

## A Stabilized $\mu\text{-}\eta^2\text{:}\eta^2$ Peroxodicopper(II) Complex with a Secondary Diamine Ligand and Its Tyrosinase-like Reactivity

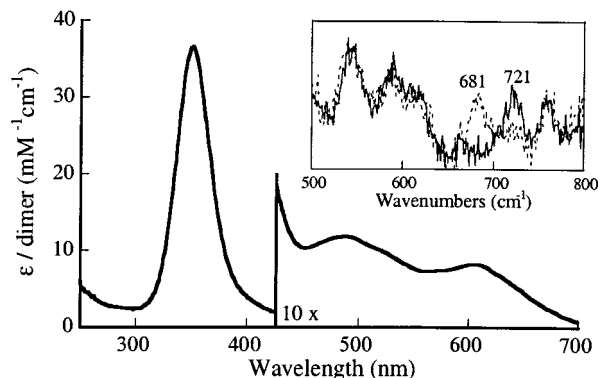
Liviu M. Mirica,<sup>†</sup> Michael Vance,<sup>†</sup> Deanne Jackson Rudd,<sup>†</sup> Britt Hedman,<sup>†,‡</sup> Keith O. Hodgson,<sup>†,‡</sup> Edward I. Solomon,<sup>†</sup> and T. D. P. Stack<sup>\*,†</sup>

Department of Chemistry, Stanford University, California 94305, and Stanford Synchrotron Radiation Laboratory, SLAC, Stanford University, California 94309

Received May 14, 2002; Revised Manuscript Received June 18, 2002

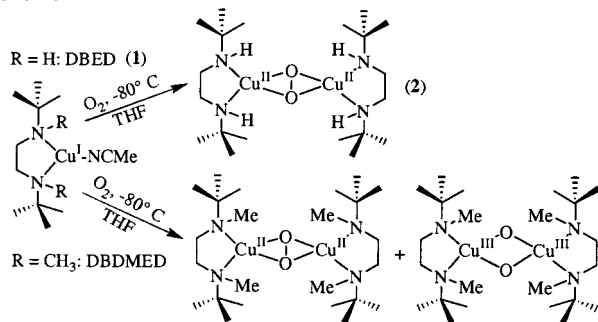
The activation of dioxygen ( $\text{O}_2$ ) by Cu(I) complexes is known to play an important role in biological and industrial oxidation processes.<sup>1–3</sup> The structure–reactivity relationships of the binuclear copper enzymes, such as tyrosinase, have been extensively investigated, and model complexes have aided these studies.<sup>4–6</sup> In line with the native systems, most model complexes use facial-capping trinitrogen ligation of the copper, and all such structurally characterized Cu– $\text{O}_2$  species exhibit a weak association with the axial nitrogen ligand. An emerging trend exists in which bidentate nitrogenous ligands are used, and such ligation does not generally compromise the stability of the formed Cu– $\text{O}_2$  complexes. A reactivity advantage with externally added substrates may also be realized as the Cu/ $\text{O}_2$  cores are potentially more accessible.<sup>7,8</sup> Bidentate ligation of peralkylated diamine ligands (PDL) to Cu(I) is sufficient to allow  $\text{O}_2$  activation to yield either a pure bis  $\mu$ -oxodicopper(III) species (**O**),<sup>3,9,10</sup> or an equilibrium mixture of the isoelectronic  $\mu\text{-}\eta^2\text{:}\eta^2$ -peroxodicopper(II) (**P**) and **O** species.<sup>11</sup> Here we report a stabilized **P** complex that employs a bidentate secondary diamine ligand (DBED, Scheme 1). Beyond potential biological relevance, our interest in the Cu(I)–DBED/ $\text{O}_2$  reactivity stems from its use in the catalytic oxidative polymerization of phenols to the thermoplastic polyphenylene oxide (PPO).<sup>12,13</sup>

