J. Am. Chem. Soc. 1991, 113, 7603–7608

A Molecular Mechanics Study of Dioxygen Binding by Lacunar Cobalt Dioxygen Carriers

Wang-Kan Lin,[†] Nathaniel W. Alcock,[*,‡] and Daryle H. Busch[*,†,§]

Contribution from the Chemistry Departments, The Ohio State University, Columbus, Ohio 43210, The University of Kansas, Lawrence, Kansas 66045, and The University of Warwick, Coventry CV4 7AL, England. *Received September 4, 1990*

Abstract: The dioxygen affinities of the lacunar cyclidene complexes of cobalt(II) are uniquely controlled by variations in the size, shape, and flexibility of cavities within which the O_2 binds to the cobalt. A molecular mechanics model reproduces the geometries of both *single-conformation* hosts and *dual-conformation* hosts and their dioxygen binding with good fidelity. The noncomplementary basis for the control of the O_2 affinities by the *single-conformation* hosts is explained. It is shown that the role of the *dual conformations* for the other species involves switching from a noncomplementary structure to a complementary one with the result that the maximum strength of binding is achieved. The latter behavior is predicted for a number of complexes of this class.

Introduction

The timely subjects of inclusion chemistry and, more generally, supramolecular chemistry relate closely to molecular organization. In classical coordination chemistry, including the chelate, macrocyclic, cryptate, and template effects,[1] the foremost conclusion is that the maximum strength of binding between metal ion and ligand, or guest and host, is attained by adding maximum constraint[2] to ultimate complementarity.[3] If it fits (geometrically and electronically), the ligand (host) that is most constrained, topologically and rigidly, will form the strongest union with its metal ion (guest).[1] When function is involved, and not simply maximized binding, then an equally valuable requirement may be *limited flexibility*—in addition to or rather than maximum constraint. The study reported here displays clearly (1) how noncomplementarity can be used to adjust the affinity of a union and (2) how limited flexibility can serve to optimize a given interaction.

We have previously[4-7] used detailed crystal structure information to examine the interrelationships between the cyclidene complexes as host molecules, with a coordination site within their host cavity, and their guest ligands. Others have applied molecular mechanics calculations to the binding of dioxygen and carbon monoxide by superstructured porphyrin complexes.[8,9] Here we apply the techniques of molecular mechanics (MM) to the cyclidene systems. Our aim is 3-fold: to illustrate the evolving principles of molecular organization, to assess the validity of the molecular mechanics techniques in relation to this broad area of inclusion chemistry, and to gain further understanding of the factors controlling the abilities of the cyclidene complexes to bind small molecules (selecting dioxygen as a key example for study). We have used the MM2/MMP2 program of Allinger,[10] with modifications to extend its applicability to metal complexes.

The pioneering work in extending molecular mechanics methods to coordination compounds was carried out in the 1970s.[10,11,12] Snow[13] and associates first modified the computer program of Boyd[14] and used it to study cobalt(III) complexes of polydentate ligands.[13,15,16] Brubaker et al.[12,17] also studied polydentate ligands and their cobalt(III) complexes, including cage structures. The Busch group initiated study of various simple diamine ligands and their substituted derivatives[11] and then proceeded to examine macrocyclic complexes.[18] Using Snow's modification of the Boyd program, a group led by Buckingham also contributed strongly to those early developments.[19] Recent studies have extended the early interest in macrocycles[17b,c] to strain energy contributions to chemical reactions,[17b,d,18c] investigating both substitution reactions and electron-transfer processes. To obtain insight into the complementarity of metal ion and ligand, Martin, DeHayes, Zompa, and Busch first explored the problem of defining the size of the cavity within a tetradentate macrocyclic ligand.[18a] Their model, which minimizes the influence of the metal ion on the hole size (M–N force constants of zero), effectively gives a number appropriate to the free ligand properly oriented for chelation. Hancock et al.[20] suggested that the aperture in the free ligand

---

[*] To whom correspondence should be addressed.

[†] The Ohio State University.

[‡] The University of Warwick.

[§] The University of Kansas. Address correspondence to D.H.B. at this address.

(1) Busch, D. H.; Stephenson, N. A. *Coord. Chem. Rev.* **1990**, *100*, 119.

(2) As used here, constraints contain topological parts as in the chelate and macrocyclic effects and components due to host or ligand rigidity—as perceived in the concepts of preorganization (for example: Cram, D. J. *J. Inclusion Phenom.* **1988**, *6*, 397 and references therein) and multiple juxtapositional fixedness (Busch, D. H. *Chem. Eng. News* **1970**, *48* (June 29), 9).

(3) (a) Lehn, J.-M. *J. Inclusion Phenom.* **1988**, *6*, 351. (b) Cram, D. J. *J. Inclusion Phenom.* **1988**, *6*, 397.

(4) (a) Busch, D. H.; Stephenson, N. A. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1989**, *7*, 137. (b) Busch, D. H. *Transfus. Sangue* **1988**, *1*, 57. (c) Busch, D. H. In *Oxygen Complexes and Oxygen Activation by Transition Metals*; Martell, A. E., Sawyer, D. T., Eds.; Plenum: New York, 1988; p 61. (d) Stevens, J. C.; Jackson, P. J.; Schammel, W. P.; Christoph, G. G.; Busch, D. H. *J. Am. Chem. Soc.* **1980**, *102*, 3283. (e) Stevens, J. C.; Busch, D. H. *J. Am. Chem. Soc.* **1980**, *102*, 3285. (f) Thomas, R.; Fendrick, C. M.; Lin, W.-K.; Glogowski, M. W.; Chavan, M. Y.; Alcock, N. W.; Busch, D. H. *Inorg. Chem.* **1988**, *27*, 2534.

