Oxygenation of sulfides by bis(μ-oxo)dicopper(III) complexes. A theoretical study

Ekaterina Tkatchouk, Lioudmila Fomina, Ernesto Rivera, Serguei Fomine*

Instituto de Investigaciones en Materiales, Universidad Nacional Autónoma de México, Apartado Postal 70-360, CU, Coyoacán, México DF 04510, México

Abstract

The First computational study on the oxygenation of organic sulfides by bis(μ-oxo)dicopper(III) complexes was carried out at PWP91/LACV3P**+//PWP91/LACVP* level of theory. Two reaction paths have been explored. One is the precoordination of sulfur with copper atom followed by oxygen transfer. Another is the precoordination with oxygen. In both cases the precoordination was found to be very weak to give a detectable intermediate. The oxygen atom transfer shows activation energies of less than 10 kcal mol both in the solution and in the gas phase suggesting validity of the proposed mechanism. Dissociation of the intermediate formed after oxygen atom transfer gives free sulfoxide. Solvation plays an important role favoring the reaction and facilitating dissociation of the final complex. The ground state of all studied dicopper intermediates are open-shell singlets. Complexes **4a,b** and **5** have significant contribution from biradical structure to the ground state with antiferromagnetic coupling between copper atoms.
© 2005 Elsevier B.V. All rights reserved.

Keywords: DFT; Oxidation; Dicopper

1. Introduction

The understanding of dioxygen activation mechanism by transition metal complexes is of great importance for both the rational design of oxygenation catalysts and the understanding of action of oxygenases [1]. It has been recently paid much attention to $(\mu-\eta^2:\eta^2$ peroxo)dicopper(II) and bis(μ-oxo)dicopper(III) complexes which were considered to be possible active oxygen intermediates of copper monooxygenases carrying a binuclear metal active center [2,3].

The bis(μ-oxo)dicopper(III) complex has been shown to undergo intramolecular aliphatic ligand hydroxylation via hydrogen atom abstraction and subsequent oxygen rebound mechanism or its concerted variant [4,5]. However, little is known about oxygen transfer reaction from bis-(μ-oxo)dicopper(III) complex to exogenous substrates [6]. On the other hand it has been suggested that bis-(μ-oxo)dicopper(III) complexes are important intermediates in various oxygen transfer reactions which included but not limited to the oxidative polymerization of phenols [7], the Glaser reaction [8], oxidation of peralkylated diamines, [9] and C–H activation reactions [3].

Recently, the first study on oxidation of organic sulfides to sulfoxides by bis-(μ-oxo)dicopper(III) complexes has been published [10]. It was suggested two step mechanism where the first step is a quick association of substrate with the bis(μ-oxo)dicopper(III) complex and the second is slow intramolecular oxygen atom transfer from copper-oxo species (Scheme 1). The goal of this paper is to obtain deeper insight into the mechanism of oxidation of sulfides to sulfoxides by bis(μ-oxo)dicopper(III) complexes using quantum chemistry tools and trying to suggest the structures of the reaction intermediates.

2. Computational details

All calculations were carried out with Jaguar v 5.0 program [11]. The geometry optimizations were run using density functional theory (DFT) using PWP91 functional with LACVP* pseudopotential basis set.
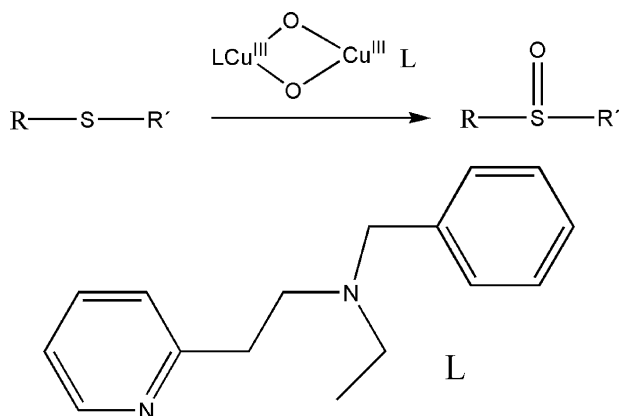
Scheme 1. Oxidation of organic sulfides by bis(μ-oxo)dicopper(III) complex.

