

Iron(III) Chloride mediated reduction of Bis(1-isoquinolylcarbonyl)amide to an Amide[†]

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Abstract. In methanol, FeCl₃ reacted readily with **L1H** (**L1H** = bis(1-isoquinolylcarbonyl)amide) and afforded a complex having the formula [Fe(**L2**)Cl₂] (**1**) {**L2**[−] = *N*-((1-isoquinolyl)(methoxy)methyl)isoquinoline-1-carboxamide ion}. This reaction involves reduction of one of the two carbonyl groups present in **L1H** to (methoxy)methyl group. A plausible mechanism for the conversion of **L1H** to **L2**[−] has been proposed. Determination of molecular structure of **1** confirmed this conversion. Fe(III) ion is surrounded by three nitrogen atoms of the ligand and two chloride ions, imparting a rare distorted trigonal bipyramidal N₃Cl₂ coordination environment.

Keywords. Reduction; Ferric chloride; Isoquinoline; Bis(carbonyl)amide.

1. Introduction

Iron(III) chloride has been known to catalyze or assist several kinds of organic reactions.^{1–3} This includes Friedel–Crafts,^{4,5} Michael addition,^{6–8} Ritter,⁹ alkylation of indoles with enamides^{10,11} and oxidation of thiols (RSH) to RSSR in the presence of butadiene.¹² Oxidation of alkanes by [Os(N)O₃][−] ion,¹³ coupling of ArMgX with alkyl halides,¹⁴ synthesis of polysubstituted benzofurans (a component in the synthesis of coumarins by Pechmann condensation) using di-*tert*-butyl peroxide, phenols and β-keto esters¹⁵ were reported. Oxygenation of cycloalkanones to oxo esters,¹⁶ oxidative coupling reactions of phenols¹⁷ and disproportionation of allylic alcohols¹⁸ were achieved using iron(III) chloride. Alkenylation of simple arenes with aryl-substituted alkynes,¹⁹ synthesis of sulfonyl amidines,²⁰ α-glycosidation,²¹ synthesis of indene derivatives,²² 1,4-addition of various thiols to α, β-unsaturated ketones,²³ preparation of cyanohydrin esters,²⁴ protection of diols and carbonyls²⁵ as well as formation of β-nitroalcohols²⁶ have also been reported.

We recently reported²⁷ the formation of bis(1-isoquinolylcarbonyl)amide (**L1H**) from 1-aminomethylisoquinoline in presence of copper(II) acetate and were

exploring the reaction of **L1H** with other transition metal ions. Herein we report a facile reaction of **L1H** with FeCl₃ that led to the formation of [Fe(**L2**)Cl₂] under ambient conditions, wherein **L2**[−] = *N*-((1-isoquinolyl)(methoxy)methyl)isoquinoline-1-carboxamide ion. This new iron(III) complex of the transformed ligand (**L2**[−]) was not accessible by conventional methods.

2. Experimental

2.1 Materials and methods

Anhydrous FeCl₃ (Merck India Ltd) and other reagent grade chemicals were used as received without further purification. Bis(1-isoquinolylcarbonyl)amide (**L1H**) was prepared using the reported procedure.^{27,28}

A Perkin–Elmer Spectrum One FT–IR spectrometer (4000–250 cm^{−1}), Perkin–Elmer Lambda 25 UV–Vis spectrometer, Perkin–Elmer Series II CHNS/O Analyzer 2400, JEOL JES FA-200 X-band EPR spectrometer, and a Lakshore VSM Setup were used for performing relevant measurements.

