Table II. Rate of Thermal Decomposition of Dioxetane **1a**

Temp, °C	$k \times 10^4$, s^{-1}	Temp, °C	$k \times 10^4$, s^{-1}
36.0	2.44[a]	57.6	28.3
40.5	4.63	59.9	37.1
51.0	14.0	63.1	54.9
54.3	20.2	65.3	74.8
$E_A = 23.6 \pm 1.6$ kcal/mol			
Log $A = 12.9 \pm 0.9$			

Determination of the Activation Energy for Thermal Decomposition of 1. The rate constants for thermolysis of diphenyldioxetane **1a** were determined in CCl_4 solution over a 20 °C range (Table II). The emission intensity of sensitized DBA (1×10^{-3} M) was followed with time. The initial concentration of **1** was 1×10^{-5} M.

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"Hydrophobic Interaction" and Solvation Energies: Discrepancies between Theory and Experimental Data

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Abstract: Prevailing descriptions of the "hydrophobic interaction" or "hydrophobic effect" are incompatible with relationships found between the structures of various nonpolar solutes and their solvation energies by water and 1-octanol. Previously reported linear relationships between partition coefficient and molecular volume actually result from compensation between relatively irregular solvation energies in water and lipid. In the partitioning of a $-CH_2-$ moiety from water into octanol, $\Delta G_{298} = -0.54$ (± 0.01) kcal/mol for favorable solvation by octanol and only $+0.18$ (± 0.01) kcal/mol for disfavorable solvation by water, whereas in the partitioning of a "CH_2-equivalent incremental molecular volume" of a rare gas, $\Delta G_{298} = -1.58$ (± 0.14) kcal/mol for favorable octanol solvation and -0.81 (± 0.03) kcal/mol for *favorable* water solvation. These two distinct linear relationships between molecular volume and solvation energy require two bulk-related modes of solute/solvent interaction. Such results appear more consistent with cavity-based models of solvation, such as the general "scaled-particle" theory. Other arguments in support of the "hydrophobic effect" are refuted.

Perhaps the most characteristic of the many physicochemical phenomena operative in a biological organism are partitioning processes, that is, the tendencies for nonpolar solutes and nonpolar portions of solutes to segregate themselves from aqueous media. For example, cell walls and internal membranes comprise highly structured lipoidal phases whose existence depends almost exclusively on partitioning. At a lower level of structural complexity, enzymes probably owe most of their affinity for substrates and their secondary structure itself to the same kinds of molecular interactions that are responsible for partitioning.[1] Consequently, it is not surprising to find that the partitioning behavior of a molecule is a major determinant of its pharmacological properties.[2]

In describing the molecular or mechanistic basis for these partitioning processes, biologically oriented chemists almost always invoke the "hydrophobic interaction", "hydrophobic effect", or "hydrophobic bond".[3] The theory of the "hydrophobic interaction" originates from the anomalously large loss of entropy which accompanies dissolution of nonpolar substances in water. From this observation, Frank, Kauzmann, Scheraga, Tanford, Ben-Naim, and others[4] have elaborated various highly ordered, entropically unfavorable arrangements

Table I. Transfer Equilibria of Some Nonpolar Solutes. Experimental Observations and Derived ΔG

	Octanol/water partition coefficient		Vapor/aqueous solution transfer		Vapor/octane solution transfer		Molecular volume,[e] Å^3 molecule
Solute	A. Obsd[a]	B. $\Delta G^b{}_{298}$ kcal/mol	C. Obsd[c] ($K \times 10^4$)	D. $\Delta G^d{}_{298}$, kcal/mol	E. Obsd[c] ($K \times 10^4$)	F. $\Delta G^d{}_{298}$, kcal/mol	
H_2	0.43	−1.67	0.14	−6.60	6.845	−4.31	11.45
He	0.28	−1.44	0.068	−7.05	2.397	−4.94	11.49
Ne	0.28	−1.44	0.081	−6.93	3.626	−4.69	15.30
Ar	0.74	−2.07	0.244	−6.27	24.26	−3.57	27.83
Kr	0.89	−2.27	0.426	−5.93	70.66	−2.93	51.28
Xe	1.28	−2.80	0.769	−5.61			58.63
CH_4	1.09	−2.54	0.255	−6.22	29.27	−3.45	28.42
C_2H_6	1.81	−3.53	0.345	−6.06	342.4	−2.00	45.41
C_3H_8	2.36	−4.28	0.255	−6.26			62.41
C_4H_{10}	2.89	−5.00	0.193	−6.43			79.39
C_5H_{12}	3.39	−5.68	0.143	−6.60			96.36
Cyclopentane	3.00	−5.15	0.965	−5.48			83.03
Cyclohexane	3.40	−5.69	0.927	−5.50			100.00
C_6H_6	2.13	−3.96	27.8	−3.38			80.33
CF_4	1.18	−2.67	0.036	−7.44	19.66	−3.69	46.40
CCl_4	2.83	−4.92	6.37	−4.37			86.82

