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Co-crystallization of isomers of iron(II) complex of a tridentate mixed amine/imine ligand in one unit cell

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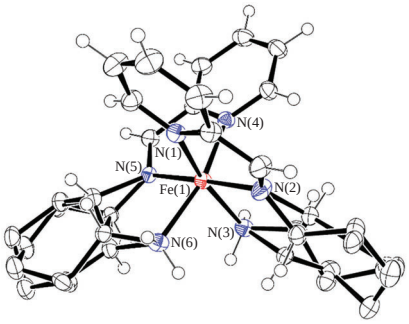
The X-ray study of an octahedral iron(II) complex with a tridentate mixed amine/imine Schiff base ligand L derived from pyridine-2-carboxaldehyde and 1,2-diaminocyclohexane revealed that its single crystals consisted of a mixture of stereoisomers co-crystallized in one unit cell. Thus, Werner-type complexes formulated as [Fe(*trans*-(1*R*,2*R*)-L)$_2$](PF$_6$)$_2$, [Fe(*trans*-(1*S*,2*S*)-L)$_2$](PF$_6$)$_2$, and [Fe(*trans*-(1*R*,2*R*)-L)(*trans*-(1*S*,2*S*)-L)](PF$_6$)$_2$ were identified within the structure. Observation of a good quality ^{1}H and ^{13}C{^{1}H} NMR spectra evidenced the low-spin configuration of the central atom.

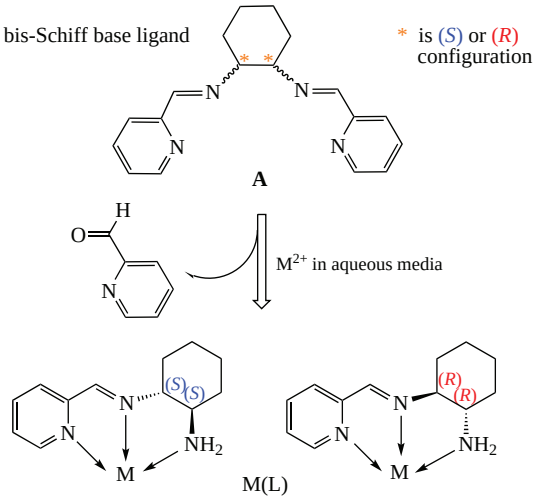


Keywords: Schiff bases, iron(II) complexes, stereoisomers, X-ray analysis, UV-visible spectra.

Iron(II) complexes are widely used in the stereospecific catalytic transformations of a large array of organic substrates.[1] The 1,2-diaminocyclohexane backbone can serve as a very simple and accessible motif for the preparation of bi-, tri-, and tetradentate chiral ligands which are potentially useful in chiral transformations. In particular, the isomeric diamines, *cis*- and *trans*-1,2-diaminocyclohexane, can undergo condensation with two equivalents of pyridine-2-carboxaldehyde to form double Schiff bases *cis*-(1*R*,2*S*)- and both the *trans*-(1*R*,2*R*) and *trans*-(1*S*,1*S*) enantiomers of *N*,*N*′-bis(pyridin-2-ylmethylene)cyclohexane-1,2-diamine of type **A**. The stereoisomers of this bis-imine have been well-characterized.[2–6] The coordination chemistry of *trans*-1,2-diaminocyclohexane derivatives has been explored more than that of their corresponding *cis*-isomers.[7] This is due, in part, to the optical activity of the *trans*-compounds which yield coordination complexes that can act as catalysts for asymmetric organic syntheses.[7] On the other hand, intensely and selectively colored with specific transition metal complexes possess certain interest for analytical chemistry, biology and biochemistry as alternative inexpensive way for their photometric detection.[8]

Preparation of metal complexes employing Schiff base **A** derived from 1,2-diaminocyclohexane was successfully accomplished in the past (Scheme 1). Surprisingly, in aqueous media transition metals do not form Werner-type complexes with two such coordinated ligands having eight N atoms in the inner sphere. Instead, hydrolysis generates rather unique tridentate neutral ligand L that has three different kinds of N atoms in the metal environment. Thus, there is NH$_2$-group (as N^{I}), imino group >C=N– (as N^{II}), and heterocyclic nitrogen from the pyridine ring (as N^{III}) making metal [MN$^{I}_2$N$^{II}_2$N$^{III}_2$] hexacoordinated environment with different donor atoms strength.

