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# Pico-meter resolution structure of the coordination sphere in the metal-binding site in a metalloprotein by NMR

Andrea Bertarello,<sup>1,4,‡</sup> Ladislav Benda,<sup>1,‡</sup> Kevin J. Sanders,<sup>1,\$</sup> Andrew J. Pell,<sup>1,¥</sup> Michael J. Knight,<sup>1</sup> Vladimir Pelmenschikov,<sup>2</sup> Leonardo Gonnelli,<sup>3</sup> Isabella C. Felli,<sup>3</sup> Martin Kaupp,<sup>2</sup> Lyndon Emsley,<sup>4,\*</sup> Roberta Pierattelli,<sup>3,\*</sup> Guido Pintacuda<sup>1,\*</sup>

<sup>1</sup>Université de Lyon, Centre de RMN à Très Hauts Champs, FRE 2034 CNRS/Université Claude Bernard Lyon 1/ENS Lyon, 5 rue de la Doua, 69100 Villeurbanne, France ; <sup>2</sup>Technische Universität Berlin, Institut für Chemie, Straße des 17 Juni 135, 10623 Berlin, Germany; <sup>3</sup>University of Florence, Department of Chemistry and Magnetic Resonance Center (CERM), Via L. Sacconi 6, 50019 Sesto Fiorentino, Italy; <sup>4</sup>École Polytechnique Fédérale de Lausanne (EPFL), Institut des Sciences et Ingénierie Chimiques, CH-1015 Lausanne, Switzerland

Supporting Information Placeholder

**ABSTRACT:** Most of our understanding of chemistry derives from atomic-level structures obtained with single crystal X-ray diffraction. Metal centers in X-ray structures of small organometallic or coordination complexes are often extremely well defined, with errors in the positions on the order of 10<sup>-4</sup>-10<sup>-5</sup> Å. Determining the metal coordination geometry to high accuracy is essential for understanding metal center reactivity, as even small structural changes can dramatically alter the metal activity. In contrast, the resolution of X-ray structures in proteins is limited typically to the order of 10<sup>-1</sup> Å. This resolution is often not sufficient to develop precise structure-activity relations for the metal sites in proteins, since the uncertainty in positions can cover all the known ranges of bond-lengths and bond-angles for a given type of metal-complex. Here we introduce a new approach that enables determination of a high-definition structure of the active site of a metalloprotein from a powder sample, by combining magic-angle spinning (MAS) nuclear magnetic resonance (NMR) spectroscopy, tailored radio-frequency (RF) irradiation schemes, and computational approaches. This allows us to overcome the "blind sphere" in paramagnetic proteins, and to observe and assign <sup>1</sup>H, <sup>13</sup>C, and <sup>15</sup>N resonances for the ligands directly coordinating the metal center. We illustrate the method by determining the bond lengths in the structure of the Co<sup>II</sup> coordination sphere at the core of human superoxide dismutase 1 (SOD) with 0.7 pm precision. The coordination geometry of the resulting structure explains the non-reactive nature of the Co<sup>II</sup>/Zn<sup>II</sup> centers in these proteins, that allows them to play a purely structural role.

### INTRODUCTION

Metal ions play an important role in many processes at the core of modern chemistry, biochemistry, and materials research, and the accurate description of their coordination environment is essential for understanding the function of organometallic catalysts and metalloenzymes.<sup>1,2</sup> The capacity of single crystal X-ray diffraction<sup>3</sup> to determine atomic positions to within 10-4-10<sup>-5</sup> Å has enabled the development of today's structure-activity based approaches to chemistry.<sup>4</sup> Indeed, high accuracy is essential for understanding metal center reactivity, as even small structural changes can dramatically alter the metal activity.<sup>5</sup> However, in proteins the resolution of crystal structures is limited typically to the order of 10-1 Å,2,6,7 mostly by the need for highly ordered crystalline samples, and this is often not sufficient to develop precise structure-activity relations for the metal sites in proteins,<sup>8</sup> since the uncertainty in positions can cover all the known ranges of bond-lengths and bond-angles for a given type of metal-complex. Metal-ligand coordination distances can be refined with X-ray absorption techniques but these approaches share many of the limitations of X-ray diffraction.9

Nuclear Magnetic Resonance (NMR) spectroscopy is a direct probe for the electronic structure and coordination geometry of metal ion complexes in the presence of paramagnetism originating from unpaired electrons, which is a common feature of many transition metal ions of biological relevance in metalloproteins. Paramagnetic metal ions induce peculiar effects on the NMR signals of the surrounding nuclei, with a well-defined dependence on the electronic configuration and coordination environment of a metal center. This results in long-range perturbations such as hyperfine shifts and NMR relaxation enhancements, which are routinely used as structural probes for proteins in both solution<sup>10,11</sup> and solid state.<sup>12-14</sup> When it comes to the proximity of a metal, however, these paramagnetic effects are the strongest, which has to date hindered the acquisition of NMR signals in the "blind sphere" around the metal ion.

MAS solid-state NMR is particularly well suited to circumvent the main barriers for the acquisition of paramagnetic signals in solution, since Curie relaxation is absent in solids,<sup>15</sup> and nuclear spin coherences can be transferred efficiently via strong dipolar couplings. However, in paramagnetic solids, additional effects broaden NMR signals and spread them over very large spectral windows. Recently, we and others have shown that these drawbacks can be significantly reduced with fast (60 kHz and above) MAS and high-power radio-frequency pulses,<sup>16,17</sup> opening the way to the detection of significantly hyperfineshifted and broadened resonances in large biomolecules.<sup>18,19</sup> Here, we show that it is possible to obtain data from the "blind sphere" of a paramagnetic Co-containing metalloprotein by combining magic-angle spinning (MAS) NMR at 100 kHz MAS rate, with tailored radio-frequency (RF) irradiation schemes and modern computational approaches. We determine the high-resolution structure of the metal coordination sphere (Fig. 1) in the core of the thermostable mutant of human super-oxide dismutase 1 in microcrystalline form containing a Co<sup>II</sup> ion (CoSOD), by measuring paramagnetic NMR effects for the <sup>1</sup>H, <sup>13</sup>C, and <sup>15</sup>N nuclei of the Co<sup>II</sup> ligands. This leads to pico-meter resolution in the precision of the bond-lengths and ±1° resolution of bond-angles in the metal center, and we show that the coordination geometry of the resulting structure is precise enough to explain the non-reactive nature of the Co<sup>II</sup>/Zn<sup>II</sup> centers in these proteins.



**Figure 1.** Structure determination of the Co<sup>II</sup> site in CoSOD. (A) Overlay of Zn<sup>II</sup> site in ten protein chains of the single-crystal Xray structure of SOD 1 (PDB code 1SOS), illustrating the crystallographic uncertainty in the metal coordination geometry and (B) the NMR ensemble of structures of the Co<sup>II</sup> complex of CoSOD. Schematic representation of the metal site (C) in the Xray ensemble and (D) in the NMR ensemble, together with the RMSDs of the metal-ligand bond lengths and ligand-metal-ligand angles RMSDs.

#### **RESULTS AND DISCUSSION**

Fast MAS rates have the multiple advantage of concentrating the signal into fewer spinning sidebands, of improving dipolar decoupling, with a benefit in sensitivity, and of removing signal overlap, with a benefit in resolution. As illustrated in Fig. 2A, tailored RF schemes (Fig. S1) at 100 kHz MAS enable the acquisition of well-resolved <sup>1</sup>H spectra, featuring resonances spanning a range of about one hundred ppm. Notably, several very broad resonances above 60 ppm and below 0 ppm which escaped detection in all previous attempts at lower MAS rates and in solution<sup>20</sup> become observable. Improved dipolar decoupling results in longer lifetimes for <sup>1</sup>H and <sup>13</sup>C coherences, which in turn allows the acquisition of 2D Transferred Echo Double Resonance (TEDOR)<sup>21,22</sup> experiments (Fig. S1) that correlate the shifts for pairs of nearby 1H,13C or 1H,15N nuclei over windows up to more than a thousand ppm (Fig. 2B-C). The addition of a spin magnetization exchange<sup>23</sup> between <sup>1</sup>H nuclei close in space extends the correlations to more distant <sup>1</sup>H.

Once the paramagnetic NMR shift tensors are acquired, a reliable assignment protocol is needed. For diamagnetic proteins

this is a well-established procedure relying on the fact that atomic nuclei in given structural environments display well-defined ranges of chemical shifts. However, strong paramagnetic interactions alter the observed shifts in a manner that is not empirically predictable and the use of theoretical modeling is of paramount importance. Only recently the theory of paramagnetic NMR shift tensors<sup>24</sup> has been developed to enable their rigorous calculation from first principles of quantum mechanics.<sup>25,26</sup>



**Figure 2**. NMR spectra of CoSOD. NMR spectra of CoSOD acquired at 100 kHz MAS ~280 K on a 500 MHz spectrometer (11.7 T). (A) <sup>1</sup>H spectrum (spin echo), (B-C) 2D <sup>1</sup>H,<sup>13</sup>C and <sup>1</sup>H,<sup>15</sup>N TEDOR spectra, acquired without (black) and with (magenta) spin magnetization exchange<sup>23</sup> between <sup>1</sup>H nuclei close in space.

We used this approach to predict the NMR shift tensors of the <sup>1</sup>H, <sup>13</sup>C, and <sup>15</sup>N nuclei in the Co<sup>II</sup>-binding complex of CoSOD. As a starting structural seed, we adopted an ensemble of ten models A-J (Fig.1 and Fig. S2) obtained from an X-ray structure of SOD 1.27 The main factor limiting the accuracy of predicted paramagnetic NMR shifts is the density functional theory (DFT) calculation of hyperfine coupling tensors. As there is currently no universally preferred density functional for hyperfine coupling,28 we adopted a previously validated approach29 and calculated the expected bounds of hyperfine couplings with PBE0 and PBE50 hybrid DFT functionals. The resulting intervals of calculated NMR shifts were then compared to the experimental data, leading to two important outcomes. First, a complete assignment was achieved for all observed <sup>1</sup>H. <sup>13</sup>C. and <sup>15</sup>N resonances, thus enhancing the so far limited set of resonances at the core of CoSOD.<sup>20</sup> Second, by selecting the models for which the agreement between experiments and calculations is satisfactory for all observed resonances, the structure of the metalbinding complex was refined as illustrated in Fig. 3. Despite a considerable uncertainty associated with the calculations, the even larger dispersion of paramagnetic shifts guarantees that this procedure has a structural discriminating power. Out of the ten models A–J, only three (C, E, F) satisfied the agreement criteria with the NMR correlation spectra. The resulting NMR structural ensemble (Fig. 1B) has a significantly better precision at the metal site than the original X-ray-based ensemble. The overall RMSD of non-hydrogen atoms of metal-binding amino-acid side chains improved from 0.16 Å for the X-ray structural ensemble to 0.09 Å for the refined ensemble, while the RMSDs for the metal-ligand bond lengths and ligand-metal-ligand angles improves by one order of magnitude (Fig. 1C-D, Table S1) to an average of 0.7 pm and  $\pm 1^{\circ}$  respectively.



**Figure 3**. Comparison between experimental and calculated NMR correlations. Experimental 2D  $^{1}$ H, $^{13}$ C (top) and  $^{1}$ H, $^{15}$ N (bottom) TEDOR spectra and the calculated areas in which we expect correlations for model A (left, blue boxes) and model F (right, red boxes). Model F is in agreement with the data, while Model A is not, and can be excluded.

With a reliable structure of the Co<sup>II</sup>-binding complex at hand, we can directly interpret the measured NMR shift pattern in terms of local structure of the metal site. The Co<sup>II</sup> ion is pseudopenta-coordinated with short bond lengths to His63  $N_{\delta 1}$ , His71  $N_{\delta 1}$ , His80  $N_{\delta 1}$ , and Asp83  $O_{\delta 1}$ , and a longer distance to Asp83  $O_{\delta 2}$  (Fig. 1. Table S1). We found that certain NMR shifts are particularly sensitive to the mode of Asp83 binding to the metal, most notably the Asp83  $C_{\beta}$  shift observed at 350 ppm. The Asp83 C<sub>β</sub> shift values calculated for the models A–J span a wide range and there is a clear correlation with the coordination distances Co-O<sub> $\delta1$ </sub> ( $r_1$ ) and Co-O<sub> $\delta2$ </sub> ( $r_2$ ) (Fig. 4 A-B). The experimental Asp83 C<sub> $\beta$ </sub> shift constrains the distances  $r_1$  and  $r_2$  to the ranges 1.94-1.96 Å and 2.68-2.82 Å, respectively. Both coordination distances are determined with a substantially better precision here than was available in the original X-ray ensemble (Fig. 4 C, Table S1), especially for the  $r_2$  distance where the variation is reduced from 1.23 Å to 0.14 Å. The variation is further reduced to 0.07 Å if we consider the distances spanned by the three structural models.

The relevance of such refinement is illustrated in a larger perspective in Fig. 4C, where the distribution of the distances obtained before and after the paramagnetic NMR structure determination is compared with all the Co complexes in the Cambridge Structural Database (CSD) featuring the same Co pattern as in SOD. The original SOD ensemble covers a large portion of the possible combinations of  $r_1$  and  $r_2$  values (369 structural motifs), and thus a correspondingly large part of the chemical activity space for Co<sup>II</sup> complexes, while the NMR refined interval discriminates a much smaller subset of 29 structural motifs (if we consider the constraints obtained from Fig. 4A-B), and an even smaller subset of only 2 structures if we consider the range delimited by the three selected structures (C,E,F). These subsets of structures significantly reduce the space of chemical properties.



**Figure 4**. Dependence of Asp83  $C_{\beta}$  NMR shift on the active site structure. (A-B) Calculated NMR shifts for the ten models A–J using PBE0 and PBE50 functionals for the hyperfine coupling, compared to the experimentally observed Asp83  $C_{\beta}$  shift, plotted as a function of (A)  $r_1$  and (B)  $r_2$  distances. The red lines (parabolic fit of the calculated data) enclose the area inside which the experimental shift is expected. The actual observed shift is indicated by the black dashed line, which by intersecting the red areas determines the  $r_1$  and  $r_2$  ranges compatible with the NMR data. (C) Distribution and average values of  $r_1$  and  $r_2$  values for all (911) tetra- (NC=4) and penta- (NC=5)

coordinated Co structural motifs with at least one carboxylate moiety as deposited in the CSD, compared to the uncertainty of  $r_1$  and  $r_2$  in CoSOD in X-ray (light magenta area, containing 368 structural motifs), and after paramagnetic NMR refinement (blue area, containing only 29 structural motifs). Average values  $r_{1av}$  and  $r_{2av}$  over all tetra-coordinated CSD complexes are shown with solid lines and the analogous values for penta-coordinated CSD complexes are shown with dashed lines.

