is used for incorporating asymmetry in the ester-imine condensation. This new synthetic strategy relies on our recent report[1e] on the possibility of using enolizable silylimines in the production of the β-lactam ring.

We began by examining the reaction between the lithium enolate of *tert*-butyl butanoate **3** and the trimethylsilylimine **2**, readily available from (*S*)-lactic aldehyde **1**[5] and lithium hexamethyldisilylamide.[6] Treatment of *tert*-butyl butanoate with lithium diisopropylamide in tetrahydrofuran followed by **2** (−78 → 25 °C overnight) gave a 96/4 mixture of the β-lactam **4** ($[\alpha]^{20}_D$ +23.5° (*c* 1.2, $CHCl_3$)) and **4a**[7] in 61% yield.

The optical purity of **4** as well as its absolute configuration was determined by completing a formal total synthesis of (+)-PS-5 **10** as outlined in Scheme II.

Treatment of **4** with aqueous HF in acetonitrile[8] gave **5** (97%) ($[\alpha]^{20}_D$ +41.8° (*c* 1.14, $CHCl_3$)) which upon oxidation by chromic acid[9] afforded **6** (76%). Baeyer–Villiger oxidation of **6** gave **7** as a single trans isomer in 72% yield ($[\alpha]^{20}_D$ +100° (*c* 1.62, $CHCl_3$)). Reaction of **7** with silyl enol ether **8** and zinc chloride[10] gave trans β-lactam **9** (67.5%) ($[\alpha]^{20}_D$ +63.9° (*c* 1.14, $CHCl_3$, lit.[4h] $[\alpha]^{20}_D$ +64.7° (*c* 1, $CHCl_3$)). Since **9** has previously been prepared in configurationally pure form and has previously been converted to (+)-PS-5 **10**,[4h] this constitutes a formal total enantioselective synthesis of (+)-PS-5 **10**.

In an alternative way **9** was obtained in two steps from **5** through a fragmentation reaction by treating a benzene solution of **5** with lead tetracetate (2 equiv) in the presence of $CaCO_3$ (5 h, reflux)[11] to give **7** and **7a** in 61% as a (30/70) cis–trans mixture and subsequent displacement of the acetoxy group via the above described procedure to give β-lactam **9** in 62% yield as a single trans isomer. By this way the lack of stereoselectivity in the formation of the C-4 stereocenter of the acetoxy derivative appears unimportant since the C-4 center is equilibrated to the more stable 4*R* configuration.

The asymmetric 1,2-lk induction[12] by the electrophilic partner observed in the ester-imine condensation could be explained by assuming a coplanarity between the oxygen and the nitrogen atoms in the imine due to the chelation by lithium cations, present in the reaction medium, and attack of the enolate from the less hindered face of the diastereotopic plane of the imine group.

Work is in progress on mechanistic aspects on the origin of the stereoselectivity of the reaction as well as on the use of other chiral silylimines.

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Registry No. **1**, 87727-28-4; **2**, 116102-34-2; **4**, 116078-97-8; **4a**, 116181-12-5; **5**, 116078-98-9; **6**, 116179-68-1; **7**, 103775-02-6; **7a**, 103775-03-7; **8**, 93788-48-8; **9**, 83997-55-1; **10**, 67007-79-8; *tert*-butyl butanoate, 2308-38-5.

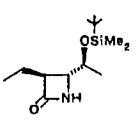
Supplementary Material Available: Preparation and physical data for compounds **4**, **4a**, **5**, **6**, **7**, **7a**, and **9** (4 pages). Ordering information is given on any current masthead page.

