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Green organometallic chemistry: $CpFe^+$-induced amination of chloroarenes in water

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Dedicated to our distinguished colleague Professor François Mathey at the occasion of his 60th birthday

Abstract

Reaction of NH_3, primary amines and non-bulky secondary amines with the complexes $[Fe^{II}Cp(\eta^6\text{-ArCl})][X]$ ($Ar = C_6H_5$ or $o\text{-}C_6H_4Cl$, $X = Cl$, BF_4 or PF_6) *in water* at room temperature gives the nucleophilic substitution products $[Fe^{II}Cp(\eta^6\text{-}ArNR^1R^2)][X]$ isolated as PF_6 salts. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Green chemistry; Water; Amination; Chloloarene; Iron

1. Introduction

Biphasic catalysis involving an aqueous phase has been a popular subject during the last two decades for catalyst recovery, in particular with the development of the water-soluble triply-sulfonated triphenylphosphine $P(m\text{-}C_6H_4SO_3^-Na^+)_3$ (TPPTS) by Kunz for the hydroformylation of propene to butyraldehyde, a process industrialized by Rhône-Poulenc [1–4]. The more recent concern for environment-safe chemistry or "green chemistry" now encourages chemists to adopt a slightly different angle that consists in completely avoiding organic solvents whenever possible and to use water as the solvent [5,6]. The amination of chloroaromatics using palladium catalysis in organic solvents has been a challenge for some time. A key step in these reactions is the oxidative addition of the aryl–halide bond [7,8]. This bond is all the more difficult to cleave as it is stronger (bond strengths: ArI < ArBr < ArCl), e.g. the chloroarenes, which are the only economically attractive halogenoarenes, are the most difficult to activate. Nucleophilic substitution of halides in halogenoaromatics usually only proceeds at high temperatures (typically 300 °C), but electron-withdrawing arene substituents such as the nitro groups or some organometallic fragments facilitate this reaction [9–11]. In particular, the isolobal 12-electron moieties $Cr(CO)_3$, $Mn(CO)_3^+$ and $CpFe^+$ are activators for these reactions [11,12]. For instance, nucleophilic substitution of chloride in the monocationic complexes $[Fe^{II}Cp(\eta^6\text{-ArCl})][PF_6]$ by a variety of nucleophiles [13–23] including NH_3 [13] and amines [13–15,19,23,24] has been carried out under mild conditions in organic solvents. We have re-investigated these reactions using water as the solvent, and now report that amination of chloroaromatics in the complexes $[Fe^{II}Cp(\eta^6\text{-ArCl})][X]$ ($X = Cl$ or PF_6) can be achieved at room temperature in water.

2. Results

The complexes $[Fe^{II}Cp(\eta^6\text{-ArCl})][X]$ ($X = Cl$, BF_4 or PF_6) are easily accessible by ligand substitution between a ring of ferrocene and the chloroaromatic in the presence of $AlCl_3$. These reactions are currently carried out in refluxing heptane or any other inert alcane around 100 °C for a few hours provided Ar does not contain a heteroatom which is incompatible with the presence of $AlCl_3$ [13,25]. Aluminum powder should not be added, unlike in the reaction with aromatics lacking the chloro substituent, because of the partial reduction of the chloroarene ligand by aluminum in the