Conventional wisdom suggests that secondary amine ligands are unsuitable for stabilizing the Cu– $\text{O}_2$  species, due to the amine protons.<sup>14,15</sup> Yet, this **P** complex exhibits thermal stability comparable to the other Cu– $\text{O}_2$  species formed using PDL.<sup>9,11,16</sup> Interestingly, this new complex exhibits tyrosinase-like reactivity by hydroxylating phenolates to catechols (vide infra), in yields comparable to those of other reported systems.<sup>17,18</sup> The reaction of *N,N'*-di-*tert*-butyl-ethylenediamine (DBED) with  $[\text{Cu}(\text{MeCN})_4](\text{X})$  ( $\text{X} = \text{CF}_3\text{SO}_3^-, \text{ClO}_4^-, \text{SbF}_6^-, \text{BF}_4^-$ ) yields a trigonal-planar Cu(I) complex,  $[(\text{DBED})\text{Cu}(\text{MeCN})](\text{X})$  (**1·X**).<sup>19</sup> Solutions of **1·X** in aprotic solvents (THF,  $\text{CH}_2\text{Cl}_2$ , acetone, toluene) react rapidly with  $\text{O}_2$  at 193 K to generate thermally sensitive dark green to orange complexes, depending on the counteranion. Spectroscopic and analytical data support a  $\mu\text{-}\eta^2\text{:}\eta^2$ -peroxodicopper(II) complex, formulated as  $[(\text{Cu}^{\text{II}}(\text{DBED}))_2(\text{O}_2)](\text{X})_2$  (**2·X<sub>2</sub>**) (vide infra).<sup>20</sup> These complexes are EPR silent, NMR active, and have a 2:1 (Cu: $\text{O}_2$ ) stoichiometry established by spectrophotometric titrations with  $\text{O}_2$ .<sup>16</sup> The complex **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** in THF exhibits characteristic LMCT absorptions,<sup>5,6,21</sup> except that the extinction coefficient of the low-energy feature at 350 nm is exceptionally large (Figure 1).<sup>22</sup> Resonance Raman (rR) spectroscopy of **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** in THF confirms a **P** structure,<sup>23</sup> with a low  $\nu_{\text{O-O}}$  = 721  $\text{cm}^{-1}$  ( $\Delta^{18}\text{O}_2$ ) =



**Figure 1.** UV–vis spectrum of **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** (THF, 193 K, [Cu]  $\approx$  1 mM). Inset: Resonance Raman spectra of **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** ( $\lambda_{\text{ex}}$  = 351.1 nm, THF, 77 K, [Cu]  $\approx$  4 mM) using  $^{16}\text{O}_2$  (solid line) or  $^{18}\text{O}_2$  (dashed line).

### Scheme 1



40  $\text{cm}^{-1}$ , Figure 1, inset), and two isotope-insensitive stretches in the 300  $\text{cm}^{-1}$  region (Table 1).<sup>16,24</sup>

Solution Cu K edge X-ray absorption spectroscopy (XAS) exhibits a preedge feature at 8979.5 eV, consistent with a Cu(II) complex.<sup>16</sup> The EXAFS fit clearly requires a Cu···Cu contribution at a distance of 3.45 Å, a distance similar to other structurally characterized **P** complexes.<sup>5,6,25</sup> The coordination around each Cu is best fit as five- rather than four-coordinate with four N/O<sup>26</sup> ligands at 1.96 Å and an additional O/N ligand at 2.53 Å.<sup>27</sup> The latter distance is consistent with an axially bound oxygen atom from a  $\text{CF}_3\text{SO}_3^-$  counteranion.<sup>10</sup> The variation of the UV–vis and rR spectra with counteranion and not with solvent suggests an intimate interaction of the counteranions with the complex. **2·(SbF<sub>6</sub>)<sub>2</sub>** exhibits the characteristic UV–vis absorptions and rR shifts of a **P** complex distinct from **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** (Table 1).

The **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** complex is remarkably stable at 193 K ( $t_{1/2} \approx$  20 days) given the secondary diamine ligation, yet decays in a first-order process at elevated temperatures ( $\Delta H^\ddagger = 14.8 \pm 0.3 \text{ kJ mol}^{-1}$ ,  $\Delta S^\ddagger = 10 \pm 1 \text{ J mol}^{-1} \text{ K}^{-1}$ ,  $T = 193\text{--}273 \text{ K}$ , THF).<sup>28</sup> Deuteration

\* To whom correspondence should be addressed. E-mail: stack@stanford.edu.

<sup>†</sup> Department of Chemistry.

