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 $d(pA)_8$.

Acknowledgment. We thank Dr. L. E. Orgel for stimulating discussions and Dr. F. Westheimer for helpful suggestions.

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.

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

Richard W. Cruse,[1a] Susan Kaderli,[1a] Kenneth D. Karlin,*,[1b] and Andreas D. Zuberbühler*,[1a]

Institute of Inorganic Chemistry
University of Basel, CH-4056 Basel, Switzerland
Department of Chemistry, State University of New York
(SUNY) at Albany, Albany, New York 12222

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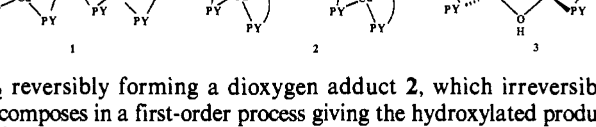
While there has been considerable recent progress in the understanding of the thermodynamics and kinetics of *reversible* reactions of dioxygen (O_2) with metalloproteins (e.g., hemoglobin, myoglobin, hemerythrin) and synthetically derived iron(II)[2-7] (and cobalt(II)) complexes,[2,7] data for Cu^I_2–O_2 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



1 2 3

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

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(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 $\Delta H_2^{*} = 47.6 \pm 0.5$ kJ/mol, $\Delta S_2^{*} = -44 \pm 2$ 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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Table I. Summary of Derived Kinetic and Thermodynamic Parameters for Reversible Dioxygen Binding Systems[f]

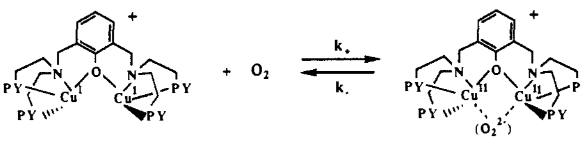
	$1 + O_2 \rightleftarrows 2 \rightarrow 3$	$4 + O_2 \rightleftarrows 5$	deoxyHc + $O_2 \rightleftarrows$ oxyHc[a]
k_{on} (M^{-1} s^{-1})	533 (k_1, -80 °C) 4570 (k_1, 20 °C)	>10^6 M^{-1} s^{-1} (k_+)	5.7×10^7 [b] 3.1×10^7 [c] 3.4×10^7 [d]
$\Delta H^\ddagger$ (kJ/mol)	8.15 ± 0.07		13[c] 31[d]
$\Delta S^\ddagger$ (J/mol-K)	-146.9 ± 0.3		-59[c] 4[d]
k_{off} (s^{-1})	1.8×10^{-5} (k_{-1}, -80 °C) 808 (k_{-1}, 20 °C)		100[b] 60[c] 1000[d]
$\Delta H^\ddagger$ (kJ/mol)	70 ± 1		59[c] 75.7[d]
$\Delta S^\ddagger$ (J/mol-K)	50 ± 6		-13[c] 71[d]
K_{eq} (k_{on}/k_{off})	2.7×10^6 (-80 °C) 6 (20 °C)	7.6×10^7 (-80 °C) 58 (20 °C)	5.7×10^5 [b] 5.2×10^5 [c]
ΔH° (kJ/mol)	-62 ± 1	-66.2 ± 0.5	-46 (20 °C)[d] -31.2[e] 12.8[e]
ΔS° (J/mol-K)	-200 ± 6	-192 ± 2	-67 (20 °C)[d] -7.5[e] 128[e]

[a] Selected data at 25 °C, see ref 2 and 6 for summaries and other data. [b] *P. interruptus* (monomer, *T*-state), ref 6. [c] *P. interruptus* (hexamer, *R*-state), ref 9a. [d] *P. interruptus* (monomer, *T*-state), ref 9a. [e] Low and high O_2 affinity forms of *L. hierosolima*, ref 9c. [f] Molar concentrations were used throughout for the calculation of kinetic and thermodynamic parameters.

one-step process; no evidence for other intermediates (e.g., mononuclear $Cu{-}O_2$) was found.

