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Solvent Pressure Effects in Free Radical Reactions. A Selectivity Inversion in Free Radical Brominations Induced by Solvent

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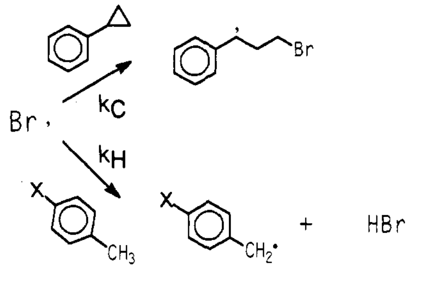
Abstract: The results reported herein demonstrate a compelling link between selectivity in free radical brominations and the internal pressure of solvent. In a study encompassing 18 solvents and/or solvent mixtures, the rate constant ratio for S_H2 ring opening of cyclopropylbenzene (k_C) vs hydrogen abstraction from toluene (k_H) by bromine atom was found to vary by nearly a factor of 20 as a function of solvent. The observed rate constant ratio correlates with the cohesive energy density of the solvent, which for the solvents utilized in this study is approximately equal to internal pressure (k_C/k_H is found to increase with increasing solvent pressure). A similar competition pitting cyclopropylbenzene against *p*-chlorotoluene shows an identical solvent effect. It is suggested that the variation in selectivity with solvent pressure arises because the volume of activation associated with k_C is more negative than that for k_H by ca. 20 cm^3/mol.

Introduction

It is widely accepted that solvent exerts only a nominal influence on reactivity and selectivity in radical reactions.[3] An important exception to this generalization is provided by Cl•, whose selectivity is markedly enhanced by complexation to aromatic solvents and CS_2.[4,5] While Br• is also known to form complexes with aromatics,[6] there are no reported examples where Br• selectivity is drastically altered by solvent. In this article, a dramatic *inversion* in Br• selectivity induced by solvent is reported.

As part of an ongoing study of the importance of stereoelectronic factors on C–H and C–C bond reactivities,[7–9] a series of experiments was performed wherein a cyclopropylarene competed with its corresponding methylarene for Br• (e.g., cyclpropylbenzene (CPB) vs toluene (TOL), Scheme I). Surprisingly, a nearly 20-fold variation in the rate constant ratio, k_C/k_H was found over several solvents. Several solvent parameters were examined, leading to the conclusion that the variation in selectivity is attributable to the internal pressure of the solvent. The effect of solvent (internal) pressure on reaction rate has been extensively reviewed[10] and is discussed in several texts dealing with chemical kinetics.[11–14] Notwithstanding, there appears to be widespread confusion in the chemical community regarding (a) the validity and applicability of solvent pressure as a factor in reaction kinetics and (b) the relationship between internal and external pressure.

Scheme I



X = H or Cl

Simply stated, for the dissolution of a substance in a solvent, a hole (cavity) must be created within the solvent to accommodate the solute, a process which requires the expenditure of energy. The amount of energy expended will depend upon the magnitude of the intermolecular forces of attraction between the solvent molecules as well as on the volume of the solute. (In effect, the solvent exerts "pressure" on the solute.) For a chemical reaction whose volume of activation is non-zero, internal pressure can affect the reaction rate in a manner similar to externally applied pressure.

Despite the general acceptance and physical basis (vide infra) for this concept, there have been relatively few clear-cut reports of solvent pressure effects on reactivity in the literature. Reichardt has noted that the solvent-dependent rate constant for the Diels–Alder dimerization of cyclopentadiene ($\Delta V^\ddagger = -23.7$ cm^3/mol) can be correlated to internal pressure, although the correlation is poor.[12] A recent report by Grieco describes a significant rate and selectivity enhancement for several intermolecular Diels–Alder reactions when carried out in 5 M $LiClO_4$ in ether.[15] It was suggested that this enhancement could be attributed to the high internal pressure of the medium. However, this interpretation has been challenged by Dailey who, on the basis of an observed first-order dependence on [Li^+], argues that the effect arises from Lewis acid catalysis by Li^+.[16]

The potential effect of internal pressure on the competition between combination (k_{comb}) and disproportionation (k_{dis}) of alkyl

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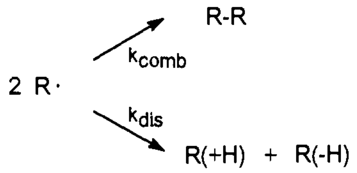
Scheme II



radicals (Scheme II) has been discussed, although it has often proven difficult to separate the role of internal pressure from that of other solvent effects, specifically polarity and viscosity.[17-23] In the case of *tert*-butyl radical, Schuh and Fischer argued that the variation in k_{comb}/k_{dis} was attributable to solvent viscosity, but the possible role of internal pressure could not be excluded.[20] In a subsequent paper, however, Neuman and Frink were able to exclude internal pressure as a contributing factor by examining the effect of *external* pressure on k_{comb}/k_{dis}.[22]

Ouellette and Williams[24] found a solvent effect on the anti→gauche conformational equilibria of 2-silabutane derivatives. Increasing solvent pressure was found to increase the population of the gauche conformation, consistent with the fact that its molar volume is ca. 4 cm^3/mol less than that of the anti conformation. Very recently, Neuman[25] found that the solvent effect on the rate of cis→trans isomerization of diazenes (RN=NR) could be directly related to internal pressure. Most intriguing was the fact that the volume of activation determined from the variation of the rate constant with internal pressure was, within experimental error, identical to that obtained by variation of *external* pressure.