This functional includes exchange: Slater local functional [12], Perdew–Wang 1991 gradient correction functional [13]; correlation: Perdew–Wang 1991 GGA-II local and nonlocal functionals [13] LACVP* basis set uses LAC pseudopotential [14] for the third row and heavier elements. Frequency calculations were run for transition state structures to make sure that a transition state (one imaginary mode) is located. Poisson–Boltzman solver [15, 16] implemented in Jaguar v 5.0 was used to calculate the solvation effects on the studied molecules in acetone at PWP91/LACVP* level of theory using gas phase geometry. In other words, the structures have not been reoptimized in the presence of solvent since it has been shown previously that reoptimization has very limited effect on the computed energies [17–21]. The choice of PWP91 functional was due to the fact that this functional reproduces correctly energies of Cu(II)–Cu(III) complexes transformation in agreement with CASSCF/CASPT2 calculations [22] and was shown to be successful in modeling of hydrogen transfer from phenols to Cu_2/O_2 core complexes [7] where popular B3LYP hybrid functional failed to improve the electronic energies of the reaction intermediates, single point energy calculations of PWP91/LACVP* optimized structures were carried out using better quality effective core potential basis set augmented by diffuse functions at heavy atoms labeled as LACV3P**+ basis set in Jaguar 5.0. For all calculations real ligands were used. The inclusion of realistic ligands and solvation effects in theoretical treatment is essential for quantitative description of the reaction energetic [7]. The geometry optimizations and single point calculations of copper containing intermediates were carried out for both singlet and triplet states. Singlet ground state the optimization and single point energy calculations were carried out using both restricted formalism and broken symmetry approach. The natural charges and spin densities were at PWP91/LACVP* level of theory using NBO 4.0 program incorporated in Jaguar 5.0.

3. Results and discussion

According to the experimental data Cu mediated oxidation of sulfides to sulfoxides is a two step process [10] involving a formation of Cu_2/O_2-sulfide complexes (Scheme 1) followed by oxygen atom transfer to sulfur giving rise sulfoxide molecule. Two different sulfides dimethylsulfide (**2a**) and 4-methoxyphenylmethyl sulfide (**2b**) which differ in size and electronodonating ability were selected to model the oxidation reaction mechanism (Scheme 2).

Two reaction paths were investigated. The first one is the complex formation with Cu center followed by the oxygen transfer to sulfur and the elimination of sulfoxide as suggested in [10]. The second one is the direct oxygen transfer to sulfur without precoordination with copper. First, the potential energy surfaces of two reaction paths were scanned along S–Cu and S–O distances using both restricted and unrestricted formalism with a step of 0.2 Å using relaxed energy scan. The points of interest were these of the highest and lowest energy, respectively, corresponding to initial structures for minimum and transition states searches.
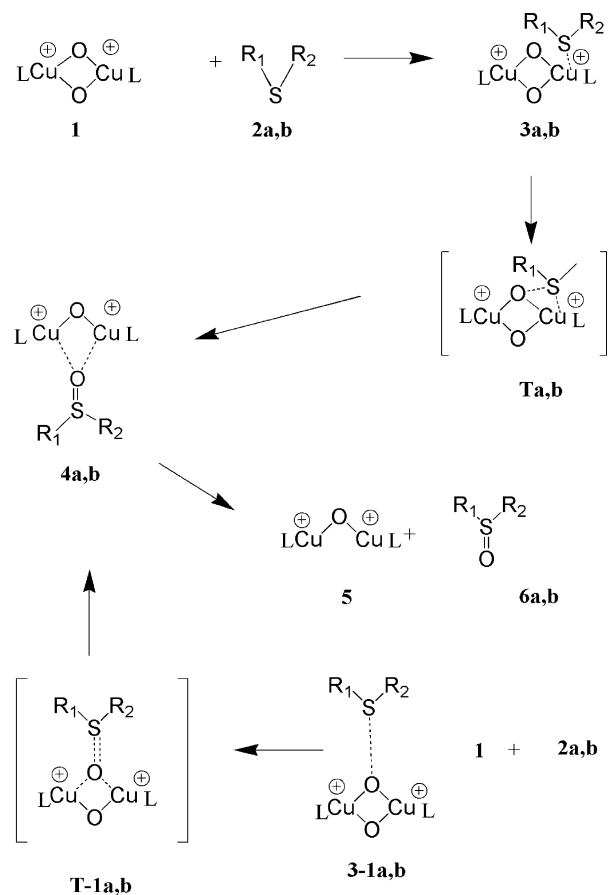
$R_1 = R_2 = CH_3$; (b) R_1 = 4-Methoxyphenyl, $R_2 = CH_3$

Scheme 2. Reaction pathways of sulfide oxidation.

Table 1
Gas phase total electronic energies (E) (a.u.) calculated at RPWP91/LACVP**+/RPWP91/LACVP* level of theory and solvation (E_s) Energy (kcal/mol) calculated at RPWP91/LACVP* level of theory for closed-shell singlet

Intermediate	E	E_s
1	−2004.791485	−118.5
2a	−477.992103	−3.2
2b	−784.221366	−6.8
3a	−2482.795153	−115.8
3b	−2789.029083	−113.8
Ta	−2482.753594	−117.8
Tb	−2789.013791	−111.6
T-1a	−2482.781769	−114.5
T-1b	−2789.021085	−111.5
3-1a	−2482.798627	−114.9
3-1b	−2789.034677	−110.5
4a	−2482.812239	−117.2
4b	−2789.047924	−112.5
5	−1929.592720	−121.0
6a	−553.182264	−8.6
6b	−859.410988	−10.6

