J. Am. Chem. Soc. 1994, 116, 5162–5166

Solvent Pressure Effects in Free Radical Reactions. 2. Reconciliation of the Gas and Condensed Phase Chlorination of Cyclopropane

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Received December 10, 1993[⊗]

Abstract: The results reported herein demonstrate that the chemoselectivity (S_H2 ring opening vs abstraction of a cyclopropyl hydrogen) associated with the free radical chlorination of cyclopropane is solvent dependent. Internal pressure is implicated as the solvent parameter responsible for the observed solvent effect. (Solvents of high internal pressure favor the S_H2 process; hydrogen abstraction becomes more important in solvents of low internal pressure or in the gas phase.) Extrapolation of the solution phase results to zero internal pressure accurately predicts the gas-phase result, suggesting that the difference in chemoselectivity between the vapor- and condensed-phase reactions is attributable to internal pressure in the condensed phase medium. No evidence for the chlorine atom cage effect is found in the chlorination of cyclopropane.

Introduction

Reaction of a radical ($X^\bullet$) with cyclopropane proceeds via two pathways: (a) S_H2 ring opening yielding $XCH_2CH_2CH_2^\bullet$ and (b) hydrogen abstraction yielding H–X and the cyclopropyl radical. The relative importance of these two pathways depends on the nature and identity of the attacking radical. The hydrogen atom abstraction pathway predominates when $X^\bullet$ is an alkoxy[3] or imidyl radical[4] whereas only ring opening is found when X = Br.[5–8]

For X = Cl, both pathways operate, and depending on the reaction conditions, variable amounts of hydrogen abstraction and ring opening are observed. In 1945, Roberts reported the vapor phase chlorination of cyclopropane (Scheme 1).[9] The major reaction products were cyclopropyl chloride and 1,1-dichlorcyclopropane. Only small amounts of ring-opened products were detected.

In contrast, Walling reported in 1962 that the ring-opening reaction predominates when the reaction is conducted in the condensed phase (Table 1).[3] This inversion in chemoselectivity between the gas- and condensed-phase results has hitherto not been satisfactorily explained.

We have recently shown that the intermolecular competition between hydrogen abstraction and S_H2 pathways in free radical brominations can be influenced by solvent.[10] Specifically, the rate constant ratio for S_H2 ring opening of phenylcyclopropane (k_C) vs hydrogen abstraction from toluene (k_H) by bromine atom (Scheme 2) was found to vary by nearly a factor of 20 as a function of solvent. This observed variation of selectivity with solvent could be correlated to the internal pressure of the solvent. Because the S_H2 process is essentially an addition reaction (i.e., two reactants $Br^\bullet$ + Ph-c-C_6H_5 generate one product $PhC^\bullet HCH_2CH_2Br$), it has a more negative activation volume ($\Delta\Delta V^\ddagger = -20$ cm^3/mol) than the hydrogen abstraction process wherein two reactants ($Br^\bullet + PhCH_3$) generate two products ($HBr + PhCH_2^\bullet$). Thus, solvents of high internal pressure tend to favor the ring opening pathway (k_C), while for solvents of low internal pressure, hydrogen abstraction (k_H) is favored.

On the basis of these earlier observations, we hypothesized that solvent internal pressure might *also* explain the discrepency between the gas- and condensed-phase chlorination of cyclopropane, since the yields of ring-opened vs hydrogen abstraction products reflect the *intramolecular* competition between k_C and k_H (Scheme 3). In this paper, we report the results of a series of experiments which confirm this hypothesis.

Experimental Section

A. General Considerations. Gas chromatographic analyses were performed on a Hewlett-Packard HP 5890A instrument equipped with FID detectors and an HP 3393A reporting integrator. Analyses were accomplished with either an SE-30 or SE-54 capillary collumn (30 × 0.25 mm). Products were identified by comparison of the retention time to that of an authentic sample and quantitated vs a measured amount of an appropriate internal standard (chlorobenzene) utilizing predetermined GLC correction factors. Cyclopropane, 2,3-dimethylbutane, 1,3-dichloropropane, Freon 113, Freon 11, CCl_4, CH_2CH_2, and $ClCH_2CH_2Cl$ were obtained from Aldrich and used without purification. Chloroform was obtained from Fisher and distilled prior to use.

