Helical Structures

DOI: 10.1002/anie.201102144

Conversion of Cobalt(II) Porphyrin into a Helical Cobalt(III) Complex of Acyclic Pentapyrrole**

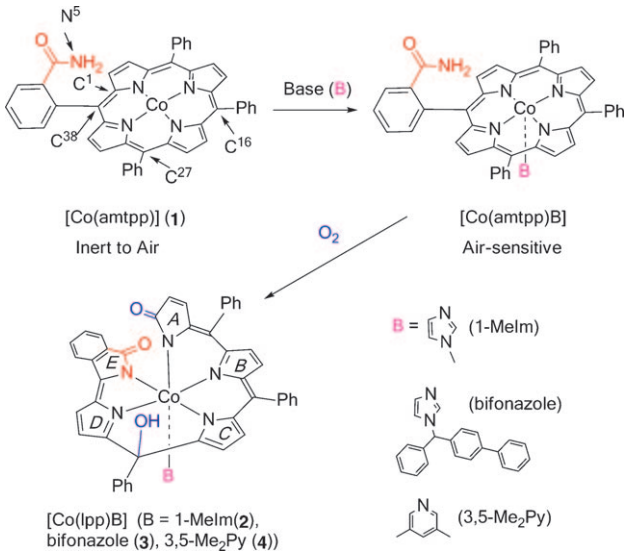
Katsunori Yamanishi, Masamichi Miyazawa, Takeshi Yairi, Shintaro Sakai, Naoko Nishina, Yasuhiro Kobori, Mitsuru Kondo, and Fumio Uchida*

In memory of Yasuo Yamamoto of Shimane University

Conversion of artificial porphyrin to acyclic polypyrrole by oxidation is important not only for model reactions of heme oxygenase (HO), which converts heme to biliverdin,[1–3] but also for the syntheses of new acyclic polypyrroles.[4–10] Biliverdin-type ligands are nonplanar tetrapyrrole derivatives and have been utilized for the syntheses of metal complexes with helical structures that are easily racemized, owing to its low steric hindrance for interconversion.[11–16] In contrast, metal complexes bearing acyclic polypyrroles constructed of more than five pyrroles are still rare because of the limited availability of synthetic routes to prepare them.[17–22] As an exceptional example, a new dicopper(II) complex bearing acyclic heptapyrrolic helices has been prepared from dicopper(II) heptaphyrin by reaction with O_2.[7] In this reaction, O_2 was not activated at the metal center but reacted with the heptaphyrin ligand directly.

Two intrinsic effects of the coordination environment around heme on the activation of the O_2 molecule have been proposed in the biological system. One is the electron donation from coordinating bases such as imidazole and thiolate at the fifth coordination site to the iron center, and the other is the hydrogen bond from the histidine residue to the O_2 molecule bound at the metal center. When these two effects contribute cooperatively, this activation mechanism is called a "push–pull" mechanism.[3,23] To mimic the pull effects, some porphyrin ligands bearing carboxylic acid, which could form a hydrogen bond to the bound O_2, have been designed and synthesized.[4,23–25] For example, Chang and co-workers have shown that Co^{II} porphyrin complex bearing naphthoic acid, [Co(npca-por)], converted to metal-free biliverdin-type acyclic polypyrrole by reaction with O_2. This reaction proceeds under ambient condition without coordination of any bases at the axial site.[4] The authors proposed that in this system, the carboxylic acid group protonated the coordinating O_2 molecule to yield a Co^{III}–OOH species as an intermediate. Although this system mimicked the pull effect well, porphyrin complexes which require both push and pull effects for the cleavage of the porphyrin ring are still not known.