Table 3
Gas phase total electronic energies (E) (a.u.) calculated at UPWP91/LACVP**+/UPWP91/LACVP* level of theory, solvation (E_s) energy (kcal/mol) calculated at UPWP91/LACVP* level of theory and unrestricted spin properties ($\langle S^2 \rangle$) for triplet state

Intermediate	E	E_s	$\langle S^2 \rangle$
1	−2004.765665	−116.0	2.015
2a	–	–	–
2b	–	–	–
3a	−2482.775261	−114.3	2.013
3b	–	–	–
Ta	−2482.767360	−115.7	2.029
Tb	−2789.010488	−110.7	2.018
T-1a	−2482.776334	−114.7	2.016
T-1b	−2789.008330	−110.7	2.030
3-1a	−2482.776576	−114.3	2.014
3-1b	−2789.025277	−110.9	2.009
4a	−2482.814050	−114.6	2.006
4b	−2789.046903	−112.3	2.005
5	−1929.597974	−117.4	2.006
6a	–	–	–
6b	–	–	–

According to calculations the ground state of molecule **1** is a singlet in accordance with experimental and theoretical data [3]. The broken symmetry approach gives the structure that is 0.34 kcal/mol lower in energy than the closed shell method (Tables 1–3). The triplet state is 16.2 kcal/mol higher in energy in gas phase. The spin density of triplet state is located almost completely at two oxygen atoms (1.4 at P_x and P_z orbitals) with small contribution (0.3) from Cu atoms (d_{xy} orbitals) Fig. 1 shows optimized geometries of complex **1** for three different theoretical approaches. As seen the closed and the open shell singlet geometries are very similar but not identical. As mentioned in [23,24] the broken symmetry solution converged to restricted solution for bis(μ-oxo)dicopper core with ammonia ligands,

Table 2
Gas phase total electronic energies (E) (a.u.) calculated at UPWP91/LACVP**+/UPWP91/LACVP* level of theory, solvation (Es) energy (kcal/mol) calculated at UPWP91/LACVP* level of theory and unrestricted spin properties ($\langle S^2 \rangle$) for open-shell broken symmetry singlet

Intermediate	E	E_s	$\langle S^2 \rangle$
1	−2004.792041	−119.1	0.000
2a	–	–	–
2b	–	–	–
3a	−2482.795153	−115.8	0.001
3b	−2789.029083	−113.8	0.000
Ta	−2482.784802	−114.9	0.000
Tb	−2789.022216	−111.5	0.437
T-1a	−2482.781769	−114.5	0.000
T-1b	−2789.020655	−111.8	0.000
3-1a	−2482.798627	−114.9	0.000
3-1b	−2789.034677	−110.6	0.000
4a	−2482.812944	−116.5	0.642
4b	−2789.049021	−112.7	0.598
5	−1929.600231	−117.5	0.237
6a	–	–	–
6b	–	–	–

however, in case of complex **1** the closed and open shell siglets are slightly different. This could be due to different stabilization of different electronic states by different ligands.

Sulfides **2a** and **2b** are able to form two types of intermolecular complexes with Cu_2/O_2 molecule **1**. One, where sulfur is predominantly linked to copper and another one where sulfur is mainly connected to oxygen. These complexes are rather weak taking into account solvation destabilizing even more these complexes making their formation even slightly endothermic for some cases as seen from Table 5. No complex was found for triplet state of **3b** while the opened-shell broken symmetry method converged here to restricted solution. In case of complex **3a** all complexes are stable at all levels of theory and similar to **3b** the triplet state was higher in energy compared to singlet states.

Fig. 2 shows optimized molecular geometries of Cu_2/O_2-sulfide complexes suggested as first intermediate in the oxidation reaction. As seen from the Tables 1–3 in all cases complexes of type **3-1** are more stable than complexes **3**. Thus, for the gas phase complex, **3-1a** is 2.2 kcal/mol more stable than **3a** and **3-1b** is 3.5 kcal/mol more stable than **3b**. Solvation decreases this energy difference still maintaining the order of stability.

The complex formation slightly distorts Cu_2/O_2 intermediate. Thus, one of Cu–O bonds elongates by 0.06–0.07 Å in case of complex **3b**.

