equiv of copper display reproducible activities under our conditions. Moreover, the relaxivity and absorbance are also well-described as linear functions of the copper content. Collectively, our data on BPAO are consistently interpreted in terms of equivalent copper sites that either bind copper independently or bind it in a highly cooperative fashion.[8] If recent determinations[8,14] are correct, each copper is associated with a quinone.

Finally, close examination of the apoprotein NMRD profiles in Figure 8A suggests that metal-depleted BPAO and PPAO are not monomeric under the conditions of the NMRD experiments. Molecular weight estimates from the data and Figure 2 of ref 44 are as follows: porcine enzyme, 500 000 Da; bovine enzyme, 900 000 Da. Assuming a molecular weight of 190 000 for the native, monomeric enzymes,[1,2] the NMRD values correspond to oligomers of two or three monomers for the porcine enzyme and of about five monomers for the bovine enzyme. Although there is considerable uncertainty in these estimates, the NMRD data strongly indicate that at least the copper-depleted enzymes associate under conditions that are similar to those used for many spectroscopic experiments, i.e., protein concentrations of a few tenths of a millimole per liter. The oligomerization is probably concentration-dependent, as analytical ultracentrifugation studies on oxidized PPAO,[27] dithionite-reduced PPAO,[51b] and oxidized BPAO[53] at protein concentrations <0.05 mM revealed no evidence of a high molecular weight species.[54]   We emphasize that the reconstitution of BPAO and PPAO with copper was carried out at low protein concentrations, i.e., under conditions where protein association should not be a factor. The NMRD results suggest that dilute protein concentrations may be preferable for the reconstitution of metal-depleted metalloenzymes; this is certainly the case for the plasma amine oxidases. Given the high paramagnetic relaxivities observed for the resting enzymes, self-association of the resting amine oxidases, if it occurs, does not appear to decrease the solvent accessibility of the Cu(II) sites.

Summary

NMRD profiles, considered together with previous studies of the copper site structure and reactivity of amine oxidases, provide strong support for multiple water ligands to Cu(II) in these enzymes. However, amine oxidases may differ in the rates of exchange of the coordinated water molecules with solvent water. A single rapidly exchanging water molecule mediates the para-magnetic contribution to solvent relaxation by BPAO and PKAO, and anions that are known to displace equatorially coordinated water from the Cu(II) ions produce only minor effects on the NMRD profiles of these enzymes. Hence, the rapidly exchanging water ligands in BPAO and PKAO are probably not equatorial; the equatorial waters must exchange slowly. The enzymes from porcine plasma and *Arthrobacter* P1 display an additional relaxation process at 25 °C, which we suggest involves rapid exchange of an equatorial water ligand; this additional relaxation process is much less evident at 5 °C, suggesting a relatively large activation energy. The NMRD profiles of BPAO, PPAO, PKAO, and APAO are quantitatively very similar at low temperature (5 °C), suggesting that the Cu(II) sites in all these enzymes contain a nonequatorial water ligand and an additional, solvent-derived ligand (either H_2O or OH^-) that is equatorial. The proteins divide into two classes characterized by the rate of exchange of this equatorial ligand. This conclusion is consistent with previous suggestions[3,9] that the Cu(II) site structure in amine oxidases has been conserved.

The relaxivity, absorption spectrum, and specific activity are linearly correlated with the copper content of both BPAO and PPAO. Our data on the porcine enzyme can be readily interpreted in terms of nearly equivalent, independent copper sites, each associated with a quinone molecule, but equally well in terms of cooperative Cu(II) binding to inequivalent sites. Either PPAO displays pronounced negative cooperativity in its reactions with substrates or carbonyl reagents or one of the quinones is simply unreactive. In contrast, the data on BPAO are fully consistent with a model involving equivalent, independent active sites containing one quinone and one Cu(II) ion in the resting state. Our data do not support previous suggestions that the copper sites in BPAO are distinguishable with regard to structure or function. One possible source for the reported variations in the properties of the bovine enzyme may be the recently discovered heterogeneity in the content of the reactive quinone.[8]

Finally, the NMRD profiles indicate that metal-depleted forms of BPAO and PPAO oligomerize under the conditions of the NMRD experiments.