(4) Isolation of (+)-PS-5: (a) Yamamoto, K.; Yoshioka, T.; Kato, Y.; Shibamoto, N.; Okamura, K.; Shimauchi, Y.; Ishikura, T. *J. Antibiot.* **1980**, *33*, 796. Synthesis of (+)-PS-5: (a) Georg, G. I.; Kant, J. *J. Org. Chem.* **1988**, *53*, 692. (b) Chiba, T.; Nakai, T. *Chem. Lett.* **1987**, 2187. (c) Corbett, D. F.; Eglington, A. J. *J. Chem. Soc., Chem. Commun.* **1980**, 1083. (d) Wasserman, H. H.; Han, W. T. *Tetrahedron Lett.* **1984**, *25*, 3747. (e) Okano, K.; Izawa, T.; Ohno, M. *Tetrahedron Lett.* **1983**, *24*, 217. (f) Hatanaka, M.; Nitta, H.; Ishimaru, T. *Tetrahedron Lett.* **1984**, *25*, 2387. (g) Kametani, T.; Honda, T.; Nakayama, A.; Sasaki, Y.; Mochizuchi, T.; Fukumoto, K. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2228. (h) Favara, D.; Omodei-Salè, A.; Consonni, P.; Depaoli, A. *Tetrahedron Lett.* **1982**, *23*, 3105. (i) Cecchi, R.; Favara, D.; Omodei-Salè, A.; Depaoli, A.; Consonni, P. *Gazz. Chim. Ital.* **1984**, *114*, 225. (j) Bateson, J. H.; Hickling, R. I.; Roberts, P. M.; Smale, T. C.; Southgate, R. *J. Chem. Soc., Chem. Commun.* **1980**, 1084. (k) Hsiao, C.-N.; Ashburn, S. P.; Miller, M. J. *Tetrahedron Lett.* **1985**, *26*, 4855. (l) Evans, D. A.; Sjogren, E. B. *Tetrahedron Lett.* **1986**, *27*, 3119. (m) Hart, D. J.; Lee, C.-S. *J. Am. Chem. Soc.* **1986**, *108*, 6054. (n) Hart, D. J.; Ha, D.-C. *J. Antibiot.* **1987**, *40*, 309.

(5) Hirama, M.; Nishizaki, I.; Shigemoto, T.; Ito, S. I. *J. Chem. Soc., Chem. Commun.* **1986**, 393.

(6) The imine **3** was prepared according to a general procedure[1e] starting from protected lactic aldehyde[5] and lithium hexamethyldisilylamide (THF, −40 °C, 40 min).

(7) Careful analysis of the 300 MHz ^1H NMR spectrum showed the presence of 4% of isomer **4a** which could be separated by flash chromatography and analyzed.



(4a)

(8) Newton, R. F.; Reynolds, D. P.; Finch, M. A. W.; Kelly, D. R.; Roberts, S. M. *Tetrahedron Lett.* **1979**, 3981.

(9) Brown, H. C.; Garg, P. C.; Liu, K. T. *J. Org. Chem.* **1971**, *36*, 387. For general reviews, see: *Chromium Oxidations in Organic Chemistry*; Cainelli, G., Cardillo, G., Eds.; Springer: Berlin, 1984.

(10) (a) Reider, P. J.; Grabowski, E. J. J. *Tetrahedron Lett.* **1982**, 2293. (b) Ueda, Y.; Roberge, G.; Vinet, V. *Can. J. Chem.* **1984**, *62*, 2936. (c) Barrett, A. G. M.; Quayle, P. *J. Chem. Soc., Chem. Commun.* **1981**, 1076.

(11) Amorosa, M.; Caglioti, L.; Cainelli, G.; Immer, H.; Keller, J.; Werli, H.; Mihailovic, M. L. J.; Schaffner, K.; Arigoni, D.; Jeger, O. *Helv. Chim. Acta* **1962**, *45*, 2674.

(12) Seebach, D.; Prelog, V. *Angew. Chem.* **1982**, *94*, 696.

Basic Polypeptides Accelerate the Hydrolysis of Ribonucleic Acids

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Polycationic polypeptides containing arginine or lysine and hydrophobic amino acids are able to accelerate oligoribonucleotide hydrolysis. The greatest effect was observed when the polypeptides are structured in β-sheets.