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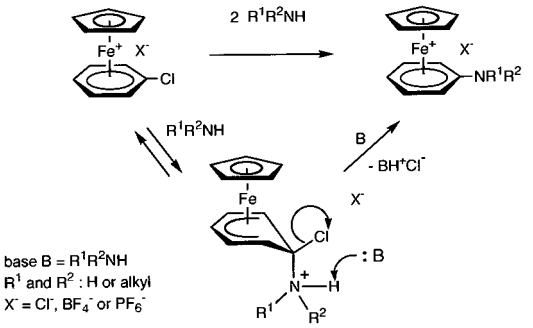
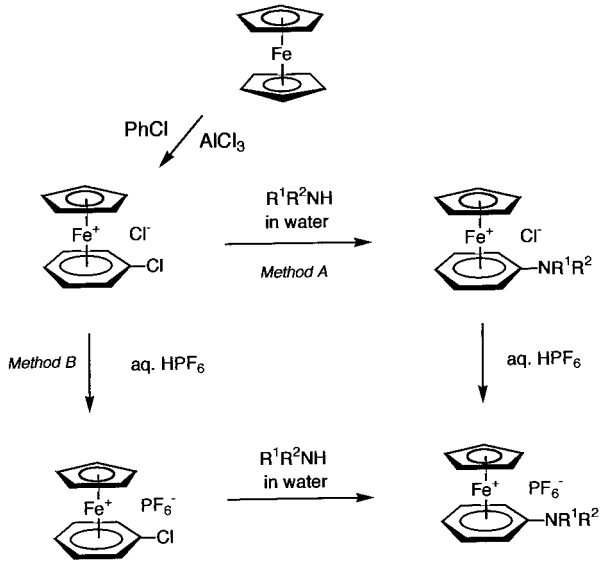
course of the reaction. After this ligand substitution reaction, slow hydrolysis by ice-water provides an aqueous phase which contains the cationic salt $[Fe^{II}Cp(\eta^6\text{-}ArCl)][Cl]$ resulting from the hydrolysis of the water-sensitive $AlCl_4^-$ anion. Then, 1 N aqueous ammonia is added in order to precipitate the Al^{3+} cations as the hydroxide $Al(OH)_3$ which is filtered off. Reactions of these organoiron salts with NH_3 and a variety of amines have been reported by the Nesmeyanov and Sutherland groups to readily proceed in methylene chloride (Scheme 1). Two strategies are possible at this stage in order to perform these reactions in water (Scheme 2):

1. Concentrate these aqueous solutions of the water-soluble organometallic chloride salt resulting from hydrolysis of the ligand substitution reaction and elimination of the Al^{3+} ions in order to carry out the nucleophilic substitution with the amine (method A). Since it is a bimolecular reaction, it should be carried out at a reasonable concentration. Aqueous HPF_6 can be added afterwards in order to precipitate, extract and purify the PF_6 organoiron salt.



Scheme 1.



Scheme 2.

2. Add aqueous $H^+PF_6^-$ in order to precipitate or further extract with methylene chloride the partly insoluble organometallic PF_6^- salt before carrying out the nucleophilic reaction in water (method B). If aqueous $H^+BF_4^-$ is added instead of $H^+PF_6^-$, the organometallic BF_4^- salt remains water soluble but can also be extracted from water using methylene chloride whereas such an extraction is too tedious with the chloride salt.

In either case, it is essential to perform the nucleophilic substitution reactions at a relatively high concentration in water in order to reduce the reaction time at room temperature. The yellow salts $[Fe^{II}Cp(\eta^6\text{-}ArCl)][PF_6]$ were also isolated, recrystallized and characterized by comparison with literature data. When the BF_4 salts were involved, they usually formed as oils because of their high hygroscopicity even if they were free of other impurities.

Reactions of the parent compound $[Fe^{II}Cp(\eta^6\text{-}C_6H_5Cl)][X]$ ($X = Cl$, BF_4 or PF_6) were carried out at the mmol scale in 5 ml water with benzylamine, phenethylamine, methylbenzylamine, dimethylamine and 7 N ammonia at room temperature and were found by ^{1}H-NMR to be complete after 5 h. The products were readily characterized using ^{1}H-NMR by comparison with literature data. Residual water was found by ^{1}H-NMR and was difficult to remove completely, the arylamine complexes being hygroscopic even as PF_6 salts. The integration showed some excess of the alkyl and aryl protons due to some $[Fe^{II}(amine)_6][PF_6]_2$ formed by decomplexation. This impurity could be removed by washing the organoiron products upon refluxing in ether or THF in which the impurities were extracted. The yields in complexes $[Fe^{II}Cp(\eta^6\text{-}ArNR^1R^2)][PF_6]$ were found to be between 50 and 70% after reprecipitation of methylene chloride solutions with diethylether.

With 7 N ammonia, the reaction was found to proceed slowly at room temperature. For instance, after 1 day, only 10% of the starting chlorobenzene complex was converted to the final aniline complex. More rapid consumption of the starting complex can be achieved within 1 day at 60 °C, giving 58% yield of aniline complex and some of the red complex $[Fe^{II}(amine)_6][PF_6]_2$.

