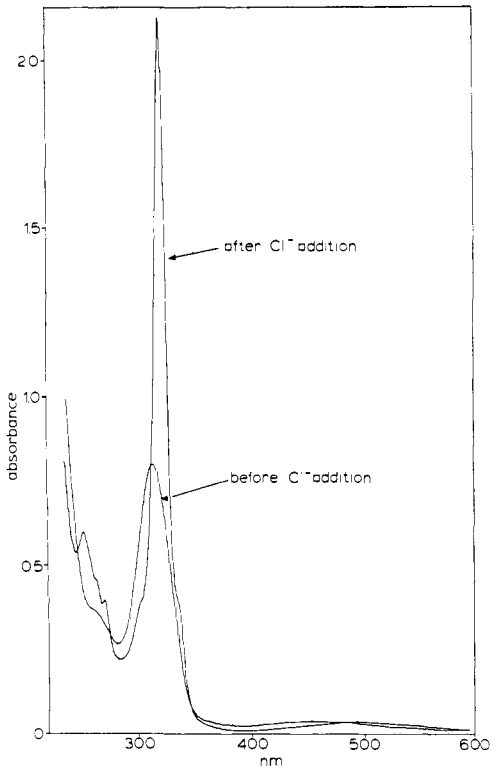

Figure 2. Spectral changes that occur after addition of 1.5 μmol of $Ph_4As^+Cl^-$ to a 10-mL acetonitrile solution containing 1.024 μmol of $[Ni_2(DMB)_4](ClO_4)_4$ and 1.036 μmol of NaSCN at 25 °C.

Importantly, titration of the halide-free complex,[16] $Ni_2(DMB)_4^{4+}$, with $Ph_4As^+Cl^-$ in acetonitrile gives a formation constant of 1.5×10^6 M^{-1} at 25 °C. For comparison, the formation constant of $NiCl^+$ in acetonitrile is 10^4 M^{-1}.[17] Further Cl^- addition has little effect on the spectrum until greater than 2 equiv have been added, at which time a steady decrease in absorbance occurs as more Cl^- is added ($NiCl_4^{2-}$ is the eventual product). Addition of SCN^- in acetonitrile to $Ni_2(DMB)_4^{4+}$ results in a visible spectrum similar to that of each of the halo complexes, indicative of square-pyramidal Ni(II).[18] [The thiocyanate complex also exhibits a peak at 310 nm, although it is less intense and much broader than in $Ni_2X(DMB)_4^{3+}$ (X = Cl, Br).] The absorbance maximizes after addition of 2 equiv of SCN^-. *Addition of 1 equiv of Cl^- to these solutions results in nearly quantitative formation of $Ni_2Cl(DMB)_4^{3+}$* (Figure 2). The remarkable preference for Cl^- over SCN^- suggests strongly that the former ion occupies the unique binding site in $Ni_2(DMB)_4^{4+}$.

The intense band at 320 nm has been studied at 20 K in poly(methyl methacrylate) films containing $Ni_2X(DMB)_4^{3+}$. Two vibrational progressions with spacings of 436 and 2174 cm^{-1} are resolved for the chloro complex. Results for the bromo complex are essentially the same. The vibrations involved are clearly the Ni-C and C≡N stretches, respectively, strongly implying that the electronic transition involves Ni(II) → π*(CNR) charge transfer. Simple theoretical considerations suggest that the transition responsible for the 320-nm system is related to the d_{z^2} → π*(CN) transitions that fall at 286[8] and 277 nm[7] in the spectra of $Ni(CN)_4^{2-}$ and $Ni(CNR)_4^{2+}$, respectively. Specifically, the 320-nm band is assigned $^1A_{1g} \rightarrow {}^1A_{2u}[a_{2u}(d_{z^2}(-) \rightarrow a_{1g}[\pi^*,p_z(+)])]$ in the $Ni_2Cl(DMB)_4^{3+}$ complex.