B. Chlorination of Cyclopropane and 1,3-dichloropropane. The typical procedure follows: One milliliter of solvent (or 1,3-dichloropropane) was placed in a ca. 1.2 mL Pyrex pressure tube (equipped with a Teflon needle valve). Cyclopropane was measured manometrically and condensed into the pressure tube via a vacuum line. Reaction mixtures were degassed 3–4× by the freeze–pump–thaw method (freezing to −196 °C and thawing at room temperature). Cl_2 was measured with a calibrated gas pipet and purified immediately before use by condensation from a trap at −78 °C directly into the degassed reaction mixture. (Typically a ≥10-fold excess of cyclopropane relative to Cl_2 was used.) The pressure tube was sealed, wrapped in aluminum foil, placed in a thermostatically maintained water bath, and equilibrated in the *dark* for 5–10 min. The reaction mixture was then irradiated with a 150-W tungsten lamp for ca. 5 min. Afterward, a measured amount of chlorobenzene (internal standard) was added, and the reaction mixture was analyzed directly by GLC in triplicate. *Important note*: Because of the volatility of cyclopropane and Cl_2, use of a pressure tube with minimal dead volume and shielding of the gas phase from light during irradiation were critical during irradiation. Failure to follow these precautions led to erratic (and irreproducible) results.

[⊗] Abstract published in *Advance ACS Abstracts*, May 15, 1994.

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Scheme 1

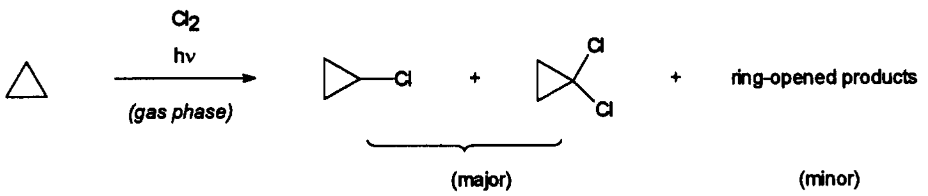
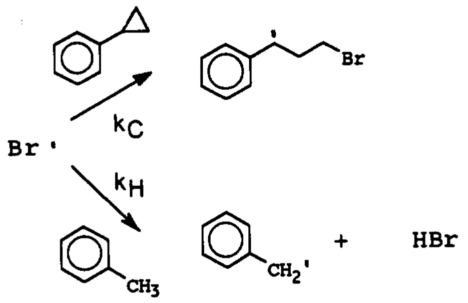


Table 1. Products/Yields Arising from the Free Radical Chlorination of Cyclopropane (Condensed Phase)[a]

solvent (temp, °C)	yield, %		
	1,3-dichloropropane	cyclopropyl chloride	1,1,3- and 1,2,3-trichloropropane
CCl_4 (0)	61.4	15.4	23.2
CCl_4 (68)	33.5	47.3	19.2
PhH (68)	42.3	48.2	9.5

[a] Data from ref 3.

Scheme 2



Results

I. The Condensed-Phase Chlorination of Cyclopropane. As reported by Walling, the major products of the condensed-phase free radical chlorination of cyclopropane are cyclopropyl chloride, 1,1-dichlorocyclopropane, 1,3-dichloropropane, 1,1,3-trichloropropane, and 1,2,3-trichloropropane, produced in quantitative yield. As anticipated, the relative yields of these products were found to vary reproducibly with solvent (Table 2). The possible formation of any of these products via polar (electrophilic) pathways was rigorously excluded because there was no detectable reaction between cyclopropane and Cl_2 in the dark.

II. Origin of 1,1,3- and 1,2,3-Trichloropropane in the Photochlorination of Cyclopropane. The results in Table 2 show that in all solvents, significant yields of trichlorides (1,1,3- and 1,2,3-trichloropropane) are produced in the photochlorination of cyclopropane. Similar observations were also reported by Walling in CCl_4 and benzene (Table 1).[3] Because these products may arise from further chlorination of *either* (or both) of the two primary reaction products (chlorocyclopropane or 1,3-dichlorocyclopropane), it is critical that the source and mechanism of formation of these products be ascertained in order to allow an accurate determination of k_C/k_H.

Initially, we thought that these trichlorides may arise from the chlorine atom "cage effect" first discovered by Skell in 1985[11] and subsequently confirmed and extended by others.[12-14] Put briefly, in the halogen atom transfer step of the free radical chlorination of an alkane ($R^\bullet + Cl_2 \rightarrow R\text{–}Cl + Cl^\bullet$), alkyl chloride and chlorine atom are initially formed as a geminate caged pair ($RCl/Cl^\bullet$). Because of the high reactivity of chlorine atom (whose bimolecular rate constants for hydrogen abstractions from alkanes are nearly diffusion-controlled), a second hydrogen can be abstracted from R–Cl at a rate competitive with cage escape. For the reaction of cyclopropane with Cl_2, it is also conceivable that S_H2 ring opening might also occur "in-cage". The possible consequences of this cage effect are summarized in Scheme 4.

