stable; Dreiding models suggest it may well be the pseudoaxial conformation.

A linear thermal cheletropic fragmentation of 1-X-3,5-cycloheptadiene is predicted to occur by an axisymmetric[10] conrotatory motion around the end carbons of the residual triene moiety.[5] However, a nonlinear cheletropic fragmentation with disrotation is also allowed thermally.[5] An equivalent analysis of the reverse addition of X to 1,3,5-hexatriene shows it should involve a linear approach of X with antarafacial bonding to the triene or a nonlinear superfacial interaction.[11] Mock[12] has observed that thermal extrusion of SO_2 from stereoisomeric sulfones structurally analogous to **1** and **2** indeed occurs by the predicted axisymmetric conrotatory path. Thus, one would predict that if the photoinduced extrusion of CO from **1** and **2** should occur by the stereochemical mode opposite to that of the analogous ground-state system studied by Mock,[12] on the assumption that orbital symmetry is the controlling factor in this system,[13] expulsion of CO along the axis of symmetry of these molecules on photoexcitation is predicted to be accompanied by disrotation in formation of the trienes, contrary to our experimental observation. Such a disrotatory extrusion of CO has been observed[3,14,15,16] on photoexcitation of bridged bicyclic analogues of these dienones, which do not have any other viable alternative.

The possibility that these stereospecific decarbonylations are not concerted seems remote, since the *cis*- and *trans*-dienones are not interconverted and since **2** shows a clear preference for forming the *Z,Z,Z*-triene **4** rather than any of the other more stable triene isomers. For a nonlinear extrusion of CO, i.e., where CO does not depart along the axis of symmetry of the starting dienones, the selection rules[5] would be reversed, consistent with the experimental observations, but there seems to be no compelling reason why such a course should be followed.[19] The precise direction of departure of CO and analogous cheleofuges is not subject to experimental verification by an ordinary stereochemical experiment but perhaps could be analyzed theoretically. Other rationalizations revolve around considerations of the stereoelectronic control exercised by the n,π^* configuration of the excited state of these cycloheptadienones,[3,13] and the rather remote possibility that the reaction is occurring on the ground-state potential surface following internal conversion from S_1. Finally, examination of Dreiding models indicates that in these twisted dienones the pseudoequatorial groups at C_2 and C_7 (H or CH_3) are nearly coplanar with the substituents (H in this instance) at C_3 and C_6, so that the conrotatory pathway (which amounts to little more than rehybridization) represents the path of least motion and would afford trienes in which these groups are on the same side (i.e., cis) of the terminal C=C bonds; disrotation would cause much greater structural distortions. On this basis, one can rationalize the preferred formation of **4** from **2** if **2** is reacting primarily through the conformation in which the methyls occupy pseudoaxial positions.

In summary, we have observed that the photochemical extrusion of CO from cycloheptadienones **1** and **2** occurs stereospecifically by the same axisymmetric conrotatory mode seen in thermal extrusion of SO_2 from the analogous sulfones.[12] Since few reactions of this type have been studied,[6,17] it remains to be seen what factors control the course of cheletropic fragmentations, particularly those induced by light.

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(10) Lemal, D. M.; McGregor, S. D. *J. Am. Chem. Soc.* **1966**, *88*, 1325.

(11) Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley/Interscience: Chichester, 1976; pp 95 ff. See also: Houk, K. N. In "Pericyclic Reactions; Marchand, A. P., Lehr, R. E., Eds.; Academic Press: New York, 1977; Vol. II, pp 181-271.

(12) Mock, W. L. *J. Am. Chem. Soc.* **1969**, *91*, 5682.

(13) A referee points out that it may well be naive to expect that a photochemical reaction proceeding via an n,π^* state with excitation localized on the carbonyl group should of necessity follow a course opposite to that dominated by the diene moiety in an analogous ground-state reaction. In the case of an n,π^* excited state, where according to the well-known description of Zimmerman[14] there is a lone electron in a p_y orbital parallel to the bonds between the carbonyl and the adjacent carbons and another electron in the antibonding π^* orbital, the stereoelectronic features of this state might well dominate the course of reaction. Some sort of twisting motion is clearly needed to generate ground-state CO, and simple considerations would lead to the expectation that a 90° twist around the C–O bond would be accompanied by rotations of the bonding orbitals of the C–O bonds in a conrotatory fashion, so as to maintain maximum bonding along the energy surface leading to the products. However, it should be kept in mind that the reactive excited state of these 3,5-cycloheptadienones is not a pure n,π^* state, so the relevance of these arguments is by no means clear at this time.