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Polymerization Mechanisms of Propellanes

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Abstract: The polymerization mechanism of [1.1.1]propellanes is studied with the concept of atomic valence numbers. SINDO1 calculations were performed on the dimerization of [1.1.1]propellane and its reaction with donor- and acceptor-substituted ethylenes. An analysis of the configuration interaction (CI) wave functions in terms of newly developed partitioning scheme allows one to classify the reactivity in diradical and zwitterionic mechanisms. An explanation is given for the copolymerization of acceptor-substituted olefins with propellanes that is in agreement with recent experimental results.

Introduction

Several years ago, we described a concept of valence with atomic, bond, and molecular valence numbers on the self-consistent field (SCF)[1] and configuration interaction (CI)[2] level. This concept was used to define diradicals and zwitterions.[3] A diradical was defined as a species where two atoms have atomic valence numbers reduced by 1 unit compared with the standard values of the atoms. These standard values are 4 for carbon, 3 for

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nitrogen and boron, 2 for oxygen, etc. A hydrocarbon would be called a diradical if the actual valence numbers of two carbon atoms are approximately 3 instead of 4. This agrees well with a definition of Berson[4] that a diradical has one bond less than prescribed by the standard rules of valence. In this concept, a zwitterion is usually a species where one atom has a reduced valence and a second atom has an increased valence. This notion cannot be applied to carbon atoms because the valence number of carbon suffers a reduction in both diradicals and zwitterions. We derived empirically the rule that diradical states are characterized by smaller molecular bond numbers[2] than zwitterionic states. Two significant applications emerged from this concept. We could explain the copolymerization of tetramethylenes by analysis of the ground-state wave function of the isolated species[5] and we also showed that the approach of a polar solvent molecule to a borderline diradical could convert the diradical to a zwitterion and in consequence the polymerization mechanism from co-polymerization to homopolymerization.[6] These findings were in excellent agreement with the work of Hall.[7]

It now seemed very challenging to see whether these ideas could be applied to the polymerization mechanism of [1.1.1]propellanes with olefins. Polymers of these compounds had been recently synthesized by Schlüter, and extensive information was obtained from these experiments.[8–10] We therefore decided to apply the valence concept also to the [1.1.1]propellanes with olefins to explain their reaction mechanisms. In connection with the present study, we refined the criterion for diradicals and zwitterions by a newly developed partitioning scheme[11] for the valence changes incurred in the molecules with respect to the standard values for atoms. In the following sections, we present SINDO1 calculations[12,13] on the dimerization of [1.1.1]propellane and donor- and acceptor-substituted ethylenepropellanes. For convenience, this name has been chosen instead of 2-(1'-bicyclo[1.1.1]pentyl)ethane-1,3'-diyl. An analysis of these wave functions by the valence concept gives an explanation for the copolymerization of acceptor-substituted compounds and the lack of observation of this polymerization of donor-substituted compounds.

Dimerization of [1.1.1]Propellane

Due to its unusual structure and bonding, [1.1.1]propellane has been the subject of much discussion.[14–19] The focus of interest was the central bond between the bridgehead carbon atoms. Calculations showed that the bond length is only slightly longer than a CC single bond. This was confirmed by vibrational spectra[20] and electronic diffraction[21] experiments. However, the bond strength and the reactivity of the bridgehead carbons were a matter of debate. Since little density was found in between these carbon atoms,[14] the conclusion that these atoms are open to radical attack[15] seemed convincing. However, Wiberg concluded that a high energy of 65 kcal/mol was needed to break the central bond and create a diradical. We suggested[22] along the lines of Hoffmann that the central bond is quite weak, with a bond valence $V_{CC} = 0.54$, and that the atoms are quite reactive toward radical attack because their atomic valence is only $V_C = 3.39$ in a SINDO1-optimized structure. The calculated geometry is close to the experimental geometry (in parentheses): $R_{CC} = 1.568$ (1.596)

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Å, $R_{CC'} = 1.553$ (1.525) Å, $R_{C'H} = 1.090$ (1.106) Å, $\theta_{CC'H} = 119.9$ (116.9)°, and $\theta_{HC'H} = 109.5$ (116.0)°.