The next step of the oxidation process is oxygen atom transfer from Cu_2/O_2 complex **1** to sulfur atom. Fig. 3 shows four different transition state structures located for oxygen atom transfer in complexes **3a,b** and **3-1a,b**. The transition states **Ta,b** connects structures **3a,b** and **4a,b**, while transition states **T-1a,b** connects complexes **3-1a,b** and compounds **4a,b**, respectively.
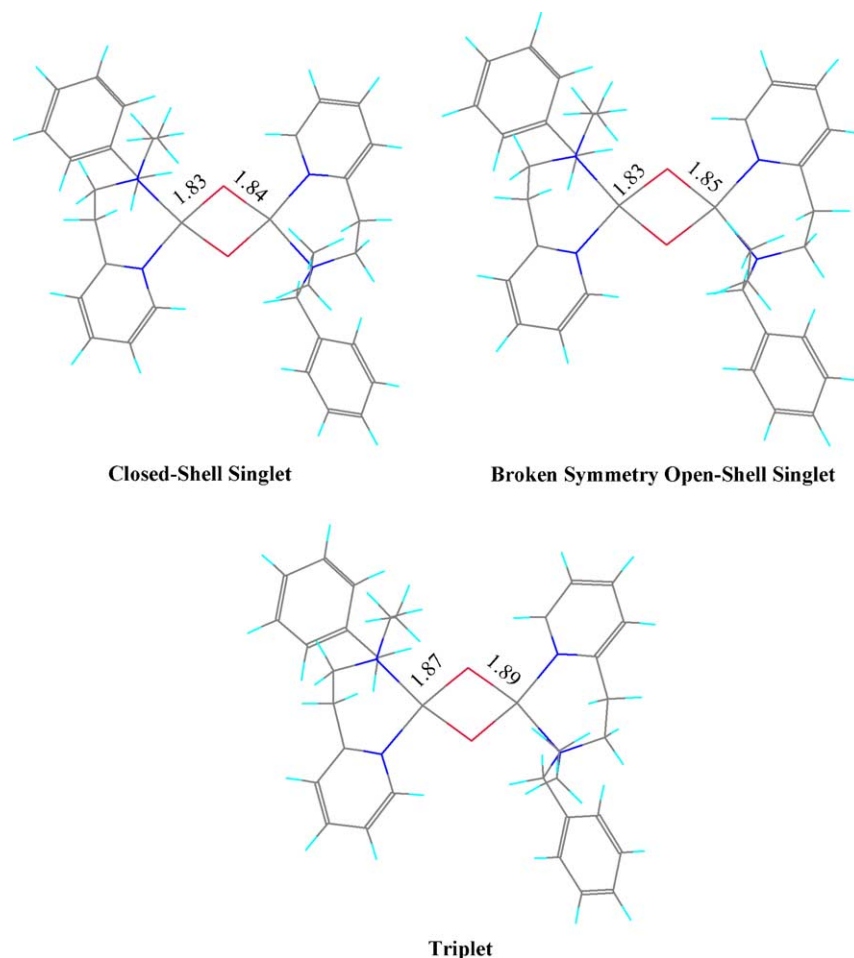
Fig. 1. Optimized molecular geometries for complex **1** for closed-shell singlet, open-shell singlet and triplet state at PWP91/LACVP* and UPWP91/LACVP* levels of theory, respectively.

As seen from the Tables 1–3 the lowest energy transition structures are located for singlet states using broken symmetry method. Restricted closed-shell singlet and triplet states give structures higher in energy. The largest energy difference in the gas phase is for **Ta** calculated using restricted closed shell method is 19 kcal/mol compared to open shell singlet using broken symmetry method. In case of **Tb**, **T-1a** and **T-1b** transition states the highest energy structures are triplets. All transition states shown in Fig. 3 are for open shell singlet using broken symmetry approach since this method gives lowest energy structures. As seen from the Table 2 oxygen transfer to **2a** should occur via transition state **Ta** as the lowest one similar to oxygen transfer to **2b** (transition state **Tb**). The energy difference, however, between **Ta** and **T-1a** is just 1.9 kcal/mol in the gas phase and 2.3 kcal/mol in solution. Therefore, **T-1a** is easily thermally accessible and could also contribute to the reaction. Similar situation holds for **Tb** and **T-1b** where the energy difference both in gas and solvated states is about 1 kcal/mol. The spin contamination for **Tb** is moderate ($\langle S^2 \rangle = 0.437$) that implies some contribution of biradical structure. As seen from the Table 4 the spin density is