<sup>‡</sup> Stanford Synchrotron Radiation Laboratory.

**Table 1.** Spectroscopic Features of **2·(X)**<sub>2</sub> in THF

complex	UV-vis features $\lambda$ , nm ( $\epsilon$ , mM <sup>-1</sup> cm <sup>-1</sup> )	rR features $\nu$ , cm <sup>-1</sup> ( $\Delta^{18}\text{O}_2$ , cm <sup>-1</sup> )
<b>2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub></b>	350 (36)	244 (0)
	485 (1.2)	313 (0)
	605 (0.9)	721 (40)
<b>2·(SbF<sub>6</sub>)<sub>2</sub></b>	353 (38)	241 (0)
	425 (1.7)	308 (0)
	472 (2.1)	728 (40)

of the N–H groups does not alter the thermal decay rate of **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** in THF at 233 K, indicating that the rate-determining step of thermal decay does not involve N–H bond cleavage.<sup>29</sup>

The stability of **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** allows the reactivity with exogenous substrates to be examined. The isoelectronic species **P** and **O** are thought to exhibit different reactivity, with the former a better oxygen-atom transfer reagent,<sup>30</sup> and the latter a better hydrogen-atom acceptor.<sup>11</sup> Consistent with these previous observations, **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** reacts stoichiometrically with PPh<sub>3</sub> at 193 K in THF to yield PPh<sub>3</sub>O (>95%) under pseudo-first-order conditions of PPh<sub>3</sub>, yet does not couple 2,4-di-*tert*-butylphenol to 3,3',5,5'-tetra-*tert*-butyl-2,2'-biphenol.<sup>31</sup> This lack of phenolic coupling supports an attenuated hydrogen-atom abstracting ability of **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>**.<sup>11</sup> The reaction of **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** with catechol, benzyl alcohol, and benzylamine gives good yields of quinone (95%), benzaldehyde (80%), and benzonitrile (70%), respectively.<sup>16</sup> The reactivity of a **P** species with the latter two substrates is unprecedented.<sup>10,32,33</sup>

In contrast to the lack of phenol reactivity, **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** reacts rapidly with sodium or lithium salts of 2,4-di-*tert*-butylphenol at 193 K, as assessed by optical spectroscopy.<sup>16,34</sup> An analysis of the products reveals a ~1:1 mixture of 3,5-di-*tert*-butylcatechol and 3,5-di-*tert*-butyl-1,2-benzoquinone as products accounting for ~80% of the oxidizing equivalents of **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>**.<sup>35</sup> The use of <sup>18</sup>O<sub>2</sub> in the formation of **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** followed by a reaction with phenolate clearly shows that a single oxygen atom is transferred to the catechol and quinone products, supporting direct oxygen-atom transfer.<sup>16</sup> This places **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** in a limited class of synthetic **P** species that efficiently hydroxylates phenolates, similar to tyrosinase.<sup>17,18</sup>

The contrast in O<sub>2</sub> reactivity between the copper complexes of DBED and its bulkier dimethylated analogue DBDMED (*N,N'*-di-*tert*-butyl-*N,N'*-di-methyl-ethylenediamine) is striking, but not unprecedented (Scheme 1).<sup>36,37</sup> Steric escalation within a series of PDL clearly shows that bulkier ligands bias the formation of the Cu–O<sub>2</sub> species toward **P** rather than **O**.<sup>10,27</sup> Yet, the less bulky DBED yields only detectable amounts of **P** while DBDMED yields an equilibrium mixture of **P** and **O**.<sup>11,38</sup> A subtle interplay of electronics and structure are obviously operative in stabilizing each isomer, ultimately controlling the reactivity with externally added substrates.

**Acknowledgment.** We thank Dr. Viswanath Mahadevan for experimental assistance and helpful discussions. Funding was provided by NIH GM50730 (T.D.P.S.), NIH DK31450 (E.I.S.), and NIH RR01209 (K.O.H.). XAS data were measured at SSRL that is supported by the Department of Energy, Office of Basic Energy Sciences. The structural molecular biology program is supported by the NIH, NCR, BTP program, and by DOE OBER.

