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Novel terpyridine-manganese(II) complexes and their potential to activate hydrogen peroxide

Torsten Wieprecht, Juntao Xia, Uwe Heinz, Josef Dannacher, Gunther Schlingloff*

Ciba Specialty Chemicals Inc., P.O. Box 1266, D-79630 Grenzach-Wyhlen, Germany

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Abstract

The ability of manganese(II) complexes with substituted terpyridine (terpy) ligands to activate hydrogen peroxide and to catalyze oxidation of the substrates Morin and Trolox C was studied in aqueous alkaline solution. Introduction of π-donor substituents as hydroxy or amine groups in the 4-positions of the pyridine rings resulted in an enhanced catalytic activity compared to the unsubstituted terpyridine-manganese(II) complex. However, the catalytic activity depends critically on the substitution pattern. Differences in the activity of catalysts towards Morin and Trolox C are discussed with respect to the mechanism of oxidation. Dissolution of isolated complexes with a ligand-to-manganese ratio of 1:1 in aqueous buffer results in formation of a mixture of 1:1 and 2:1 species. The 1:1 species was found to be the catalytically more active precursor, suggesting that free coordination sites are important for a high catalytic activity. Activity was found to be pH dependent and was highest at pH ∼10. All complexes also catalyze the disproportionation of hydrogen peroxide into oxygen and water.

Keywords: Catalysis; Oxidation; Hydrogen peroxide; Morin; Terpyridines

1. Introduction

Hydrogen peroxide and even more so, molecular oxygen are rightly considered to be the oxidants of choice for a wide range of oxidation reactions. Unfortunately, their activity is kinetically hindered under many experimental conditions, although both are potent oxidants in a thermodynamic sense. Besides the development of atom efficient processes with heterogeneous catalysts in the production of bulk chemicals, mainly with molecular oxygen as the ultimate oxidant, the design and development of soluble transition metal complexes, which are able to effectively catalyze substrate oxidation by hydrogen peroxide or molecular oxygen, has been fascinating the scientific community for decades [1–5]. The optimism about finding effective catalysts originates in the existence of numerous enzymes, which are able to activate these very oxidants [6]. Many studies exist, describing the design of complexes between transition metals and organic ligands, which structurally mimic the putative active centers of redox-active enzymes [1,2,7,8]. Moreover, model complexes have successfully been developed, possessing some potential in activating hydrogen peroxide or molecular oxygen [3,4,7,9].

Apart from its use in organic synthesis, industry is looking for hydrogen peroxide activating catalysts for a variety of other applications. Oxidation catalysts are of fundamental interest for “destructive” bleach processes, which consume the vast majority of the

* Corresponding author. Tel.: +49-7624-12-2830; fax: +49-7624-12-2885.
E-mail address: gunther.schlingloff@cibasc.com (G. Schlingloff).

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hydrogen peroxide produced worldwide [10]. Bleach processes, i.e. the oxidation and destruction of chromophores are, for example, of great importance for the pulp and paper industry, the textile industry as well as the detergent industry. From the environmental point of view complexes with iron or manganese are highly preferred, with the latter of the two having by far the richer redox chemistry. However, the application of such catalysts is often hampered by low activity and stability under the specific conditions of bleach processes (aqueous medium, high pH and elevated temperature). A problem often connected with metal complexes having organic ligands is auto-catalyzed ligand oxidation [11]. Furthermore, the existence of a thermodynamic sink, i.e. the preferred formation of insoluble metal hydroxides or oxides, limits the use of many complexes under alkaline pH. To date, only a few catalysts meet the requirements of retaining activity and stability under the aforementioned harsh reaction conditions [4]. The most prominent examples are manganese complexes derived from the ligand 1,4,7-trimethyl-1,4,7-triazacyclononane (TMTACN) [4]. Manganese complexes with TMTACN and related ligands are very potent oxidation catalysts not only in the household application of stain bleaching in laundry but also in a variety of model oxidation processes, such as oxidation of phenols [12], epoxidation [4,13–15] and dihydroxylation [16] of alkenes, C–H activation [17] and oxidation of azo-dyes [18]. For this family of catalysts, the involvement of high-valent, mono- or di-nuclear active species including species bearing μ-oxo bridged groups has been suggested to be crucial for catalytic activity [4,12,19].

Recently, high-valent manganese complexes of 2,2′:6′,2″ terpyridine (terpy) have emerged as potential oxidation catalysts [20–23]. Among others, the di-μ-oxo bridged Mn dimer $[(H_2O)terpyMn(III)(\mu\text{-}O)_2Mn(IV)terpy(H_2O)](NO_3)_3$ was synthesized in order to mimic the active center of the oxygen-evolving center of photosystem II [20,21]. The complex was shown to exert catalytic activity in aqueous solution in the presence of hypochlorite or peroxymonosulfate as oxidants [21,22]. However, catalytic activity in the presence of hydrogen peroxide as an oxidant has not yet been reported.

These findings prompted us to investigate complexes of the terpyridine family as potential catalysts for oxidation reactions with hydrogen peroxide as oxidant. A concise synthesis was developed, which enables the preparation of substituted terpyridines in multigram amounts. Studies of the oxidation of model substrates (Morin and Trolox C) by hydrogen peroxide in the presence of the respective manganese(II) complexes were carried out in order to assess their potential in catalytic oxidation reactions. Our results show that the catalytic activity is greatly enhanced by the presence of π-electron donor groups and can effectively be modulated by the substitution pattern. Complex equilibria were studied under conditions of model substrate oxidation and it was found that 2:1 and 1:1 complex species (ligand-to-Mn) coexist in solution. The dependence of the catalytic activity on the Mn(II)-to-ligand ratio and the pH was investigated. The results are discussed in terms of mechanistic aspects of the action of this new class of oxidation catalysts.

2. Experimental

2.1. Complex stability constants

2.1.1. Isothermal titration calorimetry

Isothermal titration calorimetry was performed using a MicroCal Omega high sensitivity titration calorimeter (Microcal, Norhampton, MA). Solutions were degassed under vacuum prior to use. The calorimeter was calibrated electrically. Heats of dilution were determined in control experiments and subtracted from the heats determined in the ligand-to-$MnCl_2$ titration experiments. The results of the titration experiments were fitted with the sequential binding site model provided by the Origin software (Microcal, Norhampton, MA).

2.1.2. Potentiometric measurements

Potentiometric measurements were conducted with a Titrino 751 GPD and a pH-sensitive electrode with internal reference (6.0259.100) from Metrohm AG (Switzerland). All titrations were performed in a thermostated vessel at $25.0 \pm 0.1\,^{\circ}C$ under nitrogen atmosphere. The nitrogen gas was bubbled through a solution, which was adjusted to 0.1 M ionic strength potassium chloride.

The addition of titrand and the registration of the corresponding potentials were described by a

monotone endpoint titration protocol (MET) with standard equilibrium time of 240 s for each titration point.

To ensure a stable reference potential, the pH-sensitive electrode was calibrated by titration before and after each measurement with a 2 mM hydrochloric acid solution, which was also adjusted to 0.1 mol l^{-1} ionic strength with potassium chloride. From the calibration measurements values for E° (mV) and pK_w were obtained.

Fifty milliliter of the assay solution were titrated with 0.1 M potassium hydroxide solution from Riedel-de-Haën (35125). The ionic strength of the assay solution was adjusted to 0.1 M KCl.

The titrations were fitted by the use of SUPERQUAD [24] assuming a proper model of chemical equilibria.

2.2. Oxidation reactions

Kinetics of Morin and Trolox C bleach was measured with a Cary 50 spectrophotometer (Varian, Australia). Experiments were performed in thermostated cuvettes equipped with a magnetic stirring unit. In a typical experiment, the cuvette (path length, 1 cm) was filled with 3 ml buffer solution containing 160 μM Morin or 300 μM Trolox C, 10 mM hydrogen peroxide and 2.5 μM catalyst. Bleaching of Morin was followed as the decrease in absorbance at 430 nm. Trolox C oxidation was studied at 435 nm (phenoxy radical formation) and at 260 nm (formation of the quinone).

2.3. Hydrogen peroxide decomposition

To determine the time dependence of hydrogen peroxide decomposition, 20 μM of the complex was added to 50 ml of a stirred carbonate buffer solution (10 mM, pH 10.0) containing 2 mM H_2O_2 at 40 °C. At specific times samples of 1 ml of this solution were removed. Fifty microliter 1 M hydrochloric acid, 20 μl 3% ammonium molybdate tetrahydrate solution and 20 μl of 1 M potassium iodide were added to the samples. The absorbance at 440 nm was measured 6 min after preparation of a sample. The absorbance of the samples was compared with a calibration curve in order to calculate the hydrogen peroxide concentration. In separate control experiments, the H_2O_2 concentration was also determined by means of potentiometric iodometric titration.

2.4. Synthesis of ligands and complexes

All commercial reagents were used as received unless noted otherwise. Salen complex **8** [25], and terpyridine **1** [26,27], terpyridine **2** [27,28] and terpyridine **3** [29], as well as terpy-$MnCl_2$ [30] have been described elsewhere. ^{1}H NMR spectra were recorded at 360 MHz on a Bruker BZH 360/52 instrument. IR spectra were obtained with a Nicolet 510 FT–IR S/N instrument. MALDI-TOF analyses were conducted using an Applied Biosystems Voyager 1236 instrument. Ions formed by a pulsed UV laser beam (nitrogen laser, $\lambda = 337$ nm) were accelerated by 20 kV in a 2,5 DHB matrix.

