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Steric Congestion at, and Proximity to, a Ferrous Center Leads to Hydration of α-Nitrile Substituents Forming Coordinated Carboxamides

Nasser K. Thallaj,[†,§] Pierre-Yves Orain,[‡] Aurore Thibon,[†,⊥] Martina Sandroni,[‡] Richard Welter,[∥] and Dominique Mandon*,[†,‡]

[†]Laboratoire de Chimie Biomimétique des Métaux de Transition, Institut de Chimie de Strasbourg−UMR 7177, CNRS−Université de Strasbourg, Bâtiment Le Bel, 4 rue Blaise Pascal, CS 90032, F-67081 Strasbourg Cedex, France

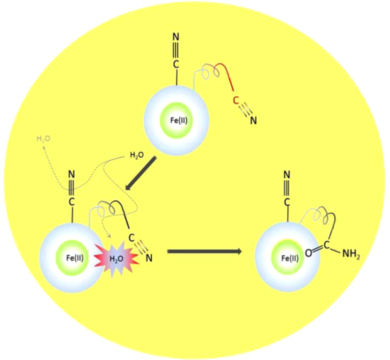
[‡]Laboratoire de Chimie, Electrochimie Moléculaires et Chimie Analytique, UMR 6521, CNRS−Université de Bretagne Occidentale, 6 Avenue Victor Le Gorgeu, CS 93837, F-29238 Brest Cedex 3, France

[§]Faculty of Applied Sciences, Department of Chemistry, Kalamoon University at Deratiah, P.O. Box 222, Deratiah, Syria

[∥]Institut de Biologie Moléculaire des Plantes, UPR CNRS 2357, Université de Strasbourg, F-67084 Strasbourg, France

[⊥]Laboratoire CLAC, Institut de Chimie de Strasbourg−UMR 7177, CNRS−Université de Strasbourg, 1 rue Blaise Pascal, F-67000 Strasbourg Cedex, France

Supporting Information



ABSTRACT: The question of the conversion of nitrile groups into amides (nitrile hydration) by action of water in mild and eco-compatible conditions and in the presence of iron is addressed in this article. We come back to the only known example of hydration of a nitrile function into carboxamide by a ferrous [Fe(II)] center in particularly mild conditions and very efficiently and demonstrate that these unusual conditions result from the occurrence of steric stress at the reaction site and formation of a more stable end product. Two bis(cyano-substituted) (tris 2-pyridyl methyl amine) ligands have been prepared, and the structures of the corresponding $FeCl_2$ complexes are reported, both in the solid state and in solution. These two ligands only differ by the position of the nitrile group on the tripod in the α and β position, respectively, with respect to the pyridine nitrogen. In any case, intramolecular coordination is impossible. Upon action of water, the nitrile groups are hydrated however only if they are located in the α position. The fact that the β-substituted β-$(NC)_2TPAFeCl_2$ complex is not water sensitive suggests that the reaction proceeds in an intramolecular way at the vicinity of the metal center. In the bis α-substituted α-$(NC)_2TPAFeCl_2$ complex, both functions are converted in a very clean fashion, pointing out that this complex exhibits ligand flexibility and is not deactivated after the first hydration. At a preparative scale, this reaction allows the one-pot conversion of the bis(cyano-substituted) tripod into a bis(amido-substituted) one in particularly mild conditions with a very good yield. Additionally, the XRD structure of a ferric compound in which the two carboxamido ligands are bound to the metal in a seven-coordinate environment is reported.

INTRODUCTION

Conversion of nitrile-containing compounds into amides in ecologically friendly conditions is a particularly challenging area in our current economical context.[1−5] The so-called nitrile hydration reactions are generally carried out in basic or acidic conditions under rigorous control to minimize formation of side products. Metal-mediated hydration of nitrile groups is an interesting alternative way,[6] for it presents some selectivity since the reaction products (the carboxamide functions) can coordinate, thus impeding further conversion into carboxylic acids or other byproducts.

Nature is able to perform such reactions: the nitrile hydratases constitute a class of enzymes with iron- or cobalt-containing active sites.[4,7−9] The promising reactivity of these biomolecules gives rise to a number of studies carried out from the biological material. However, the difficulties inherent to the extensive use of the biological media for synthesis are still inciting chemists to study more classical synthetic pathways.

A number of metal-containing complexes are able to mediate the hydration of nitriles,[10−15] and the factors affecting their reactivity have been reviewed.[6] The reaction conditions however are not always in line with the current demand in terms of eco-compatibility. In any case, it seems obvious that the nitrile has to be activated either by coordination or by interaction with its own environment, according to three different possible pathways involving (i) an inner-sphere mechanism, (ii) an outer-sphere mechanism, or (iii) a

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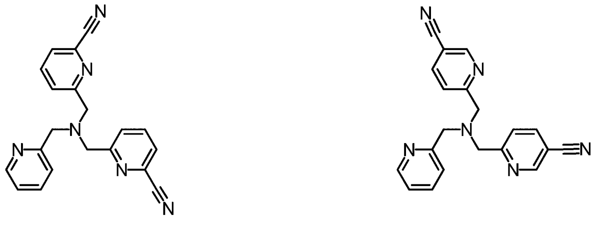
second-outer sphere mechanism.[8,16−18] From a general and fundamental point of view the question of nitrile hydration by first-row and cheap metal centers in mild conditions is of particular interest and justifies further studies.

An interesting example of a copper-mediated intramolecular hydration of a nitrile substituent of a macrocyclic tetraaza ligand was reported more than 30 years ago.[19] In that case it was proposed that a coordinated hydroxide would attack the nitrile group which is located nearby:[20−22] the reaction product is stabilized by carboxamide complexation to the metal to afford a rigid and coordinately saturated complex unable to further react. Such a reaction results from a close interaction between two potentially coordinating reactive groups to generate a very stable end product.

In a preliminary study[23] we reported the first example of conversion of a nitrile function into an amide group in mild conditions by an Fe(II) center using the (6-cyano-2-pyridylmethyl)bis(2-pyridylmethyl)amine ligand. This reaction was unusual, since weak Lewis acid centers such as Fe(II) are considered incapable to activate water. In this "outer-sphere mechanism" the first step was displacement of the coordinated chloride by water which further reacted with the neighboring nitrile to finally yield a Fe(II) carboxamido complex which was isolated and structurally characterized. However, in absolute terms we could not completely rule out that the nitrile group might be transiently coordinated to the Fe(II) atom of another complex in solution in some sort of binuclear complex, thus activating the nitrile carbon toward nucleophilic attack. Although seeming unlikely to us, this hypothesis prompted us to come back to this reaction.

We decided to address the question of an intra- vs intermolecular mechanism and prepared two different bis(cyano-substituted) ligands, the structure of which only differs by the location of the nitriles on the tripod skeleton, i.e., in the α or β position at the pyridine site. Both ligands [bis(6-cyano-2-pyridylmethyl)(2-pyridylmethyl)amine)], α-$(NC)_2$TPA, and [bis(5-cyano-2-pyridylmethyl)(2-pyridylmethyl)amine)], β-$(NC)_2$TPA, are displayed in Figure 1.



α-$(CN)_2$TPA

β-$(CN)_2$TPA

Figure 1. Two ligands of the $FeCl_2$ complexes which this work is based on.

In this article, we compare the structures in the solid state and in solution of the α-$(NC)_2TPAFeCl_2$ and β-$(NC)_2TPAFeCl_2$ complexes. Their reactivity toward water at room temperature is further examined. In both complexes the nitrile group is not able to coordinate to the metal center. We first demonstrate that two nitrile groups, when located in the α position of the bound heteroatom of the ligand, can be hydrated in a stepwise way by temporary interaction with a Fe(II) complex. During the reaction, crucial steps have been carefully studied. In particular, a bis-carboxamido Fe(II) complex (resulting from nitrile hydration) is characterized. We then show that the location of the uncoordinated nitrile groups on the tripod skeleton is crucial: when they are present at the β position, no reaction occurs. The perfect positioning of the nitrile groups when located in the α position, within a particularly flexible tripodal ligand, induces formation of π-bonded carboxamido ligand. Finally, we report a very easy and straightforward method to prepare a bis(NH_2CO)-substituted tripod from the bis-cyano precursor and the XRD structure of a ferric compound in which the two carboxamido ligands are bound to the metal in a seven-coordinate environment.

■ EXPERIMENTAL SECTION

General Considerations. Chemicals were purchased from Aldrich Chemicals and used as received. 2-Cyano-6-bromomethylpyridine was prepared according to a previously published procedure.[23] Analytical anhydrous $FeCl_2$ was obtained as a white powder by treating iron powder (ACS grade) with hydrochloric acid in the presence of methanol in an argon atmosphere. Unless otherwise stated, all solvents used during the metalation reactions and workup were distilled and dried according to standard methods.[71] Preparation and handling of all compounds were performed in an argon atmosphere using the Schlenk technique following standard procedures. Metalation of α- and β-$(NC)_2$TPA by $FeCl_2$ was carried out according to already published procedures.[27] The purity of the dry dioxygen was 99.999% (grade 5). Mass spectrometric experiments and elemental analyses were carried out, respectively, by the Service Commun de Spectrométrie de Masse and the Service Commun de Microanalyses de l'Institut de Chimie de Strasbourg (Université de Strasbourg). The molecular structure of β-$(NC)_2TPAFeCl_2$ was resolved by the Service Commun de Diffraction X de la Faculte des Sciences et Techniques de l'UBO, Brest.

Physical Methods. ^{1}H NMR data were recorded in CD_3CN for the complexes and $CDCl_3$ for the ligands at ambient temperature on a Bruker AC 300 spectrometer at 300.1300 MHz with the residual signal of CD_2HCN ($CHCl_3$) as a reference for calibration. UV−vis spectra were recorded on a Varian Cary 05 E UV/vis NIR spectrophotometer equipped with an Oxford instrument DN1704 cryostat with optically transparent Schlenk cells. Cyclic voltammetry measurements were obtained from a PAR 173A potentiostat in a 0.1 M solution of TBACl (supporting electrolyte) in acetonitrile using platinum electrodes as working and counterelectrodes and saturated calomel electrode as the reference. Potentials were calibrated by addition of ferrocene in the end of the measurements. Conductivity measurements were carried out under argon at 25 °C with a CDM 210 Radiometer Copenhagen Conductivity Meter using a Tacussel CDC745-9 electrode.

Synthesis of 3-Cyano-6-bromomethylpyridine. A 3.000 g (25.4 mmol) amount of 6-methyl-3-carbonitrile pyridine was dissolved in 100 mL of carbon tetrachloride. A 4.980 g (27.9 mmol) amount of *N*-bromosuccinimide and 0.060 g (0.25 mmol) of benzoil peroxide were added, and the reaction mixture was refluxed over 5 h. Solvent was evaporated, and the residues were chromatographed on silica gel using methylene chloride as eluent. The desired compound is a yellow oil, progressively turning red upon standing at room temperature. Obtained: 2.036 g, i.e., 41% yield. ^{1}H NMR, $CDCl_3$, δ, ppm: 8.79 (S, 1H), 7.95 (dd, 1H), 7.56 (dd, 1H), 4.53 (s, 1H).