[a] Log (concentration$_{\text{octanol}}$/concentration$_{H_2O}$) (ref 34). [b] Calculated as $2.30RT(-0.78 - \text{column A})$ where −0.78 converts the units to mole fractions. [c] Henry's law constant, in mole fraction of solute per atmosphere of solute partial pressure. (ref 28, 35 for H_2O; ref 32 for octane.) [d] Calculated as $RT \ln$ (obsd) (ref 32). The sign change (reversal of process) is intentional. Compare ref 31. [e] van der Waals or crystallographically based values (ref 36). The relationships presented in this article were not altered when molecular surface area, refractivity, or connectivity was employed as a measure of bulk instead of molecular volume.

of water molecules about a nonpolar solute, whose disruption accounts for essentially all of the energy of solute transference to a lipid phase. Attention is thereby focused on the "unique" solvation properties of water, while solvation by lipid is assumed to be a featureless process having no relevance to biological systems. Hence the adjective "hydrophobic", clearly intended to signify that partitioning phenomena result almost exclusively from repulsive interactions between water and nonpolar substances.

Various of the hydrophobic theories have been chided by Hildebrand[5] as unnecessary and castigated by Holtzer and Emerson[6] as being useless for the interpretation of experiments on urea-induced denaturation of protein and comparisons of D_2O and H_2O as solvents.[7] It is noteworthy that, according to spectral studies, little if any effect on the structure of water accompanies the dissolution of nonpolar materials.[8] The positive NMR shifts which are usually observed[9] are rather more suggestive of a decrease in hydrogen bonding, although there is also a modest decrease in the conformational lability of the water molecules.[10] In any case, interpretation of these spectral studies is seriously complicated by the polar moieties which must be attached to the "nonpolar" solutes in order to achieve sufficient solubility.

Relationship between Molecular Bulk and Partition Coefficient. The most frequently cited success of the hydrophobic models is their consistency with the data for the partitioning of a large variety of organic solutes between lipid and water. If the only important feature of the partitioning process is the ordering of water molecules about the inert solute, one would expect a linear relationship between the bulk of the solute (molecular volume or surface area) and its free energy of partitioning, with corrections for the interactions between water and any polar groups on the solute. Figure 1 exemplifies the very impressive correlations of this sort which have been presented by Hansch, Tanford, and others[11,12] in support of hydrophobic theories. Here the experimental observations for partitioning of various nonpolar solutes from a well-studied model lipid, 1-octanol, to water[13] (Table I) are transformed to free energies and plotted as a function of solute molecular volume. Least-square lines[14] are shown for the noble gases and

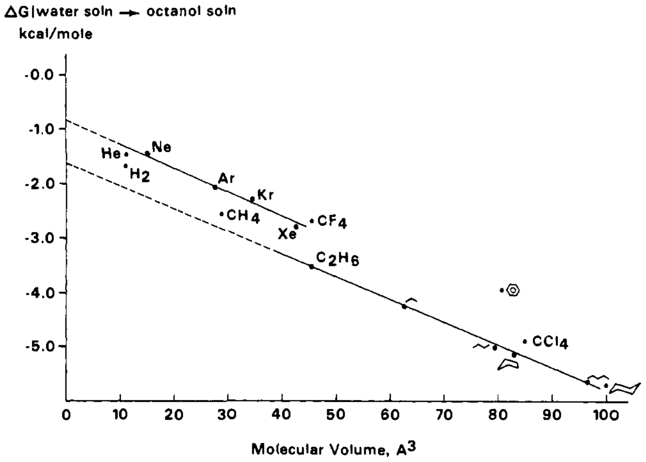

Figure 1.