2.4.1. Synthesis of terpyridine ligands

*2.4.1.1. Terpyridine **4**.* Ethyl 4-chloropicolinate [31], the procedure of *Lohse* for the preparation of the corresponding methyl ester hydrochloride was followed with minor modifications [32]. *N*,*N*′-Dimethylformamide (10.0 ml, 130 mmol) was cautiously added with stirring to thionyl chloride (295 ml, 4.06 mol) at 40 °C. After 30 min, finely powdered picolinic acid (100 g, 812 mmol) was added in 10 equal portions over 30 min, while keeping the temperature between 38 and 42 °C. The temperature is raised to 70 °C over 2 h (vigorous evolution of SO_2/HCl), and the mixture was stirred at this temperature for 1 day. Part of the volatiles (ca. 150 ml) were distilled off and replaced by toluene (ca. 150 ml), and the removal of volatiles (again ca. 150 ml) was repeated once more. Toluene was then added to a total volume of about 450 ml, and the resulting solution was poured into an ethanol–toluene solution (1:1 (v/v), 240 ml) cooled in an ice-bath. The resulting suspension was stirred overnight and concentrated to half of the volume on a rotary evaporator. The mixture was filtered at 0 °C and washed with toluene (250 ml). After drying in vacuo, ethyl 4-chloropicolinate hydrochloride was obtained as a beige solid.

The above hydrochloride was partitioned between ethyl acetate (300 ml) and water (200 ml), and quickly neutralized with aqueous sodium hydroxide (125 ml, 4 M). The aqueous layer was separated and extracted twice with ethyl acetate (200 ml each). The combined organic layers were dried over sodium sulfate (50 g), filtered and concentrated to dryness.

After distillation in vacuo (0.2 mbar, 65–70 °C), ethyl 4-chloropicolinate (75.3 g, 50% yield) was obtained as a colorless semisolid. ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 8.56$ (d, $J = 5.0$ Hz, 1H), 8.03 (d, $J = 1.8$ Hz, 1H), 7.43–7.37 (m, 1H), 4.39 (q, $J = 7.2$ Hz, 2H), 1.35 (t, $J = 7.2$ Hz, 3H).

Claisen condensation: Sodium hydride (4 g, ca. 100 mmol, ca. 60% in mineral oil) was washed twice with *n*-hexane under argon. After addition of absolute THF (100 ml), a solution of ethyl 4-chloropicolinate (18.45 g, 99.4 mmol) and acetone (2.92 ml, 39.7 mmol) in absolute THF (75 ml) was added within 2 h at 40–45 °C. After cooling to room temperature, the mixture was poured into 300 ml water with mechanical stirring. Aqueous HCl (ca. 14 ml, 6 M) was added to the resulting orange suspension within 30 min (final pH-value: 7.0–7.5). The mixture was concentrated to 2/3 of the initial volume on a rotary evaporator. After filtration at 0 °C, washing with water (100 ml) and drying in vacuo, crude 1,5-bis-(4-chlor-pyridin-2-yl)-pentan-1,3,5-trione (12.40 g, 92% yield) was obtained as a yellow solid. The product was used without further purification. ^{1}H NMR (360 MHz, $CDCl_3$), enol tautomer: 14.4 (br s, 2H); 8.49 (d, $J = 5.0$ Hz, 2H); 7.95 (d, $J = 1.8$ Hz, 2H); 7.35–7.31 (m, 2H); 6.77 (s, 2H). IR (cm^{-1}): 1619 (m), 1564 (s), 1546 (s), 1440 (m), 1374 (s), 1156 (m), 822 (w).

Pyridone formation: Aqueous ammonia (95 ml of a 25% solution) was added to the crude 1,3,5-triketone (31.1 g, 95 mmol) in 2-propanol (1.1 l), and the mixture was heated to 70 °C. Within 6 h, additional ammonia solution (3 × 30 ml) was cautiously added (at about 50 °C each). The mixture was cooled, filtered at 0 °C, and the precipitate was dried in vacuo to yield terpyridine **4** (18.3 g, 60% yield) as an off-white solid. A second, yet slightly impure crop of material (ca. 20%) can be obtained by concentration of the mother liquor. ^{1}H NMR (360 MHz, DMSO-d6): 11.12 (s, 1H); 8.64 (d, $J = 5.1$ Hz, 2H); 8.58 (s, 2H); 7.87 (s, 2H); 7.63–7.59 (m, 2H). ^{13}C NMR ($CDCl_3$): 165.6 (s, 1C), 156.5 (s, 2C), 154.9 (s, 2C), 150.2 (d, 2C), 143.6 (s, 2C), 123.7 (d, 2C), 120.2 (d, 2C), 108.5 (d, 2C).

*2.4.1.2. Terpyridine **5**.* A mixture of terpyridine **4** (6.36 g, 20 mmol), 2-(methylamino)ethanol (30.65 g, 0.4 mol, 20 equivalent) and dry zinc(II)chloride (82 mg, 0.6 mmol, 0.03 equivalent) in 2-methyl-2-butanol (100 ml) was heated under reflux for 2 days. The resulting suspension was filtered while hot. The precipitate was triturated with a minimum amount of water, filtered, and dried in vacuo to yield terpyridine **5** as an off-white solid (5.25 g, 69% yield). ^{1}H NMR (DMSO-d6): 8.23 (d, $J = 5.9$ Hz, 2H), 7.95–7.70 (m, 4H), 6.82–6.73 (m, 2H), 4.00–3.20 (m, 8H), 3.12 (s, 6H). ^{13}C NMR (DMSO-d6): 166.0 (s, 1C); 157.3 (s, 2C); 155.7 (s, 2C); 154.6 (s, 2C); 149.4 (d, 2C); 108.2 (d, 2C); 107.4 (d, 2C); 103.4 (d, 2C); 58.5 (t, 2C); 53.6 (t, 2C); 38.3 (q, 2C). $C_{21}H_{25}N_5O_3$ (395.47), calculated [%]: C 63.78, H 6.37, N 17.71; found [%]: C 63.36, H 6.21, N 17.41. IR (cm^{-1}): 3325 (m); 3256 (s); 2849 (w); 1604 (m); 1580 (s); 1514 (vs); 1444 (s); 819 (s). MALDI-TOF–MS: 396 ($[L + H]^+$).

*2.4.1.3. Terpyridine **6**.* Terpyridine **4** (7.95 g, 25 mmol) was added to PCl_5 (12.47 g, 60 mmol) in 175 ml $POCl_3$, and the mixture was heated to reflux for 1 day. After evaporation of the volatiles, ice-cold water (200 ml) was cautiously added. Aqueous sodium hydroxide (100 ml, 4M) was added and the mixture was stirred at room temperature overnight. The resulting pink solid was partitioned between chloroform (3 × 300 ml) and water (200 ml). The combined organic extracts were dried over sodium sulfate, filtered and concentrated in vacuo to yield pure terpyridine **6** [33,34] as a white solid (6.31 g, 75% yield). ^{1}H NMR (360 MHz, $CDCl_3$): 8.48 (d, $J = 5.0$ Hz, 2H), 8.45 (d, $J = 1.8$ Hz, 2H), 8.38 (s, 2H), 7.31–7.24 (m, 2H).

*2.4.1.4. Terpyridine **7**.* A mixture of terpyridine **6** (4.04 g, 12 mmol), 2-(methylamino)ethanol (48.8 ml, 610 mmol, 50 equivalent) and manganese(II)chloride tetrahydrate (5.23 g, 26.4 mmol, 2.2 equivalent) in 2-methyl-2-butanol (100 ml) was heated under reflux for 1 day. Acetonitrile:water 1:1 (50 ml) was added and the pH-value was adjusted to 12. The mixture was vigorously stirred in air for 1 day. After filtration over celite, the mother liquor was evaporated to dryness. The crude product was triturated with 20 ml water, filtered at 0 °C, and dried in vacuo. After recrystallization from aqueous methanol, ligand **7** was obtained as a white solid (3.04 g, 44% yield). ^{1}H NMR (DMSO-d6): 8.18 (d, $J = 5.9$ Hz, 2H); 7.92 (d, $J = 2.3$ Hz, 2H); 7.70 (s, 2H); 6.63 (dd, $J = 5.9, 2.3$ Hz, 2H); 4.95–4.70 (m, 3H); 3.80–3.48 (m, 14 H); 3.10 (s, 3H); 3.07 (s, 6H). ^{13}C NMR

(360 MHz, DMSO-d6): 156.4 (s, 2C); 155.7 (s, 2C); 155.3 (s, 1C); 154.4 (s, 2C); 149.2 (d, 2CH); 107.0 (d, 2CH); 103.5 (d, 2CH); 103.1 (d, 2CH); 58.5 (t, 2C); 58.2 (t, 1C); 53.7 (t, 2C); 53.6 (t, 2C); 38.6 (q, 1C); 38.3 (q, 2C). $C_{24}H_{32}N_6O_3 \cdot 1.29\ H_2O$, calculated [%]: C 60.59, H 7.33, N 17.66, H_2O 4.88; found [%]: C 60.18, H 7.26, N 17.77, H_2O 4.88. IR (cm^{-1}): 3376 (w); 2921 (w); 1580 (vs); 1538 (m); 1415 (m); 1053 (w); 994 (s); 799 (w). MALDI-TOF–MS: 453 ($[L + H]^+$).