Both $Ni_2X(DMB)_4^{3+}$ complexes react with I_2 in acetonitrile; addition of $Ph_4As^+I_3^-$ produces black microcrystalline products in 50-60% yields. These species contain none of the original counterion (PF_6^-, BPh_4^-, or BF_4^-) and are formulated as $[Ni_2X(DMB)_4](I_3)_4$ (X = Cl, Br).[19] IR spectral measurements show that the Ni-Cl-Ni stretch is at 228 cm^{-1}, whereas Ni-Br-Ni is at 165 cm^{-1}. The increase in this stretching frequency in each case is consistent with removal of an electron from the $a_{2u}[d_{z^2}(-)]$ Ni-X-Ni antibonding orbital. These species exhibit corrected molar susceptibilities (χ_m^{corr}) of 3.379×10^{-3} cgs units (X = Cl) and 3.690×10^{-3} cgs units (X = Br). (The magnetic moments are 2.82 and 3.00 μ_B, respectively.) A frozen acetonitrile solution (4 K) of the bromo complex shows an EPR signal with $g_\parallel = 2.20$, $g_\perp = 2.05$, and $A_\parallel(Br) = 185$ G. The large Br hyperfine coupling constant is similar to the value of 169 G recently obtained for $[Ni(diphos)_2Br_2]PF_6$.[20] The UV-vis spectrum of $[Ni_2Br(DMB)_4](I_3)_4$ is characteristic of I_3^-, except for a distinct shoulder at 320 nm. Details will be reported later.

Acknowledgments. We thank Steve Rice for assistance in obtaining the low-temperature electronic absorption spectra and John Lipscomb for obtaining the EPR spectrum. W.L.G. acknowledges a National Science Foundation Postdoctoral Fellowship for 1978-1979. This research was supported by National Science Foundation Grant CHE78-10530.

(16) This complex is a tractable white powder prepared from $Ni(ClO_4)_2 \cdot 6H_2O$ and DMB. The infrared spectrum indicates the presence of a small amount of an unbound isocyanide group. Anal. Calcd for $[Ni_2(DMB)_4](ClO_4)_4 \cdot 2H_2O$: C, 43.92; H, 5.85; N, 8.54. Found: C, 43.87; H, 6.02; N, 8.52.

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Hydrophobic Effect of the CH_2 Group: Enthalpy and Entropy Contributions

Sir:

Several workers[1-3] have analyzed the CH_2 increment to the free energy of partition of *n*-alkanes between water and an organic solvent into a favorable gas → organic solvent contribution and an unfavorable gas → water contribution. More recently, I showed[4] that the free energy of solution of rare gases and gaseous alkanes in nonaqueous solvents could be correlated through 1 and 2, where R_G is a solute parameter and l_G and d_G are parameters

$$\Delta G_s^\circ \text{ (in solvent)} = m\Delta G_s^\circ \text{ (in benzene)} + c \quad (1)$$

$$\Delta G_s^\circ \text{ (in solvent)} = l_G R_G + d_G \quad (2)$$

characteristic of the solvent.[5] When these equations were applied to solution in water, it was found that ΔG_s° values for rare gases were well correlated but that values for the *n*-alkanes were always more positive than those calculated by using the "rare gas line" (see Figure 1).[6] The difference may be taken as a measure of the hydrophobic effect of alkanes, and in this way, the unfavorable gas → water CH_2 contribution of 0.18 kcal mol^{-1} was dissected into a favorable normal solvent effect of 0.36 kcal mol^{-1} and an

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(5) The parameters R_G, l_G, and d_G are identical with the terms *R*, *l*, and *d* used previously.[4]

(6) In Figure 1 are also plotted points for the inorganic gases H_2, N_2, O_2, and CO; these solutes behave similarly to the rare gases in all solvents, including water.