Synthesis of α-$(NC)_2$TPA. To a solution of 1.40 g (7.1 mmol) of 2-cyano-6-bromomethylpyridine in 100 mL of CH_3CN were added 0.40 g (3.7 mmol) of picolylamine and 0.37 g (3.5 mmol) of Na_2CO_3. The reaction mixture was refluxed over 18 h. Solid residues were filtered, and the solvent was evaporated to dryness. After water was added, the mixture was extracted several times with CH_2Cl_2, and the combined organic phases were washed with water and then dried over $MgSO_4$. The solvent was evaporated, and the sticky material was extracted several times with pentane. The concentration of the pentane phases yielded 1.17 g (93%) of a white solid, which was further recrystallized in pentane. Anal. Calcd for $C_{20}H_{16}N_6$: C, 70.57; H, 4.74; N, 24.69. Found: C, 70.18; H, 4.79; N, 24.23. ^{1}H NMR, $CDCl_3$, δ, ppm: 8.54 (m, α-CH, 2H); 7.80 (dd, β-CH, 2H); 7.79 (dd, β-CH, 2H); 7.66 (td, γ-CH, 1H); 7.56 (dd, γ-CH, 2H); 7.47 (dt, β-CH, 1H); 7.17 (m, β-CH, 1H); 3.99 (s, CH_2, 4H); 3.89 (s, CH_2, 2H).

Synthesis of β-$(NC)_2$TPA. To a solution of 1.40 g (8.91 mmol) of 3-cyano-6-bromomethylpyridine in 100 mL of CH_3CN were added 0.480 g (4.46 mmol) of picolylamine and 0.55 g (4.5 mmol) of Na_2CO_3. The reaction mixture was refluxed over 16 h. The solvent was evaporated to dryness, and the residue was treated with aqueous K_2CO_3 and extracted with methylene chloride. The compound obtained upon complete evaporation of the solvent was purified by column chromatography on alumina using acetonitrile as the eluent. The desired compound is an orange oil. Obtained: 0.755 g, i.e., 50% yield. Anal. Calcd for $C_{20}H_{16}N_6$: C, 70.57; H, 4.74; N, 24.69. Found: C, 70.31; H, 4.36; N, 24.91. ^1H NMR, $CDCl_3$, δ, ppm: 8.77 (dd, α-CH, 2H); 8.53 (dq, α-CH, 1H); 7.90 (dd, β/γ-CH, 2H); 7.70 (dm, β/γ-CH, 2H); 7.64 (td, γ-CH, 1H); 7.40 (dm, β-CH, 1H); 7.16 (m, β-CH, 1H); 3.96 (s, CH_2, 4H); 3.87 (s, CH_2, 2H).

Preparation of α-$(NC)_2$TPAFeCl_2. A 150 mg (0.44 mmol) amount of free α-$(NC)_2$TPA was dissolved in a Schlenk tube containing 20 mL of dry and degassed THF. A 56 mg (0.44 mmol) amount of anhydrous $FeCl_2$ was dissolved in a second Schlenk tube containing 10 mL of dry and degassed THF. The solution of $FeCl_2$ was transferred under argon in the Schlenk containing the ligand, and the medium was stirred overnight. The solvent was then evaporated to dryness, and the compound was extracted with dry and degassed CH_3CN, filtered under inert atmosphere, and concentrated. Addition of diethyl ether afforded a red solid, which was washed thoroughly with this solvent, prior to being dried under vacuum. A 165 mg (80%) amount of α-$(NC)_2$TPAFeCl_2 with good analytical and spectroscopic data could be obtained. Anal. Calcd for $C_{20}H_{16}Cl_2FeN_6$: C, 51.42; H, 3.45; N, 17.99. Found: C, 51.21; H, 3.87; N, 18.06. IR, ATR, solid state: $\nu_{C\equiv N}$ = 2239 cm^{-1}. UV−vis: λ = 350−550 nm, broad and featureless absorption (ε = 800 L mol^{-1} cm^{-1}) at λ = 462 nm. Spectroscopic data are detailed in the text and shown in the Supporting Information.

Preparation of β-$(NC)_2$TPAFeCl_2. This complex was obtained following the same procedure from 0.126 g (0.37 mmol) of β-$(NC)_2$TPA and 0.044 g (0.35 mmol) of $FeCl_2$. Anal. Calcd for $C_{20}H_{16}Cl_2FeN_6$: C, 51.42; H, 3.45; N, 17.99. Found: C, 50.98; H, 3.92; N, 17.71. IR, ATR, solid state: $\nu_{C\equiv N}$ = 2234 cm^{-1}. UV−vis: λ = 400 nm (ε = 1600 L mol^{-1} cm^{-1}), 506 nm (shoulder, $\varepsilon_{506\ nm}$ = 1300 L mol^{-1} cm^{-1}). Spectroscopic data are detailed in the text and shown in the Supporting Information.

Hydration of α-$(NC)_2$TPAFeCl_2: Preparation of α-$H_2NCO)_2$TPAFeCl_2. A 100 mg (0.21 mmol) amount of α-$(NC)_2$TPAFeCl_2 was dissolved in a Schlenk tube containing 80 mL of dry and degassed CH_3CN. A 780 μL (43 mmol) amount of previously degassed distilled water was added. The medium became bright orange, and the color progressively turned into burgundy red. Thirty hours after the beginning of the reaction, the medium was concentrated and a purple microcrystalline solid was obtained upon slow addition of diethyl ether. It was washed and dried under vacuum. Yield: 80 mg (76%). Anal. Calcd for $C_{20}H_{20}Cl_2FeN_6O_2$: C, 47.74; H, 4.01; N, 16.70 Found: C, 47.62; H, 3.97; N, 17.01. HR-ESI-MS ([$(CONH_2)_2$TPAFeCl-H]$^+$): m/z calcd for $C_{20}H_{19}Cl_1Fe_1N_6O_2$ 466.060, found 466.059. IR, ATR, solid state: $\nu_{C=O}$ = 1664 and 1645 cm^{-1}. UV−vis: λ = 364 nm (ε = 1300 L mol^{-1} cm^{-1}) and λ = 497 nm (ε = 1660 L $mol^{-1}cm^{-1}$). Spectroscopic data are detailed in the text and shown in the Supporting Information.

Detection and Characterization of α-(NC)(H_2NCO)TPAFeCl_2. To obtain the traces displayed in Figure 4, the same procedure as indicated above was followed except that the reaction times were 8 and 18 h, respectively.

HR-ESI-MS characterization was carried out at t = 18 h. (NC)(H_2NCO)TPAFeCl^+ in CH_3CN/H_2O 80/20: m/z calcd for $C_{20}H_{18}ClFeN_6O$ 449.060, found 449.06. (NC)(H_2NCO)TPAFeCl^+ in CH_3CN: calcd for $C_{20}H_{18}ClFeN_6O$ 449.060, found 449.058. (NC)(H_2NCO)TPAFeCl^+−H in CH_3CN: calcd for $C_{20}H_{17}ClFeN_6O$ 448.060, found 448.050. All traces are given in the Supporting Information.

Preparation of {[α-$(H_2NCO)_2$TPAFe$]_2$-O}Cl_4. A 100 mg (0.21 mmol) amount of α-$(NC)_2$TPAFeCl_2 was dissolved in 100 mL of CH_3CN in a Schlenk tube. A 10 μL (0.5 mmol) amount of distilled water was introduced, and oxygen was bubbled for 15 s. The medium was stirred 48 h in a stoppered vessel. The solvent was then concentrated, and diethyl ethyl was added, allowing precipitation of a brown solid. This brown solid was recrystallized from a wet (5% H_2O) solution of CH_3CN by diffusion of diethyl ether. A 70 mg amount of analytically pure compound was obtained. Anal. Calcd for $C_{40}H_{40}Cl_4Fe_2N_{12}O_5$: C, 46.99; H, 3.94; N, 16.44. Found: C, 47.20; H, 3.51; N, 16.62. IR, ATR, solid state: $\nu_{C=O}$ = 1661 cm^{-1}. UV−vis: λ = 367 nm (ε = 3553 L mol^{-1} cm^{-1}), λ = 316 nm (ε = 3365 L mol^{-1} cm^{-1}), and λ = 500 nm (ε = 915 L mol^{-1} cm^{-1}).

Preparation of α-$(H_2NCO)_2$TPA. *i. Direct Preparation.* A 100 mg (0.29 mmol) amount of free α-$(NC)_2$TPA and 40 mg (0.31 mmol) of anhydrous $FeCl_2$ were introduced in a Schlenk tube, and 35 mL of dry and degassed CH_3CN were added under argon. The medium was stirred overnight under argon. To this medium 30 mL of distilled water was added under aerobic atmosphere. The medium was stirred for 2 days. Following, 500 mg (excess, 8.9 mmol) of solid KOH was added and the medium was vigorously stirred for 5 min. A 100 mL amount of CH_2Cl_2 and 50 mL of water were added to the medium, and the organic solution was washed with water (4 × 50 mL). The organic phase was dried over magnesium sulfate and the solvent concentrated. Addition of pentane afforded 80 mg (73%) of a white solid. HR-ESI-MS ([$(CONH_2)_2$TPA-H]$^+$): m/z calcd for $C_{20}H_{21}N_6O_2$ 377.172, found 377.170; m/z calcd for $C_{20}H_{20}N_6O_2Na$ 399.154, found 399.151. ^1H NMR, $CDCl_3$, δ, ppm: 8.53 (m, α-CH, 2H); 8.06 (d, β-CH, 2H); 7.96 (s, NH_2, 2H); 7.81 (t, γ-CH, 2H); 7.66 (m, β-CH, 1H);7.64 (d, β-CH, 2H); 7.51 (d, β-CH, 1H); 7.16 (m, γ-CH, 1H); 5.69 (s, NH_2, 2H); 3.92 (s, CH_2, 2H); 3.90 (s, CH_2, 4H). ^{13}C NMR, $CDCl_3$, δ, ppm: 166 (ipso C); 158 (C=O); 157 (ipso C); 148 (ipso C); 147 (ipso C); 137 (CH); 135 (CH); 125 (CH); 122 (CH); 121 (CH); 120 (CH); 59 (CH_2); 58 (CH_2). ^1H NMR analysis of the residues of the mother liquor showed that some ligand was still present in good amount in the sample.

ii. By Decomplexation. A 50 mg amount of α-$(H_2NCO)_2$TPAFeCl_2 (99 μmol) or {[α-$(H_2NCO)_2$TPAFe$]_2$-O}Cl_4 (49 μmol) was dissolved/suspended in a flask containing 20 mL of a 80/20 CH_3CN/H_2O mixture. A 250 mg (excess, 4.45 mmol) amount of solid KOH was added, and the medium was stirred for 5 min. A 50 mL amount of CH_2Cl_2 and 20 mL of aqueous Na_2CO_3 were added to the colorless medium, and the organic solution was washed with water (2 × 50 mL). The organic phase was dried over magnesium sulfate and the solvent concentrated. Addition of pentane allowed crystallization of a white solid whose spectroscopic properties were identical to those above described. A 33 mg amount of free ligand (90%) could be obtained.