(5) Alcock, N. W.; Lin, W.-K.; Jircitano, A.; Mokren, J. D.; Corfield, P. W. R.; Johnson, G.; Novotnak, G.; Cairns, C.; Busch, D. H. *Inorg. Chem.* **1987**, *26*, 440.

(6) Alcock, N. W.; Lin, W.-K.; Cairns, C.; Pike, G. A.; Busch, D. H. *J. Am. Chem. Soc.* **1989**, *111*, 6630.

(7) Alcock, N. W.; Padolik, P. A.; Pike, G. A.; Kojima, M.; Cairns, C. J.; Busch, D. H. *Inorg. Chem.* **1990**, *29*, 2559–2607.

(8) Hancock, R. D.; Weaving, J. S.; Marques, H. M. *J. Chem. Soc., Chem. Commun.* **1989**, 1176.

(9) Kollman, P. A.; Grootenhuis, P. D. J.; Lopez, M. A. *Pure Appl. Chem.* **1989**, *61*, 593.

(10) (a) Allinger, N.; Yuh, Y. *QCPE* **1980**, *No. 423*. (b) Allinger, N.; Sprague, J. *J. Am. Chem. Soc.* **1973**, *95*, 3893. (c) Allinger, N. *J. Am. Chem. Soc.* **1977**, *99*, 8129.

(11) DeHayes, L.; Busch, D. H. *Inorg. Chem.* **1973**, *12*, 1505, 2010.

(12) Brubaker, G.; Euler, R. *Inorg. Chem.* **1972**, *11*, 1505.

(13) Snow, M. *J. Am. Chem. Soc.* **1970**, *92*, 3617.

(14) Boyd, R. *J. Chem. Phys.* **1968**, *49*, 2574.

(15) Geue, R.; Snow, M. *Inorg. Chem.* **1977**, *16*, 231.

(16) Hambley, T.; Hawkins, C.; Palmer, J.; Snow, M. *Aust. J. Chem.* **1981**, *34*, 2525.

(17) (a) Brubaker, G.; Johnson, D. *Inorg. Chem.* **1983**, *22*, 1423. (b) Endicott, J.; Brubaker, G.; Ramasami, T.; Kuman, K.; Dwarakamath, K.; Cassel, J.; Johnson, D. *Inorg. Chem.* **1983**, *22*, 3754. (c) Brubaker, G.; Johnson, D. *Inorg. Chem.* **1984**, *23*, 1591. (d) Brubaker, G.; Johnson, D. *Inorg. Chim. Acta* **1986**, *119*, 131. (e) Brubaker, G.; Johnson, D. *Coord. Chem. Rev.* **1984**, *53*, 1.

(18) (a) Martin, L. Y.; DeHayes, L.; Zompa, L.; Busch, D. H. *J. Am. Chem. Soc.* **1974**, *96*, 4047. (b) Hung, Y.; Martin, L. Y.; Jackels, S. C.; Tait, A. M.; Busch, D. H. *J. Am. Chem. Soc.* **1977**, *99*, 4029. (c) Hung, Y.; Busch, D. H. *J. Am. Chem. Soc.* **1977**, *99*, 4977.

(19) (a) Buckingham, D.; Dwyer, M.; Gainsford, G.; Janson, H.; Marzilli, L.; Robinson, W.; Sargeson, A.; Turnbull, K. *Inorg. Chem.* **1975**, *14*, 1739. (b) Buckingham, D.; Cresswell, P.; Dellaca, R.; Dwyer, M.; Gainsford, G.; Marzilli, L.; Maxwell, I.; Robinson, W.; Sargeson, A.; Turnbull, K. *J. Am. Chem. Soc.* **1974**, *96*, 1713. (c) Buckingham, D.; Edwards, J.; McLaughlin, G. *Inorg. Chem.* **1982**, *21*, 2770.

0002-7863/91/1513-7603$02.50/0

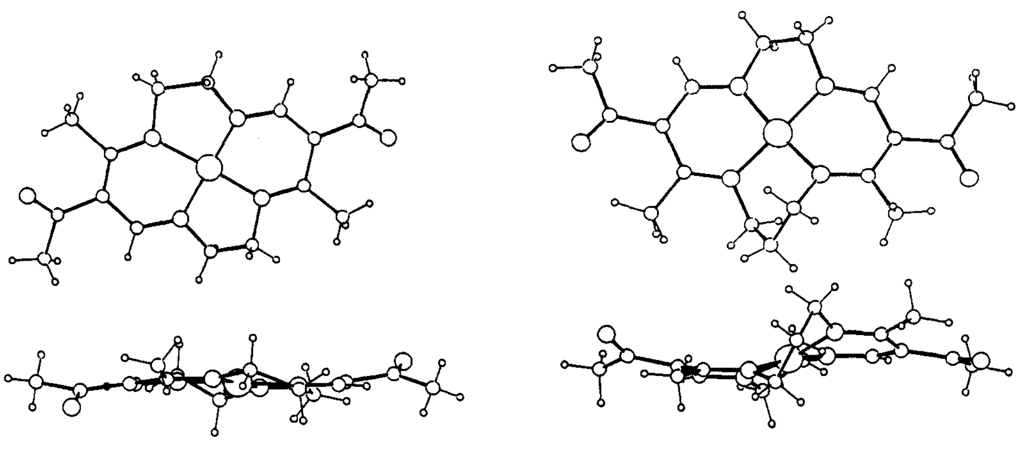
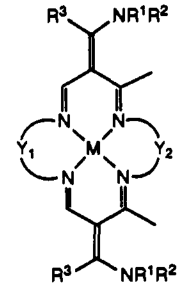

(a) (b)

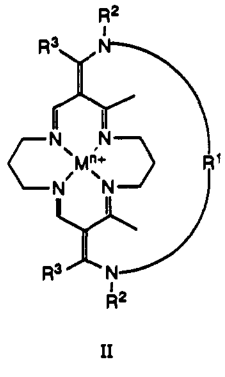
Figure 1. Structures of 14-membered (a) and 15-membered (b) macrocycles related to cyclidenes to illustrate the Z-shape and the associated chelate ring conformations.[5]

is not necessarily complementary to a metal ion, and they attempted to estimate the ideal metal–nitrogen bond distance within a coordinated macrocyclic ligand. While adopting a definition similar to that of Hancock, Drew et al.[21] assigned a high value to the M–N bond stretching force constant.

