

New chiral ligands and iron(III) complexes based on 2,6-bis(1-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-on-2-yl)pyridines

Miloš Sedlák,^{a,*} Pavel Drabina,^a Ivana Císařová,^b Aleš Růžička,^a Jiří Hanusek^a and Vladimír Macháček^a

^aDepartment of Organic Chemistry, Faculty of Chemical Technology, University of Pardubice, Nám. Čs. Legii 565, 532 10 Pardubice, Czech Republic

^bDepartment of Inorganic Chemistry, Faculty of Science, Charles University, Hlavova 2030, 128 43 Prague 2, Czech Republic

Received 7 June 2004; revised 2 August 2004; accepted 13 August 2004

Abstract—New ligands and their complexes with iron(III) chloride have been suggested and prepared: (*R,S*)-, (*R,R*)- and (*S,S*)-2,6-bis(1-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-on-2-yl) pyridines. Both the ligands and their complexes were characterised by ¹H and ¹³C NMR spectroscopy, optical rotation and X-ray diffraction.

© 2004 Elsevier Ltd. All rights reserved.

Metal complexes of heterocyclic compounds containing a stereogenic centre have been used especially as homogeneous catalysts in a number of syntheses.¹ Reviews² and monographs^{1,3–5} deal with chiral ligands possessing a chelate-forming grouping –N–C–C–N–C–C–N– that can produce stable complexes with transition metals. Connecting 1*H*-imidazol-5-ones to the 2- and 6-positions of pyridine affords new ligands structurally similar to the well-known ligands of oxazoline ('Pybox')⁵, terpyridine ('Terp')⁶ or 2,6-bis(1-methylbenzimidazol-2-yl)pyridine⁷ and 2,6-bis(imidazol-2-yl)pyridine⁸ (Fig. 1). However, no ligands based on imidazole derivatives containing stereogenic centres have been described as yet.

Functionalised 1*H*-imidazol-5-ones are well-known and commercially available herbicides^{9,10} derived from pyr-

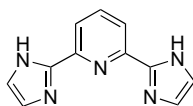


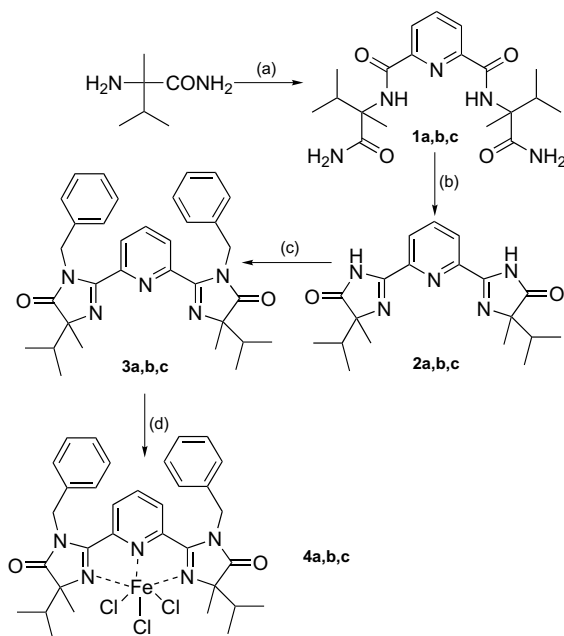
Figure 1. 2,6-Bis(imidazol-2-yl)pyridine.

idine-2,3-dicarboxylic acid. Copper(II) complexes of the herbicide *Imazapyr* (2-(4-methyl-4-isopropyl-4,5-dihydro-1*H*-imidazol-5-on-2-yl)pyridine-3-carboxylic acid) have been described.¹¹ In our previous paper we dealt with the synthesis and NMR spectra of functionalised 4,4-dialkyl-4,5-dihydro-2-phenyl-1*H*-imidazol-5-ones.¹²

The subject of the present paper is the synthesis and characterisation of new 2,6-bis(1-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-on-2-yl)pyridines and their complexes with iron(III) chloride. The complex compounds of iron or nickel represent relatively cheap catalysts and possible substitutes for platinum metals. Our ligands have the advantage of containing a quaternary asymmetric carbon atom, which prevents racemisation via cleavage of the α -hydrogen atom (for example, this takes place in the oxazolines based on natural amino acids¹³).