Action of Water on β-$(NC)_2$TPAFeCl_2. Addition of an excess of H_2O 200−500 equiv on a CD_3CN solution of the complex resulted in no other change than a neglectible downfield shift in the chemical shift of the paramagnetic ^1H NMR spectrum ($0.5 < \Delta_\delta < 1.0$ ppm) and a very small shift from 400 to 397 nm in the UV−vis spectrum (neglectible variation in the epsilon value). The traces are given in the Supporting Information.

X-ray Analysis. Single crystals of α-$(NC)_2$TPAFeCl_2·CH_3CN and {[β-$(H_2NCO)_2$TPAFe$]_2$-O}Cl_4 were mounted on a Nonius Kappa-CCD area detector diffractometer and those of β-$(NC)_2$TPAFeCl_2·CH_3CN on a Xcalibur-2 diffractometer from Oxford Diffraction (Mo Kα λ = 0.71073 Å for all complexes). Quantitative data were obtained at 173 K for all complexes. Complete conditions of data collection (Denzo software) and structure refinements are given in the Supporting Information. Cell parameters were determined from reflections taken from one set of 10 frames (1.0° steps in phi angle), each at 20 s exposure. Structures were solved using direct methods (SIR97 and 92) and refined against F^2 using the SHELXL97 software.[72] Absorption was not corrected. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were generated according to stereochemistry and refined using a riding model in SHELXL97.

Crystal data for β-$(NC)_2TPAFeCl_2 \cdot CH_3CN$: red crystals, monoclinic, space group $P2_1/c$, a = 11.0253(8) Å, b = 8.9504(6) Å, c = 25.0265(18) Å, β = 95.868(6), V = 2456.7(3) Å^3, D_{calcd} = 1.374 g·cm^{-3}, Z = 4. For 6067 unique observed reflections with $I > 2\sigma(I)$ and 290 parameters, the discrepancy indices are R = 0.0587 and R_w = 0.1292.

Crystal data for α-$(NC)_2TPAFeCl_2 \cdot CH_3CN$: red crystals, monoclinic, space group $P2_1/n$, a = 12.4650(4) Å, b = 14.2120(5) Å, c = 13.3120(5) Å, β = 102.090(2), V = 2305.95(14) Å^3, D_{calcd} = 1.464 g·cm^{-3}, Z = 4. For 5219 unique observed reflections with $I > 2\sigma(I)$ and 289 parameters, the discrepancy indices are R = 0.0528 and R_w = 0.1288.

Crystal data for $\{[\alpha\text{-}(H_2NCO)_2TPAFe]_2\text{-}O\}Cl_4$: brown crystals, monoclinic, space group $P2_1/c$, a = 11.0360(4) Å, b = 18.3800(8) Å, c = 14.3460(5) Å, β = 130.44(3), V = 2217.4(10) Å^3, D_{calcd} = 1.531 g·cm^{-3}, Z = 2. For 5499 unique observed reflections with $I > 2\sigma(I)$ and 302 parameters, the discrepancy indices are R = 0.0516 and R_w = 0.1078.

■ RESULTS

Syntheses. α-$(NC)_2TPA$ and β-$(NC)_2TPA$ were obtained by reaction of 2 equiv of 2-cyano-6-bromomethylpyridine and 3-cyano-6-bromomethylpyridine, respectively, with 1 equiv of picolylamine according to standard procedures.[24,25] The α-substituted ligand is a white powder, whereas the β-substituted one is a yellow oil. They have been fully characterized and obtained with good to excellent yields as analytically pure compound. All data are available in the Supporting Information.

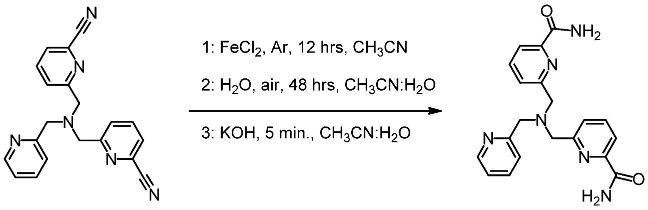
Reactivity versus Water of the Cyano-Substituted Tripods, α- and β-(CN)₂TPA. *Direct Conversion of α-(NC)₂TPA into α-(H₂NCO)₂TPA by Hydration Reaction.* The off-white solid thus obtained was complexed to $FeCl_2$ under anaerobic conditions following well-known methods,[23,25−28] and a reddish color developed progressively, accompanied by precipitation of part of the complex. Twelve hours after the beginning of the reaction, the reaction vessel was opened and distilled water was poured into the reaction mixture, affording a transparent burgundy solution. At this time, there was no longer a need for keeping the medium under inert atmosphere. The solution was simply left under stirring for 48 h at room temperature. Solid potassium hydroxide was finally added to the solution, resulting in complete bleaching. Five minutes later, the mixture was treated, and α-$(H_2NCO)_2TPA$ was recovered after precipitation as a white solid with a 73% yield as an analytically pure compound, without the need for any chromatographic separation. The product was identified by HR mass spectroscopy, and ^1H and ^{13}C NMR data confirmed the quality of the sample. All spectroscopic data are available in the Supporting Information. ^1H NMR analysis showed that the mother solutions still contained some ligand. Conversion is illustrated in Scheme 1.

Chemical Stability of β-(CN)₂TPA under the Same Conditions. When the same procedure as that described above was followed starting from the β-substituted tripod, the unmodified β-$(CN)_2TPA$ ligand was quantitatively recovered.

In order to understand the hydration reaction and the reasons for the difference of reactivity between the two ligands, we carried out a careful structural analysis of the $FeCl_2$ complexes and monitored the hydration reaction by UV−vis and ^1H NMR spectroscopy.

Structural Considerations on the FeCl₂ Complexes with the Two Tripods: Solid-State Structures. Both α-$(NC)_2TPAFeCl_2$ and β-$(NC)_2TPAFeCl_2$ complexes were prepared by well-known methods[27] upon treatment of the free ligand with $FeCl_2$. Single crystals could be obtained by slow diffusion of diethyl ether into a solution of complex in acetonitrile.

Scheme 1. Direct Hydration of α-(NC)₂TPA into α-(H₂NCO)₂TPA[a]



[a]This reaction does not occur with the β-substituted tripod β-$(CN)_2TPA$ ligand which is fully recovered in the end of the workup.

Solid-State Structure of α-(NC)₂TPAFeCl₂. The molecular structure is displayed in Figure 2. At a first glance, this structure looks similar to those already reported within the class of $FeCl_2$ complexes with moderately hindered TPA tripods,[25,29,30] i.e., the metal center lies in a six-coordinate environment, with distances supporting a high-spin state for the iron.

A more detailed examination evidences a strong elongation of the metal-to-substituted pyridines distances, with dFeN5 = 2.414(3) Å and dFeN3 = 2.325(2) Å. Moreover, a repulsive interaction between the nitriles and the chloride Cl2 causes a significant deviation from linearity of the cyano groups with C19C20N6 = 173.3° and C12C13N4 = 175.0°. Finally, the ligand skeleton is extremely distorted. The top view of the diagram does not reflect the flexibility of the ligand. Rather, this is evidenced by a side view of the structure which reveals a severe torsion of the equatorial pyridines with the dihedral angle α = 42.5°, as illustrated in Figure 3. Also, the octahedral distortion parameter[31,32] indicates significant distortion with Σ = 114°.

Solid-State Structure of β-(CN)₂TPAFeCl₂. The molecular structure is displayed in Figure 4. This is a more classical structure, the description of which is reported in order to compare the structural parameters with those of the α-substituted congener. We shall use this structure to provide a rationale for the reactivity differences between the two complexes.

The coordination polyhedron displays a distorted octahedral geometry with a six-coordinate iron center. When compared to the α-$(CN)_2TPAFeCl_2$ congener, the first difference is the shortening of the equatorial Fe−pyridine distances, with dFeN3 = 2.168(3) Å and dFeN4 = 2.164(3) Å. As a consequence, the other distances are slightly elongated with dFeN1 = 2.283(3) Å and dFeN2 = 2.234(3) Å, which however lie in the expected range for stable six-coordinate complex. Another obvious difference in this structure by contrast with the above-reported one is the absence of significant equatorial distortion, as can be seen from Figure 5. In the present case, the α angle has decreased to 4.2°. These observations obviously reflect the absence in this complex of any repulsion between the coordinated chloride ions and the nitrile functions, those being now attached to the β position. Indeed, with C11C20N6 = 178.1(5)° and C5C19N5 = 178.6(5)°, the distortion from linearity of the nitrile groups has become negligible. Finally, with Σ = 98°, a smaller distortion than that previously found with the α-substituted ligand is observed.

The main structural differences, especially the bond lengths and nitrile distortion between the two complexes α-

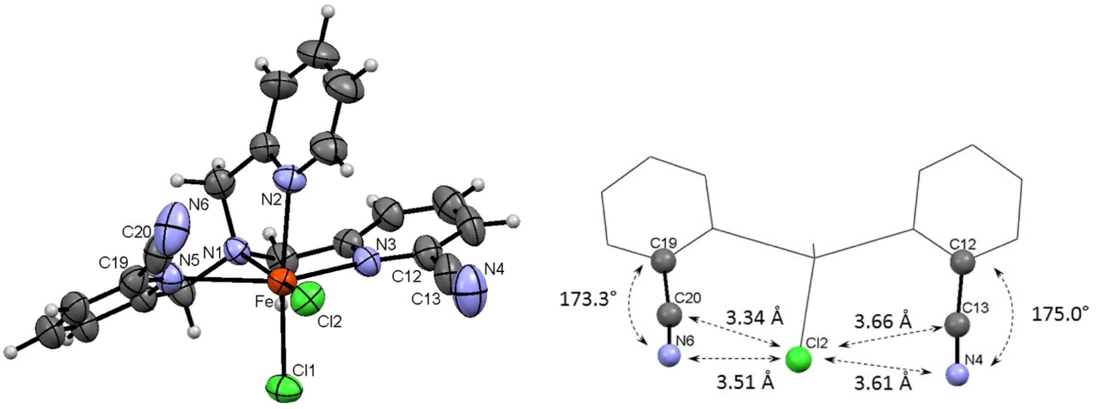


Figure 2. ORTEP diagram of α-(NC)$_2$TPAFeCl$_2$. Selected distances (Å): Fe−N5 2.414(3), Fe−N1 2.234(2), Fe−N3 2.325(2), Fe−N2 2.189(3). (Left) Top view of a fragment of molecule showing the contacts between the equatorial Cl2 and the distorted nitrile groups.