This can be of primary importance since the structural parameters are correlated to chemical properties of a species, as is e.g. the case of Zn binding proteins, where the metal-ligand distances are often indicators of a catalytic or structural role of the metal in the protein.<sup>30</sup> The uncertainty in the geometry from the X-ray ensemble is too large to distinguish these types. The refined bond lengths and bond angles we find are consistent with unreactive, structural, Zn atoms. We point out that the structural resolution we discuss here is related to the precision of the measurement. Since there are no other independent determinations with this level of resolution, it is not straightforward to assess the accuracy of the determination. That said, the comparison between the  $r_1$  and  $r_2$  ranges obtained for SOD here to those observed for all the Co<sup>II</sup> complexes in Fig.4 demonstrates consistency: the 1.94-1.96 Å range for  $r_1$  compares very well with the average value of 1.968 Å obtained for tetracoordinated Co<sup>II</sup> complexes, and the range 2.68-2.82 Å observed for  $r_2$  lies exactly in between the average values observed for tetracoordinated and pentacoordinated complexes, which is in agreement with the pseudo-pentacoordinated nature of Co in SOD. Moreover, the  $r_1$  and  $r_2$  ranges obtained from the present refinement compare well with those of some biomimetic Co and Zn complexes (the BIYHUM and BIYJAU entries in the CSD), which display a similar coordination sphere to that in SOD.<sup>31</sup> In particular, in the structure corresponding to the BIYHUM entry, the  $r_1$  and  $r_2$  distances are equal to 1.97 and 2.79 Å respectively, comparing almost perfectly with our results, and supporting the coordination geometry. This also validates the applicability in the present case of the metal substitution strategy for the study of metal binding sites in metalloproteins.

#### CONCLUSION

The understanding of the function of a metal center in a metalloprotein is intimately related to the structural environment of the metal in the protein framework, as small structural changes can alter dramatically the metal center activity. The difficulty of obtaining highly resolved structures of metal sites in proteins often represents the bottleneck for the development of precise structure-activity relations for metal sites in proteins.

We have introduced a method to determine with pico-meter precision the structure of the coordination sphere of a paramagnetic metal ion in a metalloprotein via the measurement and calculation of paramagnetic NMR shifts. Detection and assignment of NMR resonances is enabled by state-of-the-art methodology including 100 kHz MAS, tailored radiofrequency irradiation schemes, and advanced quantum chemistry modeling. The method has been applied to the CoSOD metalloprotein, where it resulted in 0.7 pm precision in the resolution of the Co<sup>II</sup> coordination sphere. The overall RMSD for all the heavy atoms in the ligands is 9 pm. In particular, the refined structure is accurate enough to be able to correlate the coordination geometry with the unreactive, structural, nature of the Zn center in SOD. Our approach provides a direct relationship between metal-ligand distances and paramagnetic NMR shifts. With ongoing progress in MAS NMR instrumentation and quantum chemistry methods, we anticipate that the approach described here will become of widespread use for the establishment of structure-activity relationships in metalloproteins. Notably, the structural resolution reported here is in terms of precision. Determining the sources of potential systematic errors in these methods, and translating that into the accuracy of the structures, will be the subject of future work.

We also note that an attractive approach would be to directly optimize structures directly against calculated paramagnetic shifts, for example in combination with MD simulations, without the need for candidate structures as inputs (here from Xray diffraction). This is currently not computationally feasible, but we expect it to become possible with future developments.

#### **EXPERIMENTAL**

#### Sample preparation

A 1H, 13C, 15N labeled sample of the thermostable mutant of human SOD was expressed and purified as described previously.14,32 Selective metalation was achieved by treating the purified protein sample with EDTA followed by dialysis into a buffer containing 20 mM sodium acetate pH 5.0, and then titrated with CoCl<sub>2</sub> to obtain stoichiometric binding. The titration was followed with solution-state NMR to check the progress of binding. For crystallization the sample of CoSOD was concentrated to 20 mg/mL in a 50 mM sodium acetate pH 5.0 buffer, mixed 1:1 with a precipitant solution of 20% PEG 4K in unbuffered water and crystals grown in sitting drops over a reservoir solution of the same precipitant supplemented with 2 M NaCl. Complete crystallization occurred in 3-4 days. The suspension of microcrystals was then packed into a 0.7 mm rotor by ultracentrifugation, using the ultra-centrifugal device provided by Giotto Biotech.33

#### NMR experiments

Paramagnetic solid-state NMR experiments were performed on a 500 MHz Bruker Avance III spectrometer with a triple-resonance 0.7 mm probe or with a 1.3 mm double-resonance probe. All experiments were performed at an estimated sample temperature of 280 K, unless specified otherwise. In all experiments the highest allowed power was used for hard and adiabatic pulses, corresponding to a  $v_1$  field of 350 kHz for <sup>1</sup>H, 190 kHz for <sup>13</sup>C, and 115 kHz for <sup>15</sup>N, respectively, on the 0.7 mm probe, and to a v1 field of 192 kHz for <sup>1</sup>H, and 175 kHz for <sup>13</sup>C, on the 1.3 mm probe. Recycle delays were set to 25 ms in <sup>1</sup>H detected experiments and 50 ms in <sup>13</sup>C detected ones. The water signal was suppressed by presaturation using a continuous pulse of 2 kHz for 10 ms. One-dimensional <sup>1</sup>H and <sup>13</sup>C spectra (Fig. 2 and Fig. S3) were acquired with a rotor synchronized spin-echo sequence at 100k Hz MAS on the 0.7 mm probe. The <sup>1</sup>H adiabatic magic angle turning (aMAT)<sup>34</sup> experiment (Fig. S4) was acquired at 40 kHz MAS on the 1.3 mm probe using six tanh/tan short high-powered adiabatic pulses (SHAPs) that swept through 10 MHz in 50 us. The <sup>13</sup>C aMAT experiment was acquired at 30 kHz MAS on the 1.3 mm probe using six tanh/tan pulses sweeping through 5 MHz in 33.33 µs. The shifts anisotropies (SAs) were estimated using the program Dmfit.<sup>35</sup> For this purpose, rows corresponding to the spinning-sideband manifold of each nucleus were extracted from the aMAT spectra and fitted separately. The <sup>1</sup>H,<sup>13</sup>C and <sup>1</sup>H,<sup>15</sup>N transferred echo double resonance (TEDOR)<sup>21,22</sup> experiments (Fig. 2) were acquired at 100 kHz MAS on the 0.7 mm probe using the same radio-frequency powers used in the 1D experiments; in both cases the recoupling period was set to four rotor periods. The <sup>1</sup>H,<sup>13</sup>C TEDOR spectrum was also acquired in a variant with spin magnetization exchange between <sup>1</sup>H nuclei close in space, using the <sup>1</sup>H-<sup>1</sup>H radio frequency driven recoupling (RFDR) scheme<sup>23,36</sup> with a mixing time of 0.64 ms. Additional experimental details, together with the pulse sequence schemes used are reported in Table S2 and Fig. S1.

#### Quantum chemistry modeling

Molecular models were built from the X-ray structure of the thermostable mutant of human Cu,Zn-SOD (PDB ID 1SOS).<sup>27</sup> The crystal unit cell of 1SOS contains ten protein chains (five dimers) labelled A–J. PNMR calculations were performed consistently for all of them, thus exploiting the structural variation naturally occurring in the crystal.

Two molecular models of the  $Co^{II}$  site (substituted for  $Zn^{II}$ ) were built for each chain (see Fig. S2): a larger one (*m1*, 86 atoms) for structure optimization, hyperfine coupling and orbital shielding calculations and a smaller one (m0, 32 atoms) for subsequent high-level *ab initio* calculations of *g*- and *D*-tensors. Each model is named after the corresponding chain in the PDB structure. The larger model m1 consists of the Co<sup>II</sup> ion in place of the native  $Zn^{II}$ , two backbone segments between  $C_{\alpha}$  atoms of residues 71-72 and 79-83, and side chains of metal-binding residues His63, His71, His80, and Asp83. All other side chains were removed and terminated with hydrogen atoms. The conformation of the metal-binding Asp83 side chain is stabilized by two hydrogen bonds to backbone amide protons of His80 and Gly72, both essential for the proper fold of the SOD Zn<sup>II</sup> (Co<sup>II</sup>) site and both properly included in model *m1*. Hydrogen atoms were added to the raw PDB structures with the Reduce tool.37

The *m1* structures were optimized at the PBE0-D3BJ<sup>38-41</sup> level in Turbomole 6.3.1.42 The conductor-like-screening model43 with a dielectric constant  $\varepsilon$  = 4.0 was used to approximately account for the protein environment. To keep the overall fold of the metal center as encoded in the X-ray structures while at the same time allowing the local structure parameters to relax after substitution of Co<sup>II</sup> for Zn<sup>II</sup> (especially the Asp83 carboxylate, Table S1), the positions of the  $C_{\alpha}$  atoms (8 atoms out of 86) were fixed in space during the optimization, and the rest was freely relaxed. A locally dense Gaussian basis set was applied, using a def2-TZVP basis for Co and def2-SVP for the maingroup elements.<sup>44</sup> From each optimized *m1* structure, a model *m0* was built by truncating *m1* and terminating with hydrogen atoms whose positions were subsequently optimized. The smaller model m0 included only the metal-binding imidazole rings of His63, His71, His80, and HCOO- of Asp83. The total charge was +1 for both models. All DFT calculations were done for the high-spin (S = 3/2) ground state of the Co<sup>II</sup> complex.

We note that vibrational effects should play a bigger role for paramagnetic NMR shifts than they do in diamagnetic NMR. We take a large part of the vibrational effects into the account by performing the full quantum mechanical structure optimization with only a few atoms anchored in space to their crystallographic positions as described above. Metal center structures obtained in this way are a harmonic average and performing molecular property calculations for these structures should usually well approximate the full vibrational average. Careful choice of the metal center model and the optimization protocol was a necessary prerequisite to ensure that each of the resulting metal center structures correctly represents the harmonic average for a given configuration of the surrounding protein chain.PNMR shift tensors were obtained according to Kurland– McGarvey theory<sup>24</sup> in its recent formulation by Vaara et al.,<sup>26</sup> where the hyperfine part of the PNMR shift tensor is expressed in terms of electron paramagnetic resonance (EPR) property tensors. EPR g- and D-tensors were calculated in model m0 applying a strongly contracted variant of the *N*-electron valencestate perturbation theory of second order (NEVPT2)<sup>45</sup> to a state-averaged complete-active-space self-consistent-field reference wave-function<sup>46,47</sup> with seven electrons in five active 3d-orbitals (SA-CASSCF(7,5)), as implemented in Orca 3.0.3.48 It is well known that standard DFT functionals dramatically underestimate the magnitude of zero-field splitting (ZFS, D-tensor) in high-spin Co<sup>II</sup> complexes and correlated multi-reference wave-function level of electronic structure theory is needed for reliable results.<sup>49-51</sup> Here, the spin-orbit part of the *D*-tensor was evaluated using quasi-degenerate perturbation theory (QDPT)<sup>52</sup> applied to the NEVPT2 electronic structure (see the calculated values in Table S3). A test CAS-CI calculation with the converged SA-CASSCF(7,5) wave-function was performed to confirm that the spin-spin part of the *D*-tensor is in this case negligible with all D<sub>SS</sub> matrix elements being smaller than 0.15 cm<sup>-1</sup>. The EPR g-tensor was calculated at the NEVPT2 level with the effective Hamiltonian approach.<sup>53</sup> For both D<sub>S0</sub> and gtensors, the spin-orbit mean-field (SOMF) approximation<sup>54,55</sup> to the spin-orbit matrix elements in Breit-Pauli form was applied. The RI technique was applied in the orbital transformation step of NEVPT2. The state averaging in SA-CASSCF involved all 10 quartet and 40 doublet roots implied by the (7,5) active space, all equally weighted. In the multi-reference wavefunction calculations we used the def2-TZVPD basis for Co and def2-SVPD for the main-group elements, thus enhancing the atomic basis used in the DFT structure optimizations with diffuse functions optimized for molecular properties.<sup>56</sup> The FC and SD terms of the EPR hyperfine coupling tensors for the <sup>1</sup>H, <sup>13</sup>C, and <sup>15</sup>N nuclei were calculated on model *m1* using the PBE038,39 and PBE50 functionals including 25% and 50% of Hartree-Fock exchange admixture, respectively. GIAO orbital shielding tensors<sup>57</sup> were calculated at PBE0 level with Gaussian.<sup>58</sup> In the DFT hyperfine coupling and orbital shielding calculations the def2-TZVPD and IGLO-III59 basis sets for Co and main-group elements, respectively, were employed.

Isotropic shifts  $\delta_{\kappa}$  were obtained from the total (orbital plus hyperfine) isotropic nuclear shieldings  $\sigma_{\kappa}$  as

$$\delta_K = \sigma_K^{\text{ref}} - \sigma_K \tag{1}$$

where  $\sigma_{K}^{\text{ref}}$  is the reference nuclear shielding for a nucleus K. The calculations required to obtain  $\sigma_{K}^{\text{ref}}$  for <sup>1</sup>H, <sup>13</sup>C, and <sup>15</sup>N nuclei were performed with Gaussian at conditions corresponding to the experimental NMR reference measurements<sup>60</sup> (see Table S4). The molecule of tetramethylsilane (TMS) was optimized at PBE0-D3BJ/6-311++G(d,p) level with the polarizable continuum model (PCM) for the chloroform solvent. The <sup>1</sup>H and <sup>13</sup>C orbital shielding in TMS was calculated at the GIAO-PBE0/IGLO-III level with PCM (chloroform). In the case of the <sup>15</sup>N reference shielding, to avoid the difficult modeling of liquid ammonia, we employed nitromethane as an easy-to-model secondary standard. The <sup>15</sup>N reference shielding was calculated according to the expression

$$\sigma^{\rm NH_3(l)} = \sigma^{\rm CH_3NO_2(l)} + \frac{\Xi^{\rm CH_3NO_2(l)}}{\Xi^{\rm NH_3(l)}} - 1$$
(2)

where  $\sigma^{\text{CH}_3\text{NO}_2(l)}$  is the isotropic shielding of neat liquid nitromethane and  $\Xi^{\text{CH}_3\text{NO}_2(l)}/\Xi^{\text{NH}_3(l)} - 1 = 380.5$  ppm is the isotropic shift of nitromethane relative to the primary reference NH<sub>3</sub> (*l*) expressed in terms of standardized resonance frequency ratios.<sup>60</sup> The structure of nitromethane was optimized at the PBE0-D3BJ/6-311++G(d,p) level with PCM (nitromethane). The <sup>15</sup>N orbital shielding tensor was calculated at the GIAO-PBE0/IGLO-III level with PCM (nitromethane). The calculations revealed that the isotropic *g*-value had a rather stable value of 2.22-2.23 among all models (Table S3), comparing nearly perfectly with the experimental value of 2.24.<sup>61</sup> The absolute value of the zero-field splitting |D| varied between 5.1–7.5 cm<sup>-1</sup> in the calculations which is somewhat lower than the previously measured value of 10.8 cm<sup>-1.61</sup> This difference is likely caused by a combination of factors. We cannot exclude effects beyond the NEVPT2 computational level and those not captured by our molecular models of limited size. Furthermore, the experimental *D*-value obtained by a fitting of temperature-dependent paramagnetic susceptibility data might be somewhat inaccurate since a simplified Hamiltonian with isotropic *q*-tensor and axial zero-field splitting was assumed.61 Nevertheless, the uncertainty of the PNMR shifts (rows in Tables S5 and S6) was to a large extent dominated by that of the EPR hyperfine couplings.

