oxygen-based macrocyclic ligands, crown ethers,[11-13] our attention recently shifted to nitrogen-[14-17] and sulfur-based[18,19] macrocyclic ligands. Additionally, we have also recently begun an investigation into the organoaluminum chemistry of open-chain multidentate amines.[20-22] An examination of the organoaluminum chemistry of multidentate phosphorus ligands represents a logical extension of this work.

As can be seen from Figure 1, $[Al(CH_3)][(C_6H_5)_2P(O)CP(O)(C_6H_5)_2]_2[Al(CH_3)_2]_2$ contains two bis(diphenylphosphinoyl)methanide units bridged by three organoaluminum moieties: two dimethylaluminum fragments and one methylaluminum fragment. Particularly significant is the fact that the central aluminum atom, in addition to being bonded to one methyl carbon atom and one oxygen atom of each ligand, is also bonded to the methylene carbon atom of each ligand. Thus, the title compound results from a condensation reaction in which four $Al-CH_3$ bonds were cleaved in addition to all four C-H bonds of the methylene carbon atoms of the two ligands. Methane was eliminated during the course of the reaction. Such condensation reactions are well documented for Al-R/N-H systems.[23-31] Characteristically, such systems eliminate alkane while reaction products are Al-N cages possessing Al_2N_2 fragments. To the best of our knowledge, the title compound represents the first report of a condensation product resulting from cleavage of Al-R and C-H fragments. Furthermore, it is quite unusual for the methylene hydrogen atoms of a bis(diphenylphosphino)methane-based bidentate ligand to exhibit such reactivity. Indeed, in the recently reported product $[Al(CH_3)]_2[(C_6H_5)_2PCH_2P(C_6H_5)_2]$, isolated from reaction of trimethylaluminum with bis(diphenylphosphino)methane, the methylene hydrogen atoms proved to be completely inert to reaction with $Al(CH_3)_3$ as only the 2:1 (AlR_3 to ligand) complex was observed.[32] The observed lability of the methylene hydrogen atoms of bis(diphenylphosphinoyl)methane is undoubtedly due to increased acidity resulting from the presence of the oxygen atoms.

Several points are worthy of note regarding structure and bonding in $[Al(CH_3)][(C_6H_5)_2P(O)CP(O)(C_6H_5)_2]_2[Al(CH_3)_2]_2$. The molecule contains a 2-fold axis of rotation containing atoms Al2 and C28. The central aluminum atom, Al2, is five-coordinate being bonded to one methyl carbon atom in addition to the two central methanide carbon atoms of the two ligands. These four atoms constitute a plane. The coordination sphere of the pentacoordinate aluminum atom is completed by an oxygen atom from each ligand situated on either side of the AlC_3 plane. The O-Al-O bond angle is 163.3 (2)°, while the mean C-Al-C bond angle of the central AlC_3 plane is 120°. The coordination geometry of Al2, thus, may be described as trigonal bipyramidal. The variation in Al-O distances in the title compound is worthy of note. At a distance of 1.772 (4) Å the Al1-O1 bond is quite strong. This distance is placed in perspective when one considers the value of 2.02 (2) Å for the Al-O interaction found in the bis(trimethylaluminum)dioxane adduct $[Al(CH_3)_3]_2[C_4H_8O_2]$.[33] Conversely, the Al2-O2 distance of 2.174 (4) Å must be considered quite long. The mean Al-C distance in the title compound of 1.986 (9) Å is within the expected range. With P-C bond distances of 1.680 (6) Å and 1.672 (6) Å for P1-C1 and P2-C1, respectively, it is reasonable to assume resonance stabilized double bond character over these two bonds.

Although Lewis base species possessing C-H fragments are generally quite inert to reaction with AlR_3, the isolation of the title compound indicates, that under appropriate conditions, facile Al-R and C-H bond cleavage can occur resulting in interesting organoaluminum products. Additional studies on related ligands and organoaluminum species are forthcoming.

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Supplementary Material Available: Tables of crystal data, bond distances and angles, final fractional coordinates, and thermal parameters (4 pages); a listing of observed and calculated structure factors (8 pages). Ordering information is given on any current masthead page.

