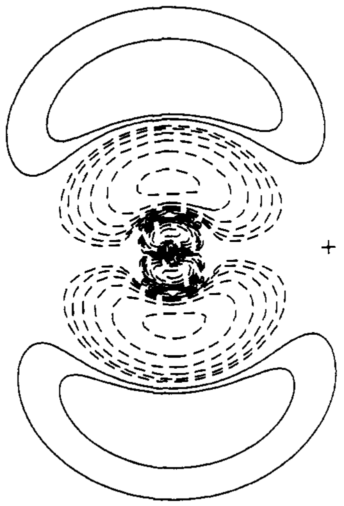

Figure 3. Electron density difference map of the highest occupied molecular orbitals of AsH_3-SeH_3^+ in the planar form. The plane is perpendicular to the plane of the molecules. The contour levels are 0.032, 0.016, 0.008, 0.004, 0.002, 0.001, −0.001, −0.002, −0.004, −0.008, −0.016, −0.032, −0.064, −0.128, and −0.256.

Table IV. Inversion Barriers for AH_3 and AH_3^+ Molecules

Molecule	Barrier[a]	Molecule	Barrier[a]
NH_3	6[b]	H_3O^+	1-2[c,d]
PH_3	36[e]	H_3S^+	32[f]
AsH_3	46[g]	H_3Se^+	30[g]

[a] Kilocalories/mole. [b] References 2 and 3. [c] S. Novick, R. M. Stevens, and W. Klemperer, unpublished results. [d] R. Ahlrichs, F. Driessler, H. Lischka, V. Staemmler, and W. Kutzelnigg, *J. Chem. Phys.*, **62**, 1235 (1975). [e] Reference 5. [f] References 1 and 8. [g] This work.

relative barrier heights. Further work on other molecules in this series is anticipated to elucidate these trends more clearly.

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Nature of the Iron-Oxygen Bond in Oxyhemoglobin

Sir:

The nature of the iron-oxygen bond in oxyhemoglobin has been a controversial problem for decades. Although x-ray data from model compounds[1]-support the bent Fe-O(1)-O(2) geometry proposed by Pauling,[2] questions concerned with the details of the bonding, including the charge on the oxygen (O_2 or O_2^-),[2-4] have not been resolved. In this communication we present the results of two quantum mechanical calculations which support a *neutral* oxygen model and show that it is consistent with Mossbauer and vibrational spectra data that have been interpreted as favoring a Fe^{+3}-O_2^- unit. Analysis of the electronic structure shows that it can be considered to arise from the interaction of an iron porphine moiety and an O_2 molecule with both species in either $S = 0$ or $S = 1$ valence states; the latter corresponds to ozone-like bonding, an analogy mentioned by Pauling[2] and emphasized recently by Goddard and Olafson.[4]

The system treated consists of a planar iron porphine with an imidazole group and an oxygen molecule as axial ligands. The geometry is that given by Collman et al.;[1] the porphine is in the xy plane with the x and y axes bisecting the N-Fe-N angles and both the imidazole and the FeO_2 unit are in the yz plane. The first calculation is of the extended SCF-CI Pariser-Parr-Pople (PPP) type.[5] It includes the iron 3d, 4s, and 4p orbitals, the oxygen 2s and 2p orbitals, the nitrogen lone-pair σ orbitals, and the π orbitals of the porphine and imidazole. The iron, porphine, and imidazole parameters were taken from ref 5 and those for oxygen from a PPP study of ozone.[6] The second calculation employs the Xα multiple scattering method,[7] which has been shown to yield excellent results for copper porphine.[8]

The charge distribution obtained in the PPP calculation corresponds to a neutral oxygen (O(1), +0.14; O(2), −0.08), an iron atom with net charge +0.44, and an imidazole group with a charge of +0.31. For the Xα wave function, a simple decomposition into atomic charges has been found not to be meaningful.[8] However, the charge distributions obtained from other calculations do correlate with the Xα atomic potentials. These indicate that in the O_2 unit the atoms are very similar to each other and to a free oxygen atom, with O(1) slightly positive. The Fe potential is that appropriate for a positive iron (+0.1).

