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Redox-Switchable Catalysis

Redox Control of a Dendritic Ferrocenyl-Based Homogeneous Catalyst**

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Abstract: *The application of a dendrimer in a redox-switchable catalytic process is reported. A monomeric and the corresponding dendritic ferrocenylphosphane ligand were used to develop well-defined controllable catalysts with distinct redox states. The corresponding ruthenium(II) complexes catalyze the isomerization of the allylic alcohol 1-octen-3-ol. By adding a chemical oxidant or reductant, it was possible to reversibly switch the catalytic activity of the complexes. On oxidation, the ferrocenium moiety withdraws electron density from the phosphane, thereby lowering its basicity. The resulting electron-poor ruthenium center shows much lower activity for the redox isomerization and the reaction rate is markedly reduced.*

Redox-switchable catalysis (RSC) is a field of growing importance, in which redox-active functionality is incorporated within a ligand framework to allow the catalytic activity of the coordinated metal centers to be influenced in situ.[1] Oxidation and reduction influence the electron-donating ability of the ligand and thus result in altered activity or selectivity of the catalyst, which may facilitate a new transformation altogether. The ultimate goal is to design a catalyst that displays orthogonal activity for different substrates on changing its electronic nature.

Wrighton et al. were the first to describe the concept of RSC for a rhodium(I) bisphosphino cobaltocene complex.[2] While the catalytic hydrogenation of cyclohexene is approximately 16 times faster with the reduced complex, the (chemically) oxidized complex is the faster and more durable hydrosilylation catalyst. This original outcome was explained by a more electron-rich rhodium center in the reduced form promoting oxidative addition of H_2.

Following the pioneering work of Wrighton et al., RSC has been applied to several areas of homogeneous catalysis, such as ring-opening polymerization,[3] ring-closing metathesis,[4] and the Mitsunobu reaction.[5] Thus catalysts have been switched to change the solubility of the catalyst (for catalyst recycling)[4b] or to modulate the activity of the transition metal (electronic communication between the redox-active group and the catalytic center). However, so far no reports have involved dendritic phosphane-containing ligands (Scheme 1).

Owing to the well-defined and hyperbranched molecular architecture of dendrimers, the concentration and location of the immobilized catalyst can be precisely controlled.[6] Catalytic sites grafted to the surface of dendrimers are in close proximity to each other, and the resulting high local catalyst concentration may cause a "positive dendritic effect", that is, an increase in activity with increasing generations.[7] Additionally, dendritic catalysts are nano-objects that can be easily separated by precipitation or nanofiltration. Herein, we report the first example of redox-switchable catalysis with a dendritic catalyst.

Ferrocene is a widely used redox-active group because it can be easily functionalized and displays a high degree of reversibility. For our study, we employed the unsymmetrically disubstituted 1,1′-ferrocenylphosphane **1**, in which one cyclopentadienyl ring is substituted with an anchoring group for linkage to the dendrimers (Scheme 2). According to Allgeier and Mirkin, **1** belongs to the class of substitutionally inert redox-active ligands.[1] Monomeric ferrocenylphosphane ligand (**1-ML**) was synthesized for comparison with the dendritic ligand in catalytic testing.

The ferrocenylphosphane ligand **1** was synthesized from 1,1′-dibromoferrocene[8] through two successive Negishi cross-coupling reactions (Scheme 2a,b), followed by deprotection of the phenol linker (Scheme 2c) and reduction of the phosphane sulfide (Scheme 2d). The corresponding monomeric ligand **1-ML** contains an anisole group instead of the phenol substituent. The grafting experiments were performed with a slight excess of **1** with respect to the terminal $P(S)Cl_2$ groups of the dendrimer (Scheme 2e). The progress of the reaction was monitored by ^{31}P NMR spectroscopy. The dendritic ligand was obtained by precipitation in high yield and purity. The corresponding heterobimetallic complexes were obtained by reaction of the monomeric (**1-ML**) and dendritic (**1-G_1**) phosphane ligands with $[\{Ru(p\text{-cym})Cl_2\}_2]$ (Scheme 2i,f).