for the straight-chain hydrocarbon series ethane through pentane.[15] As can be seen, there is a linear increase in "hydrophobicity" as solute volume increases, which is otherwise independent of structure except for a slight tendency for alkyl hydrocarbons to be more hydrophobic than other nonpolar solutes.[12] From the slope of the least-square lines, the transfer energy of each incremental $-CH_2-$ is found to be −0.72 (±0.02) kcal/mol,[14] in reasonable agreement with calculated values using the hydrophobic bond theory.[16] Finally, extrapolation of the least-squares lines suggests that nonpolar solutes having zero volume have a nearly zero energy of partitioning.[17]

Relationship between Molecular Bulk and Solvation Energies. The purpose of the present study is to examine this agreement between the hydrophobic models and partitioning studies in greater depth. The partitioning equilibrium will be dissected into its two components—solvation by water and solvation by 1-octanol. To the extent that the hydrophobic theories are correct in ascribing a dominant role to bulk-dependent repulsions between water and solute, a plot of solvation free energy by water against molecular bulk should resemble Figure 1,

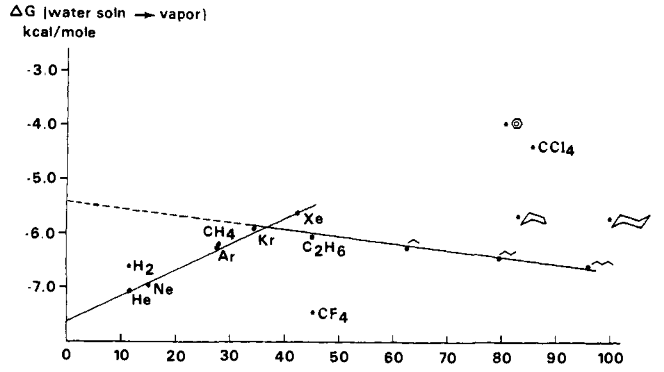

Figure 2.

while a plot of ΔG_S by octanol against bulk should be an almost horizontal line.

Such free energies of solvation are available directly from experiment, as the equilibrium observed in the transfer of the solute from its own vapor phase into dilute solution. Since the interactions among solute molecules in the gas phase are negligible, the magnitudes of these Henry's law constants or "gas solubilities" are influenced *only* by solute/solvent interactions.

Thus from the numerous literature data for the solubilities in water of the rare gases and hydrocarbons (Table I), Figure 2 was readily constructed. This plot of free energy of transference from the gas state to aqueous solution as a function of molecular volume is to be compared with to Figure 1. The free energies of transference from the vapor state to octanol, found as the differences of columns D and B in Table I,[18] are similarly plotted in Figure 3. The nearer a solute is to the top of Figure 2 or Figure 3, the more soluble it is in that solvent.[19]

Deficiency in the hydrophobic bonding theory is evident simply on comparison of the three figures. If interaction with water is the interesting feature of the partitioning process, a resemblance between Figure 1 and 2 and a featureless Figure 3 would have been expected. In fact it is Figure 3 which resembles Figure 2 and Figure 1 which is relatively featureless. It appears that the simple linear relationships exemplified in Figure 1 result from the mutual compensation of some relatively complex interactions of solute with water and octanol. Intuitively one therefore suspects that solvation by water and by octanol must have many common features; otherwise they would scarcely balance one another so well.[20] Figures 2 and 3 define additional relationships which are difficult to reconcile with the "hydrophobic effect" interpretation of partitioning phenomena:

1. The individual components of the energy for transfer of $-CH_2-$ from water to octanol can be evaluated from the appropriate slopes, as with Figure 1, to be +0.18 (±0.01) kcal/mol of "repulsive" ΔG between $-CH_2-$ and water and −0.54 (±0.02) kcal/mol of "attractive" ΔG between $-CH_2-$ and octanol, in agreement with scattered earlier results.[21] Evidently "the correct interpretation of the hydrophobic effect, assigning the predominant role to the properties of water per se",[22] must in fact be the incorrect interpretation insofar as the overall energetics of partitioning are concerned.