To test the charge distributions, we consider first the electric field gradient tensor (EFG) at the iron nucleus evaluated from the Mössbauer spectrum. Since the EFG depends upon the individual orbital populations, we compare four different FeO_2

Table I. 3d Electronic Populations and Mossbauer Parameters

	Method	Ab initio[a]	GVB[b]	PPP[c]	$X\alpha$[c]	exp[d]
Electronic population	$3d_{xy}$	0.33	0.0	0.56	0.81	
	$3d_{z^2}$	0.22	1.0	0.53	1.09	
	$3d_{xz}$	1.90	1.0	1.36	1.66	
	$3d_{yz}$	1.96	2.0	1.74	2.00	
	$3d_{x^2-y^2}$	1.91	2.0	2.00	1.98	
EFG tensor[e]	V_{xx}	0.0	3.85	0.16	1.15	
	V_{yy}	−0.35	−1.93	−2.02	−1.43	
	V_{zz}	0.35	−1.93	+1.85	0.29	
Quadrupole splitting[f]	ΔE_Q	0.40	3.85	−2.24	−1.52	−2.11
Asymmetry parameter	η	1.0	0.0	0.84	0.60	0.23

[a] Reference 9. [b] Reference 4. [c] Present calculations. [d] Reference 11. [e] The components of EFG along the molecular axes are expressed in the ^{57}Fe Mossbauer unit of millimeters/second.[10] The quadrupole moment of ^{57}Fe was taken to be 0.20 b, the Sternheimer factor $(1 - R)$ was set equal to 0.68, and a radial factor $\langle r^{-3} \rangle$ of 4.90 au was used. For the $X\alpha$ results the radial factors are obtained from the calculated 3d wave functions.[8] The off-diagonal EFG components are negligible. [f] PPP calculation which takes into account the 4p electrons and the ligand contributions gives a quadrupole splitting ΔE_Q of −2.34 mm/s and 0.09, −2.07, and 1.98 for V_{xx}, V_{yy}, and V_{zz}, respectively.

calculations (ab initio SCF,[9] idealized GVB,[4] and the two present calculations) that all yield an essentially neutral oxygen. We assume that the dominant contribution to the EFG values come from the iron 3d orbitals, whose occupancies are shown in Table I. It is clear that both the ab initio SCF and GVB results are in disagreement with experiment; the first because the quadrupole splitting is much too small, and the second because it yields a positive principal component perpendicular to the heme plane and a zero asymmetry parameter. Both of the present calculations are in approximate agreement with Mössbauer data;[10,11] that is, the largest principal component has the correct magnitude and sign and is in the heme plane, although the calculated asymmetry parameter is somewhat too large. The two calculations differ in the orientation of the smallest component, but data are not available to determine which is correct.[11,12]

The oxygen stretching frequencies observed in myoglobin (1103 cm^{-1}),[13] in hemoglobin (1107 cm^{-1}),[14] and in model compounds (~1160 cm^{-1}),[15] have been cited as evidence for the Fe^{+3}-O_2^- structure, since they fall in the range found for superoxide complexes (1100-1150 cm^{-1}),[15,16] while the stretching frequencies for the O_2 molecule are 1556 cm^{-1} for the $^3\Sigma_g^-$ state and 1484 cm^{-1} for the $^1\Delta_g$ state.[17] A result that appears to have been neglected is that the force constant of the O-O bond in ozone is 6.16 mdyn/Å,[18] a value in the O_2^- range (5.7-6.2 mdyn/Å).[19] This suggests that a neutral O_2 unit can have the observed frequency.[20] Clearly what is important are the various bond orders. The total PPP bond order for the O_2 in heme O_2 is 1.60, which may be compared with the values for O_2 (2.0 for $^3\Sigma_g^-$ and $^1\Delta_g$), O_2^- (1.5), and O_3 (1.65).