2.4.2. Syntheses of catalysts

*2.4.2.1. Complex **1**-$MnCl_2$.* Ligand **1** [27] (249 mg, 1 mmol) was added to a stirred solution of $MnCl_2 \cdot 4H_2O$ (198 mg, 1 mmol) in ethanol (10 ml) and the mixture was stirred for 1 day at ambient temperature. After filtration and drying, the complex **1**-$MnCl_2$ was obtained as a light-yellow powder (349 mg, 93% yield). $C_{15}H_{11}Cl_2MnN_3O$ (375.12), calculated [%]: C 48.03, H 2.96, N 11.20, Mn 14.65; found [%]: C 48.22, H 3.14, N 11.13, Mn 14.6. IR (cm^{-1}): 3082 (br, vs), 1613 (s), 1600 (s), 1558 (s), 1429 (m), 1224 (s), 1011 (m), 798 (m). MALDI-TOF–MS: 339 ($[M - Cl]^+$); 250 ($[L + H]^+$). UV-Vis (10 mM carbonate buffer, pH 10.0): 281 nm (28700 $(M\,cm)^{-1}$); 321 (9250 $(M\,cm)^{-1}$).

*2.4.2.2. Complex **3**-$MnCl_2$.* Ligand **3** [29] (6.83 g, 22.3 mmol) was added, in five portions over a period of 30 min to an ethanolic solution (150 ml) of $MnCl_2 \cdot 4H_2O$ (4.41 g, 22.3 mmol). The mixture was stirred at room temperature for 18 h. After filtration and drying, the complex **3**-$MnCl_2$ was obtained as a light-yellow powder (8.85 g, 92% yield). $C_{18}H_{18}Cl_2MnN_4O$ (432.21), calculated [%]: C 50.02, H 4.20, N 12.96, Mn 12.71, Cl 16.41; found [%]: C 49.90, H 4.12, N 12.78, Mn 12.9, Cl 16.33. IR (cm^{-1}): 3484 (m), 1610 (vs), 1600 (vs), 1532 (m), 1039 (m), 1013 (vs), 793 (s), 786 (m). MALDI-TOF–MS: 396 ($[M - Cl]^+$); 307 ($[L + H]^+$). UV-Vis (10 mM carbonate buffer, pH 10.0): 222 nm (26200 $(M\,cm)^{-1}$); 281 (24600 $(M\,cm)^{-1}$); 320 nm (11800 $(M\,cm)^{-1}$).

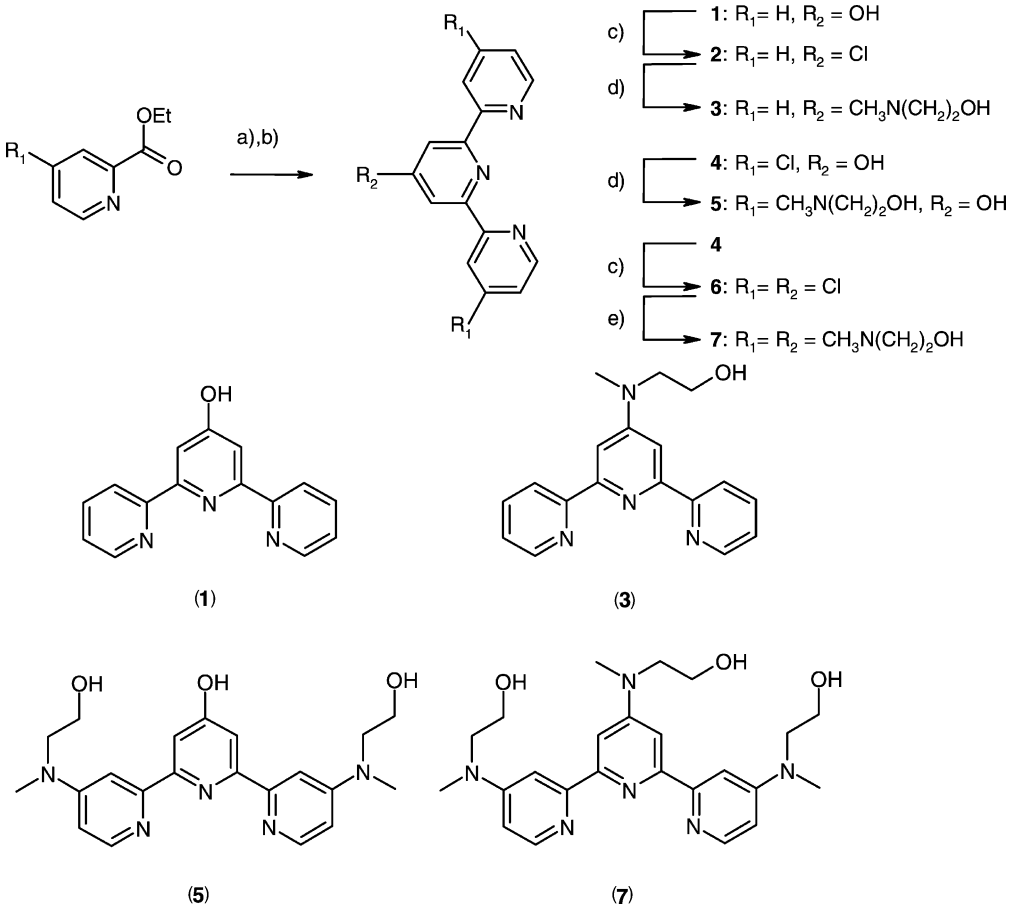
*2.4.2.3. Complex **5**-$MnCl_2$.* Ligand **5** (3.56 g, 9 mmol) was added to a stirred solution of $MnCl_2 \cdot 4H_2O$ (1.78 g, 9 mmol) in ethanol (60 ml), and the mixture was stirred at ambient temperature for 16 h. After filtration and drying, the complex **5**-$MnCl_2$ was obtained as a light-yellow powder (4.05 g, 86% yield). $C_{21}H_{25}Cl_2MnN_5O_3 \cdot 0.16H_2O$ (524.19), calculated [%]: C 48.12, H 4.87, N 13.36, Mn 10.48, Cl 13.53, H_2O 0.55; found [%]: C 48.17, H 4.90, N 13.27, Cl 13.41, Mn 10.7, H_2O 0.54. IR (cm^{-1}): 1605 (vs), 1579 (m), 1535 (m), 1500 (m), 1011 (vs). MALDI-TOF–MS: 485 ($[M - Cl]^+$); 396 ($[L + H]^+$). UV-Vis (10 mM carbonate buffer, pH 10.0): 228 nm (31,100 $(M\,cm)^{-1}$); 270 nm (45,250 $(M\,cm)^{-1}$); 312 nm (19,800 $(M\,cm)^{-1}$).

*2.4.2.4. Complex **7**-$MnCl_2$.* Ligand **7** (996 mg, 2.2 mmol) was added to a stirred solution of $MnCl_2 \cdot 4H_2O$ (435 mg, 2.2 mmol) in ethanol (15 ml) and the mixture was stirred at ambient temperature for 16 h. After filtration and drying, the complex **7**-$MnCl_2$ was obtained as a light-yellow powder (1.14 g, 88% yield). $C_{24}H_{32}Cl_2N_6O_3MnCl_2 \cdot 0.47H_2O$ (586.87), calculated [%]: C 49.12, H 5.66, N 14.32, Mn 9.36, H_2O 1.44; found [%]: C 48.98, H 5.73, N 14.00, Mn 9.24, H_2O 1.45. IR (cm^{-1}): 3383 (br), 1605 (vs), 1535 (s), 1518 (m), 1014 (s). MALDI-TOF–MS: 542 ($[M - Cl]^+$); 453 ($[L + H]^+$). UV-Vis (10 mM carbonate buffer, pH 10.0): 230 nm (35,800 $(M\,cm)^{-1}$); 275 nm (50,500 $(M\,cm)^{-1}$); 306 nm (21,650 $(M\,cm)^{-1}$).

3. Results and discussion

3.1. Synthesis of ligands and complexes

A vast number of methods are known for the synthesis of substituted terpyridines, most of which make use of either 2-acetyl pyridines or derivatives of α-picolinates, respectively. However, only a few terpyridines bearing heteroatom substitutents were published so far. Potts and Konwar [26] and Constable and Ward [27] followed a two-fold Claisen condensation approach for the preparation of a 1,3,5-triketone from ethyl picolinate and acetone, which was subsequently cyclized with ammonium acetate to give 4′-hydroxyterpyridine (**1**) (Scheme 1). The latter ligand can be further modified upon treatment with a chlorinating agent to yield the 4′-chloro derivative **2** [27,28]. Following Constable's protocol but using catalytic amounts of zinc(II)chloride instead of over-stoichiometric iron(II)chloride as a promoter



Scheme 1. Synthesis of electron-rich terpyridine ligands. (a) ethyl picolinate or ethyl 4-chloropicolinate, acetone, sodium hydride, THF, 50 °C, 85% yield (wt. of ethyl picolinate), 92% yield (wt. of ethyl 4-chloropicolinate); (b) NH_4OAc (for **1**) or NH_4OH (for **4**), *i*-PrOH, 60 °C, 65% yield (compound **1**), 60% yield (compound **4**); c) PCl_5, $POCl_3$, reflux, 60% yield (compound **2**), 75% yield (compound **6**); (d) $CH_3NH(CH_2)_2OH$ (excess), catalyst $ZnCl_2$, 2-methyl-2-butanol, reflux, 85% yield (compound **3**), 69% yield (compound **5**); (e) $CH_3NH(CH_2)_2OH$ (excess), $Mn(OAc)_2{\cdot}4H_2O$, 2-methyl-2-butanol, reflux, 44% yield (compound **7**).

for the dehalo-amination, we obtained the known terpyridine **3** [29]. New ligands **5** and **7** bearing amine substituents in the outer rings were obtained in a similar manner starting from di- and tri-chloroterpyridines **4** and **6** [33,34], respectively.