localized at sulfur and oxygen atoms which can be considered as an indication for partial electron transfer from sulfur to oxygen atoms. The formation of S–O bond is accompanied by breaking of one of the Cu–O bond. Another feature of the located transition states is that in spite of difference in geometries **Ta**, **T-1a** and **Tb**, **T1** are very close by energy implying a rather shallow maximums on the potential energy surface in the vicinity of the saddle point. Oxygen transfer is completed in intermediates **4a,b** (Fig. 4) where one O–Cu bond is completely broken and formed sulfoxide fragment is linked to one of the copper atom of dicopper complex via oxygen atom. The S–O bond length (1.59–1.60 Å) is a bit large that in free sulfoxide molecule (1.52 Å). Similar to other intermediates the most stable structures are generated for the open-shell singlet (Tables 1–3) when using unrestricted open shell formalism, while the triplet and closed shell singlets gave structures higher in energy. In the case of **4a** the triplet state is 0.7 kcal/mol more stable compared to open-shell singlet (Tables 2 and 3). However, open-shell singlet is better solvated compared with triplet state reverting the stability in solution. As a result, the open-shell singlet is 1.2 kcal/mol more
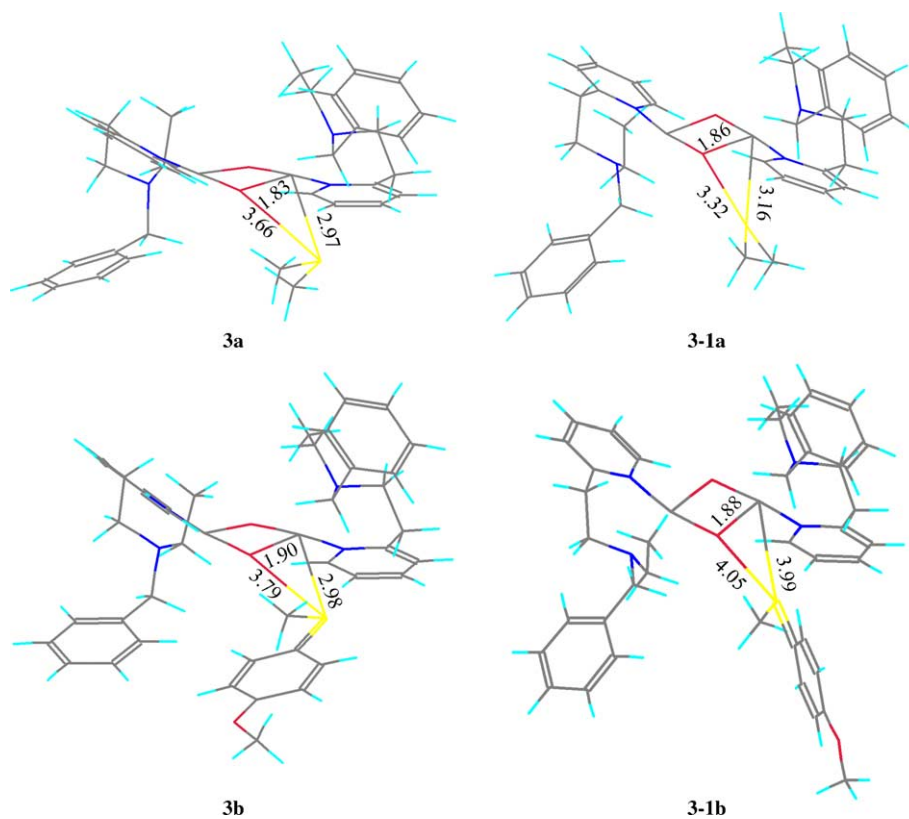
Fig. 2. Optimized geometries of intermediates **3a**, **3-1a**, **3b** and **3-1b** for open-shell singlet states at UPWP91/LACVP* level of theory.
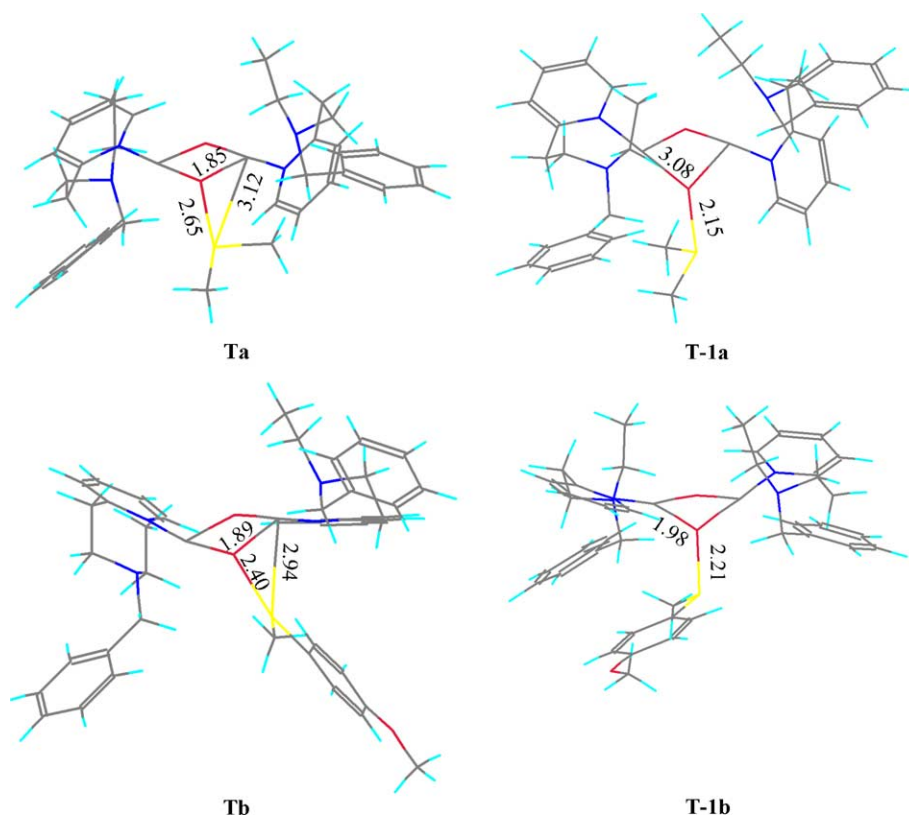