#### NMR resonance assignment strategy

Full assignment of paramagnetically shifted resonances of Co<sup>II-</sup> binding residues of SOD is reported in Table S7. The general assignment strategy is based on the comparison between experimental and calculated isotropic paramagnetic NMR shifts (Table S7) and shift anisotropies (SAs, Table S8). Depending on the quality of the experimental data for a given atom, we provide an unambiguous or just a tentative assignment. We note that, while we made use of previously published solution NMR <sup>1</sup>H assignment to validate our method,<sup>20,62</sup> the combination of the experimental and calculated data would have allowed a complete assignment even without any prior <sup>1</sup>H NMR information, just by comparing the calculated shift intervals with the experimental shifts.

Unambiguously assigned resonances. From the comparison of the <sup>1</sup>H spin-echo spectrum (Fig. 2) with the previously published <sup>1</sup>H solution spectrum<sup>20,62</sup> it is evident that the pattern of the observed shifts is preserved, and thus the available solution assignment can be transferred to the solid state. In particular, His71  $H_{\epsilon 2}$  and  $H_{\delta 2}$ , His80  $H_{\epsilon 2}$  and  $H_{\delta 2}$ , His63  $H_{\delta 2}$ , and Asp83  $H_{\beta 1}$ and  $H_{\beta 2}$  are readily assigned. The His63  $H_{\epsilon 2}$  resonance is not observed. This might be due to chemical exchange phenomena occurring at this solvent-exposed site, as was already noticed in solution.<sup>20</sup> All these nuclei can be correlated in the solid state with the directly attached <sup>13</sup>C or <sup>15</sup>N nuclei through the <sup>1</sup>H,<sup>13</sup>C and <sup>1</sup>H,<sup>15</sup>N TEDOR spectra (Fig. 2). Thus, we assigned His63, His71, and His80 C<sub> $\delta2$ </sub>, His71 and His80 N<sub> $\epsilon2$ </sub>, and Asp83 C<sub> $\beta$ </sub>. The  $^1\text{H}, ^{13}\text{C}$  TEDOR experiment with the RFDR mixing provided an additional confirmation of the assignment, displaying correlations between  $C_{\delta 2}$  and  $H_{\epsilon 2}$  nuclei in His71 and His80 (Fig. 2).

The assignment made then validates our computational approach. Notably, for model F all the observed resonances in the TEDOR spectra lie in the corresponding calculated intervals, indicating that our computational approach offers a reliable PNMR shift prediction.

*Tentatively assigned resonances.* Once the computational approach is validated, the calculated data can be used to assign all the other observed resonances in the <sup>1</sup>H and <sup>13</sup>C 1D spectra to the corresponding nuclei.

Two very broadened resonances appear in the <sup>1</sup>H spin-echo spectrum at 82 and 68 ppm, both characterized by a very large SA. Based on calculations these peaks might be assigned to H<sub>\epsilon1</sub> of His80 and His71, respectively. We note that, in principle, H<sub>\epsilon1</sub>-C<sub>\epsilon1</sub> correlations should be observable in the <sup>1</sup>H,<sup>13</sup>C TEDOR spectrum. However, strong relaxation effects due the metal proximity prevent the observation of these correlations. His63 H<sub>\epsilon1</sub> is not observed even in the <sup>1</sup>H spin-echo spectrum, but it is expected to be appreciably broadened because of relaxation

effects. Based on calculations this signal is probably overlapped with stronger <sup>1</sup>H signals around 50 ppm.

Broad resonances appearing at -26, -13, and -8 ppm in the <sup>1</sup>H spin-echo spectrum can be tentatively assigned to His63 H<sub>β1</sub>, His71 H<sub>β2</sub> and His71 H<sub>β1</sub> nuclei, respectively (Fig. S5). Note that the calculated SAs (Table S8) of all Co<sup>II</sup>-binding residues strongly differ between H<sub>β2</sub> and H<sub>β1</sub>, and thus they might be used to stereo-specifically distinguish between the H<sub>β</sub> nuclei. Moreover, His71 H<sub>β2</sub> at -13 ppm correlates in the TEDOR spectrum with a <sup>13</sup>C nucleus resonating at 119 ppm (not shown), which is then assigned to His71 C<sub>β</sub>. No TEDOR correlations are observed for the other two negatively shifted <sup>1</sup>H resonances, probably again because of strong relaxation effects. The calculations indicate that His80 H<sub>β1</sub>, H<sub>β2</sub>, His63 H<sub>β2</sub>, and Asp83 H<sub>α</sub> are probably buried in the diamagnetic bulk.

In the <sup>13</sup>C spin-echo and aMAT spectra unassigned resonances show up at 1210, 960, 915, 775, 358, and 220 ppm (Fig. S3). Based on calculations, the resonance at 1210 ppm can be assigned to His80  $C_{\epsilon 1}$ , while the resonances at 960 and 915 ppm likely belong to His63 and His71 H<sub>ɛ1</sub>, respectively, although the reversed assignment cannot be completely excluded given the proximity of the two peaks and the computational uncertainty. The calculated ranges for Cy of His71 and His80 almost coincide, and the calculated SAs are also very similar. The broad signal at 775 ppm can thus be assigned to either of the two or to both of them. The peak at 358 ppm is most likely assignable to His63 C<sub>v</sub>, although in the absence of the experimental SA value the assignment to His63 C<sub>β</sub> cannot be completely excluded. Finally, the signal observed in <sup>13</sup>C aMAT at 220 ppm coincides with the calculated shift ranges of His63 C<sub>B</sub> and Asp83 C<sub>g</sub> but only Asp83  $C_{\alpha}$  gives acceptable agreement between the experimental and calculated SA values. Unassigned remain His63 C<sub>β</sub>, His80  $C_{\beta}$ , and Asp83  $C_{\gamma}$ , all of which, according to the calculations, are likely buried in the diamagnetic bulk.

In summary, the metal center of SOD contains eighteen <sup>1</sup>H, fifteen <sup>13</sup>C, and six <sup>15</sup>N atoms in the contact-shift regime. We observed and at least tentatively assigned twelve <sup>1</sup>H, eleven <sup>13</sup>C, and two <sup>15</sup>N resonances, and based on calculations predicted the likely positions and anisotropies of all remaining signals.

### ASSOCIATED CONTENT

#### Supporting Information

NMR pulse sequence schemes, NMR acquisition parameters additional <sup>13</sup>C and <sup>1</sup>H spectra, EPR parameters for the Co<sup>II</sup> center of CoSOD, selected structure parameters of the metal coordination in SOD, reference isotropic shielding, calculated paramagnetic NMR shifts with PBE0 and PBE50 hyperfine coupling, assignment of <sup>1</sup>H, <sup>13</sup>C, and <sup>15</sup>N paramagnetic NMR shifts and shift anisotropies, Cartesian coordinates of molecular models (PDF). The Supporting Information is available free of charge on the ACS Publications website.

The NMR raw data have been deposited at: [will be added on publication] as detailled in the SI.

### **AUTHOR INFORMATION**

Corresponding Authors

Lyndon Emsley (lyndon.emsley@epfl.ch), Roberta Pierattelli (roberta.pierattelli@unifi.it), Guido Pintacuda (guido.pintacuda@ens-lyon.fr)

#### Author Contributions

‡These authors contributed equally.

#### Present Addresses

<sup>\$</sup>McMaster University, 1280 Main St. West, Hamilton, Ontario L8S 4K1, Canada

<sup>¥</sup>Stockholm University, Department of Materials and Environmental Chemistry, Arrhenius Laboratory, SE-106 91 Stockholm, Sweden.

#### Notes

The authors declare no competing financial interests.

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# **Supporting Information**

# Pico-meter resolution structure of the coordination sphere in the metal-binding site in a metalloprotein by NMR

Andrea Bertarello,<sup>1,4,‡</sup> Ladislav Benda,<sup>1,‡</sup> Kevin J. Sanders,<sup>1,\$</sup> Andrew J. Pell,<sup>1,¥</sup> Michael J. Knight,<sup>1</sup> Vladimir Pelmenschikov,<sup>2</sup> Leonardo Gonnelli,<sup>3</sup> Isabella C. Felli,<sup>3</sup> Martin Kaupp,<sup>2</sup> Lyndon Emsley,<sup>4,\*</sup> Roberta Pierattelli,<sup>3,\*</sup> Guido Pintacuda<sup>1,\*</sup>

<sup>1</sup>Université de Lyon, Centre de RMN à Très Hauts Champs, FRE 2034 CNRS/Université Claude Bernard Lyon 1/ENS Lyon, 5 rue de la Doua, 69100 Villeurbanne, France ; <sup>2</sup>Technische Universität Berlin, Institut für Chemie, Straße des 17 Juni 135, 10623 Berlin, Germany; <sup>3</sup>University of Florence, Department of Chemistry and Magnetic Resonance Center (CERM), Via L. Sacconi 6, 50019 Sesto Fiorentino, Italy; <sup>4</sup>École Polytechnique Fédérale de Lausanne (EPFL), Institut des Sciences et Ingénierie Chimiques, CH-1015 Lausanne, Switzerland

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Table S8. Paramagnetic NMR shift anisotropies.

Cartesian coordinates of molecular models.

The NMR raw data are available from [link to be added on publication] in the JCAMP-DX version 6.0 standard and the original TopSpin data. Data are made available under the license CC-BY-4.0 (Creative Commons Attribution-ShareAlike 4.0 International)

## Figure S1. Pulse sequence schemes used in the present work.

- (A) Spin echo.  $\tau_r$  indicates the rotor period.
- (B) aMAT (adapted from ref. (34))
- (C) <sup>1</sup>H,X TEDOR (where X indicates either <sup>13</sup>C or <sup>15</sup>N). N is an integer and k is an odd integer.
- (D)<sup>1</sup>H,X TEDOR (where X indicates <sup>13</sup>C in this work) with spin magnetization exchange between <sup>1</sup>H nuclei close in space via RFDR mixing. N and n are integers and k is an odd integer.



# Figure S2. Molecular models used for quantum chemistry calculations

Left: the larger model m1 used for DFT structure optimization and hyperfine coupling calculations. Right: the smaller model m0 used for ab initio calculations of g- and D-tensors, showing the spin-density distribution (from a SA-CASSCF(7,5) calculation, 0.002 a.u. isosurface).



# Figure S3. Additional <sup>13</sup>C spectra.

<sup>13</sup>C spin-echo spectrum (blue) and projection from the <sup>13</sup>C aMAT spectrum (magenta), with assignment of observable peaks and comparison with the calculated <sup>13</sup>C shift ranges for model F. <sup>13</sup>C spin-echo spectrum was acquired at 100 kHz MAS, ~280 K on a 500 MHz spectrometer (11.7 T) while the <sup>13</sup>C aMAT spectrum was acquired at 30 kHz MAS, ~280 K on a 500 MHz spectrometer (11.7 T).



(\*) Assigned based on calculations; see the "Assignment strategy" section and discussion therein.

# Figure S4. <sup>1</sup>H aMAT spectrum.

(A) <sup>1</sup>H aMAT spectrum acquired at 40 kHz MAS, ~280 K on a 500 MHz spectrometer (11.7 T). (B) The row corresponding to His71  $H_{\delta 2}$  spinning-sideband manifold (blue) and the fitted profile (magenta).



# Figure S5. Additional <sup>1</sup>H spectra.

<sup>1</sup>H spin-echo spectrum, acquired at 100 kHz MAS, with assignment of observable peaks and comparison with the calculated <sup>1</sup>H shift ranges for model F.



(\*) Assigned based on calculations; see the "Assignment strategy" section and discussion therein.

# Figure S6. Spinning sidebands manifold of His71 $H_{\epsilon 1}$ and His80 $H_{\epsilon 1}$ .

Full <sup>1</sup>H spin-echo spectrum, acquired at 100 kHz MAS, with zooms on the spinning sidebands manifold of His71  $H_{\epsilon 1}$  and His80  $H_{\epsilon 1}$  resonances.



# Table S1. Selected structure parameters of the metal coordination in SOD.

	Α	В	С	D	Е	F	G	Н	Ι	J	RMSD
Optimized structures:											
<i>r</i> (Co–His63 Nठ1) <sup><i>a</i></sup>	2.036	2.034	2.045	2.029	2.046	2.042	2.035	2.037	2.044	2.046	1.700·10 <sup>-3</sup> °
<i>r</i> (Co–His71 Nठ1) <sup>a</sup>	2.054	2.047	2.048	2.057	2.046	2.048	2.051	2.052	2.053	2.052	9.428·10 <sup>-4</sup> °
<i>r</i> (Co–His80 Nठ1) <sup>a</sup>	2.048	2.033	2.033	2.047	2.036	2.036	2.033	2.049	2.045	2.036	1.414·10 <sup>-3</sup> ¢
<i>r</i> (Co–Asp83 Oδ1) <sup>a</sup>	1.991	1.935	1.947	1.966	1.939	1.945	1.940	1.973	1.924	1.974	3.399·10 <sup>-3</sup> °
<i>r</i> (Co–Asp83 Οδ2) <sup>a</sup>	2.508	2.833	2.777	2.631	2.828	2.762	2.814	2.598	2.871	2.663	2.825·10 <sup>-2</sup> °
Δ <i>r</i> (Co–Oδ) <sup>a</sup>	0.517	0.898	0.831	0.665	0.889	0.816	0.874	0.624	0.947	0.688	-
Θ(His63 Nδ1–Co–His71 Nδ1) <sup>b</sup>	99.2	101.3	103.8	100.2	102.1	102.8	102.0	98.6	101.2	103.0	0.488 <sup>c</sup>
Θ <i>(</i> His71 Nδ1–Co–His80 Nδ1) <sup>b</sup>	123.0	124.2	119.4	123.3	123.0	120.1	124.3	123.2	120.9	119.3	1.377 <i>°</i>
Θ(His80 Nδ1–Co–Asp83 Oδ1) <sup>b</sup>	119.7	115.0	117.7	119.8	116.5	117.4	113.8	120.3	113.1	121.4	0.705 <sup>c</sup>
Θ(Asp83 Oδ1–Co– His63 Nδ1) <sup>b</sup>	109.7	104.3	101.3	106.7	104.3	101.4	103.9	109.2	105.4	107.9	1.559 <i>°</i>
PDB structures:											
r(Zn–His63 Nδ1) <sup>a</sup>	2.102	2.121	2.079	2.125	2.124	2.088	2.071	2.109	2.106	2.078	1.916·10 <sup>-2 d</sup>
r(Zn–His71 Nδ1) <sup>a</sup>	2.058	2.076	2.062	2.081	2.097	2.050	2.070	2.051	2.053	2.068	1.426·10 <sup>-2 d</sup>
r(Zn–His80 Nδ1) <sup>a</sup>	2.044	2.055	2.046	2.093	2.079	2.063	2.053	2.085	2.042	2.061	1.700·10 <sup>-2 d</sup>
<i>r</i> (Zn–Asp83 Об1) <sup>a</sup>	1.923	1.966	1.943	1.955	1.964	1.951	1.948	1.919	1.947	1.934	1.495·10 <sup>-2 d</sup>
<i>r</i> (Zn–Asp83 Об2) <sup>a</sup>	3.038	2.937	3.742	2.890	2.512	3.160	2.692	3.191	2.817	2.999	3.157·10 <sup>-1 d</sup>
$\Delta r$ (Zn–O $\delta$ ) <sup>a</sup>	0.772	0.701	1.115	0.972	1.799	0.935	0.548	1.209	0.745	1.272	-
Θ <i>(</i> His63 Nδ1–Co–His71 Nδ1) <sup>b</sup>	105.0	99.5	106.8	107.9	118.4	111.2	112.4	104.5	103.5	113.5	5.326 <sup>d</sup>
Θ(His71 Νδ1–Co–His80 Νδ1) <sup>b</sup>	112.4	132.5	111.0	116.4	112.0	112.9	121.1	119.9	129.3	103.2	8.396 <sup>d</sup>
Θ(His80 Nδ1–Co–Asp83 Oδ1) <sup>b</sup>	111.4	100.8	98.4	110.3	101.3	101.9	107.3	96.9	97.5	107.8	5.125 <sup>d</sup>
Θ(Asp83 Οδ1–Co– His63 Nδ1) <sup>b</sup>	116.8	105.9	132.8	117.2	101.8	114.6	102.7	121.5	107.6	118.7	9.100 <sup>d</sup>

<sup>*a*</sup> Distance in Å. <sup>*b*</sup> Angles in °. <sup>*c*</sup> Models C, E, F. <sup>*d*</sup> Models A-J.

