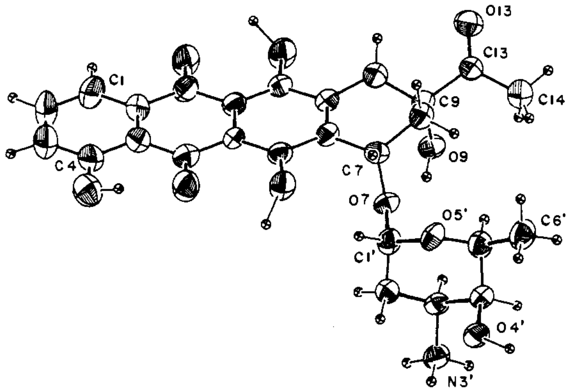

Figure 1. A perspective representation of the structure of carminomycin 1. A hydrogen atom on C10 is hidden from view.

size for data collection were obtained from ethanol–toluene. The observed Laué symmetry and extinctions correspond to the monoclinic space group $P2_1$ with $a = 20.027$ (4) Å, $b = 5.487$ (1) Å, $c = 11.900$ (2) Å, $\beta = 93.710$ (3)°; $Z = 2$; $\rho_{\text{calcd}} = 1.445$ g/cm^3 for $C_{26}H_{30}O_{11}NCl$, $\rho_{\text{obsd}} = 1.42$ g/cm^3. Diffraction intensities were measured in the θ–2θ scan mode using Ni-filtered Cu K$\bar{\alpha}$ radiation on a Syntex P$\bar{1}$ diffractometer; of the 2779 reflections examined within the limits of the diffractometer ($\sin \theta/\lambda \leq 0.609$), a total of 2631 unique reflections were retained as objectively observed. No corrections were applied for either absorption or extinction.

The structure was readily solved by direct methods using the MULTAN-74 system of programs.[12] Large block least-squares refinement[13] of the structure with anisotropic thermal parameters and fixed hydrogen positions (351 independent variables in four blocks) yielded a standard residual $R = 0.0710$ for all observed data; a weighted residual $R_w = (\sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2)^{1/2}$ of 0.0752 was obtained with $w = 1/\sigma_{F^2}$. All hydrogen positions had been observed in a difference synthesis based on a refined anisotropic model and the C–H atoms were placed at idealized positions. All others were placed as found in the map.

The perspective view shown in Figure 1 displays the essential configurational and conformational features of the molecule. The six chiral centers are C7 (*S*), C9 (*S*), C1′ (*R*), C3′ (*S*), C4′ (*S*), and C5′ (*S*). Since the configuration of the daunosamine unit of carminomycin I has been shown to be the same as that obtained from daunomycin[7] whose absolute configuration is known,[2,3] carminomycin I is herein shown (Figure 1) in the correct enantiomorphic form.

The structure of carminomycin I originally proposed[7] is in complete accord with the results of this crystal structure analysis, and with the stereochemistry at C7 now established is shown to be the desmethyl derivative of daunomycin with identical configurations at all chiral centers.

Investigation of the structural details of carminomycin reveals some interesting bonding patterns which affect the conformation of the molecule; these will be discussed in a detailed presentation of the structure.

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Electronic Structure and Electric Field Gradients in Oxyhemoglobin and -cytochrome P-450 Model Compounds

Sir:

The large quadrupole splittings observed in the Mössbauer resonance spectra of oxyhemoglobin (oxy Hb)[1] and oxycytochrome P-450[2] are thought to be anomalous for low spin ferrous heme complexes. These results have been used[1,2] to support the proposal[3,4] that these complexes, while formally Fe(II)–O_2, are best described by a Fe(III)–O_2^- configuration in which two unpaired electrons couple

Table I. Variation of Electric Field Gradients and Quadrupole Splittings with Oxygen Geometry in a Model Oxy Hb Compound in Fe(II)–O_2 Configurations

