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A Theoretical Investigation of the Copper–Superoxide System. A Model for the Mechanism of Copper–Zinc Superoxide Dismutase

M. ROSI, A. SGAMELLOTTI, F. TARANTELLI

Department of Chemistry, University of Perugia, Italy

I. BERTINI and C. LUCHINAT

Department of Chemistry, University of Florence, Italy

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The superoxide ion in water is unstable with respect to dioxygen and hydrogen peroxide [1]. Copper–zinc superoxide dismutase (SOD) is a highly efficient catalyst of the dismutation [2]. Although it has not been definitely proved, it is often assumed that electron transfer between copper and superoxide occurs through direct binding [3–5]. In particular, it is believed that the reaction occurs in the following two steps:

$$Cu^{2+} + O_2^{-} \rightleftharpoons Cu^{+} + O_2 \qquad (1)$$

$$Cu^{+} + O_2^{-} + 2H^{+} \rightleftharpoons Cu^{2+} + H_2O_2 \qquad (2)$$

We have been trying to understand such electron transfer through *ab initio* treatments of model systems. In the meantime a paper has appeared in which the energies of the various intermediates of a model system of SOD interacting with O_2^- are calculated through a Hartree–Fock pseudopotential approach [6]. The SOD model consists of three ammonia nitrogens plus an imidazolate ion bridging the copper ion with a proton. Under these circumstances the Cu^{2+}–superoxide system is stabilized by hydrogen bonding with an NH_4^+ ion which simulates arginine 141 of SOD [7]. In other words there is no way to describe the system as Cu^+-triplet dioxygen and then to transfer the electron from superoxide to copper.

Our calculations have shown that when only copper(II) and superoxide are considered (with a Cu–O distance of 1.9 Å, an O–O distance of 1.3 Å, and a Cu–O–O angle of 136°), the only stable species is Cu^+–O_2, which is also stable with respect to dissociation (Fig. 1).

When an ammonia interacts with copper(II) (for example with a Cu–N distance of 2.07 Å and an N–Cu–O angle of 90°), the stable species is still Cu^+–O_2, which is however unstable with respect to dissociation. It is interesting to note that the major effect of NH_3 is that of increasing the electronic charge density on copper and thus to destabilize the Cu^+–O_2 system (Fig. 1).

If a proton of NH_4^+ is allowed to interact with Cu^{2+} and O_2^-, the only stable species is described as Cu^{2+} and superoxide. It is a sufficiently weak H–––O interaction, as weak as the interaction due to a very large hydrogen bond distance such as 2.5 Å, to stabilize the above species with respect to copper(I)–dioxygen. The effect of an ammonium proton at the same distance on the bare copper(II)–superoxide system still gives a stable Cu^+–O_2 species, which is unstable with respect to dissociation.

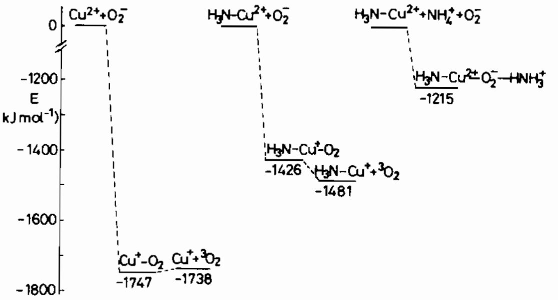

Fig. 1. Energies of the investigated systems relative to the separated species.

The simultaneous effects of a single nitrogen donor to copper(II) and of a hydrogen bond between the distal oxygen and ammonium definitely stabilize the Cu^{2+}–O_2^- species (Fig. 1). These results are in agreement with the previous publication in which four nitrogens were considered to interact with the copper ion [6].

As far as the mechanism of action of SOD is concerned, these calculations show that the mechanism which requires interaction of superoxide with both copper(II) and arginine 141 [7] cannot associate copper(I) and dioxygen with a single superoxide ion involved in the process. As previously suggested [6], a second superoxide is required to reduce the Cu^{2+}–O_2^- species to Cu^+–O_2^-. Whereas the results of the previous theoretical calculations were bound to a particular $CuN_4(H^+)$ model, we have shown that every copper(II) complex (with more than one electron donor ligand) will give a Cu^{2+}–O_2^- adduct without copper reduction, provided that the distal superoxide oxygen is allowed to form even a weak hydrogen bond.

The calculations were performed within the Hartree–Fock all-electron formalism, using contracted Gaussian basis sets of double zeta for the valence and single zeta quality for the core orbitals.

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References

1 I. Fridovich, *Adv. Enzymol., 41,* 35 (1974).

2 J. S. Valentine and M. W. Pantoliano, in T. G. Spiro (ed.), 'Metal Ions in Biology, Vol. 3', Wiley, New York, 1981, p. 291.

3 J. A. Fee, in H. Sigel (ed.), 'Metal Ions in Biological Systems, Vol. 13', Marcel Dekker, New York, 1981, p. 259.

4 A. Rigo, P. Viglino and G. Rotilio, *Biochem. Biophys. Res. Commun., 63,* 1013 (1975).

5 I. Bertini and C. Luchinat, in E. Clementi (ed.), 'Structure and Dynamics of Nucleic Acids, Proteins and Membranes', Adenine, in press.

6 R. Osman and H. Basch, *J. Am. Chem. Soc., 106,* 5710 (1984).

7 J. A. Tainer E. D. Getzoff, J. S. Richardson and D. C. Richardson, *Nature (London), 306,* 284 (1983).