Experimental Section

General Considerations. Gas chromatographic analyses were performed on a Hewlett-Packard HP 5890A equipped with FID detectors and an HP 3393A reporting integrator. Analyses were accomplished on either a 15- or 30-m SE-54 column (0.25 mm diameter). Solvents were obtained from Aldrich (bromobenzene, α-bromonaphthalene, butane, carbon disulfide, chlorobenzene, *p*-chlorotoluene, *o*-dichlorobenzene, Freon 11, and Freon 113), Fisher (benzene, chloroform, ethylene dibromide, ethylene dichloride, methylene chloride, and pentane), EM Science (carbon tetrachloride), and PCR Inc. (Freon 112) and were dried and distilled prior to use. *N*-Bromosuccinimide (Aldrich) was recrystallized from water and dried in vacuo. Toluene, cyclopropylbenzene, and *p*-chlorotoluene (Aldrich) were distilled prior to use.

Competition Experiments. General. The relative rate constants k_C/k_H (Scheme I) were obtained via the competitive free radical bromination of cyclopropylbenzene (CPB) vs toluene (TOL) or cyclopropylbenzene vs *p*-chlorotoluene (PCTOL). All reactions were run to a low percent conversion (i.e., $[PhCH_3]_0, [Ph\text{-}c\text{-}C_3H_5]_0 \geq 10[Br_2]_0$), which (a) effectively prevented further bromination of the primary reaction products (e.g., $PhCH_2Br \rightarrow PhCHBr_2$, etc.) and (b) allowed the assumption that the initial and final concentrations of the two competitors were equal. As noted in our earlier work,[9] yields were essentially quantitative. Product yields were determined by GLC, and the selectivity was calculated using eq 1.

$$\frac{k_C}{k_H} = \frac{\text{yield of PhCHBrCH}_2\text{CH}_2\text{Br}}{\text{yield of PhCH}_2\text{Br}} \frac{[\text{PhCH}_3]_0}{[\text{Ph-c-C}_3\text{H}_5]_0} \qquad (1)$$

Competitive Photobromination of Cyclopropylbenzene/Toluene. Typical Procedure. Toluene (0.845 g, 9.17 mmol), 1.29 g of cyclopropylbenzene (10.9 mmol), and 1.33 g of *o*-dichlorobenzene (9.03 mmol, internal standard for GLC analysis) were placed in a 25-mL volumetric flask and diluted to volume with the desired solvent. A 5.0-mL aliquot of this stock solution was transferred to a 30-mL Pyrex pressure tube (equipped with an O-ringed Teflon needle valve). The appropriate HBr scavenger (NBS, K_2CO_3, or epoxide) was added, and the solution was degassed 4× by the freeze–pump–thaw method. Bromine (ca. 10 μL, 0.2 mmol) was FPT degassed and distilled (via vacuum line) into the reaction mixture at -196 °C. The pressure tube was sealed, and the reaction mixture was allowed to warm to 21 (±1) °C in total darkness. The reaction mixture was allowed to thermally equilibrate (ca. 5 min) and was then irradiated with a 450-W medium-pressure mercury arc lamp at a distance of 2 ft through two Pyrex layers. Complete discharge of Br_2 color occurred within 2–5 min. Afterward, the solution was analyzed in triplicate via GLC. All competitions in each solvent were performed in triplicate (at least). Mean values of k_C/k_H (±one standard deviation) are summarized in Table III.

Competitive Photobromination of Cyclopropylbenzene/Toluene in Butane. Toluene (200 μL, 1.88 mmol), 290 μL of phenylcyclopropane (2.31 mmol), 200 μL of *o*-dichlorobenzene (1.78 mmol, internal standard for GLC), and 100 μL of 1,2-epoxybutane (1.16 mmol) were combined in a 30-mL Pyrex pressure tube. The mixture was cooled to -196 °C, and butane was condensed into the pressure tube (vacuum line) to a total volume of ca. 5 mL. The reaction mixture was FPT degassed 4×. Bromine (ca. 10 μL, 0.2 mmol) was FPT degassed and distilled (vacuum line) into the pressure tube. After sealing, the pressure tube was warmed to 21 (± 1) °C in the dark and irradiated (see above) for 2–5 min. After reaction, the mixture was cooled to -196 °C and 5–10 mL of CCl_4 was distilled into the pressure tube (vacuum line). The solution was warmed and analyzed by GLC. (The addition of CCl_4 served to lower the vapor pressure of the solution so that GLC analysis could be performed more conveniently.) Results from these experiments are also summarized in Table III.

Competitive Photobromination of Cyclopropylbenzene/*p*-Chlorotoluene. Typical Procedure. The cyclopropylbenzene/*p*-chlorotoluene competitions were conducted in exactly the same manner (and on the same scale) as the cyclopropylbenzene/toluene competions described above. The results are summarized in Table IV.

Competitive Photobromination of Toluene/*p*-Chlorotoluene. Typical Procedure. Toluene/*p*-chlorotoluene competitions for Br• were conducted in the same manner (and on the same scale) as the CPB/TOL and CPB/PCTOL competitions. The results are summarized in Table V.

Viscosity Measurements. Viscosities of the stock solutions were determined relative to trichlorofluoromethane (Freon 11, $\eta = 0.42$) using an Ostwald microviscometer according to eq 2,[26] where ρ_s, t_s, and η_s refer to the density, time required to flow through the capillary, and viscosity of the test solution, respectively, and ρ_{std}, t_{std}, and η_{std} are the corresponding parameters for Freon 11. Absolute viscosities for the cyclopropylbenzene/toluene stock solutions are summarized in Table III and are in excellent agreement with the literature values reported for each solvent.

$$\frac{\eta_s}{\eta_{std}} = \frac{t_s}{t_{std}} \frac{\rho_s}{\rho_{std}} \qquad (2)$$

Results and Discussion

I. HBr Scavenging. Possible variation in k_C/k_H arising from diffusive HBr reversal (reaction of HBr generated during the course of the reaction with $PhCH_2^•$ to regenerate toluene)[27,28] was minimized by conducting the reaction in the presence of an appropriate HBr scavenger such as K_2CO_3, NBS, or an epoxide. As illustrated by the results given in Table I, within experimental error, all methods of HBr scavenging were found to yield identical results. Most noteworthy were the runs carried out in the presence of an epoxide, which is generally regarded as the most reliable and efficient method of HBr scavenging. With a 25-fold variation in epoxide concentration, no significant variation in k_C/k_H was observed (Table II).