$\Upsilon_{N_{pyr}\text{-Fe-O-O}}$	0°	25°	45°[c]	135°[c]	45°	45°	45°	45°	45°	45°
$\theta_{\text{Fe-O-O}}$	135°	135°	135°	135°	180°	160°	135°	110°	101°	90°
$V_{xx}{}^b$	−2.65	−1.92	−0.79	−0.80	+0.67	−0.49	−0.79	−0.79	−0.74	+0.26
$V_{yy}{}^b$	+0.89	+0.17	−0.97	−0.98	−2.48	−1.30	−0.97	−0.88	−0.87	−1.32
$V_{zz}{}^b$	+1.76	+1.75	+1.76	+1.79	+1.81	+1.79	+1.76	+1.67	+1.61	+1.06
$\Delta E_Q{}^a$	−2.74	−2.17	+1.79	+1.82	−2.61	+1.89	+1.79	+1.70	+1.64	−1.42
η^a	0.33	0.82	0.10	0.10	0.46	0.45	0.10	0.05	0.08	0.61

[a] ΔE_Q in mm/sec calculated from $\Delta E_Q = 8(1 - R)Qq(1 + \eta^2/3)^{1/2}$ where $(1 - R)$ = Sternheimer shielding factor = 0.68, Q = 0.187 Barns, $\langle r^{-3}\rangle$ = 5.00 au, and V_{ii} ordered such that $q \equiv$ largest magnitude V_{ii} and $0 \leqslant \eta \leqslant 1$. Sign of ΔE_Q is sign of largest magnitude V_{ii}. [b] Principal axis values given are very nearly along the chosen molecular axis. The porphine plane is xy with pyrrole nitrogens along $\pm x$, $\pm y$; ligands are along z. When the V_{ii} values are used in the above expression to calculate ΔE_Q they are ordered as indicated in (a). [c] Two crystallographically distinguishable conformers with Fe–O_2 plane nearly perpendicular (Υ = 45°) and parallel (Υ = 135°) to the imidazole plane. Note similar V_{ii} and ΔE_Q values.

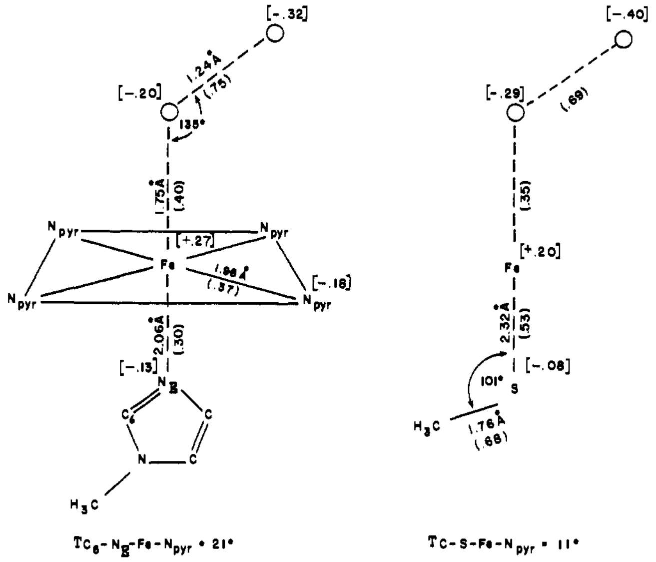

Figure 1. X-Ray structure geometry, calculated net atomic charges [$\pm q_A$], and bond densities (ρ_{AB}) for oxy Hb and oxycytochrome P-450 model compounds.

to form the diamagnetic ground state. The recent synthesis and structure determination of chemical models for oxy Hb[5] and cytochrome P-450[6,7] which reproduce properties of the intact protein have made it possible to investigate the correlation between the nature of the iron-oxygen bond and the observed quadrupole splitting.