X-ray crystallographic data were collected using Bruker SMART APEX-CCD diffractometer with Mo Kα radiation (λ = 0.71073 Å). The intensity data were corrected for Lorentz and polarization effects and empirical absorption corrections was applied using SAINT program.²⁹ The structure was solved by direct

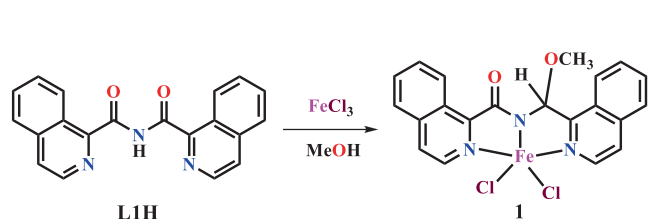
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[†]Dedicated to Professor Animesh Chakravorty on the occasion of his 80th birth anniversary.

methods using SHELXS-97.^{30,31} Non-hydrogen atoms located from the difference Fourier maps were refined anisotropically by full-matrix least-squares on F^2 using SHELXL-97.^{30,31} All hydrogen atoms were included at the calculated positions and refined isotropically using a riding model.

2.2 Synthesis

2.2a $[Fe(L2)Cl_2](1)$: To a methanolic solution (20 mL) of $FeCl_3$ (16.0 mg, 0.1 mmol) solid **L1H** (33.0 mg, 0.1 mmol) was added and stirred for 8 h. The reaction mixture was left undisturbed and after 4 days red crystals of **1** were isolated. Yield: 30.0 mg, 64%. IR (KBr) ν_{max} (cm^{-1}): 3438, 1719, 1651, 1618, 1588, 1500, 1449, 1432, 1394, 1382, 1356, 1331, 1289, 1255, 1190, 1152, 1092, 1054, 1017, 903, 878, 867, 824, 750, 672, 654, 628, 609, 572, 507, 489, 473, 415, 386, 356. Anal. calcd for $C_{21}H_{16}N_3O_2Cl_2Fe$: C 53.77; H 3.44; N 8.96%. Found: C 53.57; H 3.40; N 8.89%. UV-Vis [λ_{max} , nm (ϵ , $M^{-1}cm^{-1}$), MeOH]: 370(9425), 335(15180), 325(15570). EPR (DMF solution, 77 K): $g_{eff} = 4.27$; μ_{eff} (polycrystalline, 25°C) = 5.60 B.M.



Scheme 1. Synthesis.

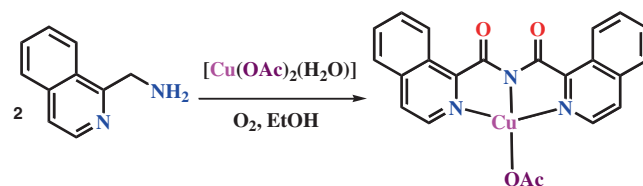
3. Results and Discussion

3.1 Synthesis

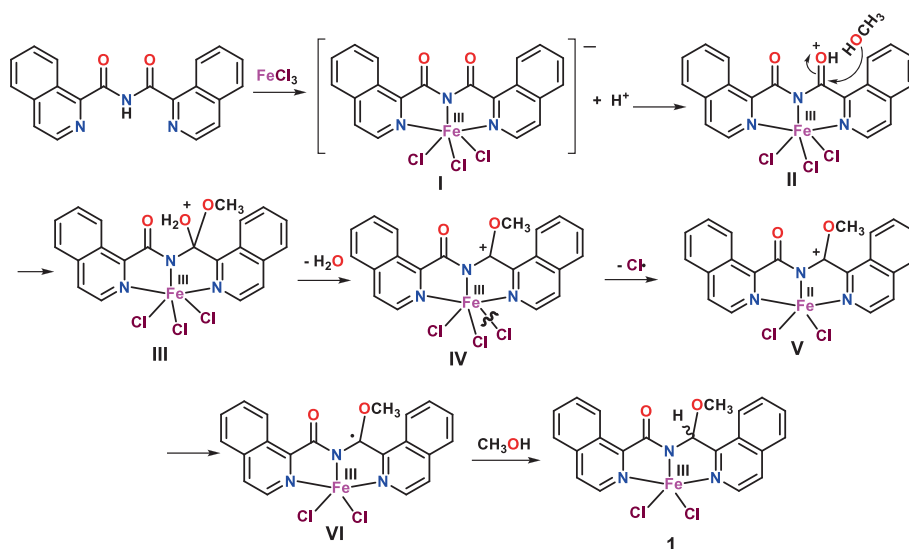
On stirring **L1H** with anhydrous $FeCl_3$ in methanol, a yellowish red solution was obtained, which on standing afforded red crystals of **1**. The molecular structure of **1** has been determined (*vide infra*) and the composition $[Fe(L2)Cl_2]$ has been formulated (scheme 1). During the course of the reaction, reactivity at the carbonyl function of the ligand has been enhanced upon coordination and one of the two carbonyl groups of bis(1-isoquinolylcarbonyl)amide has been reduced³² to (methoxy)methyl group. It is relevant to note that bis(2-pyridylcarbonyl)amine (**L3H**) having a similar ligand framework has been reported to react with $FeCl_3$ resulting in the formation of $[Fe(L3)Cl_2(H_2O)]$ and $[Fe(L3)_2]^+$ species, without any change in **L3H**.³³ To the best of our knowledge this is the first example of reduction of dicarbonylamides, in which one carbonyl group has been converted to a (methoxy)methyl group.