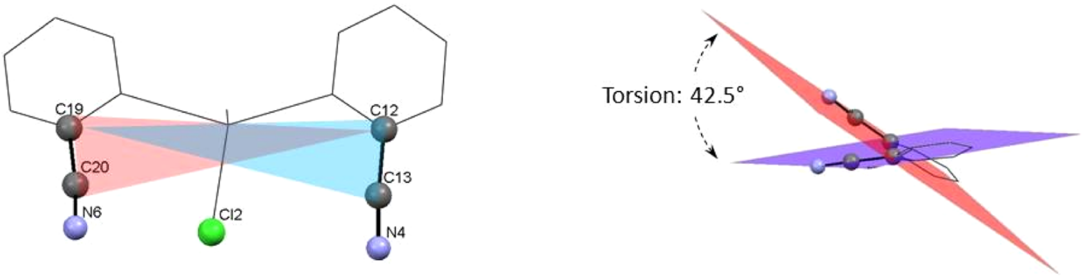


Figure 3. Top and side view of a fragment of molecule showing the dihedral angle of the equatorial pyridines around the C19−C12 axis.

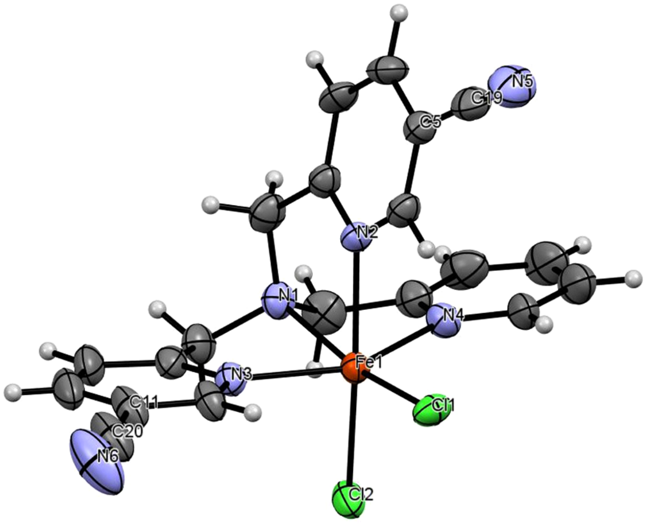


Figure 4. ORTEP diagram of β-(NC)$_2$TPAFeCl$_2$. Selected distances (Å): Fe−N3 2.168(3), Fe−N1 2.283(3), Fe−N4 2.164(3), Fe−N2 2.234(3).

(NC)$_2$TPAFeCl$_2$ and β-(NC)$_2$TPAFeCl$_2$, are summarized in Table 1.

Spectroscopic Studies in Solution of the FeCl$_2$ Complexes with the Two Tripods. *Spectroscopic Data for α-(NC)$_2$TPAFeCl$_2$.* By contrast to most of its parent TPA-type complexes which generally display a yellow color, α-(NC)$_2$TPAFeCl$_2$ was found to be a red compound. In solution, a broad and featureless MLCT absorption in the UV−vis was observed between 350 and 550 nm (ε = 800 L mol^{-1} cm^{-1} at λ = 462 nm). The molecular conductivity measurement of a 2 mM solution yielded Λ = 21 S cm^2 mol^{-1}, indicating a neutral electrolytic behavior of the compound in solution at this concentration.[33,34] In cyclic voltammetry, a quasi-reversible wave assigned to the redox Fe(III)/Fe(II) couple was measured at $E_{1/2}$ = −380 mV vs Fc/Fc$^+$ (i_{pc}/i_{pa} = 0.85).[35] This value lies at the upper limit within the potential range typically corresponding to five-coordinate compounds.[36−39] The ^{1}H NMR spectrum of the complex exhibited very broad resonances at δ = 66 ($\Delta_{\nu1/2}$ = 1100 Hz), 56 ($\Delta_{\nu1/2}$ = 400 Hz), 53 ($\Delta_{\nu1/2}$ = 140 Hz), 40 ($\Delta_{\nu1/2}$ = 400 Hz), and 28 ppm ($\Delta_{\nu1/2}$ = 650 Hz) and poorly defined signals in the diamagnetic region between

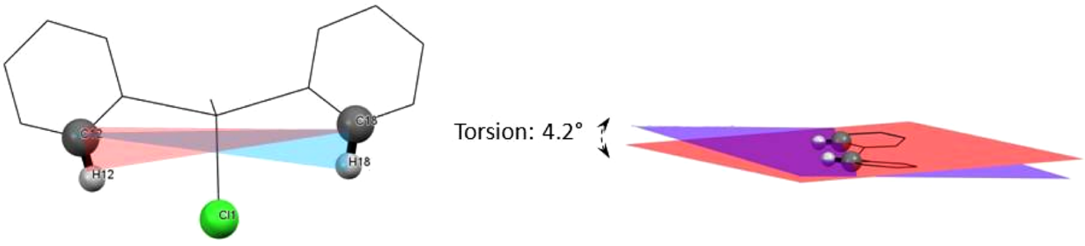


Figure 5. Top and side view of a fragment of molecule showing the dihedral angle of the equatorial pyridines around the C12−C18 axis.

Table 1. Metal-to-Ligand Bond Lengths (Angstroms) and Distortion of the Nitrile Groups (degrees) in α-$(NC)_2TPAFeCl_2$ and β-$(NC)_2TPAFeCl_2$[a]

	α-$(NC)_2TPAFeCl_2$	β-$(NC)_2TPAFeCl_2$
Fe−Cl, trans-amine	Cl2 2.3217(8)	Cl1 2.3216(10)
Fe−Cl, trans-pyr	Cl1 2.3976(10)	Cl2 2.4404(11)
Fe−amine	N1 2.234(2)	N1 2.283(3)
Fe−pyr, trans-Cl	N2 2.189(3)	N2 2.234(3)
Fe−pyridine	N3 2.325(3)	N4 2.164(3)
Fe−pyridine	N5 2.414(3)	N3 2.168(3)
nitrile distortion	C19C20N6 173.4(4)	C11C20N6 178.1(5)
nitrile distortion	C12C13N4 174.9(4)	C5C19N5 178.6(5)
Σ (dev. from 90°)	114	98

[a] Σ: octahedral distortion parameter according to refs 31 and 32.

10 and 0 ppm. All data were consistent with the presence of a κ^3 coordination mode of the ligand in solution.[36]

Spectroscopic Data for β-$(CN)_2TPAFeCl_2$. This complex also displayed a red color, due to a broad MLCT absorption between 340 and 550 nm, with a maximum at $\lambda = 400$ nm ($\varepsilon = 1600$ L mol^{-1} cm^{-1}). The high molecular extinction coefficient corresponds to coordination of the three pyridyl units.[27,36] The molecular conductivity of a 1.5 mM solution in acetonitrile yielded $\Lambda = 18$ S cm^2 mol^{-1}, in line with a negligible dissociation of the complex in these conditions. The cyclic voltammogram of the complex exhibited an irreversible Fe(III)/Fe(II) couple at $E_a = -100$ mV vs Fc/Fc^+, in line with a six-coordinate compound in which the iron center is ligated to an electro-deficient tripod.[30,36−41] Another difference with α-$(CN)_2TPAFeCl_2$ is evidenced in the ^1H NMR spectrum of β-$(CN)_2TPAFeCl_2$. This new complex displays sharp absorptions at $\delta = 51$ ($\Delta_{\nu 1/2} = 70$ Hz), 47 ($\Delta_{\nu 1/2} = 65$ Hz), 43 ($\Delta_{\nu 1/2} = 140$ Hz), 28 ($\Delta_{\nu 1/2} = 44$ Hz), and 25 ppm ($\Delta_{\nu 1/2} = 35$ Hz) corresponding to the β and γ protons of the coordinated pyridines. It was shown in the past[27,36] that sharp signals (for paramagnetic NMR) of this type are benchmarks for six coordination within this class of complexes.

Structure of the Complexes in Solution. The correlation between the spectroscopic properties and the geometry of the complexes in solution within this class of compounds is now well established.[27,36] The most significant patterns are the Fe(III)/Fe(II) redox potentials ($E_{a/c/E1/2}$), the molecular extinction coefficients of the MLCT bands in UV−vis (ε), and the midintensity width of the signals in ^1H NMR ($\Delta_{\nu 1/2}$). In the present case these values differ very significantly from one complex to the other. They are reported in Table 2. Low $E_{1/2}$ and ε values and large resonances in NMR are benchmarks of five-coordinate complexes in solution:[27,36] this is the case for α-$(NC)_2TPAFeCl_2$ only. In fact, a five-coordinate geometry for this complex in solution was expected from the bond elongations and distortion which were observed in the solid state (vide supra). Such a difference between solid state and solution has already been reported in related complexes.[30,37,41] By contrast, the solid-state structure of the β-$(NC)_2TPAFeCl_2$ congener is retained in solution, as expected for a moderately distorted complex. This is shown in Scheme 2.

Table 2. Spectroscopic Data in Solution of Complexes α-$(NC)_2TPAFeCl_2$ and β-$(NC)_2TPAFeCl_2$

	α-$(NC)_2TPAFeCl_2$	β-$(NC)_2TPAFeCl_2$
λ_{MLCT}, nm (ε, L mol^{-1} cm^{-1})	350−550 (800 at 462 nm)	340−550 (1600 at 400)
Λ, S cm^2mol^{-1}	21	18
$E_{1/2}$, mV/Fc/Fc^+ (i_{pc}/i_{pa})	−380 (0.85)	irreversible
E_a, mV/Fc/Fc^+		−100
δ, ^1H NMR, ppm (midintensity width, Hz)	66−28 (1100−140)	51−25 (140−35)

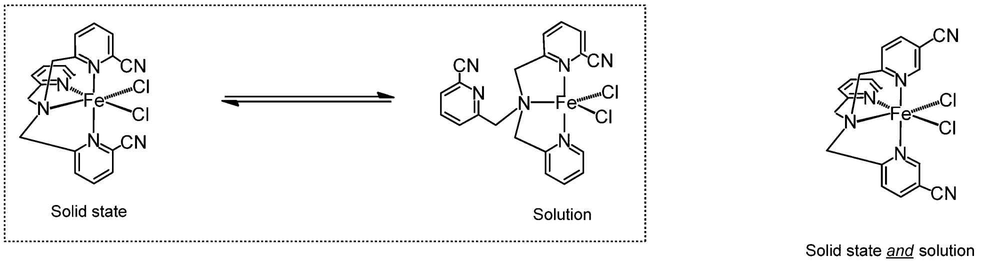
Experimental Insights into the Hydration Reaction of α-$(NC)_2TPAFeCl_2$ into α-$(H_2NCO)_2TPAFeCl_2$: UV−Vis and ^1H NMR Monitoring. At preparative scale when water is poured in the medium under normal laboratory atmosphere (vide supra) it cannot be ruled out that the α-$(NC)_2TPAFeCl_2$ present in the medium is first converted into some ferric species. To establish whether Fe(II) rather than Fe(III) could be responsible for the hydration, the reaction was followed under strictly anaerobic conditions.