Recently, we designed a new porphyrin ligand (amtpp; Scheme 1) that has an amide group in the *ortho* position of a phenyl ring of tetraphenylporphyrin (H_2tpp) to mimic the pull effect by histidine residue in the biological system. We found that the imidazole adduct [Co(amtpp)(1-MeIm)] (1-MeIm = 1-methylimidazole) activated O_2, thus converting to a new Co^{III} helical complex with a coiled acyclic pentapyrrole-type ligand, despite the fact that the Co^{II} complex [Co(amtpp)] (**1**) was inert to air (Scheme 1). Moreover, we have found that chiral axial ligands (*S*)-nicotine and (*S*)-cotinine induced the (*M*)-helical form preferentially in this conversion system. Herein, we report the synthesis and structure of the Co-amtpp complex and the unique porphyrin conversion reaction.



Scheme 1. Conversion of **1** to helical complexes by addition of bases.

H_2amtpp was prepared from the precursor H_2CNtpp, which has a CN group in the *ortho* position of a phenyl ring of

[*] K. Yamanishi, M. Miyazawa, T. Yairi, S. Sakai, Dr. N. Nishina, Prof. Y. Kobori
Department of Chemistry, Shizuoka University (Japan)
Prof. M. Kondo
Center for Instrumental Analysis, Shizuoka University
836 Ohya, Suruga-ku, Shizuoka 422-8529 (Japan)
Fax: (+81) 54-238-4763
E-mail: scmkond@ipc.shizuoka.ac.jp
F. Uchida
Hautform Devision, Fuji Chemical Co. Ltd. (Japan)

[**] This work was supported by Ministry of Education, Culture, Sports, Science and Technology (Japan). M.K. thanks R. Ikeya and K. Terasaki of the Center for Instrumental Analysis in Shizuoka University for support in obtaining the X-ray diffraction data and elemental analysis data.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201102144.

H_2tpp. Complex **1** was obtained as an air-stable purple crystalline solid by the reaction of $Co(CH_3COO)_2$ with H_2amtpp in $CHCl_3$/MeOH. The structure of **1** was determined by a single-crystal X-ray analysis,[26] which revealed a dimer in the solid state formed by coordination of the amide oxygen atom to the Co^{II} center in an adjacent unit (Co–O 2.2724(7) Å, Figure 1). The synthetic procedures, detailed crystal analysis data, and spectral data are summarized in the Supporting Information.

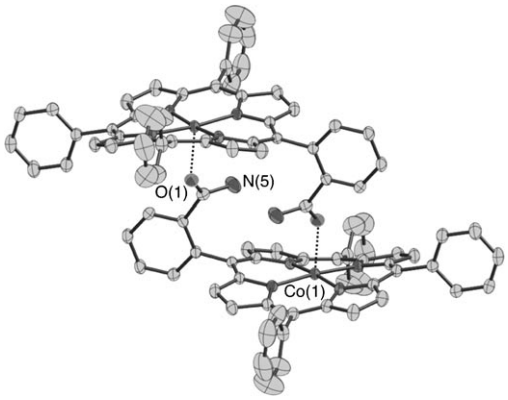


Figure 1. Crystal structure of **1**, which showed a dimeric form by coordination of the amide oxygen atom O(1) to the Co^{II} center in the adjacent molecule. Thermal ellipsoids are scaled to the 30% probability level. Hydrogen atoms are omitted for clarity.

In spite of the inertness of **1** to air, addition of 1-methylimidazole (1-MeIm) to **1** in $CHCl_3$ under O_2 or air caused a drastic color change of the solution from deep red-purple to brownish green within a few days. Diffusion of *n*-hexane into the solution led to precipitation of a new Co^{III} complex [Co(lpp)(1-MeIm)] (**2**) as deep greenish crystals in about 59% yield. The structure of lpp and the corresponding complex is illustrated in Scheme 1. The structure of **2** was clarified by single-crystal X-ray diffraction.[26] The numbering scheme of **1** is shown in Scheme 1, including designations of the three pyrroles (*B*, *C*, *D*) and the two derivative rings (*A*, *E*) of **2** referred to in the structural descriptions.