To find a suitable chemical oxidant and reductant for the redox switch, the complexes were investigated electrochemically. The Fe^{II}/Fe^{III} redox potential does not change significantly on complexation, and both Fe^{II} and Ru^{II} undergo well separated, fully reversible one-electron redox processes (Table 1). Both dendritic and monomeric complexes show

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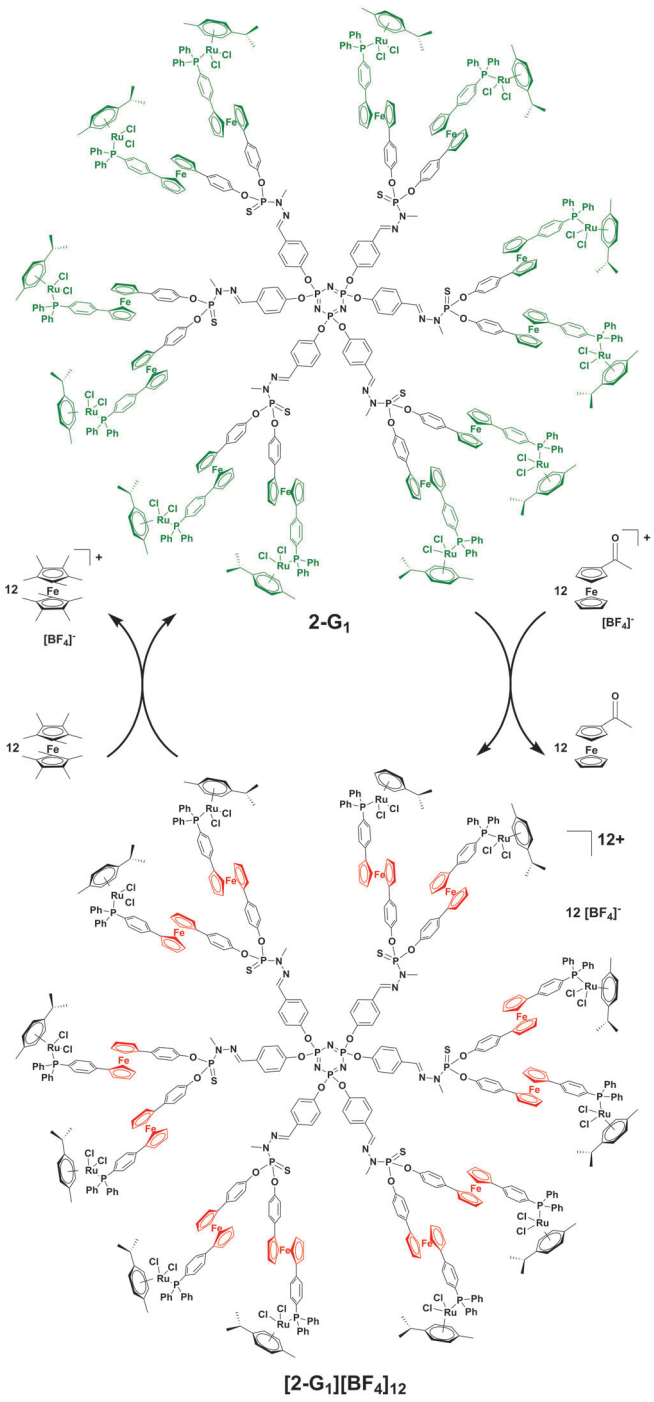
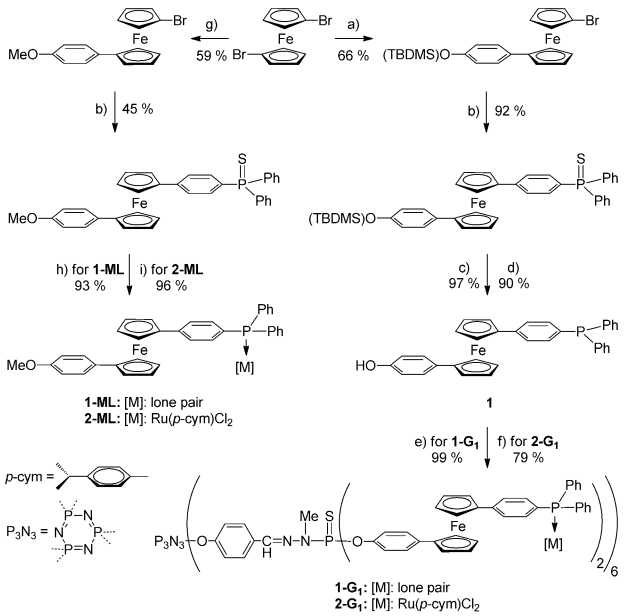


