

Aminopyridine Iron Catecholate Complexes as Models for Intradiol Catechol Dioxygenases. Synthesis, Structure, Reactivity, and Spectroscopic Studies

Pierre Mialane,^{1a} Luba Tchertanov,^{1b} Frédéric Banse,^{1a} Joelle Sainton,^{1a} and Jean-Jacques Girerd^{*,1a}

Laboratoire de Chimie Inorganique, UMR CNRS 8613, Institut de Chimie Moléculaire d'Orsay, Université Paris-Sud, 91405 Orsay, France, and Institut de Chimie des Substances Naturelles, UPR CNRS 2301, 91198 Gif-sur-Yvette, France

Received October 21, 1998

Four new Fe(III) catecholate complexes, [(bispicMe₂en)Fe^{III}(DBC)]⁺, [(bispicCl₂Me₂en)Fe^{III}(DBC)]⁺, [(trispicMeen)Fe^{III}(DBC)]⁺, and [(BQPA)Fe^{III}(DBC)]⁺, which all contain aminopyridine ligands, were synthesized. The structure of [(bispicMe₂en)Fe^{III}(DBC)]⁺ was determined by X-ray diffraction. It crystallizes in the triclinic space group *P*1̄ with *a* = 10.666(3) Å, *b* = 13.467(5) Å, *c* = 17.685(2) Å, α = 93.46(2)°, β = 93.68(2)°, γ = 109.0(3)°, *V* = 2387.4 Å³, and *Z* = 2. All of these complexes were found to be active toward oxidation of catechol by O₂ in DMF at 20 °C to afford intradiol cleavage products. The catechol was quantitatively oxidized, mainly (90%) into 3,5-di-*tert*-butyl-5-(carboxymethyl)-2-furanone. Reaction rates were measured, and for the first three (topologically similar) complexes, a correlation of the second-order kinetic constants *k* with the optical parameters of the two LMCT O(DBC) → Fe(III) bands was found. In particular, *k* increases with the ε_{max} of the charge-transfer bands. The *k* value of the complex [(BQPA)Fe^{III}(DBC)]⁺, containing a tripodal ligand, is smaller than expected on the basis of these correlations. This discrepancy could be related to steric hindrance induced by the BQPA ligand. However, the much lower activity of the bispicen-Fe(III)-type complexes compared to that of the [(TPA)Fe^{III}(DBC)]⁺ complex synthesized by Jang et al. (*J. Am. Chem. Soc.* **1991**, *113*, 9200–9204), despite similar ε_{max} values, shows that a knowledge of optical and NMR parameters values is not sufficient to explain the dioxygenase activity rate. In their study of protocatechuate 3,4-dioxygenase, Orville et al. (*Biochemistry* **1997**, *36*, 10052–10066) suggested that asymmetric chelation of the catecholate to Fe(III) is of great importance in the efficiency of the intradiol dioxygenase reaction. Indeed, a comparison of the X-ray structures of [(TPA)Fe^{III}(DBC)]⁺ and [(bispicMe₂en)Fe^{III}(DBC)]⁺ shows that the Fe(III)–O bonds differ by 0.019 Å in the former and are identical in the latter. Asymmetry could also play a role in the model complexes. An alternative explanation is the possible existence of a low-spin state for [(TPA)Fe^{III}(DBC)]⁺, as recently identified in [(TPA)Fe^{III}(cat)]⁺ by Simaan et al. (*Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 196–198).

Catechol dioxygenases catalyze the last step in the degradation of aromatic compounds. They have been extensively studied from both biochemical and chemical modeling points of view.² Intradiol dioxygenases contain in the active site an Fe(III) ion coordinated to two tyrosine groups, two histidines, and an OH[−] anion. This structure has been inferred from model studies and confirmed by X-ray diffraction.³ The group of L. Que has made a major contribution to the modeling of intradiol dioxygenases. In their early studies, they developed models with Fe(salen)X.⁴ These complexes showed a very weak dioxygenase activity, despite a structure similar to that of the enzyme active site. Extensive work has been done in order to increase the reaction rate. The group of Que insisted on the importance of using an auxiliary ligand favoring the electron transfer from the catecho-

late group to the Fe(III),⁵ and along this line, they demonstrated the rapid stoichiometric oxidation of catechol in the [(TPA)Fe(DBC)]⁺ complex.⁶ In 1995, Koch and Krüger discovered the catalysis of the same reaction by an Fe(III) complex of *N,N'*-dimethyl-2,11-diaza[3.3](2,6)pyridinophane.⁷ The macrocyclic nature of that ligand certainly contributes to the stabilization of the corresponding Fe(III) complex, even in the presence of an excess of catecholate in catalytic conditions. Duda et al.⁸ used an Fe(III) complex of a TPA analogue in which one pyridine group was replaced by *N*-methylimidazole to achieve an efficient catalysis. Funabiki et al.⁹ have shown that the Fe(III) complex with TPA itself can catalyze the oxygenative cleavage of chlorocatechols.