A. Effect of Cyclopropane Concentration on Trichloride Yield. Experimentally, the cage effect was excluded by examining the effect of alkane concentration on the poly- to monochloride ratio (P/M).[11-14] In an inert solvent (e.g., CCl_4), polychloride formation is most important at low alkane concentrations. At low alkane concentrations, the cage walls are comprised mostly of inert solvent, and the in-cage reaction of $RCl/Cl^\bullet$ is competitive with diffusion out of the cage. However, as the alkane concentration is increased P/M decreases smoothly. This trend is observed because at high alkane concentrations, the alkane becomes an increasingly important constituent of the cage walls. The chlorine atom in the geminate $RCl/Cl^\bullet$ caged pair preferentially reacts with the alkane comprising the cage walls via hydrogen abstraction, rather than RCl.

The data summarized in Table 3 demonstrate that the relative yield of the two trichlorides is not affected by cyclopropane concentration. (In fact, rather than a decrease, there is a slight increase in the relative yield of the trichlorides with increasing cyclopropane concentration). These results suggest that the chlorine atom cage effect is inoperative in the free radical chlorination of cyclopropane. Similarly, the fact that trichloride formation is significant in benzene solvent (Table 1) corroborates this hypothesis, since aromatic solvents have been shown to suppress the cage effect.[13] (The absense of a detectable cage effect in this system is attributable to the fact that cyclopropane and 1,3-dichloropropane are significantly less reactive than alkanes toward $Cl^\bullet$, vide infra).

B. Relative Reactivity of 1,3-Dichloropropane and Cyclopropane toward Chlorine Atom. Because some of the products resulting from the photochlorination of cyclopropane and 1,3-dichloropropane are the same, a direct competition experiment between these two substrates for $Cl^\bullet$ was not feasible. Instead, we chose to perform competitions pitting these substrates against a third substrate, 2,3-dimethylbutane (23DMB).

Competition experiments pitting 23DMB vs cyclopropane for $Cl^\bullet$ (20 °C, CCl_4 solvent) yielded $k_{DMB}/(k_C + k_H) = 265 \pm 13$.[15] A similar competition pitting 23DMB against 1,3-dichlorocyclopropane (13DCP) for $Cl^\bullet$ yielded $k_{DMB}/k_{13DCP} = 10.8 \pm 0.5$.[16] Consequently, in terms of reactivity toward chlorine atom 2,3-dimethylbutane (1.0) > 1,3-dichlorocyclopropane (0.093) > cyclopropane (0.0038). The diminished reactivity of 1,3-dichloropropane relative to 23DMB is attributable to the well-documented polar effect of the chloro substituents.[17] Hydrogen abstraction from cyclopropane is sluggish due the C–H bond being stronger in cyclopropane than in ordinary alkanes.[18] It is

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(15) $k_{DMB}/(k_C + k_H)$ = (yield of all DMB derived products) ÷ (yield of all cyclopropane derived products) × ($[C_3H_6]_i/[23DMB]_i$).

(16) $k_{DMB}/(k_{13DCP})$ = (yield of all DMB derived products) ÷ (yield of 1,1,3- and 1,2,3-trichloropropane) × ($[13DCP]_i/[23DMB]_i$).

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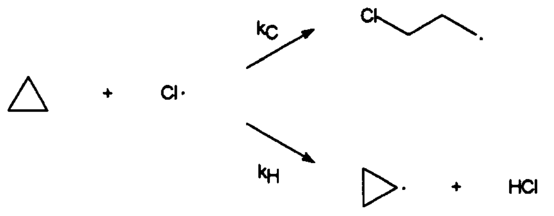
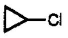
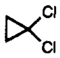
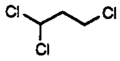
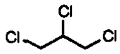
Scheme 3