Scheme 1. Redox reaction of the dendritic catalyst **2-G$_1$** (green = active catalyst; red = poorly active ligand).



Scheme 2. Synthetic pathway to monomer **ML** and dendrimer **G$_1$** terminated by **1** or [**1**-Ru(*p*-cym)Cl$_2$]: a) *n*BuLi, ZnCl$_2$, [Pd(PPh$_3$)$_4$], 4-Br-C$_6$H$_4$-O(TBDMS); b) *n*BuLi, ZnCl$_2$, [Pd(PPh$_3$)$_4$], 4-Br-C$_6$H$_4$-P(S)Ph$_2$; c) TBAF·3 H$_2$O, THF, 3 h, RT; d) Raney nickel, toluene, MeCN, 12 h, RT; e) 14 equiv **1**, **G$_1$**, Cs$_2$CO$_3$, THF, 12 h, RT; f) **1-G$_1$**, 6 equiv [{Ru(*p*-cym)Cl$_2$}$_2$], CH$_2$Cl$_2$, 2 h, RT; g) *n*BuLi, ZnCl$_2$, [Pd(PPh$_3$)$_4$], 4-Br-C$_6$H$_4$-OMe; h) Raney nickel, toluene, MeCN, 72 h, 80 °C; i) **1-ML**, 0.5 equiv [{Ru(*p*-cym)Cl$_2$}$_2$], CH$_2$Cl$_2$, 2 h, RT; TBDMS = *tert.*-butyldimethylsilyl, TBAF = tetra-*n*-butylammonium fluoride, **ML** = monomeric ligand, **G$_1$** = 1st generation dendrimer, *p*-cym = *p*-cymene.

Table 1: Electrochemical data for **1-ML**, **2-ML**, **1-G$_1$**, and **2-G$_1$**.[a]

Compound	$E_{1/2}$ (Fe^{II}/Fe^{III}) [V]	$E_{1/2}$ (Ru^{II}/Ru^{III}) [V]
1-ML	0.59	–
2-ML	0.57	1.19
1-G$_1$	0.59	–
2-G$_1$	0.58	1.27

[a] Data obtained from CV and square-wave voltammetry in THF with 0.1 M [*n*Bu$_4$N][PF$_6$] electrolyte and referenced against SCE.

similar redox behaviors, with a potential window between 0.6 and 1.1 V for a prospective chemical oxidant. It is also noteworthy that the dendritic complexes only show a single Fe^{II} redox wave. Therefore, the structurally flexible dendrimer undergoes fast rotational changes in solution that ensure that all 12 ferrocene moieties are oxidized on the electrochemical timescale. Of the chemical oxidants studied, [Fe{η^5-C$_5$H$_4$C(O)Me}Cp][BF$_4$][9] was found to be the most promising candidate for RSC ($E_{1/2}$ = 0.78 V vs. SCE in THF) since it can oxidize all of the ferrocene units but does not interfere with the Ru^{II} redox process.