3.2 Plausible mechanism

A plausible mechanism for this conversion has been proposed in scheme 2. First step is formation of



Scheme 3. Formation of **L1H** from 1-aminomethylisoquinoline.



Scheme 2. Plausible mechanism for the formation of **1** from **L1H**.

simple monochelate of $\mathbf{L1}^-$ having the composition $[\text{Fe}(\mathbf{L1})\text{Cl}_3]^-$ (**I**). Upon reaction of FeCl_3 with $\mathbf{L1H}$ a proton will be released which will attach to one of the carbonyl oxygen atoms as in **II**. This will polarize the carbonyl group, which will become susceptible to nucleophilic attack by CH_3OH molecule and a concomitant proton shift will lead to intermediate **III**. Elimination of a water molecule from **III** will yield cation **IV**, which could undergoes a homolytic cleavage at one of the Fe(III)-Cl bonds. This will release a Cl atom and intermediate **V** containing five-coordinated iron(II) center. Iron(II) could transfer one electron to the electrophilic carbon to generate a radical intermediate **VI**, containing five-coordinated iron(III) center. This radical could abstract H atom from MeOH leading to the final product **1**.

It is also important to note here that different dicarbonylamides are formed from appropriately substituted pyridine nucleus having an *ortho* aminomethyl group in presence of copper(II) acetate.^{30,31} This conversion involves oxidation of the methylene group and coupling of the bond between nitrogen and carbon in N-C(=O) . However, thus formed (from 1-aminomethylisoquinoline in presence of copper(II) acetate, scheme 3) dicarbonyl group in $\mathbf{L1H}$ undergoes a reduction in presence of iron(III) chloride. It is also important to note that penta-coordinated iron(III) complexes find application as efficient catalysts for the cross-coupling reaction between arylmagnesium bromides and alkyl halides.^{34,35}

3.3 Optical Spectra and Magnetism

The IR spectrum of free $\mathbf{L1H}$ shows ν_{CO} around 1745 cm^{-1} ,^{30,31} which is lowered to the range $1690\text{--}1710\text{ cm}^{-1}$ upon coordination to a metal center as observed in the complexes $[\text{Cu}(\mathbf{L1})(\text{H}_2\text{O})_2]\text{ClO}_4$ and $[\text{Ni}(\mathbf{L1})_2]$. Compound **1** shows a characteristic 1719 cm^{-1}

peak for ν_{CO} . In addition, a strong peak for $\nu_{\text{C-O}}$ at $\sim 1250\text{ cm}^{-1}$ and $\nu_{\text{Fe-Cl}}$ peaks at ~ 386 and 356 cm^{-1} were noted. Methanol solution of **1** shows allowed transitions in the UV region with the peak at 370 nm tailing into visible region and thus accounting for red/yellow color of compound. Since in the case of high-spin d^5 complexes, $d-d$ transitions are both Laporte and spin forbidden, such transitions are not observed in **1**. The room temperature magnetic moment of polycrystalline samples of **1** has the value of 5.60 B.M. which is less than the spin-only value of 5.92 B.M. At 77 K , EPR spectrum of **1** (DMF solution) shows a

Table 1. Crystallographic Data for **1**.