The location of certain peaks in the resonant Raman spectrum of oxyhemoglobin has also been used to suggest an Fe^{+3}-O_2^- structure.[21] Since the observed vibrational modes are dominated by porphyrin internal coordinates, the specific bond orders involved rather than the iron orbital populations would have to be compared before drawing any conclusions.[22]

For an analysis of the FeO_2 bonding it is useful to compare the calculated results with appropriate reference states. One possibility is a low spin ($S = 0$) iron porphine and a low spin oxygen molecule ($S = 0$) with a doubly occupied in-plane π_g^* orbital (π_g^s), which has a lower energy than the empty out-of-plane π_g^* orbital (π_g^a). Comparison of these two separated species with the bonded heme-O_2 system shows a significant reduction of the iron $3d_{xz}$ population (1.75 → 1.36) due to donation into the π_g^a orbital of the oxygen, and an increase in the 4s (0.33 → 0.52), $4p_z$ (0.09 → 0.33), and $3d_{z^2}$ (0.17 → 0.53) populations due to σ donation from O_2 and the imidazole ligand; the other iron 3d populations are essentially unaltered. It is primarily the back-donation of electrons into the π_g^a antibonding orbital that causes the reduction in the O-O bond order; the calculated value is 0.77 in heme-O_2 relative to unity in the O_2 ($S = 0$) molecule. An alternative reference state involves an iron porphine ($S = 1$) and an O_2 molecule ($S = 1$) with populations Fe $((x^2 - y^2)^2(yz)^2(xz)^1(z^2)^1)$ and O_2 $((\pi_g^s)^1(\pi_g^a)^1)$ that correspond to the idealized ozone-like model.[4] On bonding, the four electrons in the orbitals antisymmetric with respect to the FeO_2 plane (xz on Fe, p_x on O(1) and O(2)) are found to be nearly equally distributed over the three atoms, leading to 1.36 rather than 1.0 in the iron $3d_{xz}$ orbital; this is consistent with the PPP ozone results.[6] The iron $3d_{z^2}$ population is considerably less than the ideal value of unity, but the total population in the $4p_z$ and $3d_{z^2}$ orbitals is 0.86, which is near to the value of 0.87 found for the $2p_z$ orbital of the terminal oxygen in ozone.[6]

An essential element in the MO formulation of ozone is the empty low-lying π^* orbital ($2b_1$). The double excitation $1a_2^2 \rightarrow 2b_1^2$ makes the dominant contribution in a configuration interaction calculation[23] and is required to obtain a $^1A_1$ ground state below the $^3B_2$ state. Also, a number of the low-lying singlet and triplet states arise from excitations into the $2b_1$ orbital.[4,6,23,24] Corresponding behavior is found in CI calculations for the oxygenated heme; in particular, doubly excited $\pi \rightarrow \pi^*$ configurations in the FeO_2 unit are essential to obtain a singlet ground state. A Weiss type[4] charge-transfer state with O_2^- appears at ~1.4 eV above the ground state. (The lowest triplet is at 1.2 eV; this appears to be in disagreement with recently reported measurements of the magnetic susceptibility of oxyhemoglobin.[25]) Details will be presented in separate publication.

In conclusion, it is clear that the emphasis on the Fe^{+2}-O_2 vs. Fe^{+3}-O_2^- dichotomy in discussions of oxyhemoglobin is simplistic. The essential element in interpreting the available data is not the overall charge distribution but the nature of the bonding and the attendant orbital populations and bond orders. The "superoxo" formulation (Fe^{+3}-O_2^- formal oxidation state) that has been stressed recently may be of some heuristic value.[16,26] However, it seems to us to be inappropriate since it has little basis in terms of the electronic structure of FeO_2.[27] Our calculations show *no* net charge transfer to oxygen, in contrast to the result for the true superoxide ion found in molecules like NaO_2.[28] A much better first-order model is provided by the correspondence between ozone and the FeO_2 unit, although descriptions starting with the interaction of two neutral $S = 0$ or $S = 1$ (ozone-like, see above) moieties are both valid; a linear combination of the two would be appropriate in a valence-bond treatment.[29] Finally, it should be noted that the role of the porphyrin and imidazole in modulating the iron populations cannot be neglected.[2]

