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Fluorocarbon Soluble Copper(II) Carboxylate Complexes with Nonfluoroponytailed Nitrogen Ligands as Precatalysts for the Oxidation of Alkenols and Alcohols under Fluorous Biphasic or Thermomorphic Modes: Structural and Mechanistic Aspects

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This fluorous biphasic catalysis (FBC) contribution was focused on the synthesis and characterization of new fluorous soluble R_f-Cu(II) carboxylate complexes containing nonfluoroponytailed ligands and defines their role as precatalysts for the FBC oxidation of alkenols and alcohols in the presence of 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO)/O_2. In this FBC approach, we have utilized the phase-switching technique of Vincent et al. (*J. Am. Chem. Soc.* **2002**, *124*, 12942) to solubilize the nonfluoroponytailed ligands, *N*-1,4,7-Me_3TACN, **2**, and *N*-1,4,7-pentamethyldiethylenetriamine (PMDETA), **3**, by reaction with a fluorous solvent-soluble copper (II) dimeric complex, $[Cu(\{C_8F_{17}(CH_2)_2\}_2CHCO_2)_2]_2$, **1**. Moreover, the reaction of nonfluoroponytailed ligands **2** and **3** with **1** afforded new perfluoroheptane-soluble Cu(II) complexes, $[Cu(\{C_8F_{17}(CH_2)_2\}_2CHCO_2)_2($**2**$)]$, **4**, and $[Cu(\{C_8F_{17}(CH_2)_2\}_2CHCO_2)_2$ $($**3**$)]$, **5**, respectively. The known Cu(II) complex, **1**, was further characterized by electron paramagnetic resonance (EPR) spectroscopy confirming its dimeric structure, while **4** and **5** were characterized by elemental analysis, IR, diffuse reflectance UV–vis, and EPR spectroscopy. Furthermore, **1**, **4**, and **5** were evaluated as precatalysts for alkenol and alcohol oxidation. The oxidation reactions of alkenols and alcohols in the presence of TEMPO/O_2 proceeded under FBC conditions for **1**, **4**, and **5**, but 1-octanol was unreactive under single-phase FBC conditions at 90 °C with TEMPO/O_2. The thermomorphic property of **5**, soluble in chlorobenzene/toluene at 90 °C but insoluble at room temperature, was also evaluated in the selective oxidation of *p*-nitrobenzyl alcohol to *p*-nitrobenzaldehyde. Plausible mechanisms concerning these FBC/thermomorphic oxidation reactions will be discussed.

Introduction

The selective, catalytic synthesis of aldehydes and ketones from alcohols still represents a cornerstone for global industrial research for the preparation of a variety of important intermediates.[1] Homogeneous catalytic oxidation is more selective to the above-mentioned aldehyde and ketone products, and the reactions are carried out at lower temperatures in comparison to those of heterogeneous catalytic oxidation. Thus, the development of a homogeneous oxidation process for conversion of alkenols and alcohols to aldehydes and ketones has been an important goal in numerous industrial and academic laboratories.[1]

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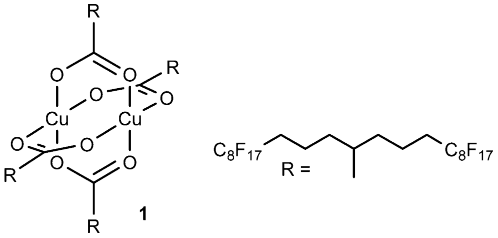
In order for this process to be industrially important for economical and environmental concerns, new and innovative approaches for the separation of the homogeneous catalyst from the oxidation products are still needed. Approximately 10 years ago, Horváth and Rábai introduced the concept of *Fluorous Biphasic Catalysis* (FBC),[2] and they demonstrated that, by using fluorocarbon solvents and modifying the homogeneous catalyst ligand structure with long-chain perfluoroalkane derivatives, fluoroponytails, to make the precatalyst soluble in the fluorocarbon phase, the products of the catalytic reaction would be soluble in a separate solvent phase that is immiscible in the fluorocarbon phase; by removing this second phase, the products are easily separated from the precatalyst and recycled. It should also be clearly noted that the solubility of the products of alcohol oxidation, the aldehydes and ketones, is extremely low or nonexistent in perfluoroalkanes and perfluoroethers.[3] This latter critical characteristic, and the fact that perfluoroalkanes and perfluoroethers are very interesting for their nonpolarity and extremely low intermolecular forces, makes them ideal solvents for homogeneous biphasic catalytic processes.

The FBC concept has now been amply demonstrated with many examples of classic organic catalytic reactions being converted to the FBC paradigm,[4,5] among them oxidation reactions.[5,6] However, there is still an urgent need to synthesize and fully characterize new fluoroponytailed ligands and their metal complexes, for structural identification, solubility in fluorocarbon solvents, thermomorphic properties, and the additional need to understand the mechanisms of the oxidation chemistry, under FBC reaction conditions.[5a] Moreover, we recently utilized fluoroponytailed ligands to solubilize fluoroponytailed metal carboxylate complexes that, themselves, were not totally soluble in perfluorocarbons.[5a,6] For example, the use of fluorocarbon soluble ligands, R_f-TACN and R_f-bipyridine, with $[Cu(O_2C(CH_2)_2C_8F_{17})_2]$ to form fluorocarbon soluble Cu(II) complexes, $[Cu(R_f\text{-TACN})(O_2C(CH_2)_2C_8F_{17})_2]$ and $[Cu(R_f\text{-bipyridine})(O_2C(CH_2)_2C_8F_{17})_2]$, which were oxidation precatalysts for alkane and alkene functionalization, was reported.[5] Furthermore, the oxidation of 4-nitrobenzyl alcohol to 4-nitrobenzaldehyde under single-phase FBC reaction conditions at 90 °C in the presence of TEMPO/O_2 was demonstrated for $[Cu(R_f\text{-TACN})(O_2C(CH_2)_2C_8F_{17})_2]$.