Figure 2 shows the molecular structure of **2**. The distorted octahedral center is coordinated in a helical manner by the lpp framework. The unit cell contains enantiomeric pairs of helical complexes. The parts of the lpp ligand that originated from the amide group (red) and additional oxo and hydroxy groups (blue) are highlighted in

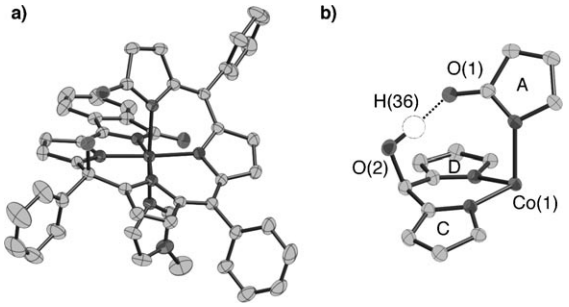
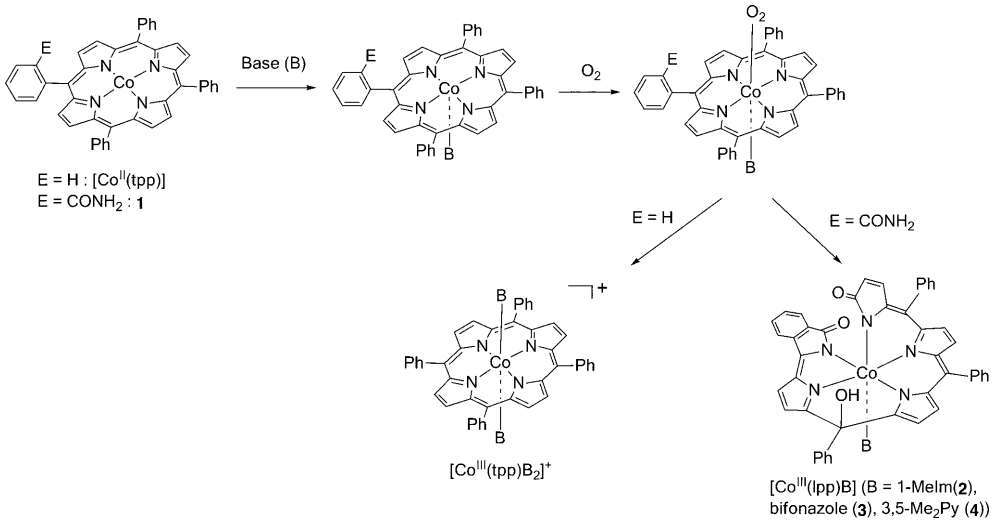


Figure 2. a) Crystal structure of **2**. Thermal ellipsoids are scaled to the 30% probability level. Hydrogen atoms are omitted for clarity. b) Hydrogen bond between hydroxy O(2)–H(36) and carbonyl O(1).

Scheme 1. As for the conversion to **2**, the $C^1{=}C^{38}$ bond of **1** was cleaved, and C^{38} formed a new bond with the amide nitrogen atom N^5 to produce the oxoisoindole ring *E*. The nitrogen atom of this resulting ring was completely deprotonated and coordinated to the Co^{III} center. Carbon atom C^1 was oxidized to bear a carbonyl group ($C^1{=}O$).

This reaction sequence, involving C=C bond cleavage and production of a C=O group, is similar to the conversion from porphyrin to biliverdin observed in biological systems[1–3] and in [Co(npca-por)].[4] A hydroxy group was regiospecifically added at the C^{27} position to give an sp^3-hybridized carbon atom in **2**, and the hydroxy group was oriented to the side where the amide group originally existed. This incorporated hydroxy group forms an intramolecular hydrogen bond with an oxygen atom of the terminal carbonyl $C^1{=}O$ (O(1)···O(2) 2.592(3) Å) as shown in Figure 2b. The obtained sp^3 carbon atom breaks the conjugation of the pentapyrrole framework. The sixth coordination site was occupied by 1-MeIm.

As illustrated in Scheme 2, it has been shown that [Co^{II}(tpp)B], which was prepared by treatment of [Co^{II}(tpp)] with bases such as 1-MeIm, produced [Co(tpp)B(O_2)] in solution.[27] The obtained Co···O_2 adduct did not cleave the porphyrin ring, but led to production of $[Co^{III}(tpp)B_2]^+$.[28] In contrast, the corresponding Co···O_2 adduct obtained from **1**



Scheme 2. Comparison of reactivity between [Co(tpp)B(O_2)] and [Co(amtpp)B(O_2)].

cleaved the C=C bond of the porphyrin ring to produce the helical complex **2**.

