-dried ethanol. When ligands HL2 and HL3 were reacted with FeCl₂ under the same conditions, no identifiable products formed.



Scheme 5. Synthesis of dinuclear iron complex 1a.

Magnetic susceptibility

All four complexes **1**, **1a**, **2** and **3** contain a paramagnetic highspin iron center. The magnetic moments were experimentally determined with the help of a magnetic susceptibility balance (see Experimental Section). The number of unpaired electrons was calculated by applying the spin-only formula.²⁶ Data is summarized in Table 1. In case of the mononuclear complexes **1-3** the determined numbers of unpaired electrons agree quite well with the expected 5 unpaired electrons for a high-spin d⁵ metal center and definitively rules out a low-spin configuration. For the dinuclear complex **1a** a value of 3.89 unpaired electrons for both iron centers was experimentally determined indicating antiferromagnetic coupling via the oxygen bridge.²⁷

Complex	μeff	experimental
		no. of unpaired electrons
1	6.09	5
1a	4.79 ^a	3.89 ^ª
2	6.10	5
3	5.27	5

^a antiferromagnetic coupling in the dinuclear species

Molecular structures of complexes 1 and 1a

The molecular structures of complex **1** and **1a** were determined by single crystal X-ray diffraction analysis. Single crystals of **1** were obtained by slow evaporation of an acetone solution at room temperature and for **1a** by slow evaporation

from a concentrated solution in DMSO at room temperature. Molecular views for **1** and **1a** are displayed in Figure 2 and Figure 3, selected bond angles and lengths are given in Table 2, crystallographic data and refinement parameters can be found in the SI.



Figure 2. Molecular view of the mononuclear complex **1** showing the numbering scheme of the non-carbon atoms. Hydrogen atoms have been omitted for clarity.



Figure 3. Molecular view of the dinuclear complex **1a** showing the numbering scheme of the non-carbon atoms. Hydrogen atoms have been omitted for clarity.

Table 2. Selected bond lengths (Å) and angles (°) of compounds 1 and 1a

	1	1a	1a		
		Fe1 fragment	Fe2 fragment		
Fe1-Cl1/O1	2.2703(3)	1.7898(11)	Fe2-01	1.7893(11)	
Fe1-O21	1.8630(9)	1.9098(11)	Fe2-O61	1.8993(11)	
Fe1-O41	1.8583(8)	1.8986(11)	Fe2-081	1.9094(11)	
Fe1-N12	2.1201(9)	2.1531(13)	Fe2-N52	2.1273(13)	
Fe1-N32	2.1309(9)	2.1246(13)	Fe2-N72	2.1580(13)	
Fe1-O1-Fe2	-	179.86(9)	-	-	
N12-Fe1-N32	170.68(4)	172.76(5)	N52-Fe2-N72	172.41(5)	
021-Fe1-041	125.49(4)	120.59(5)	061-Fe2-081	119.45(5)	

Complex 1 shows a trigonal-bipyramidal coordination with small deviations from ideal geometry of the iron atom with the N atoms in axial positions (N12–Fe1–N32 170.68(4)°, O41–Fe1–O21 125.49(4)°, O21–Fe1–Cl1 119.59(3)°, O41–Fe1–Cl1 114.91(3)°). All the other bond lengths and angels compare well with previously published, fivefold coordinated iron(III) complexes equipped with bidentate *N*,*O*-ligands.^{27,28}

Complex **1a** shows approx. D_2 symmetry, with the Fe atoms having trigonal-bipyramidal surroundings (N12–Fe1–N32 172.76(5)Å, N52–Fe2–N72 172.41(5)Å) and are connected by a linear O bridge (O1–Fe1 1.7898(11)Å, O1–Fe2 1.7893(11)Å; Fe1–O1–Fe2 179.86(9)°). Dinuclear μ -oxido iron(III) complexes