The opposite modified paradigm would be the solubilization of nonfluoroponytailed ligands with a fluorocarbon soluble metal carboxylate. This was demonstrated by Vincent et al.,[7] with a fluorocarbon soluble bis-fluoroponytailed copper(II) dimer complex, $[Cu(\{C_8F_{17}(CH_2)_2\}_2CHCO_2)_2]_2$, **1**, that was able to reversibly phase transfer several nonfluoroponytailed pyridyl-tagged ligands, a pyridyl-substituted porphyrin and a dipyridyl-substituted C_{60} fullerene, through coordination of the pyridyl groups to **1**. Importantly, to our knowledge, just one report has emanated that utilizes this approach for FBC experiments, which is also the focus of this contribution. Thus, Deelman et al. have reported the use of highly fluorous solvent-soluble and weakly coordinating tetraphenylborate anions to solubilize cationic complexes, such as $[(COD)Rh(dppb)]^+$, for the hydrogenation of octenes.[8]

Therefore, in this manuscript, we report on the utilization of the previously reported fluorous solvent-soluble copper (II) dimeric complex, **1**, that we further characterized by electron paramagnetic resonance (EPR) spectroscopy to solubilize 1,4,7-Me_3-TACN, **2**, and *N*-1,4,7-pentamethyldiethylenetriamine (PMDETA), **3**, and thus, form the fluorocarbon soluble Cu(II) complexes $[Cu(\{C_8F_{17}(CH_2)_2\}_2CHCO_2)_2]$, **4**, and $[Cu(\{C_8F_{17}(CH_2)_2\}_2CHCO_2)_2]$, **5**, respectively. Furthermore, the oxidation of alcohols to aldehydes and a ketone, under FBC conditions, has also been performed with 2,2,6,6-tetramethylpiperidinyl-1-oxy (TEMPO) and oxygen gas at 90 °C: one phase during reaction, two phases on cooling to room temperature. In addition, the thermomorphic properties of **5** were also evaluated in the absence of a fluorocarbon solvent; the organic solvent was soluble at 90 °C but insoluble at room temperature. We will also provide EPR results to ascertain the fate of the Cu(II) precatalysts andpresent plausible mechanisms for all of these transformations under FBC and thermomorphic conditions.



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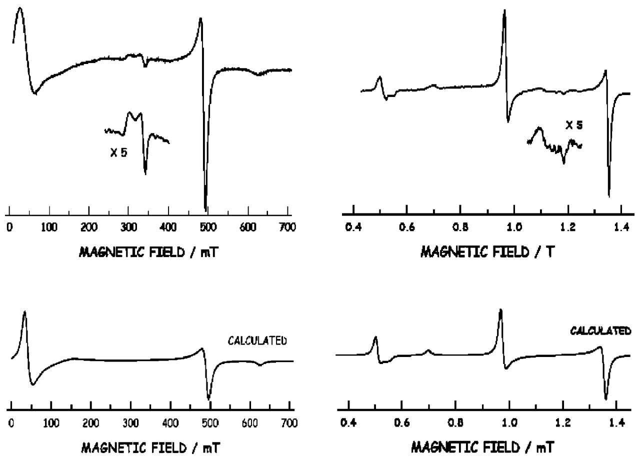

Figure 1. X-band (left spectra) and Q-band (right spectra) experimental and calculated EPR spectra of **1**.

Results and Discussion

Recently, a fluorocarbon soluble bis-fluoroponytailed acid, $[(C_8F_{17}(CH_2)_3)_2CHCO_2H]$, allowed the preparation of the highly fluorous Cu(II) compound, $[Cu(\{C_8F_{17}(CH_2)_3\}CHCO_2)_2]_2$, **1**.[7a] This Cu(II) complex with eight perfluorooctyl chains was found to be soluble in perfluorocarbons at room temperature (fluorine content, 64%) in contrast to the partial solubility of the Cu(II) complex derived from the commercial fluorous acid with only one fluoropontytail, $[Cu(C_8F_{17}(CH_2)_2CO_2)_2]_2$, (fluorine content 62%). Although the synthesis and characterization of **1** had been partially described previously,[7a] we will present a more comprehensive structural characterization based on extensive EPR studies of **1**.