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Table I. Effect of Different HBr Scanvengers on k_C/k_H in Cyclopropylbenzene/Toluene Competitions for Br$^\bullet$ [a]

k_C/k_H[b]	HBr scavenger
1.00 ± 0.06	K_2CO_3[c]
0.96 ± 0.03	*N*-bromosuccinimide (NBS)[c]
1.06 ± 0.05	0.2 M 1,2-epoxybutane

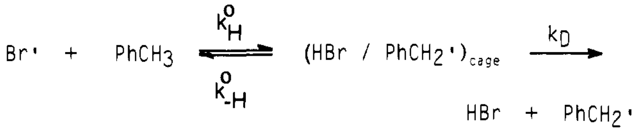
[a] 1,1,2-Trichloro-1,2,2-trifluoroethane (Freon 113) solvent at 21 °C. [b] Average of three determinations ± one standard deviation. [c] Heterogeneous HBr scavenger (K_2CO_3 and NBS were insoluble in Freon 113).

Table II. Effect of Epoxide Concentration on k_C/k_H in Cyclopropylbenzene/Toluene Competitions for Br$^\bullet$

[1,2-epoxybutane], M	k_C/k_H[a]
0.046	2.6 ± 0.3
0.23	2.4 ± 0.2
1.1	2.7 ± 0.3

[a] CS_2 solvent at 21 °C; average of three determinations ± one standard deviation.

Scheme III



$$Br^\bullet + PhCH_3 \underset{k^o_{-H}}{\overset{k^o_H}{\rightleftharpoons}} (HBr / PhCH_2^\bullet)_{cage} \xrightarrow{k_D} HBr + PhCH_2^\bullet$$

As reported previously,[9] solutions of CPB/Br_2 are stable in the dark for short periods of time (ca. 5–10 min) in CCl_4. Upon irradiation (450-W Hg arc lamp), 1,3-dibromo-1-phenylpropane is formed in nearly quantitative yield. With prolonged exposure to Br_2 (dark), (*p*-bromophenyl)cyclopropane is formed via an electrophilic aromatic substitution process. While small amounts of the EAS product are detected in some of our competition experiments, this does not distort the derived value of k_C/k_H since (a) the polar and free radical pathways are independent (i.e., each gives rise to a different product) and (b) the fact that $[Ph\text{-}c\text{-}C_3H_5]_o \gg [Br_2]_o$ ensures that the concentration of Ph-c-C_3H_5 does not change appreciably.

II. Cyclopropylbenzene/Toluene Competitions for Br$^\bullet$. As the data in Table III and IV demonstrate, k_C/k_H varies by nearly a factor of 20 over the range of solvents examined. For the CPB/TOL competition, a complete selectivity inversion is observed (from a minimum value of 0.51 in butane to a maximum value of 9.7 in α-bromonaphthalene). Several possible factors such as solvent viscosity, polarity, and internal pressure were examined in order to explain this unexpected solvent effect.

A. Solvent Viscosity. Tanner has proposed that "in-cage" HBr reversal may distort relative rate constants for hydrogen abstraction from toluenes and substituted toluenes (Scheme III), where back-reaction of the benzyl radical/HBr geminate pair (k^o–H) is competitive with diffusion out of the cage (k_D).[29-31] Mathematical models analogous to those used to quantitate the efficiency of geminate radical pair combination vs diffusion are applicable to Scheme III. From the steady-state approximation

$$k_{H,obsd} = \frac{k^o_H k_D}{k^o_{-H} + k_D} = k^o_H(1 - \beta) \qquad (3)$$

where β represents the cage efficiency defined as $k^o_{-H}/(k^o_{-H} + k_D)$.

For combination/diffusion of geminate radical pairs, relationships between β and solvent viscosity (η) have been derived on the basis of the parameter $F = 1/\beta - 1$, which for Scheme III is equivalent to k_D/k^o_{-H}. Thus, the observed value of k_C/k_H can be rewritten on the basis of eq 3 and F:

$$\frac{k_C}{k_H} = \frac{k_C}{k^o_H}(1 + F^{-1}) = \frac{k_C}{k^o_H} + \frac{k_C}{k^o_H}F^{-1} \qquad (4)$$

The Noyes model[36] predicts an inverse relationship between F and η ($F \propto \eta^{-1}$). If k_C and k^o_H are assumed to be viscosity independent,[37] on the basis of eq 4 it is anticipated that a plot of k_C/k_H vs η would be linear if geminate HBr reversal were responsible for the observed solvent effect. Utilization of the data in Table III results in a modest correlation ($R^2 = 0.6175$) between k_C/k_H and η for the cyclopropylbenzene/toluene system (Figure 1), primarily due to the data point corresponding to α-bromonaphthalene. When this single data point is excluded from the regression analysis, any perceivable correlation to viscosity vanishes ($R^2 = 0.0586$).