# Table S2. NMR acquisition parameters.

Spectrum	Max indirect evolution	Spectral window (ppm)	Scans per point	Experimental time
<sup>1</sup> H spin echo	-	1500	92160	2 h
<sup>13</sup> C spin echo	-	2980	614400	12.5 h
<sup>1</sup> H, <sup>15</sup> N TEDOR	0.2 ms	1500 (1H)	27136	10 h
		1971 ( <sup>15</sup> N)		
<sup>1</sup> H, <sup>13</sup> C TEDOR	0.2 ms	1500 (1H)	10240	6.5 h
		794 ( <sup>13</sup> C)		
<sup>1</sup> H, <sup>13</sup> C TEDOR	0.2 ms	1500 (1H)	25600	14 h
(with RFDR mix- ing)		794 ( <sup>13</sup> C)		
<sup>1</sup> H aMAT	0.325 ms	800 (ω₂)	5120	10.5 h
		400 (ω <sub>1</sub> )		
<sup>13</sup> C aMAT	0.633 ms	1986 (ω₂)	24832	4.4 d
		1758 (ω <sub>1</sub> )		

# Table S3. EPR parameters for the Co<sup>II</sup> center of CoSOD.

Summary of EPR parameters for the Co<sup>II</sup> center of CoSOD calculated at NEVPT2 level, compared to the available experimental data.

EPR parameter	Α	В	С	D	Е	F	G	н	Ι	J	<b>EXP</b> <sup>a</sup>
<b>G</b> iso	2.231	2.222	2.222	2.229	2.223	2.221	2.224	2.231	2.227	2.226	2.24
<i>g</i> 11	2.183	2.178	2.196	2.180	2.183	2.192	2.179	2.185	2.180	2.196	
<b>g</b> 22	2.236	2.232	2.219	2.229	2.229	2.223	2.235	2.231	2.230	2.216	
<b>g</b> 33	2.274	2.257	2.251	2.277	2.256	2.247	2.258	2.276	2.269	2.265	
<b>g</b> aniso	0.064	0.052	0.043	0.072	0.050	0.039	0.051	0.068	0.064	0.059	
D <sub>11</sub> <sup>b</sup>	4.676	4.618	3.275	4.980	4.483	3.523	4.624	4.817	4.916	3.538	
D22 <sup>b</sup>	- 0.509	- 1.287	0.140	- 0.161	- 0.743	- 0.398	- 1.721	- 0.069	- 1.105	0.985	
D <sub>33</sub> <sup>b</sup>	- 4.168	- 3.331	- 3.415	- 4.819	- 3.740	- 3.125	- 2.903	- 4.749	- 3.811	- 4.524	
۱ <i>D</i> ۱ <i>۵</i>	7.01	6.93	5.12	7.47	6.72	5.28	6.94	7.23	7.37	6.79	10.8
E/D	0.261	0.148	0.306	0.312	0.223	0.258	0.085	0.324	0.184	0.188	
Q11 <sup><i>c</i></sup>	13.9	8.7	9.3	11.0	4.2	11.0	10.4	10.8	8.6	18.0	
Q <sub>22</sub> <sup>c</sup>	7.0	14.0	4.4	6.1	9.2	6.6	15.9	9.1	5.8	12.1	
<b>Q</b> 33 <sup><i>c</i></sup>	12.0	16.3	8.4	9.2	9.1	11.6	17.5	8.0	6.4	16.5	

<sup>*a*</sup> Taken from ref. (61).

<sup>*b*</sup> In cm<sup>-1</sup>. Principal values of the traceless *D*-tensor ( $D_{ii}$ , ii = 11, 22, 33) sorted in mutual correspondence with the principal values of the *g*-tensor ( $g_{ii}$ ) such that the principal axes of the two tensors with the same label approximately coincide.

<sup>c</sup> Angular deviation (in degree) between corresponding principal axes of the *g*- and *D*-tensors.

# Table S4. Reference isotropic shielding.

Calculated reference isotropic shielding values (in ppm).

Nucleus	Experimental NMR reference	$\sigma_{K}^{ m ref}$
۱H	TMS <sup>a</sup>	31.6
<sup>13</sup> C	TMS <sup>a</sup>	185.7
<sup>15</sup> N	NH <sub>3</sub> ( <i>I</i> )	218.7

<sup>*a*</sup> 1 % solution with CDCl<sub>3</sub> solvent.

# Table S5. Calculated paramagnetic NMR shifts with PBE0 hyperfine coupling.

Residue	Atom	Α	В	С	D	Е	F	G	н	I	J
His63	Сβ	300	280	264	294	261	308	274	300	335	246
	Cõ2	790	771	735	792	758	741	760	797	698	794
	Cɛ1	947	956	995	948	921	979	967	961	976	863
	Сү	570	533	562	538	525	525	555	543	456	621
	Ηβ2	-1	1	0	5	0	2	-3	-1	-3	-3
	Ηβ1	-14	-17	-7	-13	-14	-17	-14	-16	-22	-13
	Ηδ2	55	50	49	53	48	48	49	55	45	54
	Hɛ1	57	59	59	56	59	58	64	55	59	58
	Hɛ2	78	74	69	77	72	72	72	79	72	72
	Νδ1	17338	16426	16056	17236	16506	16210	15962	17735	15398	17187
	Νε2	1296	1268	1282	1320	1266	1264	1248	1318	1219	1280
His71	Сβ	204	216	184	211	199	184	212	215	175	188
	Cõ2	706	677	693	694	663	695	660	704	696	686
	Cɛ1	961	862	879	883	926	898	879	914	920	936
	Сү	807	854	911	762	877	879	820	833	846	868
	Ηβ2	-17	-16	-7	-17	-14	-8	-18	-16	-15	-7
	Ηβ1	-2	1	0	0	-3	0	0	-1	-3	-1
	Ηδ2	64	63	64	61	63	63	61	65	62	63
	Hɛ1	94	86	95	87	90	89	80	96	83	97
	Hɛ2	69	65	58	70	60	60	63	70	61	59
	Nō1	16296	15373	15339	15970	15155	15363	15326	16109	15684	15442
	Νε2	1291	1235	1277	1249	1274	1276	1231	1278	1288	1290
His80	Сβ	153	92	131	150	107	126	79	162	90	199
	Cõ2	585	568	548	551	563	545	562	573	536	596
	Cɛ1	1299	1306	1331	1297	1308	1327	1267	1315	1244	1352
	Сү	726	908	870	804	901	872	911	789	944	827
	Ηβ2	-1	5	-2	-4	3	0	6	-5	13	-12
	Ηβ1	5	4	3	4	3	5	5	3	9	-1
	Ηδ2	59	59	60	60	60	59	58	60	61	60
	Hɛ1	93	101	108	99	105	107	96	97	111	98
	Hɛ2	62	47	50	55	50	48	45	61	40	65
	Νδ1	13710	11663	11870	12651	11981	11778	11506	13180	11961	13588
	Νε2	1355	1360	1374	1341	1364	1357	1338	1345	1355	1377
Asp83	Ca	288	256	244	270	236	262	240	272	256	243
	Сβ	215	568	475	328	531	477	581	258	621	292
	Сү	-127	-2	-62	-88	-48	-44	-21	-108	81	-65
	Ηα	5	7	7	8	7	8	6	7	7	7
	Ηβ2	59	46	49	49	42	49	28	58	47	59
	Ηβ1	27	40	42	34	45	39	57	31	40	32

# Table S6. Calculated PNMR shifts with PBE50 hyperfine coupling.

Residue	Atom	Α	в	С	D	Е	F	G	н	I	J
His63	Сβ	226	214	201	223	198	236	208	226	260	187
	Cō2	636	607	577	630	601	586	601	637	547	640
	Cɛ1	711	728	749	716	693	741	737	723	761	619
	Сү	415	384	413	388	378	373	401	388	320	463
	Ηβ2	-3	-2	-2	2	-3	-3	-5	-4	-9	-6
	Ηβ1	-16	-17	-9	-15	-15	-17	-16	-18	-21	-14
	Ηδ2	38	34	34	37	32	32	33	37	30	36
	Hɛ1	43	45	43	42	44	42	49	41	44	43
	Hɛ2	63	59	55	62	58	58	58	64	58	58
	Νδ1	14875	13907	13638	14699	14040	13759	13498	15163	12993	14684
	Νε2	954	934	951	972	931	934	920	968	904	932
His71	Сβ	154	163	141	160	151	141	160	162	134	141
	Cõ2	544	521	526	536	504	527	504	545	529	522
	Cɛ1	652	598	597	610	645	613	613	620	642	625
	Сү	612	668	724	572	691	692	639	636	656	693
	Ηβ2	-15	-14	-5	-14	-12	-6	-16	-13	-13	-6
	Ηβ1	-3	-1	0	-1	-3	-1	-2	-2	-3	-1
	Ηδ2	44	45	46	42	45	45	43	44	45	45
	Hɛ1	78	71	77	74	74	73	66	81	68	79
	Hɛ2	53	50	44	54	46	45	49	53	47	44
	Nō1	13571	12860	12795	13352	12647	12830	12800	13437	13155	12847
	Νε2	968	937	969	942	970	969	934	960	980	972
His80	Сβ	123	81	108	122	92	104	73	131	77	160
	Cõ2	434	412	400	408	409	399	406	427	390	446
	Cɛ1	932	931	946	926	933	938	896	943	869	971
	Сү	566	740	708	645	730	714	747	618	794	638
	Ηβ2	-1	7	0	-3	5	2	8	-4	14	-11
	Ηβ1	4	5	4	4	4	5	6	2	10	-2
	Ηδ2	45	47	47	46	48	47	46	45	49	45
	Hɛ1	73	78	85	78	82	83	73	77	85	80
	Hɛ2	48	37	39	43	39	37	35	47	30	50
	Nō1	11332	9663	9838	10454	9949	9742	9500	10925	9888	11280
	Νε2	1031	1048	1057	1025	1053	1041	1030	1028	1029	1055
Asp83	Са	191	170	163	180	157	174	158	180	170	163
	Сβ	100	369	299	189	340	299	378	135	410	163
	Сү	-35	72	14	-9	37	23	51	-16	147	16
	Ηα	6	7	8	8	8	8	6	8	7	8
	Ηβ2	34	23	25	26	20	26	13	31	24	31
	Ηβ1	17	24	25	22	27	24	35	20	24	20

# Table S7. Assignment of <sup>1</sup>H, <sup>13</sup>C, and <sup>15</sup>N paramagnetic NMR shifts.

Assignment of the experimental <sup>1</sup>H, <sup>13</sup>C, and <sup>15</sup>N paramagnetic NMR shifts (in ppm) of the Co<sup>II</sup>-binding residues of CoSOD and comparison with the calculated data for model F.<sup>*a*</sup> Numbers in italics indicate a tentative assignment.

		Experiment	Expe	eriment	Calculation				
		(solution NMR) <sup>20</sup>	(MAS	S NMR)	ŀ	PBE0 <sup>b</sup>	Pl	3 <i>E50</i> <sup>b</sup>	
Residue	Atom type	۱H	۱H	<sup>13</sup> C/ <sup>15</sup> N	۱H	<sup>13</sup> C/ <sup>15</sup> N	۱H	<sup>13</sup> C/ <sup>15</sup> N	
His63	β1	-	-26	_	-17	308	-17	236	
	β2	-	-	-	2	500	-3	200	
	γ			358		525		373	
	δ1			-		16210		13759	
	δ2	46	45	631	48	741	32	586	
	ε1	-	-	960	58	979	42	741	
	ε2	-	-	-	72	1265	58	934	
His71	β1	-	-8	119	0	184	-1	141	
	β2	-	-13	110	-8	104	-6	171	
	γ			775		879		692	
	δ1			-		15363		12830	
	δ2	56	56	600	63	695	45	527	
	ε1	-	68	915	89	898	73	613	
	ε2	49	51	1034	63	1276	49	969	
His80	β1	-	-	_	5	126	5	104	
	β2	-	-		0	120	2	101	
	Y			775		872		714	
	δ1			-		11778		9742	
	δ2	49	50	458	59	545	47	399	
	ε1	-	82	1210	107	1327	83	938	
	ε2	39	38	1095	48	1357	37	1041	
Asp83	α	-	-	220	8	262	8	174	
	β1	36 (43)	36	350	39	477	24	299	
	β2	43 (36)	43	000	49	.,,	26	200	
	Y			-		-44		23	

<sup>*a*</sup> Structure optimized as described in the "Materials and methods" section.

<sup>*b*</sup> Method for hyperfine coupling.

(-) Atom unassigned.

## Table S8. Paramagnetic NMR shift anisotropies.

Experimental paramagnetic NMR shift anisotropies (SAs, in ppm, defined as  $\delta_{ZZ} - \delta_{iso}$  in Haeberlen convention (60)) for the <sup>1</sup>H, <sup>13</sup>C, and <sup>15</sup>N nuclei of the Co<sup>II</sup>-binding residues of CoSOD and comparison with the calculated data for model F.<sup>*a*</sup> Numbers in italics indicate a tentative assignment.