**Supporting Information Available:** Experimental details including synthetic procedures, UV-vis, resonance Raman, spectrophotometric titration, XAS, kinetic measurements, and product analysis (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

## References

(1) Solomon, E. I.; Sundaram, U. M.; Machonkin, T. E. *Chem. Rev.* **1996**, *96*, 2563.

- (2) Blackman, A. G.; Tolman, W. B. *Struct. Bonding (Berlin)* **2000**, *97*, 179.
- (3) Mahadevan, V.; Klein Gebbink, R. J. M.; Stack, T. D. P. *Curr. Opin. Chem. Biol.* **2000**, *4*, 228.
- (4) Karlin, K. D.; Haka, M. S.; Cruse, R. W.; Meyer, G. J.; Farooq, A.; Gultneh, Y.; Hayes, J. C.; Zubieta, J. *J. Am. Chem. Soc.* **1988**, *110*, 1196.
- (5) Kitajima, N.; Fujisawa, K.; Fujimoto, C.; Moro-oka, Y.; Hashimoto, S.; Kitagawa, T.; Toriumi, K.; Tatsumi, K.; Nakamura, A. *J. Am. Chem. Soc.* **1992**, *114*, 1277.
- (6) Kodera, M.; Katayama, K.; Tachi, Y.; Kano, K.; Hirota, S.; Fujinami, S.; Suzuki, M. *J. Am. Chem. Soc.* **1999**, *121*, 11006.
- (7) Cole, A. P.; Root, D. E.; Mukherjee, P.; Solomon, E. I.; Stack, T. D. P. *Science* **1996**, *273*, 1848.
- (8) Holland, P. L.; Rodgers, K. R.; Tolman, W. B. *Angew. Chem., Int. Ed.* **1999**, *38*, 1139.
- (9) Mahadevan, V.; Hou, Z. G.; Cole, A. P.; Root, D. E.; Lal, T. K.; Solomon, E. I.; Stack, T. D. P. *J. Am. Chem. Soc.* **1997**, *119*, 11996.
- (10) Mahadevan, V.; DuBois, J. L.; Hedman, B.; Hodgson, K. O.; Stack, T. D. P. *J. Am. Chem. Soc.* **1999**, *121*, 5583.
- (11) Mahadevan, V.; Henson, M. J.; Solomon, E. I.; Stack, T. D. P. *J. Am. Chem. Soc.* **2000**, *122*, 10249.
- (12) DBED is used with Cu(I) as a catalyst for the synthesis of PPO: Aycock, D.; Abolins, V.; White, D. M. *Encyclopedia of Polymer Science and Engineering*, 2nd ed.; John Wiley & Sons: New York, 1986; Vol. 13, p 1. The investigation of the Cu–O<sub>2</sub> species formed using DBED could provide a chemically plausible intermediate for the oxidative polymerization of phenols.
- (13) Higashimura, H.; Fujisawa, K.; Moro-oka, Y.; Kubota, M.; Shiga, A.; Terahara, A.; Uyama, H.; Kobayashi, S. *J. Am. Chem. Soc.* **1998**, *120*, 8529.
- (14) Mandal, S.; Macikenas, D.; Protasiewicz, J. D.; Sayre, L. M. *J. Org. Chem.* **2000**, *65*, 4804.
- (15) Schindler, S. *Eur. J. Inorg. Chem.* **2000**, 2311. A *trans*- $\eta$ -1,2-peroxodicycopper(II) complex has been synthesized using a secondary triamine ligand (Schatz, M.; Becker, M.; Walter, O.; Liehr, G.; Schindler, S. *Inorg. Chim. Acta* **2001**, *324*, 173).
- (16) See Supporting Information.
- (17) Santagostini, L.; Gullotti, M.; Monzani, E.; Casella, L.; Dillinger, R.; Tuzcek, F. *Chem. Eur. J.* **2000**, *6*, 519.
- (18) Itoh, S.; Kumei, H.; Taki, M.; Nagatomo, S.; Kitagawa, T.; Fukuzumi, S. *J. Am. Chem. Soc.* **2001**, *123*, 6708.
- (19) Complex **1·(CF<sub>3</sub>SO<sub>3</sub>)** has been characterized by single-crystal X-ray diffraction.