For conversion from **1** to **2**, we monitored ESR spectra of the reaction mixture of **1** with 1-MeIm and O_2 to obtain insight into the reaction process. The measurement was carried out at 77 K. The reaction mixture of **1** with 1-MeIm under Ar revealed an ESR signal ascribed to the five-coordinated Co^{II} complex,[27] thus indicating the formation of [Co(amtpp)(1-MeIm)]. The reaction mixture after O_2 bubbling revealed a signal ascribed to [Co(amtpp)(1-MeIm)(O_2)] within 12 h, the spectrum of which was similar to various Co···O_2 adducts bearing porphyrin[27] and other chelate ligands.[29] The intensity of the ESR signal gradually decreased, and a new intense signal at $g = 2.0035$ developed within the next two days. This signal, which disappears within a week, can be assigned to the organic radical species. (The ESR spectra and analyzed parameters are shown in the Supporting Information.) This observation does not contradict the reaction mechanism proposed by Chang and coworkers.[4] They also observed organic radical species during the conversion of their Co^{II} complex to metal-free biliverdin by O_2 activation.

Meanwhile, we confirmed that similar conversion from **1** to the {Co^{III}(lpp)} complex was also induced by addition of other imidazole and pyridine bases. Treatment of **1** with (*rac*)-bifonazole and 3,5-dimethylpyridine (3,5-Me_2Py) in a $CHCl_3$ solution in air produced [Co(lpp)((*rac*)-bifonazole)] (**3r**) and [Co(lpp)(3,5-Me_2Py)] (**4**) in about 46 and 44% yield. The structures were characterized by single-crystal X-ray analyses.[26] Their helical frameworks and absorption spectra were essentially same as those of **2** (see the Supporting Information).

Although **2** was formed as a racemate, we succeeded in chiral separation and characterizations of the enantiomers. The chiral separation of **2** was carried out by high-performance liquid chromatography (HPLC) using a chiral separation column (Daicel CHIRALPAK IA). The first and second fractions were assigned to {Co^{III}(lpp)} complexes with (*P*)- and (*M*)-forms; the absolute configurations were determined by single-crystal X-ray diffraction.[26] Figure 3 shows the circular dichroism (CD) and absorption spectra of (*P*)- and (*M*)-[Co(lpp)(1-MeIm)], which are designated as (*P*)-**2** and (*M*)-**2**. The CD spectra of the enantiomers are almost perfect mirror images of each other. This chiral structure was retained without racemization in a $CHCl_3$ solution after heating at 50 °C for 24 h (see the Supporting Information).

The formation of helical complex **2** from **1** by addition of axial ligands prompted us to study the chiral induction of the helical {Co(lpp)} framework by addition of chiral axial ligands. To this end, we selected (*S*)-bifonazole,[30] (*S*)-nicotine, and (*S*)-cotinine (Scheme 3). The addition of each chiral axial ligand to **1** in $CHCl_3$ successfully produced [Co(lpp)B] helical complexes, as confirmed by elemental analyses and absorption and NMR spectra (see the Supporting Information). Although our first attempt at chiral induction by combination of **1** and (*S*)-bifonazole was unsuccessful, treatment of **1** with the other two chiral ligands produced (*M*)-[Co(lpp)B] preferentially. Figure 4 shows the CD and absorption spectra of the obtained complexes