The transition metal catalyzed isomerization of allylic alcohols, which is a useful and atom-economical synthetic process en route to saturated carbonyl compounds,[10] was chosen to illustrate the use of metallodendritic catalysts in RSC. As a result of the well-known ability of transition metals to facilitate the migration of carbon–carbon double bonds, the allylic alcohol is turned into an enol, which then readily isomerizes into the corresponding carbonyl compound.[11] Besides rhodium(I), ruthenium(II) is predominantly used for this transformation.[12] This reaction has already been applied in numerous multistep syntheses,[13] as well as with metallodendritic catalysts.[14] Complexes such as [(η^6-arene)RuCl$_2$(L)], in which L is a monodentate phosphane ligand (PPh_3 or analogues), show particularly high activity.[12,15]

Since a poorly soluble base is used for activation,[16] an induction period is observed that corresponds to formation of the active species.[12] To minimize this effect and obtain more easily comparable results, the catalyst was preheated with Cs_2CO_3 in THF for 5 min at 60 °C. Both **2-ML** and **2-G$_1$** show high catalytic activity in the conversion of 1-octen-3-ol to 3-octanone, but the dendritic catalyst **2-G$_1$** shows higher activity than **2-ML** (60 min, TOF 400) and leads to full conversion after 40 min (TOF 600). This outcome can be explained by the increased stability of the dendritic catalyst or by cooperative effects of neighboring catalytic entities on substrate migration or the stabilization of transition states.

After examining the catalytic properties of **2-ML** and **2-G$_1$**, the monomeric complex **2-ML** was used in RSC (Figure 1). On oxidation with 1 equiv of [Fe{η^5-$C_5H_4C(O)Me$}Cp][BF_4] the reaction rate was markedly reduced. After reduction with [FeCp*$_2$] (Cp* = C_5Me_5),[9] full conversion was observed with a degree of activity similar (96 %) to that of the original catalyst before oxidation. Since the oxidized catalyst does not precipitate from the reaction mixture, these findings, in accord with Wrighton's previous work,[2] clearly demonstrate an electronic effect of the redox-active ligand. Once the ferrocene is oxidized, Fe^{III} withdraws electron density from the phosphane and thus decreases its basicity. Consequently, the decrease in electron density in the Ru–P bond creates an electron-poor transition metal and thus a far less active catalyst for the isomerization of allylic alcohols. In this manner, it is possible to reversibly tune the electronic properties of the ruthenium catalyst in situ.

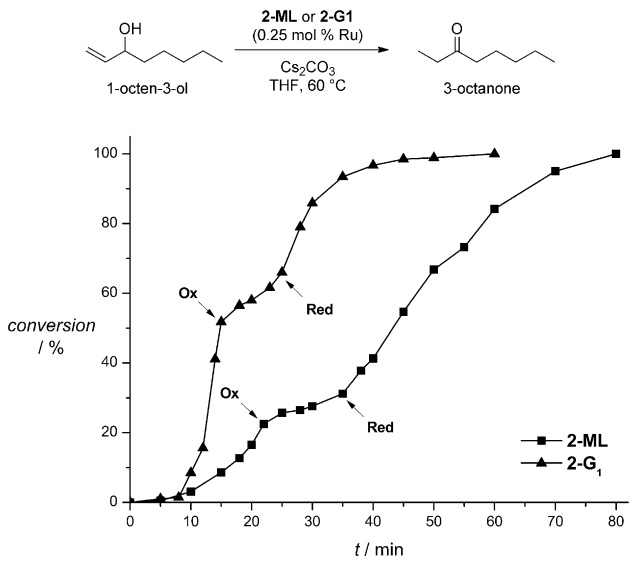


Figure 1. Plot of conversion versus time: redox-switched isomerization of 1-octen-3-ol catalyzed by **2-ML** (black squares) and **2-G$_1$** (blue triangles); monitored by GC–MS; conditions: 0.25 mol% ruthenium, 0.625 mol% Cs_2CO_3 in THF at 60 °C (preheating); Ox: 1 equiv [Fe{η^5-$C_5H_4C(O)Me$}Cp][BF_4]; Red: 1 equiv [FeCp*$_2$] (Cp* = C_5Me_5).