In this work, we employed direct one-pot interaction between the aldehyde and the diamine in the presence of the Mohr salt (Scheme 2). Thus, stereoisomers of octahedral iron(II) complexes **1** of ligand L *via* self-assembly were formed, which is a common synthetic technique, usually *via* condensation, for preparing metal complexes of ligands, that are otherwise difficult to produce.[9–12] Stereoisomers of the dark blue iron(II) complex **1** of mixed amine/imine tridentate ligands formulated as



Scheme 1 Stereoisomers of tridentate ligand L derived from the ‘one arm hydrolysis’ of the initial tetradentate Schiff base.

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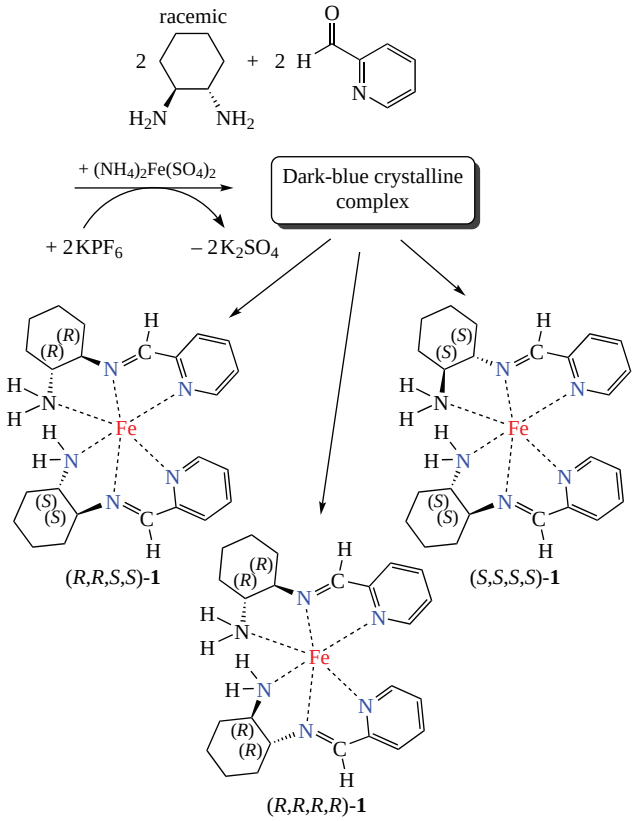

Scheme 2 Alternative way of preparing Fe^{II} complex **1** using the tridentate ligand L and possible stereoisomers of resulting complex.

$[Fe(trans\text{-}L)_2](PF_6)_2$ were obtained (*cf.* ref. 12). The tridentate ligands are resulted from the condensation of *trans*-1,2-cyclohexanediamine and pyridine-2-carboxaldehyde (2 mol of each per 1 mol of iron), with one of two heterocyclic moieties being lost during the reaction (see Scheme 1). Purification takes advantage of the solubility of the hexafluorophosphate salts in organic solvents, namely dichloromethane, and is achieved by washing aqueous solutions of the sulfate with dichloromethane in the presence of KPF_6. The synthesis results in a product being a mixture formulated as stereoisomeric solvate complexes of formula $[FeL_2](PF_6)_2$ (for details, see Online Supplementary Materials, sections S1–S6).

The target cationic complex represents a very dark dichroic solid: blue on reflected light and red on transient light. The complex demonstrates a good quality of NMR spectra which indicates $^1A_{1g}$ (d^6) low-spin state of the metal center. Growing of suitable crystals for the X-ray analysis was possible from propionitrile solutions using the vapor diffusion method with more volatile ether being the 'pushing' solvent. The synthesized Fe^{II} complex was characterized by elemental analysis on C,H,N content and studied by several conventional physical methods including the X-ray crystallography (see Online Supplementary Materials, sections S2–S8).‡