favored by high internal pressure solvents

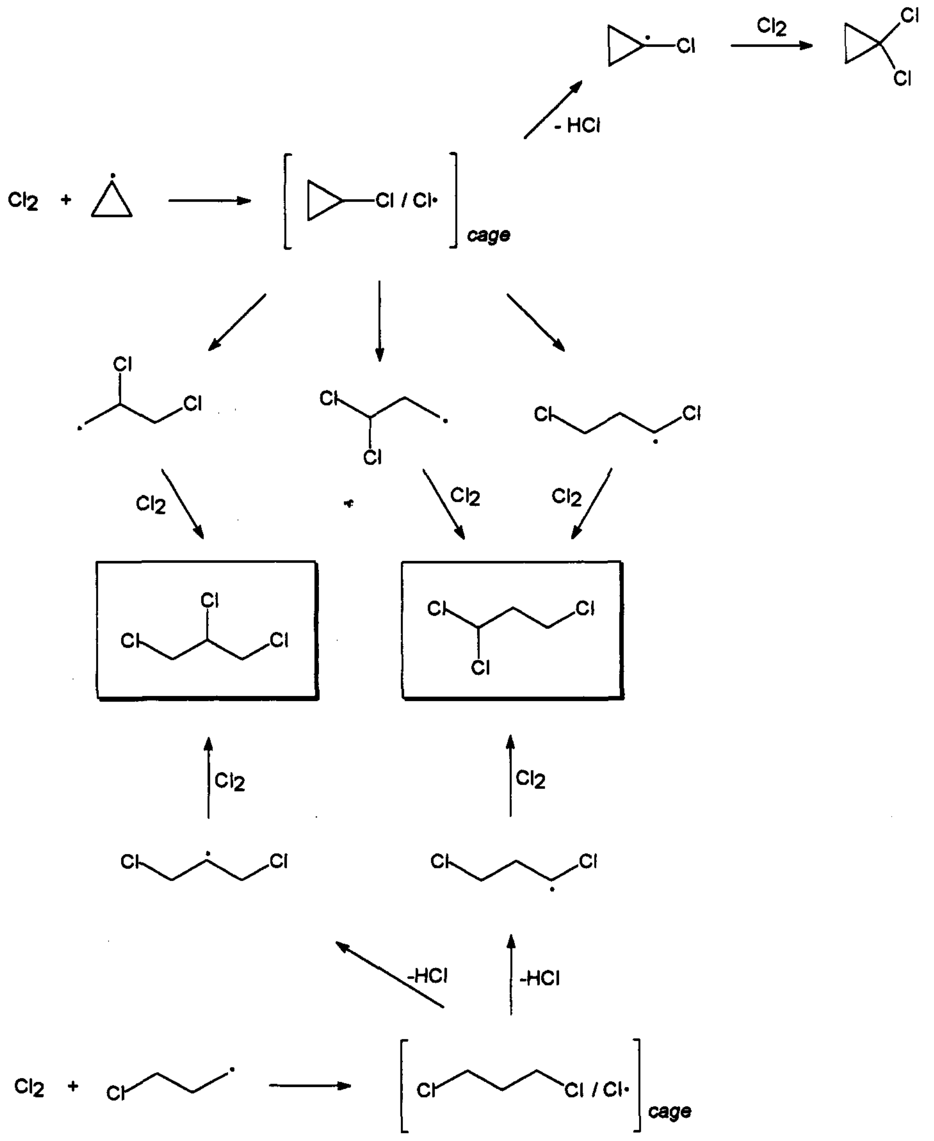
favored by solvents of low internal pressure or the gas phase

Table 2. Free Radical Chlorination (%) of Cyclopropane in Several Solvents and in the Gas Phase at 21 °C

solvent						$k_{C}k_{H}$[a]
gas phase	71	6.3	12	5.7	5.4	0.25 ± 0.05
$CF_2ClCFCl_2$	14	0.6	66	12	8.2	6.7 ± 0.5
$CFCl_3$	11	0.4	67	13	8.7	7.9 ± 1.8
CCl_4	6.2	*b*	77	10	7.1	15 ± 0.4
$CHCl_3$	1.7	*b*	94	2.3	1.6	58 ± 3
CH_2Cl_2	1.4	*b*	96	1.4	1.1	72 ± 7
$ClCH_2CH_2Cl$	1.1	*b*	97	1.2	1.1	93 ± 16

[a] The concentrations of reactants were held constant for all of these experiments (0.12 mmol Cl_2 and 1.7 mmol cyclopropane in 1.0 mL solvent). k_C/k_H = (total yield of 1,3-dichloropropane + 1,1,3-trichloropropane + 1,2,3-trichloropropane) ÷ (total yield of cyclopropyl chloride + 1,1-dichlorocyclopropane). Reported value represents the average of three trials ± one standard deviation. [b] None detected.