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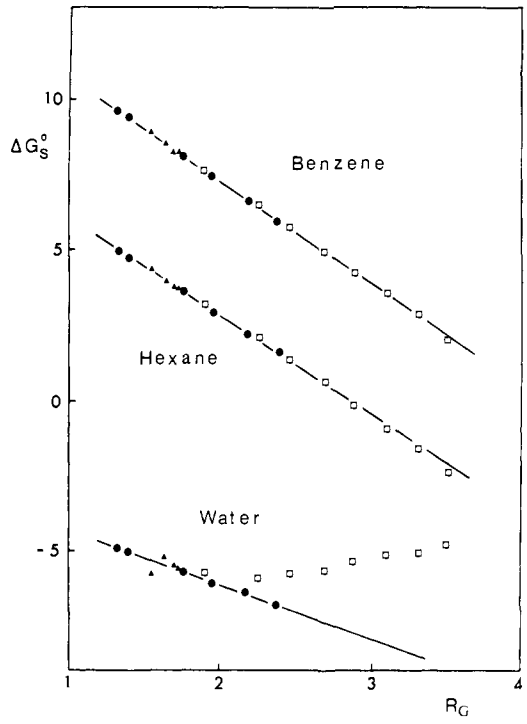

Figure 1. Plot of ΔG_s° (kcal mol^{-1}) against the solute parameter R_G. Values for benzene have been increased by 4 kcal mol^{-1} and those for water decreased by 12 kcal mol^{-1} on the graph. Rare gases (●); inorganic gases (▲); C_1–C_8 *n*-alkanes (□).

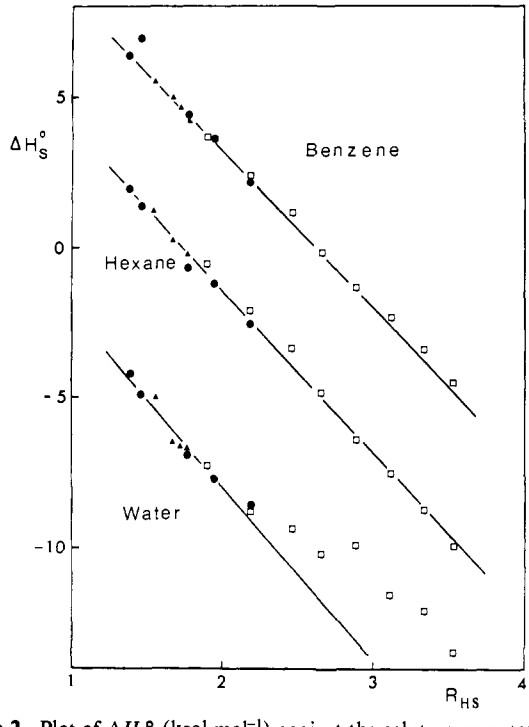

Figure 2. Plot of ΔH_s° (kcal mol^{-1}) against the solute parameter R_{HS}. Values for benzene have been increased by 4 kcal mol^{-1} and those for water decreased by 4 kcal mol^{-1} on the graph. Symbols as in Figure 1.

unfavorable hydrophobic effect of 0.54 kcal mol^{-1}.

I now report that ΔH_s° and ΔS_s° (or $-T\Delta S_s^\circ$) values for rare gases, inorganic gases, and the *n*-alkanes are also correlated by equations analagous to eq 1 and 2 in nonaqueous solvents; Figures 2 and 3 show results of applying eq 3 and 4 to data on solution