We concentrated our study on the synthesis, characterization, and mechanism of catecholate degradation for a series of [LFe^{III}(DBC)]⁺ complexes in which L is a ligand of the bispicen

- (1) (a) Université Paris-Sud. (b) Institut de Chimie des Substances Naturelles.
- (2) (a) Lipscomb, J. D.; Orville, A. M. In *Metal Ions in Biological Systems*; Sigel, H., Sigel, A., Eds.; Marcel Dekker: New York, 1992; Vol. 28, pp 243–298. (b) Que, L., Jr. In *Iron Carriers and Iron Proteins*; Loehr, T. M., Ed.; VCH: New York, 1989; pp 467–524.
- (3) Ohlendorf, D. H.; Orville, A. M.; Lipscomb, J. D. *J. Mol. Biol.* **1994**, *244*, 586–608.
- (4) (a) Lauffer, R. B.; Heistand, R. H., II; Que, L., Jr. *Inorg. Chem.* **1983**, *22*, 50–55. (b) Heistand, R. H., II; Roe, A. L.; Que, L., Jr. *Inorg. Chem.* **1982**, *21*, 676–681.

- (5) Lauffer, R. B.; Heistand, R. H., II; Que, L., Jr. *J. Am. Chem. Soc.* **1981**, *103*, 3947–3949.
- (6) Jang, H. G.; Cox, D. D.; Que, L., Jr. *J. Am. Chem. Soc.* **1991**, *113*, 9200–9204.
- (7) Koch, W. O.; Krüger, H.-J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2671–2674.
- (8) Duda, M.; Pascaly, M.; Krebs, B. *Chem. Commun.* **1997**, 835.
- (9) Funabiki, T.; Yamazaki, T.; Fukui, A.; Tanaka, T.; Yoshida, S. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 513.

family. To this set, we added the complex $[(\text{BQPA})\text{Fe}^{\text{III}}(\text{DBC})]^+$, where BQPA is the bis(2-quinolylmethyl)(2-pyridylmethyl)amine ligand, which is a strong π -acceptor. The goal of this study is the elucidation of the role of electronic, steric, and symmetry factors in the process of catecholate degradation.

Experimental Section

Materials. Aerobic conditions were used for ligand syntheses, whereas complex syntheses were performed under anaerobic conditions. Chemical starting materials were purchased from Aldrich and used as received. Solvents were dried before use.

Ligand Preparation. Bis(2-quinolylmethyl)(2-pyridylmethyl)amine (BQPA). To a solution of 2-aminomethylpyridine (1.06 g, 10 mmol) in 50 mL of acetonitrile was added a solution of 2-chloromethylquinoline·HCl (4.3 g, 20 mmol) in 50 mL of acetonitrile. Then, 7 g of sodium carbonate was added, and the mixture was stirred for 2 days at 50 °C. After filtration, the solvent was evaporated under vacuum. The orange powder collected was recrystallized in hexane to give a yellow, microcrystalline powder (yield, 80%). ^1H NMR (250 MHz): δ 8.5 (d, 1H, H-py), 8.1 (d, 2H, H-qui), 8.0 (d, 2H, H-qui), 7.7 (m, 8H, H-qui), 7.5 (m, 2H, H-py), 7.1 (t, 1H, H-py), 4.1 (s, 4H, CH₂-qui), 3.9 (s, 2H, CH₂-py).

***N,N'*-Dimethyl-*N,N'*-bis(2-pyridylmethyl)ethane-1,2-diamine (BispicMe₂en).** The ligand bispicMe₂en was synthesized as previously described.¹⁰

***N,N'*-Dimethyl-*N,N'*-bis(4-chloro-2-pyridylmethyl)ethane-1,2-diamine (BispicCl₂Me₂en).** The ligand bispicCl₂Me₂en was a gift from Professor J.-B. Verlhac (University of Bordeaux, Bordeaux, France).¹¹

***N*-Methyl-*N,N',N''*-tris(2-pyridylmethyl)ethane-1,2-diamine (TrispicMeen).** The ligand trispicMeen was synthesized as previously described.¹² This ligand has also been described by Bernal et al.¹³

Preparation of Complexes. [(BQPA)Fe^{III}(DBC)]BPh₄. A solution of BQPA (390 mg, 1 mmol) in 10 mL of ethanol was added under argon to anhydrous FeCl₃ (162 mg, 1 mmol) dissolved in 10 mL of ethanol. The yellow mixture was stirred at room temperature for 30 min, and DBCH₂ (222 mg, 1 mmol) dissolved in 5 mL of ethanol was then added, followed by a dropwise addition of triethylamine (280 μL , 2 mmol) in 5 mL of ethanol. The solution turned blue, and sodium tetraphenylborate (342 mg, 1 mmol) in 5 mL of ethanol was added. A deep blue powder immediately precipitated and was filtered and washed with a small amount of ethanol. Anal. Found: C, 78.0; H, 6.3; N, 5.7. Calcd for C₆₄H₆₄N₄O₂FeB: C, 77.5; H, 6.3; N, 5.9.