We observed in this study a quite rare phenomenon of co-crystallization of stereoisomers of one compound in the same unit cell. The rarity of such findings is explained in vast experimental evidence of the old principle '*Puris omnia pura*' (Latin: To the pure, all things are pure). In general, the formation of pure crystalline solids from the mixture is by far the predominant process that requires minimum energy for the alignment of same molecules and formation of the crystal lattice. Thus, from the mixture of stable compounds in solution separate crystallization of individual components occurred in a sequence dictated by their solubility. Nevertheless, co-crystallization phenomenon of chemically and structurally diverse compounds does happen and is widely studied. This is always the process of coexistence in one crystal lattice of two different chemical compounds with one of the most vivid examples being the co-crystallization of 2,4,6-trinitrobenzoic acid and indole-3-acetic acid. However, the great application for co-crystallization was found in pharmaceutical chemistry and industry.[13] Herein co-crystallization is a process by which the molecular interactions can be altered to optimize the drug properties.[14] Co-crystals always comprise a multicomponent system of structurally different compounds: active pharmaceutical ingredient (API) with a stoichiometric amount of a pharmaceutically acceptable benign co-former incorporated in the crystal lattice.[15,16] Variable intermolecular interactions facilitate the process of co-crystallization. Speaking of co-crystallization of the stereoisomers of the same compound, we should point out a great scarcity of such examples. One of the best documented cases was detection of such behavior in the chemistry of oximes. Thus, Antony Spek reported several cases of co-crystallization of *syn*- and *anti*-diastereomers of oximes.[17] We presented our earlier finding of the same phenomenon during investigations of cyanoximes.[18] In the latter case it was clearly shown that the coexistence of two diastereomers in one unit cell of the same crystal symmetry is because of their very similar molecular volume and H-bonding patterns. In all these cases co-crystallization of stereoisomers resembled two-positional disorder, which was not the case at all.

In the presented work we report another rare case of co-crystallization of three stereoisomers in one crystal lattice, but this time without any stabilizing or helpful effect of the H-bonding. The first indication of co-crystallization arose from the $^{13}C\{^1H\}$ NMR spectra of analytically pure compound, which showed a 'doubling' of each peak, with one set belonging to enantiomers $[Fe(trans\text{-}(1R,2R)L)_2](PF_6)_2$ and $[Fe(trans\text{-}(1S,2S)L)_2](PF_6)_2$ that are not possible to independently observe in a non-chiral solvent. The second set of peaks belongs to their diastereomers $[Fe(trans\text{-}(1R,2R)L)(trans\text{-}(1S,2S)L)](PF_6)_2$ (see Online Supplementary Materials, sections S2, S5). We have not attempted a separation of these stereoisomers being aware of considerable difficulties involved in the process of work with a small amount of the obtained complex and its insufficient stability of Fe^{II} species to variable chromatographic techniques carried out normally in a an open air. The UV-visible spectrum of the complex evidenced high intensity CT bands (Figure 1). These intense bands are sensitive to the solvent which is an additional confirmation to their CT character. An example of full

‡ *Crystallographic data for* **1**. Crystals of $C_{31}H_{49}F_{12}FeN_7OP_2$ (M = 881.09) are monoclinic, space group $P2_1/c$, at 120 K, a = 9.3699(7), b = 20.0609(15) and c = 21.0430(16) Å, β = 100.187(1)°, V = 1102.5(6) Å^3, Z = 4, d_{calc} = 1.503 g cm^{-3}, μ(MoKα) = 0.564 mm^{-1}, F(000) = 1822; 61453 reflections were measured and 4553 independent reflections (R_{int} = 0.0288) were used in further refinement. The refinement converged to wR_2 = 0.0975 and GOF = 1.034 for all independent reflections [R_1 = 0.0398 was calculated against F for 9383 observed reflections with $I > 2\sigma(I)$].

The measurements were performed on a Bruker Apex 2 diffractometer with CCD camera using graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å). The structure was solved by direct methods, and the non-hydrogen atoms were located from the trial structure and then refined anisotropically with SHELXTL using a full-matrix least-squares procedure based on F^2. The hydrogen atoms were fixed geometrically at calculated positions and were allowed to ride on the parent atoms.

