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Quantum Chemical Approach to the Assignment of Iron−Catecholate Vibrations and Isotopic Substitution Shifts

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In this communication we report the use of quantum chemical model calculations to assign iron−catecholate vibrations and to get quantitative predictions of the isotopic shifts. This study will show how such a new approach may increase the potential of vibrational spectroscopy,[1−3] especially the resonance Raman technique,[4−7] in studies of metalloproteins. Full geometry optimizations and vibrational analyses were performed for catechol and [Fe(catecholate)]$^{2-}$, and with the latter, the $^{16/18}$O, $^{54/57}$Fe, and $^{1/2}$H isotopic substitution shifts were obtained. They were successfully matched to the experimental pattern (Figure 1)[6] and allowed more precise assignments of the observed bands.

The great interest in these calculations stems from the use of catecholate type ligands as spectroscopic probes for non-heme iron proteins.[8−16] However, the assignment of the metal−catecholate vibrational frequencies is not straightforward, even with isotopic labeling. Particularly the nature of the C═O and Fe—O vibrations and the existence of a chelate vibration mode have been questioned.[6] Although the isotopic shifts can, in principle, be predicted after a complete normal coordinate analysis of the spectrum, this is not always possible. Then one often has to rely on the diatomic harmonic oscillator (DHO) for a rough estimation of the shifts, but this model has obvious shortcomings since it cannot take into account the true nature of the vibrations.[1]

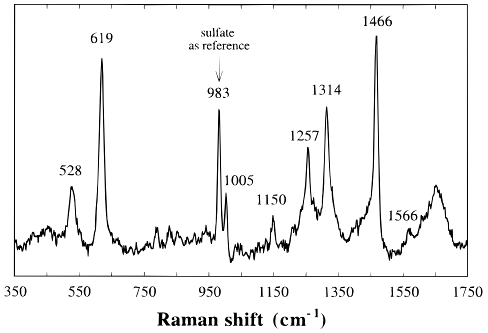

Figure 1. Resonance Raman spectrum of the catechol−tyrosine hydroxylase complex[6] obtained on a ≈1 mM sample (120 μL) in a spinning cell at 5 °C (90° scattering geometry) using a 606 nm excitation wavelength, a scan rate of 2 cm^{-1}/s, a 4 cm^{-1} slit, and accumulation of 40 scans.

Table 1. Selected Experimental Vibrations for Fe(III)−Catecholate Complexes Compared to Frequencies Calculated for [Fe(catecholate)]$^{2-}$ by DFT

vibrations all A_1	cald Fe^0cat^{2-} [a]	expt	
		TH-cat[b]	$Fe^{III}PDA(cat)^-$ [c]
ν CC	1537	1566	1573
ν CC + δ CH	1494	1466	1469
ν CC	1351	1314	1308
ν C−O/7a	1292	1257	1250
δ CH	1116	1150	1145
ring	761		792
ν Fe−O	583	619	633
δ,ν-chelate	489	528	523
ν Fe−O	283		310

[a] This work. [b] Reference 6. [c] Reference 8. These experimental values are representative; more examples can be found in the literature.

Density functional theory (DFT) calculations[17] on free catechol gave a geometry[18] and frequencies in good agreement with experimental data, as expected in view of recent results on related phenoxy systems.[19,20] There is no complete consensus in the literature on the vibration modes in the experimental spectra,[21,22] and we were able to verify and clarify the proposed assignments (see supporting information).

To model the iron−catecholate bonding we used [Fe(catecholate)]$^{2-}$.[23] This model fulfills the following criteria: (1) It allows for fast frequency evaluation on a relatively advanced theoretical level. (2) The catecholate remains in its original oxidation state. (3) The optimized geometry comes reasonably close to observed parameters for Fe(III)−catecholate complexes.[24] (4) The population analysis of the catecholate