		Experiment		Calculation					
				F	PBE0 <sup>b</sup>	PB	E50 <sup>b</sup>		
Residue	Atom type	۱H	<sup>13</sup> C/ <sup>15</sup> N	۱H	<sup>13</sup> C/ <sup>15</sup> N	۱H	<sup>13</sup> C/ <sup>15</sup> N		
His63	β1	618 <sup>c</sup>	_	495	582	486	573		
	β2	-	_	871	502	858	0,0		
	Y		-		925		887		
	δ1		-		4239		3654		
	δ2	188	381	181	335	175	325		
	ε1	-	-	724	791	714	789		
	ε2	-	-	205	314	196	305		
His71	β1	232	_	239	183	234	475		
	β2	780 °	_	617	400	607	475		
	γ		1019		857		810		
	δ1		-		4237		3602		
	δ2	184	381	170	378	165	356		
	ε1	795 °	-	835	1040	822	1025		
	ε2	223	-	204	416	197	389		
His80	β1	-	_	334	561	327	552		
	β2	-		956	501	943	552		
	γ		1019		912		858		
	δ1		-		4408		3813		
	δ2	199	405	172	378	165	362		
	ε1	994 <sup>c</sup>	-	784	989	770	959		
	ε2	257	-	207	499	198	469		
Asp83	α	-	309	332	276	314	256		
	β1	201	_	277	497	265	421		
	β2	211	_	247		234	741		
	Y		-		1162		1141		

<sup>a</sup> Structure optimized as described in the "Materials and methods" section.

<sup>b</sup> Method for hyperfine coupling.

<sup>c</sup> Estimated from <sup>1</sup>H spin echo.

(-) Atom unassigned or SA not measurable.

## Cartesian coordinates of molecular models

32			
1S0S	.A model m0		
Co	-0.0242546	0.1605536	-0.3265478
Н	1.7076856	-2.5647321	0.4842243
С	1.9176107	-1.7474495	1.1699444
N	1.3085046	-0.5119577	1.0573960
С	2.7669911	-1.7038601	2.2481675
С	1.7774254	0.2488030	2.0378232
N	2.6582408	-0.4404712	2.7716836
Н	3.4228875	-2.4538182	2.6799148
Н	1.4998462	1.2827071	2.2314129
Н	3.1565346	-0.0853514	3.5804428
Н	0.4146576	3.5313186	-0.5989040
С	-0.2521549	3.2621232	0.2164180
N	-0.5283384	1.9501894	0.5455545
С	-0.9706774	4.0742706	1.0588063
С	-1.3863500	1.9722419	1.5565091
N	-1.6707631	3.2389857	1.8891444
Н	-1.0419809	5.1567282	1.1197652
Н	-1.8134210	1.1019318	2.0521591
Н	-2.3004123	3.5241700	2.6316032
Н	-0.1358088	-1.2562540	-3.3364084
С	0.7494183	-0.6333511	-3.2374147
N	1.0513282	0.0316070	-2.0651440
С	1.7081004	-0.3163726	-4.1686739
С	2.1696158	0.7107871	-2.2808597
N	2.5827533	0.5283201	-3.5410943
Н	1.8384915	-0.6243519	-5.2025500
Н	2.6972699	1.3296598	-1.5587992
Н	3.4093113	0.9463235	-3.9554560
Н	-3.5939903	-0.4902475	-0.9356988
С	-2.5191806	-0.2123368	-0.9342619
0	-1.7374072	-0.8376142	-0.1487169
0	-2.0662745	0.6868892	-1.6834229

32			
1505	B.B model m0		
Co	-0.0280725	0.2037086	-0.2585425
н	-3.2337965	0.0963939	0.5811312
С	-2.5966248	-0.0843209	1.4435240
N	-1.2223120	-0.1897439	1.3397977
С	-2.9354546	-0.2413988	2.7651894
С	-0.7517149	-0.4008740	2.5625885
N	-1.7587170	-0.4347515	3.4420413
н	-3.8963688	-0.2248320	3.2710407
Н	0.2929076	-0.5371205	2.8323866
Н	-1.6627949	-0.5816541	4.4410515
Н	2.7651300	-1.7918221	-0.3530286
С	2.8595232	-0.9517398	0.3306420
N	1.8315052	-0.0596241	0.5546074
С	3.9386653	-0.5590803	1.0847755
С	2.2802086	0.8462123	1.4152201
N	3.5462544	0.5690991	1.7545855
Н	4.9376804	-0.9766365	1.1740239
Н	1.7205712	1.6995229	1.7953069
Н	4.1126582	1.1090858	2.4003552
Н	-1.3999808	0.8021586	-3.2324817
С	-1.2684374	-0.2648908	-3.0701019
N	-0.7016629	-0.7698333	-1.9107375
С	-1.5649343	-1.3257271	-3.8908179
С	-0.6730100	-2.0903730	-2.0344101
N	-1.1799164	-2.4529545	-3.2179021
Н	-2.0151779	-1.3654083	-4.8786980
н	-0.3077515	-2.7985245	-1.2935890
Н	-1.2652408	-3.4071622	-3.5524396
Н	1.1143942	3.6884432	-1.0324162
С	0.9289862	2.5936254	-1.1103128
0	-0.0247007	2.1342280	-0.3908291
0	1.6029067	1.8716301	-1.8659729

32			
1505	S.C model m0		
Co	-0.0508109	-0.1697423	-0.2546018
Н	1.3896976	2.6871649	0.5969086
С	1.1056607	2.1182934	1.4790181
N	0.3593196	0.9570255	1.4014918
С	1.3873059	2.3579657	2.8014212
С	0.1987222	0.5156352	2.6424546
N	0.8075731	1.3353490	3.5067299
Н	1.9438028	3.1532224	3.2885596
Н	-0.3487799	-0.3744516	2.9431939
Н	0.8337615	1.2167309	4.5137877
Н	-3.2169257	-1.5637667	-0.4731070
С	-2.5447672	-2.0964757	0.1946697
N	-1.2594834	-1.6613411	0.4575039
С	-2.7512103	-3.2584698	0.8998659
С	-0.7112410	-2.5427361	1.2848773
N	-1.5870902	-3.5142308	1.5722261
Н	-3.6176733	-3.9112032	0.9614474
Н	0.3065596	-2.5104091	1.6713507
Н	-1.4096320	-4.3025739	2.1857982
Н	0.8367259	0.8380007	-3.3102054
С	-0.1303701	1.2445809	-3.0262552
N	-0.7014720	0.9946392	-1.7885757
С	-1.0105888	2.0157616	-3.7464235
С	-1.8746930	1.6125991	-1.7663354
N	-2.0914312	2.2282932	-2.9338511
Н	-0.9507133	2.4316702	-4.7481390
Н	-2.5699350	1.6432865	-0.9296378
Н	-2.9191172	2.7673834	-3.1667405
Н	2.3516374	-2.8334349	-1.3267378
С	1.5005472	-2.1178673	-1.2886571
0	1.6291757	-1.1234868	-0.4935972
0	0.4832282	-2.2713817	-1.9901701

32			
1505	S.D model m0		
Co	0.1971505	-0.1756679	-0.3185337
Н	-1.7885051	2.4293635	0.1709105
С	-1.8704885	1.7174053	0.9884740
N	-1.1791566	0.5204472	1.0000283
С	-2.6110711	1.7882735	2.1424916
С	-1.4943817	-0.1066758	2.1254712
N	-2.3541839	0.6319555	2.8353620
Н	-3.2827183	2.5517921	2.5229654
Н	-1.1221386	-1.0788147	2.4413336
Н	-2.7462093	0.3753639	3.7349257
Н	-0.0891626	-3.5469984	-0.5512897
С	0.5296150	-3.2468653	0.2907281
N	0.7446285	-1.9239787	0.6176782
С	1.2320711	-4.0274593	1.1760045
С	1.5543185	-1.9072785	1.6685843
N	1.8635007	-3.1609015	2.0289919
Н	1.3409428	-5.1060764	1.2509846
Н	1.9286290	-1.0192762	2.1753989
Н	2.4658546	-3.4180515	2.8039590
Н	0.4506584	1.2662940	-3.3318491
С	-0.3847684	0.5717761	-3.2981970
N	-0.7202940	-0.1198596	-2.1472312
С	-1.2406742	0.1760659	-4.2966471
С	-1.7607167	-0.8868835	-2.4453145
N	-2.0890139	-0.7380527	-3.7335759
Н	-1.3123157	0.4675277	-5.3407365
Н	-2.2915940	-1.5462727	-1.7627082
Н	-2.8433361	-1.2247008	-4.2067544
Н	3.8212555	0.5434920	-0.3920378
С	2.7770077	0.2418062	-0.6236368
0	1.8404534	0.8614229	-0.0190966
0	2.5207153	-0.6557497	-1.4547320

32			
1505	.E model m0		
Co	-0.0087296	-0.0564847	-0.4509002
Н	3.1500158	-0.0872481	0.5757333
С	2.4780220	0.1458157	1.3980952
N	1.1167073	0.3112794	1.2171286
С	2.7544174	0.3175345	2.7325567
С	0.5953049	0.5757362	2.4084217
N	1.5547906	0.5834970	3.3406831
Н	3.6856088	0.2680403	3.2893586
Н	-0.4531637	0.7713130	2.6204534
Н	1.4140307	0.7593340	4.3297547
Н	-2.8124163	1.8664189	-0.9308429
С	-2.9364611	1.1111971	-0.1589718
N	-1.9082962	0.2773073	0.2330468
С	-4.0535793	0.7830930	0.5710219
С	-2.3965056	-0.5329745	1.1645928
N	-3.6859855	-0.2492866	1.3914256
H	-5.0603438	1.1911478	0.5533895
H	-1.8510019	-1.3257495	1.6740313
H	-4.2830420	-0.7233021	2.0607983
H	1.5176961	-0.5560553	-3.3687705
С	1.4458832	0.5046687	-3.1422252
N	0.8069116	0.9737530	-2.0054660
С	1.8984066	1.5913759	-3.8502047
С	0.8851469	2.2974612	-2.0319576
N	1.5313130	2.6977785	-3.1333348
Н	2.4532877	1.6607705	-4.7816120
Н	0.5055183	2.9794906	-1.2737646
H	1.7219612	3.6623909	-3.3839898
H	-1.1849034	-3.5131767	-1.2794696
С	-0.9643568	-2.4249982	-1.3561034
0	-0.0203866	-1.9894166	-0.6042863
0	-1.5877951	-1.6873026	-2.1377104

32			
1505	.F model m0		
Co	0.0222598	-0.0767906	-0.3417255
Н	-1.2285894	2.9124039	0.3125503
С	-0.9368480	2.4064549	1.2296345
N	-0.5091188	1.0920725	1.2461499
С	-0.9021173	2.8811352	2.5182657
С	-0.2257223	0.7891934	2.5069720
N	-0.4495590	1.8466385	3.2951841
Н	-1.1498827	3.8519935	2.9376123
Н	0.1261129	-0.1722341	2.8736531
Н	-0.3109729	1.8723549	4.2997526
Н	-0.5556112	-3.4602170	-0.0987345
С	0.3051053	-3.1271372	0.4756094
N	0.6721594	-1.7979718	0.5580899
С	1.2064376	-3.8637486	1.2059259
С	1.7666469	-1.7417737	1.3076097
N	2.1098721	-2.9706720	1.7153969
Н	1.2775059	-4.9337599	1.3804794
Н	2.3275735	-0.8420150	1.5565707
Н	2.9069076	-3.1943240	2.3019636
Н	-0.6252381	0.7665598	-3.5220274
С	-1.4717504	0.2618905	-3.0637771
N	-1.4554863	-0.1502248	-1.7405957
С	-2.6726843	-0.1198284	-3.6093747
С	-2.6183824	-0.7428305	-1.5031009
N	-3.3674401	-0.7469994	-2.6112031
H	-3.0829335	0.0156429	-4.6060915
Н	-2.9447330	-1.1587020	-0.5520858
Н	-4.2986338	-1.1423786	-2.6883346
Н	3.4134991	0.2650833	-1.8792626
С	2.3599112	-0.0228558	-1.6681614
0	1.7124215	0.7304565	-0.8665869
0	1.8370622	-1.0245145	-2.1951125

32			
1509	S.G model m0		
C0	0 0566633	-0 0034000	-0 3652699
н	3 3196080	-0 1217816	0 2965850
c	2.7263951	-0.2025422	1.2041575
N	1.3503920	-0.0650730	1.2046537
c	3,1288790	-0.4500106	2.4935493
c	0.9424606	-0.2252086	2.4575855
N	1,9891676	-0.4612193	3.2554513
н	4.1118770	-0.6201181	2,9225118
н	-0.0849875	-0.1682213	2.8092434
н	1,9425241	-0.6188126	4.2563521
н	-2.8242140	1.7986710	0.0617967
С	-2.8545436	0.8253415	0.5447219
N	-1.7631478	-0.0175452	0.5816490
С	-3.8996806	0.2007091	1.1815351
С	-2.1426504	-1.1199588	1.2169090
N	-3.4243464	-1.0159549	1.5923584
н	-4.9240103	0.5191964	1.3548106
н	-1.5255208	-1.9975948	1.4033871
н	-3.9475986	-1.7238638	2.0968699
н	1.2642551	0.1524161	-3.4532975
С	1.1069155	1.1490978	-3.0492027
N	0.6059392	1.3567065	-1.7729542
С	1.3075556	2.3778637	-3.6279520
С	0.5223011	2.6689248	-1.5967978
N	0.9316127	3.3082343	-2.6980955
Н	1.6848561	2.6556583	-4.6082222
н	0.1847489	3.1770290	-0.6959445
н	0.9601117	4.3156977	-2.8152927
н	-1.2312468	-3.1538864	-1.9093801
С	-1.0068870	-2.0788895	-1.7278329
0	0.0238012	-1.8311746	-1.0137141
0	-1.7141031	-1.1754538	-2.2118231

32			
1SOS.H model m0			
Co	0.2066505	-0.0389056	-0.4364822
Н	-1.3643744	-2.8665010	0.3435441
С	-0.7016356	-2.5518742	1.1459881
N	0.0490409	-1.3941215	1.0758708
С	-0.4412086	-3.1533365	2.3528018
С	0.7379555	-1.3026923	2.2056080
N	0.4646844	-2.3477161	2.9950999
Н	-0.8221764	-4.0663912	2.8001107
Н	1.4295145	-0.5053265	2.4690083
Н	0.8607352	-2.5106163	3.9143536
Н	3.3229572	1.3286513	-0.1112203
С	2.5811432	1.8183885	0.5147194
N	1.2633311	1.4103777	0.5597200
С	2.7212717	2.9041828	1.3435693
С	0.6293732	2.2251107	1.3921088
N	1.4826355	3.1353605	1.8815714
Н	3.5854835	3.5211992	1.5737463
Н	-0.4274256	2.1792361	1.6497477
Н	1.2439638	3.8709403	2.5380792
Н	-0.4810053	-1.1071838	-3.5145877
С	0.4843678	-1.4821399	-3.1842788
N	1.0050866	-1.1760402	-1.9418225
С	1.3975570	-2.2609696	-3.8521750
С	2.1881220	-1.7700566	-1.8613136
N	2.4548021	-2.4222582	-2.9993547
Н	1.3762155	-2.7061893	-4.8430801
Н	2.8608067	-1.7549191	-1.0071582
Н	3.3004479	-2.9495150	-3.1901816
Н	-2.1324804	2.5687745	-1.6317335
С	-1.3103326	1.8384700	-1.4751507
0	-1.5317406	0.8620187	-0.6824354
0	-0.2070129	1.9517483	-2.0530949