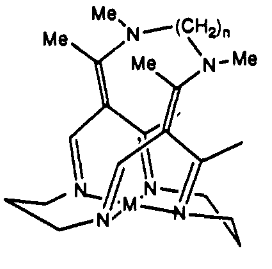
The following discussion begins with consideration of the geometries of the unbridged cyclidenes (structure I), establishing the causes of the saddle shape of the cyclidenes and ring-size/metal–donor distance relationships. It then proceeds to treat polymethylene-bridged [16]cyclidenes (structures II and III) in two groups, respectively, those with short polymethylene chains (from three to five carbons) and those having chains of intermediate length (six to eight carbons).



I



II



III

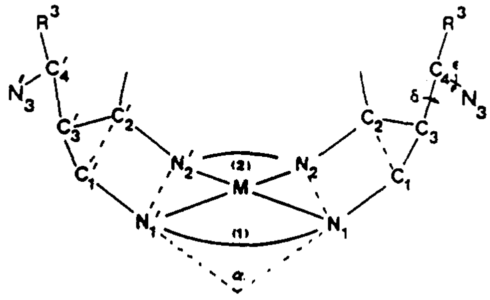


Figure 2. Parameters for defining the width of the cavity in the cyclidene complexes: α, the saddle angle; C4–C4' or N3–N3'.

Results and Discussion

Unbridged Cyclidene Complexes. The 15-membered and 16-membered cyclidene macrocycles have structures that inherently contain clefts,[5] and this greatly facilitates the synthesis of species containing cavities.[4] The 14-, 15-, and 16-membered-ring cyclidenes (structure I) differ in the number of methylene groups in their saturated chelate rings. The most stable conformation for dimethylene, or ethylene, groups in chelate rings[22] is gauche, and this conformation imposes a "Z-shape" on the overall macrocycle[5] (side view, Figure 1a). In contrast, the presence of the two 6-membered saturated chelate rings in the 16-membered cyclidene produces the U-shape exclusively.[5] The 15-membered cyclidenes can adopt the Z-shape (Figure 1b) or the U-shape, and in either case, one saturated chelate ring has an unfavorable conformation.[5] Figure 2 defines parameters that show the width of the cavity: the N3–N3' or C4–C4' distance and α, the angle between the N1–N2–C1–C2 and N1'–N2'–C1'–C2' planes. α measures the folding toward each other of the unsaturated chelate rings of the cyclidene complex.[5]

Figure 3 and Table S1 (supplementary material) summarize the results of calculations based on the Hancock model[20] for a 15-membered cyclidene complex. In these calculations, the conformational energies were monitored while the constant representing the M–N bond distance was varied from 1.60 to 2.20 Å. Significant conclusions are as follows: the Z-shaped species is favored at most M–N distances; the Z-shaped species is considerably more size-selective toward metal ions than is the U-shaped species (steeper minimum); and the width of the cleft increases with the M–N distance (N3–N3' from 6.06 to 6.54 Å for M–N from 1.8 to 2.2 Å).

For the 16-membered cyclidene complex (Figure 4, supplemental Table S2), the U-shape is always lower in energy, as expected on the basis of the conformational preferences of the two 6-membered chelate rings. Further, the minima are very shallow, indicating relatively little size selectivity on the part of this species. The best fit is achieved with a metal to nitrogen bond

---

(20) (a) Thom, V.; Fox, C.; Boeyens, J.; Hancock, R. *J. Am. Chem. Soc.* **1984**, *106*, 5947. (b) Thom, V.; Hoskon, G.; Hancock, R. *Inorg. Chem.* **1985**, *24*, 3378. (c) Hancock, R. *J. Chem. Soc., Dalton Trans.* **1986**, 1081.

(21) (a) Drew, M.; Yates, P. *J. Chem. Soc., Dalton Trans.* **1985**, 1829. (b) Drew, M.; Rice, D.; Silong, S.; Yates, P. *J. Chem. Soc., Dalton Trans.* **1986**, 1081.

(22) Corey, E. J.; Bailar, J. C. *J. Am. Chem. Soc.* **1959**, *81*, 2620.