EPR Structural Studies of 1. The Cu(II) carboxylates have been described as a well-known family of air-stable complexes formed by two Cu(II) ions bridged symmetrically by four carboxylate ligands.[9] The EPR spectra of solid, powdered samples of **1** were measured at room temperature in X-band and Q-band (Figure 1). The EPR signals clearly indicated the presence of a Cu(II) magnetic dimer and can be described by the following spin Hamiltonian equation:

$$H = \mu_B\{g_\perp(B_xS_x + B_yS_y) + g_\parallel B_zS_z\} + D\{S_z^2 - 1/3S(S + 1)\}$$

$S = 1$
μ_B = Bohr magneton
g = principal values of the gyromagnetic tensor
D = zero-field splitting

The analysis of the EPR spectra was performed following a procedure previously described,[10−13] and the values obtained for the parameters of the spin Hamiltonian were: $g_\parallel = 2.062(5)$, $g_\perp = 2.364(5)$, and $D = 10.96(10)$ GHz. The calculated X- and Q-band EPR spectra shown in Figure 1 were in excellent agreement with the experimental spectra with the peak widths being the only differences found. This was due to the calculation method; i.e., (a) introduction of a Lorentzian line-shape analysis with isotropic width, 10.2 mT for X-band measurements and 12.0 mT for Q-band measurements and (b) no introduction of the hyperfine interaction with the copper nuclei. This interaction is usually strongly anisotropic, which would explain the observed differences with the peak widths. Both spectra displayed a minor signal centered at 330 mT (X-band) and 1.1 T (Q-band). This signal isdue to a paramagnetic entity ($S = {}^1/_2$) with nearly axial symmetry, whose gyromagnetic tensor was determined by $g_\parallel \approx 2.32$ and $g_\perp \approx 2.07$, and is typical for monomeric or isolated Cu(II) complexes. Such contamination by a small amount (<5%) of monomeric Cu(II) has been previously observed in other solid samples of Cu(II)−carboxylate dimers.[9d]

The obtained values for the spin Hamiltonian parameters ($g_\parallel$, $g_\perp$, and D) are very similar to those obtained for different Cu(II) dimers containing bridging carboxylates, and Table 1 contains the spin Hamiltonian parameters for **1** and several dinuclear Cu(II)−carboxylate complexes of this structural type.[13−17] The ensemble of data confirms the proposed dimeric structure for **1**.

Preparation of Perfluorocarbon Soluble Monomeric Cu(II) Complexes. In view of the previously described hydrocarbon/perfluorocarbon phase-switching behavior of nitrogen ligands coordinated to **1**, we decided to use this new paradigm to solubilize nonfluoroponytailed nitrogen ligands by reaction with **1** and then utilize these as precatalysts in FBC oxidation chemistry. In this manner, we were able to synthesize and isolate Cu(II) complexes analogous to the previously reported fluorocarbon soluble $[Cu(C_8F_{17}(CH_2)_2CO_2)_2(R_f\text{-TACN})]$ complex.[5a] The thesis was that these novel complexes, of the formula $[Cu(\{C_8F_{17}(CH_2)_3\}CHCO_2)_2(L)]$, should have high solubility in perfluorocarbons and possibly have thermomorphic properties **(**highly temperature-dependent *liquid*/*solid* phase miscibilities**)** in organic solvents. Gladysz et al., in particular,[18] and others[19,20] have applied this thermomorphic concept to fluorous compounds and showed that some solid fluorous compounds, displaying extremely low solubility in conventional hydrocarbon solvents at room temperature, become

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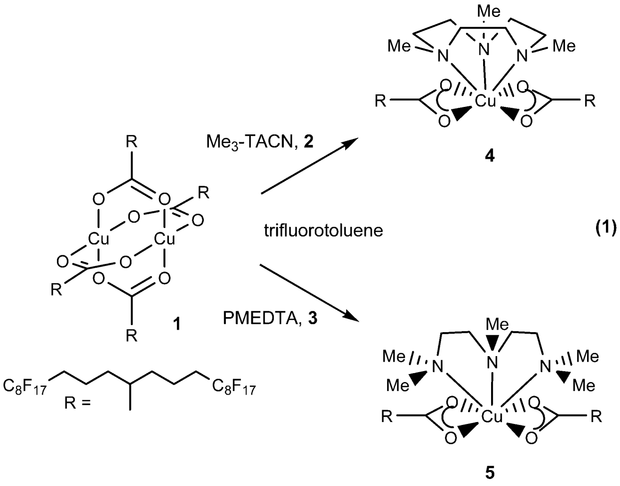
Table 1. Spin Hamiltonian Parameters for Some Cu(II) Dimers Compared to Those of **1**

compd	g_x	g_y	g_z	D(GHz)	E(GHz)	ref
1	2.062		2.364	10.96	–	–
$[CuAc_2]_2$	2.08	2.08	2.42	10.19	0.30	13
$[CuAc_2]_2$	2.053	2.093	2.344	10.34	0.15	14
$[Cu_2(niflumate)_4(H_2O)_2]_4DMF$	2.075		2.36	10.79	–	15
$[Cu_2(niflumate)_4(DMSO)_2]$	2.075		2.36	10.79	–	15
$[Cu_2(O_2CCH{=}CHCH_3)_4(DMF)_2]$	2.0735(12)	2.0769(12)	2.3648(12)	−10.04	0.01	16
$[Cu_2(Sup)_2CH_3CN]_2$	2.070	2.022	2.285	10.43	−0.15	17

highly soluble at higher temperatures, allowing their straightforward recovery by filtration or adsorption onto Teflon solid supports.[21]

The addition of nitrogen ligands **2** or **3** to trifluoromethylbenzene solutions of **1** provided novel **4** and **5**, which were isolated and characterized (eq 1). The addition of the ligands **2** and **3** to trifluoromethylbenzene or perfluoroheptane solutions of **1** provided a change of color from turquoise-blue to dark-green or dark-blue, leading after isolation to **4** or **5** in 40 and 85% yield, respectively.