[(BispicMe₂en)Fe^{III}(DBC)]BPh₄. A solution of bispicMe₂en (270 mg, 1 mmol) in 10 mL of methanol was added to a solution of anhydrous FeCl₃ (162 mg, 1 mmol) in 25 mL of methanol. The mixture was stirred at room temperature for 30 min, after which DBCH₂ (222 mg, 1 mmol) and 2 mmol of triethylamine (280 μL , 2 mmol) dissolved in 10 mL of methanol were added. The mixture was stirred at room temperature for 30 min, and then sodium tetraphenylborate (342 mg, 1 mmol) in 5 mL of methanol was added. A purple powder precipitated, which was filtered and washed with 10 mL of methanol and then recrystallized in acetonitrile under a nitrogen flow. Crystals of [(bispicMe₂en)Fe^{III}(DBC)]BPh₄ suitable for X-ray diffraction studies were obtained. Anal. Found: C, 74.8; H, 7.2; N, 6.5; Fe, 6.4. Calcd for C₅₄H₆₂N₄O₂FeB: C, 74.0; H, 7.2; N, 6.5; Fe, 6.4.

[(BispicCl₂Me₂en)Fe^{III}(DBC)]BPh₄·CH₃OH. Synthesis of this complex is identical to that described for [(bispicMe₂en)Fe^{III}(DBC)]BPh₄. Anal. Found: C, 69.3; H, 6.5; N, 6.0; Cl, 7.6. Calcd for C₅₄H₆₀N₄O₂Cl₂FeB: C, 68.8; H, 6.5; N, 5.9; Cl, 7.9.

Table 1. Crystallographic Data for [(BispicMe₂en)Fe^{III}(DBC)]BPh₄

formula	C ₅₄ H ₆₂ N ₄ O ₂
fw	865.74
radiation	Mo K α (0.71073 Å)
temp, K	294(2)
space group	$P\bar{1}$
<i>a</i> , Å	10.666(3)
<i>b</i> , Å	13.467(5)
<i>c</i> , Å	17.685(2)
α , deg	93.46(2)
β , deg	93.68(2)
γ , deg	109.0(3)
<i>V</i> , Å ³	2387.4(11)
<i>Z</i>	2
μ , mm ⁻¹	0.360
<i>N</i> _{meas}	11152
<i>N</i> _{obs}	10958
<i>R</i>	0.0393
<i>R</i> _w	0.0903

[(TrispicMeen)Fe^{III}(DBC)]BPh₄. A solution of trispicMeen (227 mg, 1 mmol) in 10 mL of ethanol was added to a solution of anhydrous FeCl₃ (162 mg, 1 mmol) in 10 mL of ethanol. The resulting yellow solution was stirred for 30 min at room temperature. A solution of DBCH₂ (222 mg, 1 mmol) in 5 mL of ethanol was then added, followed by a dropwise addition of triethylamine (280 μL , 2 mmol) in 5 mL of ethanol. The blue solution was stirred for 30 min at 50 °C and then allowed to cool to room temperature, and sodium tetraphenylborate (342 mg, 1 mmol) was added. Finally, 10 mL of distilled water was very slowly added while the solution was vigorously stirred at -15 °C for 1 h. A blue powder precipitated and was filtered and washed with a small amount of ethanol. Anal. Found: C, 74.6; H, 6.9; N, 7.4; Fe, 5.9; B, 1.1. Calcd for C₅₉H₆₅N₅O₂FeB: C, 74.1; H, 6.9; N, 7.4; Fe, 6.1; B, 1.0.

Studies of Oxygenated Products. The following procedure was used for all of the complexes described. A solution of 0.5 mmol of complex in 5 mL of DMF was stirred at room temperature with bubbling oxygen. When the solution turned brown, the mixture was dried under vacuum. The brown oil obtained was diluted with water (pH 8), extracted with ether, and dried under vacuum. The pH of the remaining aqueous solution was decreased to a value of 2 by addition of a 0.01 N HCl solution, and the second oil was extracted with ether and dried. The two oils were studied by ^1H NMR and infrared spectroscopy.

NMR Studies. NMR spectra were recorded on a Bruker AM250 spectrometer using CDCl₃ or CD₃CN as the internal lock. *T*₁ values were determined using an inversion-recovery pulse sequence (π - τ - $\pi/2$ -ACQ).

UV-Vis Studies. Spectra and kinetic studies were recorded at 20 °C in DMF with a Varian Cary 5E spectrophotometer.

Crystallographic Data Collection and Refinement of Structure. [(BispicMe₂en)Fe^{III}(DBC)]BPh₄. A single crystal of dimensions 0.33 × 0.15 × 0.10 mm³ was mounted on a four-circle Philips PW1100 diffractometer with graphite monochromated Mo K α radiation ($\lambda = 0.71073$ Å). The unit cell was obtained by least-squares procedures based on the 2θ values of the 25 reflections measured ($8.4^\circ < 2\theta < 14.4^\circ$). All reflection intensities were collected at room temperature in the range $4^\circ < 2\theta < 40^\circ$ for $-14 < h < 13$, $-17 < k < 17$, and $0 < l < 23$. A total of 10 958 independent reflections was collected. The structure was solved by direct methods (SHELXS86)¹⁴ and refined by full least-squares approximation based on *F*². Crystallographic data are presented in Table 1. Refinement was anisotropic for all non-H atoms. Hydrogen positions were calculated by assuming geometrical positions and were included in the structural model. Clusters of electronic residual appeared in a subsequent *F*_o - *F*_c synthesis. Anisotropic full-matrix least-squares refinement of this structural model was continued until convergence when *R* = 0.0393 and *R*_w = 0.0903 for all 10 958 reflections. The final difference map showed the largest residual peaks of 0.331 and -0.234 eÅ⁻³ (the latter being on a symmetry center).