When mixing an aqueous solution of alternating poly(Leu-Lys) to an aqueous solution of ApAp at pH 8, the solution becomes turbid reflecting the formation of a complex. The mixture was analyzed as a function of time by reversed-phase HPLC, after complete dissociation of the complex. Poly(Leu-Lys) stimulates strongly the rate of hydrolysis as compared to the control run in the absence of polypeptide (Figure 1). From the pseudo-first-order kinetics it can be calculated that the hydrolysis rate is increased by a factor of about 150. HPLC chromatograms show that the hydrolysis produces 2′:3′ cyclic AMP (A > p) together with A2′p and A3′p. This suggests that the polypeptide accelerates the classical alkaline hydrolysis of RNA[1] which is known to proceed in two steps: cleavage of the phosphodiester bond and subsequent formation of a 2′:3′ cyclic phosphate (A > p) followed by the opening of the cycle in a second step. The acceleration of the hydrolysis affects essentially the first step of the mechanism since it has been found that poly(Leu-Lys) increases the rate of A > p hydrolysis only by a factor 5 to produce A2′p and A3′p monomers in a 1.14 ratio in favor of A2′p.

The activity of poly(Leu-Lys) was extended to a mixture of oligo(A)s up to the 25-mer which is well resolved by HPLC on RPC5[2,3] and which can be cheaply obtained on a large scale from commercially available poly A.[4] In a preliminary publication,[5]

(1) Brown, D. M.; Todd, A. R. *The Nucleic Acids*; Chargraff E., Davidson, J. N., Eds.; Academic Press: New York, 1955; Vol. 1, pp 409–445.

(2) Pearson, R. L.; Weiss, J. F.; Kelmers, A. D. *Biochim. Biophys. Acta* **1971**, *228*, 770.

(3) Joyce, G. F.; Inoue, T.; Orgel, L. E. *J. Mol. Evol.* **1984**, *176*, 279.

0002-7863/88/1510-6880$01.50/0

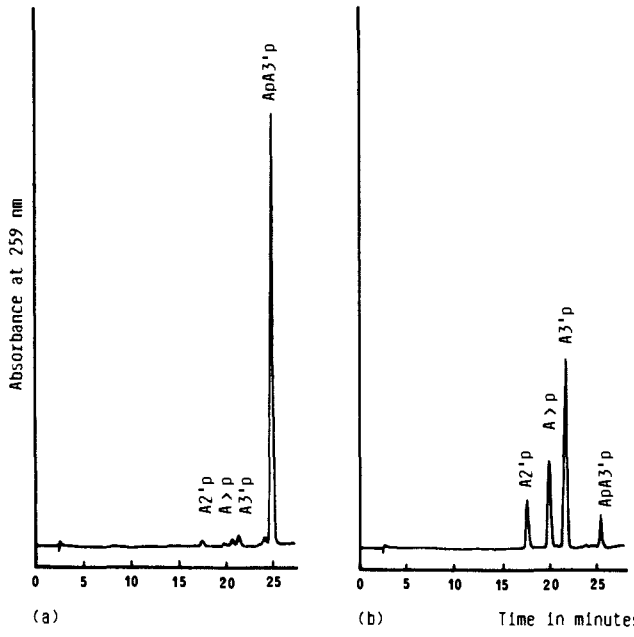

Figure 1. Reversed phase HPLC profiles of the reaction products of the hydrolysis of ApAp: (a) control; (b) in the presence of poly(Leu-Lys). Reaction conditions: 50 °C, 7 days, 0.1 M Gly-Gly buffer pH 8; ApAp: 9.7×10^{-4} M in PO_4^-; poly(Leu-Lys): 2.4×10^{-3} M in Lys^+. Analyses were run on a C18 lichrospher 5 μm column Merck with a 0–50% linear elution gradient of KH_2PO_4 0.02 M, pH 4.5, and methanol/water (3:2) solution over 30 min with a flow rate of 1 mL/mn.