Reactivity of α-$(NC)_2TPAFeCl_2$ with water: as shown in Figure 6, addition of 200 equiv of degassed H_2O under argon to a $C = 1.5 \times 10^{-3}$ M solution resulted in the progressive raise of two new absorptions observed in UV−vis at $\lambda = 368$ ($\varepsilon = 1300$ L mol^{-1} cm^{-1}) and 505 nm ($\varepsilon = 1660$ L mol^{-1} cm^{-1}). The reaction was considered to be complete over 30 h, the time by which no further spectroscopic changes could be observed. Similar time ranges were observed upon work with more dilute ($C = 10^{-4}$ M) or concentrated ($C = 10^{-2}$ M) solutions. The first absorption was assigned to the standard MLCT transition observed with $FeCl_2$ complexes. The second one is similar in energy and intensity to the value reported in a ferrous compound with a similar pivaloylamido-substituted $TPA^{2C(O)NHtBu}$ tripod, prepared by conventional ways (i.e., from an already existing pivaloylamido-substituted pyridine).[42] It has recently been shown that this absorption reflects the coordination of the carbonyl groups within a seven-coordinate environment.[42,43] In the present case, we proposed that the two nitrile groups of the α-$(NC)_2TPA$ tripod were converted into amide functions yielding the α-$(H_2NCO)_2TPAFeCl_2$ complex, the carbonyl groups of the ligand being bound to the metal center.

The reaction was performed on a preparative scale, and progressive conversion of α-$(NC)_2TPAFeCl_2$ into this new Fe(II) species was monitored by ^1H NMR. Aliquots of the reaction mixture were taken and treated (evaporation and careful washing with diethyl ether followed by vacuum drying) 8, 18, and 30 h following addition of water. The result is shown in Figure 7. The broad lines of the starting material, typical for five-coordinate Fe(II) species, were finally converted into clean and sharp signals, indicating a serious modification in the coordination geometry at the metal site which remains in the high-spin Fe(II) state. The intermediate traces showed the presence of a mixture consisting of the starting material and some end product, together with an intermediate species assigned to the mixed cyano/carboxamido α-$(NC)(H_2NCO)$-$TPAFeCl_2$ complex (vide infra).

To get insight into the nature of this intermediate species, the $t = 18$ h medium was submitted to mass spectroscopy analysis. A clean molecular ion was detected at $m/z = 449.060$. We noted that this $m/z = 449.60$ value may account for either the monocarboxamido α-$(NC)(CONH_2)TPAFeCl^+$ species or the mono aquo adduct α-$(NC)_2TPAFe(OH_2)Cl^+$. As this latter hypothesis is unlikely because of an already strong MLCT band at $t = 18$ h in UV−vis, we ran an IR spectrum on the $t = 18$ h sample. Indeed, the presence of both a nitrile group and a carboxamido function on the ligand was confirmed by the observation in the IR spectroscopy of a nitrile and carboxamido

Scheme 2. Changes in Geometry of the Metal Center in the Complexes as a Function of the State (solid vs solution)[a]



[a] For α-$(NC)_2TPAFeCl_2$, we propose uncoordination of the nitrile-substituted pyridine for steric reasons.[27,37]

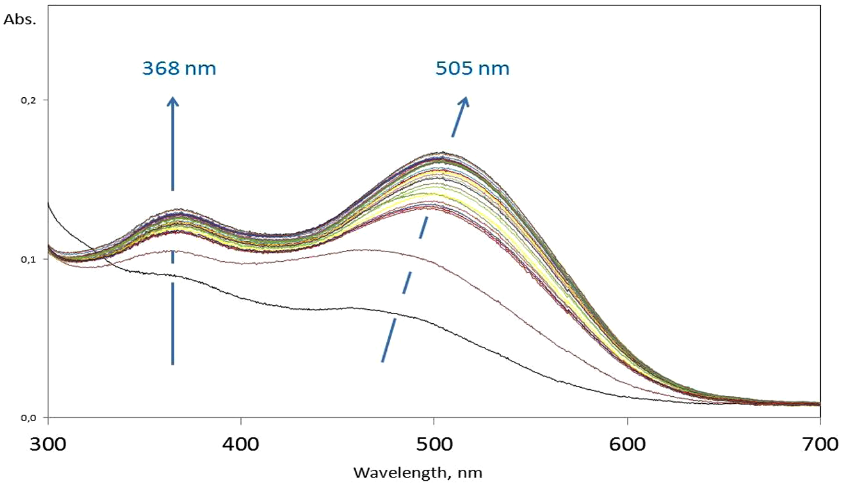


Figure 6. UV−vis spectral absorption changes upon addition of 200 equiv of distilled water to a solution of α-$(NC)_2TPAFeCl_2$ in acetonitrile: 1 scan/h, 30 h total time, C = 1.5 mM.

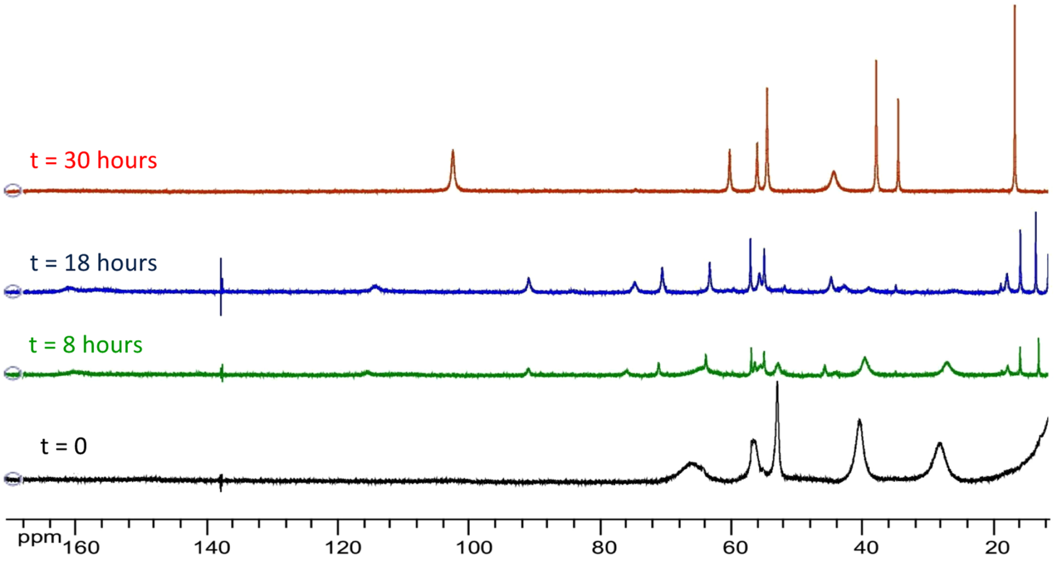
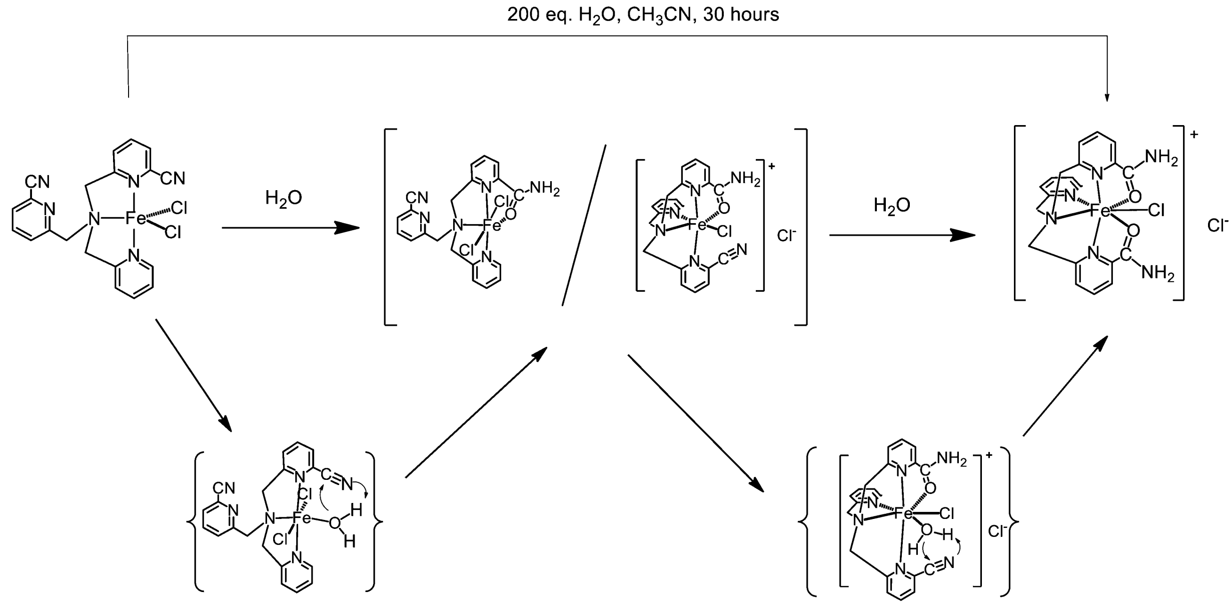


Figure 7. ^1H NMR monitoring (CD_3CN, paramagnetic area) of the conversion of α-$(NC)_2TPAFeCl_2$ into α-$(H_2NCO)_2TPAFeCl_2$: (black) t = 0; (green) t = 8 h; (blue) t = 18 h; (red) t = 30 h. The sharp signals of the end product are assigned to the γ,γ' and β, β' protons of the pyridines. See Supporting Information for full assignment and references.

vibration, respectively, at $\nu_{C\equiv N}$ = 2240 cm^{-1} and $\nu_{C=O}$ = 1662 cm^{-1}. The trace is displayed in the Supporting Information.

In the end, i.e., 30 h after addition of water, the reaction was stopped and a dark purple solid could be isolated. Its UV−vis spectrum was identical to that obtained as described above. HRMS measurements indicated the presence of the α-$(H_2NCO)_2TPAFeCl^{+2}$ ion with m/z = 233.533 and α-$(H_2NCO)_2TPAFeCl^{+}$ − H at m/z = 466.059 (all MS data available in the Supporting Information). Infrared measurements indicated the disappearance of the $\nu_{C\equiv N}$ = 2239 cm^{-1} band of the starting material and the presence of two new intense bands at $\nu_{C=O}$ = 1645 and 1664 cm^{-1} in line with the

Scheme 3. Hydration Reaction Reported in the Present Study[a]



[a]The presence of the intermediate species as the mono-carboxamido compound drawn in square brackets (top line) is proposed on the basis of its detection by HRMS in the reaction medium. In the bis-carboxamido ferrous species, the iron has been drawn as a seven-coordinate center on the basis of similar spectroscopic properties to that reported with a parent compound fully characterized in ref .42. Species in brackets (bottom line) are proposed as short-lived intermediates.