Using geometries obtained from x-ray analysis of the porphin ring[8] and axial ligands[7,8] (Figure 1) as input to a molecular orbital program based on the iterative extended Hückel method,[9] detailed descriptions of the valence electron distribution and bonding in both the oxy Hb and oxy P-450 compounds were obtained. The calculated electron distributions were then used in a properties program to calculate the nine components of the electric field gradient tensor, principal axis values, anisotropy, and quadrupole splittings. Details of the formulation of this program are presented elsewhere.[10]

In the model oxy Hb compound, crystallographic data indicated a large disorder and consequent ambiguity in the position of the second oxygen atom due to rotations about the iron-oxygen bond.[5,8] Consequently, we have varied both the N_{pyr}-Fe-O-O torsion angle (Υ) and the Fe-O-O bond angle (θ) in our study.

The results of these calculations for a ground state Fe(II)-O_2 configuration are summarized in Table I. They indicate that each geometric variation considered produces a large quadrupole splitting. Further, the magnitude and sign of the principal axis values of the field gradient tensor are very sensitive to oxygen geometry. The results also show that both the negative sign of the field gradient and its observed decrease with temperature can be accounted for by rotations about the iron-oxygen bond involving energy barriers which we calculate to be less than 5 kcal/mol.

Using the same methods, the electron distribution and electric field gradients of a model high spin deoxy ferrous Hb complex were also calculated. In this model the O_2 ligand was removed, the imidazole ligand retained, and the Fe moved 0.42 Å out of the mean plane of the pyrrole nitrogens consistent with a recent x-ray analysis of a similar compound.[11] Our results yield a calculated value of ΔE_Q = +2.61 mm/sec, comparing favorably with the experimental low temperature value of +2.28. More significantly, our methods reproduce the striking experimental result of equal and opposite values of ΔE_Q for the high spin deoxy ferrous and the low spin oxy ferrous compounds.

Two Fe(III)-O_2^- configurations were also considered, formed respectively by electron transfer from $\pi_d \rightarrow \pi_O{}^*$ and $\sigma_{d_{xy}} \rightarrow \pi_O{}^*$. The former yielded a positive field gradient of ΔE_Q = +1.61 mm/sec and η = 0.03 while the latter yielded a value of ΔE_Q = −1.33 mm/sec and η = 0.07. Further investigations of the details of such charge transfer configurations, including geometry variation and the mechanism resulting in singlet ground states, are now in progress. Our results, however, indicate that it is not necessary to invoke such configurations to account for both the magnitude and sign of the field gradient.

A model oxy P-450 compound was constructed using methyl mercaptide (SCH_3^-) to replace the axial imidazole ligand. The positions of the sulfur and carbon were taken from the crystal structure of a high spin ferric P-450 model compound with a p-nitrobenzenethiolate ion as an axial ligand.[7] A preliminary calculation for one geometry of this species in a Fe(II)-O_2 configuration with the oxygen molecule at θ = 135° and Υ = 45° yielded a value of ΔE_Q = ±2.06 mm/sec and η = 1 indicating a large field gradient similar to oxy Hb, but with greater anisotropy.

Promotion of an electron from $\sigma_{d_{xy}} \rightarrow \pi_O{}^*$ to form a Fe(III)-O_2^- configuration yielded ΔE_Q = −2.15 and η = 0.52, in agreement with experimental observation of ΔE_Q = −2.15 and $\eta \leq 0.5$.[12] Further studies are in progress to resolve the question of whether a single geometry of a Fe(II)-O_2 configuration or a Fe(III)-O_2^- configuration can best account for the negative sign and lack of temperature dependence of the oxygenated ferrous P-450 complex.

An examination of the calculated valence electron distributions indicates the origin of the magnitude and sign of the electric field gradient as well as the enhanced rhombicity of the model oxy P-450 complexes. The large magnitude of the field gradient in the Fe(II)-O_2 configuration of both complexes is due to significant delocalization (covalency) in each iron-ligand bond (Figure 1). This delocalization results in partial population of the d_{z^2} and $d_{x^2-y^2}$ orbitals (forward donation) and depopulation of the d_{xz} and d_{yz} orbitals (back-donation), and consequently a significant deviation from the spherical symmetry associated with the totally localized low spin ferrous configuration $(d_{xy})^2$ $(d_{xz})^2$ $(d_{yz})^2$. It is also of interest to note that the delocalized Fe(II)-O_2 configuration leads to a substantial negative charge on the oxygen ligand and a weakening of the O_2 bond in keeping with recent experimental observations.[13,14]