Table I. Influence of the Polypeptide Conformation[a]

polypeptides	% of hydrolyzed phosphodiester bonds	polypeptides	% of hydrolyzed phosphodiester bonds
poly(Leu-Lys)[15]	85	poly Lys	27.1
poly(Arg-Leu)[16]	68	poly(Arg-Thr-Lys-Pro)[8]	4.1
poly(Ala-Lys)	33.1	free lysine	2.1
poly(Leu-Lys-Lys-Leu)[6]	58	control	1.6

[a] Experimental conditions: 50 °C, 7 days, Gly-Gly buffer 0.05 M, pH 8, oligo(A)s: 4.87×10^{-3} M; polypeptides: 1.22×10^{-2} M in lysine. The concentration of each oligomer was calculated from the area of the HPLC peak with a correction for hypochromicity.[17,18] For a given mixture, the overall number of phosphodiester bonds was obtained by counting one bond for the dimer plus two bonds for the trimer, etc.

we reported that arginine-containing sequential polypeptides interact with oligo(A)s to form water-insoluble complexes. Complete precipitation of the oligo(A)s was achieved for an Arg^+/PO_4^- ratio of about 2. The polypeptides were found to increase the rate of oligo(A)s hydrolysis. Again, poly(Leu-Lys) accelerates strongly the hydrolysis (Figure 2), L-lysyl residues being more active than L-arginyl ones (Table I). The very short oligonucleotides (monomer and dimer) produced during the hydrolysis reaction were analyzed by reverse phase HPLC on C18. We found A3'p, A2'p, and A > p suggesting a base-induced hydrolysis. The rate of A2'p over A3'p is very close to that found with the control (1.25 and 1.16, respectively). Poly(Leu-Lys) was compared to alternating

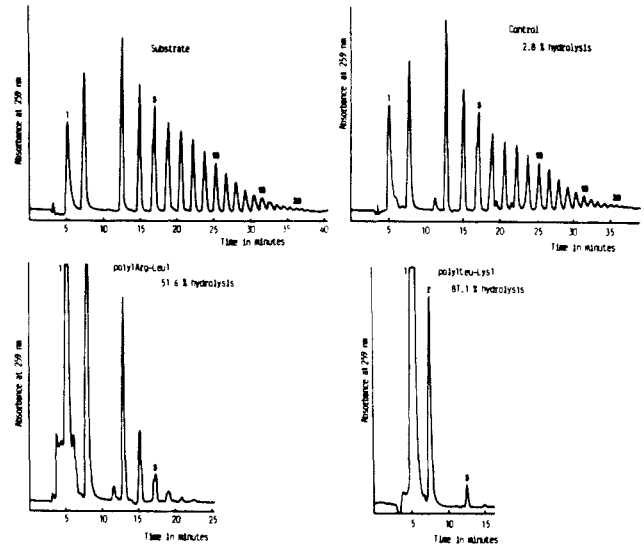

Figure 2. RPC5 HPLC elution profiles of the reaction products of the hydrolysis of 1-25 oligo(A)s: oligo(A)s used as substrate, control, in the presence of poly(Arg-Leu), in the presence of poly(Leu-Lys). Percent of hydrolysis states for the percent of hydrolyzed phosphodiester bonds. Reaction conditions: 50 °C, 2 weeks, 0.05 M Gly-Gly buffer pH 8; oligo(A)s: 4.87×10^{-3} M; poly(Leu-Lys): 1.22×10^{-2} M in Lys^+. Separations were performed on a HITACHI HPLC system with a linear gradient from 0 to 0.04 M $NaClO_4$ at pH 12 in 0.002 M Tris.

poly(Ala-Lys): the activity increases with hydrophobicity (Table I). Poly(Leu-Lys) appears to be also active on poly A, poly U, poly G, and poly C.