To the best of our knowledge, 4,4″-diamino-4′-hydroxy-terpyridines have not been described before. The new reaction sequence for the 4,4′,4″-triamino-substituted ligands compares favorably with the alternative procedure starting from 2,2′:6′,2″-terpyridine 1,1′,1″-trioxide introduced by Case [33]. Employing these methods, we synthesized a broad variety of ligands on a multigram scale.

With ligands **1**, **3**, **5**, and **7** in hand, we focused on the synthesis of the corresponding manganese(II) complexes. Stirring equimolar amounts of ligand and manganese(II)chloride tetrahydrate in methanol or ethanol gave catalysts **1**-$MnCl_2$, **3**-$MnCl_2$, **5**-$MnCl_2$, and **7**-$MnCl_2$ as yellow powders in high yield.

3.2. Complex equilibria in solution

Given the ability to chelate with the nitrogen atoms of all pyridine rings, one can assume a meridional coordination mode for terpyridines with most transition metal ions. In solution, an equilibrium of different

complexes bearing one (1:1) or two (2:1) ligands per central ion can thus be expected. Working with a 1:1 stoichiometry seemed appropriate for our purpose, since the existence of "free" coordination sites (i.e. in alkaline aqueous solution: easily exchangeable hydroxo or aqua ligands) is considered to be of importance for catalytic activity. Furthermore, a 1:1 stoichiometry allows in principle the formation of di-μ-oxo bridged dimers, thereby stabilizing manganese in its higher oxidation states (e.g. III/IV or IV/IV). In contrast, a 2:1 complex is considered as coordinatively saturated, preventing the coordination and thereby activation of an oxidant (e.g. perhydroxyl ion) as expected for an ionic oxidation mechanism.

However, the formal ratio of metal ion-to-ligand in solution or the stoichiometry in the solid state tells nothing about the complex species, which are finally present in aqueous solution. This in particular holds true in case of Mn(II) complexes, which are known to be kinetically labile [35]. In order to have a closer look at the complex species present in aqueous and alkaline solutions, a Job plot analysis was performed at pH 10 and 23 °C (Fig. 1) [36]. The maximum excess absorbance was observed for a ligand/(manganese + ligand) ratio α of ~0.67 for all catalysts corresponding to a stoichiometric ratio of two ligands per Mn. Hence, a 2:1 species dominates for each of the ligands at pH 10.

However, for catalysts **5**-$MnCl_2$ and **7**-$MnCl_2$ an additional non-linearity was observed at α ~0.5, probably caused by a partially hidden local maximum. A maximum at $\alpha = 0.5$ points to the existence of a 1:1 complex (Fig. 1(b)). Although these maxima are not very sharp and less pronounced they could be reproduced in several experiments. Two maxima within one Job plot point to an equilibrium of 2:1 and 1:1 species under the present experimental conditions.

Although a second maximum was not observed for catalysts **1**-$MnCl_2$ and **3**-$MnCl_2$, the existence of a 1:1 species in addition to the 2:1 species cannot be excluded from the Job plot analysis. To obtain a more comprehensive picture of complex equilibria in solution, we studied in more detail complex formation between manganese and ligand **1** by means of isothermal titration calorimetry (ITC) and potentiomeric titrations. In a typical ITC experiment, the calorimeter cell contained 80 μM of $MnCl_2$ (10 mM carbonate buffer, pH 9.4, 28 °C). Small aliquots of a 2 mM ligand solution (same buffer) were injected into the calorimeter cell. After integration of the heat flow for each injection (Fig. 2(A)), the heat of injection versus molar ratio of ligand-to-Mn curve was fitted with the sequential binding site model provided by the Origin software (Fig. 2(B)). Best fit was obtained with $\log \beta_{(1\,1\,0)} = 7.3$ and $\log \beta_{(1\,2\,0)} = 13.3$ (for definition, see Table 1). The heat of complex formation was found to be exothermic with about $-4.7\,\text{kcal mol}^{-1}$ for the first complexation step and $-3.3\,\text{kcal mol}^{-1}$ for the second complexation step.

Table 1
Overall ligand protonation and complex formation constants ($\log \beta_{(x\,y\,z)}$) of the species $Mn_xL_yH_z$ at 25 °C and 0.1 mol l^{-1} KCl with L, ligand **1**

x y z	$\log \beta_{(x\,y\,z)}$[a]
0 1 1	8.78 (1)[b]
0 1 2	12.07 (2)
0 1 3	15.30 (3)
1 1 0	7.9 (1)
1 1 1	12.6 (1)
1 2 0	13.9 (4)
1 2 1	20.3 (2)
1 2 2	25.9 (1)

The complex formation constants were determined by potentiometric titrations of solutions containing manganese(II)chloride and L in a ratio of 1:1 and 1:2 with c(L) = 1.0 mM.

[a] $\beta_{(x\,y\,z)} = [M_xL_yH_z][M]^{x-}[L]^{y-}[H]^{z-}$.

[b] In parentheses are the triple standard deviations given by the program SUPERQUAD.

As an alternative to the abovementioned ITC methods, we also determined the complex formation constants with manganese(II) over a broad pH range by potentiometric, as well as spectrophotometric titrations (Table 1). In addition, these methods provide the protonation constants of the ligand and the complexes. The extent to which the pH value of the metal-containing system is lowered in comparison to the titration curve of ligand **1** alone, is an indication for the stability of the existing complexes. Thus, the corresponding species distribution can be calculated with a suitable iteration program using an appropriate chemical model (see Section 2). Best fits were obtained with the following assumptions: at low pH value (pH 2) the ligand is in its three-fold protonated state and no complex is formed. Raising the pH value initiates complexation of manganese(II) by one or two ligand molecules. Complexes are partially protonated in the intermediate pH range (MnLH and MnL_2H_2). Upon

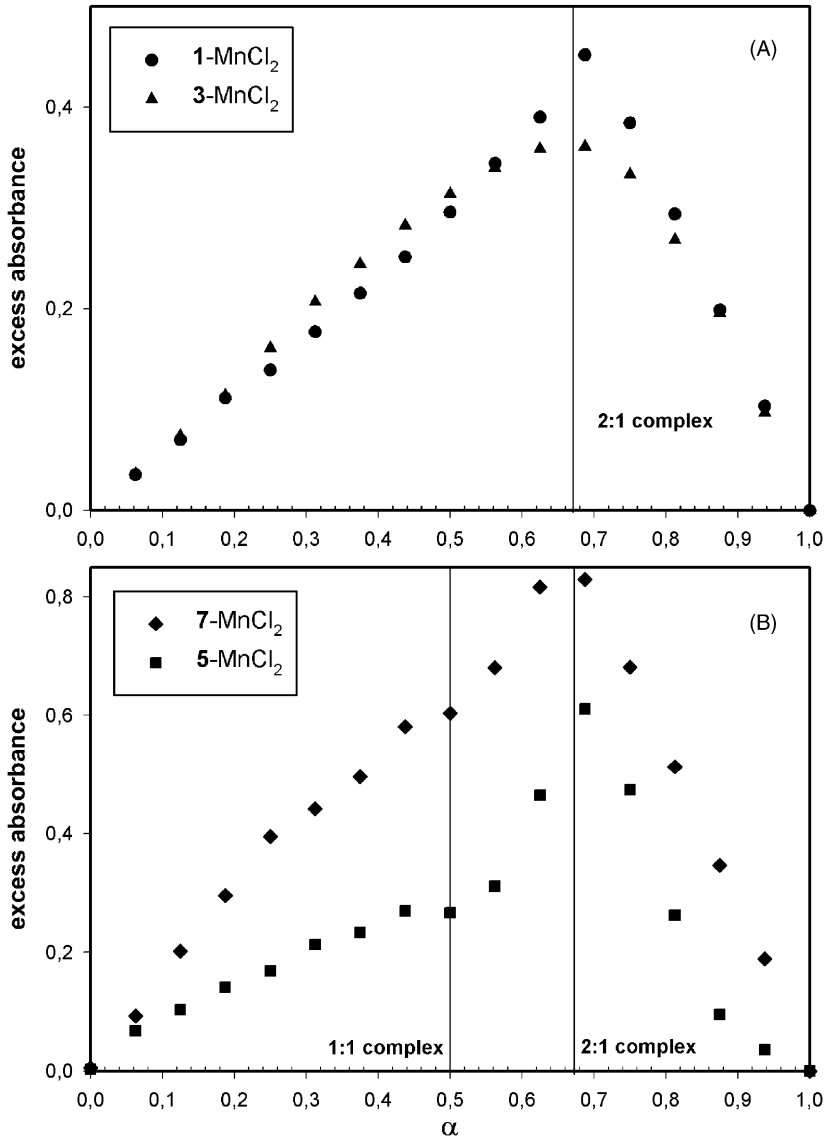


Fig. 1. Job plot analysis of complex formation. Experiments were run in 10 mM carbonate buffer pH 10.0 at 23 °C. The sum of concentration of ligand and manganese was 80 μM.

further addition of potassium hydroxide solution, MnL_2H_2 is deprotonated to MnL_2H ($pK_{a(MnL_2H_2)}$ = 5.6), and at higher pH-values, finally, to MnL_2 ($pK_{a(MnL_2H)}$ = 6.4). Likewise, the 1:1 complex MnLH is deprotonated to MnL ($pK_{a(MnLH)} = 4.7$).