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of the type [L₂Fe-O-FeL₂] with four bidentate ligands are rather scarce in literature.^{27,29,30} The almost ideal linear arrangement of the Fe-O-Fe core (179.86(9)°) in **1a** indicates the low steric bulk of ligand moiety **L1**, which otherwise has been shown to cause significant distortion from linearity (135-180°).³⁰ Also the lack of a sixth ligand in the solid state structure of **1**, where often an H₂O molecule is coordinated, points to an excellent Lewis basicity of the pyrazole moiety in ligand **L1**. The small steric bulk in combination with the excellent donor capabilities of ligand **HL1**, as deduced from the solid state structures, might explain the unusual catalytic activity in oxidations reactions of complexes **1-3**.

Oxidation of alcohols

Complexes **1**, **2** and **3**, their *in situ* generated analogues **IS1–IS3** as well as the dinuclear complex **1a** were screened in the catalytic direct one-pot synthesis of carboxylic acids from three different benzylic alcohol substrates (**S1-S3**) using H_2O_2 as oxidizing agent (Scheme 6).



Scheme 6. General scheme of the direct one-pot synthesis of carboxylic acids

The oxidation of benzyl alcohol (PhCH₂OH) to benzaldehyde (PhCHO) and benzoic acid (PhCOOH) was chosen as benchmark reaction for the oxidation of alcohols. Because ligand HL3 is commercially available complex 3 was used for the optimization of the reaction conditions with respect to the addition time of H₂O₂, loading of H₂O₂, solvent, total volume of the solvent and catalyst loading. The best activity was observed with 6 equiv. of H_2O_2 (with respect to substrate) with an addition time of 80 min via syringe pump and a catalyst loading of 4 mol% in a total of 2 mL CH₃CN. Thus, standard conditions for all catalytic experiments were 2 mL of CH₃CN with 4 mol% of catalyst 1, 2 and 3 and 6 equiv. H₂O₂ added over a period of 80 min at 70 °C, unless stated otherwise. For the dinuclear complex 1a both 2 and 4 mol% of catalyst loading were used, in order to test if only one or both Fe centers become active catalysts. Oxidation reactions with in situ generated complexes IS1-IS3 were also performed under the same conditions by simply mixing the required amounts of FeCl₃·6H₂O and ligands HL1-HL3 (Scheme 6). For further investigations of the reaction kinetics benzaldehyde (PhCHO, S4) was also screened as substrate (vide infra). Apart from the desired product (carboxylic acid) and the corresponding aldehyde (in some cases up to 25%, e.g. in Table 4, entry 13) no other side products were detected in oxidation reactions of substrates S1-S3. A summary of all yields can be found in Table 6.

The oxidation of **S1** is catalyzed by isolated complexes **1**, **1a**, **2** and **3** (Table 4, entries 1, 2, 5 and 7) as well as by using *in situ* generated systems **IS1-IS3** (Table 3, entries 4, 6 and 8) with various yields of acid (31-94%) and high selectivities (>96%). Complete overview of the data is given in Table 4. No side-products were observed during the catalysis reaction, only remaining alcohol, the intermediate aldehyde and the resulting acid were detected.

Table 3. Iron-catalyzed	l oxidation o	of S1	with	H_2O_2
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Entry	Cat.	Conv. ^a	Acid ^a	Aldehyd ^a	Select. ^b
		[%]	[%]	[%]	[%]
1	1	91	81	10	89
2	1a	56	31	25	55
3°	1a	79	56	23	71
4	IS1	97	93	4	96
5	2	93	86	7	92
6	IS2	96	94	2	98
7	3	95	89	6	94
8	183	97	93	4	96
9	-	0	0	0	0
10 ^d	1	0	0	0	0
11	FeCl ₃ · 6H ₂ O	0	0	0	0
Lit.13	[Co]	-	76	-	-

^a Conversion and yield were determined by HPLC analysis. ^b Selectivity refers to benzoic acid. ^c 4 mol% of **1a** was used. ^d no hydrogen peroxide was added.