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The X-ray Structure of Flavohemoglobin: A Semisynthetic Hydroxylase†

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Hemoglobin (Hb) catalyzes monoxygenase reactions in a cytochrome P-450-like manner.[1] This activity requires cytochrome P-450 reductase, which transfers electrons between the two-electron donor, NAD(P)H, and the single-electron acceptor, the

† E. T. Kaiser passed away on July 18, 1988. We would like to dedicate this paper to his memory.

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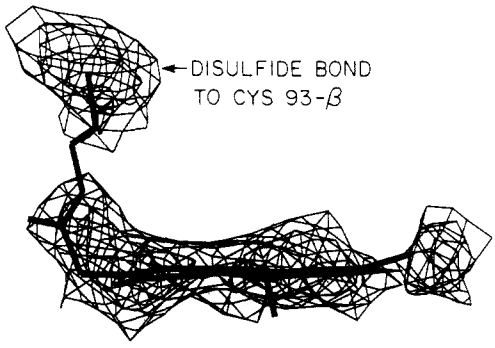

Figure 1. Electron density for the flavin viewed edge on, calculated by using Fourier coefficients $(2F_o - F_c)e^{i\alpha_c}$. F_o and F_c are observed and calculated structure factor amplitudes, and α_c is the calculated phase. The model used was the final refined structure, omitting the flavin. Contours are at 1 and 2 standard deviations. Note the strong electron density for the disulfide bond. The electron density level for the isoalloxazine ring is not as high as for some of the surrounding side-chains, indicating that the flavin is either very mobile or is bound with less than unit occupancy. The density is particularly weak for the ring farthest from the disulfide bond and there is almost no density for the cyano group. This could be the result of a high degree of libration or else due to more than one mode of binding, with the ring system rotated by 180° about the long axis.

heme iron. It has been shown that Hb with a flavin (I) attached to the β-subunits (by modification of a cysteine, β93) acts as a P-450-like enzyme without requiring the reductase.[1] Since the orientation of the flavin and its distance from the heme iron are important factors in determining the rate of electron transfer, design of further flavo-Hb enzymes would be aided by a knowledge of the structure and environment of the bound flavin. We have therefore crystallized flavo-Hb and determined its structure.

Flavo-Hb in the carbon-monoxy form[2] was crystallized by the method of Perutz[3] from 2.8 M phosphate buffer. Large (0.25–0.5 mm) crystals grew in about 3 weeks. A single crystal was mounted in a quartz capillary in an atmosphere of CO and was observed to give strong diffraction beyond 2.5 Å resolution. Data to 2.5 Å were collected at room temperature.[4] The best structure of liganded Hb available in the protein data bank[5] is that of oxy-Hb;[7] this was used to initiate least-squares refinement against the X-ray data by using the program X-PLOR,[8] a version of CHARMM[9] modified for crystallographic calculations. Electron density maps calculated by using this model showed a long flat feature near Cys93β which was recognizable as the flavin (Figure 1). The maps also showed that the positions of the last four residues in the β-chain are different with respect to oxy-Hb. These residues are partially disordered in oxy-Hb and CO-Hb, and the data for flavo-Hb show that His143β is well localized in its new position but that Lys144β, Tyr145β, and His146β do not have density which can be unambiguously interpreted. The isoalloxazine ring is on the surface of the protein and is not constrained by crystal contacts; while the model we have built and refined appears to be the most likely structure, the disorder in the neighboring side-chains prevents us from ruling out other binding modes for the flavin. Apart from the changes in the C-terminal region of the β-chain there are no significant perturbations in the structure. The final refined model has an *R*-factor of 21% with good stereochemistry (rms deviation of bond lengths and angles from ideality is 0.016 Å and 3.4°, respectively).

The flavin is readily accessible for reaction with NAD(P)H. In our model the si face is partially buried, interacting mainly with the side-chain of His143β, but the high mobility of the C-terminus is likely to result in this face being transiently exposed. Direct contact between the heme and the flavin is impossible because of a large number of intervening residues (Figure 2). The distance from the center of the isoalloxazine ring to the iron atom of the β-heme of the same subunit is 14 Å. The other heme groups are substantially more distant, the distances to the iron atom from the flavin being 28 and 35 Å for the two α-hemes and 25 Å for the other β-heme. The flavin–iron distance is similar to the distances between the iron atom and the nearest of a number of ruthenium groups attached to the surface of myoglobin and cytochrome-*c*, where fast electron transfer is observed.[10]