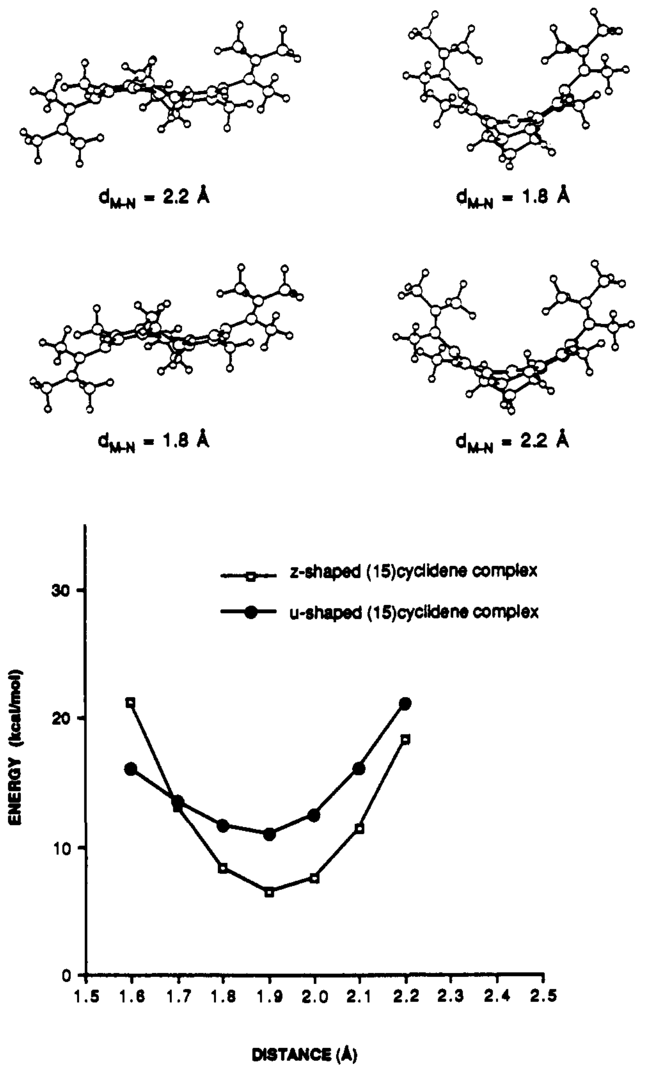


Figure 3. M–N bond distance dependence of conformational energy for [15]cyclidene complexes: top, edge views of Z-shaped (left) and U-shaped complexes (right) at extreme M–N distances; bottom, graph of energy versus M–N.

distance of about 1.90 Å, with the hole size of the standard U-shaped conformer being slightly smaller than that of the Z-shaped conformer. For comparison, the observed M–N bond distances in the cyclidene complexes (all U-shaped) vary from a minimum of 1.89 Å for Ni(II) to about 2.12 Å for Fe(II).[6,21] In fact, Ni(II), which shows the best fit, is located rather precisely within the N_4 coordination plane[6] while the larger Fe(II) is displaced from the coordination plane by 0.55 Å.[23]

Lacunar Cyclidene Complexes. We consider only the simplest bridges, comprising R^1 = polymethylene chains $-(CH_2)_n-$, with n = 3–8 (structures II and III), and $R^2 = R^3$ = Me. For convenience, the chain length of the bridge is indicated by a simple abbreviation; C4 indicates a $(CH_2)_4$-bridged cyclidene complex. The conformations of the bridging group have been examined in detail, both by analyzing the results of the X-ray crystal structure determinations[6] and through the present MM calculations. When the torsional angles of the C–C bonds in the bridging group are discussed, the following conformations have been labeled as indicated:

torsion angle, deg	0	60	120	180	−120	−60
label		g_1	e_1	a	e_2	g_2
type	eclipsed	gauche	eclipsed	anti	eclipsed	gauche

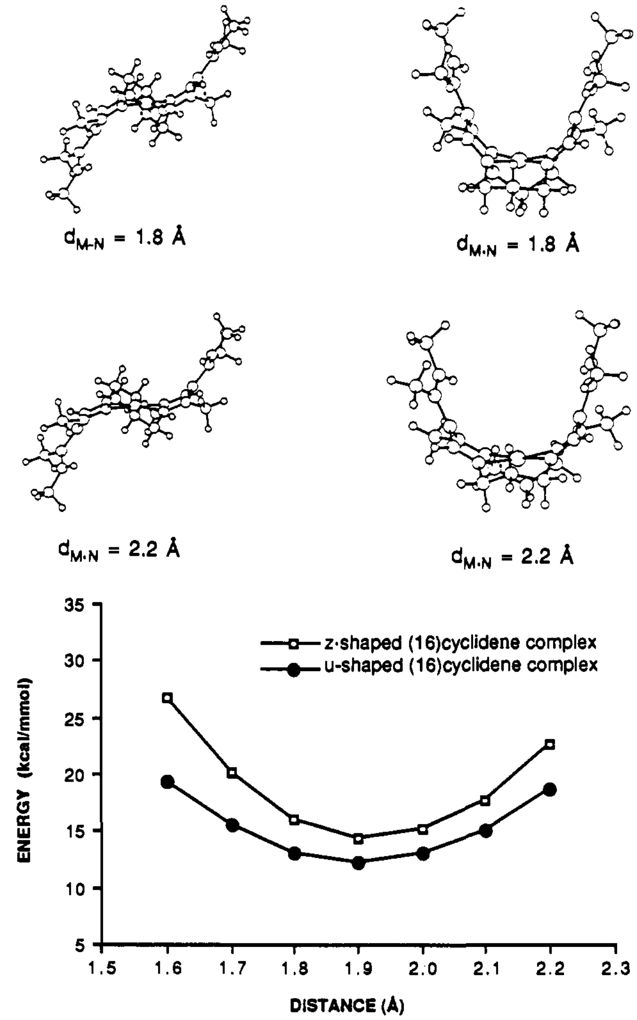


Figure 4. M–N bond distance dependence of conformational energy for [16]cyclidene complexes: top, edge views of Z-shaped (left) and U-shaped complexes (right) at extreme M–N distances; bottom, graph of energy versus M–N.