An alternative model for the diffusive behavior of geminate radical pairs developed by Koenig[38] predicts that F is proportional to $\eta^{-1/2}$. On the basis of eq 4, k_C/k_H is expected to be linearly related to $\eta^{1/2}$. The correlation between k_C/k_H and $\eta^{1/2}$ is slightly worse ($R^2 = 0.5252$). As above, the modest correlation which is observed arises primarily from the contribution of the data point corresponding to α-bromonaphthalene. Omission of this point from the analysis extinguishes the correlation ($R^2 = 0.0676$).

Both the Noyes and Koenig models accurately predict the kinetic behavior of caged radical pairs as a function of solution viscosity (excellent linear correlations between rate constants or product yields vs $1/\eta$ or $\eta^{-1/2}$ are observed). Consequently, the poor correlation observed between k_C/k_H and either η or $\eta^{1/2}$ provides a strong indication that the observed solvent effect is not attributable to solution viscosity and, hence, geminate HBr reversal.

B. Solvent Polarity. The potential contribution of solvent polarity to the observed variation of k_C/k_H was addressed by examining the relationship between selectivity and the dielectric constant (ϵ) of the solvent. The selection of ϵ as a measure of solvent was based primarily on the fact that it was the *only* parameter available for many of the solvents utilized in this study (all of which are essentially nonpolar).[39] No significant correlation between k_C/k_H and ϵ is observed ($R^2 = 0.2277$).

An alternative test of the role of solvent polarity based upon the Kirkwood formulation[12] was attempted. For the reaction A + B → C, the effect of solvent dielectric constant is described by eq 5, where μ and r refer to the dipole moments and radii, respectively, of the reacting species and transition state. As demonstrated by the plot of ln (k_C/k_H) vs the Kirkwood function $(\epsilon - 1)/(2\epsilon + 1)$ presented in Figure 2, the correlation is poor ($R^2 = 0.6399$).

$$\ln k = \ln k_o - \frac{1}{4\pi\epsilon_o}\frac{N}{RT}\frac{(\epsilon - 1)}{(2\epsilon + 1)}(\mu_A{}^2/r_A{}^3 + \mu_B{}^2/r_B{}^2 - \mu_\ddagger{}^2/r_\ddagger{}^3) \qquad (5)$$

On the basis of these arguments, solvent polarity does not appear to be the source of the observed solvent effect. This conclusion is reasonable since the ρ value for hydrogen abstraction from substituted toluenes ($\rho = -1.76$) is nearly identical to that reported

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[37] Both k_C and k_H fall well below the diffusion-controlled limit and are ca. 10^5 M^{-1} s^{-1} (ref 9).

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[39] While other, and undoubtedly better, measures of solvent polarity are available, most of the data available deal with solvents substantially more polar than those utilized in this study.

Table III. Rate Constant Ratio k_C/k_H as a Function of Solvent for Cyclopropylbenzene/Toluene Competitions for Br• at 21 °C

solvent	k_C/k_H[a]	dielectric constant (ϵ)[b]	viscosity (η), cP[c]	Hildebrand parameter (δ),[d] cal$^{1/2}$ cm$^{-3/2}$	internal pressure (P_i),[e] cal cm^{-3}
α-$C_{10}H_7Br$	9.7 ± 1 (4)	4.83	3.0	10.6	
$BrCH_2CH_2Br$	4.3 ± 0.1 (3)	4.78	1.4	9.7	107.8
$ClCH_2CH_2Cl$	4.2 ± 0.5 (5)	10.4	0.74	9.8	102
PhBr	4.0 ± 0.1 (3)	5.4	1.1	9.9	
CH_2Cl_2	3.9 ± 0.1 (3)	8.9	0.47	9.7	97.5
PhCl	3.6 ± 0.1 (3)	5.62	0.73	9.5	
$CHCl_3$	3.3 ± 0.1 (3)	4.7	0.59	9.3	88.3
PhH	2.9 ± 0.2 (9)	2.28	0.61	9.2	90.5
CS_2	2.5 ± 0.1 (7)	2.64	0.38	10	90
$CFCl_2CFCl_2CCl_4$ (1:3.5)	2.0 ± 0.1 (3)		1.0		
$CFCl_2CFCl_2$ CCl_4 (1:6)	1.9 ± 0.1 (3)		1.0		
CCl_4	1.8 ± 0.2 (6)	2.23	0.82	8.6	82.4
$CFCl_2CFCl_2$	1.5 ± 0.1 (3)	2.52	1.1	7.8	
$CFCl_2CFCl_2$:$CF_2ClCFCl_2$ (3:1)	1.5 ± 0.1 (3)		1.1		
$CFCl_3$	1.2 ± 0.1 (3)	2.28	0.42	8	
$CF_2ClCFCl_2$	1.0 ± 0.1 (9)	2.41	0.66	7.3	63.8
n-C_5H_{12}	0.57 ± 0.1 (3)	1.84	0.27	7	54.8
n-C_4H_{10}	0.51 ± 0.05 (3)			6.8	

[a] Average value ± one standard deviation; number of experiments appears in parentheses. [b] Values taken from ref 32 for all solvents except the Freons. Values for the Freon solvents were obtained from ref 33. [c] Measured. [d] Values taken from ref 34. [e] Values taken from ref 35.