(14) Zimmerman, H. E. *Adv. Photochem.* **1963**, *1*, 183. Zimmerman, H. E.; Schuster, D. I. *J. Am. Chem. Soc.* **1961**, *83*, 4486; **1962**, *84*, 4527. Zimmerman, H. E. *Top. Curr. Chem.* **1982**, *100*, 45.

(15) Paquette, L. A.; Meisinger, R. H.; Wingard, R. E., Jr. *J. Am. Chem. Soc.* **1973**, *95*, 2230. Antkowiak, T. A.; Sanders, D. C.; Trimitsis, J. B.; Press, J. B.; Schechter, H. *Ibid.* **1972**, *94*, 5366.

(16) Mukai, T.; Aksaki, Y.; Hagiwara, T. *J. Am. Chem. Soc.* **1972**, *94*, 675. Houk, K. N.; Northington, D. J. *Ibid.* **1972**, *94*, 1387. Schuster, D. I.; Stoute, V. A. *Mol. Photochem.* **1978**, *9*, 93.

(17) The same stereospecificity was observed in a photochemical and thermal retrograde homo-Diels-Alder reaction involving extrusion of nitrogen. Other electronic factors may be operating in that system that may not be appropriate to the present case. See: Berson, J. A.; Olin, S. S. *J. Am. Chem. Soc.* **1970**, *92*, 1086.

(18) Wang, L.; Schuster, D. I.; van der Veen, J. M. *Tetrahedron Lett.*, in press.

(19) However, see Schippers et al. (Schippers, P. H.; van der Ploeg, J. P. M.; Dekkers, H. P. J. M. *J. Am. Chem. Soc.* **1983**, *105*, 84) for evidence of distortion of $^1n,\pi^*$ states of β,γ-enones.

Cooperative Dioxygen Binding by Cobalt(II) Gable Porphyrin in Homogeneous Solution

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The nature of cooperativity in protein action has been gradually elucidated in recent years. Cooperative dioxygen binding by hemoglobin, for example, is now reasonably understood as follows. The O_2 affinity of the T state is remarkably reduced due to intersubunit interaction, but the T state is converted to a high affinity form, R state, on O_2 binding. This conformation change induces the T → R conformation change in the remaining vacant binding sites of the tetrameric protein. Similarly, successive O_2 binding further drives the conformation change. Thus O_2 affinity finally approaches the "normal" value of myoglobin.[1] Among the events involved, the most important yet perhaps most difficult to understand seems to be the structural change of the "coupling site" that transfers the information for O_2 binding from one binding site to the other. In order to gain more insights into the mechanism of information transmission by the structural change of the coupling site, several attempts have been made to *mimic* the cooperative dioxygen binding by using solid metalloporphyrin[2,3] or metalloporphyrin attached to a polymer.[4] Although these systems showed large Hill coefficients, this is primarily due to multisite interaction.[5] Mechanistic details on the molecular basis have not yet been clarified.

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(1) Perutz, M. F. *Ann. Rev. Biochem.* **1979**, *48*, 327-386. See also ref 13b and Traylor et al. (Traylor, T. G.; Mitchell, M. J.; Ciccone, J. P.; Nelson, S. *J. Am. Chem. Soc.* **1982**, *104*, 4986-4989), reporting $n = 2.1$ for the CN^- binding by a heme dimer.[5]

(2) Jamson, G. B.; Molinaro, F. S.; Ibers, J. A.; Collman, J. P.; Brauman, J. I.; Rose, E.; Suslick, K. S. *J. Am. Chem. Soc.* **1980**, *102*, 3224-3237.

(3) Collman, J. P.; Brauman, J. I.; Rose, E.; Suslick, K. S. *Proc. Natl. Acad. Sci. U.S.A.* **1978**, *75*, 1052-1055.

(4) Tsuchida, E.; Hasegawa, E.; Honda, K. *Biochim. Biophys. Acta* **1976**, *427*, 520-529.

(5) Theoretical maximum of n for the m-site cooperative system is m.