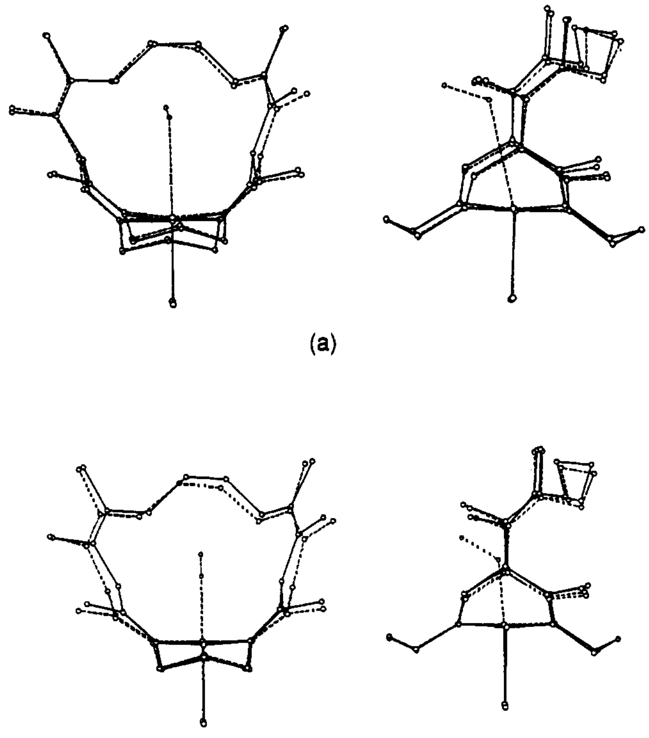
Four series of MM calculations that have been performed are contained in supplemental Tables S1–S8. (1) The first set examined, the 4-coordinate complexes, included more than one conformer for some of the complexes. (2) Since axial ligands must be present in order for oxygen binding to occur, calculations have been made on 5-coordinate species with an axial base opposite the oxygen-binding site. Experimentally, pyridine and N-methylimidazole most commonly serve in this role; however, their structural complexity complicates the modeling process unnecessarily, and a chloride ion was chosen as a fifth ligand for these calculations. These 5-coordinate species provide the baseline for calculation of oxygen-binding effects. Addition of an O_2 molecule was modeled in two ways. In series 1a, the O_2 is rigidly bound in the pocket (the rigid-bonding model). Reasonably high values for the force constants were used to evaluate the effects of the rigidly bound dioxygen on the cavity (k_{M-N} = 5.0 mdyn/Å and k_{N-M-O} = 0.50 mdyn Å/rad^2). In series 1b, a "soft-bonding model" was used to more nearly approximate the effect when an O_2 molecule first approaches the pocket (k_{M-N} = 2.0 mdyn/Å and k_{N-M-O} = 0.25 mdyn Å/rad^2 with the M–O distance about 3.0 Å). In all cases, the central metal was chosen to be cobalt.

Species with Short Polymethylene Bridges—Exploiting Noncomplementarity To Control O_2 Affinity. The X-ray crystal structures[6] of lacunar cyclidene species having short bridging polymethylene chains (C3–C5) are characterized by single conformations for the bridging moieties and by relatively inflexible cavity sizes and shapes. It is illuminating to discuss them individually.

C3-Bridged Lacunar Cyclidene Complexes (Supplemental Table

---

[23] Herron, N.; Zimmer, L. L.; Grzybowski, J. J.; Olszanski, D. J.; Jackels, S. C.; Callahan, R. W.; Cameron, J. H.; Christoph, G. G.; Busch, D. H. *J. Am. Chem. Soc.* **1983**, *105*, 6585.


(a)

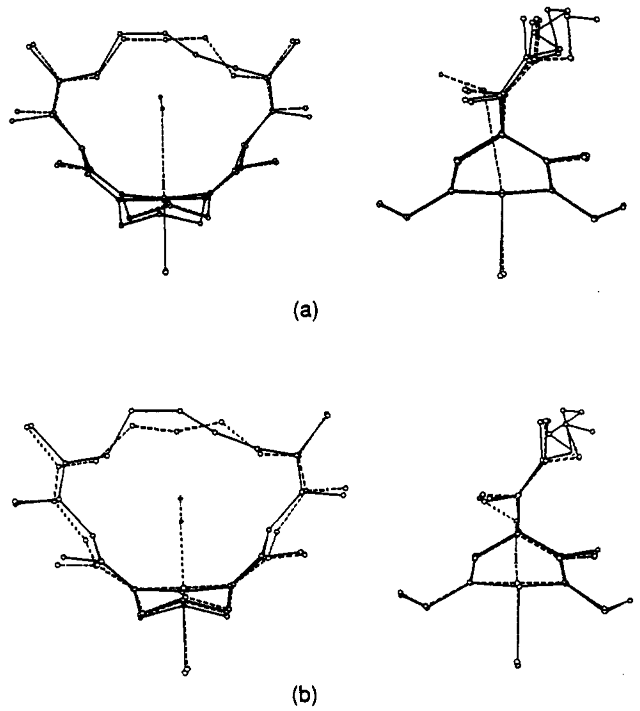
(b)

Figure 5. Soft- (a) and rigid-bonding (b) models for the O_2 adduct of the C4-bridged cyclidene complex of cobalt. Solid lines are the MM structure of the 5-coordinate complex; broken lines are the MM structure of the O_2 adduct.

S3). The crystal structure[6] of a Cu(II) lacunar cyclidene complex bridged by $-(CH_2)_3-$ shows that the short bridging group, in the extended **a–a** conformation, can only just span the two sides of the macrocycle and gives the smallest cavity in the cyclidene family of ligands. Its width C4–C4′ is 5.759 Å, and its cavity height, defined by the distance between the metal atom and the closest hydrogen atom on the middle carbon of the bridge, is 3.53 Å. The small and rigid cavity makes the complex unsuitable for dioxygen binding. The MM calculation (**M3a** in supplemental Table S3) reproduces the crystallographic dimensions well and confirms that the short bridging group produces considerable strain. The high conformational energy results mainly from large torsional and one to four van der Waals (vdw) interactions.