The highest yield of benzoic acid (94%) with an excellent selectivity (98%) for the oxidation of **S1** was obtained by using the in situ system IS2 (Table 3, entry 6). The oxidation with the analogous isolated complex 2 (Table 3, entry 5) yielded 86% of benzoic acid with a 92% selectivity. Comparison of mononuclear complex 1 to dinuclear 1a (Table 3, entries 1, 2 and 3) indicates that only one Fe center in 1a becomes an active catalyst. At 2 mol% catalyst loading of 1a the yield of benzoic acid is only 31%, at 4 mol% loading the yield increases to 56%. Nevertheless this is still far below the yield with 1 (81%). The in situ generated analogue IS1 showed a better catalytic activity with a yield of acid of 93% with a high selectivity (Table 3, entry 4). In general, in situ systems (Table 3, entries 4, 6 and 8) showed higher catalytic activities than their isolated analogues in the oxidation of S1 (Table 3, entries 1, 3, 5 and 7). In order to obtain more mechanistic information the kinetic conversion profile of substrate S1 was investigated with catalyst 3. As seen in Figure 4 the oxidation of S1 to aldehyde and acid occurs at essentially the same rate within the first ten minutes, without an induction time. The detected amount of the intermediate aldehyde confirms the initial oxidation of S1 to benzaldehyde. From 10 to 25 minutes, the amount of PhCHO remains roughly constant while the concentration of product PhCOOH steadily increases. Because the second oxidation from PhCHO to PhCOOH occurs at the same rate as the oxidation of S1 to PhCHO, this first oxidation step could therefore represent the rate determining step.

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Figure 4. Oxidation of ${\bf S1}$ showing the concomitant formation of acid and aldehyde; 1 mmol substrate, 4 mol% ${\bf 3}$, 6 equiv. H_2O_2, 70 °C, 2 mL CH_3CN.

The oxidation of **S2** is catalyzed by both the isolated complexes **1**, **1a**, **2** and **3** (Table 5, entries 14, 15, 17 and 19) as well as by using *in situ* generated systems **IS1-IS3** (Table 5, entries 16, 18 and 20) in good to high yields (58-96%) with good selectivities for the mononuclear catalysts (83-98%).

Table 4. Iron-catalyzed oxidation of $\ensuremath{\text{S2}}$ with $\ensuremath{\text{H}_2\text{O}_2}$

Entry	Cat.	Conv.ª [%]	Acid ^a [%]	Aldehyde ^a [%]	Select. ^b [%]
12	1	93	77	16	83
13 ^c	1 a	83	58	25	70
14	IS1	98	96	2	98
15	2	93	80	13	86
16	IS2	98	95	3	97
17	3	96	90	4	94
18	IS3	98	95	3	97
Lit.13	[Co]	-	74	-	-

 a Conversion and yield were determined by HPCL analysis. b Selectivity refers to benzoic acid. c 0.02 mmol of 1a was used.

Compared to the oxidation of **S1**, **S2** behaves quite similar. The highest yield of 4-chlorobenzoic acid (96%) with a high selectivity (98%) was obtained by using the *in situ* system **IS1** (Table 4, entry 14). The oxidation with the isolated mononuclear analogue **1** (Table 4, entry 12) yielded 77% of the acid with slightly reduced selectivity (83%). The dinuclear iron complex **1a** (Table 4, entry 13) again showed the lowest activity and selectivity (58% yield acid, 70% selectivity). *In situ* generated catalysts (Table 4, entries 14, 16 and 18) showed higher activities as well as higher selectivities towards the formation of the acid than their isolated analogues (Table 4, entries 12, 13, 15 and 17).

The oxidation of **S3** is again catalyzed by all four isolated complexes **1**, **1a**, **2** and **3** (Table 5, entries 19, 20, 22 and 24) as well as by using *in situ* generated systems **IS1-IS3** (Table 5, entries 21, 23 and 25) in good yields to high yields (61-86%) with high selectivities (83-92%).