It should be noted that the complex stability constants of manganese(II) with ligand **1** are comparably low. This leads to only a small pH-difference between ligand titration and metal-ligand titration causing a reduced reproducibility between two independent measurements. We repeated the titrations several times and found variations in the $\log \beta$ values of about ±5%.

The results obtained with the potentiometric titrations are in good agreement with the results of the ITC measurements. Hence, both the methods are

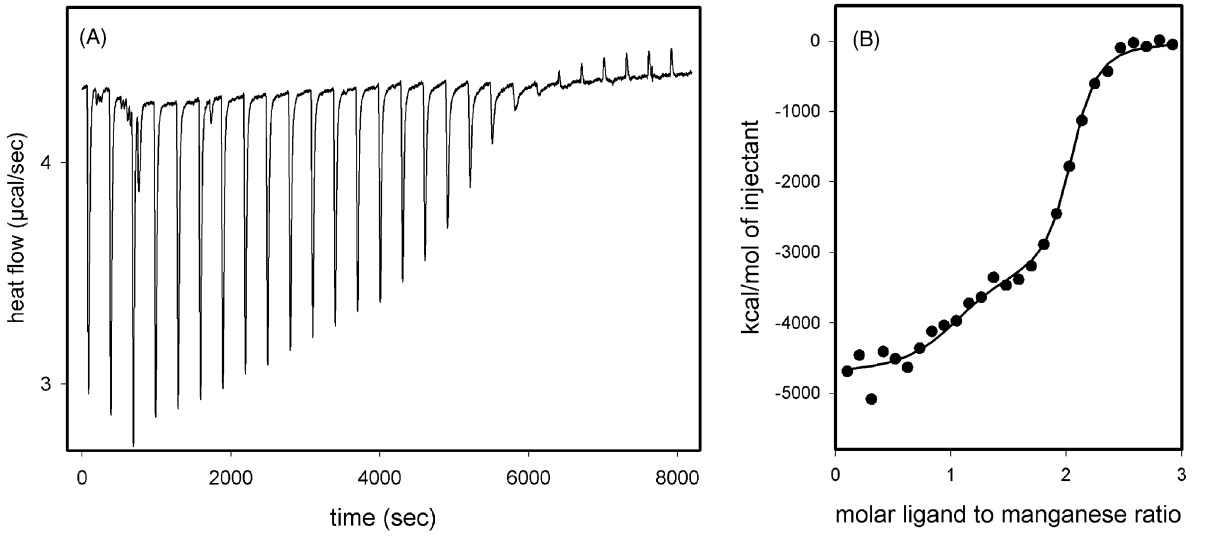


Fig. 2. Isothermal titration calorimetry of $MnCl_2$ with ligand **1**. (A) Heat flow for the injection of aliquots of ligand into a $MnCl_2$ solution at 28 °C. (B) Integrated heat of injection and best fit of a sequential binding site model to the experimental data.

appropriate tools to determine complex formation constants of terpyridine-manganese complexes. Whereas, ITC yields as additional information the complex formation enthalpies, potentiometric titration reveals a whole set of stability constants of protonated and deprotonated species over a broad pH range.

It is instructive to compare complex formation constants of ligand **1** with Mn(II) with those of terpyridine. By means of potentiometric titration $\log \beta_{(1\,1\,0)}$ and $\log \beta_{(1\,2\,0)}$ of the terpyridine-manganese system were determined to be 5.1 and 9.2 in water, respectively [37]. Thus, introduction of a hydroxy group in the 4′-position considerably enhances the complex formation constants for each complexation step by about 2 orders of magnitude.

Applying the complex stability constants to a 1:1 solution of 10 μM **1**-$MnCl_2$, ∼75% of the ligand are involved in a 1:1 complex and ∼23% in a 2:1 complex at pH 10. This confirms indeed the assumption of a mixture of 1:1 and 2:1 complex species in an aqueous, alkaline solution.

3.3. Catalysis of Morin oxidation

To assess the ability of the complexes to activate H_2O_2 and to catalyze oxidations in aqueous solution at pH 10 (10 mM carbonate buffer), we selected Morin (3,5,7,2′,4′-pentahydroxyflavone) as a model substrate. This polyphenol is one of numerous flavonoid plant dyes, which was shown to possess antioxidant activity [19]. A polyphenolic structure is a common element of chromophores present in fruit, vegetable and tea. Very often such chromophores are the target of bleach processes. Therefore, polyphenolic compounds serve frequently as model substrates for these processes [38,39].[1]

Fig. 3 shows the time dependence of the absorbance at 410 nm of a solution containing 160 μM Morin, 10 mM H_2O_2 and 2.5 μM of a Mn complex (10 mM carbonate buffer, pH 10.0, 23 °C). Thus, a decrease of the absorbance with time reflects oxidative degradation of Morin and can hence be considered as a measure for the catalytic activity of the complex.

Apart from the catalysts shown in Scheme 1, the figure includes data observed for $MnCl_2$, the Mn(III) complex of *N*,*N*′-bis[4-(dimethylamino)salicylidene]-1,2-ethylenediamine (**8**), the Mn(II) complex with unsubstituted terpyridine (terpy-$MnCl_2$) and the complex $[LMn(IV)(\mu\text{-}O)_3Mn(IV)L]^{2+}$, with L being 1,4,7-trimethyl-1,4,7-triazacyclononane (Mn-TMTACN) (see Scheme 2).

[1] Further studies show also the formation of epoxides from olefins working with our Mn-terpy catalysts (work in progress).

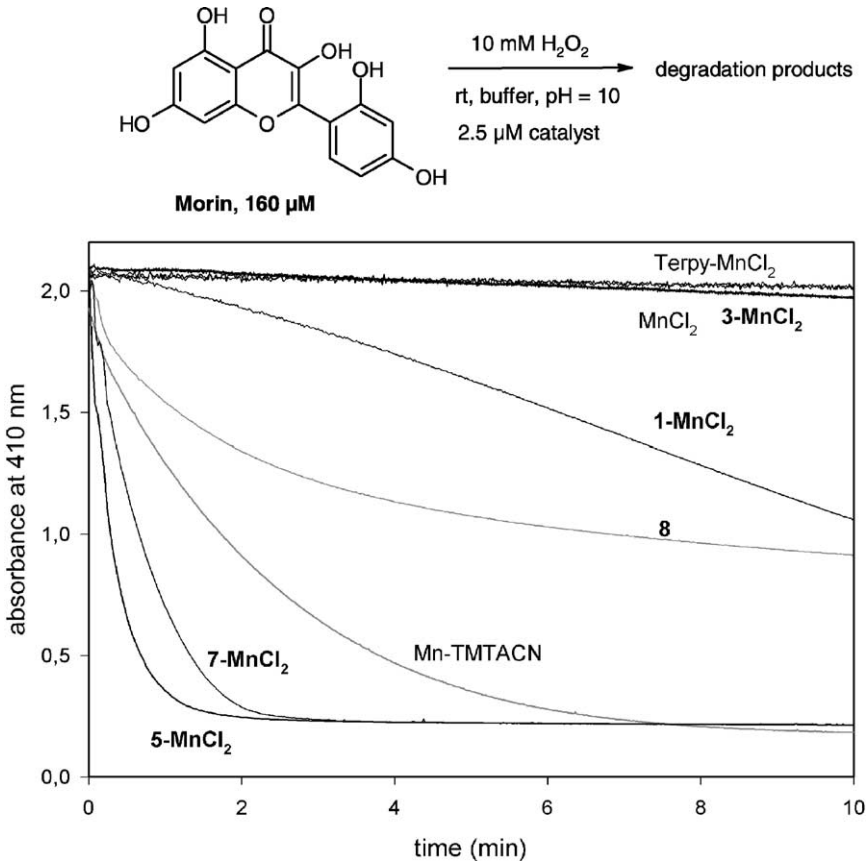
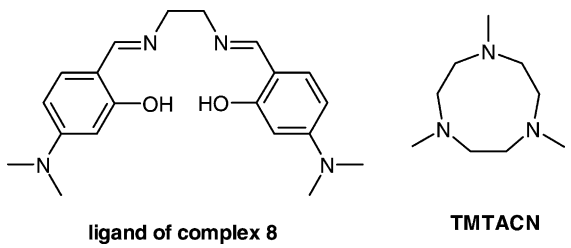


Fig. 3. Time dependence of Morin oxidation by H_2O_2 in the presence of different metal complexes at 23 °C as followed by UV-Vis spectroscopy at 410 nm. The solution contained 160 μM Morin, 10 mM H_2O_2 and 2.5 μM complex (basis: Mn) in 10 mM carbonate buffer pH 10.