32			
1505	S.I model m0		
Co	-0.0509751	-0.1181646	-0.2388187
н	1.0144625	-3.0842872	0.7501795
c	0.5736821	-2.5398834	1,5816884
N	0.1455051	-1.2303010	1.4647778
c	0.3268252	-2.9545918	2.8680725
c	-0.3429606	-0.8718221	2.6469040
N	-0.2505904	-1.8896015	3.5096473
н	0.5013550	-3.9025281	3.3691894
н	-0.7516066	0.1014073	2.9079164
Н	-0.5562587	-1.8704631	4.4769929
Н	0.4031615	3.2662214	0.0151633
С	-0.5327436	2.9316155	0.4554384
N	-0.8966734	1.6001424	0.5013869
С	-1.5407420	3.6686797	1.0311313
С	-2.0931368	1.5414418	1.0741557
N	-2.5043419	2.7718931	1.4089965
Н	-1.6479110	4.7390907	1.1851745
Н	-2.6794585	0.6404554	1.2492947
Н	-3.3826732	2.9934847	1.8666647
Н	1.2214674	-0.9270521	-3.3275392
С	1.9202368	-0.3714976	-2.7080797
N	1.6417376	-0.0480018	-1.3843649
С	3.1401793	0.1769218	-3.0212516
С	2.6772124	0.6430766	-0.9268654
N	3.5889003	0.8052632	-1.8905300
Н	3.7179028	0.1634807	-3.9405726
Н	2.7941303	1.0253997	0.0854841
Н	4.4650706	1.3070355	-1.7889724
Н	-3.0711285	-0.4150316	-2.4431354
С	-2.0706581	-0.1078222	-2.0627568
0	-1.5617221	-0.8655564	-1.1673526
0	-1.4924730	0.9012486	-2.5026042

32					
1SOS	1SOS.J model m0				
Co	0.1028925	-0.2350574	-0.3215807		
Н	-3.2395125	-0.2325901	0.1981290		
С	-2.6898661	-0.5398459	1.0843755		
N	-1.3058723	-0.5939064	1.1181990		
С	-3.1567383	-0.9238437	2.3174788		
С	-0.9605891	-0.9990257	2.3331377		
N	-2.0516982	-1.2052854	3.0789765		
Н	-4.1658820	-1.0143298	2.7079228		
Н	0.0561208	-1.1531557	2.6880974		
Н	-2.0554604	-1.5152534	4.0445246		
Н	2.8829444	-2.2749528	-0.0410638		
С	2.9201105	-1.3947626	0.5958328		
N	1.8699611	-0.4998441	0.6873304		
С	3.9357838	-0.9421410	1.4026130		
С	2.2486206	0.4598076	1.5226172		
N	3.4880510	0.2202103	1.9701964		
Н	4.9240900	-1.3490849	1.5987690		
Н	1.6577290	1.3290554	1.8077910		
Н	4.0010904	0.8046089	2.6216688		
Н	-1.0887072	-0.3080680	-3.3729451		
С	-0.9777089	-1.3203284	-2.9920066		
N	-0.4431746	-1.5817181	-1.7474803		
С	-1.2753079	-2.5197639	-3.5917672		
С	-0.4353751	-2.8989482	-1.5955048		
N	-0.9227565	-3.4897755	-2.6938090		
Н	-1.7014081	-2.7537094	-4.5635388		
Н	-0.1058189	-3.4456159	-0.7150326		
Н	-1.0148835	-4.4909701	-2.8306332		
Н	1.3557210	3.0274460	-1.6252299		
С	1.1190932	1.9580294	-1.4383641		
0	0.1139406	1.7046582	-0.6899052		
0	1.7962525	1.0347217	-1.9373154		

86			
1SOS	.A model m1	0 1605536	-0 3265479
Н	3.5628330	-3.8748569	0.4071192
С	2.4919993	-4.1079988	0.5099999
н С	2.2531176	-4.9111011 -2 8807672	-0.2010744
c	1.9176112	-1.7474500	1.1699447
N	1.3085050	-0.5119578	1.0573963
C	2.7669919	-1.7038606	2.2481681
N	2.6582415	-0.4404713	2.03/8238
Н	2.3240031	-4.5014439	1.5240550
H	1.7773168	-2.5310067	-0.7938663
н н	0.5600082	-3.1390034	0.32/4026
н	1.4998466	1.2827075	2.2314135
Н	3.1565355	-0.0853514	3.5804438
H	0.6369302	3.6024590	-3.0955846
c	-1.2784723	4.2136922	-2.4399447
0	-1.1988190	5.4276123	-2.5735401
C	0.6098995	3.6420727	-0.9369264
N	-0.5283385	3.2621241	0.2164181
C	-0.9706777	4.0742717	1.0588066
С	-1.3863504	1.9722425	1.5565095
N H	-1.6707636	3.2389866	1.8891449
н	1.5750099	3.1166810	-0.8727699
Н	0.8320383	4.7171473	-0.8767715
Н	-1.0419812	5.1567296	1.1197655
Н	-2.3004129	3.5241710	2.6316039
N	-2.4384241	3.5343955	-2.3762088
С	-3.6839990	4.2269988	-2.4099993
н Н	-4.4215450	3.681/441 2.5428931	-3.0183597
Н	-4.1114061	4.3678539	-1.4016197
Н	-3.5228579	5.2190457	-2.8501501
H C	-3.5146656	2.2108454	-6.2987101
c	-2.6192178	0.4313719	-5.5382220
0	-2.6494105	-0.2046992	-6.5811812
Н	-4.3819893	1.4580600	-4.9410931
п N	-1.8935957	0.0020632	-4.4701032
С	-1.3529996	-1.3189996	-4.5199987
C	-2.4661670	-2.3678024	-4.4146593
c	-3.5121/54	-2.1384596	-3.8245215
C	0.7494185	-0.6333513	-3.2374156
N	1.0513285	0.0316070	-2.0651446
C C	2 1696164	-0.3163/27	-4.1686/51
N	2.5827540	0.5283202	-3.5410953
Н	-2.0535936	0.4060246	-3.5444995
H	-0.8353239	-1.4505585	-5.4835144
Н	0.0173340	-2.6067603	-3.4848679
Н	1.8384920	-0.6243521	-5.2025515
H	2.6972707	1.3296602	-1.5587996
н N	-2.1666087	-3.5917466	-3.9554571
C	-3.1459991	-4.6479987	-4.8679986
C	-3.5165764	-5.1576362	-3.4986855
о н	-4.5604029	-5.4969189	-3.3109564
н	-1.3552121	-3.6978231	-5.4966276
Н	-4.0885152	-4.3264633	-5.3377069
N C	-2.6019408	-4.9127118	-2.5377762
c	-3.3064291	-4.0499658	-0.2997711
0	-3.2049741	-4.1276027	0.9152938
Н н	-1.7553566	-4.4231045	-2.7975385
л Н	-3.0040015	-5.6683133	-1.1442400 -0.6849661
N	-3.8359346	-2.9915094	-0.9475036
С	-4.3669988	-1.8389995	-0.2529999
н С	-5.4666884 -3.9865199	-1.901/578	-U.1892668 -0.9447195
c	-2.5191813	-0.2123369	-0.9342622
0	-1.7374077	-0.8376144	-0.1487169
0	-2.0662751	0.6868894	-1.6834234
л Н	-3.9733544	-2.9943881	0.7717912
н	-4.3104785	-0.5407785	-1.9969927
Н	-4.5044657	0.3037409	-0.4633428

86			
ISOS	B model ml	0 2027007	0 2595426
н	-0.0280725	_1 3139181	0 7381179
c	-4.9269986	-0.2439999	0.4909999
H	-5.5285065	-0.0584852	-0.4096968
С	-3.4796316	0.1760896	0.2689646
C	-2.5966255	-0.0843209	1.4435244
N	-1.2223123	-0.189/440	1.3397981
c	-2.9354554	-0.2413969	2.7031902
N	-1.7587175	-0.4347516	3.4420423
н	-5.3870175	0.3246435	1.3141692
н	-3.0598547	-0.3531381	-0.6015486
н	-3.4275250	1.2527605	0.0248158
Н	-3.8963699	-0.2248321	3.2710416
н	0.2929077	-0.5371207	2.8323874
п	-1.002/954	-0.3010343	-2 8298029
C	3.0009992	-1.4919996	-2.1119994
c	4.3633372	-0.8444873	-2.1961550
0	5.3823660	-1.5218820	-2.1604312
С	2.7911621	-2.0345769	-0.6896546
С	2.8595240	-0.9517401	0.3306421
N	1.8315057	-0.0596241	0.5546076
c	3.9386664	-0.5590805	1.084//58
N	3 5462554	0.6462125	1 7545860
н	2.2032924	-0.7789035	-2.3720946
н	1.8277167	-2.5615966	-0.6191425
Н	3.5754015	-2.7743668	-0.4756822
Н	4.9376818	-0.9766368	1.1740242
н	1.7205717	1.6995234	1.7953074
H	4.1126594	1.1090861	2.4003559
N	4.3643326	0.50528/1	-2.2469658
н	5.6058856	2.0434617	-2.9573596
н	3.4783377	1.0039831	-2.1579999
Н	5.7514252	1.7143078	-1.2079505
Н	6.4234165	0.5553930	-2.3882622
н	3.1781004	1.4926487	-6.4286139
C	2.7079992	1.9249995	-5.5359984
C	1.2116900	1.856/254	-5.6868551
н	2 9988941	2.0527799	-6.7529201
н	3.0729561	1.4146465	-4.6347083
N	0.5117688	1.5820803	-4.5535244
С	-0.9109997	1.7799995	-4.5699987
С	-1.2388832	3.2582381	-4.6003743
0	-0.5450070	4.0898753	-4.0345292
C	-1.549928/	1.1854354	-3.2980599
N	-0.7016631	-0.7698335	-1.9107380
c	-1.5649347	-1.3257275	-3.8908190
С	-0.6730102	-2.0903736	-2.0344107
N	-1.1799167	-2.4529552	-3.2179030
Н	0.9841406	1.6592234	-3.6482968
Н	-1.3216279	1.2934771	-5.4682335
H	-1.21/1/65	1.7597201	-2.4203410
н	-2.0151785	-1.3654087	-4.8786994
н	-0.3077516	-2.7985253	-1.2935894
Н	-1.2652412	-3.4071632	-3.5524406
N	-2.4172135	3.5561108	-5.1779297
С	-2.8809992	4.9079986	-5.1709985
C	-3.133643/	5.4759030	-3.7897502
о н	-3.1988294	0.0/01882	-3.6019457
н	-2.8860207	2.8638675	-5.7493751
н	-2.1622382	5.5868086	-5.6555429
N	-3.2897989	4.5488101	-2.8188323
С	-3.5079990	4.8999986	-1.4579996
C	-2.3227385	4.7725708	-0.5003725
U U	-2.5324404	4.6525914	0.6984979
н Н	-3.2/80186 -3.8172326	3.3/41032 5.9574487	-3.08/1862 -1.4326438
н	-4.3272740	4.3127802	-1.0178043
N	-1.0949798	4.8658335	-1.0433801
С	0.1120000	4.8319986	-0.2409999
Н	0.4577788	5.8584865	-0.0287940
С	1.2084301	4.0693932	-0.9657022
C	0.9289865	2.5936261	-1.1103131
0	-0.024/00/	2.1342280 1.8716306	-0.3908292 -1.8659734
н	-1.0035453	4.9195586	-2.0565642
Н	-0.1439582	4.3567090	0.7141957
Н	1.3907926	4.4767483	-1.9728557
Н	2.1638531	4.1657581	-0.4233454

#### 1SOS.C model m1 Co -0.0508109 -0.1697423 -0.2546019 Н 1,4218104 4.8725708 1.2375982 2.1079994 4.2629988 0.6299998 С Н 2.3481609 4.8302919 -0.2798850 С 1.4880256 2.9191081 0.2808015 č 1.1056610 2.1182940 1.4790185 N 0.3593197 0.9570258 1.4014922 С 1.3873063 2.3579664 2.8014220 С 0.1987223 0.5156353 2.6424553 Ν 0.8075733 1.3353494 3.5067309 Н 3.0428264 4.1395683 1.1987361 н 0.5902690 3.0656239 -0.3422190 н 2.1872106 2.3259210 -0.3353549н 1.9438033 3.1532233 3.2885605 -0.3487800 -0.3744517 2.9431947 Η Н 0.8337617 1.2167312 4.5137890 -3.9944659 -1.3429966 -2.8669423 Н -3.2169991 -1.8099995 С -2.2459994 С -3.2922787 -3.2931842-2.4128812 0 -4.3585780-3.8934382-2.3866363 c -3.4826949 -1.4460757 -0.7683166 С -2.5447679 -2.0964763 0.1946698 N C -1.2594838 -2.7512111 -1.6613416 -3.2584707 0.4575040 0.8998662 -2.5427368 С -0.7112412 1.2848777 Ν -1.5870906 -3.5142318 1.5722265 н -2.2369373-1.4207350-2.5609372-3.4561649 -0.3544453 -0.6385570 Н -4.5034513 -1.7649001 -0.5123390 Н н -3.6176743 -3.9112043 0.9614477 0.3065597 -2.51040981.6713512 Η Н -1.4096324 -4.3025751 2.1857988 Ν -2.0909291 -3.8907758 -2.5291501 С -2.0029994-5.3129985-2.5719993н -1.2994964 -5.6445584 -3.3503584 Н -1.2412624 -3.3434471 -2.3887713 н -1.6702217 -5.7356702 -1.6075997-2.7932419 -2.9996066 -5.7139681 Н Н -0.6515169 -3.5549375 -6.5771963 -0.1400000 -3.2979991 -5.6419984 С С 0.4917500 -1.9202530-5.79733720.8819554 -1.5068722 -6.8785448 0 0.6621292 -4.0304954 -5.4663093 Н н -0.8460532-3.3447509-4.8007323 -4.6655276 Ν 0.6204203 -1.1647398 С 1.4559996 0.0160000 -4.6739987 С 2.9476682 -0.4121967 -4.6760232 0 3,2883067 -1.4445626 -4.1149887 0.8248028 1.2622107 -3.3746709 С С -0.1303701 1.2445812 -3.0262560 Ν -0.7014722 0.9946395 -1.7885762 С -1.0105891 2.0157622 -3.7464246С -1.8746935 1.6125996 -1.7663359 Ν -2.0914318 2.2282938 -2.9338519 н 0.5069673 -1.6269009 -3.7585785 1.2236591 0.6179343 -5.5649673 Η Н 1.6631885 0.2372850 -2.5345770 н 1.8901320 1.7279761 -3.4458292 н -0.95071362,4316709 -4.7481403-2.5699357 -0.9296381 Н 1.6432870 -2.9191180 2.7673842 -3.1667414 Н Ν 3.8537768 0.4433427 -5.2025470 -5.2469985 С 5.2709985 0.1130000 С 5.9649337 0.0102749 -3.8790413 0 7.0382415 -0.5565776 -3.7980474 5.7879717 0.8830424 -5.8353563 н н 3.5224447 1.2305601 -5.7481854 5.4335299 -0.8578308 -5.7373134 Н Ν 5.3378535 0.5728838 -2.8112414 5.8269984 0.4669999 -1.4489996С С -0.6061032 5.1871674 -0.6226471 0 5.3358633 -0.6175589 0.6074402 -2.9822116 -1.4987450 н 4.4656969 1.0584127 6.9054530 0.2524531 Н Н 5.7027982 1.4214746 -0.9183304 Ν 4.5190229 -1.5704933 -1.2826730С 3,9039989 -2.6819992 -0.6069998 Н 4.5987616 -3.5388878 -0.5593704 C C 2.6301437 -3.1195145 -1.3158553 1,5005476 -2.1178679-1.28865751.6291762 -0.4935973 0 -1.1234871 0 0.4832283 -2.2713823 -1.9901707 4.4087132 н -1.4941139 -2.2922122 Η 3.6964335 -2.3675426 0.4245976 Н 2.8191471 -3.3657887 -2.3722860 н 2.2443791 -4.0440959 -0.8552224