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(17) Full geometry optimizations and vibrational analyses were performed for catechol and [Fe(catecholate)]$^{2-}$ using the DGauss 2.3 and 3.0 DFT program (Andzelm, J.; Wimmer, E. *J. Chem. Phys.* **1992**, *96*, 1280), included in the UniChem package from Cray Research Inc. The VWN functional was used (Vosko, S. H.; Wilk, L.; Nusair, M. *Can. J. Phys.* **1980**, *58*, 1200). For the nonlocal corrections to the exchange-correlation energy, the Becke−Perdew functional (Becke, A. D. *J. Chem. Phys.* **1988**, *88*, 2547. Becke, A. D. *Phys. Rev.* **1988**, *A28*, 3098. Perdew, J. P. *Phys. Rev.* **1986**, *B33*, 8822), including a gradient-corrected exchange, was applied self-consistently. A double ζ split-valence plus polarization basis set optimized for DFT calculations was used. (Godbout, N.; Salahub, D. R.; Andzelm, J.; Wimmer, E. *Can. J. Chem.* **1992**, *70*, 560). The contracted basis sets had the following composition: H [2s], C, N, O [3s,2p,1d] Fe [5s,3p,2d]. The geometry optimizations and the vibrational analyses were made by analytical determinations of the first and second derivatives of the total energy. No symmetry constraints were used. The calculations on the [Fe(catecholate)]$^{2-}$ complex were made on the $S = 0$ state in a RHF manner while for the [Fe(catecholate)(NH$_3$)$_2$(H$_2$O)$_2$]$^+$ we used the $S = {}^5/_2$ spin state in an UHF type calculation.

(18) Calculated (experimental): C1−O, 1.38 (1.37); C1−C2, 1.42 (1.39); C2−C3, 1.40 (1.38); C3−C4, 1.41 (1.39); O−C1−C2, 117° (117−121°). According to experimental data from the hydrogen-bonded catechol dimer (Wunderlich, H. v.; Mootz, D. *Acta Crystallogr.* **1971**, *B27*, 1684), in the crystal structure the molecule is not C_{2v} symmetric.

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Table 2. Isotopic Shifts Calculated by DFT for $[Fe(catecholate)]^{2-}$ and by the DHO-Model, Compared to Experimental Data for Tyrosine Hydroxylase Fe(III) Complexes with Catecholates

vibration mode all A_1	ν DFT (cm^{-1})	$^{57/54}Fe$ (cm^{-1})			$^{18/16}O$ (cm^{-1})			D/H (cm^{-1})	
		DFT	DHO[a]	exptl[b]	DFT	DHO[c]	exptl	DFT	exptl[d]
ν CC	1537							27	30
ν C−O/7a	1292				15	32	5−9	88	57
ν Fe−O	583	0.3	4	<1	10	29	12	14	10, 10[e]
δ,ν-chelate	489	0.1	3	<1	20	24	18−19	6	6, 4[e]
ν Fe−O	283	5	2	−	1	0	−	3	3[e]

[a] Fe−O vibration. [b] Reference 6, average values for noradrenaline and dopamine. [c] C−O vibration; [d] Reference 6, catecholate. [e] Reference 26, [Fe(PDA) catecholate]$^-$.

ligand does not differ too much from that of the more elaborate model complex $[Fe(catecholate)(NH_3)_2(H_2O)_2]^+$.[25] The main conclusion when comparing $[Fe(catecholate)(NH_3)_2(H_2O)_2]^+$ and $[Fe(catecholate)]^{2-}$ is that the Fe−O interaction should be weaker in the smaller model compound, and thus we would expect less perturbed catecholate vibrations and lower Fe−O frequencies in $[Fe(catecholate)]^{2-}$ compared to experimental data.

We report in Table 1 the calculated frequencies (only A_1 modes because these are the ones observed in resonance Raman) important for the identification of the Fe−catecholate unit together with experimental data[6,8] (see also supporting information). For the $[Fe(catecholate)]^{2-}$ model complex the calculated frequencies with mainly catecholate contributions are generally 2−3% too high. As foreseen, the Fe−O vibrations are lower than the observed experimental frequencies.

We find one more Fe−O A_1-vibration mode in our calculations than has hitherto been implicated by experiments. This falls at 283 cm^{-1} and can by extrapolation be predicted at 305−330 cm^{-1}, which allows us to assign the unattributed 310 cm^{-1} band from the model complex $[Fe(PDA)(catecholate)]^-$ to this mode.[8]

Furthermore, the assignment of the experimental bands at ~520 cm^{-1} as chelate modes is confirmed.[6] This is in fact a 50/50 mixture of δ Fe−O and ν Fe−O vibrations, and we propose to call it a *δ,ν-chelate* vibration. We also note that the band at 1292 cm^{-1} appears to contain equal proportions of ν C−O and δ C−H (type 7a in Wilson's nomenclature) contrary to the usual assignment as ν C−O. We suggest replacing the old notation of ν C−O with ν C−O/7a. Figure 2 displays the most important vibrational modes as calculated by DFT.