(14) Sheldrick, G. M. *SHELXS86: Program for the Solution of Crystal Structures*; University of Göttingen: Göttingen, Germany, 1986.

(10) Toftlund, H.; Pedersen, E.; Yde-Andersen, S. *Acta Chem. Scand., Ser. A* **1984**, *38*, 429.

(11) Delroisse, M. Thesis, Université de Bordeaux I, Bordeaux, France, 1995. Delroisse, M.; Rabion, A.; Chardac, F.; Tétard, D.; Verlhac, J.-B.; Fraisse, L.; Séris, J.-L. *J. Chem. Soc., Chem. Commun.* **1995**, 949.

(12) Nivorozhkin, A. L.; Anxolabéhère-Mallart, E.; Mialane, P.; Davydov, R.; Guilhem, J.; César, M.; Audière, J.-P.; Girerd, J.-J.; Styring, S.; Schussler, L.; Seris, J.-L. *Inorg. Chem.* **1997**, *36*, 846-853.

(13) Bernal, I.; Jensen, I. M.; Jensen, K. B.; McKenzie, C. J.; Toftlund, H.; Tuchagues, J. P. *J. Chem. Soc., Dalton Trans.* **1995**, 3667.

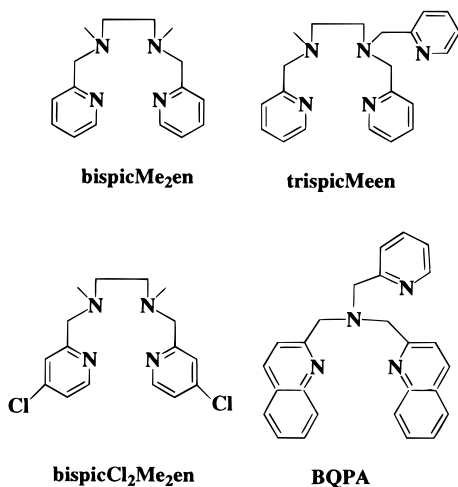


Figure 1. Ligands used in this study.

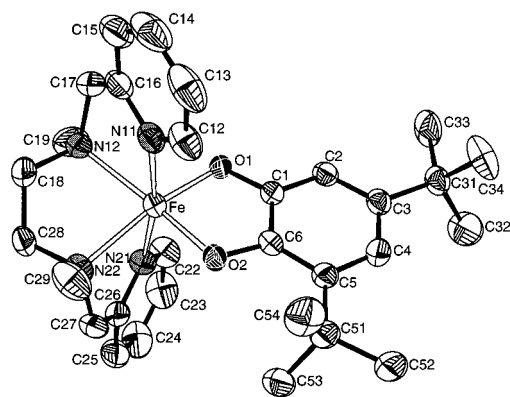


Figure 2. Structure of the [(bispicMe₂en)Fe(DBC)]⁺ dication showing the 50% probability thermal ellipsoids and atom-labeling scheme. Hydrogen atoms are omitted for clarity.

Results and Discussion

The ligands used in this study are represented in Figure 1. The ligands bispicMe₂en and bispicCl₂Me₂en are of the linear tetradentate type. The chloropyridine derivative was used to study the electronic effect of the chloro substituent. The influence of an extra pyridine group was studied with the pentadentate ligand trispicMeen. The ligand BQPA is a tetradentate tripodal analogue of TPA. Elementary analyses and spectroscopic data show that every compound contains the [LFe^{III}(DBC)]⁺ entity. In the case of [(bispicMe₂en)Fe^{III}(DBC)]BPh₄, the structure was determined by X-ray diffraction.

Structure of [(BispicMe₂en)Fe^{III}(DBC)]BPh₄. The [(bispicMe₂en)Fe^{III}(DBC)]⁺ cation is represented in Figure 2. It has a distorted octahedral geometry, the catechololate dianion being chelated to Fe(III). As usual, the bispicMe₂en ligand has the *cis* α configuration. This structure has already been noted by Glerup et al.¹⁵ and by Arulsamy et al.¹⁶ The metal–ligand bond distances (Table 2) are Fe–N(pyridine) = 2.163(6) and 2.176(7) Å, Fe–N(amine) = 2.210(4) and 2.205(4) Å, and Fe–O = 1.914(4) and 1.914(2) Å. As expected, the Fe–O distances are similar to each other for [(bispicMe₂en)Fe^{III}(DBC)]⁺ and [(L–N₄Me₂)Fe^{III}(Cat)]⁺ [1.915(3) and 1.903(3) Å, respectively].⁷ In [(TPA)Fe^{III}(DBC)]⁺,⁶ the chelation of catechololate is slightly