Formula	$\text{C}_{21}\text{H}_{16}\text{N}_3\text{O}_2\text{Cl}_2\text{Fe}$
Formula weight	469.12
T , K	296(2)
Crystal system	Monoclinic
Space group	$P2_1/n$
a , Å	14.4079(10)
b , Å	9.0517(5)
c , Å	15.6056(10)
α , deg	90.00
β , deg	104.923(4)
γ , deg	90.00
V , Å ³	1966.6(2)
Z	4
D_{calcd} , gcm^{-3}	1.584
μ , mm^{-1}	1.062
GOF ^a on F^2	1.036
$R[I > 2\sigma(I)]$	^b $R_1 = 0.0557$; ^c $wR_2 = 0.1115$
Rindices (all data)	^b $R_1 = 0.1164$; ^c $wR_2 = 0.1320$

^aGOF = $[\sum [w(F_0^2 - F_c^2)^2] / M - N]^{1/2}$ (M = number of reflections, N = number of parameters refined).

^b $R_1 = \sum \|F_0\| - \|Fc\| / \sum \|F_0\|$.

^c $wR_2 = [\sum [w(F_0^2 - F_c^2)^2] / \sum [w(F_0^2)^2]]^{1/2}$.

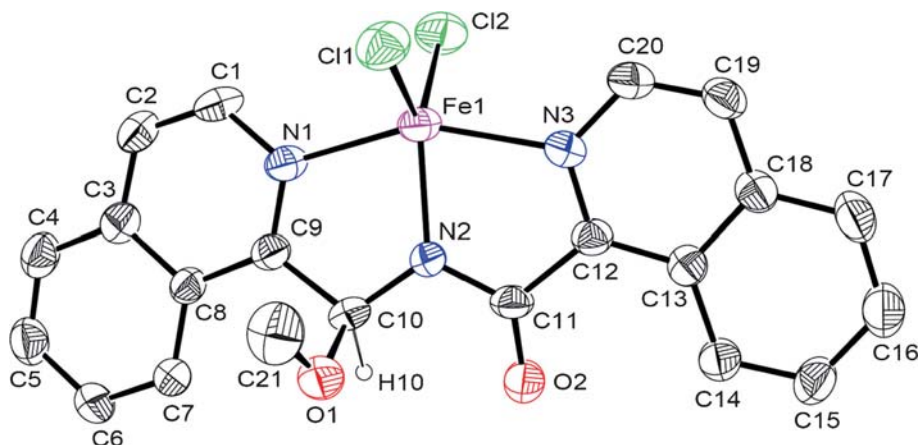


Figure 1. ORTEP (30% probability ellipsoids) diagram of **1**; hydrogen atoms except H10 were omitted for clarity.

broad signal centered at $g_{eff} = 4.27$. These features are consistent with the presence of high-spin d^5 iron(III) center.³³

3.4 Molecular Structure

The molecular structure of **1** has been determined by single crystal X-ray diffraction method and its ORTEP diagram is displayed in figure 1. The crystallographic data and selected bond parameters are listed in tables 1 and 2, respectively. The compound crystallized in $P2_1/n$ space group and the trivalent iron is penta-coordinated with $L2^-$ bound as an end-cap tridentate chelating ligand. The geometry around Fe(III) can be best described as distorted trigonal bipyramidal containing a unique $N_C(N_E)_2Cl_2$ (N_C = amide-N; N_E = pyridyl-N) distorted trigonal plane having angles

Table 2. Selected bond distances (Å) and angles (°).