Terpy-$MnCl_2$ and **3**-$MnCl_2$ show the lowest activity of the terpyridine complexes studied. In both the instances, the decline of the absorbance at 410 nm is comparable to that induced by $MnCl_2$ alone. The activity of the terpyridine complexes increases significantly in the order of **3**-$MnCl_2$ < **1**-$MnCl_2$ < **7**-$MnCl_2$ < **5**-$MnCl_2$. Hence, by incorporating electron-donating groups in the respective 4-positions of the pyridine rings, the catalyst activity can be considerably enhanced. A three-fold substitution (**5**-$MnCl_2$: *N*,*O*,*N*-pattern; **7**-$MnCl_2$: *N*,*N*,*N*-pattern) results obviously in a higher catalytic activity than a sole substitution at the central pyridine ring of the ligand. Furthermore, catalysts with a hydroxy group in the 4′-position are more active than the analog complexes with the amine substituted ligand (cf. **1**-$MnCl_2$ with **5**-$MnCl_2$ and **3**-$MnCl_2$ with **7**-$MnCl_2$). The two complexes with three-fold ligand substitution, **5**-$MnCl_2$ and **7**-$MnCl_2$, show an even higher activity in oxidizing Morin than Mn-TMTACN. The latter complex was previously shown to be a highly effective bleach catalyst under aqueous, alkaline



Scheme 2. Other ligands used for Mn-catalyzed Morin oxidations.

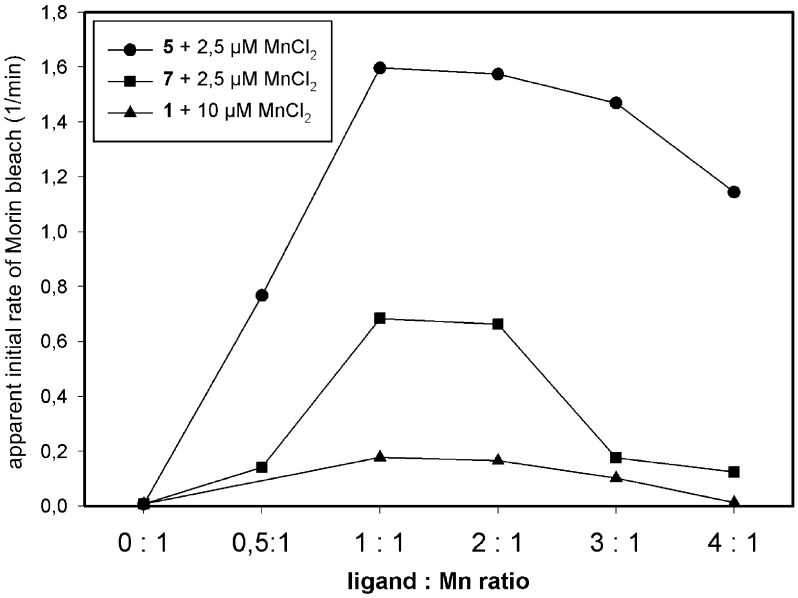


Fig. 4. Apparent initial rate of Morin bleach ($(dA/dt)/A$, at $t = 0$ with A being the absorbance at 410 nm) of different ligand-to-manganese ratios of ligands **1**, **5** and **7** at pH 10.0. The solution contained 160 μM Morin, 10 mM H_2O_2 and 2.5 μM complex (basis: Mn) in 10 mM carbonate buffer pH 10.

conditions [4,12,18]. It is interesting to note the quite different kinetic behavior of salen complex **8**. Following a fast initial drop in absorbance, the activity slows down after about 2–3 min. This is indicative of complex destruction due to ligand oxidation. In general, Mn-salen complexes are easily oxidatively destroyed in the presence of hydrogen peroxide in alkaline and aqueous solutions [11]. In contrast, the Mn-terpyridine complexes studied herein are much more robust against ligand oxidation as has also been confirmed by UV-Vis spectroscopy (data not shown).

The abovementioned bleach experiments were also carried out at elevated temperature (40 °C). With the exception of terpy-$MnCl_2$, Morin bleaching was faster than at 23 °C. However, the order of activity of the Mn-terpyridine complexes was unchanged.

Furthermore, the influence of the anion on the bleach activity has been studied (not shown). Complexes prepared with manganese(II) acetate or manganese(II) sulfate showed identical bleach activities as the complexes prepared with manganese(II)chloride. Most likely these anions dissociate from the manganese under the present reaction conditions (aqueous solution, high pH).

3.4. Dependence of catalytic effect on ligand-to-manganese ratio

The existence of an equilibrium between 1:1 and 2:1 complexes in alkaline aqueous solution raises the question of which species is the catalytically more suitable precursor. Therefore, we measured the catalysis of Morin oxidation by hydrogen peroxide with solutions containing ligand-to-manganese ratios between 1:1 and 4:1. (Fig. 4; Catalyst **3** was omitted because of the low activity of its Mn(II) complex) For all catalysts studied, increasing the ligand-to-manganese ratio significantly decreased the bleaching activity.

Terpyridine-manganese(II) complexes are known to be kinetically labile on the time scale of our experiments [35]. Hence, the complex equilibrium is driven more towards $Mn(terpy)_2^{2+}$ in the presence of excess of ligand. Our data demonstrate that a 1:1 species in solution possesses a higher catalytic activity than the corresponding 2:1 complex. This is in line with the suggestion that one prerequisite for an effective oxidation catalyst is the presence of free (i.e. occupied by weak and labile co-ligands) coordination sites [6,40]. Our data do not rule out any residual

catalytic activity of the 2:1 complex, e.g. through outer sphere electron transfer. Moreover, even if the 2:1 complex is not catalytically active and is the only complex species present in a solution, addition of the oxidant (hydrogen peroxide) might modify the equilibrium by the formation of new species such as terpyridine-Mn 1:1 complexes with perhydroxyl as co-ligand or complexes with Mn in a higher oxidation state. A shift of the equilibrium from 2:1 species to 1:1 species, as could be caused by the addition of perhydroxyl, may account for the experimental finding that a 2:1 stoichiometry shows the same or only slightly reduced activity as the respective 1:1 stoichiometry. Naturally, this effect plays a minor role as higher the ligand-to-manganese ratio, explaining the continuous decrease in activity with increasing ligand concentrations.

3.5. Dependence of Morin bleach on pH

The catalytic activity of terpyridine-manganese(II) complexes is expected to depend on the pH value of the aqueous solution. We have studied the pH dependence of Morin oxidation of the complexes **1**-$MnCl_2$, **5**-$MnCl_2$ and **7**-$MnCl_2$ between pH 7.9 and pH 11. Table 2 summarizes the results given as the apparent initial reaction rate ($(dA/dt)/A$ at $t = 0$ with A being the absorbance at 410 nm).

For all the catalysts, the initial rate of oxidation increases with increasing pH and goes through a maximum, which is found at pH ∼9.1 for **1**-$MnCl_2$ and at pH ∼10 for **5**-$MnCl_2$ and **7**-$MnCl_2$. The activity is very low in the pH range between 7.9 and 8.5 for **1**-$MnCl_2$ and **7**-$MnCl_2$. In contrast, the activity of **5**-$MnCl_2$ is surprisingly high even at a low pH of 7.9. Activity is generally influenced by the protonation state of the substrate, the catalyst, H_2O_2 and the solvent. The pK_a values of Morin are 3.5 and 8.1 [41]. Thus, at pH values below 9 the loss in activity might in part be caused by the protonation of the Morin. Furthermore, assuming that hydrogen peroxide is activated by a direct interaction with the metal center of the complex, oxidation is expected to be favored by a high pH because of the larger concentration of the perhydroxyl anion (HOO^- is more nucleophilic than H_2O_2). For an overall peroxide concentration of 10 mM, the concentration of HOO^- is only 2.4 μM at pH 8 but 234 μM at pH 10. On the other hand, at very large pH values, the complexes may be destroyed by the formation of the mineral forms of manganese. This could account for the drop in activity observed for all three catalysts at pH 11. Although it is difficult to discuss the pH dependence in terms of each of the aspects given above, the activity of terpyridine-Mn complexes in activating hydrogen peroxide is strongly favored by an (moderately) alkaline pH and vanishes completely at acidic pH values (not shown). This finding is in line with the pH dependence of bleach processes catalyzed by Mn-TMTACN [4].

Table 2
The pH dependence of the apparent initial rate of Morin oxidation k_0 at 23 °C[a]

pH	k_0 (1 min^{-1}) **1**-$MnCl_2$	k_0 (1 min^{-1}) **5**-$MnCl_2$	k_0 (1 min^{-1}) **7**-$MnCl_2$
7.9[b]	0.003	0.35	0.01
8.5[b]	0.025	0.51	0.03
9.1[c]	0.072	1.44	0.32
10.0[c]	0.050	1.84	0.82
11.0[c]	0.021	1.24	0.67

[a] Sample contained 160 μM Morin, 10 mM H_2O_2, and 2.5 μM complex.
[b] 10 mM phosphate buffer.
[c] 10 mM carbonate buffer.

3.6. Catalyzed disproportionation of hydrogen peroxide

The concurrent catalytic disproportionation of H_2O_2 is a general property of transition metal complexes possessing catalytic activity towards organic substrates. In biological systems, H_2O_2 is a byproduct of many oxidation processes and its catalase-induced decomposition is essential because of its high toxicity [42].

Of course, for oxidations as used in organic synthesis or bleach processes, the non-productive decomposition of hydrogen peroxide is generally unwanted.