It is now suggestive to study the central bond properties by stepwise saturation of the bridgehead carbon atoms. If one hydrogen is added, the central bond is lengthened to 1.675 Å and its bond valence is reduced to $V_{CC} = 0.22$ in a SINDO1-optimized structure. The radical bridgehead carbon has now a valence number of $V_C = 2.91$, whereas the saturated bridgehead carbon has a valence number of $V_C = 3.90$. If both bridgehead carbons are saturated by H atoms, the CC bond length increases to 1.81 Å and the bond valence is further reduced to 0.07. Both bridgehead carbons have atomic valencies of 3.95.

From the valence reduction of the bridgehead carbons of the free [1.1.1]propellane and their characterization as almost radical centers, it would be suggestive to classify this compound as a diradical. It is now most important to realize that this classification is not supported by our newly developed valence-reduction partitioning scheme.[11] This scheme distinguishes between a SCF ΔV_M^{RHF} term and a CI ΔV_M^{CI} term of the total valence change ΔV_M of a molecule M. If $\Delta V_M^{RHF} \approx 2$ and $\Delta V_M^{CI} \ll 1$, the structure is called a zwitterion, whereas it is called a diradical if $\Delta V_M^{RHF} \ll 1$ and $\Delta V_M^{CI} \approx 2$. A 1,n-dipole is a compound with $|\Delta V_M^{RHF}|^2 + |\Delta V_M^{CI}|^2 > 1$.

For [1.1.1]propellane, $\Delta V_M^{RHF} = 1.31$ and $\Delta V_M^{CI} = 0.10$. Therefore, this compound should be classified as either a zwitterion or a 1,2-dipole. Due to the symmetry of the molecule, there is no charge shift or dipole moment. In the terminology of Salem and Rowland,[23] it is not a diradical because it does not have singlet–triplet degeneracy. This insight is necessary for the understanding of the polymerization mechanism of the homo-polymerization of [1.1.1]propellane, which is not understood as of now. Michl[24] achieved homopolymerization of propellanes with radical-chain starters. In experiments by Schlüter,[8,9] polymerization occurs under exclusion of light and chain starters. Analogous to the spontaneous polymerization of olefins,[7] one could postulate an intermediate responsible for initiation of the reaction. In the following text, we discuss the possibility of a propellane dimer as such an intermediate. A naive approach would be to assume that the propellane is a diradical where two of four radical centers of two propellanes react spontaneously to form a bond. However, from our valence analysis [1.1.1]propellane should not behave like a diradical. Indeed, a SINDO1 calculation does not show an energy minimum for the dimer on a 10 × 10 CI surface with three double excitations and six single excitations from the highest occupied to the three lowest unoccupied MO's. We cannot exclude that a small minimum exists, but it would be too weak to initiate polymerization. Figure 1a shows the energy dependence of the lowest singlet S_0 and the triplet T_1 of the dimer on the intermolecular distance between the two monomers. A corresponding Figure 1b was obtained from UHF calculations. Both figures show a triplet minimum but no minimum on the singlet surface. In the UHF calculation, the singlet and triplet curves are quite close for intermolecular distances below 1.5 Å. It is therefore suggestive to postulate that the dimer is formed on the T_1 surface by collision of two monomers followed by intersystem crossing. The structure of the UHF triplets T_1 of dimer and trimer is in Figure 2. The calculations do not account for the possibility of reaction with the walls of the vessel or impurities.