Basic copolypeptides with alternating hydrophilic and hydrophobic residues adopt a random coil conformation in pure water due to charge repulsions. In the presence of oligo(A)s, poly(Leu-Lys) transforms into a β-sheet structure as indicated by the infrared spectrum (amide I vibration at 1630 cm^{-1} with a shoulder at 1690 cm^{-1}) which can be considered as the result of electrostatic interactions between phosphate and amino groups. The activity of poly(Leu-Lys) was compared to that of sequential poly(Leu-Lys-Lys-Leu) which is known to adopt an α-helical conformation[6] and to that of poly lysine and poly(Arg-Thr-Lys-Pro) which do not adopt any structured conformation at pH 8.[7,8] Table I indicates that β-sheets of poly(Leu-Lys) have the highest activity. It is known that alternating polypeptides based on hydrophilic and hydrophobic residues built up asymmetric β-sheets with all the hydrophilic side-chains on one side of the sheet.[9] Along a given β-strand the distance between two consecutive positively charged side-chains is about 6.9 Å[10] which is compatible with the distance of 6.2 Å separating two phosphate groups in the single stranded helical structure of poly(A) (from ref 11).

When increasing the ionic strength in the reaction mixture, the formation of the complexes becomes unlikely. For instance, a 2 M $NaClO_4$ salinity completely dissociates preformed complexes.[5] With $NaClO_4$ molarity varying from 0 to 2 M, the percentage of hydrolyzed phosphodiester bonds dropped from 85% to 7.3%, whereas the hydrolysis in the control remained very low (1.9% without $NaClO_4$ and 5.4% in 2 M $NaClO_4$), suggesting that the cleavage reaction is directly related to the complex formation.[12]

(4) Reactions were carried out in stoppered siliconized glass tubes. In a typical hydrolysis experiment, 20 μL of 0.0375 M aqueous solution of polypeptide (by weight) was left overnight at 4 °C. A freshly prepared 0.015 M aqueous solution (20 μL) of oligo(A)s up to the 25-mer (quantified by UV) was added, and molarities were expressed in basic amino acids and in phosphate, respectively. A Lys^+/PO_4^- of 2.5 was taken to ensure a complete oligoribonucleotides complexation.[7] The precipitate was left for 15 min before addition of 20 μL of 0.15 M glycylglycine/NaOH pH 8 buffer. Experiments were run at 50 °C. At the end of the reaction, the complexes were dissociated by addition of sodium perchlorate to a final 2 M concentration. Oligo(A)s up to the 25-mer were obtained by basic hydrolysis of poly(A) in KOH 0.2 M at room temperature for 12 h.

(5) Barbier, B.; Brack, A. *Origins of Life* **1987**, *17*, 381.

(6) Barbier, B.; Perello, M.; Brack, A. *Collect. Czech. Chem. Commun.*, in press.

(7) Epand, R. E.; Wheeler, G. E.; Moscarello, M. A. *Biopolymers* **1974**, *13*, 359.

(8) Trudelle, Y.; Brack, A.; Delmas, A.; Pedoussaut, S.; Rivaille, P. *Int. J. Peptide Protein Res.* **1987**, *30*, 56.

(9) Brack, A.; Orgel, L. E. *Nature (London)* **1975**, *256*, 383.

(10) Arnott, S.; Dover, S. D.; Elliott, A. *J. Mol. Biol.* **1967**, *30*, 201.

(11) Saenger, W.; Riecke, J.; Suck, D. *J. Mol. Biol.* **1975**, *93*, 529.

(12) The possible introduction of some contaminants added together with the polypeptides in the reaction milieu (nucleases, metal ions...) can be excluded: comparable amounts of A2'p and A3'p are formed while nucleases would give only A3'p; the polypeptide activity is not base-specific; additon of EDTA had very little influence on the hydrolsysis; some polypeptides prepared according to the same procedure exhibited very different behavior, i.e., poly(Leu-Lys) and poly(D,L-Leu-D,L-Lys).