- (20) The formation of **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** follows a second-order process with a rate of  $3.0(3) \times 10^2 \text{ M}^{-1} \text{ s}^{-1}$  (THF, –80 °C, 1 atm O<sub>2</sub>), as assessed by the formation of the 350 nm LMCT. This is in agreement with the well-established mechanism of reaction of Cu(I) complexes with O<sub>2</sub> for peroxo or bis-oxo species (Karlin, K. D.; Kaderli, S.; Zuberbühler, A. D. *Acc. Chem. Res.* **1997**, *30*, 139).
- (21) Cahoy, J.; Holland, P. L.; Tolman, W. B. *Inorg. Chem.* **1999**, *38*, 2161.
- (22) The unique absorption spectra of these complexes are currently under investigation.
- (23) Henson, M. J.; Mukherjee, P.; Root, D. E.; Stack, T. D. P.; Solomon, E. I. *J. Am. Chem. Soc.* **1999**, *121*, 10332.
- (24) Henson, M. J.; Mahadevan, V.; Stack, T. D. P.; Solomon, E. I. *Inorg. Chem.* **2001**, *40*, 5068.
- (25) Hu, Z. B.; Williams, R. D.; Tran, D.; Spiro, T. G.; Gorun, S. M. *J. Am. Chem. Soc.* **2000**, *122*, 3556.
- (26) EXAFS analysis typically cannot distinguish between atoms that differ in Z by 1 (e.g., O and N) (Scott, R. A. *Methods Enzymol.* **1985**, *117*, 414). Given the *k* range of the EXAFS data ( $k = 3\text{--}12.5 \text{ \AA}^{-1}$ ), any difference in *R* less than 0.17 Å between ligands in the first coordination shell (at 1.96 Å) could not be resolved.
- (27) Inclusion in the least-squares fits to the data of the fifth ligand reduced the normalized error ( $\chi^2$ ) from 0.22 to 0.17 (G. N. George, SSRL, EXAFSPAK calculation of normalized error).
- (28) Recovery of only 50% of the ligand (by ammonia workup) suggests an intramolecular ligand oxidation during the thermal decay (see Supporting Information).
- (29) When **2·(CF<sub>3</sub>SO<sub>3</sub>)<sub>2</sub>** is warmed exposed to air, the bis-hydroxycopper complex is formed, similar to other Cu–O<sub>2</sub> complexes.<sup>32</sup>
- (30) Pidcock, E.; Obias, H. V.; Zhang, C. X.; Karlin, K. D.; Solomon, E. I. *J. Am. Chem. Soc.* **1998**, *120*, 7841.
- (31) Most Cu–O<sub>2</sub> model complexes react with phenols to give the C–C coupling dimer through a hydrogen-atom abstraction mechanism.
- (32) Obias, H. V.; Lin, Y.; Murthy, N. N.; Pidcock, E.; Solomon, E. I.; Ralle, M.; Blackburn, N. J.; Neuhold, Y. M.; Zuberbühler, A. D.; Karlin, K. D. *J. Am. Chem. Soc.* **1998**, *120*, 12960.
- (33) Except for one system,<sup>10</sup> no appreciable amounts of benzyl alcohol or benzylamine were oxidized by other Cu/O<sub>2</sub> species previously studied.
- (34) To prevent oxidation by O<sub>2</sub>, solutions were deoxygenated by bubbling N<sub>2</sub> for 15 min before addition of substrates.
- (35) Assuming 2 equiv of **2·(X)** are needed for formation of 1 equiv of quinone from phenolate with no Cu(I) formation.
- (36) Liang, H.-C.; Zhang, C. X.; Henson, M. J.; Sommer, R. D.; Hatwell, K. R.; Kaderli, S.; Zuberbühler, A. D.; Rheingold, A. L.; Solomon, E. I.; Karlin, K. D. *J. Am. Chem. Soc.* **2002**, *124*, 4170.
- (37) Taki, M.; Teramae, S.; Nagatomo, S.; Tachi, Y.; Kitagawa, T.; Itoh, S.; Fukuzumi, S. *J. Am. Chem. Soc.* **2002**, *124*, 6367.
- (38) The equilibrium mixture of **P** and **O** formed using DBDMED did not hydroxylate phenolates in appreciable yields.

JA026905P