(1)

The structures depicted in eq 1 are tentatively proposed on the basis of the following structural data. The stoichiometries of **4** and **5** were confirmed by elemental analysis and revealed a metal/carboxylate/nitrogen ligand ratio of 1:2:1. Their IR spectra showed that for **4** and **5**, the two carboxylates were coordinating most probably in the chelate mode, as opposed to $[Cu(C_8F_{17}(CH_2)_2CO_2)_2(R_f\text{-TACN})]$ for which the carboxylates ligands were coordinated to the Cu(II) center in a monodentate fashion.[5a] The coordination mode of the carboxylates was suggested by the small differences, $\Delta\nu = 149\ cm^{-1}$, **4**; $\Delta\nu = 112\ cm^{-1}$, **5**, observed between the asymmetric and symmetric C−O stretches; $\nu = 1611$ and $1462\ cm^{-1}$, **4**; $\nu = 1576$ and $1464\ cm^{-1}$, **5**.[22,23]

The monomeric nature of these compounds was clearly demonstrated by EPR studies of solid powdered samples of **4** and **5** at room temperature (RT). The X-band spectra are shown in Figure 2, and in both cases, they showed signals that can be assigned to isolated monomeric compounds.[24] The signals can be interpreted as being due to a paramagnetic entity ($S = {}^1/_2$) whose principal gyromagnetic values are determined by $g_1 = 2.065(5)$, $g_2 = 2.140(5)$, $g_3 = 2.270(2)$ (**4**) and $g_1 = 2.050(5)$, $g_2 = 2.122(5)$, $g_3 = 2.260(2)$ (**5**). In both cases, the low field component (g_3) displayed a resolved hyperfine structure with a nuclei of spin $I = {}^1/_2$ with effective coupling constants of $A_3 = 492(10)$ MHz (**4**) and $A_3 = 497(10)$ MHz (**5**). The other contributions (g_1 and g_2) are not resolved, indicating that the effective coupling constants are lower than 50 (**4**) or 25 MHz (**5**).

Table 2. Solubility of **1**, **4**, and **5** in Different Solvents[a]

complex	perfluoro-heptane	trifluoro-toluene	toluene	chloro-benzene	Et_2O	CH_2Cl_2	hexane
1 (RT)[b]	s	ps	ns	ns	ns	ns	ns
1 (Δ)[c]	s	s	ns	ns	ns	ns	ns
4 (RT)[b]	s	ps	ns	ns	ns	s	ns
4 (Δ)[c]	s	ps	ns	ps	ps	s	ns
5 (RT)[b]	s	ps	ns	ns	ps	s	ns
5 (Δ)[c]	s	s	s	s	ps	s	ns

[a] 3.5×10^{-3} mmol in 0.5 mL of solvent. s = soluble; ps = partially soluble; ns = no solubility. [b] Room temperature. [c] Reflux temperature or 80 °C for the following solvents: trifluorotoluene, clorobenzene, and toluene.

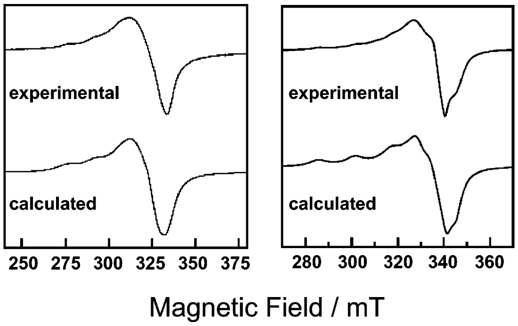


Figure 2. Experimental (X-band, RT) and calculated EPR spectra of **4** (left spectra) and **5** (right spectra).

Our attempts at obtaining single crystals for X-ray analysis of **1**, **4**, and **5** have not been successful. The solubilities of **1**, **4**, and **5** in different solvents at RT or higher temperatures, either reflux temperature or 80 °C, are shown in Table 2. Whereas **1** was soluble only in perfluorocarbons and insoluble in hydrocarbons, novel complexes **4** and **5** were not only fluorocarbon solvent-soluble, but they were found to also be soluble in dichloromethane at room temperature. Interestingly, these novel complexes, especially **5**, displayed good thermomorphic properties. They were insoluble at room temperature in solvents such as toluene and chlorobenzene

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Scheme 1. FBC Oxidation of 4-Nitrobenzyl Alcohol with Precatalysts, **1**, **4**, or **5**

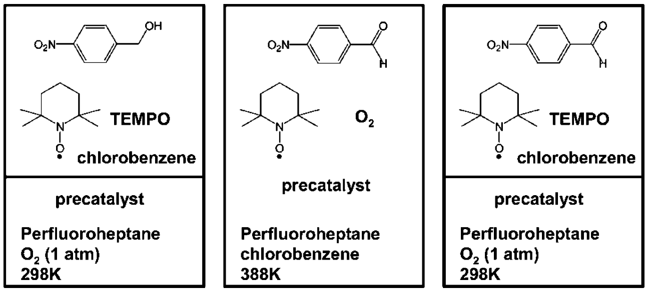


Table 3. Oxidation of 4-Nitrobenzyl Alcohol under FBC Conditions Using **1**[a]

run	conversion (%)[b]	TON
1	100	29
2	100	29
3	100	29
4	75	21
5	45	13
6	9	3

[a] TEMPO (6 mol %), **1** (3.5 mol %), 90 °C, O_2, 8 h. [b] Measured by ^{1}H NMR.