$$\Delta H_s^\circ \text{ (in solvent)} = l_H R_{HS} + d_H \quad (3)$$

$$-T\Delta S_s^\circ \text{ (in solvent)} = l_S R_{HS} + d_S \quad (4)$$

in hexane and benzene.[7] The same procedure may be applied

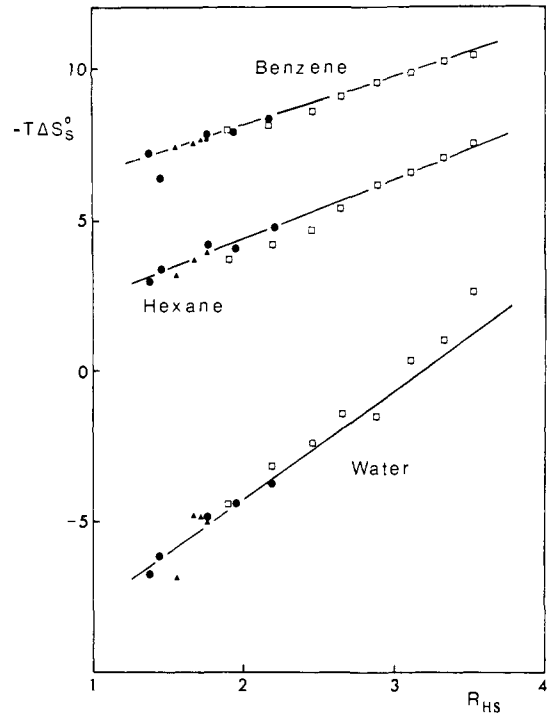

Figure 3. Plot of $-T\Delta S_s^\circ$ (kcal mol^{-1}) against the solute parameter R_{HS}. Values for benzene have been increased by 4 kcal mol^{-1} and those for water decreased by 12 kcal mol^{-1} on the graph. Symbols as in Figure 1.

Table I. Analysis of the CH_2 Group Hydrophobic Effect in *n*-Alkanes (kcal mol^{-1}) at 298 K

process	ΔG°	ΔH°	$-T\Delta S^\circ$
hexane solution → gas[a]	0.74	1.32	−0.58
gas → water, normal solvent effect[b]	−0.37	−1.21	0.84
gas → water, hydrophobic effect[c]	0.54	0.46	0.08
hexane solution → water[a]	0.91	0.57	0.34

[a] Observed values. [b] Obtained from the observed total gas → water parameter less the calculated parameter for the hydrophobic effect. [c] Calculated as described in the text.

to solution in water, using literature values for rare gases, inorganic gases, C_1–C_4 *n*-alkanes,[8] *n*-pentane and *n*-hexane,[9] and *n*-heptane and *n*-octane.[10] Although values of ΔH_s° for rare and inorganic gases in water are correlated by eq 3, those for the *n*-alkanes do not fall on the rare gas line. As with the ΔG_s° values, the overall partition of alkanes between, e.g., hexane and water can be dissected into a gas → hexane and a gas → water enthalpic contribution, and using the rare gas line in Figure 2 it is now possible to further dissect the gas → water CH_2 contribution into a normal solvent effect and a true hydrophobic effect. The divergence of the observed ΔH_s° values for gaseous *n*-alkanes in water from the rare gas line is of the same magnitude as is the corresponding divergence in ΔG_s° values. It therefore follows that the rare gas line for $-T\Delta S_s^\circ$ values in water must lie close to the observed values for *n*-alkanes. Indeed, eq 4 very nearly correlates all the $-T\Delta S_s^\circ$ values for all the solutes in water, so that the entropic contribution to the hydrophobic CH_2 free-energy increment is very small; a summary of the numerical values is in Table I. The conclusion that the major contribution to the hydrophobic CH_2

(7) For a given solute, the parameter R_{HS} is usually close to, but not identical with, R_G. The standard states used in the entropy calculations are 1 atm (gas) and unit mole fraction (solution), as before.[4]

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free-energy increment is an enthalpic effect and not an entropic effect is quite contrary to previous analyses[11] and contrary also to suggestions[12-14] that restriction of internal motion of hydrocarbon chains in water is an important feature.

Finally, I wish to point out that the hydrophobic effect can most logically be discussed only by assessing the expected thermodynamic parameters for solution in water in the absence of any unusual or hydrophobic effect. Thus, $\Delta G_t°$ for transfer of *n*-hexane from *n*-hexane solvent to water is very positive (7.8 kcal mol^{-1}); however, not all of this is due to a hydrophobic effect, because $\Delta G_t°$ for transfer from *n*-hexane solvent to many other solvents is also positive, e.g., 2.6 kcal mol^{-1} to Me_2SO and 3.9 kcal mol^{-1} to ethylene glycol. Only by factoring out the expected or normal solvent effect for transfer to water can the unusual or hydrophobic effect quantitatively be obtained. Similarly, $\Delta H_t°$ for transfer of *n*-hexane from *n*-hexane solvent to water is 0; this does not mean that there is no enthalpic contribution to the hydrophobic effect but is the result of a positive hydrophobic enthalpic effect (about 2.5 kcal mol^{-1}) in combination with a negative normal solvent effect for transfer to water.