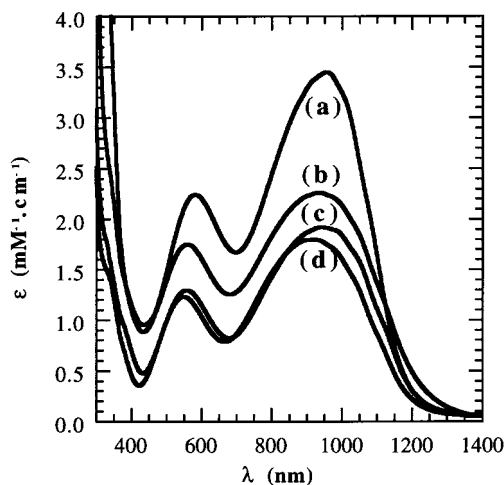


Figure 3. UV–visible spectra in DMF at 20 °C of the complexes (a) [(BQPA)Fe^{III}(DBC)]⁺, (b) [(trispicMeen)Fe^{III}(DBC)]⁺, (c) [(bispicCl₂Me₂en)Fe^{III}(DBC)]⁺, and (d) [(bispicMe₂en)Fe^{III}(DBC)]⁺.

Table 2. Selected Bond Lengths (Å) and Angles (deg) for [(BispicMe₂en)Fe^{III}(DBC)]BPh₄

Fe–O(2)	1.914(4)	C(1)–O(1)	1.344(3)
Fe–O(1)	1.914(2)	C(6)–O(2)	1.346(2)
Fe–N(11)	2.163(6)	C(1)–C(2)	1.391(3)
Fe–N(21)	2.176(7)	C(2)–C(3)	1.384(3)
Fe–N(22)	2.205(4)	C(3)–C(4)	1.399(3)
Fe–N(12)	2.210(4)	C(4)–C(5)	1.393(3)
		C(5)–C(6)	1.403(3)
		C(6)–C(1)	1.418(3)
O(2)–Fe–O(1)	85.72(6)		
O(2)–Fe–N(11)	94.69(13)		
O(1)–Fe–N(11)	94.1(2)		
O(2)–Fe–N(21)	94.05(9)		
O(1)–Fe–N(21)	91.1(2)		
N(11)–Fe–N(21)	170.15(7)		
O(2)–Fe–N(22)	90.85(8)		
O(1)–Fe–N(22)	166.01(6)		
N(11)–Fe–N(22)	99.7(2)		
N(21)–Fe–N(22)	75.6(2)		
O(2)–Fe–N(12)	166.83(7)		
O(1)–Fe–N(12)	103.51(7)		
N(11)–Fe–N(12)	75.52(11)		
N(21)–Fe–N(12)	95.12(8)		
N(22)–Fe–N(12)	82.32(8)		

asymmetric [1.917(3) and 1.898(2) Å], but the asymmetry is more pronounced for [(BPG)Fe^{III}(DBC)]⁺ [1.989(2) and 1.889(2) Å]. In [(bispicMe₂en)Fe^{III}(DBC)]⁺, the catechololate dianion presents C–O distances of 1.344(3) and 1.346(2) Å and C–C distances between 1.384(3) and 1.418(3) Å. The analogous distances in [(TPA)Fe^{III}(DBC)]⁺ are very close.⁶ These values for the catechololate dianion are quite different from those observed for the semiquinonato DBSQ^{•-} anion in the [LFe^{III}(DBSQ)] complex, where LH₂ = *N,N'*-bis(4-methyl-6-*tert*-butyl-2-methylphenolato)-*N,N'*-bismethyl-1,2-diaminoethane.¹⁸

UV–Visible Spectroscopy. The electronic absorption spectra of the [LFe^{III}(DBC)]⁺ complexes in DMF solution (Figure 3) exhibit two prominent bands, one in the visible (λ_1 = 550–582 nm) region and one in the NIR (λ_2 = 925–957 nm) (Table 3). The same type of spectrum has been observed in [(BPG)Fe^{III}(DBC)]⁺,^{17,19} [(TPA)Fe^{III}(DBC)]⁺,⁶ [(NTA)Fe^{III}(DBC)]²⁻,^{17,19} [(L–N₄Me₂)Fe^{III}(DBC)]⁺,⁷ and [(SS–CTH)Fe^{III}(DBC)]⁺.²⁰ The

(15) Glerup, J.; Goodson, P. A.; Hazell, A.; Hazell, R.; Hodgson, D. J.; McKenzie, C. J.; Michelsen, K.; Rychlewska, U.; Toftlund, H. *Inorg. Chem.* **1994**, *33*, 4105–4111.

(16) Arulsamy, N.; Hodgson, D. J.; Glerup, J. *Inorg. Chim. Acta* **1993**, *209*, 61.

(17) Cox, D. D.; Que, L., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 8085–8092.

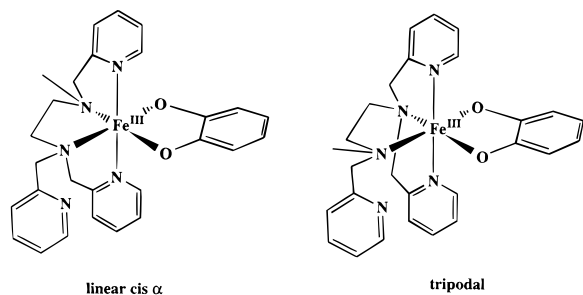
(18) Mialane, P.; Anxolabéhère-Mallart, E.; Blondin, G.; Nivorozhkin, A. L.; Guilhem, J.; Tchertanova, L.; Cesario, M.; Ravi, N.; Bominaar, E.; Girerd, J.-J.; Münck, E. *Inorg. Chim. Acta* **1997**, *263*, 367.