86			
1S0S	.D model m1		
Co	0.1971506	-0.1756679	-0.3185338
C	-2.7599992	3.8429989	-0.0550000
н	-2.6373131	4.5198629	-0.9114127
С	-1.7533942	2.7012097	-0.1281314
С	-1.8704890	1.7174058	0.9884743
N	-1.1791569	0.5204473	1.0000286
c	-1.4943821	-0.1066758	2.1254718
N	-2.3541846	0.6319557	2.8353628
н	-2.6254809	4.4364208	0.8619338
H	-1.8668058	2.1558188	-1.0800252
H H	-0./230543	3.1008215	-0.1316/26
н	-1.1221389	-1.0788150	2.4413343
Н	-2.7462101	0.3753640	3.7349267
Н	-0.0874763	-3.6330862	-3.0776318
C	0.5329999	-3.3559991	-2.2129994
0	1 7098295	-4.2113134 -5 4231158	-2.2152/40
c	-0.2394705	-3.6545661	-0.9168364
С	0.5296151	-3.2468662	0.2907282
N	0.7446287	-1.9239792	0.6176784
C	1.2320/14	-4.0274604	1.1760048
N	1.8635012	-3.1609024	2.0289925
н	0.7845334	-2.2898020	-2.2859438
н	-1.2196900	-3.1557068	-0.9225436
Н	-0.4371273	-4.7349967	-0.8681427
H	1.3409432	-5.1060778	1.2509850
н	2.4658553	-3.4180525	2.8039598
N	2.8981337	-3.5387306	-1.9343079
С	4.1169988	-4.2389988	-1.6939995
н	4.3660725	-4.2773922	-0.6187713
H H	2.8446139	-2.5391000	-1./305/54
н	4.9607853	-3.7674556	-2.2214022
н	4.1492456	-2.2398783	-5.7258949
С	3.9029989	-1.6469995	-4.8359986
С	3.1272320	-0.4304932	-5.2366267
О Н	3.2348814	0.1138785	-6.3244226
н	3.3689624	-2.2699880	-4.1064529
N	2.3011726	0.0491251	-4.2702320
С	1.7809995	1.3729996	-4.4049988
С	2.8855737	2.3985777	-4.1123392
C	0.6882717	2.1296894	-3.3677046
c	-0.3847685	0.5717763	-3.2981979
N	-0.7202942	-0.1198596	-2.1472318
С	-1.2406745	0.1760659	-4.2966483
C	-1.7607172	-0.8868837	-2.4453152
н	2.4344057	-0.2883282	-3.3134926
н	1.3908754	1.5080620	-5.4248171
н	1.1670011	1.6501192	-2.3515076
н	0.2342096	2.5965706	-3.5145537
н	-1.3123161	0.46/52/8	-5.340/380
н	-2.8433369	-1.2247011	-4.2067556
N	2.6953897	3.6367268	-4.6149780
С	3.6769990	4.6719987	-4.4049988
С	3.8427680	5.1387879	-2.9675671
О Н	4.8338492	5.7623480	-2.6358162
н	1.9831056	3.7750610	-5.3219795
Н	4.6757296	4.3422564	-4.7303471
N	2.8301571	4.8342832	-2.1225796
C	2.8589992	5.1809985	-0.7319998
0	3.2429924	4.0488279 4 1482487	0.2364/14
н	2.0317183	4.3385952	-2.4984108
Н	3.6033215	5.9811711	-0.5994000
Н	1.8863519	5.5653116	-0.3952223
N	3.9404938	3.0126709	-0.2749739
с Н	4.3019988 5.4159070	1.9821798	0.3239999
c	4.2004798	0.5874421	-0.2705880
С	2.7770085	0.2418063	-0.6236370
0	1.8404539	0.8614231	-0.0190966
О н	2.5207160	-0.6557499	-1.4547324
Н	3.7456922	2.9804903	1.4322455
Н	4.7750370	0.6157511	-1.2095086
н	4,6025787	-0.2665324	0.3009085

86	D madal mi		
Co	-0.0087296	-0.0564847	-0.4509003
Н	5.0447252	1.1272711	0.9213154
С н	4.8769986	0.0810000	0.6249998
C	3.4150104	-0.1687309	0.2800077
C	2.4780227	0.1458157	1.3980956
C	2.7544182	0.3175346	2.7325575
С	0.5953051	0.5757364	2.4084224
N H	1.5547910	0.5834972	3.3406840
Н	3.1238561	0.4344028	-0.5955303
Н	3.2680162	-1.2225859	-0.0180068
н Н	-0.4531638	0.2680404	3.2893595
Н	1.4140311	0.7593342	4.3297559
H	-3.0287791	2.2236529	-3.4206988
c	-4.5212593	0.9355010	-2.6937074
0	-5.5029821	1.6590372	-2.5868632
C	-2.8333355	2.0909268	-1.2778295
N	-1.9082967	0.2773074	0.2330469
С	-4.0535804	0.7830932	0.5710221
C N	-2.3965063	-0.5329746	1.1645931
н	-2.4012149	0.6608734	-2.8510233
Н	-1.8300592	2.5408625	-1.2902356
н н	-3.5498828	2.906614/	-1.1039/9/
Н	-1.8510024	-1.3257499	1.6740318
Н	-4.2830432	-0.7233023	2.0607989
N C	-4.5693219	-0.3949366	-2.8546929
Н	-5.8420300	-1.8107469	-3.6977991
Н н	-3.7121830	-0.9358049	-2.7660163
Н	-6.5866580	-0.2751613	-3.1628204
Н	-2.9339145	-1.7978620	-6.7872156
C C	-2.4959993	-1.9059995	-5.7879984 -5.8877451
õ	-0.3765490	-2.0744484	-6.8949607
Н	-2.7214275	-2.9168278	-5.4138084
H N	-2.9422239	-1.3192414	-4.7705448
С	1.0679997	-1.5429996	-4.6989987
C	1.3238074	-3.0653355	-4.5715071
c	1.6686419	-0.9478208	-3.4080362
С	1.4458836	0.5046688	-3.1422261
N C	1.8984071	0.9/3/533	-2.0054666
c	0.8851471	2.2974618	-2.0319582
N	1.5313134	2.6977793	-3.1333357
Н	1.5560168	-1.1391905	-5.5974527
H	1.2785673	-1.5162075	-2.5493748
н н	2.7543413	-1.1356117	-3.4333442 -4.7816133
н	0.5055184	2.9794914	-1.2737650
H	1.7219617	3.6623919	-3.3839908
N C	2.7629992	-4.9759986	-4.9799986
С	2.9498368	-5.5937706	-3.5901917
О Н	2.8584675	-6.7998568 -5 1816532	-3.4550125
н	3.0896800	-2.9656190	-5.5983901
Н	1.9381529	-5.5389516	-5.4409520
N C	3.2255/84	-4./490838 -5.1889985	-2.563/530
c	2.0680318	-5.0194043	-0.3570201
0	2.1233532	-5.1006480	0.8619409
п Н	3.5687836	-6.2634521	-2.7733403
Н	4.1465835	-4.6702326	-0.6716461
N C	0.9333472	-4.8288623	-1.0479769
н	-0.7713012	-5.7060523	-0.1975750
C	-1.3130987	-3.8883191	-1.2111587
0	-0.96435/1	-2.4249989 -1.9894172	-1.3561038
0	-1.5877955	-1.6873031	-2.1377110
H H	0.9617893	-4.7387595	-2.0612947
H	-1.4285685	-4.2998262	-2.2259243
Н	-2.3153538	-3.9292371	-0.7534238

86	D		
Co	0.0222598	-0.0767906	-0.3417256
H	-3.3008283	3.7750143	0.6558414
С Н	-2.3919993	4.1929988	-0.7529062
С	-1.3384157	3.1133371	-0.0225918
C N	-0.9368483	2.4064556	1.2296348
C	-0.9021176	2.8811360	2.5182664
С	-0.2257224	0.7891936	2.5069727
N H	-0.4495591	1.8466390	3.2951850 0.8616371
Н	-1.7102193	2.3604945	-0.7357740
Н Н	-0.4364916	3.5514014	-0.4868126
Н	0.1261129	-0.1722341	2.8736539
Н	-0.3109730	1.8723554	4.2997538
н С	-1.2605675 -0.4279999	-4.1838241 -3.7329990	-2.4230922
c	0.7834479	-4.6264821	-2.0173533
0	0.6990053	-5.8363095	-1.8498326
c	0.3051054	-3.1271381	0.4756095
N	0.6721596	-1.7979723	0.5580901
C C	1.2064379	-3.8637497 -1.7417742	1.2059262
N	2.1098727	-2.9706728	1.7153974
H	-0.2346087	-2.7289738	-2.2726037
н Н	-1.0768259	-4.6440948	-0.2529449
Н	1.2775063	-4.9337613	1.3804798
H H	2.3275742	-0.8420152	1.5565711
N	1.9400985	-3.9851030	-2.2915500
С	3.1929991	-4.6869987	-2.3849993
н Н	1.9484510	-2.9634237	-2.2932528
Н	3.8379772	-4.4882668	-1.5122384
H H	2.9820124	-5.7629752	-2.4218852
C	1.9809994	-2.6259993	-5.6649984
C	1.1638759	-1.3977821	-5.9465919
н	3.0430925	-2.3364491	-5.6238595
Н	1.7183083	-3.0959648	-4.7074456
N C	0.7687935	-0.7096148	-4.8425175
c	1.3623818	1.6360810	-5.2862452
0	2.4964351	1.4304108	-4.8797209
c	-1.4717508	0.2618906	-3.0637780
N	-1.4554867	-0.1502248	-1.7405962
C C	-2.6726851	-0.1198284 -0.7428307	-3.6093757
N	-3.3674410	-0.7469996	-2.6112038
H	1.2073503	-0.9216641	-3.9418127
п Н	0.4112453	1.2173090	-2.9346416
Н	-0.7981086	2.1064553	-3.8511636
н н	-3.0829344 -2.9447338	0.0156429	-4.6060928
н	-4.2986350	-1.1423789	-2.6883354
N	1.0109239	2.8182883	-5.8562853
c	2.6265982	4.5330909	-4.9570520
0	3.6760519	5.1379835	-5.0761432
н Н	1.4/2530/ 0.0909273	4.646/946 2.8944531	-6.2741922
Н	2.8071376	3.4773230	-6.7689285
N	1.9505554	4.4202419	-3.7920363
c	3.1114393	3.9144684	-1.6307596
0	3.2698180	4.1863862	-0.4495985
н Н	1.0734962 3.2414886	3.9150456 5.6822011	-3.7969393 -2.8117887
Н	1.6862463	5.4578482	-1.9846439
N	3.5129924	2.7596481	-2.1973063
H H	4.1869988 5.2820691	1.8410573	-1.4449996 -1.5281068
С	3.7969505	0.3416259	-1.9342948
C O	2.3599119	-0.0228558	-1.6681619
õ	1.8370627	-1.0245148	-2.1951131
H	3.3404737	2.5971805	-3.1872922
н Н	3.9199159	0.2245643	-0.3888580 -3.0145584
Н	4.4198961	-0.4218135	-1.4386553

#### 1SOS.G model m1 Co 0.0566633 -0.0034000 -0.3652700 Н 5,1878647 1.0541264 0.8523278 0.1430000 0.2549999 С 5.0349986 Н 5.6000891 0.2464455 -0.6816497 С 3.5562790 -0.0869873 -0.0306129 C 2.7263959 -0.2025423 1.2041578 1.3503924 -0.0650730 Ν 1,2046540 С 3.1288799 -0.4500107 2.4935500 С 0.9424609 -0.2252087 2,4575862 Ν 1.9891682 -0.4612194 3.2554522 Н 5.4714758 -0.7028249 0.8086875 н 3.1545016 0.7373089 -0.6427963 н 3,4244135 -1.0036695-0.63367514.1118782 -0.6201183 н 2.9225126 -0.0849875 -0.1682213 2.8092442 Н Н 1,9425246 -0.6188128 4.2563533 -3.0734897 2,9162673 -2.1862330 Н -1.6979995 -3.1279991 1.9309995 С С -4.4763217 1.3722536 -1.9053529 0 -5.5023005 1,9977883 -1.6708914С -2.8615317 2.1191718 -0.1937378 С -2.8545444 0.8253417 0.5447221 Ν -1.7631483-0.01754520.5816492 1.1815354 c -3.8996817 0.2007092 -2.1426510 С -1.1199591 1.2169093 N -3.4243474-1.0159552 1.5923588 -2.3524644н 1,2886381 -2.1391911-1.9046037 2.6387455 -0.0388520 Η -3.6464809 2.7663331 0.2232896 Н н -4.9240117 0.5191965 1.3548110 -1.5255212 -1.99759541.4033875 Η Н -3.9475997 -1.7238643 2.0968705 Ν -4.4368080 0.0991538 -2.3172742 С -5.6549984 -0.6009998-2.3989993Н -5.6286618 -1.3496970 -3.2056104 Н -3.5475284 -0.4021176 -2.3304737 н -5.9051088-1.1301142-1.4606625-6.4663698 0.1079488 -2.6033829 Η Н -3.5735318 -0.3758578 -6.4655954 -3.0059992 -0.6479998 -5.5679984 С С -1.5275104-0.5493257-5.8709072 -7.0033543 -1.0733254 -0.6045342 0 -3.2407794 -1.6923789 -5.3080778 Н н -3.3042907-0.0137444-4.7226657 Ν -0.7163924 -0.4112587 -4.7854295 С 0.6999998 -0.5559998 -4.9279986 С 1.0567995 -2.0764187 -5.1970862 0 0.3377672 -2.9440233 -4.72206741.4170666 -0.2006898 -3.6111750 С С 1.1490981 1.1069158 -3.0492036 Ν 0.6059394 1.3567069 -1.7729547С 1.3075560 2.3778644 -3.6279530 0.5223012 2.6689255 -1.5967982 С Ν 0.9316130 3.3082352 -2.6980963 н -1.1148729-0.6074534-3.8631515 0.0648893 -5.7644502 1.0560813 Η н 1.1665554 -0.9625378 -2.8574427 н 2.5031496 -0.2772981-3.7827379 н 1.6848566 2,6556590 -4.60822350.1847490 3.1770299 -0.6959447 Н 0.9601120 4.3156989 -2.8152935 Н Ν 2,2173779 -2.3895771 -5.8367256 -3.7719989 -6.1229983 С 2.6469993 С 2.9354473 -4.6246991 -4.8840089 0 2.9496025 -5.8378251 -4.9767554 3.5585923 -6.7334573н -3.7235158н 2.7235329 -1.6421362 -6.2977993 1.8782412 -4.3132467 -6.6934459 Н Ν 3.1797466 -3.9592748-3.72647983.3729991 -4.6199987 -2.4579993С -1.5419770 С 2.1334520 -4.6694737 0 2.2824954 -4.9511407 -0.3614134 н 3,1720276 -2.9474773-3.7590491-5.6619838 -2.6595201 3.6649765 Η Н 4.1815085 -4.1480585 -1.8829507 Ν 0.9321111 -4.4346722 -2.1084169 -0.3169999-4.4839987 С -1.3589996Н -0.7235412 -5.5103193 -1.3760715 -1.3430354 -3.5308817 -1.9348184 С С -1.0068873-2.0788901-1.72783340.0238012 -1.8311751 0 -1.0137144 0 -1.7141036 -1.1754541 -2.2118237 н 0.8838552 -4.1753126 -3.0925514Η -0.0839388 -4.2410815 -0.3135888 Н -1.4857368 -3.6876565 -3.0156702 н -2.3275786 -3.7071435 -1.4711781