Fig. 3. Optimized geometries of transition states **Ta**, **T-1a**, **Tb** and **T-1b** for open-shell singlet states at UPWP91/LACVP* level of theory.

Table 4
Natural spin density distribution in selected reaction intermediates obtained for open-shell singlet states at UPWP91/LACVP* level of theory (only shown values large than 0.15)

Intermediate	Cu_1	Cu_2	O_1	O_2	S
4a	−0.25	0.32	−0.17		
4a[a]	0.35	0.45	0.62		
4b	−0.23	0.30	−0.17		
5	−0.17	0.17	–	–	
Tb			−0.15		0.18

[a] Triplet state.

4a

4b

5
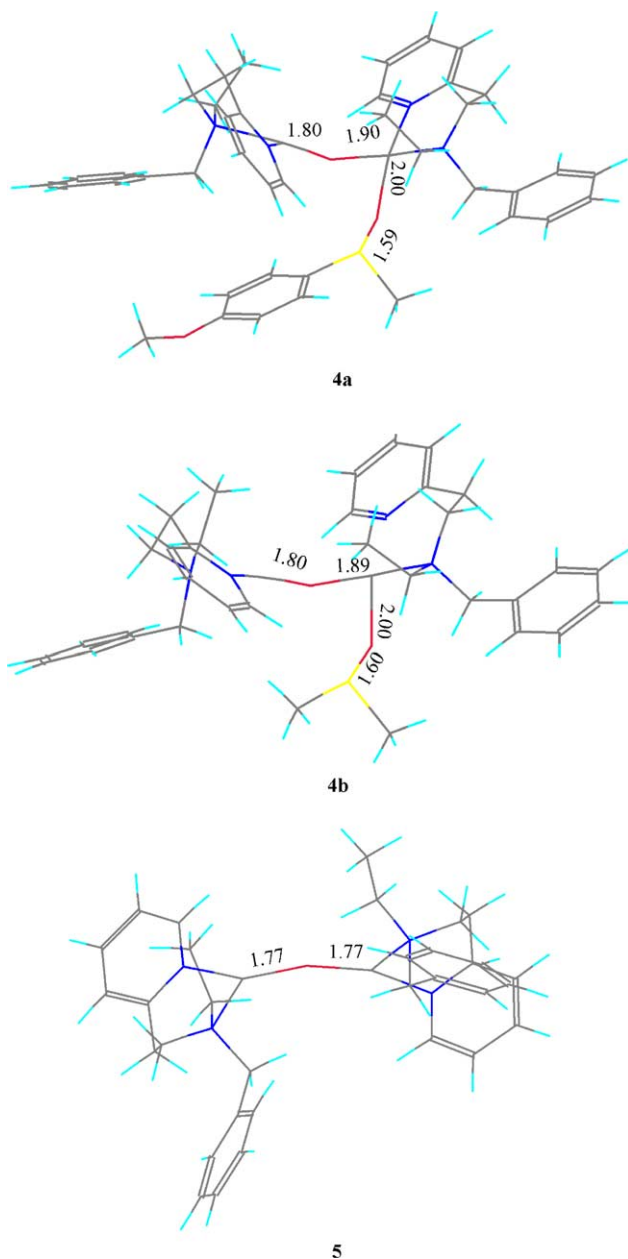
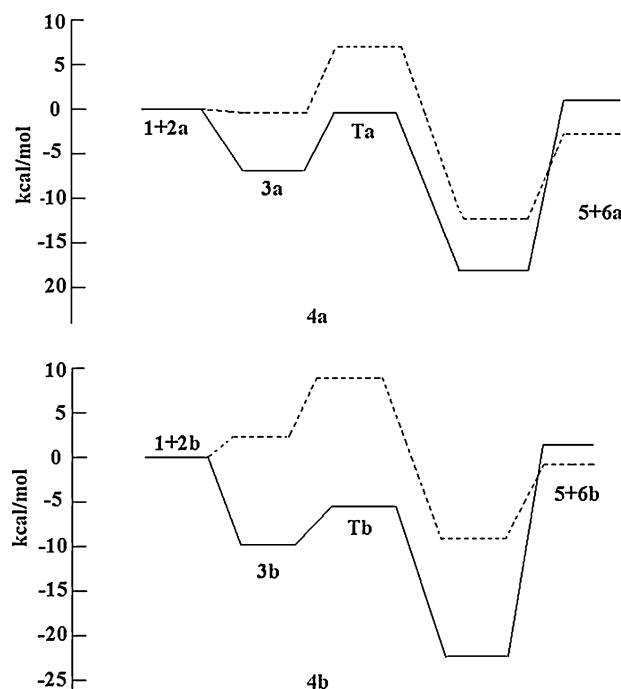Fig. 4. Optimized geometries of reaction intermediates 4a, 4b and 5 for open-shell singlet states at UPWP91/LACVP* level of theory.