Homochiral polypeptides, poly(L-Leu-L-Lys), and poly(D-Leu-D-Lys) exhibited the same activity (66.2% and 68.8% hydrolysis, respectively), whereas the racemic polypeptide, poly(D,L-Leu-D,L-Lys), which is unable to adopt a β-sheet structure,[13,14] is less active (only 27% hydrolysis).

The base-induced hydrolysis involves both hydroxyl groups of the ribose. Thus, deoxyribonucleotides should not be sensitive to the action of basic polypeptides. Indeed, poly(Leu-Lys) had no activity on $d(pA)_8$.

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Registry No. Poly(A), 24937-83-5; poly(u), 27416-86-0; poly(G), 25191-14-4; poly(C), 30811-80-4; poly(Leu-Lys), 66826-32-2; poly-(Leu-Lys), SRU, 64809-02-5; poly(Arg-Leu), 94798-15-9; poly(Arg-Leu), SRU, 99266-08-7; poly(Ala-Lys), 99163-80-1; poly(Ala-Lys), SRU, 32104-73-7; poly(Leu-Lys-Lys-Leu), 116054-08-1; poly(Leu-Lys-Lys-Leu), SRU, 88992-25-0; poly(Lys), 25104-18-1; poly(Lys), SRU, 38000-06-5; poly(Arg-Thr-Lys-Pro), 116054-10-5; poly(Arg-Thr-Lys-Pro), SRU, 112710-32-4; Au, 7440-57-5; $HS(CH_2)_{10}CH_3$, 5332-52-5; $HS(CH_2)_{10}CO_2H$, 71310-21-9; $HS(CH_2)_{10}CH_2OH$, 73768-94-2; $HS(CH_2)_{10}CH_2Br$, 116129-34-1.

(13) Brack, A.; Spach, G. *J. Mol. Evol.* **1979**, *13*, 35.
(14) Spach, G.; Brack, A. *J. Mol. Evol.* **1979**, *13*, 47.
(15) Brack, A.; Caille, A. *Int. J. Peptide Protein Res.* **1978**, *11*, 128.
(16) Barbier, B.; Caille, A.; Brack, A. *Biopolymers* **1984**, *23*, 2299.
(17) Michelson, A. M. *The Chemistry of Nucleosides and Nucleotides*; Academic Press: London and New York, 1963.
(18) Ayad, S. R.; Blamire, J. *Techniques of Nucleic Acid Fractionation*, J. Wiley and Sons Ltd.: 1972.

Kinetic and Thermodynamic Studies on the Reaction of O_2 with Two Dinuclear Copper(I) Complexes

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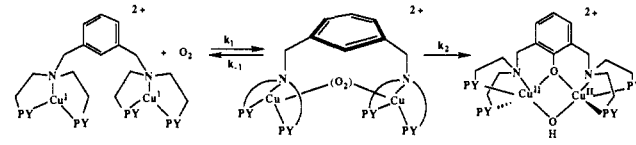
While there has been considerable recent progress in the understanding of the thermodynamics and kinetics of *reversible* reactions of dioxygen (O_2) with metalloproteins (e.g., hemoglobin, myoglobin, hemerythrin) and synthetically derived iron(II)[2-7] (and cobalt(II)) complexes,[2,7] data for Cu^1_2–O_2 binding in the oxygen carrier hemocyanin (Hc)[2a,c,6,8,9] are limited, and no kinetic/thermodynamic information has been available for synthetic copper–dioxygen systems.[10-13] Such information is of critical importance in determining the contributions of environmental factors such as ligation, coordination geometries, and medium effects toward O_2 affinities and differential binding of O_2/CO.[2,3,13] Elucidation of these factors is necessary in the development of (i) an understanding of biological dioxygen utilization, (ii) practical dioxygen carriers,[2b,3,13] and (iii) the field of metal-catalyzed oxidations/oxygenations with molecular oxygen.[14] Here, we report the first thermodynamic and kinetic data for two synthetic systems in which dinuclear copper(I) complexes exhibit reversible O_2-binding behavior.

