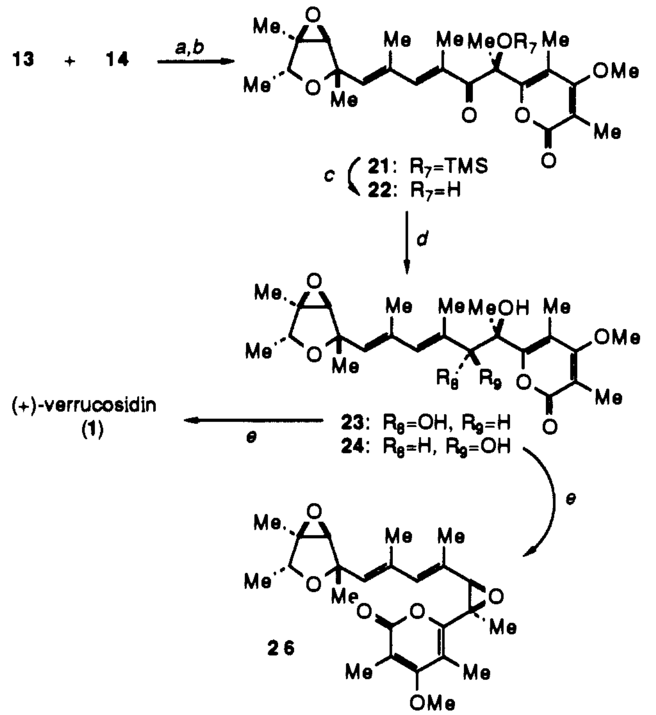
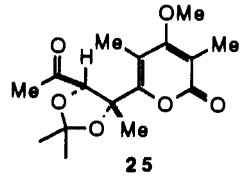
Scheme III[a]



[a] (a) LiN(TMS)$_2$, THF, −78 °C (77% based on consumed SM). (b) TFAA, DMAP, DBU, CH_2Cl_2, −40 to 0 °C (83%). (c) CsF, EtOH, room temperature (90%). (d) 1 equiv of $NaBH_4$–0.5 equiv of *d*-tartaric acid–1 equiv of $PrCl_3 \cdot 6H_2O$, 2-propanol, 0 °C (85%). (e) Martin's sulfurane (80%).

and reduction of the resulting α-hydroxy enone **22** with LAH (at −78 °C) or $NaBH_4$–$CeCl_3$ (at −23 °C)[13] gave inseparable 1:2 or 3:2 mixtures of diols **23** and **24**, respectively. In our hands, both reduction reactions gave poorer stereoselectivity than reported by Takano. More significantly, however, our unequivocal stereochemical assignment (vide infra) of **23** and **24** reveals that the stereostructures of these diols should be reassigned as shown in Scheme III. After considerable experimentation with several hydride reagents, the stereoselective (∼5:1) reduction of **22** leading to diol **23** was accomplished by the use of a sodium acyloxyborohydride[14] derived from $NaBH_4$ and tartaric acid in the presence of a lanthanide. On the other hand, diol **24** can be prepared stereoselectively (≥10:1) by LAH or $NaBH_4$ reduction of **21** followed by desilylation.[15] The stereochemical assignment of the diols was secured at this juncture by the conversion [(1) 2,2-dimethoxypropane, *p*-TsOH; (2) OsO_4–$NaIO_4$] of **24** to ketone **25** and an independent synthesis of the latter ketone starting from



25

pyrone **16**.[16] Finally, treatment of a 5:1 mixture of diols **23** and **24** with Martin's sulfurane[17] stereoselectively afforded **1** and its epimer **26** in the same ratio. The synthetic substance was found to be identical in every aspect with an authentic sample of verrucosidin.[18]

Acknowledgment. We are grateful to the National Institutes of Health (GM 35956) for financial support. We also thank Professors Thomas and Constance Harris of this department for providing an authentic sample of the natural (+)-verrucosidin.

Supplementary Material Available: Description of the preparation of ketone **25** and $^1H/^{13}C$ NMR spectra for key intermediates (27 pages). Ordering information is given on any current masthead page.

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[15] The observed 1,2-asymmetric induction can be rationalized by the open-chain Felkin–Anh model. See, for example: (a) Overman, L. E.; McCready, R. J. *Tetrahedron Lett.* **1982**, *23*, 2355. (b) Nakata, T.; Tanaka, T.; Oishi, T. *Ibid.* **1983**, *24*, 2653.