The systems suggested by us can be relatively easily synthesised and/or further modified. The stereogenic centre of the imidazolone ring is derived from easily available, optically pure (*R*)-2-amino-2,3-dimethylbutanamide and (*S*)-2-amino-2,3-dimethylbutanamide.^{10,14} First we prepared the respective acylated butanamides¹⁵ **1a,b** (*R,R*) and **1c** (*S,S*) by reaction of pyridine-2,6-dicarboxylic acid dichloride with racemic 2-amino-2,3-dimethylbutanamide, (*R*)-2-amino-2,3-dimethylbutanamide, and

* Corresponding author. Tel.: +420 466 037 015; fax: +420 466 037 068; e-mail: milos.sedlak@upce.cz



Scheme 1. Reagents and conditions: (a) 2,6-py(COCl)₂/TEA, CH₂Cl₂, rt overnight; (b) CH₃ONa/CH₃OH rt 48 h; (c) PhCH₂Br/K₂CO₃, DMF reflux 48 h; (d) FeCl₃, MeOH rt overnight.

(*S*)-2-amino-2,3-dimethylbutanamide. From the ¹H NMR spectra we calculated that **1a** contained about 20% of a mixture of **1b** (*R,R*) and **1c** (*S,S*) and 80% of the *meso*-form (*R,S*). Ring closure¹⁶ of **1a** gave an analogous mixture of cyclic compounds, whose crystallisation provided only the *meso*-form **2a** (*R,S*) as the least soluble component. The optically pure 2,6-bis(4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-on-2-yl)pyridines **2b** (*R,R*) and **2c** (*S,S*) were prepared in the same way from amides **1b** (*R,R*) and **1c** (*S,S*). In an analogous manner,¹⁷ benzylation¹⁸ of the *meso*-form **2a** (*R,S*), **2b** (*R,R*) and **2c** (*S,S*) gave the respective 2,6-bis(1-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-on-2-yl)pyridines (**Scheme 1**): **3a** (*R,S*), **3b** (*R,R*) and **3c** (*S,S*). Using ¹⁵N NMR, we confirmed the presence of three types of nitrogen atoms: δ 78 (*P_y*), δ 109 (*C=N*), δ 222 (*Bz-N*).

The molecular structure of compound **3c** (*S,S*) was obtained by X-ray techniques (**Fig. 2**, ORTEP—40% probability level). Only one molecule of two from the crystalline unit cell is shown; the hydrogen atoms are omitted for clarity. Selected interatomic distances [Å] and angles [°]: N11 C12 1.384(2), N11 C15 1.404(2), C12 O11 1.216(2), C13 N14 1.473(2), N14 C15 1.276(2), C16 N17 1.342(2), N17 C18 1.347(2), C18 C112 1.483(2), C112 N116 1.284(2), C112 N113 1.401(2), N113 C114 1.379(2), N113 C128 1.464(2), C114 O12 1.215(2), C115 N116 1.480(2), C12–N11–C15 107.08(13), C13–N14–C15 107.2(1), N14–C15–C16 121.0(1), C16–N17–C18 117.4(2), C18–C112–N116 123.3(1), N17–C18–C12 116.3(3), C112–N116–C115 106.3(1).

The bond distances and angles of the two crystallographically independent molecules were unexceptional,

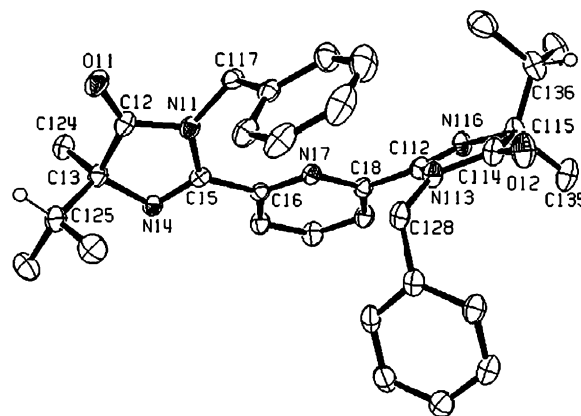


Figure 2. ORTEP representation of the structure of compound **3c**.

confirming the proposed structure and aromaticity of the corresponding rings. In both molecules, the imidazole rings deviate from the pyridine plane (**Fig. 1**, the torsion angles indicating this shape are: C19 C18 C112 N113 –136.0(2)°, C111 C16 C15 N11 –157.4(1)° and 136.1(2), 150.2(2) for the second molecule, respectively) in mutually opposite fashion. Three nitrogen atoms bearing benzyl groups (N11 and N113) are turned towards the pyridine nitrogen (N17) and the benzyl groups are situated in face of this atom.