2. The solvation energy/solute bulk relationships for the rare gases in the two solvents are also linear but have slopes which differ greatly from the slopes for straight chain hydrocarbons in the corresponding solvents. In terms of the "$-CH_2-$ molar volume units" employed above, the molecular volume dependencies of rare gas solvation energies are −1.58 (±0.14) kcal/mol for octanol and −0.81 (±0.03) kcal/mol for water. Note that aqueous solubility of rare gases *increases* with solute bulk, in direct opposition to the prediction of hydrophobic interaction theory for these nonpolar solutes. Therefore the simplest mathematical relationship between solvation energies and molecular volumes that can fit both hydrocarbon data and noble gas data must have the functional form

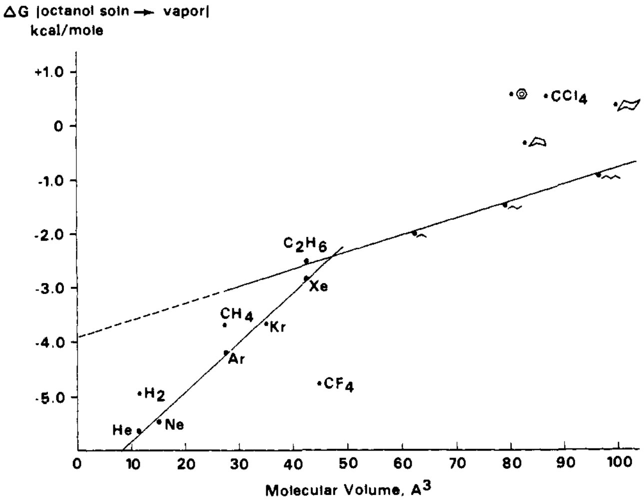

Figure 3.

$$\Delta G = (a + b)\mathrm{MV} + C$$

where a and b are linearly independent constants, characteristic of solute structure type and solvent. Furthermore, at least for water, a and b must have different signs.

3. The intercepts of the four lines all suggest that $\Delta G_{(\mathrm{MV}=0)}$ for a nonpolar solute in either water or lipid is far from zero.[23] Therefore formation of a cavity of any size in either solvent appears to be a highly energy-demanding step. However, increasing the size of a cavity which is formed and filled is evidently an energy-yielding process (except for the series of hydrocarbons in water).

4. Qualitatively it is noteworthy that cyclic alkanes are much more soluble than straight-chain alkanes of similar bulk, for example, cyclohexane, surprisingly, being more hydrophilic than methane.[24] Furthermore, CF_4 is less solvated and CCl_4 more solvated than the alkanes, and CH_4 and H_2 are intermediate between the rare gases and the alkanes. It may be tempting to use these deviations as reason to seek a substitute for molecular volume as a measure of bulk. However, the extraordinarily high linearities indicated by the least-squares lines[11] do suggest that, within a series where "other things" should be equal, molecular volume effects play dominant, if multiple, roles.

The purpose of this article is to call attention to discrepancies between existing theory and experiment, not to offer alternative theories. However, it should be noted that all these relationships appear to be readily explicable in terms of the various cavity models of solvation, in which energies are calculated first for creation of a suitably sized solvent cavity and then for the interactions between solvent and a solute molecule introduced into the cavity.[25] The overall similarity between Figures 2 and 3 is not surprising if the mechanisms of solvation by water and lipid are fundamentally similar. The "$(a + b)$" dependency of solvation energies on molecular volume is an expected consequence of the cavity theories, because two types of volume dependency are implicit in its expanded equations. A "repulsive" solvation energy of cavity formation, which evidently increases directly with molecular bulk, is opposed by an "attractive" solvation energy which is proportional to solute polarizability; polarizability in turn is proportional to molecular volume.[26] Finally, a nonzero $\Delta G_{(\mathrm{MV}=0)}$ observation is predicted by the scaled particle theory, where a portion of the nonzero intercept provides an estimate of the volume of a solvent molecule.[27]

It also should be noted that the supposedly "anomalous" thermodynamic properties of water as a solvent have been shown to arise, using the scaled particle cavity theory,[28] as a natural consequence of the small size of water molecules[29] and its thermal expansion coefficient. Not only are results calculated from this theory equal to the hydrophobic bond theory in their agreement with experiment, they are markedly superior in the number of adjustable parameters required.

Additional Failings of the Hydrophobic Theories. Objections to these arguments raised by advocates of the hydrophobic effect are the observation that water is, after all, unique among biologically encountered liquids in its disaffinity for hydrocarbons, and therefore partitioning phenomena *must* be primarily water related, and more specifically reiteration of the admittedly anomalous entropy decrease accompanying transfer of a hydrocarbon from lipid to water at ambient temperatures. For example, at 298 K the solvation entropy for methane in water is -32.1 cal/mol deg[31] and in octane only -14.8 cal/mol deg.[32]

While these two objections do not really answer the points raised in this article, they do merit the following, apparently novel, arguments in rebuttal. The ΔG for transference of a $-CH_2$-sized moiety from water to a lipid phase in fact depends very much upon the nature of the lipid phase, varying from -0.36 kcal/mol for 2-butanone to -0.80 kcal/mol for many lipids such as benzene.[30] With the affinity of 2-butanone for $-CH_2-$ thus being nearer to that of water than to that of benzene, water's disaffinity for hydrocarbons would seem to be a matter of slight degree rather than of "uniqueness".