Figure 3. The initial biphasic system at RT with the upper chlorobenzene layer and the perfluoroheptane lower layer containing precatalyst **1**.

but became soluble at higher temperatures (80 °C). This property was subsequently utilized for catalyst recovery experiments in nonfluorous solvents.[18−21]

FBC Alcohol Oxidation Studies. The initial FBC mode at room temperature (Scheme 1) included precatalyst **1** in the lower perfluoroheptane layer, whereas the substrate alcohol, chlorobenzene, and TEMPO were in the upper organic layer. Conversion to the aldehyde was performed at 90 °C in a now single homogeneous phase under an oxygen atmosphere.

The FBC oxidation of 4-nitrobenzyl alcohol to 4-nitrobenzylaldehyde, with **1** as a precatalyst, was demonstrated with five runs (Table 3). A photograph of the FBC system can be seen in Figure 3, with **1** dissolved in the lower fluorous phase and the substrate alcohol and TEMPO in chlorobenzene contained in the upper phase.

Interestingly, **1** alone displays very good catalytic activity, with complete conversion of the alcohol in 8 h. Recycling has been achieved after decantation, and the perfluoroheptane phase was reused for the subsequent runs. The catalytic activity for **1** was maintained during three catalytic cycles and then showed a significant decrease in its activity.

We chose three additional alcohols as substrates for their FBC oxidation using **1** as the precatalyst. The oxidation of aryl alcohols and alkenols proceeded with moderate to high conversions (Table 4, entries 2 and 1, respectively), but the oxidation of an aliphatic, secondary alcohol, 2-octanol, was not successful (entry 4).

We decided to test the catalytic behavior of novel Cu(II) complexes, **4** and **5**, under FBC conditions for the oxidation of 4-nitrobenzyl alcohol to 4-nitrobenzylaldehyde and then compare the results to those obtained for the Cu(II) dimer complex, **1**. These complexes could, in principle, be more stable than the precursor synthon, **1**. The catalytic activities and recycle abilities for **4** and **5** are shown in Table 5.

4 behaved as a precatalyst for the oxidation of 4-nitrobenzyl alcohol to 4-nitrobenzylaldehyde and could also be recycled without a major loss of activity during three consecutive runs; The catalytic activity and recycle ability for **5** were very similar to those displayed by **4**; in comparison, **1** could be recycled for four runs. We surmised that the catalytic performances of **4** and **5** might be affected by “precatalyst leaching” into the hydrocarbon phase. However, this was not the case because the Cu content in the hydrocarbon phase, measured by ICP for precatalyst **5**, after every catalytic run had taken place was very negligible, (Table 6), and even after the fourth run, it accounted for only 1% of the initial amount of **5**. However, we found that the final recovered fluorous phase had become colorless, most plausibly due to reduction to the Cu(I) species that may

Table 4. Oxidation of Various Alcohols to Aldehydes and a Ketone under FBC Conditions, Using **1**[a]

entry	catalyst	alcohol	conversion (%)[b]	TON
1	**1**	2-cyclohexen-1-ol	100	29
2	**1**	benzyl alcohol	60	17
3	RFP, **1**[c]	benzyl alcohol	40	12
4	**1**	2-octanol	0	−

[a] TEMPO (6 mol %), **1** (3.5 mol %), 90 °C, O_2, 8 h. [b] Measured by ^{1}H NMR. [c] Recovered fluorous phase.

Table 5. Oxidation of 4-Nitrobenzyl Alcohol under FBC Conditions Using **4** or **5** as Precatalysts[a]

run	catalyst	conversion (%)[b]	TON	run	catalyst	conversion (%)[b]	TON
1	**4**	99	28	1	**5**	95	27
2	RFP 1[c]	98	28	2	RFP 1[c]	98	28
3	RFP 2[c]	95	27	3	RFP 2[c]	96	27
4	RFP 3[c]	53	15	4	RFP 3[c]	40	11
5	RFP 4[c]	0	−	5	RFP 4[c]	0	−

[a] TEMPO (6 mol %), **4** (3.5 mol %) and Me_3-TACN or PMDETA (1:1), 90 °C, O_2, 8 h. [b] Measured by ^{1}H NMR. [c] Recovered fluorous phase.

Table 6. Amount of Cu Leaching during the FBC Oxidation with **5**

run	Cu content (ppt)[a]
1	4.3
2	2.2
3	3.5

[a] Measured by ICP for data in Table 6; ppt (pg/mL).