The reactions of ligands **3a,b**, and **3c** with anhydrous ferric chloride in methanol gave the complexes¹⁹ **4a** (*R,S*): C₃₃H₃₇Cl₃FeN₅O₂ (697.88) and **4b** (*R,R*). In the case of complex **4c** (*S,S*) the molecular structure was confirmed by X-ray techniques (**Fig. 3**, ORTEP—40% probability level; the molecule of **4a** is placed in a special position on a two-fold axis going through atoms Fe1, N1 and C4 in the crystal structure, however, the position of some atoms does not fulfil this symmetry exactly and these are disordered, most significantly C11. Only one position of the disordered atoms is shown and the hydrogens are omitted for clarity). Selected interatomic distances [Å] and angles [°]: Fe1 C11 2.268(4), Fe1 C12 2.337(1), Fe1 N1 2.167(3), Fe1 N6 2.127(3), N1 C2

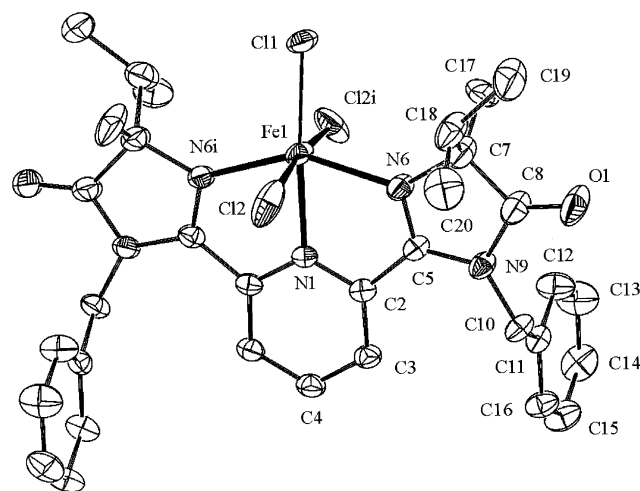


Figure 3. ORTEP representation of the structure of complex **4c**.

1.337(4) 1.414, C2 C5 1.485(5), C5 N6 1.290(4), N6 C7 1.492(5) Cl1 Fe1 Cl2 103.7(1), Cl1 Fe1 Cl2ⁱ 87.5(1), Cl1 Fe1 N6 104.1(1), N6 Fe1 N6ⁱ 147.3(1), Cl1 Fe1 N1 171.7(1), Cl2 Fe1 Cl2ⁱ 168.77(5), Cl1 Fe1 N6ⁱ 108.3(1), N1 Fe1 N6 73.64(9). Symmetry code (i): 1/4-y, 1/4-x, 1/4-y.

The iron coordination geometry in **4a** (Fig. 3) is a distorted octahedral with three nitrogen atoms relatively strongly bonded to the iron centre. The largest deviation from the ideal geometry is the N6 Fe1 N6ⁱ angle. In comparison with the free ligand, both the pyridine and imidazole rings are coplanar and the aminobenzyl groups are turned away from the ligand coordination core. The benzyl moieties are situated above and below the ligand coordination plane (Fig. 3). The bond lengths and angles are very similar to previously published data for some examples of meridionally co-ordinated iron(III) complexes by N₃Cl₃ donor sets (tridentate ligands).²⁰

Acknowledgements

The authors wish to acknowledge Professor Jitka Moravcová (Institute of Chemical Technology Prague) for determinations of optical rotatory power and the financial support by the grant Agency of the Czech Republic (Grant No. 203/04/0646).