The first case involves a copper monooxygenase model system,[15,16] where the kinetic analysis[17,18] indicates that **1** reacts with



O_2 reversibly forming a dioxygen adduct **2**, which irreversibly decomposes in a first-order process giving the hydroxylated product **3**.[18] The spectrum of the intermediate, **2**, has a typical absorption band at 435 nm[17c] in accord with that of related complexes $[Cu_2(L)(O_2)]^{2+}$ (L = dinucleating ligand), which are stable at low temperature.[12a,15b] The O_2-binding process is effectively a

(1) (a) University of Basel. (b) State University of New York (SUNY) at Albany.
(2) (a) Niederhoffer, E. C.; Timmons, J. H.; Martell, A. E. *Chem. Rev.* **1984**, 137-203. (b) *Oxygen Complexes and Oxygen Activation by Transition Metals*; Martell, A. E., Sawyer, D. T., Eds.; Plenum: New York, 1988. (c) Wilkens, R. G. in ref 2b, pp 49-60.
(3) Traylor, T. G.; Traylor, P. S. *Ann. Rev. Biophys. Bioeng.* **1982**, *11*, 105-127.
(4) Collman, J. P.; Halpert, T. R.; Suslick, K. S. In *Metal Ion Activation of Dioxygen: Metal Ions in Biology*; Spiro, T. G., Ed.; Wiley-Interscience: New York, 1980; Volume 2, pp 1-72.
(5) Jameson, G. B.; Ibers, J. A. *Comments Inorg. Chem.* **1983**, *2*, 97.
(6) Armstrong, G. D.; Sykes, A. G. *Inorg. Chem.* **1986**, *25*, 3135-3139.
(7) Jones, R. D.; Sommerville, D. A.; Basolo, F. *Chem. Rev.* **1979**, *2*, 139.
(8) (a) Solomon, E. I.; Penfield, K. W.; Wilcox, D. E. *Struct. Bonding (Berlin)* **1983**, *53*, 1-57. Solomon, E. I. In *Metal Ions in Biology*; Spiro, T. G., Ed.; Wiley-Interscience: New York, 1981; Vol. 3, pp 44-108. (b) Lontie, R.; Witters, R. *Met. Ions Biol. Syst.* **1981**, *13*, 229-258.
(9) (a) Antonini, E.; Brunori, M.; Colosimo, A.; Kuiper, H. A.; Zolla, L. *Biophys. Chem.* **1983**, *18*, 117-124. (b) Klarman, A.; Daniel, E. *Biochemistry* **1980**, *19*, 5176-5180. (c) Er-el, Z.; Shaklai, N.; Daniel, E. *J. Mol. Biol.* **1972**, *64*, 341-352.
(10) See the following lead references to studies involving Cu(I)/O_2 kinetic studies: (a) Zuberbühler, A. D. *Metal Ions Biol. Syst.* **1976**, *5*, 325-368. (b) Gampp, H.; Zuberbühler, A. D. *Ibid.* **1981**, *12*, 133-190. (c) Zuberbühler, A. D. In *Copper Coordination Chemistry: Biochemical and Inorganic Perspectives*; Karlin, K. D., Zubieta, J., Eds.; Adenine: Guilderland, NY, 1983; pp 237-258. (d) Davies, G.; El-Sayed, M. A. *Comments Inorg. Chem.* **1985**, *4*, 151-162. (e) Graham, D. R.; Marshall, L. E.; Reich, K. A.; Sigman, D. S. *J. Am. Chem. Soc.* **1980**, *102*, 5419-5421. (f) Goldstein, S.; Czapski, G. *J. Am. Chem. Soc.* **1986**, *108*, 2244-2250, and references therein.
(11) A summary of copper complex systems reported to bind O_2 reversibly can be found in ref 12 and in the following: Karlin, K. D.; Gultneh, Y. *Prog. Inorg. Chem.* **1987**, *35*, 219-327.