To demonstrate that RSC can also be applied to dendrimers, it is necessary to investigate the reversibility of the dendritic redox event during the reaction. Therefore, the experiment was repeated with the dendritic complex **2-G$_1$**. One equivalent of [Fe{η^5-$C_5H_4C(O)Me$}Cp][BF_4] was added, and subsequently the activity of the dendrimer dropped significantly (Figure 1). In contrast to **2-ML**, the oxidized species [**2-G$_1$**][BF_4]$_{12}$ partly precipitates from the reaction mixture, as was anticipated given its high positive charge. However, [**2-G$_1$**][BF_4]$_{12}$ is still slightly soluble in THF, showing 8 % of the original activity of **2-G$_1$**. On reduction with [FeCp*$_2$], **2-G$_1$** was reformed and a significant increase in catalytic activity was observed. In the case of the dendritic redox event, a combination of electronic communication and an additional solubility effect is assumed. Figure 2 illustrates

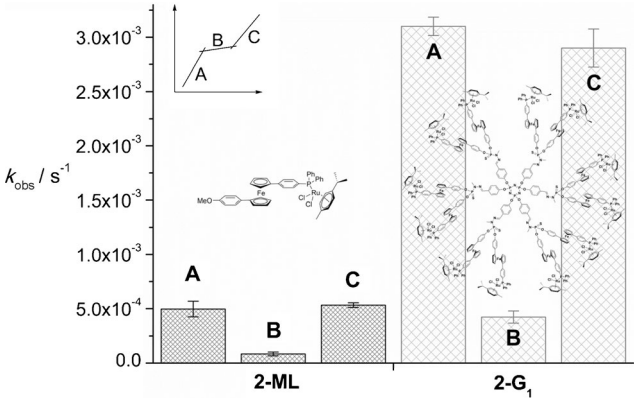


Figure 2. Comparison of the experimental rate constants k_{obs} derived from linear regression of the RSC sectors A, B, and C: redox-switched isomerization of 1-octen-3-ol catalyzed by **2-ML** (left) and **2-G$_1$** (right).

the difference in reaction kinetics between the monomeric and dendritic redox events. The plots of conversion versus time were classified into three RSC sectors: A (before oxidation), B (after oxidation), and C (after reduction). The experimental rate constants k_{obs} could be observed by linear regression of the sectors (see the Supporting Information). In sector A, the rate constant of this pseudo-first-order reaction is increased six-fold by using the dendritic catalyst. In both cases, the decrease in the reaction rate upon oxidation is remarkable considering that only one electron is removed from the conjugated π system. The similarity of the rate constants in sectors C and A proves the reversibility of both redox events. These outcomes are interesting firstly for the investigation of orthogonal activity by using different substrates in the same reaction and secondly for facile catalyst recovery (by simple filtration).[4b]

In conclusion, the first application of a dendritic transition metal complex in redox-switchable catalysis and the first example of a redox-switchable isomerization of an allylic alcohol were achieved by employing a phosphane ligand that contains a redox-active ferrocene moiety closely connected to the catalytic center through a conjugated π system. As expected, the dendritic catalyst **2-G$_1$** partly precipitates on oxidation, and this observation suggests that loss of catalytic activity could be partly due to reduced solubility. However, the oxidized monomeric catalyst [**2-ML**][BF_4] and some of the oxidized dendrimer [**2-G$_1$**][BF_4]$_{12}$ remain in solution. Thus, the reversible nature of the redox event is clearly derived

from electronic communication of the redox-active phosphane ligand and the catalytically active transition metal, ruthenium(II). These findings extend the field of stimuli-responsive catalysts to redox-switchable phosphane ligands. Redox control not only enables a better understanding of catalytic mechanisms but also facilitates the development of catalysts with in situ orthogonal activity for different substrates. Moreover, dendritic catalysts can bridge the gap between homogeneous and heterogeneous catalysis.

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