The CCDC 2295664 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

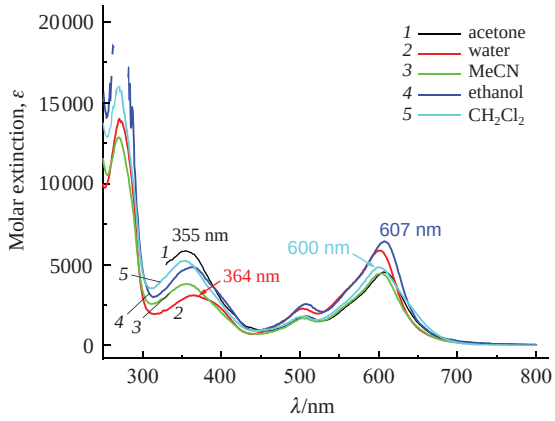

Figure 1 Electronic spectra of [Fe(*trans*-L)$_2$](PF$_6$)$_2$ complex **1** in several solvents showing its solvatochromic behavior.

line shape analysis of electronic spectrum of the co-crystallized mixture of stereoisomers of [Fe(*trans*-L)$_2$](PF$_6$)$_2$ complex is presented in Online Supplementary Materials (section S6).

The asymmetric unit (ASU) in a remarkable structure of [Fe(*trans*-L)$_2$](PF$_6$)$_2$ complex **1** (Figure 2 and Online Supplementary Materials, section S9) highlights three disordered fragments: 1) non-volatile solvent for crystallization, propionitrile; 2) volatile diethyl ether solvent used for vapor diffusion method of crystal growth; 3) disordered PF_6^- anion. In all three cases it was successfully modeled as a two-positional disorder (see Online Supplementary Materials, sections S10–S12). It is a rare and quite unusual phenomenon bearing in mind that all disordered species possess different site occupancies. Also, one of the parts of the cyclohexyl rings represents the bright manifestation of co-crystallized mixture of Fe^{II} complex stereoisomers, but not a disorder! Thus, careful analysis of the crystal structure revealed the presence of all three stereoisomers, which are shown in Figure 3 where all of them are drawn separately.

The tridentate ligands adopt a meridional configuration around the metal center, giving a distorted octahedral N6 coordination environment of two tridentate ligands. Severely rhombic distortion in geometry of Fe^{II} environment is shown in Figure 4. There is a very pronounced contraction of Fe–N bonds (being 1.895 Å on average) stemming from two imino nitrogen atoms across each other with the N(5)–Fe(1)–N(2) angle of 177.49°. It should be mentioned that these bonds are very short indeed and evidenced the low-spin $^1A_{1g}$ state of the metal center. The second longest bonds are between Fe and N-atoms of pyridine averaging to 1.967 Å. For iron(II) complexes there are empirically established below 1.98 Å cut-off bond lengths that indicate its low-spin character.[19] In our case of

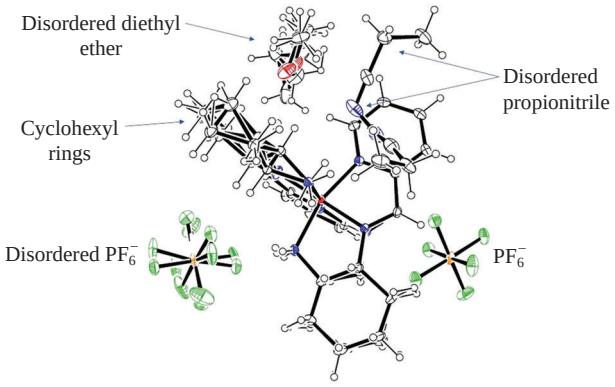

Figure 2 The ASU in the structure of the Fe^{II} complex showing disordered fragments and overall (superimposed) structure of the metal-centered cation as a co-crystallized mixture of isomers.