References and notes

- Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; John Wiley & Sons: New York, 2000.
- Pfaltz, A. *J. Heterocycl. Chem.* **1999**, *36*, 1437.
- Seyden-Penne, J. In *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*; John Wiley & Sons: New York, 1995.
- Organic Synthesis Highlights III*; Mulzer, J., Waldmann, H., Eds.; Wiley-VCH: Weinheim, 1998.
- Doyle, M. P.; McKervey, M. A.; Ye, T. In *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley & Sons: New York, 1998.
- (a) *Progress in Inorganic Chemistry*; Karlin, K. D., Ed.; John Wiley & Sons: New York, 1999; Vol. 48; (b) Enright, D.; Gambarotta, S.; Yap, G.; Budzelaar, P. *Angew. Chem., Int. Ed.* **2002**, *41*, 3873.
- Addison, A. W.; Burman, S.; Wahlgren, C. G.; Rajan, O. A.; Rowe, T. M.; Sinn, E. *J. Chem. Soc., Dalton Trans.* **1987**, 2621.
- (a) Carina, R. F.; Verzeznassi, L.; Bernardinelli, G.; Williams, A. F. *Chem. Commun.* **1998**, 2681; (b) Stupka, G.; Gremaud, L.; Bernardinelli, G.; Williams, A. F. *J. Chem. Soc., Dalton Trans.* **2004**, 407.
- Weplo, P. *J. Pestic. Sci.* **1990**, *39*, 293.
- (a) Gastrock, W. H.; Wepplo, P. J. U.S. 4,683,324, 1987, American Cyanamid Company; (b) *Chem. Abstr.* **1987**, *107*, 198332.
- Duda, A. M.; Dyba, M.; Kozłowski, H.; Micera, G.; Pusino, A. *J. Agric. Food Chem.* **1996**, *44*, 3698.
- Sedlák, M.; Halama, A.; Mitaš, P.; Kaválek, J.; Macháček, V. *J. Heterocycl. Chem.* **1997**, *34*, 1227.
- George, T.; Mabon, R.; Sweeney, G.; Sweeney, J. B.; Tavassoli, A. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2529.
- Schoemaker, P. J. H.; Kamphuis, J. *Tetrahedron: Asymmetry* **1993**, *6*, 113.
- (Racemic)-pyridine-2,6-dicarboxylic acid bis-[(1-carbamoyl-1,2-dimethylpropyl)-amide] (**1a**): A solution of 2-amino-2,3-dimethylbutanamide (1.3 g, 10 mmol) and triethylamine (2.1 mL, 15 mmol) in dry dichloromethane (25 mL) was cooled to 0 °C and treated with a solution of pyridine-2,6-dicarboxylic acid dichloride (1.02 g, 5 mmol) in dichloromethane (15 mL) added over 15 min. The mixture was stirred overnight, whereupon the solution was evaporated until dry. The residue was recrystallised from water to give 1.5 g of the product (77%), mp 250–260 °C (a 4:1 mixture of the *meso*-form and racemate). Data for the *meso*-form ¹H NMR (DMSO-*d*₆ 500 MHz, ppm): δ 8.75 (s, 2H, NH), 8.25 (m, 3H, PyH), 7.41 (br s, 2H, NH₂), 7.24 (br s, 2H, NH₂), 2.31 (sp, 2H, *i*PrCH), 1.63 (s, 6H, CH₃), 1.05 (d, ³J = 6.8 Hz, 6H, *i*PrCH₃), 0.97 (d, ³J = 6.8, 6H, *i*PrCH₃). ¹³C NMR (DMSO-*d*₆ 125 MHz, ppm): δ 174.7 (CONH₂), 161.9 (CONH), 149.1 (PyC₂, C₆), 139.9 (PyC₄), 124.1 (PyC₃, C₅), 62.5 (C_q), 34.9 (*i*PrCH), 17.6 (CH₃), 17.5 (*i*PrCH₃), 17.4 (*i*PrCH₃). For C₁₉H₂₉N₅O₄ (391.47) calculated: C, 58.30; H, 7.47; N, 17.89%; found: C, 58.75; H, 7.18; N, 17.56%. (*R,R*)-Pyridine-2,6-dicarboxylic acid bis-[(1-carbamoyl-1,2-dimethylpropyl)-amide] (**1b**): 52% yield, mp = 227–230 °C, [α]_D²⁵ = –63.5 (c = 1, CH₃OH). ¹H NMR (DMSO-*d*₆ 500 MHz, ppm): δ 8.67 (br s, 2H, NH), 8.25 (m, 3H, PyH), 7.41 (br s, 2H, NH₂), 7.18 (br s, 2H, NH₂), 2.27 (sep, ³J = 6.8, 2H, *i*PrCH), 1.62 (s, 6H, CH₃), 1.05 (d, ³J = 6.8 Hz, 6H, *i*PrCH₃), 1.01 (d, ³J = 6.8 Hz, 6H, *i*PrCH₃). ¹³C NMR (DMSO-*d*₆ 125 MHz, ppm): δ 174.5 (CONH₂), 161.9 (PyCONH), 149.2 (PyC₂, C₆), 139.9 (PyC₄), 124.1 (PyC₃, C₅), 62.5 (C_q), δ 35.1 (*i*PrCH), 17.9 (CH₃), 17.4 (*i*PrCH₃), 17.35 (*i*PrCH₃). The elemental analysis is comparable with that of **1a**. (*S,S*)-Pyridine-2,6-dicarboxylic acid bis-[(1-carbamoyl-1,2-dimethylpropyl)-amide] (**1c**): 45% yield, mp 230–233 °C, [α]_D²⁵ = 63.0 (c = 0.9, CH₃OH). Elemental analysis is comparable with that of **1a** (**1b**), ¹H and ¹³C NMR spectra are identical with those of the (*R,R*)-isomer.
- (*R,S*)-2,6-Bis(4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-on-2-yl)pyridine (**2a**): A mixture of **1a** (780 mg, 2 mmol) and 20 mL 1 M CH₃ONa (20 mmol) was stirred at room temperature. After 24 h, the mixture was neutralised with concd HCl to pH ~7 and evaporated to dryness. The residue was treated with water (10 mL), and the suspension formed was filtered and washed with hexane to give 0.57 g of the product (80%), mp 302–303 °C. ¹H NMR (DMSO-*d*₆ 500 MHz, ppm): δ 11.59 (s, 2H, NH), 8.39 (d, ³J = 7.9, 2H, PyH₃, H₅), 8.23 (t, ³J = 7.9, 1H, PyH₄), 2.02 (sep, ³J = 6.8, 2H, *i*PrCH), 1.34 (s, 6H, CH₃), 1.04 (d, ³J = 6.8, 6H, *i*PrCH₃), 0.84 (d, ³J = 6.8, 6H, *i*PrCH₃). ¹³C NMR (DMSO-*d*₆ 125 MHz, ppm): δ 186.9 (C=O), 158.4 (C=N), 146.2 (PyC₂, C₆), 139.4 (PyC₄), 123.5 (PyC₃, C₅), 75.5 (C_q), 34.3 (*i*PrCH), 21.2 (CH₃), 17.0 (*i*PrCH₃), 16.80 (*i*PrCH₃). For C₁₉H₂₅N₅O₂ (355.44) calculated: C, 64.20; H, 7.09; N, 19.70%; found: C, 64.18; H, 7.10; N, 19.65%. (*R,R*)-2,6-Bis(4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-on-2-yl)pyridine (**2b**): 71% yield, mp 284–286 °C, [α]_D²⁵ = 32.0 (c = 1, CH₃OH). The elemental analysis is comparable with that of **2a**. (*S,S*)-2,6-Bis(4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-on-2-yl)pyridine (**2c**): 69% yield, mp 281–283 °C, [α]_D²⁵ = –32.3 (c = 1, CH₃OH). Elemental analysis is comparable with that of **2a** (**2b**), ¹H and ¹³C NMR spectra are identical with those of the (*R,R*)-isomer.
- Sedlák, M.; Šimůnek, P.; Antonietti, M. *J. Heterocycl. Chem.* **2003**, *40*, 671.
- (*R,S*)-2,6-Bis(1-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-on-2-yl)pyridine (**3a**): A mixture of **2a**