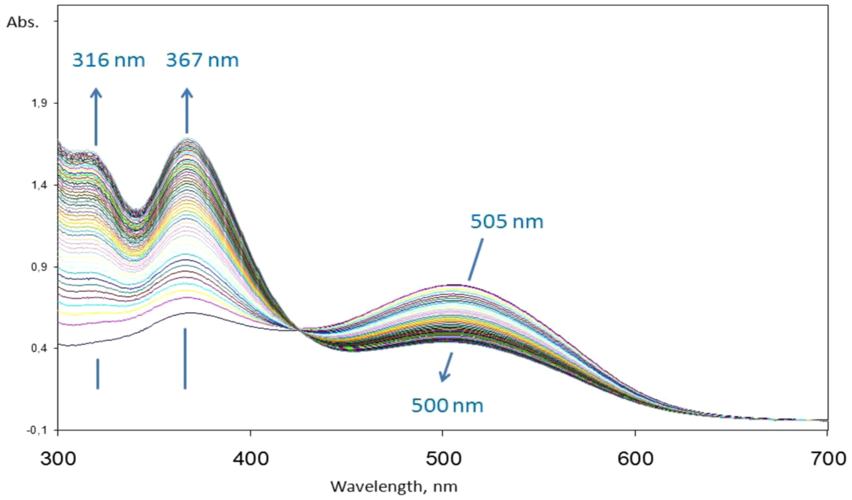


Figure 8. Forty-eight hour conversion of α-$(H_2NCO)_2$TPAFeCl_2 into {[α-$(H_2NCO)_2$TPAFe]$_2$-O}Cl_4 in CH_3CN/H_2O 80/20, monitored by UV–vis spectroscopy.

presence of a bound amide function.[44] Finally, elemental analysis was also carried out and confirmed the formulation of the complex. Taken together, all collected data indicate formation of the bis-carboxamido α-$(H_2NCO)_2$TPAFeCl_2 species, drawn in Scheme 3 as a seven-coordinate complex by analogy to the above-mentioned Fe(II) complex with the parent TPA$^{2C(O)NHtBu}$ tripod.[42] In view of further reactivity studies, it should be mentioned that this complex is poorly soluble in acetonitrile and should be studied in solution in a mixture CH_3CN/H_2O 80/20.

Full Stability of β-$(NC)_2$TPFeCl_2 when Exposed to Water. The same experiments were carried out on the β-substituted congener. Addition of 200–500 equiv of H_2O to a solution of β-$(CN)_2$TPAFeCl_2 in CH_3CN had negligible effects on the UV–vis and ^{1}H NMR spectra of the complex, indicating no change in the structure of the ligand. Following unsuccessful attempts to convert the ligand in a preparative way (vide supra), this confirmed the inertness of the tripod in β-$(CN)_2$TPAFeCl_2 when exposed to water. All data and experimental traces are given in the Supporting Information.

Oxidation of α-$(H_2NCO)_2$TPAFeCl_2: κ^6 Coordination Mode of α-$(H_2NCO)_2$TPA. *Reactivity of α-$(H_2NCO)_2$TPAFeCl_2 with Oxygen.* As displayed in Figure 8, bubbling O_2 in a CH_3CN/H_2O solution of the complex resulted in the appearance of a new band at $\lambda = 316$ nm ($\varepsilon = 3365$ L mol^{-1} cm^{-1}) and an important increase of a signal at $\lambda = 367$ nm ($\varepsilon = 3553$ L mol^{-1} cm^{-1}). This particular pattern is the distinctive mark of the presence of a diferric μ-oxo species.[25,26,38] The third absorption indicating amide coordination decreased in intensity and was slightly shifted to $\lambda = 500$ nm, with $\varepsilon = 915$ L mol^{-1} cm^{-1}. UV−vis data of the amido-coordinated complexes are summarized in Table 3.

Table 3. Spectroscopic Data in Solution of the Amido-Coordinated Complexes α-$(H_2NCO)_2TPAFeCl_2$ and $\{[\alpha$-$(H_2NCO)_2TPAFe]_2$-$O\}Cl_4$

	λ_{MLCT}, nm (ε, L mol^{-1} cm^{-1})
α-$(H_2NCO)_2TPAFeCl_2$	368 (1300), 505 (1660)
$\{[\alpha$-$(H_2NCO)_2TPAFe]_2$-$O\}Cl_4$	316 (3365), 367 (3553), 500 (915)

The reaction occurred slowly and was considered to be complete over 48 h.

As shown in Scheme 4, it was reproduced at the preparative scale, and after workup a dark brown compound was isolated and first characterized by elemental analysis, which was consistent with the presence of the μ-oxo diferric complex $([\alpha$-$(H_2NCO)_2TPAFe]_2$-$O)(Cl)_4$. Its UV−vis spectrum was identical to that detected in the course of the reaction monitoring. In infrared spectroscopy, the carbonyl vibration was measured at $\nu_{C=O}$ = 1661 cm^{-1}, in line with weak coordination to the metal center.

Single crystals of this compound could be obtained by diffusion of diethyl ether in an acetonitrile solution, and its ORTEP diagram is displayed in Figure 9.

The structure of the $\{[\alpha$-$(H_2NCO)_2TPAFe]_2$-$O\}^{4+}$ ion is similar to that of the recently reported $[(TPA_2^{C(O)NHtBu}Fe)_2$-$O]^{4+}$ one, in which the pivaloylamido-substitued tripod was synthesized by conventional methods.[42] This compound belongs to the class of ferric complexes in which the metal is seven coordinate.[42,45−51] In the present case the nitrogen atoms from the substituted pyridines together with the oxygen atoms from the amide are coplanar and define an equatorial plane. The amine nitrogen atom N2 is displaced 0.38 Å from this plane. Thus, the geometry is consistent with a slightly distorted pentagonal bipyramidal structure. The longest distance is that between the iron atom and the central amine, with *d*Fe−N2 = 2.360(2) Å, the shortest been the one between the metal and the pyridine trans to the μ-oxo group, *d*Fe−N1 2.154(2) Å. The Fe−O3−Fe segment is linear, and the intermetallic distance *d*Fe−Fe = 3.54 Å lies in the expected range for μ-oxo diferric complexes.[25,52,53]

Recovery of the Free α-$(H_2NCO)_2TPA$ Tripod by Decomplexation. Treatment of either α-$(H_2NCO)_2TPAFeCl_2$ or $\{[\alpha$-$(H_2NCO)_2TPAFe]_2$-$O\}Cl_4$ by KOH in a mixture of CH_3CN/H_2O resulted in immediate bleaching. A standard extraction of the medium at neutral pH by methylene chloride afforded the free tripod in a very clean way as a white-off solid, whose spectroscopic data were identical to those indicated above.

DISCUSSION

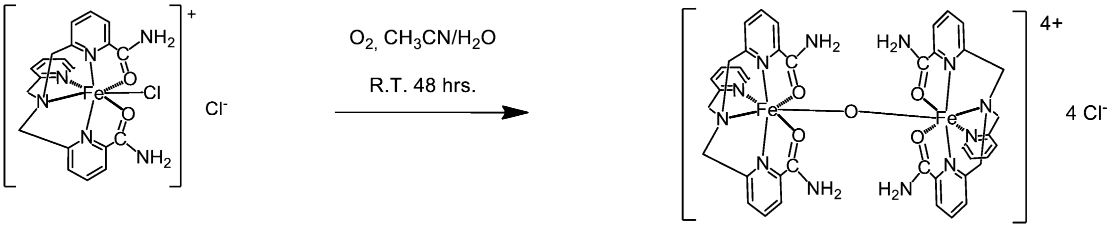
Nitrile groups are considered as thermodynamically unstable functions, while being kinetically inert[54] their conversion into amide requires harsh conditions or activation by metal centers with or without adjuvants.[1−6,55] In many cases, nitrile hydration by metal centers involves nucleophilic attack of an hydroxide group on a coordinated nitrile.[1,6] In the iron chemistry of TPA-type tripods, the hydration of a coordinated nitrile into an acetamide[53] and acetate[56] has been reported within dinuclear Fe(III) complexes. This is not unexpected at a ferric center, since Fe(III) is also found at the active site of nitrile hydratase.[4,5,7,8] In the present case, the hydration reaction is performed by a ferrous Fe(II) center, which is unusual.

The following lines aim at replacing this reaction in the context of the chemistry of aminomethylpyridine-containing complexes and more generally with Fe(II) centers.

Both Complexes Display Relatively High Redox Potentials. The redox potentials measured in this work both stand at the upper limit of the reported range for this kind of complexes,[36] those being either five or six coordinate. Obviously, tripods with electron-withdrawing groups afford complexes with an increased Lewis acid character. This indicates that the metal center, although being Fe(II), must be electron deficient, at least with respect to standard Fe(II) complexes. It is also likely that in the intermediate steps, i.e., those in which water coordinates, both tripods act as κ^4 ligands: if so, the potentials should not differ by much whether the ligand is α- or β-substituted. In any case, both complexes should display an increased propensity to activate a coordinated water molecule, even in the Fe(II) state.

Coordination of Nitriles to the Fe(II) Center. The coordination of acetonitrile to Fe(II) centers is known in the chemistry of aminomethylpyridyl-containing ligands. Many structures are known,[57−60] either in the solid state or in solution, examples of which are shown in Figure 10. We recently reported the structure of a bis-aquo Fe(II) complex with a TPA-type tripod.[59] All these complexes are extremely stable, and as cationic species or/and simply because the ligands are substituted with electron-withdrawing groups, they exhibit high redox couples. As a consequence, the metal center must be electron deficient, and even an Fe(II) center should be able to activate a coordinated molecule. For instance, we could envisage that in Figure 10A one acetonitrile might be replaced by water which would hydrate the second ancillary ligand. This might also be the case in the Fe(II) complex of the bpmpn ligand displayed in Figure 10C: one acetonitrile and one water molecule are ideally placed in cis position to be able to react each with the other.[61] To our knowledge, there is no mention that any complex of this kind could lead to the corresponding amides by any treatment.

Scheme 4. Oxidation of α-$(H_2NCO)_2TPAFeCl_2$ Yielding $\{[\alpha$-$(H_2NCO)_2TPAFe]_2$-$O\}Cl_4$



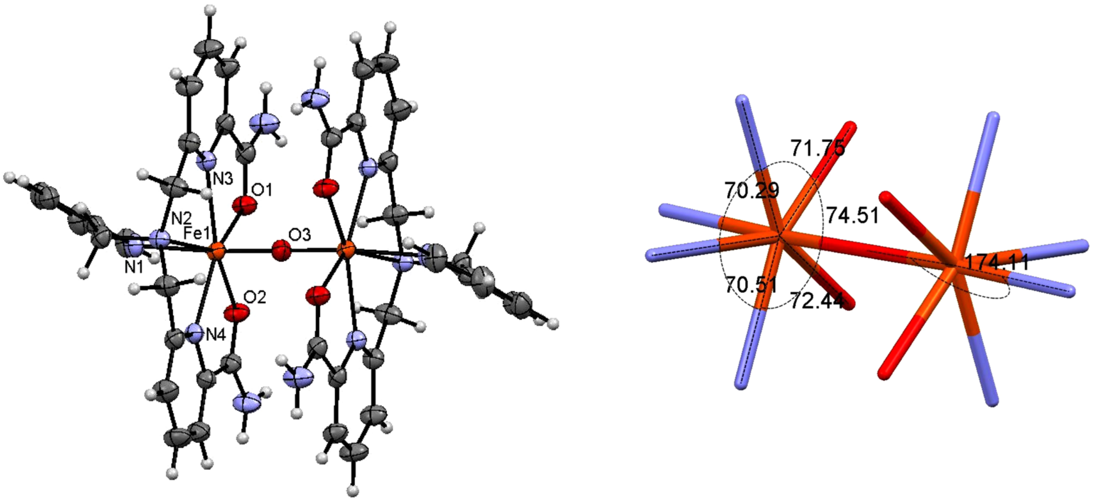


Figure 9. ORTEP diagram of the {[α-$(H_2NCO)_2$TPAFe$]_2$-O}$^{4+}$ ion, and coordination skeleton with the main angles. Chloride ions are omitted for clarity. Selected distances (Å): Fe−O1 2.1616(18), Fe−O2 2.1439(18), Fe−O3 1.7703(5), Fe−N1 2.154(2), Fe−N2 2.360(2), Fe−N3 2.229(2), Fe−N4 2.212(2), Fe−Fe 3.541(5). This complex has inversion symmetry with O3 occupying the inversion center: bond distances and angles are identical for the inversion counterpart.