In regard to the anomalously large entropy of solvation of hydrocarbons, it is a surprisingly little noticed fact that the entropy of solvation by water of an *incremental* $-CH_2-$ is quite unremarkable. For water, the difference in ΔS_{H_2O} of solvation between ethane and methane and the average difference along the methane-butane series are -4.2 and -3.3 cal/mol deg per $-CH_2-$, respectively;[31] for comparison the ethane/methane ΔS differences in some typical nonpolar solvents are -1.5 cal/mol deg in heptane, -2.9 cal/mol deg in cyclohexane, -1.4 cal/mol deg in acetone, and -1.9 cal/mol deg in chlorobenzene.[32] Whatever may be the mechanistic origin of the anomalous ΔS for water solvation of a nonpolar solute, the fact that this ΔS is not notably solute bulk dependent excludes the "hydrophobic" interpretation, that is, an ordering of water molecules immediately adjacent to a nonpolar surface.[33]

Conclusion

The preceding analysis of the partitioning process leaves little if any experimental evidence remaining to support the notion of a specifically "hydrophobic" effect. At the molecular level, individual solvation energies reflect relatively small differences between much larger attractive and repulsive interactions, operating in both the water and the lipid phases. The overall process is much better characterized energetically as "lipophilic". The widespread citation of hydrophobic theories in textbooks of biochemistry, and their exclusive and uncritical invocation in the scientific literature which treat partitioning phenomena in a biological context, seem entirely unwarranted by the experimental data.

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(14) All uncertainties cited in this article are 95% confidence intervals derived from the standard error of the least-squares slope estimate. A $-CH_2-$ unit is assumed to have a volume of 16.94 Å (negligible uncertainty, ref 36).

(15) The regression equations are (see ref 14)

$$\Delta G = -0.837\ (\pm 0.228) - 0.044\ (\pm 0.008) \times \mathrm{MV}.$$

noble gases,
$H_2O \rightarrow$ octanol, 298 K ($r = 0.988$, $s = 0.102$)

$$\Delta G = -1.63\ (\pm 0.09) - 0.042\ (\pm 0.001) \times \mathrm{MV}$$

hydrocarbons,
$H_2O \rightarrow$ octanol, 298 K ($r = 0.9998$, $s = 0.024$)

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(17) In studies involving organic compounds only, there has been a tendency to force a zero intercept, either explicitly (G. G. Nys and R. F. Rekker, *Eur. J. Med. Chem.*, **5**, 521 (1973)) or implicitly, by assigning to $-CH_3$ a bulk some two to four times that of $-CH_2-$, thus moving the regression line for hydrocarbons in Figure 1 far to the right (ref 4e, p 8; S. S. Davis, *J. Pharm. Pharmacol.*, **25**, 293 (1973); ref 35). The latter procedure ignores independent bulk data and usually imposes a negative bulk on tertiary and quaternary carbon.

(18) To corroborate the proposition that this subtraction procedure indeed yields the octanol solvation energy of a solute, these differences have been compared with measured ΔG_{298} for transfer of some of the solutes from the vapor state to *octane* solutions (columns E and F of Table I). Regression yields the following relationship (See ref 14):

$$\text{column F} = 0.20\ (\pm 0.74) + 0.895\ (\pm 0.168) \times (\text{column D} - \text{column B})$$

($r = 0.975$, $s = 0.231$)

The nearly unit slope and negligible intercept of this satisfactory correlation support the treatments made of these partition coefficient data for estimating the interaction energy between these solutes and a hydrocarbon (lipid) solvent.