Scheme 2. Oxidation of *p*-Nitrobenzyl Alcohol Using **5** in a Thermomorphic Mode

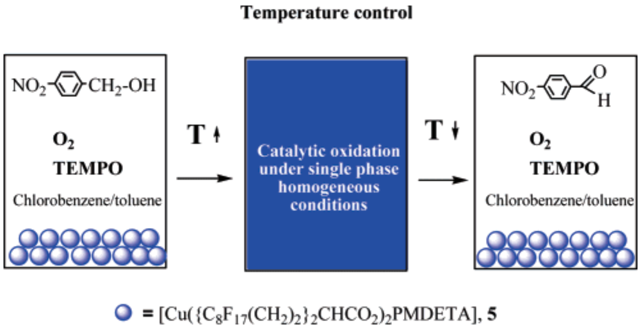


Table 7. Oxidation of 4-Nitrobenzyl Alcohol in Chlorobenzene/Toluene (1:3) Using Thermomorphic **5** as a Precatalyst[a]

catalyst	catalyst amount (g)	recovered catalyst (%)	conversion (%)[b]	TON
5	0.046	–	97	28
RS 1[c]	0.040	87	91	26
RS 2[c]	0.037	91	64	18
RS 3[c]	0.029	78	35	10

[a] Conditions: 1 mL of chlorobenzene, 3 mL of toluene, 4-nitrobenzyl alcohol, TEMPO (6 mol %) and solid **5** (0.0046 g, 3.5 mol %), 90 °C, O_2, 8 h. [b] Measured by ^{1}H NMR. [c] Recovered solid from previous run.

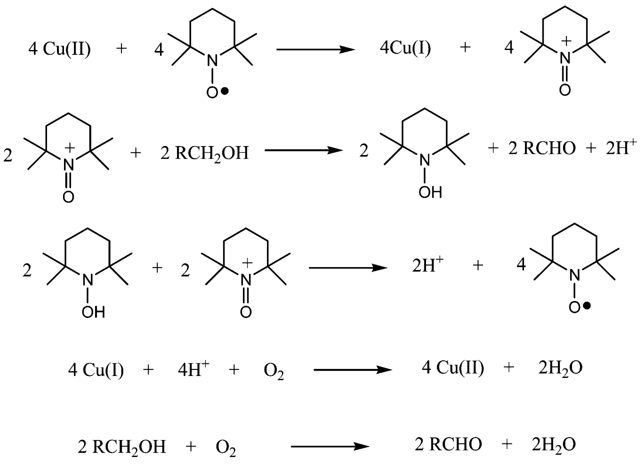
end the catalytic cycle. This was further confirmed by EPR studies of the fluorous phase after reaction, which showed a silent Cu(I) spectrum. Further studies will attempt to assess the structure of such Cu(I) species. Clearly, we have found that the amino ligands do not increase the catalytic activity of Cu(II)−carboxylate complexes in FBC oxidation of alcohols to aldehydes in the presence of TEMPO/O_2.

Thermomorphic Properties of 5 in the Oxidation of 4-Nitrobenzyl Alcohol in the Absence of Fluorous Solvents. There have been relatively few examples of the use of thermomorphic fluoroponytailed complexes, such as **5**, that have been utilized in catalysis studies (Scheme 2).[18−21] As we stated, **5** has excellent thermomorphic properties that show insolubility in solvents, such as toluene and chlorobenzene, at room temperature but show solubility at 80 °C in these same solvents. We performed the oxidation of 4-nitrobenzyl alcohol in a mixture of toluene/chlorobenzene (3:1) using solid **5** as a precatalyst with TEMPO/O_2 at 90 °C. The precatalyst became completely soluble after 1 h of reaction. After the reaction had taken place (8 h), solid **5** could be recovered via filtration techniques.

Table 7 depicts the catalytic activity and the amount of precatalyst recovered after each catalytic run. The oxidation of 4-nitrobenzyl alcohol was demonstrated for three runs without a major loss of catalytic activity. The amount of precatalyst recovered ranged from 80 to 90%.

Mechanism and Fate of 1, 4, and 5 as Precatalysts in the Oxidation of 4-Nitrobenzyl Alcohol under FBC Conditions. A plausible mechanism for this FBC oxidation was proposed on the basis of EPR experiments and was postulated to involve the reduction of the Cu(II) complex to Cu(I) by the TEMPO radical, which was then oxidized again to the initial Cu(II) complex by O_2 while also regenerating TEMPO and producing the aldehyde.[5a] The mechanism was similar to the one reported by Semmelhack et al.[25] for the oxidation of alcohols to aldehydes, with oxygen and Cu(II) ions, mediated by a nitrosonium ion that was generated from the TEMPO radical (Scheme 3). This catalytic cycle was based on the reactions and electrochemical studies that indicated that Cu(II) could indeed oxidize TEMPO to the nitrosonium ion and, in that process, become reduced to Cu(I).

Scheme 3. Semmelhack Mechanism for the Oxidation of Alcohols to Aldehydes Mediated by Cu(II), TEMPO, and O_2[25]



We carried out our standard EPR catalytic experiment (Figure 4, spectra a−c, Experimental Section) with **4**. **4** was dissolved in perfluoroheptane; then to the reaction mixture were added chlorobenzene, TEMPO, and 4-nitrobenzyl alcohol. The reaction started at 90 °C in the presence of O_2, and after 1.2 h (Figure 4), followed by cooling to room temperature, an aliquot was removed from the perfluoroheptane phase and immediately frozen at 77 K in an EPR tube. The spectrum shows a narrow central signal at about $g = 2.006$, which can be associated with the TEMPO radical. The spectrum of the reaction mixture also has a Cu(II) signal, with $g_{\|} = 2.26(1)$ and $g_{\perp} = 2.06(1)$, $A_{\|} = 520(5)$ MHz and $A_{\perp} < 50$ MHz. After 4 h, the signals due to the Cu(II) species disappeared, whereas the signal due to TEMPO decreased (Figure 4, spectrum b). After 8 h, we observed a recovery of the signal corresponding to the Cu(II) species (Figure 4,