We have tested the ability of the terpyridine-Mn complexes to catalyze H_2O_2 disproportionation in the absence of organic substrates. Fig. 5 shows the time dependence of H_2O_2 decomposition in alkaline aqueous solution (10 mM carbonate buffer, pH 10.0, $T = 40$ °C). H_2O_2 consumption is highest for **5**-$MnCl_2$ and decreases in the order **5**-$MnCl_2$ > **7**-$MnCl_2$ ≫ **1**-$MnCl_2$ ≈ **3**-$MnCl_2$. Interestingly, the

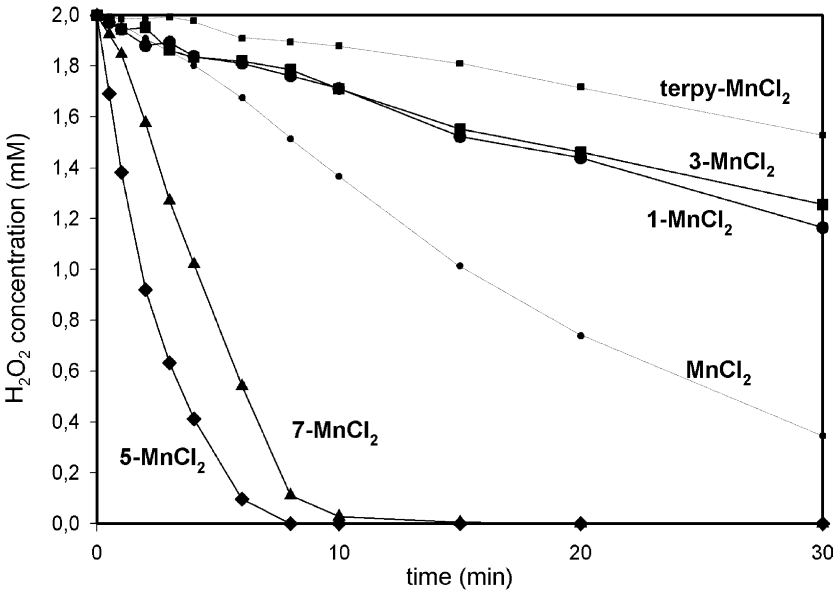
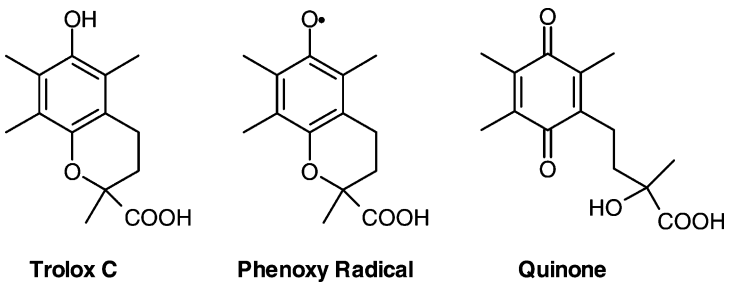


Fig. 5. Time dependence of complex-induced H_2O_2 decomposition to molecular oxygen and water. Solutions contained 2 mM H_2O_2 and 20 μM complex (10 mM carbonate buffer, pH 10.0 at 40 °C).

catalase activity of $MnCl_2$ is distinctly larger than that of **1**-$MnCl_2$, **3**-$MnCl_2$ and terpy-$MnCl_2$ under the present conditions. This is in contrast to the catalytic activity in oxidation processes of organic substrate (cf. Morin bleach), where the activity of both Mn(II) and terpy-$MnCl_2$ is very low, but that of **1**-$MnCl_2$ is distinctly higher. Unlike Morin bleach, catalase activity could not be quenched by a large ligand-to-manganese ratio (not shown), indicating that both 1:1 and 2:1 complexes possess catalase activity. This again indicates a complicated mechanism of action, which is different from that of substrate oxidation catalysis.

3.7. Oxidation of Trolox C via one-electron oxidation steps

It is generally accepted that polyhydroxyflavins such as Morin can be oxidized by many different mechanisms. Consequently, we sought for a phenol with a more defined degradation behavior. The water-soluble Vitamin E analog Trolox C is such a compound [43]. Trolox C was previously shown to be oxidized by a sequence of two initial one-electron oxidation steps [44]. The primary oxidation product of Trolox C is a sterically hindered phenoxy radical with a comparably long life-time (Scheme 3).



Scheme 3. Structure of the Vitamin E analog Trolox C and its degradation products.

A second one-electron oxidation step includes the disproportionation of two phenoxy radicals to Trolox C and the oxidation product 1,4-benzoquinone as the final products [43,44]. The formation and decay of the intermediate phenoxy radical can conveniently be followed by UV-Vis spectroscopy because of its characteristic absorbance at 435 nm [12,44,45]. Mn-TMTACN was previously shown to effectively catalyze the oxidation of Trolox C by H_2O_2 via an initial one-electron oxidation step as described earlier [12]. In principle, two mechanisms can account for an one-electron oxidation catalyzed by a transition metal complex. (i) The electron can be transferred directly from the substrate to the manganese cation or by an outer sphere mechanism. (ii) The catalyst produces primary radicals, such as superoxide or hydroxyl radicals, which subsequently react with Trolox C to form the Trolox C–phenoxy radical. In fact, it is well-known that Trolox C cleanly reacts with a broad range of inorganic radicals [44,45].

We have compared the ability of the terpyridine complexes **5**-$MnCl_2$ and **7**-$MnCl_2$ with that of Mn-TMTACN to oxidize Trolox C. Fig. 6 shows the time dependence of the UV-Vis signals at 260 and 435 nm of a solution containing 300 μM Trolox C, 2.5 μM complex (**5**-$MnCl_2$, **7**-$MnCl_2$ or Mn-TMTACN on Mn basis) and 10 mM H_2O_2 (10 mM carbonate buffer pH 10, 23 °C).

As shown previously, Trolox C oxidation catalyzed by Mn-TMTACN is accompanied by a fast build-up of the phenoxy radical (435 nm), and by the formation of the Trolox C–quinone reaction product (characteristic absorbance at 260 nm) [12]. The maximum concentration of the phenoxy radical is reached after about 2 min and the concentration then drops moderately with increasing time. In the presence of **5**-$MnCl_2$, Trolox C oxidation proceeds initially only slightly slower than for Mn-TMTACN. In contrast, the catalytic activity of **7**-$MnCl_2$ is distinctly weaker, as is evident not only by a much slower build-up of the absorbance of the

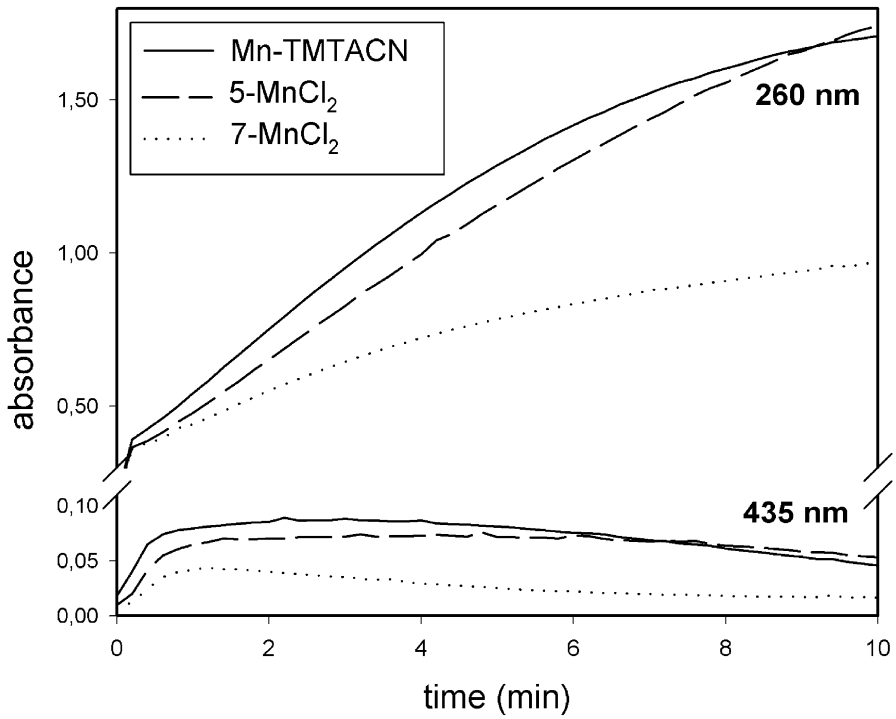


Fig. 6. Time dependence of UV-Vis traces at 260 nm (indicating build-up of the quinone reaction product) and at 435 nm (indicating formation of the phenoxy radical) of catalysts **5**-$MnCl_2$, **7**-$MnCl_2$ and Mn-TMTACN. Solutions contained 300 μM Trolox C, 2.5 μM complex and 10 mM H_2O_2 (10 mM carbonate buffer, pH 10, 23 °C).

reaction product at 260 nm, but also by a lower steady state concentration of the phenoxy radical (see trace at 435 nm). It is instructive to compare activity of the catalysts on Trolox C with that on Morin. Both the catalysts **5**-$MnCl_2$ and **7**-$MnCl_2$ show a distinctly higher activity than Mn-TMTACN in oxidizing Morin, but the latter catalyst shows the highest activity for Trolox C. This can also be expressed by the ratios of the apparent initial reaction rates $V_{app}^{Morin}/V_{app}^{Trolox}$, which amount to 2.9 for Mn-TMTACN, 13.0 for **5**-$MnCl_2$ and 8.5 for **7**-$MnCl_2$. The larger this ratio, the higher is the activity on Morin compared with Trolox C. Hence, although Morin and Trolox C possess very similar oxidation potentials (Morin: 0.34 V versus NHE, Trolox C: 0.31 V, versus NHE, pH 7.4, 50 mM phosphate buffer) the catalysts behave rather differently on both substrates [46]. This can be caused by different mechanisms of substrate oxidation. While Trolox C is oxidized by an initial one-electron oxidation step, Morin can be oxidized by many different mechanisms. A lower activity of the terpyridine catalysts on Trolox C suggests that in contrast to Mn-TMTACN an initial one-electron oxidation step is not the prevailing reaction path made accessibly by these catalysts. Although it is premature to draw conclusions at this point, the question arises whether or not Mn-TMTACN might have a higher tendency to transform hydrogen peroxide into reactive primary radicals than the terpyridine catalysts.