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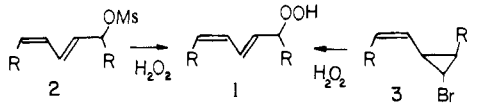
A New Route to Lipid Hydroperoxides: Orbital Symmetry Controlled Ring Opening of Vinylcyclopropyl Bromides

Sir:

Recent reports that diene hydroperoxides are formed from polyunsaturated fatty acids by enzymes present in platelets and polymorphonuclear leukocytes have stimulated interest in this class of compounds. Arachidonic acid (5,8,11,14-eicosatetraenoic acid, 20:4), for example, is converted to 12-(hydroperoxy)eicosatetraenoic acid (12-HPETE) by a platelet enzyme,[1,2] and an enzyme present in leukocytes converts this fatty acid into 5-(hydroperoxy)eicosatetraenoic acid[3] (5-HPETE). The spectrum of biological activity of these hydroperoxides remains to be fully determined, but it has been suggested that these compounds play an important role in inflammation. 5-HPETE, in particular, is the proposed intermediate in the biosynthesis of SRS-A,[3] a compound believed to be involved in the allergic response.

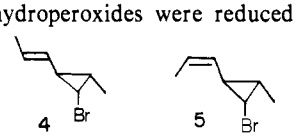
Fatty acid hydroperoxides are also formed in free-radical autoxidation, and random oxidation of lipid may play an important biological role. It has, in fact, been suggested that heart attacks and strokes may be essentially lipid peroxidation diseases.[4,5]

While we have earlier reported on chromatographic methods for purification of fatty acid hydroperoxides formed by singlet oxygen[6] or free-radical oxidation[7] of the fatty acid, these procedures, while convenient, provide relatively low conversion from fatty acid to isolated hydroperoxide products. Recently, direct peroxide displacement to diene mesylates (prepared in an elegant scheme from the starting fatty acid) **2** → **1** has been used[8,9] to

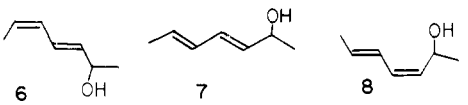


prepare specific diene hydroperoxides. We have also utilized direct peroxide displacement[10,11] (silver ion assisted displacement of halides)[12,13] for preparation of prostaglandin endoperoxides and allylic hydroperoxides, and we report here a method for the preparation of lipid hydroperoxides by the use of this silver ion/hydrogen peroxide reagent. The known orbital symmetry control of stereochemistry in the ring opening of cyclopropyl halides[14] suggested that the route **3** → **1** might provide a vehicle for the preparation of the target compound. While the reaction of alkyl-substituted cyclopropyl halides has been studied extensively[14,15] with regard to mechanism, vinylcyclopropyl halides like **3**, on the other hand, have not been thoroughly investigated.[16]

Treatment of the model bromides **4** or **5**[17] with excess silver trifluoroacetate/hydrogen peroxide in diethyl ether at 25 °C led to a mixture of geometric isomers of 2-(hydroperoxy)-3,5-heptadiene. The hydroperoxides were reduced with triphenyl-



phosphine, and the resulting alcohols were analyzed on a 25-m SCOT Carbowax column. The product alcohols **6**-**8** were in-



dependently prepared by reduction of the known[18] 3,5-heptadien-2-ones with lithium aluminum hydride. Bromide **4** leads to a 50:50 mixture of alcohols **6** and **7** while **5** gives a 92:8 mixture of these diene alcohols. None of the *cis,trans*-diene alcohol **8** was detected in the reaction of either **4** or **5** with Ag^+/H_2O_2.

With the validity of the approach established, we next sought a route that would be generally useful for the preparation of trans,cis- and trans,trans-substituted diene hydroperoxides. Lipid hydroperoxides with both trans,cis and trans,trans stereochemistry are formed in autoxidation, and the factors that control product stereochemistry in free-radical oxidation have only recently been established.[19] We chose the 12-hydroperoxides **15a** and **15b** as target molecules since they are representative of the general class of fatty acid hydroperoxides, and we had earlier[6] prepared these compounds by singlet oxygen methods.

The synthesis, which is general for fatty acid hydroperoxides, proceeds[20] from the dihydropyran **9** to **10** by addition of di-

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