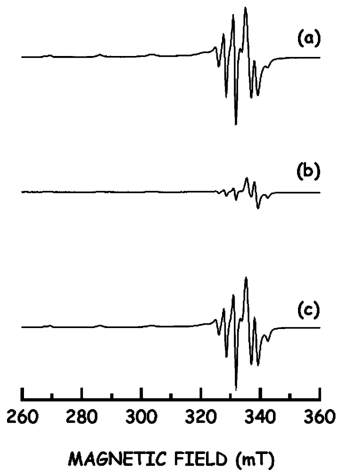


Figure 4. X-band EPR spectra of the perfluoroheptane layer during the course of the oxidation of 4-nitrobenzyl alcohol with **4** and measured at liquid nitrogen. (a) 1.2 h; (b) 4 h; (c) 8 h.

spectrum c) and of the signal assigned to the TEMPO radical. Therefore, these data were similar to those of the mechanism proposed previously, in accordance with the Semmelhack mechanism, shown in Scheme 3.[5a,25]

Conclusions

We have shown that we are able to totally solubilize nonfluoroponytailed ligands, such as **2** and **3**, in fluorocarbon solvents by a phase-switch process, which occurs by reaction with the fully fluorocarbon-soluble Cu(II) complex, **1**, to provide **4** and **5**. The dimeric nature of **1** was unambiguously ascertained by EPR spectroscopy, whereas novel complexes **4** and **5** were characterized by EPR, IR, and UV−vis solid-state spectroscopy. These complexes were used as precatalysts in the FBC oxidation of an alkenol, 2-cyclohexen-1-ol, benzyl alcohol, and *p*-nitrobenzyl alcohol, whereas the only example of a straight-chain aliphatic alcohol, 2-octanol, was unreactive. Interestingly, the Cu(II)−carboxylate dimer **1** was found to be the more active precatalyst. We have concluded that beyond efficient solubilization of the nonfluoroponytailed ligands into the coordination sphere of the fluorocarbon soluble Cu(II) complex, **1**, the benefits in catalytic activity were minimal in FBC oxidation reactions of alcohols with **4** and **5**. However, we have further demonstrated that the thermomorphic mode can be utilized in nonfluorous solvent, oxidation catalytic experiments with **5**. More studies are necessary to fully understand the role of fluorous solvent-soluble metal carboxylates in other catalytic reactions, but clearly, these simple complexes, such as **1**, could be FBC candidates as precatalysts for many classical organic reactions.[26]

Experimental Section

General Procedures. All manipulations involving air-sensitive reagents and hygroscopic Me_3-TACN were performed under an inert atmosphere of dry argon with the use of Schlenk techniques, and all solvents were dried and degassed before use. $[\{C_8F_{17}(CH_2)_3\}_2CHCOOH]$,[7] was prepared as described previously in a three-step procedure starting from diethyl malonate and $C_8F_{17}(CH_2)_3I$.[7b] The fluorocarbon solvents, and some starting perfluoro derivatives, were purchased from ABCR GMBH & Co., and alcohols and ligands *N*-1,4,7-Me_3TACN and PMDETA were from Aldrich Chemical Co. The oxidant, TEMPO, was a commercial product from Avocado, and all were used without further purification. ^1H, $^{13}C\{^1H\}$, and ^{19}F NMR spectra were obtained on a 300 MHz Varian-GEMINI 2000 apparatus in $CDCl_3$ solutions; chemical shifts are quoted relative to $SiMe_4$ (external, ^1H and $^{13}C\{^1H\}$) and $CFCl_3$ (external ^{19}F). C, H, N elemental analyses were performed with a Perkin-Elmer 2400 microanalyzer, whereas mass spectra (LSIMS, 3-nitrobenzyl alcohol as matrix) were obtained on a VG Autospec spectrometer using a Cesium gun. The IR spectra were recorded on a Perkin-Elmer Spectrum One FT-IR instrument in a Universal ATR Sampling Accessory. The diffuse reflectance spectra were recorded on a Cary 500 scan UV−vis−NIR spectrophotometer. The electron paramagnetic resonance (EPR) spectra were measured on a Bruker ESP380E spectrometer working either at X-band or Q-band. In the X-band experiment, an ER4102st cavity was used; the frequency was determined with a Hewlett-Packard HP5350B frequency counter. Powdered samples as well as solutions were introduced in a standard EPR quartz tube (707-SQ from Wilmad). The spectra of powdered samples were recorded at RT. To follow catalytic experiments, aliquots of the perfluoroheptane layer were removed and immediately frozen at liquid nitrogen temperature (LNT). These frozen solutions were measured at LNT using an immersion quartz Dewar. The microwave frequency was determined. For detecting Cu(II) complexes, the X-band conditions were as follows: 3320 ± 125 mT scan range, 2 mW microwave power, 9.51 GHz microwave frecuency, RT or LNT, 0.4 mT modulation amplitude, 100 kHz modulation frequency, conversion time, 163.84 msg. In the case of the Q-band experiment, the conditions were as follows: 750 ± 650 mT scan range, 2.52 mW microwave power, 33.9 GHz microwave frecuency, RT, 0.4 mT modulation amplitude, 100 kHz modulation frequency, conversion time, 327 msg.

