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The Pyridyl-Tag Strategy Applied to the Hydrocarbon/Perfluorocarbon Phase-Switching of a Porphyrin and a Fullerene

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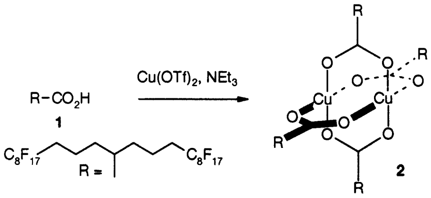
The use of perfluorocarbons as reaction media to perform catalytic reactions, or as a labeling phase for reactants, substrates, and products, is receiving considerable interest.[1] The so-called "fluorous techniques" are now considered as powerful tools for the rapid, simple, and efficient purification of complex reaction mixtures.[2] Fluorophilic ligands and reactants are obtained by the irreversible and covalent attachment of a fluorous domain, for example, at least one lipophobic perfluoroalkyl chain ($-C_nF_{2n+1}$, $n > 5$). In "fluorous synthesis" techniques, substrates and/or products were first attached to cleavable "heavy fluorous" tris-(perfluoroalkyl-alkyl)-tin or -silyl tags through Sn−N, Sn−C, or Si−O bonds.[3] "Light fluorous tags" such as fluorous acyl groups or a fluorous Boc group with fewer fluorine atoms were also developed.[4]

Recently, Ley and co-workers reported a new substrate phase-switch method using bipyridine-tagged substrates that could be immobilized on a copper(II)-carboxylate resin through reversible metal coordination.[5] For a long time, we have been interested in the use of fluorinated carboxylates as ligating counteranions to favor the solubilization of transition metal complexes in perfluorocarbons.[6] We recently reported that Mn(II)- and Co(II)-carboxylate complexes of bis-perfluorooctylpropyl carboxylic acid **1** were highly fluorophilic.[7] It was then anticipated that perfluorocarbon solutions of metal-carboxylate could represent a new labeling phase for pyridyl-tagged molecules. Herein we report the preparation of the copper(II)-carboxylate complex **2** and its application to the hydrocarbon/perfluorocarbon phase-switching of a porphyrin and a fullerene.

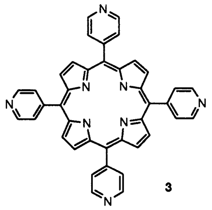
Copper(II) carboxylates are a well-known family of air-stable complexes formed by two Cu^{2+} ions bridged symmetrically by four carboxylate ligands.[8] This rigid and well-defined "paddle-wheel" structure (eq 1) posseses two accessible axial coordination sites for ligands such as pyridine derivatives.

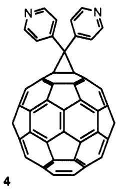


(1)

Copper(II)-carboxylate complex **2** thus appeared as a good candidate for a heavy fluorous inorganic phase-switch. Complex **2** was prepared in high yield (>95%) by reacting 2 equiv of the triethylammonium salt of **1** with $Cu(OTf)_2$ in acetone.[9] Complex **2**, with eight perfluorooctyl fragments and a 63.9% fluorine content, is highly fluorophilic and dissolves readily in perfluorocarbons under gentle heating to break the crystal packing forces. Once dissolved, the partition coefficient is 100% in favor of the fluorous phase whatever the organic solvent employed, as checked by UV−vis spectroscopy.

To demonstrate the efficiency of our phase-switching strategy, we choose as pyridyl-tagged molecules the commercially available 5,10,15,20-tetra(4-pyridyl)porphyrin **3** and the C_{60} fullerene dipyridyl monoadduct **4** recently reported by Diederich and co-workers.[10] Porphyrins and fullerenes are prototypical examples of molecules for which solubilization in perfluorocarbons is really challenging because of their size and relatively high polarity. Moreover, due to their excellent O_2 photosensitizing properties, they represent important target molecules for which solubilization in perfluorocarbons could find useful applications such as in photodynamic therapy (PDT)[11] or in oxidation reactions. To date, only two examples of perfluorosoluble porphyrins,[12] and one example of perfluorosoluble fullerene,[13] have been reported. The solubilization of a *meso*-aryl-substituted porphyrin was achieved by covalently linking eight perfluorooctyl chains (seven steps, 3% overall yield), whereas six perfluorooctyl chains were required in the case of the fullerene.





When a chloroform solution of the porphyrin **3** (0.1 mM, 2 mL) is layered on a perfluorodecalin solution of complex **2** (3.25 mM, 1.5 mL), a red and blue biphasic system is formed (Figure 1). Upon stirring, rapid bleaching of the upper phase is observed, while the perfluorocarbon phase turns to a homogeneous dark blue solution (Figure 1).

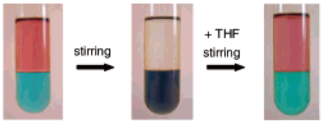


Figure 1. Photographs of a phase-switching experiment between a chloroform solution of **3** (upper phase) and a perfluorodecalin solution of **2** (lower phase).