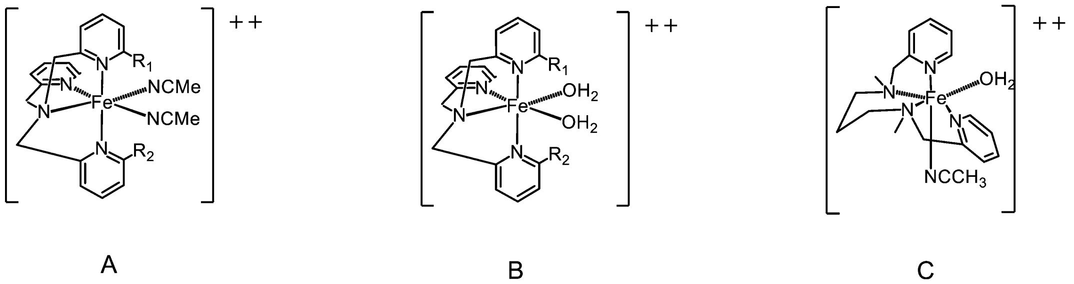


Figure 10. Examples of chemically stable bis-acetonitrile or bis-aquo cations with high redox couples (A and B, see refs 57−60). Precursors are triflate- or perchlorate-bound complexes. (A and B) Ancillary ligands (NCMe or H_2O) can bind and exchange each other by a simple control of the ligand concentration. (C) Example of a stable mixed acetonitrile/aquo complex characterized by X-ray diffraction analysis; see ref 61.

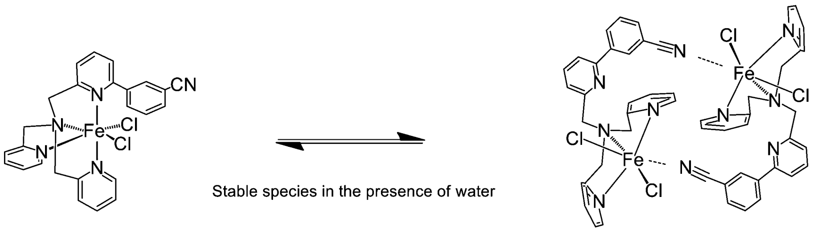


Figure 11. Example of a complex with a nitrile-substituted TPA ligand in which the nitrile is ideally positioned to undergo hydration by action of water. This complex is stable in wet conditions; see ref 41.

Finally, Figure 11 illustrates a case of a binuclear assembly, where the nitrile is not coordinated and water can bind to the metal:[41] in such a case, the position of the reagents would also be ideal to promote nitrile hydration. However, even in wet conditions, the hydration of the nitrile could never be observed.

It thus appears that the only coordination of the reagents to an Fe(II) center, even with a high redox couple as found in cationic species, or simply a good positioning in cis position, as illustrated in Figures 10C and 11, do not define sufficient conditions to ensure nitrile hydration.

Coordination of Water to the Fe(II) Center. We recently showed that the dissociation equilibrium of the chloride ions is displaced toward uncoordination as better as the coordination polyhedron is sterically constrained.[25,29,59] Acetonitrile[29] or dioxygen,[25,59] − which is a weak ligand−can easily when used in excess, replace the ancillary chloride ions. In the present case, we also work with an excess of water. Considering this, the coordination of water to the metal center is more than likely. Numerous examples can be found in the literature where a water molecule is coordinated to a metal center that, in turn, facilitates its deprotonation, increasing its nucleophilicity and ability to attack neighboring groups.[1,6,62] We believe that this is what happens here, even if for stability reasons we could not detect these aquo-substituted species. We suggest that the instability of the aquo species results from a fast hydration reaction due to the perfect positioning of both reagents within the complex as outlined below and displayed in Figure 12.

Ideal Positioning of the Nitrile Group in α-$(NC)_2$TPAFeCl_2. From the structure analysis of α-$(NC)_2$TPAFeCl_2 in the solid state and in solution the proximity

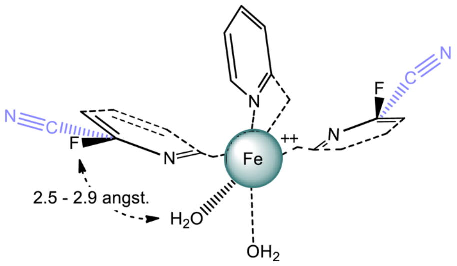


Figure 12. Short water-substituent distance in the crystallographically characterized $[F_2TPAFe(H_2O)_2]^{+2}$ dication according to ref[59] (black drawing). The light blue adds-on feature the presence of the two nitrile groups instead of fluorine atoms, within a hypothetical six-coordinate bis aquo α-$(NC)_2TPAFe(H_2O)_2$.

of the nitrile groups with the reaction center is obvious. What about a hypothetical complex with aquo groups instead of chloride ions? We need to focus on the intermediate step that in which water is coordinated instead of chloride and for which we have no crystal structure. We do, however, have XRD data on the bis-aquo complex $[F_2TPAFe(H_2O)_2]^{+2}$,[59] which show by comparison with $F_2TPAFeCl_2$ (i) that replacement of a chloride ligand by a water molecule provides a more compact coordination polyhedron and (ii) that short distances between the coordinated water proton and the substituent can be measured in the 2.5−2.9 Å range. Thus, coming back to our present study, the nitrile in the α-position of the pyridine should be kept even closer to the ancillary ligand within an aquo complex as shown in Figure 12 than in the chloro one.

■ CONCLUSION

Intramolecular Nitrile Hydration Reaction at an Fe(II) Site as a Result of Combined Steric and Positioning Effects. The fact that the β-substituted β-$(NC)_2TPAFeCl_2$ is not water sensitive suggests the involvement of an intramolecular hydration reaction of α-$(NC)_2TPAFeCl_2$, the nitrile being ideally positioned and kept in place by the ligand skeleton. In the end, the reaction product is stabilized by carboxamide coordination to the metal, but it is also probably stabilized relative to the starting material by release of steric strain. In fact, in the present case, all structural and electronic ingredients favor the reaction to take place in unexpected conditions, i.e., by a ferrous Fe(II) center at room temperature. To our knowledge, the present study together with our preliminary communication of 2008 represent the only case of a nitrile hydration with ferrous Fe(II).

Synthetic Interest: Easy Preparation of α-$(H_2NCO)_2$TPA. The hydration reaction which is described in the present study is not devoid of interest in itself. The presence of amide substituents at the secondary coordination sphere of tripodal ligands may have dramatic effects on the reactivity of metal sites.[63−67] RNHCO-substituted tripods are known, but their preparation requires working from picolinic acid in harsh conditions[42,68,69] (by contrast with RCONH-substituted ones which can be easily obtained from the commercially available amino-substituted pyridines). CN-substituted TPA-type tripods are easy to prepare with good to excellent yields and constitute simple precursors of H_2NCO-substituted ligands.

Coordination Chemistry. As expected, α-$(H_2NCO)_2TPAFeCl_2$ reacts with O_2 to yield a μ-oxo diferric species. This reaction, which has been thoroughly described in the past,[25,26,37] generally involves ligand exchange steps[59,63] and proceeds very smoothly in the present case. This reflects a relative rigidity and excellent stability of the coordination polyhedron within the ferrous precursor in which the tripod is tightly bound in a κ^5 mode. The structure of the μ-oxo $\{[\alpha$-$(H_2NCO)_2TPAFe]_2$-$O\}^{4+}$ represents one of the few examples of seven-coordinate Fe complexes.[42,51,70]

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

All synthetic details, including preparation and characterization of all compounds mentioned; experimental details for the hydration reaction; for the three reported structures, crystallographic files in CIF format have been deposited. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Phone. ++33 (0)298 016 028. Fax: ++33 (0)298 017 001. E-mail: dominique.mandon@univ-brest.fr.

Notes

The authors declare no competing financial interest.

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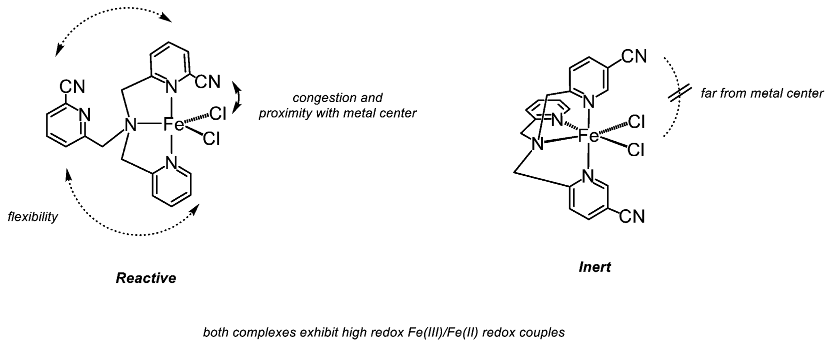

Figure 13. α-$(NC)_2TPAFeCl_2$ complex exhibits flexibility, and by contrast with its β-$(NC)_2TPAFeCl_2$ congener, the cyano groups are ideally placed to be hydrated.

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■ REFERENCES

(1) Ahmed, T. J.; Knapp, S. M. M.; Tyler, D. R. *Coord. Chem. Rev.* **2011**, *255*, 949−974.

(2) Garcia-Alvarez, R. C. P.; Cadierno, V. *Green Chem.* **2013**, *15*, 46−66.

(3) Kukushkin, V. Y.; Pombeiro, A. J. L. *Chem. Rev.* **2002**, 1771−1802.

(4) Mascharak, P. K. *Coord. Chem. Rev.* **2002**, *225*, 201−214.

(5) Kobayashi, M.; Shimizu, S. *Curr. Opin. Chem. Biol.* **2000**, 95−102.

(6) Kukushkin, V. Y.; Pombeiro, A. J. L. *Inorg. Chim. Acta* **2005**, *358*, 1−21.

(7) Prasad, S. B.; T, C. *Biotechnol. Adv.* **2010**, *28*, 725−741.

(8) Shen, Y. D. F.; Gao, W.; Wang, A.; Chen, C. *Afr. J. Microbiol. Res.* **2012**, *6*, 6114−6121.

(9) Rao, S.; Holz, R. C. *Biochemistry* **2008**, *47*, 12057−12064.