Synthesis of $[Cu(\{C_8F_{17}(CH_2)_3\}_2CHCOO)_2(Me_3\text{-}TACN)]$, 4. **1** (0.2022 g, 0.1 mmol) was partly dissolved in 3 mL of trifluorotoluene, and the ligand Me_3-TACN (21.31 μL, 0.1 mmol) was added. The resulting olive-green solution was reacted for 1 h at RT. The solvent was concentrated to ca. 0.5 mL via flash distillation, and 2 mL of perfluoroheptane was then added. The solution was cooled to −40 °C (5 days). **4** precipitated as a dark-green solid in 40% yield (0.0877 g). Elemental anal. calcd for $C_{57}H_{47}O_4N_3F_{68}Cu$: C 31.21, H 2.16, N 1.92; found: C 30.94, H 2.02, N 1.61. IR: carboxylate bands $\nu = 1611$ and 1462 cm^{-1}. LSIMS−MS: *m/z* 2051 (7%), [M − (TACN-Me_3) + NMe].

Synthesis of $[Cu(\{C_8F_{17}(CH_2)_3\}_2CHCOO)_2(PMDETA)]$, 5. 1 (0.2022 g, 0.1 mmol) was partly dissolved in 3 mL of trifluorotoluene, and the ligand PMDETA (20.87 μL, 0.1 mmol) was added. The resulting solution was reacted for 1 h at RT, giving a dark-blue solution that was allowed to react for a further 23 h. The solvent was removed to ca. 0.5 mL via flash distillation, and 5 mL of toluene was then added. The solution was cooled to −40 °C (12 h), and **5** precipitated as a dark-blue solid in 86% yield (0.1867 g). Elemental anal. calcd for $C_{57}H_{49}O_4N_3F_{68}Cu$: C 31.18, H 2.25, N 1.91; found: C 31.04, H 2.21, N 2.13. IR: carboxylate bands $\nu =$ 1576 and 1464 cm^{-1}. LSIMS−MS: *m/z* 2025 (37%), [M − N5].

Standard Catalytic Oxidation of Alcohols under FBC Conditions. A 25-mL Schlenk tube, previously purged with Ar, was charged with **1**, **4**, or **5** (3.5 mol %). **1** was added as a solid (0.021 mmol, 0.0425 g) in 2 mL of perfluoroheptane, while **4** and **5** were prepared in situ as follows: to a solution of **1** in perfluoroheptane, Me_3-TACN (0.021 mmol, 4.07 μL) was added for the preparation of **4**, or PMDETA (0.021 mmol, 4.8 μL) was added for the preparation of **5**. The resulting perfluoroheptane solutions were allowed to react for a further 1 h at RT. The hydrocarbon phase (upper layer of the biphasic system) consisted of 0.60 mmol of 4-nitrobenzyl alcohol (0.0093 g) in 2 mL of chlorobenzene. Then 6 mol % (0.036 mmol, 0.0053 g) of TEMPO was added, and the biphasic reaction mixture was stirred under an O_2 atmosphere at 90 °C (during 8 h, see Tables 3 and 5). The formation of other aldehydes, with **1** as a catalyst, was performed in the manner as described above, starting from the indicated alcohols (see Table 4). After the reaction had taken place, the Schlenk tube was cooled to room temperature, and the two phases were separated by decantation. The fluorous phase was washed with chlorobenzene (3 × 2 mL), and the combined organic layers were diluted with 30 mL of Et_2O and washed successively with brine (40 mL) and water (40 mL). After drying ($MgSO_4$), filtration, and complete evaporation

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(25) Semmelhack, M. F.; Schmid, C. R.; Cortés, D. A.; Chou, C. S. *J. Am. Chem. Soc.* **1984**, *106*, 3374.

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of the solvent under reduced pressure, the crude product was weighed and analyzed by ^{1}H NMR. The fluorous phase was separated and used directly, after adding 0.5 mL of perfluoroheptane, for further catalytic runs.

Catalytic Oxidation of 4-Nitrobenzyl Alcohol in the Absence of Fluorous Solvents. A 25-mL Schlenk tube, previously purged with Ar, was charged with **5** (3.5 mol %, 0.021 mmol, 0.0460 g), 3 mL of toluene, and 1 mL of chlorobenzene. Then, 0.60 mmol of 4-nitrobenzyl alcohol (0.093 g) and 6 mol % (0.036 mmol, 0.0053 g) of TEMPO were added, and the reaction mixture was stirred under an O_2 atmosphere at 90 °C for 8 h (see Table 7). After 1 h at 90 °C, **5** was found to be solubilized in the reaction medium. After the reaction had taken place, the reaction mixture was cooled, and **5** precipitated under vacuum and was weighed and then recycled for further runs. The identification of 4-nitrobenzylaldehyde and the analysis of the entire reaction mixture by ^{1}H NMR were accomplished as described above.

EPR−FBC Experiment. Using standard oxidation conditions for 4-nitrobenzylic alcohol, as outlined in the Experimental Section using **4** as the precatalyst, aliquots of the perfluoroheptane layer were removed, after cooling the reaction mixture to RT, and were immediately frozen at LNT in an EPR tube (Figure 4, EPR spectra a−c).

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