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Table I. Cooperative Parameters of O_2 Binding by Cobalt(gable)[a]

diimidazolylmethane concn $\times 10^{-3}$, M	0	2	7	15	20	112
$n \pm 0.1$[b]	1.0	1.2	1.5	1.5	1.5	1.3
$P_{1/2}{}^{O_2}$, mmHg	2300 ± 200	158 ± 10	160 ± 6	151 ± 19	143 ± 5	129 ± 10

[a] $Co^{II}(TPP)$ (*N*-methylimidazole): $n = 1.1 \pm 0.1$, $P_{1/2} = 56 \pm 7$ mmHg. $Co^{II}(TPP)$ (diimidazolylmethane): $n = 0.9 \pm 0.1$, $P_{1/2} = 110 \pm 11$ mmHg. [b] Statistical error estimated from three to five independent runs.

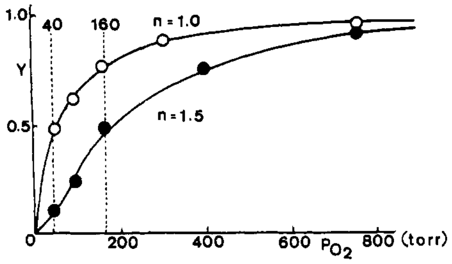
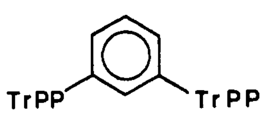


Figure 1. Partial O_2 pressure vs. fractional saturation: (○) (TPP)-$Co^{II}(L)$; (●) (gable)$Co^{II}_2(\overset{L}{\underset{L}{|}})$; −20 °C, DMF. $[Co^{II}_2(gable)] = 2.0 \times 10^{-6}$ M, $[L\text{–}L] = 15 \times 10^{-3}$M; $[Co(TPP)] = 2.0 \times 10^{-6}$M, $[L] = 0.04$ M.

We report the first successful example of cooperative dioxygen binding by a dimeric metalloporphyrin in a homogeneous solution via a structural change–information transmission mechanism. Previously described "gable porphyrin" **1** was used in this study.



1

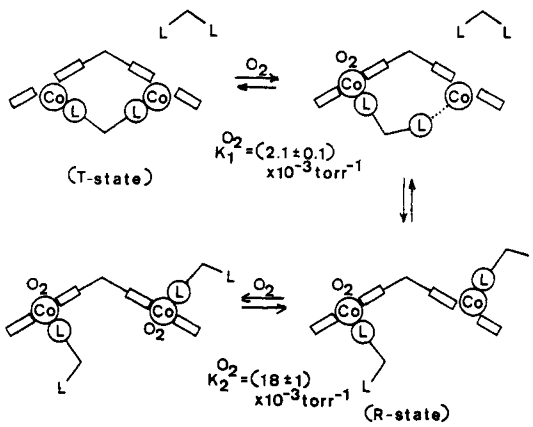
TrPP ; triphenylporphinyl

The bis(cobalt(II)) complex Co^{II}_2(gable) was prepared from 60 mg of $CoCl_2$ and 10 mg of gable porphyrin, **1**[6] in 30 mL DMF under Ar. O_2 binding with this complex was studied in the presence of an appropriate ligand in DMF under N_2–O_2 at −20 °C, where concentrations of oxy- and deoxy-Co^{II}_2(gable) ligand were determined by the absorptions at 411 and 430 nm, respectively.

The Co^{II}_2(gable) complex binds various bases as the fifth ligand very similarly to Co(TPP).[7] The base binding was measured in DMF at −20 °C by following the electronic spectrum change when the solution was titrated with the base. During the titration, clear isosbestic points were observed at 418 and 432 nm for Co(TPP) with 1-MeImd, 414 and 434 for Co(TPP) with $(Imd)_2CH_2$, 410 and 430 for Co_2(gable) with 1-MeImd, and 413 for Co_2(gable) with $(Imd)_2CH_2$. Association constants of imidazole complexes are as follows: (L)Co^{II}(TPP), $(2.3 \pm 0.5) \times 10^3$ M^{-1}; (L-L)-Co^{II}(TPP), $(3.0 \pm 0.4) \times 10^3$ M^{-1}; $(L_2)Co^{II}_2$(gable), $(2.2 \pm 0.6) \times 10^3$ M^{-1}; $(\overset{L}{\underset{L}{|}})Co^{II}_2$(gable) (bridging), $(4 \pm 2) \times 10^6$ M^{-1}, where L = 1-methylimidazole and L–L = *N,N′*-diimidazolylmethane. The two Co^{II}(TPP) moieties of Co^{II}_2(gable) have practically the same association constants toward L (K_L), which are also nearly the same as K_L for monomeric Co^{II}(TPP), indicating that the simple base binds normally. Interestingly, a bridging bifunctional ligand showed an unusually large association constant toward Co^{II}_2(gable) but not for Co^{II}(TPP), indicating the two-site ligation of nearly additive energetics; $\Delta G_{LL}(\text{gable}) = 2\Delta G_{LL}(\text{TPP})$.[8]