We have also studied the structure of the dimer and trimer of [1.1.1]propellane with hydrogens at the bridgehead atoms. These are called staffanes by Michl.[24] They turn out to be stable singlets in our calculations, in agreement with experiment.

Reaction of [1.1.1]Propellane with Olefins

We had recently studied the initiation of polymerization of tetramethylenes.[6] Here, it was determined that classification of the ground state of planar arrangements of substituted tetramethylenes as diradical or zwitterion is responsible for the initiation of copolymerization or homopolymerization. An analogous study

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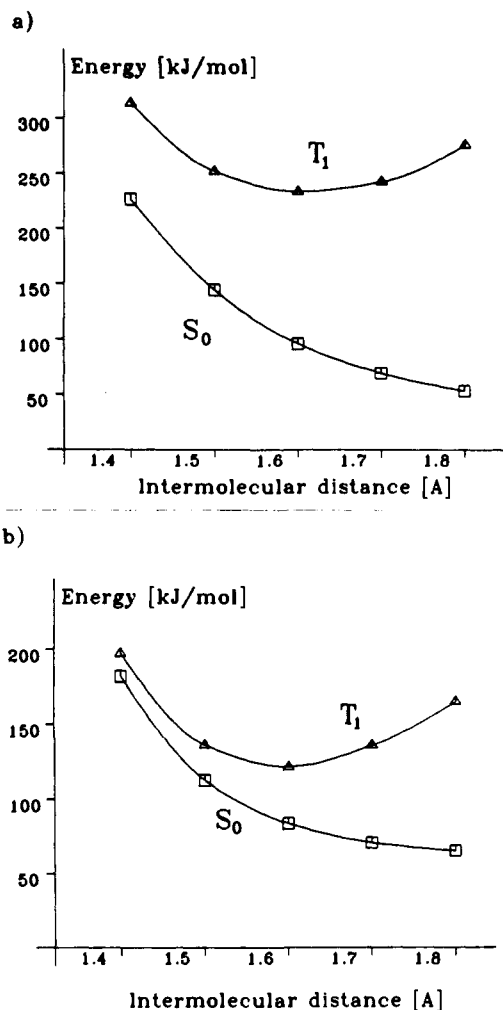(24) Kazynski, P.; Michl, J. *J. Am. Chem. Soc.* **1988**, *110*, 5525.

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a)

b)

Figure 1. Lowest singlet (S_0) and triplet (T_1) potential energy curves of [1.1.1]propellane dimer for (a) 10 × 10 CI and (b) UHF vs intermolecular distance.
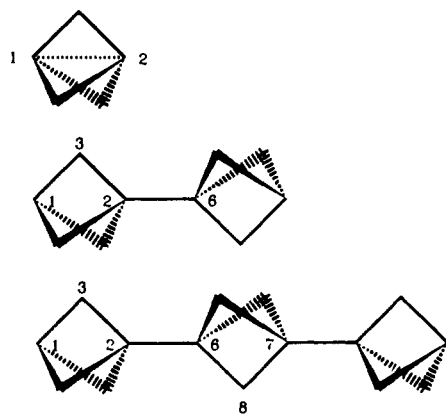

Figure 2. Structure of RHF singlet S_0 of the monomer and UHF triplets T_1 of the dimer and trimer of [1.1.1]propellane.

was now performed for ethylenepropellanes, i.e., systems built from [1.1.1]propellane and substituted ethylenes. If the outer methylene group with the substituents R_1 and R_2 is in the plane (Figure 3a), the combined system can exist on a flat plateau as a twixtyl.[25] We found that the perpendicular arrangement (Figure 3b) led to dissociation into [1.1.1]propellane and olefins. Therefore, the planar arrangement was analyzed by the valence analysis scheme proposed by us.[11]
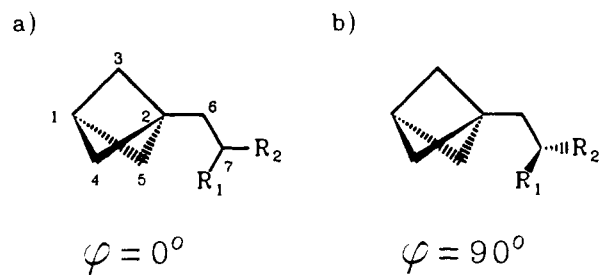
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a)   b)

$$\varphi = 0^\circ \qquad \varphi = 90^\circ$$

Figure 3. Conformations of ethylenepropellane: (a) in-plane and (b) perpendicular arrangement of outer methylene group.