Table 5. Iron-catalyzed oxidation of $\mathbf{S3}$ with H_2O_2

Entry	Cat.	Conv. ^a [%]	Acid ^a [%]	Aldehyde ^a [%]	Select. ^b [%]
19	1	90	76	14	84
20 ^c	1a	83	61	22	75
21	IS1	93	86	7	92
22	2	84	70	16	83
23	IS2	94	86	8	91
24	3	93	84	9	90
25	IS3	92	80	12	87
Lit.13	[Co]	-	74	-	-

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 $^{\rm a}$ Conversion and yield were determined by HPCL analysis. $^{\rm b}$ Selectivity refers to benzoic acid. $^{\rm c}$ 0.02 mmol of 1a was used.

Again the highest yield of the corresponding acid (86%) with the best selectivity (92%) was obtained by using the *in situ* systems **IS1** and **IS2** (Table 5, entries 21 and 23). Similar to the oxidation of substrates **S1** and **S2** the oxidation of **S3** with the isolated mononuclear complex **1** (Table 5, entry 19) lower yields of the acid (76%) in contrast to the *in situ* system **IS1** were obtained. Again the dinuclear iron complex **1a** (Table 5, entry 20) resulted in lowest yield of the corresponding carboxylic acid (61%). In contrast to previous results of **S1** and **S2** the isolated analogue **3** showed a more less similar catalytic activity and selectivity than the *in situ* generated system **IS3** (Table 5, entries 24 and 25). The other two *in situ* generated systems **IS1** and **IS2** (Table 5, entries 21 and 23) were showing higher catalytic activities than their isolated analogues **1** and **2** (Table 5, entries 19, 20 and 22).

It is known that iron complexes are capable of decompose H_2O_2 forming OH' radicals (Fenton chemistry).³¹ Such radical based reactions lead to low selectivities and result in undefined polymeric materials. In our case the mononuclear complexes **1-3** as well as their *in situ* generated analogues **IS1-3** showed high selectivities for the two oxidation products, without any other side products being detected. Therefore a radical pathway seems unlikely during the oxidation of the substrates **S1-S3**.

The results with in situ generated complexes as well as with the isolated complexes are better than those with the best previously described cobalt-based system of Punniyamurthy et al. with H₂O₂ as the terminal oxidant, as less oxidant and shorter reaction times were required.¹³ For the cobalt-based system 6-9 hours reaction time and high amounts of the oxidant H₂O₂ (20 equiv.) were required. In the benchmark reaction of benzyl alcohol S1 the catalytic system of Punniyamurthy et al. was able to oxidize S1 to benzoic acid in 81-95% yield vs. 76% (Table 6). Furthermore, our catalytic system has the added value of using non-toxic iron instead of cobalt. It was also demonstrated that the oxygen bridged diiron complex 1a is able to catalyze to formation of the acid from primary alcohols, albeit with lowest activities and selectivities of all tested complexes (Table 6). In case of HL1 based systems the catalytic activity decreases from in situ prepared complex IS1 to isolated iron complex 1 for all three