[16] A similar degradation of diol **23** gave a diastereomeric ketone of **25**.

[17] Martin, J. C.; Franz, J. A.; Arhart, R. J. *J. Am. Chem. Soc.* **1974**, *96*, 4604.

[18] Similarly, diol **24** was converted smoothly into *epi*-verrucosidin (**26**).

EXAFS Studies of Nickel(II) and Nickel(I) Factor 430 M. Conformational Flexibility of the F430 Skeleton

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Factor 430 (F430) is a Ni(II) tetrapyrrole (corphin) found in methyl coenzyme M reductase, the enzyme that catalyzes the terminal stages of the conversion of carbon dioxide in methane biogenesis.[1-3] F430 can be reduced to Ni(I) in vitro[4] and in vivo,[5] and Ni(I) has been implicated as a catalytic transient in the enzymic methanogenesis.[5] Ni(I) F430 M (the pentamethyl ester of F430) has also been shown to react with methyl halides and sulfonium salts to yield methane.[6] The conformations of F430 that control the reactions are unknown,[7] as are the consequences of metal reduction. F430 is deduced to exist as hexacoordinated, high-spin (HS) Ni(II) with oxygen axial ligands in vivo,[8] and Ni–N distances of 2.10 Å have been determined by EXAFS for extracted HS F430 in aqueous solutions.[9]

We present here EXAFS results for the low-spin (LS) Ni(II) form of F430 M[10] and for its paramagnetic Ni(I) reduction in-

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[6] Jaun, B.; Pfaltz, A. *J. Chem. Soc., Chem. Commun.* **1988**, 293.

[7] Based on corphin models,[3d] F430 is expected to be planar or significantly puckered, with long or short Ni–N distances, respectively, in the high- and low-spin Ni(II) forms.

[8] Cheesman, M. R.; Ankel-Fuchs, D.; Thauer, R. K.; Thompson, A. J. *Biochem. J.* **1989**, *260*, 613.

[9] Shiemke, A. K.; Kaplan, W. A.; Hamilton, C. L.; Shelnutt, J. A.; Scott, R. A. *J. Biol. Chem.* **1989**, *264*, 7276.

termediate. The significant differences in Ni–N bond lengths found for the low- and high-spin[9] Ni(II), 1.90 vs 2.10 Å, demonstrate the considerable conformational flexibility of the F430 skeleton. Not surprisingly, therefore, the macrocycle can readily accommodate the structural changes observed on reduction to Ni(I): a distortion occurs around the Ni, with *two* sets of Ni(I)–N distances of 1.88 and 2.03 Å.

LS Ni(II) F430 M undergoes reversible one-electron electrochemical reductions in tetrahydrofuran (THF),[4] dimethylformamide,[4] and butyronitrile.[15] Reduction can also be accomplished with Na–Hg amalgam in THF to yield characteristic optical and EPR spectra.[4] The *g* values of the latter are diagnostic of Ni(I) with the unpaired electron localized in a $d_{x^2-y^2}$ orbital.[4] X-ray absorption experiments[16-18] were thus carried out in THF on the LS Ni(II) and the chemically reduced Ni(I)[19] forms of F430 M in anaerobic cells, previously described,[20] that allowed EXAFS, optical, and EPR data to be acquired on the same sample in both redox states.

Near-edge X-ray absorption spectra for the Ni(II) and Ni(I) complexes are shown in Figure 1. The Ni(II) form clearly exhibits the preedge features associated with tetracoordinate, planar geometries around the metal, and the spectrum resembles those reported for the LS 12,13-diepimer of F430 in aqueous solution.[9] Upon reduction, the edge shifts to lower energies by 2–3 eV but maintains the features of a four-coordinate species, i.e., there is no axial ligand tightly bound to the Ni(I). These results parallel those observed for isobacteriochlorin (iBC)[17,21] and tetraaza[18,21] complexes of Ni(I) and LS Ni(II).

Analysis[16-18] of the EXAFS results for the LS Ni(II) F430 M complex yields an average Ni–N bond length of 1.90 (±0.02) Å, Figure 1, with no evidence of a large spread in distances, i.e., within the uncertainty of the measurement, the Ni(II)–N distances are equivalent.