(12) (a) 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*, 1196-1207. (b) Karlin, K. D.; Cruse, R. W.; Gultneh, Y.; Farooq, A.; Hayes, J. C.; Zubieta, J. *J. Am. Chem. Soc.* **1987**, *109*, 2668-2679. (c) We have recently described a new reversible O_2-binding complex system in which an X-ray structure reveals that the dioxygen ligand is bound as a trans μ-1,2-peroxo group in a $\{LCu\text{-}(O_2)\text{-}CuL\}^{2+}$ moiety. See: Jacobson, R. R.; Tyeklar, Z.; Farooq, A.; Karlin, K. D.; Liu, S.; Zubieta, J. *J. Am. Chem. Soc.* **1988**, *110*, 3690-3692.
(13) Delgado, R.; Glogowski, M. W.; Busch, D. H. *J. Am. Chem. Soc.* **1987**, *109*, 6855-6857, and references cited therein.
(14) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidations of Organic Compounds*; Academic Press: New York, 1981.
(15) (a) Karlin, K. D.; Gultneh, Y.; Hayes, J. C.; Cruse, R. W.; McKown, J.; Hutchinson, J. P.; Zubieta, J. *J. Am. Chem. Soc.* **1984**, *106*, 2121-2128. (b) Tyeklar, Z.; Ghosh, P.; Karlin, K. D.; Farooq, A.; Cohen, B. I.; Cruse, R. W.; Gultneh, Y.; Haka, M. S.; Jacobson, R. R.; Zubieta, J. In *Metal Clusters in Proteins*; Que, L., Jr., Ed.; ACS Symposium Series 372; American Chemical Society: Washington, DC, 1988; pp 85-104.
(16) We have also studied the kinetics of the related hydroxylation, starting from a dicopper(II) complex containing the same *m*-xylyl dinucleating ligand, which reacts with H_2O_2 in aqueous dimethyl formamide to produce **3**. See: Cruse, R. W.; Kaderli, S.; Meyer, C. J.; Zuberbühler, A. D.; Karlin, K. D. *J. Am. Chem. Soc.* **1988**, *110*, 5020-5024.
(17) (a) Reactions rates were followed spectrophotometrically (Zeiss diode-array) by using a thermostatted all-glass HI-TECH Scientific stopped-flow sample handling unit. Data obtained were transferred to a 300-series Hewlett-Packard computer for analysis. (b) Conversion of two exponentials into a scheme consisting of k_1, k_{-1}, and k_2 is, e.g., described by the following: Rodiguin, N. M.; Rodiguina, E. N. *Consecutive Chemical Reactions*; D. Van Nostrand Co., Inc.: Princeton, NJ, 1964. As an alternative, some of the experiments were evaluated by numerical integration of the appropriate set of differential equations. (c) Plots of the temperature dependence of the kinetic parameters, log (k/T) versus $1/T$ for k_1, k_{-1}, and k_2 (thermal reaction only) (Figure 1) and of the experimentally observed UV–vis spectra of species **1-3** (Figure 2) are included as Supplementary Material.
(18) (a) In fact, k_2 is composed of a thermal and of a photochemical temperature-independent term. The latter becomes dominant below −50 °C. The photochemical decomposition will be discussed elsewhere. (b) Determined values for k_2 (s^{-1}) are 0.0028 (−80 °C) and 104 (20 °C) with $\Delta H_2^{\ddagger} = 47.6 \pm 0.5$ kJ/mol, $\Delta S_2^{\ddagger} = -44 \pm 2$ J/mol-K. (c) Preliminary experiments indicate the absence of any significant effect upon k_2 for the reaction of O_2 with the deuteriated *m*-xylyl analogue complex. This is in accord with our related study starting with Cu(II) and H_2O_2,[16] pointing to a very reactive hydroxylating species.

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