The sign of the field gradient in the Fe(II)-O_2 configuration appears to be determined by the extent of differential participation of the d_{xz} and d_{yz} orbitals in π bonding to the axial ligands. In the oxy Hb complex, there is no appreciable π character in the iron-imidazole bond. Hence, the sign of the field gradient is largely determined by π bonding to the oxygen, accounting for its dependence on rotation about the Fe-O_2 bond. In the oxy P-450 species, however, there is significant π character in both the iron-oxygen and iron-sulfur bonds. As a result, the geometry of both axial ligands should affect the sign and the magnitude of the field gradient.

The presence of π character in the Fe(II)-SCH_3^- bond and its absence in the Fe(II)-imidazole bond also account for the difference in the observed rhombicity in the two species. While each type of axial ligand creates a geometric rhombicity in its complex by mixing with the d_{xz} and d_{yz} orbitals, the SCH_3^- ligand effectively transmits this rhombicity to the electron density around the iron nucleus while the σ-bonded imidazole ligand does not.

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Book Reviews

Crystal Growth Theory and Techniques. Volume 1. Edited by C. H. L. GOODMAN (Standard Telecommunication Laboratories). Plenum Press, New York, N.Y. 1974. ix + 300 pp. $28.00.

The field of single crystal growth is already of considerable interest and promises to gain additional importance as the technological application of single crystals expands. This book is the first of a series designed to cover specialized areas of crystal growth. It emphasizes the experimental aspects and usually treats only the more recent and advanced theoretical developments. There is some overlap among the contributors, but it is not serious. The first chapter by D. W. Shaw discusses vapor-phase epitaxial growth of semiconductors. Its theoretical treatment will be difficult going for those not well acquainted with the field. In Chapter 2, E. Kaldis reviews the principles of vapor growth of single crystals. His approach should be of interest to the active experimentalist. He emphasizes the physical implications of theory and treats experimental techniques in considerable detail. The author's plans of expanding this work into a monograph should be welcomed. G. A. Wolff and A. I. Mlavsky cover two travelling solvent techniques, the travelling solvent method and the travelling heater method. Their review is concise, and, although experimental methods and problems are discussed quite successfully, other topics, especially crystal growth of peritectic compounds, are too brief and suffer from space limitations. Finally, D. W. Jones considers the growth of crystals of refractory metals. His review includes liquid state growth, and he continually stresses the difficulties experienced in preparing refractory metal crystals. The volume also contains a materials index which readers should find helpful.

With the exception of the last chapter, most of the experimental information is concerned with electronic materials. This is hardly surprising; it merely reflects one of the major application areas for single crystals. Nonetheless, the emphasis on experimental techniques should be of value to crystal growers in general and to those who wish to join their ranks.

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Modern Developments in Thermodynamics. By B. GAL-OR (Technion, Israel Institute of Technology). Halsted Press, New York, N.Y. 1974. xxvii + 457 pp. $24.50.

This book is an interdisciplinary collective treatise with 37 contributors. The disciplines include chemistry, physics, physiology, aerospace, electrical engineering, aeronautics, radiophysics, philosophy, astronomy, and mathematics. The book is an outgrowth of the International Symposium "A Critical Review of Thermodynamics" (Pittsburgh, Pa., April 1969).

The editor, Dr. Gal-Or, has done an excellent job of answering his question in the preface "What is new in thermodynamics?". And there are new things in thermodynamics, not just new applications but new thoughts about the fundamental concepts themselves. The main concern of the book is with the arrow of time and the origin of irreversibility.

In order to follow the formalized arguments in some of the sections the reader will need to be well versed in statistical and quantum mechanics. The book should prove thought-provoking to advanced chemists, engineers, physicists, astronomers, and especially to philosophers of science.

Walter S. Hamilton, *Texas Woman's University*