As can be seen from the data (Table I), the rapid reaction of O_2 with the dicopper(I) complex **1** is characterized by the expected low activation enthalpy and a large negative activation entropy. The spectroscopic observation of the dioxygen/copper complex intermediate (**2**) is facilitated by the favorable relative rates of formation of **2** and its decomposition to **3**, i.e., $k_1[O_2] > k_2$ at low temperatures ($[O_2] = 2 \times 10^{-3}$ M).[18b,c] The thermodynamic stability of the dioxygen/copper adduct (intermediate) is clearly derived from the strong binding ($\Delta H^\circ = -62 \pm 1$ kJ/mol). The disappearance of the $Cu_2{-}O_2$ adduct at room temperature is not due to unfavorable kinetics but rather the thermodynamics, with a negative entropy $\Delta S^\circ = -200 \pm 6$ J/mol-K.

We have also examined another reversible Cu(I)/O_2 binding system, **4** + $O_2 \rightleftarrows$ **5**.[12b,15b] The analysis also provides for the existence of a simple reversible system, and the values of ΔH° and ΔS° determined are very close to those obtained for the system **1** $\rightleftarrows$ **2** (Table I).[19] However, the rate of reaction with dioxygen was too fast to be measured even at -100 °C, indicating $k_+ > 1 \times 10^6$ M^{-1} s^{-1}. Forcing the two copper(I) ions into close proximity by the presence of a bridging phenoxo ligand in **4** apparently causes a dramatic enhancement of the rate of reaction with O_2.



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5

The data obtained here may be compared to those reported for various hemocyanins (Table I).[2a,c,6,9] The *on* rates for oxygenation (k_{on}) of hemocyanins are on the order of 10^6–10^7 M^{-1} s^{-1}.[2c,6] Such values are not approached for reactions of O_2 with **1**, but apparently they are in **4** (Table I), suggesting the importance of the protein matrix in holding the Cu(I) ions in close proximity, probably with the aid of a bridging ligand.[20] The O_2-binding affinities of hemocyanins (25 °C) are in the range of 10^5–10^6 M^{-1}.[2a,c,6] Our synthetic systems approach such values but only at low temperatures. The large negative standard enthalpy and entropy of dioxygen binding observed in our systems (Table I) appear to be typical for synthetic or biological Fe or Co dioxygen carriers.[2a,c,7,13] However, ΔH° and ΔS° values for hemocyanins[2a,c,9] are less negative, or even positive, depending on the form of this highly cooperative O_2-binding protein.[8,9,21,22] Since a large negative ΔS° can be accounted for in large part by the loss of degrees of freedom of O_2 upon coordination,[23] the small (negative or positive) ΔS° values for hemocyanins are likely due to favorable protein conformational and Cu-ligating changes associated with dioxygen binding.[21,22]

Further kinetic/thermodynamic investigations are planned within the several families of dioxygen carriers in our hands.

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Registry No. 1, 82281-84-3; **4**, 90065-16-0; O_2, 7782-44-7; monooxygenase, 9038-14-6.

Supplementary Material Available: Figure 1, with plots of the temperature dependence of the kinetic parameters, k_1, k_{-1}, and k_2, and Figure 2, showing UV–vis spectra typically observed (-95 °C in CH_2Cl_2) for species **1**–**3** (2 pages). Ordering information is given on any current masthead page.

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(19) Thermodynamic parameters were obtained from an analysis of the temperature dependence of UV–vis spectra of **4** and **5**. Details will be presented elsewhere.

(20) A bridging ligand for the copper ions in oxy-Hc (most likely OH^- or H_2O) has been implicated. See ref 12 for recent discussions and the following: Wilcox, D. E.; Long, J. R.; Solomon, E. I. *J. Am. Chem. Soc.* **1984**, *106*, 2186–2194. The reversible binding of O_2 to give $Cu_2{-}O_2$ complexes having no bridging ligand other than O_2^{2-} itself is known.[12,15b]

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