(1.78 g, 5 mmol), potassium carbonate (1.8 g, 13 mmol), benzyl bromide (2.05 g, 12 mmol), potassium iodide (50 mg) and dimethylformamide (15 mL) was refluxed for 48 h. Then, the mixture was filtered and the insoluble portion was washed with 20 mL DMF. The combined filtrates were evaporated in vacuo until dry. The residue was dissolved in 150 mL ethyl acetate and the solution was filtered through silica gel. The filtrate was evaporated to dryness and the residue was recrystallised from petroleum ether to give 1.4 g of the product (52%), mp 101–105 °C. ¹H NMR (DMSO-*d*₆, 500 MHz, ppm): δ 8.01 (m, 3H, *Py*), 7.18 (m, 6H, *PhH*₃, *H*₄), 6.90 (m, 4H, *PhH*₂), 4.60 and 4.68 (2 × d, ²*J* = 15.8, 4H, *BzCH*₂), 2.11 (sep, ³*J* = 6.8, 2H, *iPrCH*), 1.40 (s, 6H, *CH*₃), 1.06 (d, ³*J* = 6.8, 6H, *iPrCH*₃), 0.88 (d, ³*J* = 6.8, 6H, *iPrCH*₃). ¹³C NMR (DMSO-*d*₆, 125 MHz, ppm): δ 185.7 (C=O), 158.3 (C=N), 147.9 (*PyC*₂, *C*₆), 139.1 (*PyC*₄), 137.5 (*PyC*₃, *C*₅), 128.5 (*PhC*₂, *C*₆), 127.2 (*PhC*₁), 126.4 (*PhC*₃, *C*₅), 125.8 (*PhC*₄), 73.4 (*C*_q), 44.0 (*BzCH*₂), 34.3 (*iPrCH*), 21.4 (*CH*₃), 17.0 (*iPrCH*₃), 16.8 (*iPrCH*₃). ¹⁵N NMR (NMR (DMSO-*d*₆, 50 MHz, ppm): δ -78 (*Py*), δ -109 (C=N), -222 (*Bz-N*). For C₃₃H₃₇N₅O₂ (535.70) calculated: C, 73.99; H, 6.96; N, 13.07%; found: C, 73.93; H, 7.18; N, 12.97%. (*R,R*)-2,6-Bis(1-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-on-2-yl)pyridine (**3b**): 46% yield, mp 102–104 °C, [α]_D²⁵ = 26.0 (*c* = 0.5, CH₃OH). The elemental analysis is comparable with that of **3a**. ¹H and ¹³C NMR spectra are identical with those of **3a**. (*S,S*)-2,6-Bis(1-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-on-2-yl)pyridine (**3c**): 53% yield, mp = 103–105 °C, [α]_D²⁵ = 25.9 (*c* = 0.5, CH₃OH). The elemental analysis is comparable with that of **3a** (**3b**), ¹H and ¹³C NMR spectra are identical