In contrast to the Ni(II) spectra, the Ni(I) complex gives rise to an attenuated first shell transform amplitude (Figure 1). Acceptable fits to the isolated oscillations require *two* distinct sets of Ni(I)–N distances of 1.88 (±0.03) and 2.03 (±0.03) Å, using the recently characterized Ni(I) tetraaza compound[18] as an EXAFS standard. Reduction of LS Ni(II) to Ni(I) in F430 M thus induces a distortion of the nitrogens around the metal. Similar deformations accompany the reduction to Ni(I) in an iBC derivative[17] (average Ni(II)–N = 1.93 (±0.02) Å; Ni(I)–N = 1.85 (±0.05) *and* 2.00 (±0.03) Å, obtained by EXAFS), and in the above-mentioned tetraaza complex[18] (average Ni(II)–N = 1.93 (±0.02) Å, Ni(I)–N = 1.97 (±0.02) *and* 2.06 (±0.02) Å, EXAFS results). The validity of the EXAFS analyses and results for the Ni(I) species is supported by the subsequent crystallographic refinement of the Ni(I) tetraaza compound by Fujita and Szalda[18] that yielded Ni(I)–N values of 1.988 (7) and 2.068 (7) Å, and 1.979 (7) and 2.063 (7) Å for the two independent molecules in the unit cell. (The Ni(I) atom is strictly in plane.)

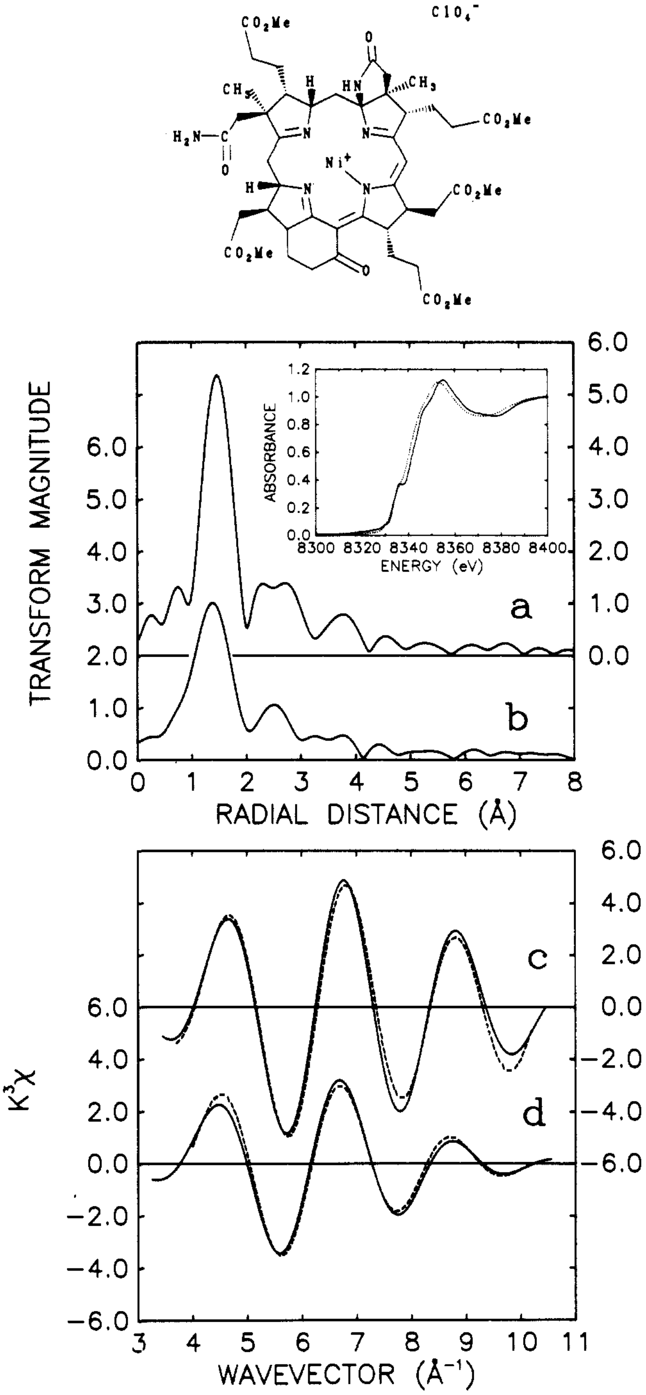

Figure 1. Structural formula of F430 M and X-ray absorption results for LS Ni(II) and Ni(I) F430 M, in THF at 298 K. Insert: Nickel K-edge spectra: Ni(II) (—) and Ni(I) (···). Top: Fourier transforms of k^3 weighted EXAFS oscillations: (a) Ni(II) and (b) Ni(I). Bottom: Isolated first-shell EXAFS oscillations (—) and nonlinear least-squares fits (- - -) for (c) Ni(II), 4 N at 1.90 Å, and (d) Ni(I), 2 N at 1.88 Å, 2 N at 2.03 Å.