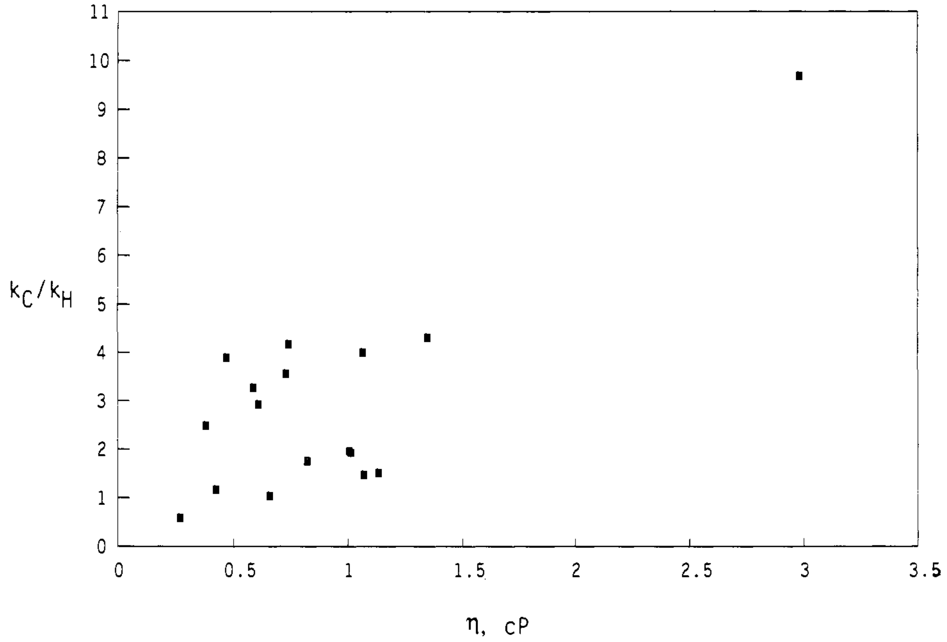

Figure 1. Variation of k_C/k_H with solution viscosity (CPB/TOL competitions).

for the S_H2 reaction between Br• and substituted cyclopropylbenzenes ($\rho = -1.84$), suggesting that both reactions proceed via transition states of similar polarity.[40]

C. Internal Pressure (Physical Basis and Interpretation of the Cavity Model). The internal pressure of a liquid (P_i) is a differential quantity which is defined as the energy change that accompanies a small volume change: $P_i = (\delta E/\delta V)_T$.[41] A related quantity is the cohesive energy density (ced), which is *approximately* related to internal pressure:

$$\text{ced} = \frac{\Delta E_V}{V_M} = \frac{\Delta H_V - RT}{V_M} = \delta^2 \qquad (6)$$

where ΔE_V and ΔH_V are the energy and enthalpy of vaporization for the pure liquid, respectively. The Hildebrand solubility parameter (δ) is equal to the square root of ced. (Values of δ and P_i for the solvents used in this work are tabulated in Table III.)

Qualitatively, P_i can be viewed as the pressure exerted by a solvent on a solute. Thus, internal pressure may alter a rate constant in a manner similar to externally applied pressure. The purpose of this section is to review the relationship between internal pressure, external pressure, and activation volumes as these concepts pertain to chemical reactivity.

1. External Pressure. The effect of pressure on a solution rate constant is expressed by eq 7, where $\Delta V^{\ddagger}$ is defined as the volume of activation (the difference between the molar volumes of the reactants and the transition state). Experimentally, $\Delta V^{\ddagger}$ is obtained by observing the effect of externally applied pressure on the rate constant in accordance with eq 7.[42]

$$(\delta \ln k/\delta P)_T = -\Delta V^{\ddagger}/RT \qquad (7)$$

2. Internal Pressure. For the dissolution to occur, a cavity must be created within the solvent to accommodate the solute. The work required to create this cavity will have an effect on the activity of the solute. Hildebrand developed an expression (eq 8) which describes the activity coefficient of the solute (i), where $V_{m,i}$ and $V_{m,s}$ are the molar volume of the solute and solvent,

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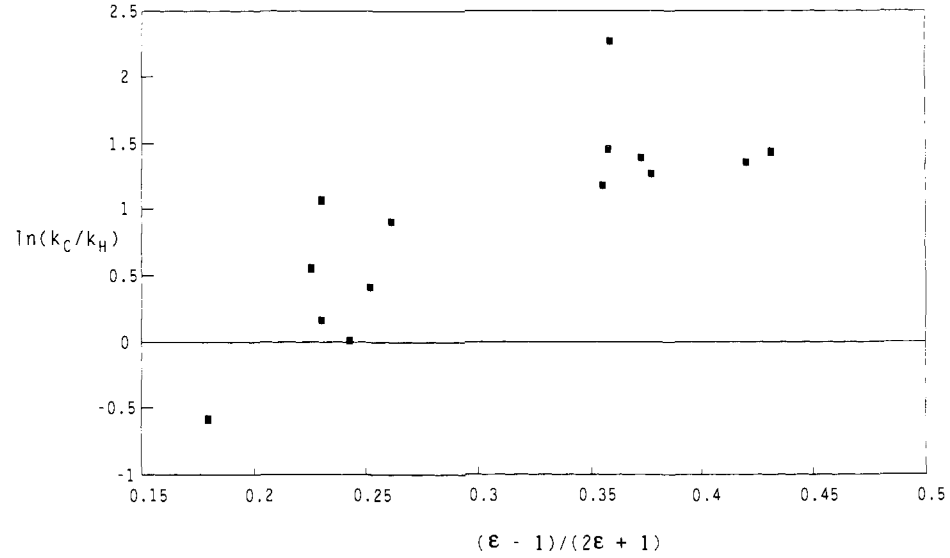

Figure 2. Variation of ln (k_C/k_H) with the Kirkwood function ((ϵ − 1)/(2ϵ + 1); CPB/TOL competitions).

respectively, ϕ_s is the volume fraction of the solvent, and $\Delta E_{v,i}$ and $\Delta E_{v,s}$ are the energy of vaporization of the pure solute and solvent, respectively.[10-14]

$$RT\ln f_i = V_{m,i}\phi_s^2[(\Delta E_{v,i}/V_{m,i})^{1/2} - (\Delta E_{v,s}/V_{m,s})^{1/2}]^2 \qquad (8)$$