Since the flavin binds to a disordered region on the surface, it is surprising that localized electron density is observed for the isoalloxazine ring. One reason for this may be that the isoalloxazine ring interacts favorably with the symmetry-related flavin on the other β-subunit. The flavin binds very close to the 2-fold axis of the Hb tetramer. In our structure the two flavins are aligned so that they are virtually in the same plane, and the cyano groups are almost in contact (Figure 3). The proximity of the flavins suggests that in the tetrameric form of flavo-Hb electrons

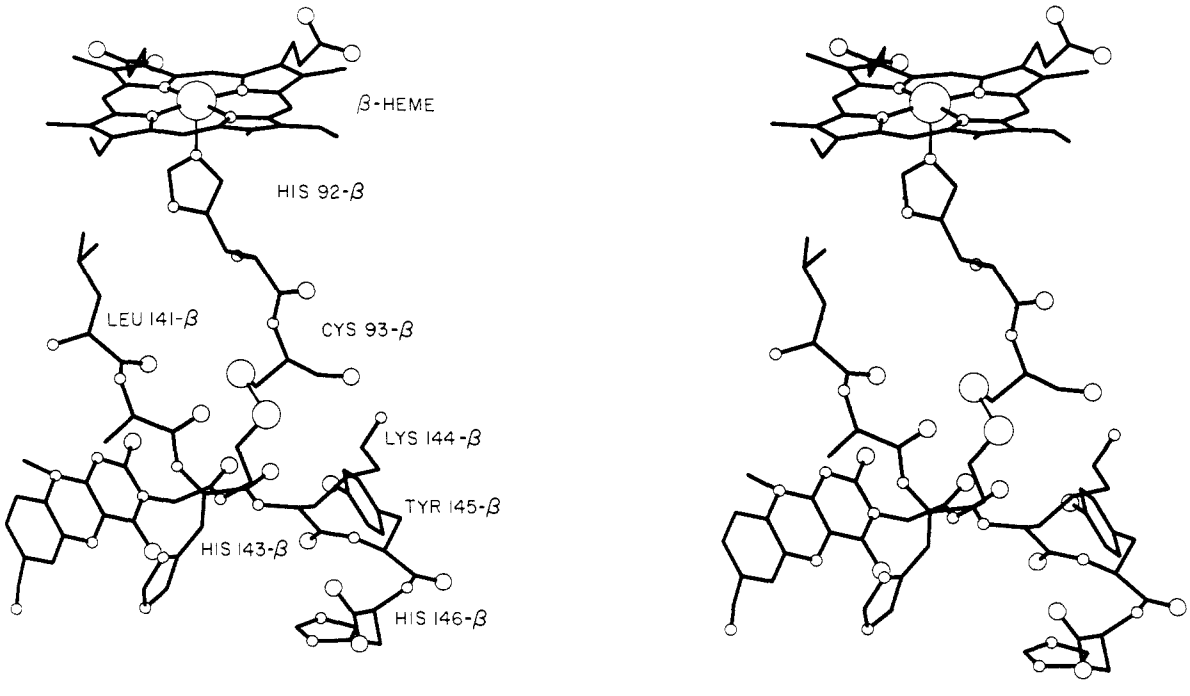

Figure 2. Stereoview of the binding site of the flavin. In Figures 2 and 3 carbon atoms are not shown explicitly, and nitrogen, oxygen, sulfur, and iron are represented by spheres of increasing size. In oxy-Hb the side-chain of His143β occupies the position of the isoalloxazine ring, and Tyr145β is close to the flavin linker arm. The placement of residues β144-β146 is uncertain due to disorder.

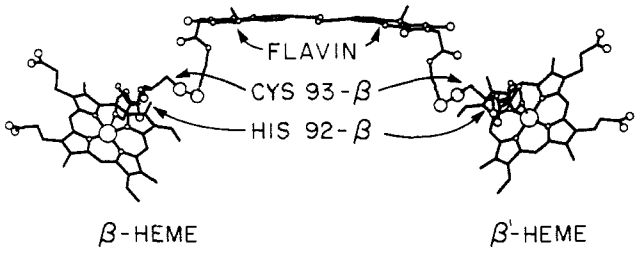

Figure 3. The interaction of the symmetry-related flavins and heme groups of the two β-chains in a tetrameric molecule. The cyano groups are roughly 3 Å apart. The long axes of the isoalloxazine rings are not colinear; they are approximately parallel but displaced by about 1.4 Å in the plane of the rings.

donated by NAD(P)H to one flavin may also be transferred to the second flavin and subsequently to the second β-heme.