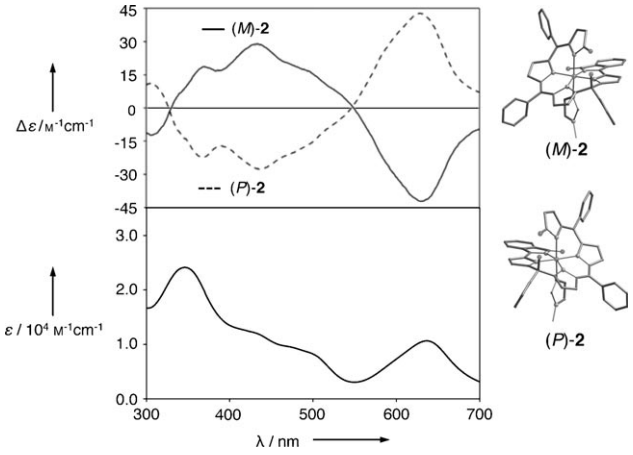
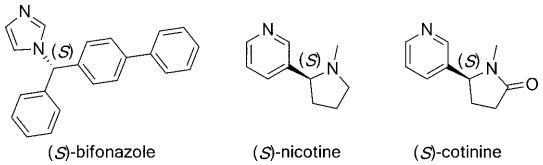


Figure 3. CD spectra (top) of separated (*P*)-**2** (-----) and (*M*)-**2** (——) and the absorption spectrum of **2** (bottom). The absolute structures of each form determined by single-crystal X-ray analysis are shown on the right.



Scheme 3. Structures of (*S*)-bifonazole, (*S*)-nicotine, and (*S*)-cotinine.

[Co(lpp)B] (B = (*S*)-nicotine (**5**), (*S*)-cotinine (**6**), and (*S*)-bifonazole (**3S**)). While **3S** did not show meaningful CD peaks, **5** and **6** revealed CD peaks with a similar pattern to (*M*)-**2**. Obviously, (*S*)-nicotine and (*S*)-cotinine preferentially induced [Co(lpp)B] having an (*M*)-conformation helical framework. Their enantiomeric excess (*ee*) values were estimated to be about 14 and 16%, respectively, by the HPLC analyses. These results demonstrated that the chirality of the axial ligand affected the induced helicity of {Co(lpp)} formed in the conversion.

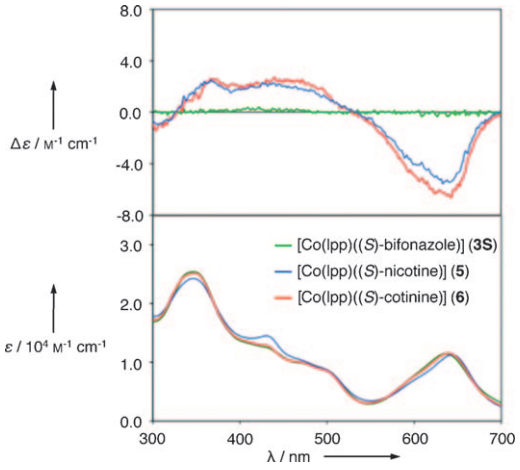


Figure 4. CD (top) and absorption spectra (bottom) of reaction product of **1** with (*S*)-bifonazole (green), (*S*)-nicotine (blue), and (*S*)-cotinine (red) in $CHCl_3$.

In summary, we have shown that [Co(amtpp)] (**1**) was converted to new complexes [Co(lpp)B] by addition of various bases in O_2 or air. In this reaction, coordination of bases at the fifth coordination position and amide groups in the phenyl ring cooperatively contribute to the conversion reaction by activation of the O_2 molecule, which could largely mimic the push–pull mechanism in the biological system. The obtained complex showed a unique helical structure defined by an acyclic pentapyrrole-type ligand in which the amide group was converted to an oxoisoindole ring that binds to the Co^{III} center. Although **2** was isolated as a racemate, the enantiomers could be separated, and the absolute structures and absorption properties of each were characterized. We have also shown that the addition of chiral axial ligands (*S*)-nicotine and (*S*)-cotinine produced [Co(lpp)B] complexes in the (*M*)-configuration in 14 and 16% *ee*. This is the first example of conversion of a porphyrin complex to helical metal complexes with coordinating acyclic pentapyrrole-type ligands. Further studies of the conversion reaction are currently underway.