(19) The corresponding regression equations are (see ref 14)
water solution → vapor:

$$\Delta G_{298}\text{, noble gases} = -7.63\ (\pm 0.08) + 0.048\ (\pm 0.002) \times \mathrm{MV}$$
$$(r = 0.999,\ s = 0.036)$$
$$\Delta G_{298}\text{, hydrocarbons} = -5.59\ (\pm 0.04) - 0.0105\ (\pm 0.0006) \times \mathrm{MV}$$
$$(r = 0.999,\ s = 0.012)$$

octanol solution → vapor:

$$\Delta G_{298}\text{, noble gases} = -6.79\ (\pm 0.24) + 0.093\ (\pm 0.008) \times \mathrm{MV}$$
$$(r = 0.997,\ s = 0.109)$$
$$\Delta G_{298}\text{, hydrocarbons} = -3.97\ (\pm 0.06) + 0.0317\ (\pm 0.0008) \times \mathrm{MV}$$
$$(r = 0.9998,\ s = 0.015)$$

(20) One feature common to all gas → solution transfers is the associated loss of translational and rotational degrees of freedom. The resulting free-energy

changes may be large enough (~1 kcal/mol) to require consideration. However, the series of compounds within the figures which would seem most likely to exhibit this effect, the hydrocarbons with their numerous rotational degrees of freedom in the gas state, are one of the two series showing the greatest regularity. Thus additional explanation of the irregularities in Figures 2 and 3 must be sought.

(21) G. L. Amidon, S. H. Yalkowsky, S. T. Anik, and S. C. Valvani, *J. Phys. Chem.*, **79**, 2239 (1975); P. Mookerjee, *Adv. Colloid Interface Sci.*, **1**, 241 (1967); J. A. V. Butler, C. M. Ramachandani, and D. W. Thomson, *J. Chem. Soc.*, 952 (1935).

(22) Reference 4e, p 3.

(23) The *absolute* values of ΔG in solute transfer processes will depend on the standard state convention, since the relative number of molecules in the two phases varies during the transfer process. In keeping with most workers in this field (ref 4e, 28, 32), mole fractions are used here, but conventional concentrations are equally satisfactory (ref 12, 35) if ideal mixing entropy is then explicitly considered. In any case, the choice of standard state does not significantly influence the *relative* values of ΔG, on which most of these arguments are based; furthermore, none of the usual standard state conventions produce nonzero $\Delta G_{(MV=0)}$. (See also ref 27.)

(24) This surprising observation was independently noted and also found inexplicable by hermann (ref 25). The marked increase in hydrophilicity when a hydrocarbon chain is cyclized persists as unsaturations are successively introduced into the hydrocarbons (C. McAuliffe, *J. Phys. Chem.*, **70**, 1267 (1966)).

(25) The "scaled particle" theory is reviewed by R. A. Pierotti, *Chem. Rev.*, **76**, 717 (1976). A somewhat different cavity model is due to R. O. Neff and D. A. McQuarrie, *J. Phys. Chem.*, **77**, 413 (1973). Cavity models may also be regarded as a first-order truncation of the highly successful Barker–Henderson perturbational treatment of solutions (R. B. Hermann, *J. Phys. Chem.*, **79**, 163 (1975)).

(26) See, for example, S. Glasstone, "Textbook of Physical Chemistry", Van Nostrand, Princeton, N.J., 1946, Chapter 5.

(27) Most of the intercept is accounted for by $RT \ln (RT/\bar{V}$ solvent), the chemical potential of the solvent required with this standard state convention, which is −4.27 kcal/mol for pure water and −2.99 kcal/mol for pure octanol.

(28) R. A. Pierotti, *J. Phys. Chem.*, **69**, 281 (1965); H. D. Nelson and C. L. deLigny, *Recl. Trav. Chim. Pays-Bas*, **87**, 623 (1968). With regard to the free energy of cavity formation, water is by no means a unique solvent, iodobenzene and nitrobenzene being comparable and hydrazine even greater (E. Wilhelm and R. Battino, *J. Chem. Phys.*, **56**, 563 (1972)).

(29) M. Lucas, *J. Phys. Chem.*, **80**, 359 (1976).

(30) Derived in a straightforward manner from empirical linear equations relating log (partition coefficients) between water and various lipid phases (A. Leo, C. Hansch, and D. Elkins, *Chem. Rev.*, **71**, 525 (1971), and ref 34), assuming the ΔG of −0.72 kcal/mol for partitioning of $-CH_2-$ from water to octanol.

(31) E. Wilhelm, R. Battino, and R. J. Wilcox, *Chem. Rev.*, **77**, 219 (1977).

(32) E. Wilhelm and R. Battino, *Chem. Rev.*, **73**, 1 (1973).