with those of the (*R,R*)-isomer. *Crystal data* for **3c**: C₃₃H₃₇N₅O₂ *M* = 535.70, monoclinic, *a* = 37.5360(6), *b* = 15.3370(2), *c* = 10.5450(2) Å, β = 104.9240(7)°, *V* = 5865.87(16) Å³, *T* = 150(2), space group *C*2, *Z* = 8, μ(*MoK*_α) = 0.077 mm⁻¹, 40,843 reflections measured, 13,341 unique (*R*_{int} = 0.039), which were used in all calculations, the final *R*₁ = 0.040. CCDC 236299.

19. *Complex 4a*: A solution of **3a** (107 mg, 0.2 mmol) and anhydrous ferric chloride (32.5 mg, 0.2 mmol) in absolute methanol (25 mL) was stirred overnight. The suspension obtained was evaporated to a volume of ca 5 mL, and the separated crystals were collected by filtration, washed with ether and dried to give 100 mg of the product (71%). For C₃₃H₃₇Cl₃FeN₅O₂ (697.88) calculated C, 56.79; H, 5.34; N, 10.04%; found: C, 56.75; H, 5.36; N, 10.04%. *Crystal data* for **4a**: C₃₃H₃₇Cl₃FeN₅O₂ *M* = 697.88, tetragonal, *a* = 17.2950(2), *c* = 45.4100(4) Å, *V* = 13582.9(3) Å³, *T* = 150(2), space group *I*4₁*acd*, *Z* = 16, μ(*MoK*_α) = 0.717 mm⁻¹, 97309 reflections measured, 3748 unique (*R*_{int} = 0.039), which were used in all calculations, the final *R*₁ = 0.074. CCDC 236300. *Complex 4b*: 75% yield, [α]_D²⁵ = 49.7 (*c* = 0.2, DMF). For C₃₃H₃₇Cl₃FeN₅O₂ (697.88) calculated: C, 56.79; H, 5.34; N, 10.04%; found: C, 57.06; H, 5.56; N, 10.11%. *Complex 4c*: 73% yield, [α]_D²⁵ = 50.0 (*c* = 0.2, DMF). For C₃₃H₃₇Cl₃FeN₅O₂ (697.88) calculated: C, 56.79; H, 5.34; N, 10.04%; found: C, 56.95; H, 5.57; N, 10.03%.
20. (a) Cotton, S. A.; Franckevicius, V.; Fawcett, J. *Polyhedron* **2002**, *21*, 2055; (b) Adams, H.; Bailey, N. A.; Crane, J. D.; Fenton, D. E.; Latour, J.-M.; Williams, J. M. *J. Chem. Soc., Dalton Trans.* **1990**, 1727.