C4-Bridged Cyclidene Complexes (Supplemental Table S4, Figure 5). The crystal structure of a copper(II) C4-bridged complex (**4**) shows that the cavity of the C4-cyclidene complex is rather small. Its width, defined by the C4–C4′ distance, is 5.89 Å and height (M to central bond midpoint) is 5.42 Å; refinement by molecular mechanics produces little change in these dimensions (**M4a** in supplemental Table S4). However, binding a fifth ligand on the coordination site opposite the cavity (**M4b**) causes the cavity to become significantly more narrow.

Dioxygen binding has been observed for this complex although the K_{O_2} values are small. The results of modeling this process are also included in supplemental Table S4 (**M4c,d**), and the resulting structures are superimposed on that of the 5-coordinate complex without dioxygen in Figure 5. Binding the O_2 molecule at the sixth coordination position results in an increase in the width of the cleft, within which it binds, and the angle α is increased from 90.4 to 98.9° in the soft-bonding model and to 106.6° in the rigid-bonding model. Correspondingly, N3–N3′ increases from 5.346 to 5.451 and to 5.521 Å, respectively. The bridging group is pushed backward when O_2 is bound, though the chain has relatively little flexibility in this direction. From the changes in going from the vacant cavity to the soft- and then to the rigid-binding model, it is apparent that the cavity width of the vacant structure requires more modification to accommodate the O_2 than does the cavity height. These adjustments are essential to achieve some minimal degree of complementarity between the cavity and the guest ligand. Distortions are also experienced by the bound O_2. Because the cavity size is relatively small, the O–metal bond is not perpendicular to the N_4 plane but rises at angles of 76.2° from the plane in the soft-bonding model and 82.0° from the plane in the rigid-bonding model. As Figure 5 dramatizes, the cavity tends to extrude the guest O_2 molecule. The implicit repulsion serves to reduce the dioxygen affinity of the cobalt(II) complex of this ligand (vide infra).


(a)

(b)

Figure 6. Soft- (a) and rigid-bonding (b) models for the O_2 adduct of the C5-bridged cyclidene complex of cobalt. Solid lines are the MM structure of the 5-coordinate complex; broken lines are the MM structure of the O_2 adduct.

C5-Bridged Cyclidene Complexes (Supplemental Table S5, Figure 6). Three crystal structures of C5-bridged cyclidene complexes have been determined, two of which are 6-coordinate. They have C4–C4′ distances of 6.55 Å for the 4-coordinate complex and 6.67 and 6.76 Å for 6-coordinate complexes.

Two possible conformers have been examined by using the MM method. One is derived from the crystal structure and has the sequence of torsion angles a–e$_2$–e$_1$–a while the other was assembled by molecular graphics and has an extended $-(CH_2)_5-$ chain with anti conformations in all four C–C bonds of the bridging group. The latter gives a length between bridgehead nitrogen atoms of 7.63 Å. The calculations (**M5a2**, supplemental Table S5) confirm that this conformer is not preferred, since it has a conformational energy of 58.12 kcal/mol as compared with 45.71 kcal/mol for the conformer found in the crystal structure (**M5a1**). The increase of the conformation energy suggests that the bridging length of 7.41 Å considerably exceeds the optimum width of the cyclidene unit. In particular, the C3–C4 vinyl bonds have high torsional energy in this hypothetical conformation. In contrast, in the observed conformer, the eclipsed conformations of the two central C–C atoms of the bridge indicate that the chain is compressed to less than its ideal length. The MM calculation (**M5a1**) seems slightly to overemphasize the force exerted by the bridge, since the calculated cavity width is somewhat larger than that observed in the crystal structure.

When dioxygen is bound to the complex (Figure 6), the saddle angle, α, changes from 97.7 to 102.4° in the soft-bonding model and to 110.7° in the rigid-bonding model. These values can be compared with the values obtained from the crystal structures[6] of complexes **L5a** and **L5b**, in which CO and NSC are bound to the metal, 103.8 and 105.6°, respectively (supplemental Table

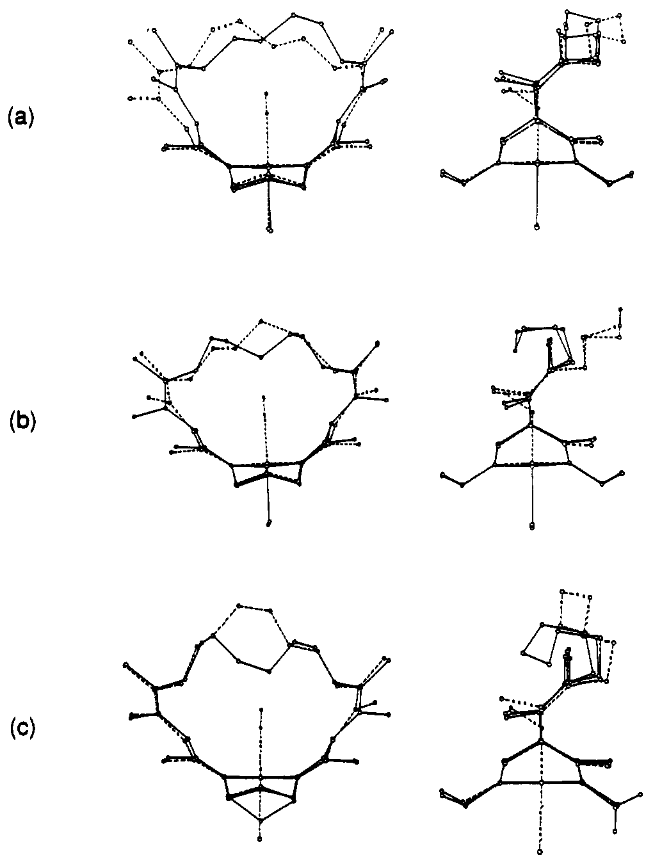


Figure 7. Rigid-bonding models for O_2 adducts of C6- (a), C7- (b), and C8-bridged (c) [16]cyclidene complexes.