The above results lead us to the following conclusions:

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[10] F430 M was a generous gift from Andrew F. Kolodziej of the Massachusetts Institute of Technology and was prepared as follows: *Methanobacterium thermoautotrophicum* strain H was grown as described by Schonheit et al.[11] F430 was isolated by the method of Diekert et al.,[12] and epimeric forms of F430 separated as described by Shiemke et al.[13] F430 was esterified with diazomethane and purified by TLC according to Pfaltz et al.[14] The final product gave a single spot on TLC. Its molecular weight (parent peak 975.5, FAB-MS) agreed with the reported value for F430 M,[14] as did its optical spectrum in tetrahydrofuran.[4] A complete description of the preparation will be presented elsewhere by A. F. Kolodziej, C. T. Walsh, and W. H. Orme-Johnson.

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[15] In butyronitrile, $E_{1/2}$ for F430 M = –0.95 V vs SCE and –1.41 V vs Fc/Fc⁺. For diepimeric F430 M, $E_{1/2}$ = –1.03 V vs SCE and –1.48 V vs Fc/Fc⁺ (0.1 M Bu_4NClO_4).

[16] Data were collected in the fluorescence mode on beam line X11A of the National Synchrotron Light Source at BNL by using Si 111 crystals. Additional details of the analyses can be found in refs 17 and 18.

[17] Furenlid, L. R.; Renner, M. W.; Smith, K. M.; Fajer, J. *J. Am. Chem. Soc.* **1990**, *112*, 1634.

[18] Furenlid, L. R.; Renner, M. W.; Szalda, D. J.; Fujita, E. *J. Am. Chem. Soc.*, in press.

[19] The optical and EPR spectra of Ni(I) F430 M obtained here agree with those previously reported.[4] λ_{max} = 754, 382, and 270 nm; *g* values: 2.062, 2.074, and 2.250 with a_N = 9.5 G. (Spectra are included in the supplementary material.) On the basis of the optical spectra, samples still comprised ≥80% Ni(I) after 8 h of EXAFS data collection.

[20] Furenlid, L. R.; Renner, M. W.; Fajer, J. *Rev. Sci. Instrum.* **1990**, *61*, 1326.

[21] The iBC and tetraaza ligands are anhydromesorhodochlorin XV methyl ester with ring C also saturated[17] and 5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradeca-4,11-diene,[18] respectively.

1. The low- and high-spin Ni(II) forms of F430 span a Ni–N range of 1.9–2.1 Å. On the basis of a series of model hydroporphyrins, corphins, and tetraaza complexes,[3,17,18] these distances reflect changes from puckered to planar macrocycle conformations, i.e., the F430 skeleton is quite flexible.
2. The Ni(II)–N distances of 1.9 and 2.1 Å found for low- and high-spin F430, respectively, match almost exactly the *strain-free* Ni(II)–N distances of 1.91 and 2.10 Å calculated for low- and high-spin Ni(II) polyamines by molecular mechanics.[22]
3. The Ni(II)–N distances of LS F430 and its 12,13-diepimer[9] are the same within experimental error. The observed different affinities for axial ligands of the two compounds[3,9] are, therefore, not due to significant differences in the equatorial nitrogens and may reflect steric constraints due to the different conformation of the diepimer,[3d] instead.
4. Since the F430 skeleton is flexible enough to accommodate changes of 0.2 Å around Ni(II), it can equally accommodate the distortion concomitant with reduction to Ni(I).

Acknowledgment. We are indebted to Andrew F. Kolodziej for the preparation of F430 M as part of a methanogenesis project directed by Christopher T. Walsh of the Harvard Medical School and William H. Orme-Johnson of the Massachusetts Institute of Technology and supported by National Institutes of Health Grant GM3-1574. We thank Profs. Walsh and Orme-Johnson for their assistance. The work at BNL was supported by the Division of Chemical Sciences, U.S. Department of Energy, under Contract DE-AC02-76CH00016. EXAFS experiments were performed at beam line X-11A of the National Synchrotron Light Source at BNL. X-11A is supported by the Division of Materials Sciences, U.S. Department of Energy, under Contract DE-FG05-89ER45384.