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substrates (Table 6). Interestingly the pyrazole based complexes 1 and 2 showed significantly lower catalytic activities compared to their in situ generated analogues IS1 and IS2, whereas the difference in activity is less pronounced for the triazole based systems 3 and IS3 (Table 6). Comparing the activities for all substrates S1-S3 of all isolated complexes 1, 1a, 2 and 3, complex 3 equipped with a triazole based ligand is the most effective in the oxidation of alcohol substrates (Table 6). The investigation of S2, that contains an electron withdrawing chloro substituent in para-position, showed a slightly higher yield of the corresponding acid compared to the oxidation of S1 (Table 6). However, for substrate S3, that contains an even more electron withdrawing -NO2 group in para-position, a slight decrease in conversion of alcohol compared to the overall conversion of S1 and S2, respectively (Table 6) is observed. Therefore the functional group located in para-position to the alcohol in the phenyl ring of the substrate does have an effect on the catalytically activity of the systems used. However more substrates with different functional groups would have to be tested to establish a trend. The better catalytic activities of the in situ generated complexes IS1 and IS2 compared to 1 and 2 could be explained by the possible formation of different, more active iron species present in solution. The catalytically active species is in all systems as yet unclear as complexes 1, 1a, 2 and 3 are only pre-catalysts. However, it seems likely that the in situ formed catalysts of the systems IS1 and IS2 are not only comprised of the isolated complexes 1 and 1a or 2, but also consist of other catalytically active complexes that lead to higher overall activities and thus selectivity towards the acid. It is feasible that the presence of these other additional species result in higher yields if these complexes are catalytic active. Finally we also tested the aliphatic substrate 1-octene with complex 3, but did not observe any conversion to the respective aldehyde or acid.

Table 6. Summary of yields of benzoic acid

	1	2	3	IS1	IS2	IS3	[Co] ¹³	1a
S1	81	86	89	93	94	93	76	56
S2	77	80	90	96	95	95	74	58
S3	76	70	84	86	86	80	74	61

Conclusions

The oxidation of substrates **S1-S3** to their corresponding carboxylic acids is achieved by using well-characterized, isolated iron(III) complexes **1**, **1a**, **2** and **3** as well as by using their analogous *in situ* prepared complexes **IS1-IS3**. It can be concluded that in principle the synthesized iron(III) complexes **1**, **1a**, **2** and **3** and the *in situ* systems **IS1-IS3** showed better catalytic activities toward the oxidation of **S1-S3** than the best previously described cobalt-based system with hydrogen peroxide as the terminal oxidant with the added value of exhibiting more environmentally friendly reaction conditions.¹³ The oxygen-bridged dinuclear complex **1a** is the least catalytically active catalyst compared to the mononuclear iron

complexes **1-3**. An advantage of using well-characterized isolated complexes as catalysts is the defined structure of the compound that allows for mechanistic investigations. *In situ* generated catalysts may be easier to prepare and show a higher conversion of the substrate **S1-S3** with excellent activities and selectivities, but the structures of the catalytically active compounds remain unknown, providing less mechanistic and no structural information for further catalyst improvement. Future work based on these results involves the investigation of other alcoholic substrates (e.g. primary aliphatic alcohols, secondary alcohols etc.).

Experimental

General

The iron precursors FeCl₃, FeCl₃·6H₂O, FeCl₂, H₂O₂ (30% aq.) and HL3 were purchased from Sigma Aldrich and used as received. Ligands HL1 and HL2 were prepared according to literature procedures.²⁴ Chemicals were purchased from commercial sources and were used without further purification. All reactions were carried out under air unless stated otherwise. NMR spectra were recorded with a Bruker (300 MHz) instrument. Chemical shifts are given in ppm and are referenced to residual protons in the solvent. Signals are described as s (singlet), bs (broad singlet), d (doublet), dd (doublet of doublet), t (triplet), m (multiplet) and coupling constants (J) are given in Hertz (Hz). Mass spectra were recorded with an Agilent 5973 MSD-Direct Probe using the EI ionization technique. Samples for infrared spectroscopy were measured on a Bruker Optics ALPHA FT-IR Spectrometer equipped with an ATR diamond probe head. A J-Kem Scientific dual syringe pump (model 2250) in combination with a JKem Infinity Controller was used for the slow addition of the oxidation agent H₂O₂. HPLC measurements were performed on an Agilent 1200 Series Rapid Resolution LC System equipped with a ZORBAX Eclipse XDB-C18 column coupled to a diode array detector (DAD) Agilent G1315D. Susceptibility measurements were performed on a MSB Auto Magnetic Susceptibility Balance of Johnson Matthey. Elemental analyses were carried out using a Heraeus Vario Elementar automatic analyzer at the University of Technology Graz.