Fig. 5. Energy profiles for the oxidation of sulfides 2a and 2b by complex 1 at UPWP91/LACV3P**+/UPWP91/LACVP* level of theory. Solid lines are the gas phase energies, dotted lines are the solution phase energies (acetone).

stable when solvation is taken into account. The moderate spin contamination found for open-shell singlet structures 4a,b shows that there is a contributions from biradical structures (Table 4) implying antiferromagnetic coupling for Cu atoms. The dissociation of complexes 4a,b produces sulfoxides 6a,b and binuclear Cu complex 5 (Fig. 4). Again, the broken symmetry open-shell singlet is the lowest energy structure among the closed-shell singlet and the triplet states (4.7 and 1.7 kcal/mol in the gas phase, respectively). The spin contamination for open-shell singlet of dinuclear complex 5 (0.237) shows that the ground state is somewhat biradical by nature with antiferromagnetic coupling between Cu atoms (Table 4).

Fig. 5 and Table 5 show the energy profile for oxygen transfer from complex 1 to sulfides 2a and 2b. To obtain these energy profiles the lowest energy structures were selected for each reaction intermediate except for

Table 5
Gas and solution phase reaction and activation energies energies (kcal/mol) calculated at UPWP91/LACV3P**+//UPWP91/LACVP* level of theory for more energetically favored reaction path

Reaction	E (kcal/mol)	E_s (kcal/mol)
1+2a=3a	−6.9	−0.4
3a=Ta=4a	(6.5)[a]−11.2	(7.4)[a]−11.9
4a=5+6a	19.1	9.5
1+2b=3b	−9.8	2.3
3b=Tb=4b	(4.3)[a]−12.5	(6.6)[a]−11.4
4b=5+6b	23.7	8.3

[a] Activation energy.

complexes **3** and **3-1** which were connected to the lowest energy transition states. The energy profile corresponds to open-shell singlets wavefunction for all structures involving copper atoms. As seen, the gas phase reactions corresponding to the process **1** + **2a** = **5** + **6a** and **1** + **2b** = **5** + **6b** are all slightly endothermic. Since number of particles does not change, the calculated reaction energy must be close to the free Gibbs reaction energies. The solvation effect plays an important role in the reaction energetics. Solvation destabilizes complexes **3** making them irrelevant reaction intermediates. In case of complex **3b** the binding energy is positive (Table 5). On the other hand, the dissociation of complexes **4a,b** to give final products is strongly favored by solvation. As seen from the Fig. 5 solvation favored overall reaction energetics making this reaction exothermic in solution. Since starting molecules are solvated a little better than transition states, the solvation slightly increases the activation energies of oxygen transfer. When comparing the reaction paths for the oxidation of sulfides **2a** and **2b** one can concludes that complexes **3a,b** do not probably exist due to the very low stability and the reaction proceeds directly via transition state **Ta** and **Tb** to intermediates **4a,b**. As seen, the activation energies of two reactions are similar within an error of chosen theoretical frame for the modeling. According to the experimental data [10] **2b** is more active compared to **2a** in the oxygenation reaction which can be understood in terms of dissociation energy of complexes **4a,b**. As seen from the Table 5 and the Fig. 5. **4b** has lower binding energy in solution compared to **4a**.

Since the oxygen atom transfer represents the oxidation of sulfur it is possible to monitor the oxidation process inspecting the atomic charges or the electron populations at atoms involved in this process such as sulfur and copper. Thus, the charges at copper atoms of initial complex **1** are of +1.20, while sulfur in isolated dimethylsulfide (**2a**) has charge of +0.21. The process of oxygen transfer causes significant changes. Thus, for transition state **Ta** charges at Cu atoms decreased to +1.13 and +1.15, while sulfur become more positive with a charge of +0.61. The charges of oxygen atoms do not change significantly showing electron transfer from S to Cu atoms. When oxygen transfer is completed copper atoms becomes less positive (charges +0.97 and +1.14) and sulfur shows positive charge of +1.24 (intermediate **4a**). Dissociation of **4a** gives dimethyl-sulfoxide (**6a**) (charge at S is +1.21) and intermediate **5**. The formal oxidation state of Cu in catalytic complex **1** is +3 while intermediate **5** has Cu atoms in formal oxidation state +2 which is reflected in less negative charges at Cu atoms (+0.98). Another confirmation of the oxidation state of Cu atoms in intermediate **5** is nonzero spin density on Cu atoms characteristic of formal +2 oxidation state. The charge distribution analysis for the oxygenation of **2b** gives similar results.