Received: March 27, 2011
Published online: June 6, 2011

Keywords: acyclic pentapyrroles · chirality · chromophores · helical structures · porphyrinoids

[1] M. Sono, M. P. Roach, E. D. Coulter, J. H. Dawson, *Chem. Rev.* **1996**, *96*, 2841.
[2] a) T. Matsui, M. Unno, M. Ikeda-Saito, *Acc. Chem. Res.* **2010**, *43*, 240; b) M. Unno, T. Matsui, M. Ikeda-Saito, *Nat. Prod. Rep.* **2007**, *24*, 553.
[3] S. Ozaki, M. P. Roach, T. Matsui, Y. Watanabe, *Acc. Chem. Res.* **2001**, *34*, 818.
[4] C. K. Chang, G. Avilés, N. Bag, *J. Am. Chem. Soc.* **1994**, *116*, 12127.
[5] a) A. L. Balch, M. Mazzanti, T. N. St. Claire, M. M. Olmstead, *Inorg. Chem.* **1995**, *34*, 2194; b) R. Koerner, M. M. Olmstead, P. M. Van Calcar, K. Winkler, A. L. Balch, *Inorg. Chem.* **1998**, *37*, 982; c) R. Koerner, M. M. Olmstead, A. Ozarowski, A. L. Balch, *Inorg. Chem.* **1999**, *38*, 3262.
[6] H. Furuta, H. Maeda, A. Osuka, *Org. Lett.* **2002**, *4*, 181.
[7] S. Saito, K. Furukawa, A. Osuka, *J. Am. Chem. Soc.* **2010**, *132*, 2128.
[8] a) N. Asano, S. Uemura, T. Kinugawa, H. Akasaka, T. Mizutani, *J. Org. Chem.* **2007**, *72*, 5320; b) T. Yamauchi, T. Mizutani, K. Wada, S. Horii, H. Furukawa, S. Masaoka, H.-C. Chang, S. Kitagawa, *Chem. Commun.* **2005**, 1309.
[9] J. L. Sessler, D. Seidel, *Angew. Chem.* **2003**, *115*, 5292; *Angew. Chem. Int. Ed.* **2003**, *42*, 5134.
[10] P. K. Sharma, R. Kevorkiants, S. P. de Visser, D. Kumar, S. Shaik, *Angew. Chem.* **2004**, *116*, 1149; *Angew. Chem. Int. Ed.* **2004**, *43*, 1129.
[11] a) T. Mizutani, S. Yagi, A. Honmaru, S. Murakami, M. Furusyo, T. Takagishi, H. Ogoshi, *J. Org. Chem.* **1998**, *63*, 8769; b) T. Mizutani, S. Yagi, T. Morinaga, T. Nomura, T. Takagishi, S. Kitagawa, H. Ogoshi, *J. Am. Chem. Soc.* **1999**, *121*, 754; c) T. Mizutani, S. Yagi, A. Honmaru, H. Ogoshi, *J. Am. Chem. Soc.* **1996**, *118*, 5318; d) T. Mizutani, N. Sakai, S. Yagi, T. Takagishi, S. Kitagawa, H. Ogoshi, *J. Am. Chem. Soc.* **2000**, *122*, 748.
[12] a) S. Yagi, N. Sakai, R. Yamada, H. Takahashi, T. Mizutani, T. Takagishi, S. Kitagawa, H. Ogoshi, *Chem. Commun.* **1999**, 911; b) S. Yagi, T. Morinaga, T. Nomura, T. Takagishi, T. Mizutani, S. Kitagawa, H. Ogoshi, *J. Org. Chem.* **2001**, *66*, 3848.
[13] G. Struckmeier, U. Thewalt, J.-H. Fuhrhop, *J. Am. Chem. Soc.* **1976**, *98*, 278.
[14] A. L. Balch, M. Mazzanti, B. C. Noll, M. M. Olmstead, *J. Am. Chem. Soc.* **1994**, *116*, 9114.
[15] R. Koerner, M. M. Olmstead, A. Ozarowski, S. L. Phillips, P. M. Van Calcar, K. Winkler, A. L. Balch, *J. Am. Chem. Soc.* **1998**, *120*, 1274.