For a dilute solution, $\phi_s \approx 1$, and it follows that

$$RT\ln f_i = V_{m,i}(\delta_i - \delta_s)^2 \qquad (9)$$

For a chemical reaction in solution, A + B → [transition state] → products, ln k = ln k_o + ln f_A + ln f_B − ln $f_‡$ where k_o is the rate constant in an ideal solution. Thus,

$$RT\ln k = RT\ln k_o[V_A(\delta_A - \delta_S)^2 + V_B(\delta_B - \delta_S)^2 - V_‡(\delta_‡ - \delta_S)^2] \qquad (10)$$

where V_A, V_B, and $V_‡$ refer to the molar volumes of A, B, and the transition state, respectively, and the δ's refer to the corresponding Hildebrand parameters.[10-14] Expansion of eq 10 demonstrates that the relationship between ln k and δ_S is quadratic (eq 11) and reduces to the same mathematical form as the expression (eq 7) which describes the effect of *external* pressure (if $A\delta^2 > B\delta$):

$$RT\ln(k/k_o) = A\delta_S^2 + B\delta_S + C \qquad (11)$$

where $A = -\Delta V^‡/RT$, $B = -2(V_A\delta_A + V_B\delta_B - V_‡\delta_‡)/RT$, $C = (V_A\delta_A^2 + V_B\delta_B^2 - V_‡\delta_‡^2)/RT$, and $\Delta V^‡ = V_‡ - V_A - V_B$.

There are several underlying assumptions pertaining to successful application of eq 11 to explain the solvent pressure effect. The first is that the solution is *regular* (i.e., there is a random distribution of solute and solvent molecules). Further, it is assumed that V_A, V_B, $V_‡$, δ_A, δ_B, and $\delta_‡$ are independent of solvent and, thus, can be treated as constants. As a consequence of the foregoing assumptions, specific solute–solvent interactions (e.g., ion–dipole or dipole–dipole interactions, hydrogen bonding, etc.) are not accounted for in this model. Such specific interactions may reduce the size of the cavity (e.g., electrostriction) or may alter V_A, V_B, or $V_‡$. *This model is therefore best applied to reactions of nonpolar species in nonpolar solvents.* Additionally, ced and P_i are not equivalent when there are strong intermolecular interactions (e.g., hydrogen bonding) in the solvent. Undoubtedly, failure to recognize these restrictions has resulted in several instances where the interpretation of a solvent effect as arising from internal pressure was incorrect. These instances have in turn led to a surprisingly widespread misconception that the notion of internal pressure effects on reactivity is without merit.

A very good correlation between ln (k_C/k_H) and the square of the Hildebrand parameter (δ^2 = ced, R^2 = 0.9164) is found (Figure 3). This correlation can be explained by assuming that $\Delta V^‡$ for the S_H2 process is more negative than for the hydrogen abstraction process. If we assume that the δ^2 term in eq 11 is dominant, linear least-squares analysis of the data in Figure 3 yields a slope m = 0.038 ± 0.003 cm^3/cal, corresponding to $\Delta\Delta V^‡ = \Delta V^‡_C - \Delta V^‡_H$ = −22 (±1) cm^3/mol. The correlation between ln (k_C/k_H) and P_i is even better (Figure 4, R^2 = 0.9531), although fewer data points are used because of the unavailability of P_i's for several of these solvents. The slope of the line (0.040 ± 0.003 cm^3/cal) and derived activation volume difference ($\Delta\Delta V^‡$ = −23 ± 2 cm^3/mol) are within experimental error of that obtained from the correlation to δ^2.

III. Cyclopropylbenzene/*p*-Chlorotoluene Competitions for Br•. An identical variation in k_C/k_H with solvent to that observed in the CPB/TOL system was observed for the cyclopropylbenzene/*p*-chlorotoluene (CPB vs PCTOL) competitions for Br• (Table IV). As with the CPB/TOL competitions, ln (k_C/k_H) is linearly related to both δ^2 and P_i (Figures 3 and 4) with R^2 values of 0.8650 and 0.9053, respectively. Within experimental error, the slopes of these plots (0.031 ± 0.004 cm^3/cal vs δ^2; 0.035 ± 0.004 cm^3/cal vs P_i) are identical (a) to each other and (b) to the analogous plots for the CPB/TOL competitions. The derived $\Delta\Delta V^‡$ values are 18 (±2) and 20 (±2) cm^3/mol for the δ^2 and P_i correlations, respectively.

These results are significant for several reasons. First, they demonstrate the generality of the solvent effect. Second, the fact that both the CPB/TOL and CPB/PCTOL competitions behave *identically* as a function of solvent either (a) provides additional support for the argument that geminate HBr reversal is not a significant factor in these systems or (b) means toluene and *p*-chlorotoluene display (fortuitously) an identical degree of reversal. The latter interpretation, however, is not consistent with several other observations. On the basis of the difference in reactivity, the activation energy for $ArCH_3$ + Br• → $ArCH_2$• + HBr differs by ca. 0.4 kcal/mol for TOL and PCTOL. (Utilizing MNDO, Gilliom calculates an activation energy difference of 0.7 kcal/mol.)[43] The bond dissociation energies of toluene and *p*-chlorotoluene differ by less than 0.1 kcal/mol,[44] suggesting that $\Delta H°$ for both substrates is approximately equal. On this basis, k_{-H} (Scheme III) for X = Cl is expected to be smaller than for X = H (i.e., geminate HBr reversal should be less important for *p*-chlorotoluene).