(33) However, the scaled particle theory seems to share this deficiency of predicting an unusually negative dependence of water solvation entropy on solute bulk, which is not observed experimentally (ref 29). Could there be a "colligative" ordering of the configuration of water molecules accompanying the solution process, an ordering which might be present but obscured by other processes during the dissolution of *polar* substances? Other explanations of the anomalous ΔS have been given (D. D. Eley, *Trans. Faraday Soc.*, **35**, 1281, 1421 (1939); R. E. Powell and W. M. Latimer, *J. Chem. Phys.*, **19**, 139 (1951); D. H. Everett, *Discuss. Faraday Soc.*, **24**, 216 (1957)).

(34) A. J. Leo, Pomona College Medicinal Chemistry Project, Claremont, Calif., semiannually distributed update. All values except that for H_2 also cited in ref 12.

(35) J. Hine and P. K. Mookerjee, *J. Org. Chem.*, **40**, 292 (1975).

(36) A. Bondi, *J. Phys. Chem.*, **68**, 441 (1964).

Chemiluminescence from the Base-Catalyzed Decomposition of α-Hydroperoxy Ketones. Competitive Cyclic and Acyclic Reactions

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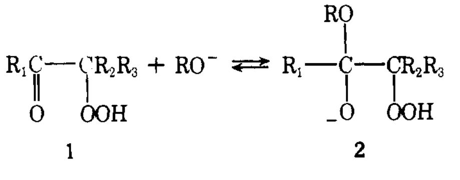
Abstract: Chemiluminescence (CL) is observed from the base-catalyzed decomposition of α-hydroperoxy ketones (**1**) in the presence of a fluorescer. The efficiency of fluorescers is in the order dibromoanthracene (DBA) ≫ diphenylanthracene (DPA) and eosin > fluorescein, suggesting a predominant formation of triplet ketone. Most peroxides exhibit the CL in the presence of DBA, although the quantum yields are low, i.e., in the range of 10^{-5}–10^{-6}. These results suggest that the chemiluminescent dioxetane mechanism is actually operating to produce triplet ketone. However, the nonchemiluminescent acyclic pathway is generally predominant in view of the ester formation, the low quantum yield of the CL, and solvent effects on the CL and the decomposition rate. The kinetics for decomposition and CL suggest competitive cyclic and acyclic pathways. Thus, the acyclic decomposition of α-hydroperoxy-α,α-diphenylacetophenone (**1j**) is too fast to compete with the dioxetane path.

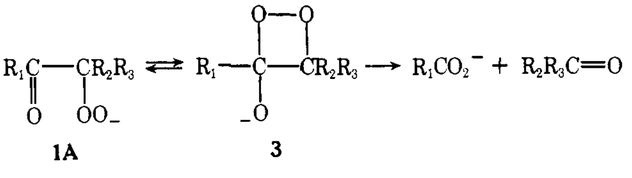
Chemiluminescence (CL) from the thermolysis of dioxetanes is efficient and an important key step for bioluminescence.[1,2] Although the observation of the CL from base-catalyzed decomposition of α-hydroperoxy ketones (**1**) suggested an operation of a dioxetane mechanism,[3] our previous report[4] has shown that the decomposition proceeds predominantly via an acyclic C=O addition mechanism (eq 1) rather than via cyclic dioxetane (eq 2).

Acyclic mechanism;[4]



$$R_1C(=O)-CR_2R_3(OOH) + RO^- \rightleftharpoons R_1-C(RO)(O^-)-CR_2R_3(OOH) \longrightarrow R_1CO_2R + R_2R_3C{=}O + HO^- \quad (1)$$

Cyclic or dioxetane mechanism;[3]



$$R_1C(=O)-CR_2R_3(OO^-) \rightleftharpoons R_1-\underset{O^-}{C}(-O-O-)CR_2R_3 \longrightarrow R_1CO_2^- + R_2R_3C{=}O \quad (2)$$

The choice of mechanism, however, was ambiguous for the case of R_1 = *i*-Pr and a question remains open about the extent of operation of the cyclic pathway for various peroxy ketones. The present paper will describe the predominance of the acyclic path (eq 1) for all substrates and the minor cyclic path (eq 2) with CL (~10^{-3}% at most) producing triplet ketone.

Results and Discussion

Decomposition Kinetics. The rate of MeONa-catalyzed decomposition of α-hydroperoxy ketones (**1**, R′OOH) was