(10) Noveron, J. C.; Olmstead, M. M.; Mascharak, P. K. *J. Am. Chem. Soc.* **2001**, *123*, 3247−3259.

(11) Crestani, M. G.; Steffen, A.; Kenwright, A. M.; Batsanov, A. S.; Howard, J. A. K.; Marder, T. B. *Organometallics* **2009**, *28*, 2904−2914.

(12) Ashraf, S. M.; Kandioller, W.; Mendoza-Ferri, M. G.; Nazarov, A. A.; Hartinger, C. G.; Keppeler, B. K. *Chem. Biodiversity* **2008**, *5*, 2060−2066.

(13) Ashraf, S. M.; Berger, I.; Nazarov, A. A.; Hartinger, C. G.; Koroteev, M. P.; Nifant'ev, E. E.; Keppler, B. K. *Chem. Biodiversity* **2008**, *5*, 1640−1644.

(14) Lung, C. W.; Zheng, W.; Zhou, Z.; Lin, Z.; Lau, C. P. *Organometallics* **2008**, *27*, 4957−4969.

(15) Daw, P.; Sinha, A.; Wahidur Rahaman, S. M.; Dinda, S.; Bera, J. K. *Organometallics* **2012**, *31*, 3790−3797.

(16) Arakawa, T.; Kawano, Y.; Kataoka, S.; Katayama, Y.; Kamiya, N.; Yohda, M.; Odaka, M. *J. Mol. Biol.* **2007**, *366*, 1497−1509.

(17) Song, L.; Wang, M.; Shi, J.; Xue, Z.; Wang, M.-X.; Qiahn, S. *Biochem. Biophys. Res. Commun.* **2007**, *362*, 319−324.

(18) Huang, W.; Jia, J.; Cummings, J.; Nelson, M.; Schneider, G.; Lindqvist, Y. *Structure* **1997**, *5*, 691−699.

(19) Schibler, W.; Kaden, T. A. *J. Chem. Soc., Chem. Commun.* **1981**, 603−604.

(20) Tschudin, D.; Kaden, T. A. *Pure Appl. Chem.* **1988**, *60*, 489−493.

(21) Siegfried, L.; Kowallick, R.; Kaden, T. A. *Supramol. Chem.* **2000**, *13*, 357−367.

(22) Siegfried, L.; Comparone, A.; Neuburger, M.; Kaden, T. A. *Dalton Trans.* **2005**, 30−36.

(23) Thallaj, N. K.; Przybilla, J.; Welter, R.; Mandon, D. *J. Am. Chem. Soc.* **2008**, *130*, 2414−2415.

(24) Chuang, C. L.; dosSantos, O.; Xu, X. D.; Canary, J. W. *Inorg. Chem.* **1997**, *36*, 1967−1972.

(25) Thallaj, N. K.; Rotthaus, O.; Benhamou, L.; Humbert, N.; Elhabiri, M.; Lachkar, M.; Welter, R.; Albrecht-Gary, A. M.; Mandon, D. *Chem.—Eur. J.* **2008**, *14*, 6742−6753.

(26) Machkour, A.; Mandon, D.; Lachkar, M.; Welter, R. *Inorg. Chem.* **2004**, *43*, 1545−1550.

(27) Mandon, D.; Machkour, A.; Goetz, S.; Welter, R. *Inorg. Chem.* **2002**, *41*, 5364−72.

(28) Machkour, A.; Mandon, D.; Lachkar, M.; Welter, R. *Eur. J. Inorg. Chem.* **2005**, 158−161.

(29) Benhamou, L.; Lachkar, M.; Mandon, D.; Welter, R. *Dalton Trans.* **2008**, 6996−7003.

(30) Jaafar, H.; Vileno, B.; Thibon, A.; Mandon, D. *Dalton Trans.* **2011**, *40*, 92−106.

(31) Drew, M. G. B.; Harding, C. J.; McKee, V.; Morgan, G. C.; Nelson, J. *J. Chem. Soc., Chem. Commun.* **1995**, 1035−1038.

(32) Deeney, F. A.; Harding, C. J.; Morgan, G. C.; McKee, V.; Nelson, J.; Teat, S. J.; Clegg, W. *J. Chem. Soc., Dalton Trans.* **1998**, 1837−1843.

(33) Geary, W. J. *Coord. Chem. Rev.* **1971**, *7*, 81−122.

(34) Hubin, T. J.; McCormick, J. M.; Collinson, S. R.; Buchalova, M.; Perkins, C. M.; Alcock, N. W.; Kahol, P. K.; Raghunatan, A.; Busch, D. H. *J. Am. Chem. Soc.* **2000**, *122*, 2512−2522.

(35) Assuming that the $E_{1/2}$ value for ferrocene is 452 mV/SCE in the presence of TBACl, the measured value lies at $E_{1/2}$ = 72 mV/SCE.

(36) Mandon, D.; Jaafar, H.; Thibon, A. *New J. Chem.* **2011**, *35*, 1986−2000.

(37) Benhamou, L.; Jaafar, H.; Thibon, A.; lachkar, M.; Mandon, D. *Inorg. Chim. Acta* **2011**, *373*, 195−200.

(38) Benhamou, L.; Machkour, A.; Rotthaus, O.; Lachkar, M.; Welter, R.; Mandon, D. *Inorg. Chem.* **2009**, *48*, 4777−86.

(39) Jaafar, H.; Louis, R.; Mandon, D. *Inorg. Chim. Acta* **2011**, *366*, 147−153.

(40) Assuming that the $E_{1/2}$ value for ferrocene is 452 mV/SCE in the presence of TBACl, the measured value lies at E_a = 352 mV/SCE.

(41) Thallaj, N. K.; Machkour, A.; Mandon, D.; Welter, R. *New J. Chem.* **2005**, *29*, 1555−1558.

(42) Soo, H. S.; Sougrati, M. T.; Grandjean, F.; Long, G. J.; Chang, C. J. *Inorg. Chim. Acta* **2011**, *369*, 82−96.

(43) We recently obtained the crystal structure of the $TPA_2^{C(O)NHtBu}Fe(II)Cl_2$ complex, which is very similar to the already reported one (seven-coordinate complex). The spectroscopic properties are identical to those of the present bis-carboxamido complex. Thibon, A., Mandon, D. Unpublished results.

(44) Thibon, A.; Karmazin-Brelot, L.; Mandon, D. *Eur. J. Inorg. Chem.* **2013**, 1118−1122.

(45) Marlin, D. S.; Olmstead, M. M.; Mascharak, P. K. *Inorg. Chim. Acta* **2000**, *297*, 16−114.

(46) Brewer, C.; Brewer, G.; Butcher, R. J.; Carpenter, E. E.; Cuenca, L.; Noll, B. C.; Scheidt, W. R.; Viragh, C.; Zavalij, P. Y.; Zielaski, D. *Dalton Trans.* **2006**, 1009−1019.

(47) Ivanovic- Burmazovic, I.; Hamza, M. S. A.; van Eldik, R. *Inorg. Chem.* **2002**, *41*, 5150−5161.

(48) Ivanovic- Burmazovic, I.; Hamza, M. S. A.; van Eldik, R. *Inorg. Chem.* **2006**, *45*, 1575−1584.

(49) Liu, G. F.; Filipovic, M.; Heinemann, F. W.; Ivanovic-Burmazovic, I. *Inorg. Chem.* **2007**, *46*, 8825−8835.

(50) Gosiewska, S.; Permentier, H. P.; Bruins, A. P.; van Koten, G.; Klein Gebbink, R. J. M. *Dalton Trans.* **2007**, 3365−3368.

(51) Machkour, A.; Thallaj, N. K.; Benhamou, L.; Lachkar, M.; Mandon, D. *Chem.—Eur. J.* **2006**, *12*, 6660−6668.

(52) Kojima, T.; Leising, R. A.; Yan, S. P.; Que, L. *J. Am. Chem. Soc.* **1993**, *115*, 11328−11335.

(53) Hazell, A.; Jensen, K. B.; McKenzie, C. J.; Toftlund, H. *Inorg. Chem.* **1994**, *33*, 3127−3134.

(54) Guthrie, J. P.; Yim, J. C-H.; Wang, Q. *J. Phys. Org. Chem.* **2014**, *27*, 27−37.

(55) Ma, X.; He, Y.; Wang, P.; Lu, M. *Appl. Organomet. Chem.* **2012**, *26*, 377−382.

(56) Do, L. H.; Xue, G.; Que, L., Jr.; Lippard, S. J. *Inorg. Chem.* **2012**, *51*, 2393−2402.

(57) Diebold, A.; Hagen, K. S. *Inorg. Chem.* **1998**, *37*, 215−223.

(58) Britovsek, G. J. P.; England, J.; White, A. J. P. *Inorg. Chem.* **2005**, *44*, 8125−8134.

(59) Benhamou, L.; Thibon, A.; Brelot, L.; Lachkar, M.; Mandon, D. *Dalton Trans.* **2012**, *41*, 14369−14380.

(60) Jensen, M. P.; Lange, S. J.; Mehn, M. P.; Que, E. L.; Que, L. *J. Am. Chem. Soc.* **2003**, *125*, 2113−2128.

(61) Mas-Balleste, R.; Costas, M.; van den Berg, T.; Que, L. *Chem.—Eur. J.* **2006**, *12*, 7489−7500.

(62) Jarenmark, M.; Carlsson, H.; Nordlander, E. *C. R. Chim.* **2007**, *10*, 433−462.

(63) Wane, A.; Thallaj, N. K.; Mandon, D. *Chem.—Eur. J.* **2009**, *15*, 10593−10602.

(64) Borovik, A. S.; Shook, R. L. *Inorg. Chem.* **2010**, *49*, 3646−3660.

(65) Jitsukawa, K.; Oka, Y.; Yamaguchi, S.; Masuda, H. *Inorg. Chem.* **2004**, *43*, 8119−8129.

(66) Harata, M.; Jitsukawa, K.; Masuda, H.; Einaga, H. *J. Am. Chem. Soc.* **1994**, *116*, 10817−10818.

(67) Harata, M.; Hasegawa, K.; Jitsukawa, K.; Masuda, H.; Einaga, H. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1031−1038.

(68) Maurin, J. K.; Lasek, W.; Gorska, A.; Switaj, T.; Jakubowska, A. B.; Kazimierczuk, Z. *Chem. Biodiversity* **2004**, *1*, 1498−1512.

(69) Mizuno, M.; Hayashi, H.; Fujinami, S.; Furutachi, H.; Nagatomo, S.; Otake, S.; Uozumi, K.; Suzuki, M.; Kitagawa, T. *Inorg. Chem.* **2003**, *42*, 8534−8544.

(70) See ref 42 for an overview of seven-coordinate Fe complexes.

(71) Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*, 4th ed.; Pergamon Press: Oxford, 1997.

(72) *Kappa CCD Operation Manual*; Nonius B.V.: Delft, The Netherlands, 1997. Sheldrick, G. M. *SHELXL97, Program for the refinement of crystal structures*; University of Göttingen: Göttingen, Germany, 1997.