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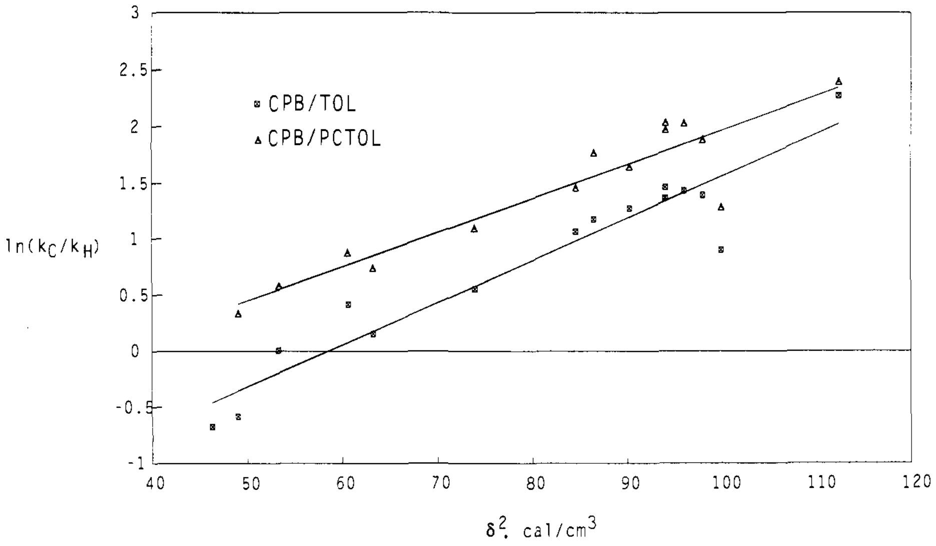


Figure 3. Variation of ln (k_C/k_H) with the cohesive energy density of the solvent (CPB/TOL and CPB/PCTOL competitions).

Table IV. Rate Constant Ratio k_C/k_H as a Function of Solvent for Cyclopropylbenzene/*p*-Chlorotoluene Competitions for Br$^•$ at 21 °C

solvent	k_C/k_H[a]	solvent	k_C/k_H[a]
α-$C_{10}H_7Br$	11 ± 1	PhH	4.3 ± 0.1
$BrCH_2CH_2Br$	7.2 ± 0.2	CS_2	3.6 ± 0.1
$ClCH_2CH_2Cl$	7.6 ± 0.4	CCl_4	3.0 ± 0.1
PhBr	6.6 ± 0.2	$CFCl_2CFCl_2$	2.4 ± 0.1
CH_2Cl_2	7.7 ± 0.4	$CFCl_3$	2.1 ± 0.1
PhCl	5.2 ± 0.6	$CF_2ClCFCl_2$	1.8 ± 0.1
$CHCl_3$	5.9 ± 0.2	*n*-C_5H_{12}	1.4 ± 0.1

[a] Average of three experiments ± one standard deviation.

Table V. Relative Reactivities of Toluene (TOL) and *p*-Chlorotoluene (PCTOL) toward Br$^•$ as a Function of Solvent

solvent	k_{PCTOL}/k_{TOL} (direct competition)[a]	k_{PCTOL}/k_{TOL} (indirect competition)[b]
α-$C_{10}H_7Br$	0.55 ± 0.04	0.87 ± 0.17
C_6H_5Br	0.55 ± 0.06	0.60 ± 0.02
C_6H_5Cl	0.61 ± 0.01	0.68 ± 0.10
C_6H_6	0.55 ± 0.02	0.68 ± 0.06
CCl_4	0.69 ± 0.02	0.59 ± 0.09
$CFCl_2CFCl_2$	0.67 ± 0.01	0.63 ± 0.07
$CFCl_3$	0.64 ± 0.01	0.56 ± 0.07
$CF_2ClCFCl_2$	0.61 ± 0.01	0.56 ± 0.08

[a] Experimentally determined via competitive bromination of toluene and *p*-chlorotoluene at 21 °C. Results represent the average of three determinations ± one standard deviation. [b] Calculated from the data in Tables III and IV: $(k_{PCTOL}/k_{TOL}) = (k_C/k_H)_{X=H}/(k_C/k_H)_{X=Cl}$.

IV. Toluene/*p*-Chlorotoluene Competitions for Br$^•$. The relative reactivity of *p*-chlorotoluene and toluene (k_{PCTOL}/k_{TOL}) for Br$^•$ was examined by direct competition in several solvents, and the results are summarized in Table V. For solvents where published values are available, the agreement with our results is excellent. Despite the fact that the solvents selected for study exhibit large variations in both viscosity and internal pressure, the variation in k_{PCTOL}/k_{TOL} is less than 10% ($k_{PCTOL}/k_{TOL} = 0.61 \pm 0.05$). The small variation in selectivity which is observed does not correlate with any of the solvent properties discussed herein. Thus, we conclude that for all practical purposes k_{PCTOL}/k_{TOL} is independent of solvent.

Finally, the data derived from both the CPB/TOL and CPB/PCTOL competitions demonstrate that our relative rate constants are both reproducible and internally consistent. For each solvent, division of k_C/k_H measured for the CPB/TOL competition by k_C/k_H measured for the CPB/PCTOL yields the relative reactivity of *p*-chlorotoluene vs toluene toward Br$^•$ (k_{PCTOL}/k_{TOL}). Within experimental error, the selectivity determined in this indirect manner was identical to that measured via direct TOL vs PCTOL competition (Table V).