Table 3. Spectroscopic and Kinetic Data

	λ_1, ϵ_1 λ_2, ϵ_2 (nm, mM ⁻¹ cm ⁻¹)	δ (4-H) ^b 5- <i>t</i> -Bu, 4-H	$k[\text{O}_2]$ ^c (s ⁻¹)	k^c (M ⁻¹ s ⁻¹)
TPA	548 (1.76) 874 (2.45)	8.7, -55.4	0.0465 ^d	15 ^d
trispicMeen	560 (1.85) 935 (2.35)	9.95, -82.0	8.68×10^{-4}	0.28
bispicCl ₂ Me ₂ en	557 (1.30) 941 (1.90)	9.7, -70.0	4.96×10^{-4}	0.16
BQPA	582 (2.23) 957 (3.45)	9.9, -89.0	4.03×10^{-4}	0.13
bispicMe ₂ en	550 (1.25) 925 (1.85)	9.0, -59.5	8.06×10^{-5}	0.026

^a In DMF. ^b In CD₃CN. ^c In DMF at 20 °C. ^d In DMF at 25 °C.

two bands have been attributed to ligand-to-metal charge transfers O(DBC) → Fe(III).^{17,20,21} Their characteristics depend on the nature of the auxiliary ligand L. The similarity between the electronic absorption spectra of the complexes [(bispicMe₂en)Fe^{III}(DBC)]⁺, [(BQPA)Fe^{III}(DBC)]⁺, [(bispicCl₂Me₂en)Fe^{III}(DBC)]⁺, and [(trispicMeen)Fe^{III}(DBC)]⁺ indicates that, in each case, the catecholato dianion is chelated to Fe(III). The bispicen moiety must present a cis α configuration in the [(bispicCl₂Me₂en)Fe^{III}(DBC)]⁺ complex, as it does in [(bispicMe₂en)Fe^{III}(DBC)]⁺. The ligand trispicMeen has been extensively studied, and it has been shown that this ligand can act as a tetradentate¹² or pentadentate ligand.^{13,22} As depicted below for the tetradentate case, two types of structure for the [(trispicMeen)Fe^{III}(DBC)]⁺ complex can be envisioned: either one with the ligand trispicMeen adopting a linear cis α mode of coordination or one in which the ligand plays the role of a tripodal ligand. Analogy with the previously characterized compound [(trispicMeen)ClFe^{III}OFe^{III}Cl(trispicMeen)]²⁺¹² is in favor of a linear cis α geometry.



The structure of the [(BQPA)Fe^{III}(DBC)]⁺ complex must be different from that of the complexes described above but similar to that of [(TPA)Fe^{III}(DBC)]⁺.⁶ However, we cannot make a conclusion about the cis or trans configuration of the two quinoline groups.

NMR Studies. The ¹H NMR spectrum of [(BQPA)Fe^{III}(DBC)]⁺ in CD₃CN shows large contact shifts. By comparison with the results by Jang et al.⁶ on [(TPA)Fe^{III}(DBC)]⁺ and by the use of T_1 values and integrations, it is possible to partially assign the resonances observed for [(BQPA)Fe^{III}(DBC)]⁺. The pyridine meta protons appear as relatively sharp features at 91

ppm with T_1 values of 0.78 ms. The pyridine ortho proton is broadened because of its proximity to the metal center and is shifted further downfield at 190 ppm. The pyridine para proton resonates in the diamagnetic region at 1.3 ppm. Additional peaks arise from the methylene protons, which appear as a broad band at 107 ppm with a T_1 value of 0.44 ms. The similarity with [(TPA)Fe^{III}(DBC)]⁺ is striking. The quinoline protons 3-H and 8-H appear at 48 and 51 ppm although we did not assign these two resonances more precisely. We tentatively assign the other quinoline protons as 4-H (1.2 ppm), 5-H and 6-H (15 ppm, which integrates for four protons), and 7-H (43 ppm). Additional peaks arise from the methylene protons, which appear as a broad band at 74 ppm with a T_1 value of 0.58 ms. The DBC 6-H and 4-H protons exhibit shift at -5 and -89 ppm, respectively. The DBC 5-*t*-Bu and 3-*t*-Bu resonances are found at 9.9 (6.0 ms) and 5.5 ppm, respectively.