Table I. Energy (ΔE), Dipole Moment (D), and Valence (ΔV) of In-Plane Ethylenepropellanes

no.	substituents		$\Delta E(S_0 - T_1)$ (kJ/mol)	D (D)	ΔV_M^{Cl} ΔV_M^{RHF}	ΔV_1^{Cl} ΔV_7^{Cl}
	R_1	R_2				
1	H	H	7.6	3.1	1.99 1.01 (D)	0.38 0.85
2	H	NH_2	133.4	14.7	0.02 2.72 (Z)	0.00 0.00
3	H	OMe	119.5	15.4	0.00 2.93 (Z)	0.00 0.00
4	H	F	14.2	1.7	1.99 1.20 (D)	0.37 0.82
5	H	Cl	12.3	1.9	1.99 1.39 (D)	0.37 0.78
6	H	CN	6.3	4.7	1.99 1.11 (D)	0.38 0.70
7	CN	CN	7.4	3.1	1.99 1.20 (D)	0.38 0.64
8	H	COMe	4.7	2.7	1.98 1.20 (D)	0.38 0.74
9	H	CO_2Me	4.2	2.3	1.98 1.46 (D)	0.39 0.75
10	OMe	OMe	120.0	11.4	0.12 3.08 (Z)	0.02 0.02
11	NH_2	NH_2	189.0	13.9	0.01 2.88 (Z)	0.00 0.00
12	H	Ph	8.1	3.0	1.97 1.16 (D)	0.36 0.60

In the following scheme, we distinguish between two terms for the total valence change in the molecule M with respect to standard values by the atoms A.

$$\Delta V_M = \Delta V_M^{RHF} + \Delta V_M^{Cl} \qquad (1)$$

with

$$\Delta V_M^{RHF} = \sum_A^{atoms} |\Delta V_A^{RHF}|$$

$$\Delta V_M^{Cl} = \sum_A^{atoms} |\Delta V_A^{Cl}|$$

The two terms result from restricted Hartree–Fock (RHF) calculations, in general given by SCF calculations on closed-shell systems or CI.
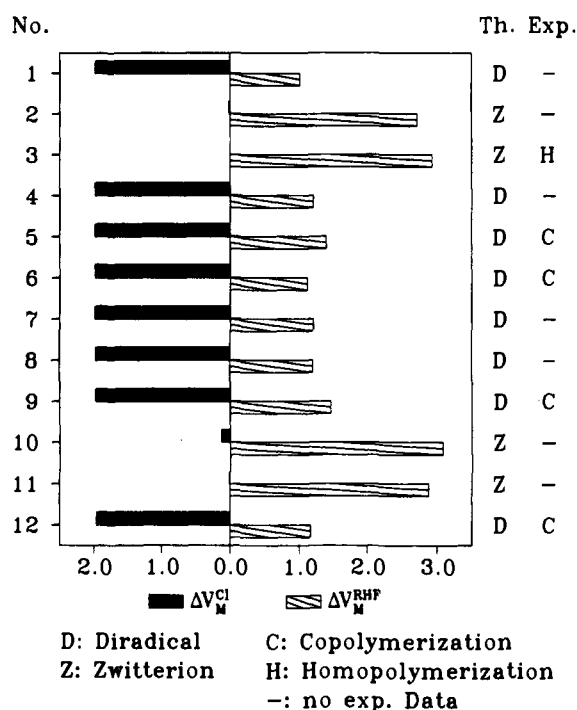
Figure 4. Comparison of theoretical and experimental data of in-plane ethylenepropellanes (numbering of compounds as in Table I).