Fe1–N1	2.125(4)	N2–Fe1–N1	77.51(16)
Fe1–N2	1.953(3)	N2–Fe1–N3	76.86(16)
Fe1–N3	2.130(4)	N1–Fe1–N3	153.62(16)
Fe1–Cl1	2.210(2)	N2–Fe1–Cl1	120.70(12)
Fe1–Cl2	2.212(2)	N1–Fe1–Cl1	99.14(11)
O1–C10	1.428(5)	N3–Fe1–Cl1	99.19(11)
O1–C21	1.474(6)	N2–Fe1–Cl2	127.37(12)
O2–C11	1.223(4)	N1–Fe1–Cl2	95.31(12)
C10–N2	1.435(6)	N3–Fe1–Cl2	95.25(12)
C11–N2	1.354(5)	C11–Fe1–Cl2	111.93(6)
		C10–O1–C21	114.1(4)
		C11–N2–C10	117.0(4)
		N2–C10–O1	114.0(4)
		O2–C11–N2	125.2(5)
		C12–C11–O2	122.3(5)
		N2–C10–C9	108.8(4)
		C12–C11–N2	112.5(4)

Table 3. Comparison of bond distances.

	Fe– N_C	Fe– N_E	Fe–Cl			
1	1.953(3)	2.125(4)	2.130(4)	2.210(2)	2.212(2)	this work
2	2.091(4)	2.222(4)	2.225(5)	2.263(2)	2.317(2)	ref ³⁷
3	2.088(4)	2.238(4)	2.250(4)	2.311(2)	2.266(2)	ref ³⁸
4	2.110(6)	2.271(6)	2.266(5)	2.312(2)	2.278(2)	ref ³⁸
5	2.229(8)	2.188(6)	2.246(7)	2.303(2)	2.298(2)	ref ³⁹
6	2.186(4)	2.213(3)	2.258(3)	2.333(1)	2.290(1)	ref ³⁹

N_C , N_E are central, terminal nitrogen atoms of ligand;

2 = [2,6-bis-[1-(2,6-diisopropylphenylimino)ethyl]pyridine] $Fe^{II}Cl_2$;

3 = (2,6-diacetylpyridinebis(2,6-diisopropylanil)) $Fe^{II}Cl_2$;

4 = (2,6-diacetylpyridinebis(2,4,6-trimethylanil)) $Fe^{II}Cl_2$;

5 = [bis(2-bromo-6-pyridylmethyl)(2-pyridylmethyl)amine] $Fe^{II}Cl_2$;

6 = [bis(2-phenyl-6-pyridylmethyl)(2-pyridylmethyl)amine] $Fe^{II}Cl_2$.

Cl1–Fe1–N2, 120.70(9)°; Cl2–Fe1–N2, 127.38(9) and Cl1–Fe1–Cl2, 111.91(5)°. As a result of severe distortion in the axial N1–Fe1–N3 angle (153.6(1)°), the calculated τ value of 0.44 is less significant in inferring the geometry.³⁶ The Fe– N_C bond is shorter than the two Fe– N_E bonds by an average of 0.176(3) Å, which can be ascribed to geometrical constraints of the ligand framework. Such a trend in which the central bond of an end-cap tridentate chelating ligand bearing geometrical constraints, being shorter than the other two, has also been observed in Fe^{II} complexes of bis-(imino)pyridines having the closely related coordination environment $Fe^{II}N_3Cl_2$.^{37,38} However such a discrepancy was not observed in complexes having flexible tripodal ligand framework.³⁹ Overall, the Fe^{III} –N distances observed in this rare example are shorter than the reported Fe^{II} –N values. Two Fe^{III} –Cl bonds having a length of 2.210(2) and 2.212(2) Å are shorter than that found (lying in the range 2.266(2)–2.312(2) Å) in closely related five-coordinated bivalent iron complex having a similar $Fe^{II}N_3Cl_2$ coordination environment reported earlier.^{37,38} In table 3, Fe–N and Fe–Cl bond distances are listed for ready comparison. It is also relevant to note that C10–O1 (1.428(5) Å) distance is longer than that of C11–O2 (1.223(5) Å).