Scheme 4



noteworthy that the rate constants for reaction of Cl• with both cyclopropane and 1,3-dichloropropane fall below the diffusion-controlled limit,[19] which confirms that no cage effect is possible in the chlorination of cyclopropane.

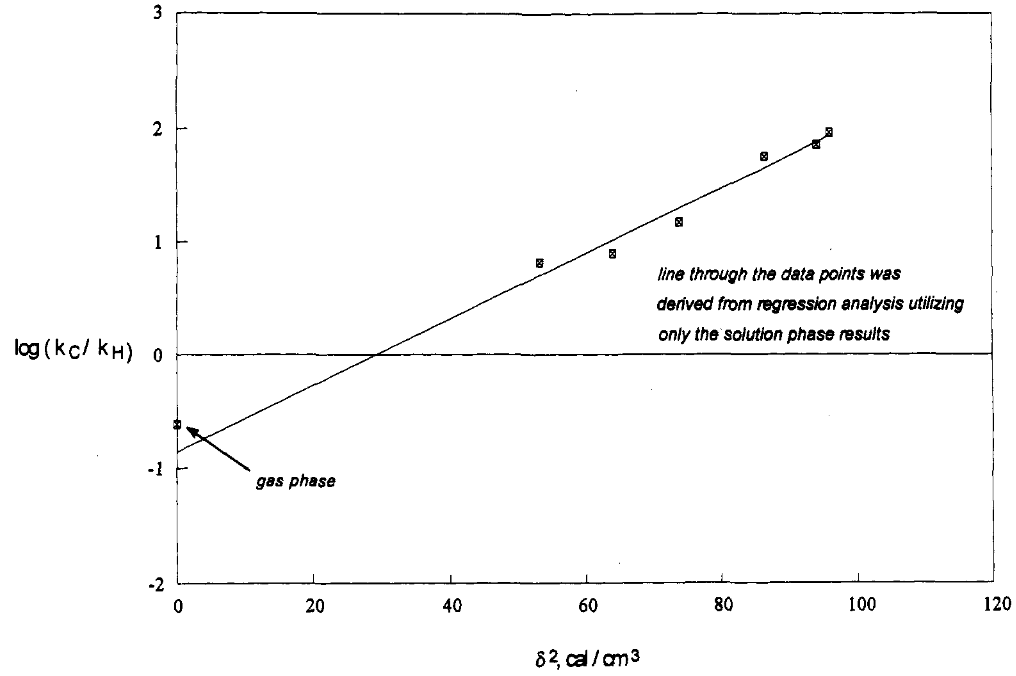


Figure 1. Variation of $\log(k_C/k_H)$ with the cohesive energy density of the solvent for the free radical chlorination of cyclopropane.

Table 3. Yield of Trichlorides Relative to Primary Chlorination Products in the Free Radical Chlorination of Cyclopropane (CCl_4 Solvent, 21 °C)

[cyclopropane], [a]*M*	rel yield of trichlorides[b]	[cyclopropane], [a]*M*	rel yield of trichlorides[b]
0.12	0.20	1.9	0.29
0.37	0.23	3.4	0.31

[a] For all experiments, the initial ratio of cyclopropane to Cl_2 was 15:1. [b] (Combined yield of 1,1,3- and 1,2,3-trichloropropane) ÷ (combined yield of cyclopropyl chloride + 1,1-dichlorocyclopropane + 1,3-dichloropropane).

C. Direct Chlorination of 1,3-Dichloropropane. Direct chlorination of 1,3-dichlorpropane at 21 °C (neat) yields 1,1,3- and 1,2,3-trichloropropane in a 1.1 (±0.1) to 1 ratio. Within experimental error, this product ratio is identical to that observed in all of our condensed-phase reactions of cyclopropane (1.3 ± 0.2). This observation provides compelling evidence that the trichlorides observed in the chlorination of cyclopropane originate from the diffusive encounter of $Cl^\bullet$ with 1,3-dichloropropane formed during the course of the reaction.

III. Calculation of k_C/k_H. Having established that, in the chlorination of cyclopropane, the trichlorides (1,1,3- and 1,2,3-trichloropropane) arise from the diffusive chlorination of one of the primary reaction products (1,3-dichlorocyclopropane), k_C/k_H can be calculated from the yield of hydrogen abstraction products (chlorocyclopropane and 1,1-dichlorocyclopropane) relative to the yield of S_H2 (and derived) products (1,3-dichlorocyclopropane and 1,1,3- and 1,2,3-trichloropropane). These relative rate constants are summarized in Table 2.