[16] J. Setsune, A. Tsukajima, N. Okazaki, J. M. Lintuluoto, M. Lintuluoto, *Angew. Chem.* **2009**, *121*, 785; *Angew. Chem. Int. Ed.* **2009**, *48*, 771.
[17] a) H. Falk, H. Flödl, *Monatsh. Chem.* **1986**, *117*, 57; b) U. G. Wagner, C. Kratky, H. Falk, H. Flödl, *Monatsh. Chem.* **1987**, *118*, 1185.
[18] D. F. Nogales, D. T. Anstine, D. A. Lightner, *Tetrahedron* **1994**, *50*, 8579.
[19] J.-Y. Shin, S. S. Hepperle, B. O. Partick, D. Dolphin, *Chem. Commun.* **2009**, 2323.
[20] Z. Gross, N. Galili, L. Simkhovich, I. Saltsman, M. Botoshansky, D. Bläser, R. Boese, I. Goldberg, *Org. Lett.* **1999**, *1*, 599.
[21] K. Okada, H. Takakura, K. Nomura, K. Saburi, *Tetrahedron Lett.* **2000**, *41*, 2915.
[22] P. Morosini, M. Scherer, S. Meyer, V. Lynch, J. L. Sessler, *J. Org. Chem.* **1997**, *62*, 8848.
[23] J. D. Soper, S. V. Kryatov, E. V. Rybak-Akimova, D. G. Nocera, *J. Am. Chem. Soc.* **2007**, *129*, 5069.
[24] C. J. Chang, L. L. Chng, D. G. Nocera, *J. Am. Chem. Soc.* **2003**, *125*, 1866.
[25] M. Harmjanz, H. S. Gill, M. J. Scott, *J. Am. Chem. Soc.* **2000**, *122*, 10476.
[26] CCDC 818717 (**1**), 818719 (**2**), 818722 ((*P*)-**2**), 818721 ((*M*)-**2**), 818720 (**3r**), and 818718 (**4**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[27] a) J. P. Collman, Y.-L. Yan, T. Eberspacher, X. Xie, E. I. Solomon, *Inorg. Chem.* **2005**, *44*, 9628; b) K. Uruma, K. Tsuge, Y. Sasaki, T. Imamura, *Chem. Lett.* **2005**, *34*, 474; c) S. van Doorslaer, A. Schweiger, B. Kräutler, *J. Phys. Chem. B* **2001**, *105*, 7554; d) K. Yamamoto, T. Kwan, *J. Catal.* **1970**, *18*, 354.
[28] J. W. Lauher, J. A. Ibers, *J. Am. Chem. Soc.* **1974**, *96*, 4447; b) F. A. Walker, *J. Am. Chem. Soc.* **1973**, *95*, 1154; c) B. Steiger, F. C. Anson, *Inorg. Chem.* **2000**, *39*, 4579; d) J. Li, B. C. Noll, A. G. Oliver, G. Ferraudi, A. G. Lappin, W. R. Scheidt, *Inorg. Chem.* **2010**, *49*, 2398; e) Z. Dokuzović, X. Ahmeti, D. Pavlović, I. Murati, S. Ašperger, *Inorg. Chem.* **1982**, *21*, 1576; f) D. V. Stynes, H. C. Stynes, J. A. Ibers, B. R. James, *J. Am. Chem. Soc.* **1973**, *95*, 1142.
[29] a) A. C. Sharma, A. S. Borovik, *J. Am. Chem. Soc.* **2000**, *122*, 8946; b) Y. Sugiura, *J. Am. Chem. Soc.* **1980**, *102*, 5216; c) B. S. Tovrog, D. J. Kitko, R. S. Drago, *J. Am. Chem. Soc.* **1976**, *98*, 5144.
[30] (*S*)-Bifonazole was separated from *rac*-bifonazole by using HPLC with chiral separation column according to: M. Botta, F. Corelli, F. Gasparrini, F. Messina, C. Mugnaini, *J. Org. Chem.* **2000**, *65*, 4736.