S5). In the soft-bonding model, the M–O bond makes a 76.3° angle to the N_4 plane, but it is almost perpendicular to the plane in the rigid-bonding model. As with C4, the chain is pushed toward the back of the cavity when O_2 is bound, though surprisingly the effect is more marked for the soft than for the rigid model. In the rigid model, the cavity has become significantly wider and lower than when O_2 is absent.

It is characteristic of these species with short polymethylene chains that they accept guest ligands within their lacunae with relatively little adjustment to the molecular void. C3 seems incapable of encompassing even such undemanding ligands as O_2, NCS, or Cl. Both C4 and C5 accept small ligands with small *increases* in the widths of their lacunar cavities and, more often than not, with very small *decreases* in their heights. Further, the metal–ligand binding parameters are altered so that both entities undergo distortions in response to their noncomplementarity. A ligand molecule bound within such a constricting cavity is substantially repelled by atoms composing the walls of the lacuna, and reduced binding affinities are to be expected.

Species Having Polymethylene Chains of Intermediate Lengths—Limited Flexibility and Maximized Binding. The X-ray crystal structures have been determined[6] for the complexes with C6, C7, and C8 bridges and for C6 complexes with small ligands occupying the lacuna. A striking contrast in conformations is found for filled and empty lacunae; the bridge changes conformation when a guest is included.

C6-Bridged Complexes (Supplemental Table S6, Figure 7a). The conformation observed for the 4-coordinated complexes (no guest ligand) has the torsional angle sequence $g_1-g_1-g_1-a-g_2$ (or its mirror-related form) for the five C–C bonds in the bridging group. A side view of this conformer (call it the *closed* conformer) shows that the bridging group folds into the open side of the cavity (Figure 7a). The other conformer (found in the 6-coordinated complexes) has a torsional sequence of $a-g_2-g_2-a-a$. In this structure (call it the *open* conformer), the chain folds out and away from the cavity, making more space for the binding of groups within. The MM calculations (**M6a1,2**) show that when the complex is 4-coordinated, the *open* conformer, having the larger cavity, has a slightly higher energy, and this is consistent with the occurrence of the *closed* conformer in the crystal structures of two examples of C6 complexes. However, since the *closed* conformer has a distance from the metal to the middle of the bridging chain of only 5.14 Å, it is not suitable for the binding of dioxygen or any other small guest ligands. In order to permit the dioxygen molecule to bind, a conversion from the *closed* conformer to the *open* conformer must occur.

Both the soft-bonding model and the rigid-bonding model were calculated for the *open* conformation. The results for the rigid model are compared with those for the 5-coordinate complex in the *closed* conformation in Figure 7a, where the two structures overlap. The saddle angle, α, increases from 99.8 to 105.3° in the soft-bonding model and to 113.7° in the rigid-bonding model. In the crystal structures of 6-coordinated complexes **L6a** and **L6b**, with ligands NCS and O_2, respectively (supplemental Table S6), this parameter is 108.8 and 106.8°, respectively. In the soft-bonding model, the M–O bond makes an angle of 84.21° to the N_4 plane, but the rigid model, this angle (88.2°) becomes very close to 90°.

C7-Bridged Complexes (Supplemental Table S7, Figure 7b). X-ray crystallographic data are only available for species having vacant cavities. The torsion angle sequence occurring for the 4-coordinated complexes, **7a** and **7b**, is $g_1-g_1-g_1-g_2-g_2-g_2$, and the associated conformation folds the center atoms of the bridge deeply into the cavity. From the side view (Figure 7b), an analogy can be made with the tail of a scorpion, which is carried folded over the back of the animal. The center methylene group approaches the metal rather closely, giving a metal–center carbon distance (in **7a**) of only 4.23 Å. The width of the cavity is, however, quite large as 7.50 Å (C4–C4′). As expected on the basis of the low "roof", calculated strain energies for 6-coordinate species having this *closed* conformation are very large. No crystal structures have been determined for 6-coordinated C7 cyclidenes, so other possible conformations of the bridging group were sought by molecular modeling. Remarkably, MM minimization led to a second conformation in which the central three methylene groups swing out of the cavity, as shown in Figure 7b. This *open* conformation has the torsion angles $a-a-e_1-g_2-a-a$. For a 4-coordinate structure with a vacant cavity, this *open* form gives a conformational energy of 53.31 kcal/mol, compared with 49.95 kcal/mol for the *closed* conformation that occurs in the crystal structure (**M7a2**).

The MM calculations show that occupation of the cavity by dioxygen or other small guest ligands will not change the cavity width appreciably, but the saddle angle, α, increases from 104.2° in the 5-coordinate to 108.1 and 115.1° in the soft- and rigid-bonding models. As with the case of the C6 complex, the height of the cavity is increased dramatically by the change from the closed to the open structure. Clearly this conformational change must accompany guest ligand binding. Further, the conformational energy of the 6-coordinate rigid-bonded structure is not much greater than the energies of the 4-coordinate and 5-coordinate complexes having the closed conformation. The position of the dioxygen molecule can be seen in Figure 7b.