The methyl of methoxy group is uniquely projected towards the metal center having the non-bonded contacts $C21 \cdots Fe1$, 3.997(5) Å and $C21 \cdots Cl1$, 4.213(5) Å. In the packing diagram, $\pi \cdots \pi$ interaction is present having the following $cg \cdots cg$ (cg = centroid) contacts: $N1C2C3C8C9$ with $N3C12C13C18C19C20$, 3.84 Å; $N1C2C3C8C9$ with $C13$ – $C18$, 3.89 Å; $C4$ – $C8$ with $C13$ – $C18$, 3.94 Å; $C4$ – $C8$ with $N3C12C13C18C19C20$, 3.95 Å. These $\pi \cdots \pi$ interactions and an intermolecular short contact ($C4 \cdots C12$, 3.378(6) Å) lead to a chain composed of same enantiomers. A perspective view of the packing diagram is shown in figure 2. An intermolecular contact $C7 \cdots O2$,

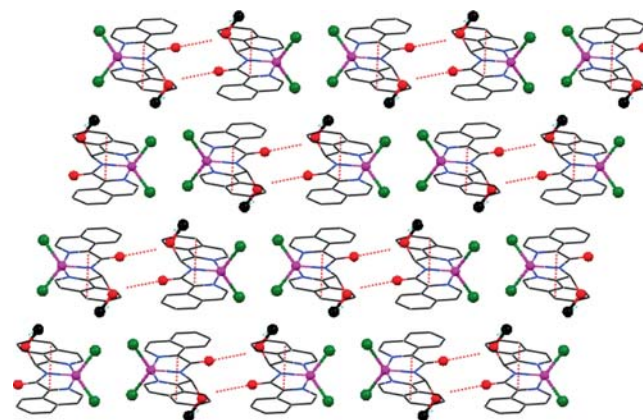


Figure 2. Packing diagram on viewing down b -axis.

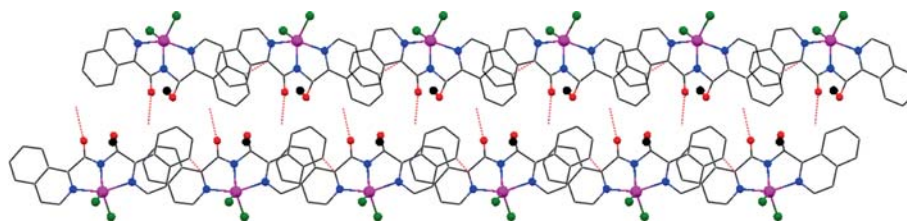


Figure 3. Double stranded chain.

3.251(6) Å, is present between the chains which link two chains containing opposite chiral carbon atoms in head-to-head fashion to double stranded chains (figure 3). Within a double strand, isoquinolyl rings are tilted such that inter-strand angle between planes of two isoquinolyl rings is 38.18° and between two planes of chelated ring Fe1N1C9C10N2C11C12N3 is 48.54°.

4. Conclusions

The ligand **L1H** reacted readily with anhydrous FeCl₃ in methanol yielding red crystals of composition [Fe(**L2**)Cl₂] in which **L2**⁻ is *N*-((1-isoquinolyl)(methoxy)methyl)isoquinoline-1-carboxamide ion. In this reaction, one of the two carbonyl groups in **L1H** has been reduced to a (methoxy)methyl group. Thus, it is important to note that iron(III) chloride reduces **L1H** but copper(II) acetate favours formation of the same from 1-aminomethylisoquinoline. Compound **1** is a rare example of penta-coordinated iron(III) complex having N₃Cl₂ environment with a distorted trigonal bipyramid geometry.

Supplementary Information (SI)

CCDC number 987001 contains the supplementary crystallographic data for complex **1**. This data can be obtained free of charge via <http://www.ccdc.ac.uk/conts/retrieving.html> or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk. IR spectrum of **1** is provided which is available at www.ias.ac.in/chemsci.

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