The nucleophilic reaction of $[Fe^{II}Cp(\eta^6\text{-}C_6H_5Cl)][PF_6]$ was also attempted with the bulkier secondary amine diethylamine in water. In this case, there was no reaction within 1 day at room temperature whereas the reaction was complete in methylene chloride. Upon heating at 50 °C for 96 h, the nucleophilic reaction occurred, but the ^{1}H-NMR spectrum of the crude reaction mixture showed an excess of ethyl protons. This was again attributed to decomplexation yielding a minor amount of $[Fe^{II}(NHEt_2)_6][PF_6]_2$ which was formed together with the aminoarene sandwich

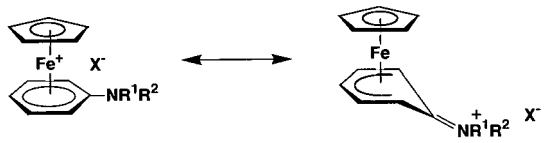


Chart 1.

complex in the ratio 1/6. The yield of isolated $[Fe^{II}Cp(\eta^6\text{-}C_6H_5NEt_2)][PF_6]$ under these conditions was 25%. Attempts to perform the nucleophilic substitution with dibenzylamine did not give the desired nucleophilic substitution product.

The complex $[Fe^{II}Cp(\eta^6\text{-}o\text{-}C_6H_4Cl_2)][PF_6]$ is also accessible in 20% yield from ferrocene and $o\text{-}C_6H_4Cl_2$ in the presence of $AlCl_3$. Reactions with benzylamine and phenethylamine were similarly carried out on the PF_6 salt in water at room temperature for 5 h and gave exclusively the monosubstitution products as already reported for the same reactions in dichloromethane. The products were purified as above by reprecipitation and the yields of the nucleophilic substitution reactions were 65%.

3. Discussion

Complexation of chloroaromatics by $CpFe^+$ leading to yellow salts not only provides a strong activator for nucleophilic substitution, but also allows solubilization of these products in water provided the counter cation is not too large (BPh_4^- would be too large an anion). The large water solubility of the chloride and BF_4^- organoiron salts and the modest solubility of the PF_6^- ones render reactions in water possible. This brings flexibility to the reaction procedure since the nucleophilic substitution can be achieved either before or after addition of the aqueous solution of the acid of the chosen anion provided the concentration is high enough.

The nucleophilic substitution of chloride in $[Fe^{II}Cp(\eta^6\text{-}C_6H_5Cl)][X]$ and $[Fe^{II}Cp(\eta^6\text{-}o\text{-}C_6H_4Cl_2)][X]$ can be achieved with NH_3, primary amines and to some extent with secondary amines provided the alkyl groups are not too bulky (Me, Et). The reactions with NH_3, primary amines and dimethylamine can be carried out in water at room temperature, but more forcing conditions (50 °C) are necessary with diethylamine giving a mediocre reaction yield, and dibenzylamine does not lead to the substitution product in water. This is a limitation because heating provokes decomplexation with formation of $[Fe^{II}(amine)_6][PF_6]_2$, probably occurring before the nucleophilic substitution reaction, because the chloride substituent weakens the iron–arene bond, whereas the amino group strengthens it. Even reactions at room temperature give some of this side product which limits the reaction yields; this product can be washed out using warm ethers.

Thus, it is clear that the nucleophilic substitution does not proceed quite as easily in water as in methylene chloride, although the fact that these reactions proceed in water at room temperature illustrates the impressive electron-withdrawing properties of the cationic organoiron activator. The mechanism consists in the rate-limiting nucleophilic attack of the amine onto the *ipso* carbon atom followed by the removal of HCl from the chlorocyclohexadienylammonium intermediate by excess amine [25–28]. Thus, the reaction stoichiometry required the use of two equivalents of amine. Water (in large excess) gives a hydrogen bond $H\text{–}O\text{–}H\cdots NHR_2$ which decreases the electron density on the nitrogen atom of the amine and weakens its nucleophilicity, disfavoring the nucleophilic attack.

We noticed that the complexes $[Fe^{II}Cp(\eta^6\text{-}ArNR^1R^2)][PF_6]$ formed were very robust. Usually, decomplexation of the arene ligand was obtained by UV–vis photolysis [25,29,30], but such a procedure did not work in this case, the complexes being recovered after such reactions. This is due to the electron-releasing character of the amino substituents, but also to the contribution of the cyclohexadienyliminium resonance form to the actual structure (Chart 1).

Theoretical calculations confirmed this contribution, the calculated structure showing a small but significant dihedral angle of the arene with a long distance between iron and the *ipso* carbon [31]. This strong influence of the amino substituent on the arene ligand also explains why only monosubstitution occurs with $[Fe^{II}Cp(\eta^6\text{-}o\text{-}C_6H_4Cl_2)][PF_6]$, as already reported for the reaction performed using methylene chloride as the solvent [23]. The first amino substituent deactivates the arene ligand towards the second substitution for the reasons indicated above.