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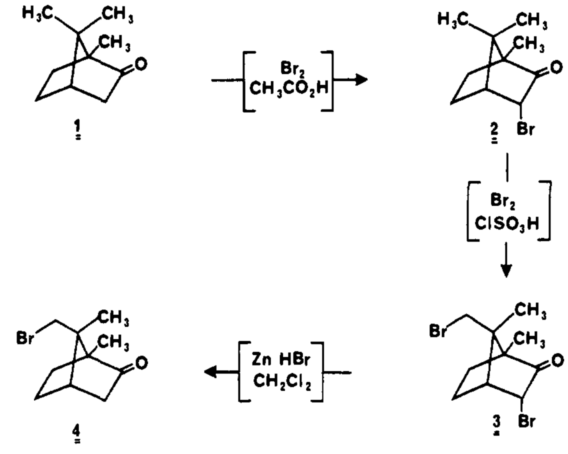
Camphorae: Chiral Intermediates for the Total Synthesis of Steroids†

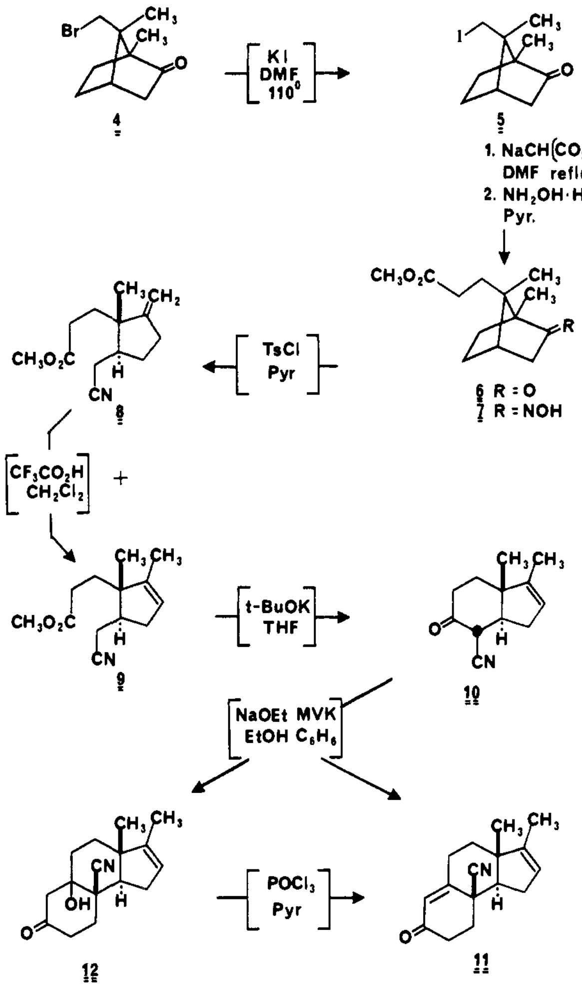
Sir:

A major effort has been devoted to the synthesis and utilization of C,D intermediates in the total synthesis of steroids.[1-4] Since the biological activity of steroids is restricted to one enantiomer, a major problem has been the development of a practical method for the production of such intermediates in chirally pure form. Recently, several ingenious solutions to this important problem have been realized and involve the employment of remarkably efficient asymmetric induction reactions.[5] Such methodology is obviously a more desirable method for achieving the necessary chirality than classical resolution by derivatization.[6] We now wish to present a fundamentally different approach to the total synthesis of chirally pure steroids, which takes advantage of (a) the natural chirality of (−)-camphor (**1**) and (b) its topology.

Scheme I



Scheme II



Direct functionalization of camphor[7] at the C-9 methyl group has been known for over 80 years.[8] Hence, preparation of (−)-π-bromocamphor[9] (**4**) can be accomplished[8a,d,e] effi-

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† Taken, in part, from the Ph.D. dissertation of F. C. A. Gaeta, Rice University, Dec 1976.