Discussion

The effect of external pressure on reaction rate is expressed by eq 1, where ΔV_{act}, the volume of activation, is equal to the difference in molar volume between the transition state and the reactants.[20]

$$(\delta \ln k/\delta P)_T = -\Delta V_{act}/RT \qquad (1)$$

The internal pressure of a liquid is a differential quantity which describes the energy change which accompanies a small change in volume ($P_i = (\delta E/\delta V)_T$).[21] Cohesive energy density (ced) is a related quantity which is described by eq 2, where ΔE_V and ΔH_V refer to the energy and enthalpy of vaporization, respectively, and V_m refers to the molar volume of the pure liquid. The Hildebrand solubility parameter (δ) is equal to $\text{ced}^{1/2}$. For solvents where the main forces of attraction are London dispersion forces (i.e., there are no orientation-dependent interactions such as hydrogen bonding or dipole–dipole interactions), $P_i \approx \delta^2$.

$$\text{ced} = \Delta E_V/V_m = -(\Delta H_V - RT)/V_m = \delta^2 \qquad (2)$$

The theory regarding the effect of internal pressure on reaction rates has been discussed.[22-26] For the reaction A + B → transition state, the effect of internal pressure on a rate constant is described by eq 3,

$$\ln(k/k_0) = A\delta_S^{\,2} + B\delta_S + C \qquad (3)$$

where $A = -\Delta V_{act}/RT$, $B = -2(V_A\delta_A + V_B\delta_B - V_\ddagger\delta_\ddagger)/RT$, and $C = V_A\delta_A^{\,2} + V_B\delta_B^{\,2} - V_\ddagger\delta_\ddagger^{\,2})/RT$ (k_o represents the rate constant in an ideal solution, V_m's and δ_m's refer to the molar volumes and Hildebrand parameters associated with A, B, and the transition state, ≠). Equation 3 predicts that internal pressure will influence reaction rates in the same direction as external pressure.[26] Typically, correlations to δ_S^2 (P_i)[27-30] or δ_S $(P_i^{1/2})$ are reported.[24,31,32]

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(19) The rate constant for $Cl^\bullet$ + 23DMB is 3×10^9 M^{-1} s^{-1} at 300 K. See: Bunce, N. J.; Ingold, K. U.; Landers, J. P.; Lusztyk, J.; Scaiano, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 5464.

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Utilizing the data in Table 2 for the chlorination of cyclopropane and in accordance with eq 2, a linear relationship between log(k_C/k_H) and δ^2 is found (Figure 1; $R^2 = 0.9588$, $m = 0.029$ (± 0.003) cm^3/cal, $b = -0.84 \pm 0.12$). The data did not show significant correlation to any other pertinent solvent parameter. For example, virtually no correlation could be found to viscosity (a plot of k_C/k_H vs η yielded a scatter with $R^2 = 0.0016$). The correlation of the data to dielectric constant was only modest [$R^2 = 0.8972$ for $\ln(k_C/k_H)$ vs the Kirkwood function, $(\epsilon - 1)/(2\epsilon + 1)$].

Within experimental error, the y intercept of the plot of log(k_C/k_H) vs δ^2 (Figure 1), corresponding to $k_C/k_H = 0.4 \pm 0.2$, is equal to the gas-phase result ($k_C/k_H = 0.25 \pm 0.05$). In other words, *extrapolation of the condensed-phase data to zero internal pressure yields the gas phase value, correctly predicting that the* S_H2 *process will predominate in the gas phase.*

Conclusion. The chemoselectivity associated with the free radical chlorination of cyclopropane is subject to a solvent effect. The relative amounts of ring-opened (S_H2) and hydrogen abstraction products correlate to the internal pressure of the solvent. Extrapolation of the solution-phase results to zero internal pressure correctly predicts the product ratio observed experimentally in the vapor phase. These observations suggest that the difference between the gas- and condensed-phase chlorination of cyclopropane can be attributable to solvent pressure effects in the latter. No evidence for the chlorine atom cage effect is detected in the cyclopropane/Cl_2 system because cyclopropane and its chlorinated derivatives are less reactive than ordinary alkanes toward chlorine atom.

Acknowledgment. We gratefully acknowledge the National Science Foundation (CHE 9113448), the U.S. Environmental Protection Agency, and the Thomas F. Jeffress and Kate Miller Jeffress Memorial Trust Fund for financial support.