Catalytic oxidation reactions

Conversion and yields were determined by HPLC; the mobile phase contained a mixture of $25\% \text{ v/v} \text{ CH}_3\text{CN}$ with $75\% \text{ v/v} \text{ H}_2\text{O}$ acidified with 0.1% v/v formic acid to achieve a separation of substrates and products. The yield of products was determined via an internal standard method, where all peak areas were referenced to the area of the internal standard. The obtained products were identified by comparison of the retention times to authentic samples; the retention times as well the peak forms were in excellent agreement. The mass balance during the analysis with HPLC of the products and the substrate added up to ~100% indicating a highly selective process. The chosen internal standard was nitrobenzene, which proved to be inert under reaction conditions. No oxidation reaction took

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place in control experiments without added catalyst or oxidant H_2O_2 . Also FeCl₃ alone proved to be inactive as a catalyst.

Magnetic susceptibility measurements

The values of mass magnetic susceptibilities χ_m for the solid samples were measured under ambient conditions, corrected for diamagnetic contributions and the number of unpaired electrons calculated by the spin-only formula.²⁶ The diamagnetic correction susceptibilities of the ligands were determined to be -1.45 $\cdot 10^{.9}$ m³/mol for HL1, -1.90 $\cdot 10^{.9}$ m³/mol for HL2 and -1.80 $\cdot 10^{.9}$ m³/mol for HL3.

X-ray crystallography

X-ray crystal structure analyses were performed on a Bruker APEX2 area detector diffractometer. All measurements were performed using graphite-monochromatized Mo Ka radiation at 100K. The structure was solved by direct methods (SHELXS-97) and refined by full-matrix least-squares techniques against F2 (SHELXL-97).³² The non-hydrogen atoms were refined with anisotropic displacement parameters without any constraints. The H atoms of the pyrazole and of the phenyl rings were put at the external bisectors of the C-C-X angles at C-H distance of 0.95Å and one common isotropic displacement parameter was refined for the H atoms of the same ring. The H atoms of the methyl groups were refined with common isotropic displacement parameters for the H atoms of the same group and idealized geometries with tetrahedral angles, enabling rotation around the N-C bond, and C-H distances of 0.98 Å. Crystallographic data for 1 and 1a have been deposited with the Cambridge Crystallographic Data Centre, CCDC 1048055 and 1048056.

General procedures for catalytic one-pot oxidation

In a standard experiment the alcohol substrate (1 mmol), the internal standard nitrobenzene (1 mmol) and the respective catalyst (1, 2, 3: 4 mol%, S/C ratio = 25:1; 1a: 2 mol%, S/C ratio = 50:1) were mixed with CH₃CN (2 mL) in a Mininert[®] glass vial closed with a screw cap containing a septum. The temperature of the reaction was kept at 70 °C using a sand bath. A hydrogen peroxide solution (6 mmol, 30% w/w in H₂O) was added to initiate the reaction over a period of 80 min via a syringe pump. Samples were directly taken out of the reaction mixture, diluted, quenched with MnO₂ and analyzed via HPLC. The identity of the oxidation products was verified by comparison to commercially available chemicals. Oxidation reactions with in situ generated complexes were prepared according to the procedure above by mixing the respective amounts of FeCl₃·6H₂O and ligands HL1, HL2 or HL3. The reaction mixture was stirred for 10min at 70 °C before the addition of H₂O₂ was started. Conversions, yields and selectivities were calculated via peak integration of the chromatograms.