As noted by Jang et al.,⁶ the more upfield proton in this type of complex corresponds to the 4-H DBC proton. This proton is recognized in this series of complexes at the following shifts: bispicMe₂en, -59.5 ppm; bispicCl₂Me₂en, -70.0 ppm; trispicMeen, -82.0 ppm; and BQPA, -89.0 ppm. For the DBC 5-*t*-Bu resonance, a similar order was observed: bispicMe₂en, 9.0 ppm; bispicCl₂Me₂en, 9.7 ppm; BQPA, 9.9 ppm; and trispicMeen, 9.95 ppm. As noted by Jang et al.,⁶ these paramagnetic shifts reflect the amount of the Fe(II)(SQ) form in the ground-state wave function, which can be written as $\Phi_{\text{Fe(III)(Cat)}} + \alpha\Phi_{\text{Fe(II)(SQ)}}$. We observed a correlation for the δ (4-H) with λ_1 values. This correlation is similar for δ (4-H) and λ_2 , but an inversion is found for [(BQPA)Fe^{III}(DBC)]⁺ and [(trispicMeen)Fe^{III}(DBC)]⁺. The correlation between δ and λ_{max} is in keeping with the idea that the lower in energy the excited Fe(II)(SQ) form is, the larger is the contribution of this excited form in the ground state. This is true because simple perturbation theory gives $\alpha = |H_{\text{AB}}|/h\nu_{\text{max}}$, where H_{AB} is the transfer integral between the d orbital and the implied π orbital and $h\nu_{\text{max}}$ is the energy gap between the states. The existence of this correlation suggests that H_{AB} does not change much in the series of complexes that we investigated. We have identified another correlation. The intensity of a CT transition is related to α^2 ,²³ so we can expect a relation between δ and ϵ_{max} . Indeed, we found that the δ (4-H) values are strictly correlated to the ϵ_1 and ϵ_2 values, as depicted in Figure 4.

It must be noticed that [(TPA)Fe^{III}(DBC)]⁺ does not follow this correlation: the molar absorptivity $\epsilon_2 = 2.45 \text{ mM}^{-1} \text{ cm}^{-1}$ is much larger than expected on the basis of the NMR shift δ (4-H) = -55.4 ppm, which is the lowest in this series of complexes.

Reactivity Studies. The reactivity of each complex with O₂ in saturating conditions was studied in DMF at 20 °C. The reaction was stopped after 6 h for [(trispicMeen)Fe^{III}(DBC)]⁺, 24 h for [(BQPA)Fe^{III}(DBC)]⁺, and 48 h for [(bispicMe₂en)Fe^{III}(DBC)]⁺ and [(bispicCl₂Me₂en)Fe^{III}(DBC)]⁺. A quantitative analysis of the reaction products was made by NMR. In every case, neither 3,5-di-*tert*-butylcatechol nor 3,5-di-*tert*-butylquinone was observed. The catechol was then quantitatively degraded. The major and almost only product (90%) is 3,5-di-*tert*-butyl-5-(carboxymethyl)-2-furanone. The muconic anhydride is always observed as a minor product (<5%). Jang et al.⁶ observed the same products, although with a larger muconic anhydride quantity. The difference could be due to the longer reaction times used here. Indeed, the furanone is the hydrolysis

(19) Cox, D. D.; Benkovic, S. J.; Bloom, L. M.; Bradley, F. C.; Que, L., Jr.; Wallick, D. E. *J. Am. Chem. Soc.* **1988**, *110*, 2026.

(20) Dei, A.; Gatteschi, D.; Pardi, L. *Inorg. Chem.* **1993**, *32*, 1389.

(21) Salama, S.; Stong, J. D.; Neilands, J. B.; Spiro, T. G. *Biochemistry* **1978**, *17*, 3781.

(22) Mialane, P.; Nivorojkine, A.; Pratviel, G.; Azéma, L.; Slany, M.; Godde, F.; Simaan, A.; Banse, F.; Kargar-Grisel, T.; Bouchoux, G.; Sainton, J.; Horner, O.; Guilhem, J.; Tchertanov, L.; Meunier, B.; Girerd, J.-J. *Inorg. Chem.* **1999**, *38*, 1085–1092.

(23) Hush, N. S. In *Progress in Inorganic Chemistry*; Cotton, F. A., Ed.; Wiley: New York, 1967; Vol. 8, p 437.

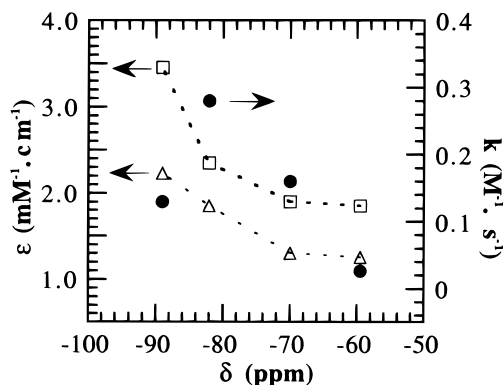


Figure 4. Correlation between δ (4-H) and ϵ_1 or ϵ_2 for the complexes [(BQPA)Fe^{III}(DBC)]⁺ ($\delta = -89.0$ ppm), [(trispicMeen)Fe^{III}(DBC)]⁺ ($\delta = -82.0$ ppm), [(bispicCl₂Me₂en)Fe^{III}(DBC)]⁺ ($\delta = -70.0$ ppm), and [(bispicMe₂en)Fe^{III}(DBC)]⁺ ($\delta = -59.5$ ppm). The second-order rate constant k in DMF at 20 °C is represented as a function of δ (4-H). For the three topologically similar complexes, k increases when the chemical shift decreases. The k value for [(BQPA)Fe^{III}(DBC)]⁺ ($\delta = -89.0$ ppm) is lower than expected (see text).

product of the anhydride, and the larger amount of anhydride was obtained for the shorter reaction time {(trispicMeen)Fe^{III}(DBC)]⁺.