V. Origin of Difference in $\Delta V^{\ddagger}$ for the S_H2 and Hydrogen Abstraction Reactions. In order to rationalize the observed variation of k_C/k_H with internal pressure, it is necessary to assume

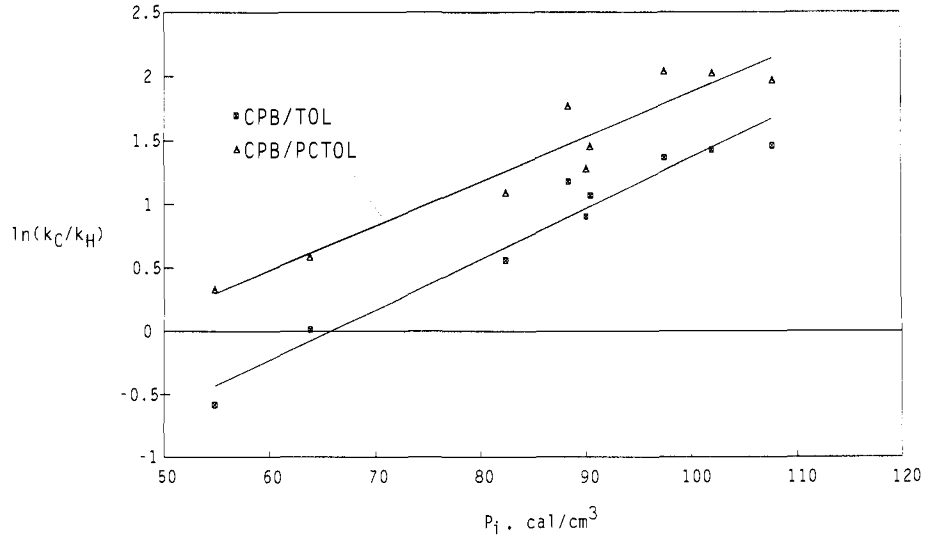
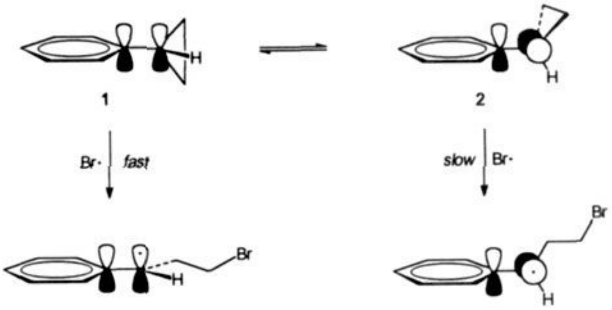


Figure 4. Variation of ln (k_C/k_H) with the internal pressure of the solvent (CPB/TOL and CPB/PCTOL competitions).

that the activation volume associated with the S_H2 (k_C) process is more negative than that associated with the hydrogen abstraction (k_H) process. Because the S_H2 process effectively involves the addition of Br• to a cyclopropane ring (i.e., two reactants generate one product), it is reasonable to suspect that the process would have a more negative activation volume than a hydrogen abstraction process (where two reactants generate two products). An estimate of $\Delta\Delta V^{\ddagger}$ based upon the linear variation of $\ln(k_C/k_H)$ with either δ^2 or P_i places it on the order of -20 cm^3/mol. While no data is available for Br• reactions specifically, the effect of external pressure on other atom abstraction and addition reactions is known, and the differences in activation volumes are consistent with this proposal. For example, $\Delta V^{\ddagger}$ for t-BuO• + $PhCH_3 \rightarrow t$-BuOH + $PhCH_2$• is -14.4 cm^3/mol.[42] In comparison, $\Delta V^{\ddagger}$ is considerably more negative for a bimolecular process which results in a single product (ca. -22 cm^3/mol for the propagation step of a free radical polymerization; ca. $-30 \rightarrow -40$ cm^3/mol for a Diels–Alder reaction).[42] On the basis of these values, a difference in the activation volume of ca. 15–30 cm^3/mol for the S_H2 and hydrogen atom abstraction processes seems plausible.

Another factor which may contribute to the observed solvent pressure effect is related to stereoelectronic factors. Cyclopropylbenzene exists in two conformations: bisected (1) and perpedicular (2). The bisected conformation is more stable by about 1.4 kcal/mol[45,46] because of favorable interactions between the cyclopropane HOMO and the aromatic LUMO.[47,48] We have previously shown that the bisected conformation is substantially more reactive toward Br• because of this favorable orbital orientation (Scheme IV).[9] We suggest that part of the variation in k_C/k_H may arise because the relative populations of these two conformations vary with internal pressure (i.e., the relative population of the more reactive bisected conformation increases with increasing solvent pressure). Future work in our laboratory will examine the effect of externally applied pressure both on k_C/k_H and on the conformational equilibrium of cyclopropylarenes.

Scheme IV



VI. Conclusions. (1) An unexpectedly large solvent effect on Br• selectivity has been discovered. (2) Internal pressure emerges as the solvent property which *best* explains the observed selectivity trend. More familiar solvent parameters such as viscosity or polarity do not adequately explain the observed solvent effect. (3) The successful correlation of our rate data with internal pressure is attributable to the fact that the systems selected for investigation closely approximate regular solutions, a necessary prerequisite for the cavity model. In this study, exclusively nonpolar solvents were utilized. Consequently, intermolecular interactions are not orientation dependent (i.e., van der Waals forces are the dominant intermolecular interaction in solution), in accord with the requirements for a regular solution. (4) On the basis of the observed solvent pressure dependence of k_C/k_H, $\Delta\Delta V^{\ddagger}$ is estimated to be -20 cm^3/mol. The fact that the same conclusion is reached by utilizing either the cohesive energy density of the solvent (δ^2) or the internal pressure (P_i) simply reflects the fact that for nonpolar solvents these parameters are approximately equal.

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