Synthesis of complexes

Synthesis of [FeCl(L1)₂] (1). To a solution of iron(III) chloride (0.485 g; 2.99 mmol) in H₂O (10 mL) a solution of **HL1** (1.052 g; 6.04 mmol) in MeOH (20 mL) was added. The resulting dark solution was stirred overnight at rt. The formed precipitate was separated by filtration, washed with H₂O and Et₂O and dried to give a dark powder of the iron complex **1**. Blue square shaped crystals, suitable for X-ray crystallography, were obtained after two days by slow evaporation of an acetone solution. Yield: 0.930 g (71%). EI-MS: m/z 437.2 [M⁺]. IR (ATR): v 1596, 1517, 1303, 1248, 861, 778, 751, 449 cm⁻¹. Anal. Calc. for C₂₀H₁₈CIFeN₄O₂: C, 54.88; H, 4.15; N, 12.80%. Found: C, 54.97; H, 3.99; N, 12.78%.

Synthesis of [{Fe(L1)₂**/**₂(μ -O)] (1a). This reaction was carried out under nitrogen using standard Schlenk techniques. To a solution of anhydrous iron(II) chloride (0.109 g; 0.86 mmol) in dry EtOH (3 mL) a solution of HL1 (0.301 g; 1.72 mmol) in dry EtOH (3 mL) was added, followed by dry NEt₃ (3.61 mmol, 503 μ I). The resulting dark red solution was stirred under refluxed for 1h, and after cooling to rt centrifuged. A light red precipitate was separated, washed twice with hot EtOH (7 mL) and THF and dried under vacuum to give 1a. Dark red crystals, suitable for X-ray crystallography, were obtained by slow evaporation of a concentrated DMSO solution. Yield: 0.263 g (74%). EI-MS: m/z 402.2 [M⁺ - OFe(L1)]. IR (ATR): v 1595, 1441, 1306, 834, 747 cm⁻¹. Anal. Calc. for C₄₀H₃₆ClFe₂N₈O₅: C, 58.56; H, 4.52; N, 13.66%. Found: C, 57.81; H, 4.26; N, 13.52%.

Synthesis of [FeCl(L₂)₂] (2). To a solution of iron(III) chloride (0.362 g; 2.23 mmol) in EtOH (10 mL) a solution of **HL2** (1.001 mg; 4.47 mmol) in EtOH (20 mL) was added. The resulting dark solution was stirred under reflux overnight. The formed black precipitate was filtered off, washed with H₂O and EtOH and dried to give a black powder of the iron complex **2**. Yield: 0.705 g (60%). EI-MS: m/z 537.2 [M⁺]. IR (ATR): v 1560, 1522, 1387, 1323, 790, 760, 738, 447 cm⁻¹. Anal. Calc. for C₂₈H₂₂ClFeN₄O₂: C, 62.53; H, 4.12; N, 10.42%. Found: C, 62.44; H, 4.07; N, 10.28%.

Synthesis of [FeCl(L3)₂] (3). Ligand **HL3** (2.048 g; 9.09 mmol) was dissolved in acetonitrile (20 mL) with gentle heating. A solution of iron(III) chloride (0.738 g; 4.55 mmol) and NEt₃ (0.835 g; 8.25 mmol) in acetonitrile (20 mL) was prepared and heated to 50 °C. To this iron precursor solution the hot ligand solution was quickly added and the resulting mixture was stirred overnight at 50 °C. The formed precipitate was filtered off, washed with H₂O and Et₂O and dried to give a greenish-black powder of iron complex **3**. Yield: 1.433 g (58%). El-MS: m/z 539.2 [M+]. IR (ATR): v 1560, 1523, 1489, 1387, 1322, 1236, 1081, 891, 790, 760, 447 cm⁻¹. IR: 1492, 1302, 806, 739, 531, 434 cm⁻¹. Anal. Calc. for C₂₇H₂₀CIFeN₆O₂: C, 57.85; H, 3.73; N, 15.57%. Found: C, 57.61; H, 3.63; N, 15.61%.

Conflicts of interest

There are no conflicts to declare.

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Direct, one-pot oxidation of benzyl alcohols to benzoic acid with H_2O_2 catalyzed by Fe(III) complexes.