In the carbon atom, the normal valence that can be used for covalent bonding is 4. This situation is realized in CH_4. In this case, the valence reduction ΔV_M is zero. However, for CH_3 the atomic valence number $V_C \approx 3$. The valence change $\Delta V_M \approx 1$. This is typical for a radical. The difference between a diradical and zwitterion in this theory is that $\Delta V_M^{Cl} \approx 2$ and $\Delta V_M^{RHF} \ll$

1 for the former and $\Delta V_M^{RHF} \approx 2$ and $\Delta V_M^{Cl} \ll 1$ for the latter.[11]

We have now collected energy, dipole moment, and valence data on twelve ethylenepropellanes in Table I. It is easy to observe that there are two groups of compounds. The first group is characterized by small singlet–triplet energy gaps, dipole moments of a few debye, and dominant ΔV_M^{Cl} terms for the valence change. These are classified as diradicals (D). The second group is characterized by large singlet–triplet energy gaps, dipole moments of >10 D, and a dominant ΔV_M^{RHF} valence change. These systems are classified as zwitterions (Z). A closer look reveals that the diradicals are acceptor-substituted ethylenepropellanes and the zwitterions donor-substituted ethylenepropellanes. Experimental observation indicates copolymerization by acceptor-substituted olefins with propellanes and homopolymerization by methoxy-substituted or no polymerization by other donor-substituted olefins. From our calculations, the following prediction emerges from comparison between theoretical and experimental data (Figure 4): We predict that, similar to the situation in tetramethylene, diradicals initiate copolymerization and that zwitterions initiate homopolymerization or no polymerization at all. For the presently known experimental data this agreement is perfect.

Conclusion

A newly introduced criterion for the distinction of diradicals and zwitterions can be successfully used to predict the polymerization mechanism of ethylenepropellanes. Acceptor-substituted ethylenepropellanes are diradicals and initiate copolymerization, whereas donor-substituted ethylenepropellanes are zwitterions and could initiate homopolymerization. [1.1.1]Propellane itself is neither a diradical nor a zwitterion but can be best characterized as a 1,2-dipole. Polymerization of pure [1.1.1]propellane therefore does not seem to proceed initially on the singlet surface but on the triplet surface where diradical properties are prevalent.

Cyclopentadienylidenecarbene: A Stable Isomer of o-Benzyne?

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Abstract: High-level ab initio quantum-mechanical studies have been performed on cyclopentadienylidenecarbene, an experimentally unknown species thought to be an important isomerization product of o-benzyne. Results suggest that cyclopentadienylidenecarbene is a shallow minimum on the PE surface, being bound by less than 5 kcal mol⁻¹. Harmonic vibrational frequencies have been evaluated at the self-consistent-field (SCF) level, together with the singlet–triplet energy difference, electron affinity, and lowest ionization energy at the configuration interaction (CI) level. The study provides the valuable detail and insight into cyclopentadienylidenecarbene necessary for its experimental detection and characterization.

Introduction

Evidence for the existence of cyclopentadienylidenecarbene (methylene, 2,4-cyclopentadien-1-ylidene), as an isomerized product of o-benzyne (1,3-cyclohexadien-5-yne) (see Figure 1), is based mainly upon the observation of ^{13}C scrambling in the biphenylamine product arising from the flash vacuum photolysis of labeled phthalic anhydride and benzocyclobutenedione.[1] Although it is thought that the interconversion is possible, it has

been pointed out recently[4] that the original experimental evidence[1–3] does not offer conclusive proof for the existence of cyclopentadienylidenecarbene. Alternative mechanisms were proposed to explain the ^{13}C scrambling.

Benzyne has received considerable attention both experimentally and theoretically because of its importance as a reactive intermediate. However, the conflicting characterization of its vibra-

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