C8-Bridged Cyclidene Complexes (Supplemental Table S8, Figure 7c). The conformational properties of C8-bridged cyclidene complexes are similar to those of their C7-bridged homologues. The bridging conformation $g_1-g_1-g_1-g_1-a-g_2-g_2$, in which the center methylene groups fold into the cavity, has been observed for 4-coordinated cyclidene complexes (complexes **8a** and **8b**). Another much more open conformer with rather more space for O_2 binding, but having almost the same conformational energy (**M8a1,2**), is generated by swinging these methylene groups out of the cavity. The *open* conformation has the torsional angle sequence $g_1-a-g_2-g_2-a-a-g_2$. The *closed* conformer has a metal–midbond distance of 4.41 Å, while the second conformer has a metal–midbond distance of 6.71 Å; this represents an enormous increase in cavity height. The cavity width seems not to be a consideration with these structures. In fact, these cyclidenes have the widest of all observed cavities in the series. It is therefore

Table I. Correlation of Strain Energy Differences, $E_6 - E_5$, and Dioxygen Affinities, K_{O_2}, for Cobalt(II) Cyclidene Complexes

complex	$E_6 - E_5$, kcal/mol	K_{O_2}, Torr^{-1} [a]	complex	$E_6 - E_5$, kcal/mol	K_{O_2}, Torr^{-1} [a]
C4	14.5	1.1×10^{-5} [b]	C7	2.57	0.62
C5	6.26	9.4×10^{-3}	C8	−0.74	0.65
C6	2.87	0.16			

[a] Reference 4c. [b] Extrapolated value.

not surprising that binding of O_2 produces only a modest increase in the saddle angle, α. The MM calculation results for C8-bridged cyclidene are given in supplemental Table S8 and in Figure 7c.

These intermediate-length polymethylene-bridged species, C6–C8, have the remarkable property of exhibiting two low-energy bridge conformations, and the interchange between them constitutes a molecular rearrangement that uniquely accommodates a guest in the cavity. The *closed* conformations minimize the size of their void, in conformity with the old saw that nature abhors a vacuum. Correspondingly, the second *open* conformation minimizes repulsions between the atoms forming the cavity and the guest molecule, thereby optimizing the binding of the guest. The strain energy advantages that are gained by this dual conformation situation may be partially offset by the less favorable entropy associated with binding to only one of the two conformations.

The dual conformations and the interchange between them is general for this set of species, and it constitutes a dramatic example of maximized binding coming about because of the enhanced complementarity that arises from limited molecular flexibility. Because noncomplementarity is imposed or removed by flipping between the two conformations, the system is exemplary of the simplest modes of molecular switching.

Ligand and Dioxygen Binding. Dioxygen affinities of the polymethylene-bridged lacunar cyclidene complexes have been measured[4c] for the C4-bridged through the C8-bridged species and show the predicted increase in dioxygen-binding ability with increasing chain length (Table I). In our calculations, the relevant energy for comparison is the *difference* between the energy of the 5-coordinate complex (without O_2 and in its optimum conformation) and that of the rigidly bound O_2 complex. This difference reflects the change in $M-O_2$ bond energy, which, in terms of electronic relationships, should otherwise be constant in all of these particular cyclidene complexes. It will be reduced if the $M-O_2$ unit cannot achieve its ideal geometry or is otherwise unfavorably constrained by the surrounding lacuna. This quantity also includes whatever increase in energy takes place in the complex, due to adoption of an alternative chain conformation or to the distortions necessary to accommodate O_2 in the cavity. These differences (Table I) show a remarkably smooth correlation with the K_{O_2} values (Figure 8).

Experimental Section

Calculations were performed with the MM2/MMP2 program of Allinger,[10] running on an IBM 3081 or a VAX 750 computer. For this work, the program was modified to treat coordination compounds. In summary, these changes involve[24] the following:

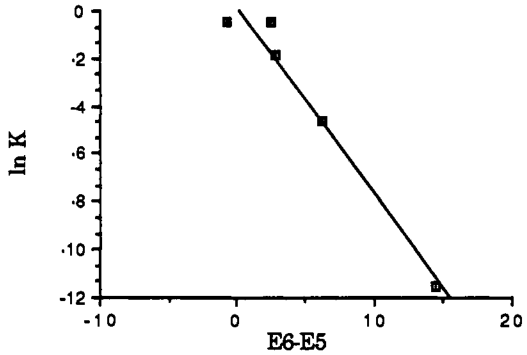


Figure 8. Correlation of the equilibrium constant for dioxygen binding, K_{O_2}, with the difference in strain energies between the 5-coordinate complex with a vacant cavity and the O_2 adduct.

(1) New atoms and their force constants were added, including N_{sp^2} (absent from the original program), Co, and Ni; stretching and dipole constants in the subroutine KBOND; torsional angle force constants in subroutine KΩ; bending force constants in subroutine Kθ; and vdW interaction force constants in subroutine KVDW. Complete listings of these parameters are given in supplemental Tables E1–E4.

(2) Two types of N–metal–N bond angle parameters were defined depending on cis and trans positioning. The changes related to this assignment were specified in subroutines EBEND (after sentence 10) and θ (in the DO 100 loop).

(3) The maximum coordination number was increased from 4 to 6. The changes were substantial and are available in the supplementary material.

(4) The convergence criterion was modified so it could be altered by the input file. This allowed us to reduce computing time for large structures far from their minimum position. Typically, for initial calculations, a criterion of 0.08 kcal/mol was used, with 0.01 kcal/mol for final cycles. The changes were substantial and are available in the supplementary material.

(5) Several data arrays were added or redimensioned so that many new parameters could be read. The changes are available in supplementary material.

Tables E1–E4 provide a full list of the parameters employed in these calculations.

Acknowledgment. Support of this research by the National Science Foundation, Grant No. CHE 8822822, and the National Institutes of Health, Grant No. GM 10040, is gratefully acknowledged. The collaboration between The Ohio State University and The University of Warwick has been supported by a NATO travel grant.

Supplementary Material Available: A textual presentation of the modifications to the MM2 computer program, Tables E1–E4, giving molecular mechanics parameters, bond stretching and bond dipole moment parameters, bond bending parameters, torsional angle parameters, and vdW parameters, and Tables S1–S8, listing calculated dimensions and energies (17 pages). Ordering information is given on any current masthead page.

---

(24) Lin, W.-K. Ph.D. Thesis, The Ohio State University, 1988.