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Ring Enlargement of Boracyclanes via Sequential One-Carbon Homologation. The First Synthesis of Boracyclanes in the Strained Medium Ring Range

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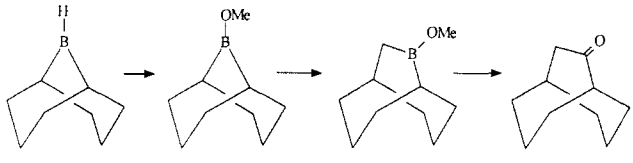
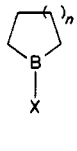
Previous attempts to achieve the synthesis of boracyclanes, $HB(CH_2)_{n-1}$ in the medium ring range (n = 9-12) have failed. However, the homologation of *B*-methoxyboracyclanes with in situ generated (chloromethyl)lithium, $LiCH_2Cl$, proceeds smoothly to furnish the next higher homologue. In this way we have successfully achieved the conversions: $MeOB(CH_2)_5 \rightarrow MeOB(CH_2)_6 \rightarrow MeOB(CH_2)_7 \rightarrow MeOB(CH_2)_8 \rightarrow MeOB(CH_2)_9 \rightarrow MeOB(CH_2)_{10} \rightarrow MeOB(CH_2)_{11}$. The yields achieved are in the range of 75-85%, and no decrease in the yield was observed in synthesizing the more strained members. Consequently, there appears to be no limit to the applicability of this procedure for the synthesis of many membered boracyclanes.

Numerous previous attempts to achieve the synthesis of medium ring boracyclanes by cyclic hydroboration of α,ω-dienes with various hydroborating agents like diborane,[1] thexylborane,[2] BH_2Cl,[3] and 9-BBN[4] have failed. Such cyclic hydroboration works well for the synthesis of five, six, and seven-membered derivatives but in general fails with higher members. In one case it was possible to achieve the formation of the eight-membered ring derivative in impure form.[3] One of the major difficulties with the synthesis of pure boracyclanes via cyclic hydroboration arises from the attack of the borane at the internal position of the diene, leading to the formation of polymeric species which upon thermal depolymerization undergo isomerization to give isomeric boracyclanes.

This long string of failures in our efforts to synthesize medium ring systems containing a boron hetero atom as part of the ring implied that the strains in these medium ring boracyclanes were too large for the relatively labile boron-carbon bonds.[5] Our present success in synthesizing and isolating such compounds and in successfully transforming them without observable molecular rearrangement opens up a major new area for the application of borane chemistry to facilitate organic synthesis. This development also opens up the possibility of increasing the size of a ring in bi- and polycyclic systems.



We recently have had considerable success in applying the Matteson homologation procedure[6] in lengthening the chain of optically active derivatives.[7] We decided to explore this procedure as a means of enlarging the size of the ring in *B*-methoxyboracyclanes. Two procedures were explored:[8] (dichloromethyl)lithium, $LiCHCl_2$ generated in situ, followed by potassium (triisopropoxy)borohydride (KIPBH) reduction, and by (chloromethyl)lithium, $LiCH_2Cl$, generated in situ. Both procedures worked entirely satisfactorily for the conversion of borinane to borepane. However, the fact that the $LiCH_2Cl$ procedure involves only a single step persuaded us to adopt this route. Indeed it worked quite satisfactorily to go stepwise from the six-membered boracyclane to the 12-membered boracyclane structure.



		ring size	
1	n = 1, X = H	5	borolane, boracyclopentane
2	n = 2, X = H	6	borinane, boracyclohexane
3	n = 3, X = H	7	borepane, boracycloheptane
4	n = 4, X = H	8	borocane, boracyclooctane
5	n = 5, X = H	9	boronane, boracyclononane
6	n = 6, X = H	10	borecane, boracyclodecane
7	n = 7, X = H	11	boracycloundecane
8	n = 8, X = H	12	boracyclododecane

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