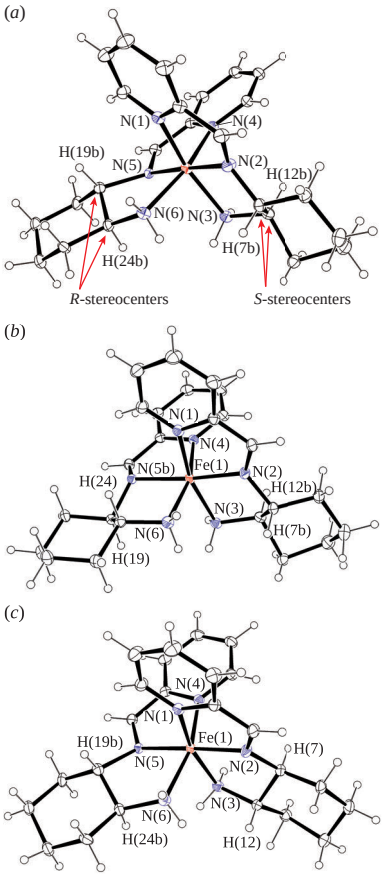

Figure 3 Details of the structure of co-crystallized mixture. (*a*) Cationic unit of one of the co-crystallized stereoisomers and this structure is formulated as the mixture of [Fe(*trans*-1*R*,2*R*-L)(*trans*-1*S*,2*S*-L)]$^{2+}$ cation; (*b*) individual structure of [Fe(*trans*-L)$_2$]$^{2+}$ unit as one of the co-crystallized stereoisomers, and its structure represents the [Fe(*trans*-1*R*,2*R*-L)$_2$]$^{2+}$ cation; (*c*) structure of [Fe(*trans*-L)$_2$]$^{2+}$ as one of the co-crystallized stereoisomers where this is the [Fe(*trans*-1*S*,2*S*-L)$_2$]$^{2+}$ cation. These ORTEP images were generated pruning overall structure displayed in Figure 1 by selective stepwise deletion of 'unwanted for the purpose' C and H atoms from overall ASU.

[Fe(*trans*-L)$_2$](PF$_6$)$_2$ there are four out of six bonds in the central atom environment that are lower than that value, which provides ligands' strong crystal field effect and assures metal center's low-spin configuration. The longest Fe–N bonds are with the amino group. In is rather interesting to rank Fe–N bond lengths in the complex according to their propensity to the π back-bonding: Fe–N(imines) > Fe–N(Py) > Fe–N(amines) (the check CIF report for this structure is presented in Online Supplementary Materials, section S13).

To the best of our knowledge, this is the first ever case where donor nitrogen atoms of three different kinds are combined in one complex! In our future work we plan to alter the tridentate

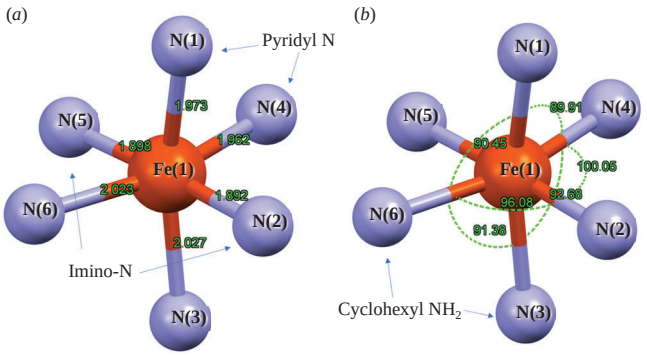

Figure 4 Geometry of Fe^{II} center in [Fe(*trans*-L)$_2$](PF$_6$)$_2$ complex **1**: (*a*) bonds; (*b*) angles.

Schiff base ligand's field by incorporating electron-withdrawing atoms and groups in its structure (CN, F, NO_2, for instance) in a hope to create suitable environment to attain the spin crossover equilibrium close to room temperature.

In summary, the synthesis of stereoisomers of [Fe(*trans*-L)$_2$](PF$_6$)$_2$ **1** was accomplished by self-assembly of two equivalents of racemic 1,2-diaminocyclohexane, two equivalents of 2-pyridine carboxaldehyde, and one equivalent of ammonium iron(II) sulfate in ethanol; followed by anion exchange with hexafluorophosphate. The formation of a compound representing a mixture of stereoisomers is proved by both single-crystal X-ray analysis and $^{13}C\{^1H\}$ NMR data showing separate ^{13}C resonances for isomers. The results of crystallography showed a very rare case of co-crystallization of stereoisomers in the same asymmetric unit of the same cell: [Fe(*trans*-(1*R*,2*R*)-L)$_2$](PF$_6$)$_2$, [Fe(*trans*-(1*S*,2*S*)-L)$_2$](PF$_6$)$_2$, and [Fe(*trans*-(1*R*,2*R*)-L)(*trans*-(1*S*,2*S*)-L)](PF$_6$)$_2$ along with two trapped solvent molecules of propionitrile and diethyl ether. Moreover, data of X-ray analysis also revealed a unique coexistence of three two-position disordered fragments in the ASU with different site occupancies: for PF_6^- 0.623/0.377, for diethyl ether 0.521/0.479, and 0.113/0.887 for propionitrile.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2024.01.014.

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