The exergonic single-electron reduction of $[Fe^{II}Cp(\eta^6\text{-}C_6H_5NEt_2)][PF_6]$ using the electron-reservoir complex $[Fe^{I}Cp(C_6Me_6)]$ [30,32] in the presence of 1 atm CO successfully led to decomplexation forming $[Fe^{II}Cp(C_6Me_6)][PF_6]$ and $[Fe^{I}Cp(CO)_2]_2$. It is also possible to carry out this decomplexation reaction in the absence of CO, which is more convenient, but chromatographic purification is then necessary in order to isolate the free aniline derivative. Despite these preliminary attempts, an extensive study with the aim to recover good yields of the free arylamines on the gramme scale with all the compounds was not carried out. Anyway, the recovery of free amines using the temporary stoichiometric complexation by transition-metal groups is not a promising strategy in view of the remarkable progress of the palladium catalyzed aryl-coupling reactions. It is hoped that this recent progress in palladium catalysis will finally provide a viable amination route of chloroaromatics [33,34]. Attempts to

use the $CpFe^+$ moiety in catalytic amounts to activate amination of chloroaromatics were not successful. The synthesis and transformation of arene complexes in water has an interest per se, however, because of the introduction of the redox center and the potential use of such organometallic materials as building blocks for molecular electronics, for instance with non-linear optical properties. Finally, it should be noted along this line that another family, the complexes [FeCp(η^6-$ArCHR^1NH_2$)][PF_6] in which the amino group is located in β position from the arene ligand, have been obtained by Moinet by reduction of the corresponding oximes [35].

4. Experimental

4.1. General

The solvents were purified as indicated elsewhere and bi-distilled water was used. The NMR spectra were recorded with a Brucker AC 200 (200MHz) spectrometer. All the complexes [FeCp(η^6-C_6H_5Cl)][X], [FeCp(η^6-*o*-$C_6H_4Cl_2$)][X] and [FeCp(η^6-$ArNR^1R^2$)][PF_6] were previously described and synthesized according to the classic known procedures [13–23]. The complexes [FeCp(η^6-$ArNR^1R^2$)][PF_6] were identified by comparison between the ^{1}H-NMR spectra recorded in CD_3COCD_3 using Me_4Si as the reference and those reported in the literature [13–23].

4.2. Procedures for the amination of the complexes [FeCp(η^6-ArCl)][X] (X = Cl, BF_4 or PF_6) in water

4.2.1. Method A

The aqueous solution resulting from slow hydrolysis with 50 g ice-water of the ligand substitution reaction between ferrocene and the arene in the presence of $AlCl_3$ (two equivalents) on a 5-mmol-scale [32,36] and addition of 1 N NH_3 until pH 10 followed by filtration and washing $Al(OH)_3$ with five times 20 ml water was concentrated under reduced pressure to 5 ml. Then 10 ml 7 N aq. NH_3 was added, and this homogeneous reaction mixture was left at room temperature (r.t.) in air for 5 h. One mmol aq. HPF_6 was added (assuming the yield of the ligand exchange reaction was not higher than 20%), which led to the precipitation of a yellow–brown solid. Extraction with twice 5 ml methylene chloride, drying the methylene chloride solution, filtration, concentration to 5 ml under reduced pressure followed by addition of 20 ml Et_2O led to the precipitation of a yellow powdery solid. This powder was washed by refluxing with 10 ml ether or THF for 2 h and filtered. The ^{1}H-NMR spectrum of the yellow complex was compared to literature data [16–22], which confirmed the structure and purity of the complex. See text for the yields.

4.2.2. Method B

1 mmol of the complex [FeCp(η^6-ArCl)][X] (X = BF_4 or PF_6) previously reported in the literature was dissolved in 5 ml water and two equivalents amine was added. The solution was left in air at r.t. for 5 h (case of the water-soluble BF_4 salt) or stirred (case of the partly soluble PF_6 salt), then extracted with twice 10 ml methylene chloride. The methylene chloride solution was dried over Na_2SO_4, filtered, concentrated under reduced pressure to 5 ml, and the organometallic salt was precipitated by addition of 20 ml ether. The resulting complex was characterized and identified by comparison with the ^{1}H-NMR data of the literature [16–22]. The yield was similar to that obtained using method A.

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