After the mixture was stirred for 30 min at 1250 rpm, almost complete extraction (99.9%) of the porphyrin into the fluorous layer is achieved as evidenced by the UV−vis absorption spectra (Figure 2). The visible spectrum of the fluorous phase corresponds to the superimposition of the porphyrin and complex **2** spectra recorded before the extraction. Clearly, under these conditions (**2**/pyridyl

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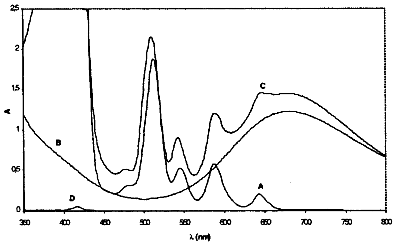

Figure 2. Absorption spectra: chloroform before (A) and after (D) extraction; perfluorodecalin before (B) and after the extraction (C).

group ratio of 6), pyridine coordination to complex **2** occurs at the solvent interface leading to perfluorosoluble [porphyrin-dicopper] supramolecular assembly. For a phase-switching technique to be synthetically useful, the release of the immobilized molecule has to be simple, rapid, and efficient. We were pleased to find that by simply adding an excess of THF (500 μL, 7700 equiv/pyridyl group) to the biphasic system, the porphyrin is quantitatively released into the hydrocarbon phase, whereas **2**, with coordinating THF ligands, is quantitatively recovered in the fluorous phase as checked accurately by UV−vis spectroscopy.[14] Thus, no leaching or decomposition of **2** is observed during the recycling process. The THF acts as a pyridine-competing ligand, the ability of THF to coordinate transition metal-carboxylate complexes being previously evidenced.[15] Interestingly, due to the high lability of the THF ligands, the perfluorocarbon solution can be reused for another "catch and release" experiment with the same efficiency, after washing the perfluorodecalin layer three times with chloroform to remove the excess solubilized THF.[16] After being washed, THF molecules are still coordinated to **2** as evidenced by UV−vis spectroscopy.[14]

We then evaluated the maximum loading capacity of a perfluorodecalin solution of complex **2** by studying a biphasic system with equimolar amounts (1 μmol) of **2** (1 mM, 1 mL of perfluorodecalin) and **3** (0.1 mM, 10 mL of chloroform). Following the disappearance of the 512 nm absorption band of the porphyrin in the chloroform phase, we found that a maximum of 0.5 μmol of **3** can be extracted, that is, 0.5 mol of porphyrin per mole of complex **2**. Under these experimental conditions (**2**/pyridyl group ratio of 0.25), the formation of a red precipitate suspended in the perfluorodecalin with the concomitant complete decoloration of the fluorous phase is observed. Even from the precipitate in suspension in the perfluorodecalin, **2** (1 μmol) and **3** (0.5 μmol) are still released and recovered quantitatively by addition of THF (1.3 mL). The precipitate that contains **2** and **3** can be isolated by filtration, the red powder obtained being totally insoluble in both organic solvents and perfluorocarbons, even upon heating. From the structural features of **2** and **3**, one could expect that polymeric supramolecular assemblies of low solubility are formed, formation that should be particularly favored when using equimolar amount of **3** and **2**. Further work is in progress to get insights into the structures of the supramolecular assemblies formed when varying the **2**/**3** ratio used and will be reported in due course. Preliminary experiments have shown that the 5-pyridyl-10,15,20-triphenylporphyrin,[17] which cannot form polymeric assemblies, is not extracted even in the presence of 100 equiv of **2**. Thus, at least a "bis-monopyridyl" tag is required to get an efficient extraction (see below with the fullerene), the poly-monopyridyl tags allowing the formation of oligomeric or polymeric assemblies.

The hydrocarbon/perfluorocarbon phase-switching of a nonfluorinated fullerene was conducted using the C_{60} fullerene dipyridyl monoadduct **4**. As demonstrated with **3**, the fullerene **4** in solution in chloroform (0.13 mM, 1 mL) is efficiently extracted (90%) into a perfluorodecalin solution of **2** (20 mM, 0.5 mL) after 30 min of stirring (1250 rpm), the extraction being quantified by following the disappearance of the 325 nm absorption band of **4** in the chloroform phase.[18] A larger amount of **2** was required for a good extraction of the dipyridyl-substituted fullerene **4** (40 equiv/pyridyl group) as compared to the tetrapyridyl porphyrin. Precipitation was never observed with the fullerene. As with **3**, the release of **4** is quantitative upon addition of THF (200 μL, 10 550 equiv/pyridyl group) to the biphasic system.

To conclude, we have shown that coordination chemistry at the dicopper complex **2** is a powerful hydrocarbon/perfluorocarbon phase-switching strategy for polypyridyl-substituted molecules. Of particular interest is the ease of both the release of the immobilized molecules and the recovery of the phase-switch **2**, just by using THF. We believe that this strategy could be applied to a large variety of copper coordinating tags, with many other types of tagged molecules, and thus should find useful applications in, for example, combinatorial synthesis. Moreover, the chemical or photophysical properties of the pyridyl-tagged molecule can potentially be studied either in organic solvents or in perfluorocarbons. The approach presented here can therefore be considered as a more general strategy than the covalent attachment of perfluoroalkyl chains, where the molecule obtained is only soluble in perfluorocarbons.

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Supporting Information Available: Detailed preparation of **2**, UV−vis spectra of **2** + THF and of the extraction of **4** in the fluorous phase (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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