#### 1SOS.H model m1 Co 0.2066506 -0.0389056 -0.4364823 Н -1.4456471-5.1331064 0.3887153 -2.2279994 С -4.3639988 0.2989999 Н -2.8880369 -4.6495532 -0.5321082 С -1.6241403 -2.9872110 0.0573994 C -0.7016358 -2.5518749 1.1459884 0.0490409 -1.3941219 Ν 1.0758711 С -0.4412087 -3.1533374 2.3528025 С 0.7379557 -1.30269272,2056086 Ν 0.4646845 -2.3477168 2.9951007 Н -2.8300722 -4.3800160 1.2200192 н -1.0686155 -2.9776495 -0.8966708 н -2.4223359-2.2305003-0.0483296 н -0.8221766 -4.0663923 2.8001115 Н 1.4295149 -0.5053266 2.4690090 Н 0.8607354 -2.51061703,9143547 4.0455301 1.0495947 -2.5090259 Н 1.5509996 3.3099991 С -1.8629995 С 3.4855316 3.0548049 -2.0597565 0 4.5956065 3.5601646 -1.9620272c 3.5850203 1.2036658 -0.3967857 С 2.5811439 1.8183890 0.5147195 N C 1.2633315 2.7212725 1.4103781 2.9041836 0.5597202 1.3435697 С 0.6293734 2.2251113 1.3921092 Ν 1.4826359 3.1353614 1.8815719 н 2.3032782 1.2246048 -2.16228643.6036792 0.1119137 -0.2574455 Н 4.5851973 1.5722218 -0.1288011 Н н 3.5854845 3.5212002 1.5737467 -0.42742571.6497482 Η 2.1792367 Н 1.2439641 3.8709414 2.5380799 N 2.3616418 3.7736833 -2.2993633 С 2.3799993 5.2189985 -2.4439993 -1.5738788 Н 1.9224905 5.7169299 Н 1.4640080 3.2903877 -2.2644508 н 3,4266403 5.5371118 -2.5231782 1.8370178 -3.3507019 Η 5.5253424 Н 1.6107482 3.2088322 -6.5020571 0.9339997 2.9939992 -5.6659984 С С 0.2753047 1,6562852 -5.8979727 -7.0161022 0.0243224 1.2321650 0 0.1506999 3.7686708 -5.6549235 Н н 1.4813733 3.0405477 -4.7148741 Ν -0.0451573 0.9457848 -4.7806070 С -0.8879998 -0.2079999 -4.9089986 С -2.3588377 0.2329683 -5.1204942 0 -2.77367131.2674344 -4.6178301-1.0524169 -0.8722856 С -3.6266881 С 0.4843679 -1.4821403 -3.1842797 Ν 1.0050869 -1.1760405-1.9418230С 1.3975574 -2.2609702 -3.8521761 2.1881226 -1.7700571 С -1.8613141 Ν 2.4548028 -2.4222589 -2.9993555 1.4145339 -0.7973865 н -0.0384765-3.8703686 -0.5495758 -5.7746784 Η Н -1.3513332 -0.4853211 -2.8138490 н -1.4970004-1.9444882-3.7949967 н 1.3762159 -2.7061901-4.84308152.8608075 -1.7549196 -1.0071585 Н 3.3004488 -2.9495158 -3.1901825 Н Ν -3.1802252 -0.6319253 -5.7615561 -5.9579983 -0.3379999 С -4.5899987 С -5.4095486 -0.2708879 -4.6820118 0 -6.4953899 0.2783795 -4.6670457 -5.0215661-1.1127203-6.6066747 н н -2.7738430 -1.4129050 -6.2630332 -4.7255201 0.6310907 -6.4614284 Н Ν -4.8491350-0.8624869-3.6030835-5.4419985 -0.8069998 -2.3039994 С С -4.9034434 0.2850936 -1.3617533 0 -5.0812944 0.1691847 -0.1582749н -3.9544257-1.3187489-3.7251740-6.5189021 -2.4273467 -0.6138115 Н Н -5.3334753 -1.7634504 -1.7739375 Ν -4.3027305 1.3481127 -1.9380363 С -3.7829989 2.4769993 -1.1829997Н -4.4580221 3.3437082 -1.2764509 C C -2.3958119 2.8689562 -1.6732001 -1.3103330 1.8384705 -1.47515110.8620189 0 -1.5317410 -0.6824356 0 -0.2070130 1.9517488 -2.0530955 н -4.1393680 1.3403262 -2.9431595 Η -3.7642035 2.1734133 -0.1276919 Н -2.4076167 3.1193403 -2.7452607 н -2.0602320 3.7827207 -1.1538369

#### 1SOS.I model m1 Co -0.0509751 -0.1181646 -0.2388188 Н 3.0488488 -3.83041641.3971148 2.2279994 -4.3149988 С 0.8499998 Н 2.6462461 -4.8164562 -0.0348685 С 1.1660157 -3.2967816 0.4386411 č 0.5736823 -2.5398841 1.5816888 0.1455051 -1.2303013 1.4647782 Ν С 0.3268253 -2.9545926 2.8680733 С -0.3429607-0.8718223 2.6469047 Ν -0.2505905 -1.8896020 3.5096483 1.8012233 Н -5.0941161 1.4994566 н 1.5957915 -2.5625670 -0.2619888 н 0.3445241 -3.7965911-0.1055079н 0.5013551 -3.9025292 3.3691903 -0.7516068 0.1014073 2.9079172 Η Н -0.5562589 -1.8704636 4.4769942 1.5127370 -2.1875098 3.8491765 Н 0.5729998 3.4739990 -1.7599995 С С -0.5267325 4.4705215 -2.0672244 0 -0.36304285,6657731 -1.8556376c 0.7033606 3.4241926 -0.2199923 С -0.5327437 2.9316163 0.4554385 N C -0.8966737 1.6001428 3.6686807 0.5013870 1.0311316 -1.5407424 С -2.0931374 1.5414422 1.0741560 Ν -2.5043426 2.7718939 1.4089969 0.3517417 н 2.4764552 -2.16321340.0765202 1.5601285 2.8041114 Н 0.9111159 4.4420003 0.1407172 Н н -1.6479115 4.7390920 1.1851748 -2.67945930.6404556 1.2492951 Η Н -3.3826741 2.9934855 1.8666652 N -1.6953332 3.9452959 -2.4940013 С -2.8699992 4.7679987 -2.6529993 -3.5676801 Н -3.4171460 4.4967098 Н -1.7779267 2.9290831 -2.5474437 н -3.5562556 4.6687391 -1.7953170-2.7162074 -2.5516785 Н 5.8160717 Н -0.8361667 3.0427133 -6.6441384 -0.9889997 2.2709994 -5.8789983 С С -0.04160811,1500407 -6.06031990.4464978 0.8073617 -7.1253302 0 Н -2.0127450 1.8787522 -5.9924058 н -0.9202146 2.7261689 -4.8810527 Ν 0.1935192 0.4900187 -4.9042205 С 0.7219998 -0.8199998 -4.9899986 С -0.3432949 -1.8102863 -5.4678292 0 -1.5316524-1.6093102 -5.2645764 -3.5393516 С 1.0670487 -1.2840971 C 1.9202373 -0.3714977 -2.7080805 Ν 1.6417381 -0.0480018 -1.3843653С 3.1401802 0.1769218 -3.0212524 С 2.6772132 0.6430768 -0.9268657 Ν 3.5889013 0.8052634 -1.8905305 н -0.40946340.6941435 -4.1025676 1.6044709 -0.8332278 -5.6444805 Н н 0.1196757 -1.4405567 -2.9991669 Н 1.5615094 -2.2679643 -3.5901137 н 3.7179038 0.1634807 -3.94057372.7941311 1.0254000 Н 0.0854841 4.4650719 1.3070359 -1.7889729 Н Ν 0.1206657 -2.9688674 -5.9795543 -0.7939998 -6.3939982 -4.0029989 С С -1.5662503 -4.6689802 -5.2695268 0 -2.5717635 -5.3128435 -5.5048483 -4.7803888 -6.9279578 н -0.2314872н 1.0989726 -3.0395086 -6.2326275 -1.5500512 -3.6037706 -7.0870309 Н Ν -1.0523069-4.5053312 -4.0292205 -5.0199986 -1.6979995-2.8619992 С С -4.0002970 -2.0574870 -2.5396240 0 -2.7816277 -4.2348276 -0.8825116 -3.9334222 -3.1762248 н -0.1990099-3.9698939 -2.3843293 -5.8209990 Н Н -0.9726710 -5.4508480 -2.1575883 Ν -3.0071647 -2.9180253 -2.7197215 С -3.8539989 -1.8969995-2.1069994-2.0721762 Н -4.9088275 -2.3798377 C C -3.4417442 -0.5055010 -2.5464135 -2.0706587 -0.1078222-2.0627574 -1.5617225 -0.8655566 0 -1.1673529 0.9012489 -2.5026049 0 -1.4924734 Н -2.7209603 -2.7724165-3.6854137 Η -3.7614831 -2.0160799 -1.0203072 Н -3.4586380 -0.3964871 -3.6419799 н -4.1558511 0.2388507 -2.1548041

#### 1SOS.J model m1 Co 0.1028925 -0.2350575 -0.3215808 Н -5.2832090-1.27303400.2915748 -4.9879986 -0.2359999 0.0710000 С Н -5.5124391 0.0774767 -0.8424720 С -3.4760813-0.1182193-0.1144007C -2.6898669 -0.5398461 1.0843758 -1.3058727 -0.5939066 Ν 1.1181993 С -3.1567392 -0.92384402.3174795 С -0.9605894 -0.9990260 2.3331384 Ν -2.0516988 -1.2052857 3.0789774 0.8941343 Н -5.3407870 0.4034695 н -3.1536545 -0.7267829 -0.9773346 н -3.20333720.9234961 -0.3611353-1.0143301 н -4.1658832 2.7079236 Η 0.0561208 -1.1531560 2.6880982 Н -2.0554610-1.5152538 4.0445257 3.3075863 -2.3555241 -3.1626837 Н -2.2389994 3.2949991 -1.7589995 С С 4.6727830 -1.6304208 -1.8288685 0 5,6739677 -2.3062795-1.6327819c 2.9446783 -2.5841243 -0.3042142 С 2.9201113 -1.3947630 0.5958330 N C 1.8699616 -0.4998442 -0.9421413 0.6873306 1.4026134 3.9357849 С 2.2486212 0.4598077 1.5226176 3.4880520 Ν 0.2202104 1.9701970 -1.5645912н 2.5355231 -2.18352341.9783253 -3.1058889 -0.2663119 Н Н 3.6981860 -3.2893355 0.0757296 н 4.9240914 -1.34908531,5987694 1.6577295 1.3290558 1.8077915 Η 4.0010915 Н 0.8046091 2.6216695 N 4.7042782 -0.3045765 -2.0840580 С 5,9489983 0.4129999 -2.1329994 5.9739138 -2.9981579 Н 1.0924264 Н 3.8256054 0.2117536 -2.1013786 н 6.1186738 1.0082960 -1.21978236.7622635 -0.3172990 -2.2249065 Η Н 3.8367636 -0.1531927 -6.2268078 3.2779991 0.3319999 -5.4169985 С С 1.8087978 0.2084376 -5.68103361.3370547 0.1501449 -6.8066694 0 3.5392636 1.4023614 -5.4194276 Н н 3.5774055 -0.0900346 -4.4487856 1.0174100 0.1963346 -4.5741237 Ν С -0.3829999 0.3799999 -4.7679987 С -0.6806468 1.8599077 -5.1430800 0 0.0116546 2.7612314 -4.6918447 С -1.1909236 0.0611987 -3.5062380 С -0.9777092 -1.3203288 -2.9920074 Ν -0.4431747 -1.5817185 -1.7474808С -1.2753083 -2.5197646-3.5917682С -0.4353752 -2.8989490 -1.5955052 Ν -0.9227568 -3.4897765 -2.6938098 н 1.4106011 0.4921435 -3.6755701 -0.7063539 -0.2672389 -5.5983183 Η Н -0.9435476 0.7872942 -2.7165241 н -2.2587681 0.2013539 -3.7384677 н -1.7014086-2.7537102-4.5635401-0.1058189 -3.4456169 -0.7150328 Н -1.0148838 -4.4909714 -2.8306340 Н Ν -1.7931587 2.1045096 -5.8787032 -6.2549982 -2.19999943.4529990 С С -2.5541833 4.3504521 -5.0806021 0 -2.5746560 5.5604266 -5.2069261 -3.07512083.3804100 -6.9151477н н -2.2553562 1.3232633 -6.3289387 -1.4020373 3.9698291 -6.8091982 Н Ν -2.84660823.7073896 -3.9267303 -3.1289991 4.3989988 -2.7079992 С С -1.9750932 4.4978143 -1.6947044 0 -2.2345898 4.7596408 -0.5293491 -3.9361865 -2.9621250 н -2.8383852 2.6959159 -3.4135836 5.4319048 Н Н -3.9758436 3.9435061 -2.1753626 Ν -0.7215113 4.3354621 -2.1674824 -1.3279996 С 0.4609999 4.4569987 Н 0.9125934 5.4568180 -1.4416604 C C 1.4975729 3.4008606 -1.6864278 1,1190935 1,9580299 -1.43836450.1139406 1.7046587 -0.6899054 0 0 1.7962530 1.0347220 -1.9373159 н -0.5873266 4.0808089 -3.1450506 -0.2860913 Η 0.1279346 4.3556417 Н 1.7873510 3.4731221 -2.7462520 н 2.4218201 3.5815579 -1.1114085