In Table 2 we have summarized the calculated isotopic shifts for $[Fe(catecholate)]^{2-}$ together with the observed values for tyrosine hydroxylase Fe(III) complexes with dopamine, noradrenaline, or catechol[6] and the model compound $[Fe(PDA)(catecholate)]^-$.[8] Calculations based on the diatomic harmonic oscillator are included as a reference. It is clear that the DHO model overestimates the isotopic shifts. On the other hand, the DFT method on the model compound $[Fe(catecholate)]^{2-}$ performs very well. Most important from the experimental point of view is that all the isotopic shifts for the two vibrations assigned to Fe−O modes are predicted within a few wavenumbers, thus fully confirming the experimental assignments. The $^{54}Fe/^{57}Fe$ shift of 0.3 cm^{-1} is furthermore in good agreement with the shift of 0.7 cm^{-1} observed for the [Fe(salen)(*p*-cresolate)] frequency at 570 cm^{-1},[27] given the experimental difficulties when measuring such small shifts.

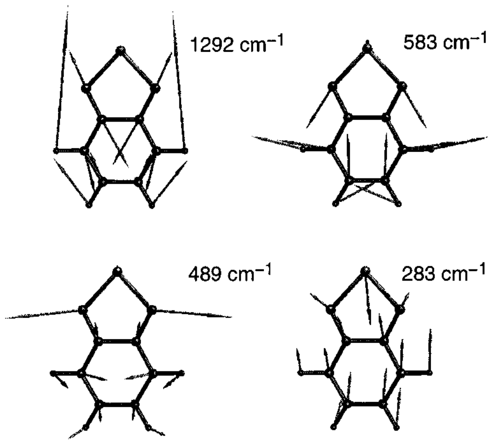

Figure 2. Selected vibrational modes for $[Fe(catecholate)]^{2-}$ calculated by DFT.

The model study also sheds some light on the puzzling absence of any $^{54}Fe/^{57}Fe$ effect in the recent resonance Raman study of tyrosine hydroxylase.[6] It appears that there should indeed be such an effect on the order of 5 cm^{-1} but only for the newly assigned ν Fe−O band predicted at 305−330 cm^{-1} in an experimental spectrum (calculated at 283 cm^{-1}).

In conclusion, the model compound $[Fe(catecholate)]^{2-}$, even though it may underestimate the Fe−O bond, gives reasonable vibrational frequencies and predicts isotope shifts which are in good agreement with experimental data. The results of this study are encouraging, and further work is in progress. It should be emphasized that a fast and reliable method to predict isotope shifts, *before* doing the labeling experiment, could save both time and money. The utility of the resonance Raman−isotopic labeling method may also be enhanced since we will have a more precise tool when interpreting the data. Especially interesting are the possibilities to model different possible structures, for example oxygen intermediates in metallobiochemistry, and then match the experimental isotopic shift pattern to the different calculated alternatives.

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Supporting Information Available: Complete listings of calculated catechol frequencies (Table 3) and $[Fe(catecholate)]^{2-}$ frequencies (Table 4) (2 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet: see any current masthead page for ordering information and Internet access instructions.

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(23) The choice of model system is of course critical. For example $[Fe(catecholate)]^+$ is not a good alternative since we would expect large electrostatic interactions between the 3+ and 2− units and, moreover, the catecholate will be oxidized to a semiquinone. Zero-valent metals with one or two ligands as model systems for organometallic reactions are discussed in the following: Blomberg, M. R. A.; Siegbahn, P. E. M.; Svensson, M.; Wennerberg, J. In *Energetics of Organometallic Speceis*; Martinho Simões, J. A., Ed.; Kluwer Academic Publishers: Dordrecht, 1992; pp 387−421.

(24) Calculated (experimental): Fe−O, 1.93 (1.92−2.01); C−O, 1.33 (1.35); C1−C2, 1.46 (1.41−1.42); C1−C6, 1.42 (1.38); O−Fe−O, 86.5° (81.3−85.2°). Experimental data from the following: Raymond, K. N.; Isied, S. S.; Brown, L. D.; Fronczek, F. R.; Nibert, J. N. *J. Am. Chem. Soc.* **1976**, *98*, 1767−1774. Jang, H. G.; Cox, D. D.; Que, L., Jr. *J. Am. Chem. Soc.* **1991**, *113*, 9200−9204.

(25) Population analysis $[Fe(catecholate)(NH_3)_2(H_2O)_2]^+/[Fe(catecholate)]^{2-}$: O, −0.42/−0.50; C1, −0.25/−0.24; C3, −0.35/−0.40; C4, −0.21/−0.29; Fe, 0.48/−0.75; total charge of the catecholate, −0.35/−1.25; overlap Fe−O, 0.56/0.26.

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