Kinetic measurements were made for all of the complexes in DMF at 20 °C. The pseudo-first-order constants were deduced from simulation, and the second-order constants were calculated using $[O_2] = 3.1 \times 10^{-3}$ M in DMF at 20 °C (Table 3).²⁴ The series does not follow that deduced from UV-vis and NMR (Figure 4) data. Nevertheless, if we focus on the topologically similar complexes [(bispicMe₂en)Fe^{III}(DBC)]⁺, [(bispicCl₂Me₂en)Fe^{III}(DBC)]⁺, and [(trispicMeen)Fe^{III}(DBC)]⁺, the correlation is verified (Figure 4). A decrease of the δ (4-H) value or an increase of the ϵ_{\max} value, both of which signify a larger contribution of the Fe(II)(SQ) form to the ground state, leads to better reactivity. The introduction of a σ -attractor group on the pyridine ring leads to an improvement of the reactivity. The k value found for the complex [(BQPA)Fe^{III}(DBC)]⁺ is smaller than expected on the basis of the large paramagnetic shift observed for the 4-H proton. We propose that this low reactivity is due to the large steric hindrance of the quinolines to the metal center, which can affect the formation of the μ -peroxo intermediate postulated in the mechanism of intradiol dioxygenases.²⁵

The complex [(TPA)Fe^{III}(DBC)]⁺, synthesized by the group of L. Que, remains the most active model complex leading to degradation of catechol. This observation is not in agreement with the correlation found here for the bispicen-type ligands. The most striking disagreement is that the [(TPA)Fe^{III}(DBC)]⁺ complex has the smallest NMR shift (δ (1H, 4-H) = -55.4 ppm) but nevertheless presents the fastest reaction. Steric considerations cannot explain this phenomenon. The high reactivity of [(TPA)Fe^{III}(DBC)]⁺ is intriguing.

One possible explanation could rely on subtle structural differences between [(TPA)Fe^{III}(DBC)]⁺ and [(bispicMe₂en)-

Fe^{III}(DBC)]⁺. For the latter, the two amino groups are trans to the two oxygens of DBC²⁻, leading to two equivalent Fe–O bonds. In contrast, for the former, one oxygen of the substrate is trans to an amino group, and the other is trans to the nitrogen of a pyridine. This asymmetry could influence the reactivity, as pointed out recently for the corresponding enzymes by Orville et al.²⁵

An alternative explanation could be related to the recent observation by Simaan et al. of a spin equilibrium in [(TPA)Fe^{III}(cat)]⁺ in the solid state. It could be that such a spin equilibrium exists in solution for [(TPA)Fe^{III}(DBC)]⁺, leading to the presence of a small fraction at room temperature of low-spin [(TPA)Fe^{III}(DBC)]⁺, and that this low-spin species is at the origin of the high reactivity observed. The problem of the spin state of Fe(III)/aminopyridine/catecholate systems must be explored in detail.

Conclusion

We isolated new molecules containing the Fe(III) catecholate motif. These complexes all presented an intradiol-type dioxygenase activity. The structure of [(bispicMe₂en)Fe^{III}(DBC)]⁺ was determined. The NMR and optical properties indicate that, for the three complexes presenting similar topological characteristics, the reactivity is correlated with the λ_{\max} value, and better with the ϵ_{\max} value, of the LMCT O(DBC) \rightarrow Fe(III) band and with the chemical shift of the 4-H proton of the DBC²⁻ ligand. These results elucidate previous suggestions by the group of Que. However, these observations cannot be extrapolated to the [(BQPA)Fe^{III}(DBC)]⁺ complex. The large steric hindrance at the metal center because of the quinoline arms must considerably decrease the rate of substrate oxidation by O₂.

The complex [(TPA)Fe^{III}(DBC)]⁺ remains the most active species synthesized to date. The remarkable activity of this complex cannot be explained by a consideration of its optical and NMR properties. Asymmetric chelation of the catecholate to Fe(III), such as that noted in the enzyme by Orville et al.,²⁵ could explain the high reactivity of [(TPA)Fe^{III}(DBC)]⁺. An alternative explanation could be a large electronic difference between this complex and the series studied here. From recent data, it seems possible that [(TPA)Fe^{III}(DBC)]⁺ presents a spin equilibrium such as that observed recently for [(TPA)Fe^{III}(cat)]⁺ in the solid state. The nature of the spin states of these Fe(III)/catecholate systems must be studied in greater detail.

Acknowledgment. This work was supported by a grant from the Elf company.

Supporting Information Available: Tables of crystal data, atomic coordinates, selected bond lengths and angles, bond lengths and angles, thermal parameters, H-atom coordinates and values of $10|F_o|$ and $10|F_c|$ for [(bispicMe₂en)Fe^{III}(DBC)]BPh₄. This material is available free of charge via the Internet at <http://pubs.acs.org>.

IC981236V

(25) Orville, A. M.; Lipscomb, J. D.; Ohlendorf, D. H. *Biochemistry* **1997**, *36*, 10052–10066.

(26) Simaan, J.; Boillot, M.-L.; Rivière, E.; Boussac, A.; Girerd, J.-J. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 196–198.

(24) James, H. J.; Broman, R. F. *Anal. Chim. Acta* **1969**, *48*, 411.