When the natural populations at Cu and S atoms are analyzed similar picture is revealed. Complex **1** shows natural valence population of 9.76 e on Cu When oxygen atom transfer is completed (complexes **4a,b**) the natural valence population increases becoming 9.96 and 9.83 e for two nonequivalent copper atoms. The intermediate **5** shows natural valence population on Cu atoms of 9.92 e. Sulfur atoms reflect the reduction of copper **2a,b** changing their valence natural population from 5.74 in sulfides to 4.66 in sulfoxides **6a,b**. These data suggest that the formal oxidation state of copper decrease from +3 in complex **1** to +2 in **4a,b** and **5**.

4. Conclusions

The ground state of all studied dicopper intermediates were found to be open-shell singlets. Complexes **4a,b** and **5** have significant contribution from biradical structure to their ground states with antiferromagnetic coupling between copper atoms. Proposed reaction mechanism includes direct oxygen transfer of sulfur with copper atoms, without precoordination, followed by the dissociation of complexes **4a,b** to give free sulfoxides **6a,b**. The formal oxidation state of copper atoms change from +3 in complex 1 to +2 in complexes **4a,b** and **5**.

Acknowledgements

References

[1] J.S. Valentine, C.S. Foote, A. Greenberg, J.F. Liebman (Eds.), Active Oxygen in Biochemistry, Chapman & Hall, London, 1995.

[2] K.D. Karlin, Z. Tyeklár (Eds.), Bioinorganic Chemistry of Copper, Chapman & Hall, New York, 1993.

[3] L. Que Jr., W.B. Tolman, Angew. Chem., Int. Ed. 41 (2002) 1114.

[4] S. Mahapatra, J.A. Halfen, W.B. Tolman, J. Am. Chem. Soc. 118 (1996) 11575.

[5] P.L. Holland, K.R. Rodgers, W.B. Tolman, Angew. Chem., Int. Ed. 38 (1999) 1139.

[6] V. Mahadevan, J.L. DuBois, B. Hedman, K.O. Hodgson, T.D.P. Stack, J. Am. Chem. Soc. 121 (1999) 5583.

[7] E. Tkatchouk, L. Fomina, L. Rumsh, S. Fomine, Macromolecules 36 (2003) 5607.

[8] L. Fomina, B. Vazquez, E. Tkatchouk, S. Fomine, Tetrahedron 58 (2002) 6741.

[9] V. Mahadevan, Z. Hou, A.P. Cole, D.E. Root, T.K. Lal, E.I. Solomon, T.D.P. Stack, J. Am. Chem. Soc. 119 (1997) 11996.

[10] M. Taki, S. Itoh, S. Fukuzumi, J. Am. Chem. Soc. 124 (2002) 998.

[11] Jaguar 5.0, Schrodinger, LLC, Portland, OR, 2003.

[12] J.C. Slater, Quantum Theory of Molecules and Solids, The Self-Consistent Field for Molecules and Solids, vol. 4, McGraw-Hill, New York, 1974.

[13] J.P. Perdew, in: P. Ziesche, H. Eschrig (Eds.), Electronic Structure Theory of Solids, Akademie, Berlin, 1991.

[14] P.J. Hay, W.R. Wadt, J. Chem. Phys. 82 (1985) 270.

[15] D.J. Tannor, B. Marten, R. Murphy, R.A. Friesner, D. Sitkoff, A. Nicholls, M. Ringnalda, W.A. Goddard, B. Honig, J. Am. Chem. Soc. 116 (1994) 11875.

[16] B. Marten, K. Kim, C. Cortis, R.A. Friesner, R.B. Murphy, M.N. Ringnalda, D. Sitkoff, B. Honig, J. Phys. Chem. 100 (1996) 11775.

[17] V. Barone, M. Cossi, J. Tomasi, J. Chem. Phys. 107 (1997) 3210.

[18] C.S. Pomeli, J. Tomasi, M. Sola, Organometallics 17 (1998) 3164.

[19] I. Cacelli, A. Ferretti, J. Chem. Phys. 109 (1998) 8583.

[20] S. Creve, H. Oevering, B.B. Coussens, Organometallics 18 (1999) 1967.

[21] F. Bernardi, A. Bottoni, G.P. Miscone, Organometallics 17 (1998) 16.

[22] M. Flock, K. Pierloot, J. Phys. Chem. A 103 (1999) 95.

[23] A. Berces, Inorg. Chem. 36 (1997) 4831.

[24] A. Berces, Int. J. Quantum Chem. 65 (1997) 1077.