4. Conclusions

By using a synthetic protocol, opening the avenue to a convenient synthesis of 4,4′,4″ π-donor substituted terpyridines, we have investigated the ability of terpy-Mn(II) complexes to activate hydrogen peroxide and to catalyze substrate oxidations. To provide a basis for the understanding of catalytic activity, complex equilibria have initially been studied in aqueous alkaline solution. It was found that dissolution of isolated complexes having a stoichiometric ligand-to-manganese ratio of 1:1 results in the establishment of an equilibrium involving both 1:1 and 2:1 complex species. The non-substituted terpy-Mn(II) complex showed only poor activity in catalyzing Morin oxidation in aqueous, alkaline solution. Activity could be considerably enhanced by incorporating hydroxo or amino groups in the 4-positions of the pyridine rings. However, the catalytic activity depends critically on the substitution pattern. Best results, which were even superior to those of Mn-TMTACN, were obtained with **5**-$MnCl_2$.and **7**-$MnCl_2$, which both bear three-fold substituted ligands. With respect to the existence of different complex species in solution it could be shown that the 1:1 species is the catalytically more active precursor. Therefore, free coordination sites are of great advantage or even necessary for catalytic activity.

Catalytic activity was found to be pH dependent for all catalysts. A maximum in activity exists at pH ∼10. Probably two opposite effects account for the maximum. The concentration of the perhydroxyl ion increases with increasing pH. The coordination of this ion to the manganese center might be the first step in a catalytic cycle involving reactive ionic intermediates. On the other hand, a high pH value favors formation of MnO_2, thereby destroying the complex. Comparing the activity of the terpyridine complexes for Trolox C oxidation with that for Morin oxidation, it becomes obvious that the relative activity of our catalysts in catalyzing Trolox C oxidation is lower than that of Mn-TMTACN. Hence, a reaction path involving one-electron oxidation steps as, for example, found in reactions of radicals, seems not to be the prevailing catalytic path made accessible by terpyridine-manganese complexes.

A major side reaction of catalytic oxidation under alkaline aqueous conditions is the non-productive hydrogen peroxide disproportionation. The activity of the terpy-Mn(II) complexes to catalyze H_2O_2 disproportionation was different from the activity to catalyze substrate oxidation, suggesting differences in the mechanism of action between both catalytic processes.

Although the detailed mechanism of hydrogen peroxide activation was not unraveled in the present study, the data suggest that the catalytic activity of terpyridine-manganese complexes depends not only on the redox potential of the complexes modulated by the π-donor substituents but also on secondary effects. Such secondary effects include the thermodynamic complex stability, the oxidative stability of the ligands, the mechanism by which a substrate can be oxidized, the pH of the solution and the extent of side reactions (e.g. catalase).

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References

[1] R. Manchanda, G.W. Brudvig, R.H. Crabtree, Coord. Chem. Rev. (1995) 1.
[2] M. Yagi, M. Kaneko, Chem. Rev. 101 (2001) 21.
[3] T.J. Collins, Acc. Chem. Res. 27 (1994) 279.
[4] R. Hage, J.E. Iburg, J. Kerschner, J.H. Koek, E.L.M. Lempers, R.J. Martens, U.S. Racherla, S.W. Russell, T. Swarthoff, M.R.P. van Vliet, J.B. Warnaar, L. van der Wolf, B. Krijnen, Nature 369 (1994) 637.
[5] I.A. Weinstock, E.M.G. Barbuzzi, M.W. Wemple, J.J. Cowan, R.S. Reiner, D.M. Sonnen, R.A. Heintz, J.S. Bond, C.L. Hill, Nature 414 (2001) 191.
[6] K. Wieghardt, Angew. Chem., Int. Ed. Engl. 28 (1989) 1153.
[7] M. Delroisse, J.-P. Verlhac, J. Chem. Soc. Chem. Comm. (1995) 949.
[8] R. Hage, Recl. Trav. Chim. Pays-Bas 115 (1996) 385.
[9] C.P. Horwitz, D.R. Fooksman, L.D. Vuocolo, S.W. Goordon-Wylie, N.J. Cox, T.J. Collins, J. Am. Chem. Soc. 120 (1998) 4867.
[10] H. Offermans, G. Dittrich, N. Steiner, Chem. Unserer Zeit 34 (2000) 150.
[11] M.F. Hazenkamp, F. Bachmann, J.J. Dannacher, G. Schlingloff, J. Surfact. Deterg. 4 (2001) 65.
[12] B.C. Gilbert, N.W.J. Kamp, S. Lindsay, J. Oakes, J. Chem. Soc. Perkin Trans. 2 (1997) 2161.
[13] A. Grenz, S. Ceccarrelli, C. Bolm, J. Chem. Soc. Chem. Commun. (2001) 1726.
[14] A. Berkessel, C.A. Sklorz, Tetrahedron Lett. 40 (1999) 7965.
[15] D.E. De Vos, T. Bein, J. Organomet. Chem. 520 (1996) 195.
[16] D.E. De Vos, S. De Wildeman, B.F. Sels, P.J. Grobet, P.A. Jacobs, Angew. Chem., Int. Ed. Engl. 38 (1999) 980.
[17] G.V. Nizova, C. Bolm, S. Ceccarelli, C. Pavan, G.B. Shul'pin, Adv. Synth. Catal. 344 (2002) 899.
[18] M.S. Newton, B.C. Gilbert, S. Lindsay, J. Oakes, J. Inorg. Biochem. 67 (1997) 212.
[19] D.E. De Vos, J.L. Meinershagen, T. Bein, Angew. Chem., Int. Ed. Engl. 35 (1996) 2211.
[20] M.-N. Collomb, A. Deronzier, A. Richardot, J. Pecaut, New J. Chem. 23 (2000) 351.
[21] J. Limburg, J.S. Vrettos, L.M. Liable-Sands, A.L. Rheingold, R.H. Crabtree, G.W. Brudvig, Science 283 (1999) 1524.
[22] J. Limburg, J.S. Vrettos, H. Chen, J.C. De Paula, R.H. Crabtree, G.W. Brudvig, J. Am. Chem. Soc. 123 (2001) 423.
[23] C. Baffert, M.-N. Collomb, A. Deronzier, J. Pecaut, J. Limburg, R.H. Crabtree, G.W. Brudvig, Inorg. Chem. 41 (2002) 1404.
[24] P. Gans, A. Sabatini, A. Vacca, J. Chem. Soc., Dalton Trans. (1985) 1195.
[25] M. Hazenkamp, F. Bachmann, C. Makowka, M.-J. Dubs, G. Richter, G. Schlingloff, J. Dannacher, Patent Appl. WO 0053708 (2000).
[26] K.T. Potts, D. Konwar, J. Org. Chem. 56 (1991) 4815.
[27] E.C. Constable, M.D. Ward, J. Chem. Soc., Dalton Trans. (1990) 1405.
[28] C.H. Weidl, A.A. Precup, C. Eschbaumer, U.S. Schubert, Polym. Mat. Sci. Eng. 84 (2001) 649.
[29] G. Lowe, A.S. Droz, T. Vilaivan, G.W. Weaver, L. Tweedale, J.M. Pratt, P. Rock, V. Yardley, S.L. Croft, J. Med. Chem. 42 (1999) 1006.
[30] C.M. Harris, T.N. Lockyer, N.C. Stephenson, Aust. J. Chem. 19 (1966) 1741.
[31] D.G. Markees, J. Org. Chem. 29 (1964) 3120.
[32] O. Lohse, Synth. Commun. 26 (1996) 2017.
[33] F.H. Case, J. Org. Chem. 27 (1962) 640.
[34] S.E. Hobert, J.T. Carney, S.D. Cummings, Inorg. Chim. Acta 318 (2001) 89.
[35] R. Hogg, R.C. Wilkins, J. Chem. Soc. (1962) 341.
[36] P. Job, Ann. Chim. 9 (1928) 113.
[37] M. Ignaczak, G. Andrijewski, Russ. J. Inorg. Chem. 37 (1992) 417.
[38] H. Blum, B. Mayer, U. Pegelow, Patent Appl. DE 19620267 (1996).
[39] H. Blum, R. Kramer, Patent Appl. WO 0032731 (1999).
[40] J. Limburg, G.W. Brudvig, R.H. Crabtree, J. Am. Chem. Soc. 119 (1997) 2761.
[41] S.V. Jovanovic, S. Steenken, M. Tosic, B. Marjanovic, M.G. Simic, J. Am. Chem. Soc. 116 (1994) 4846.
[42] D.W. Yoder, J. Hwang, J.E. Penner-Hahn, in: A. Sigel, H. Sigel (Eds.), Manganese and Its Role in Biological Systems, Marcel Dekker, New York/Basel, 2000, p. 527.
[43] M.J. Thomas, B.H.J. Bielski, J. Am. Chem. Soc. 111 (1989) 3315.
[44] D.E. Cabelli, B.H.J. Bielski, J. Free Rad. Biol. Med. 2 (1986) 71.
[45] H.S. Bisby, S. Ahmed, R.B. Cundall, Biochem. Biophys. Res. Commun. 119 (1984) 245.
[46] L.V. Jorgensen, L.H. Skibsted, Free Rad. Res. 28 (1998) 335.