The most interesting and noteworthy observation is that O_2 binding is clearly cooperative. Typical conditions: 3 mL of 2.0×10^{-6} M Co_2(gable) in DMF was equilibrated at −20 °C with 1 L of N_2–O_2 gas. Concentrations of the deoxy and oxy complexes were determined spectrophotometrically. Thus, as shown in Figure 1 the *n* value[9] estimated is 1.5 under optimal conditions (see Table I), which was obtained by plotting log $(Y/(1 - Y))$ vs. log P_{O_2}. The correlation coefficient was higher than 0.99. This is due to the retarded first O_2 binding and almost normal second O_2 binding as shown in Scheme I. This characteristic is similar to that observed for hemoglobin ($K_1 < K_2 < K_3 < K_4 \approx K$(isolated subunit)).[10] Estimated cooperative parameters are listed in Table I.

Scheme I. Schematic Representation of Cooperative O_2 Binding $K\{(L)Co^{II}(TPP)\} = (18 \pm 3) \times 10^{-3}$ $torr^{-1}$



The presently observed cooperative O_2 binding seems to be interpreted by transition from a T state to an R state (Scheme I). In the absence of O_2 and in the presence of a $(7\text{–}20) \times 10^{-3}$M concentration of the bridging bifunctional ligand, 98.0–99.99% of the Co^{II}_2(gable) should exist in a form of the bridged coordination deoxy state, which has reduced O_2 affinity (T state). When the first O_2 binds to the deoxy T state, Co^{II} prefers to take a planar coordination,[11,12] resulting in the strain increase in the ligand–Co bond. This induced strain weakens the ligand–Co bond, enabling an available free ligand to form the monooxy R state (see Scheme I; $K_2^{O_2}/K_1^{O_2} = 8.6 \pm 0.3$[13]). The present Co^{II}_2(gable) affords a chemical model of cooperative O_2 binding where O_2 transfer from Co^{II}_2(gable) to Co^{II}(TPP) by operating from 160 (lung) to 40 mmHg P_{O_2} (tissue) should amount to ca. 35% at −20 °C in DMF, similar to the hemoglobin-myoglobin transfer (35%).[14]

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[6] Tabushi, I.; Sasaki, T. *Tetrahedron Lett.* **1982**, *23*, 1913–1916.

[7] Walker, F. A. *J. Am. Chem. Soc.* **1973**, *95*, 1150–1153, 1154–1159. Walker, F. A.; Beroiz, D.; Kadish, K. M. *Ibid.* **1976**, *98*, 3484–3489.

[8] Detailed analysis of the cooperative ligation will be discussed in a full-length article.

[9] Hill, A. V. *J. Physiol. London* **1910**, *40*, IV–VIII.

[10] Tyuma, I.; Shimizu, K.; Imai, K. *Biochem. Biophys. Res. Commun.* **1971**, *43*, 423–428.

[11] Scheidt, W. R. *J. Am. Chem. Soc.* **1974**, *96*, 90–94.

[12] Dwyer, P. N.; Madura, P.; Scheidt, W. R. *J. Am. Chem. Soc.* **1974**, *96*, 4815–4819

[13] Consecutive association of a small guest, S, to a multisite binding host, H, is treated as a stepwise process throughout the paper:

$$S + H \xrightleftharpoons{K_1} S_1H \qquad K_1 \text{ in } M^{-1} \text{ (or torr}^{-1}\text{)}$$

$$S_1H + S \xrightleftharpoons{K_2} S_2H \qquad K_2 \text{ in } M^{-1} \text{ (or torr}^{-1}\text{), etc.}$$

This kind of treatment is frequently seen in the literature; see: (a) Lehn, J.-M.; Simon, J. *Helv. Chim. Acta* **1977**, *60*, 141–151. (b) Rebek, J., Jr.; Wattley, R. V.; Costello, T.; Gadwood, R.; Marshall, L. *Angew. Chem.* **1981**, *93*, 584–585 (this describes the interesting activation driven by the intramolecular conformation change in close correlation with allosterism). Numerical values of K_1 and K_2 were obtained by computer simulation.

[14] Bohr, C.; Hasselbach, K. A.; Krogh, A. *Scand. Arch. Physiol.* **1904**, *168* 402–410.