Supplementary Material Available: Optical, EPR, and EXAFS spectra of Ni(II) and Ni(I) F430 M (3 pages). Ordering information is given on any current masthead page.

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Novel Cis-Directed, Four-Electron Dioxo Oxidant

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The higher oxidation states of Ru and Os are accessible by loss of electrons and protons and metal oxo formation.[1] In complexes where there are two or more aqua ligands, oxidation state VI is attainable and several complexes having the *trans*-dioxo structure are known.[2] These complexes tend to be reactive oxidants. In this context, a *cis*-dioxo structure would be of more interest than the corresponding trans structure because of the possibility of achieving cis-directed, four-electron oxidations with the transfer of two O atoms to the same reductant. Normally, the *cis*-dioxo structure leads to an instability toward ligand loss and formation of *trans*-dioxo products. The driving force for the instability is the electronic stabilization associated with the *trans*-dioxo, d^2 electronic configuration.[2,3] We report here the preparation and characterization of *trans*-[Ru^{VI}(tpy)(O)$_2$(H$_2$O)]$^{2+}$ (**1**) (tpy is 2,2′:6′,2″-terpyridine), which overcomes this limitation. The complex is coordinatively stable yet has the desired reactivity as a cis-directed, four-electron oxidant, but in a novel and indirect way.

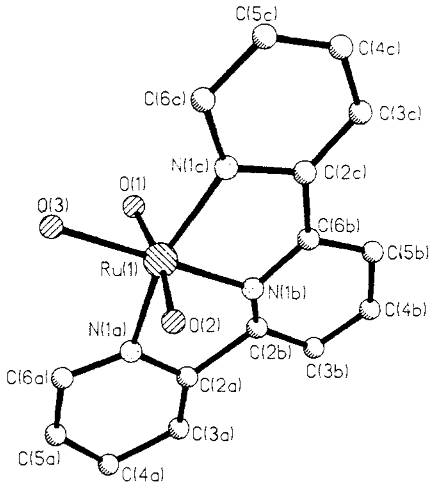

Figure 1. Crystal structure of the *trans*-[Ru(tpy)(O)$_2$(H$_2$O)]$^{2+}$ cation.

Complex **1** was prepared from [Ru^{II}(tpy)(C$_2$O$_4$)(H$_2$O)] in 2 M HClO$_4$ by the addition of excess (NH$_4$)$_2$Ce^{IV}(NO$_3$)$_6$.[4] This led to a color change from red-brown to yellow and precipitation of [Ru^{VI}(tpy)(O)$_2$(H$_2$O)](ClO$_4$)$_2$.[5] The structure of **1** has been determined by X-ray crystallography and is illustrated in Figure 1.[6] Four important features emerge from the structure: (a) the coordination geometry is approximately octahedral; (b) the disposition of the oxo groups is trans; (c) the average Ru═O bond length is 1.661 Å, compared to 2.128 Å for the Ru—O bond of the aqua group, 1.765–1.862 Å for oxo groups bound to Ru(IV), or 1.705–1.732 Å for oxo groups bound to Ru(VI);[7] and (d) the

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(4) The complex [Ru(tpy)(C$_2$O$_4$)(H$_2$O)] was prepared by heating Ru(tpy)Cl$_3$ and Na$_2$C$_2$O$_4$ is CH$_3$OH/H$_2$O under N$_2$. The complex was isolated as the monohydrate. Adeyemi, S. A.; Guadalupe, A.; Meyer, T. J., manuscript in preparation.

(5) Anal. Calcd for C$_{15}$H$_{15}$N$_3$O$_{12}$Cl$_2$Ru: C, 29.95; H, 2.49; N, 6.99; Cl, 11.80. Found: C, 29.87; H, 2.58; N, 6.87; Cl, 12.24.

(6) Data were collected on a Nicolet R3m/V diffractometer at 173 K by using Mo Kα radiation. The space group was $P2_1/n$ with a = 7.950 (13) Å, b = 18.940 (20) Å, c = 14.000 (16) Å, β = 102.08 (11)°, V = 2061 (4) Å^3, Z = 4, and FW = 599.21. For 1020 observed reflections and variables, the current discrepancy indices are R = 10.9% and R_w = 10.7%. We are currently attempting to grow crystals of higher quality in order to refine the structure further.

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