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Solvent Effects in Free Radical Halogenations: The Nature of the Br$^\bullet$/CS$_2$ "Complex"

Mitra Sadeghipour, Karen Brewer, and J. M. Tanko*

Department of Chemistry, Virginia Polytechnic Institute and State University, Blacksburg, Virginia 24061-0212

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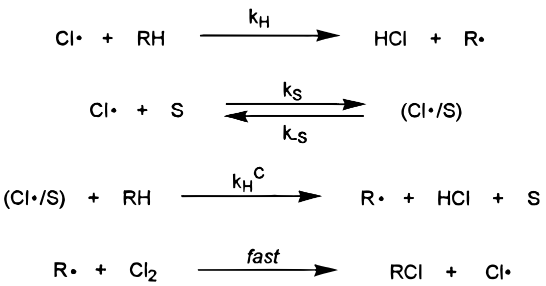
Introduction

In the late 1950s, Russell reported that high selectivities could be attained when free radical chlorinations were conducted in aromatic solvents and carbon disulfide.[1,2] As an example, for the chlorination of 2,3-dimethylbutane, the relative reactivity of the tertiary hydrogens to primary (r(3°/1°)) is 4.2 (per hydrogen) when the reaction is conducted neat (or in an inert solvent) at 25 °C. In contrast, when conducted in 8 M benzene, r(3°/1°) increases to 49.[2] Even greater selectivities are observed in carbon disulfide ($r(3°/1°) = 106$ in 8 M CS$_2$).[2]

It is generally accepted that the high selectivity observed in benzene is attributable to the formation of a Cl$^\bullet$/PhH complex. This complex has been detected spectroscopically ($\lambda_{max} = 320$, 490 nm);[3,4] however, its precise nature (π-complex vs 6-chlorocyclohexadienyl radical) remains unsettled.[4−9] Since the initial Russell report, high selectivities in alkane chlorinations have also been reported in other solvents which complex Cl$^\bullet$ (e.g., pyridine).[10,11]

The mechanism for chlorination of alkanes in complexing solvents is summarized in Scheme 1. Generally, selectivity increases with increasing concentration of the complexing solvent. Selectivity is *also* dependent on the concentration of the alkane. Specifically, selectivity increases with decreasing alkane concentrations reaching a maximum (plateau) at very low alkane concentrations (typically ≤0.1 M).[12] For free Cl$^\bullet$, the rate constants for abstraction of hydrogen from an alkane (k_H) and for complexation to solvent (k_s) are similar and at or near the diffusion-controlled limit (10^9−10^{10} M^{-1} s^{-1}).[4] Consequently, abstraction of hydrogen from RH by free Cl$^\bullet$ is competitive with complexation to solvent, and the observed selectivity reflects contributions from both free and complexed Cl$^\bullet$. At low alkane concentrations, the rate of hydrogen abstraction by free Cl$^\bullet$ is sufficiently slow that equilibrium is attained between free and complexed Cl$^\bullet$ and the observed selectivity reaches its maximum value (reflecting the equilibrium composition).

Scheme 1



$$\mathrm{Cl}\bullet + \mathrm{RH} \xrightarrow{k_H} \mathrm{HCl} + \mathrm{R}\bullet$$

$$\mathrm{Cl}\bullet + \mathrm{S} \underset{k_{-S}}{\overset{k_S}{\rightleftharpoons}} (\mathrm{Cl}\bullet/\mathrm{S})$$

$$(\mathrm{Cl}\bullet/\mathrm{S}) + \mathrm{RH} \xrightarrow{k_H{}^C} \mathrm{R}\bullet + \mathrm{HCl} + \mathrm{S}$$

$$\mathrm{R}\bullet + \mathrm{Cl_2} \xrightarrow{fast} \mathrm{RCl} + \mathrm{Cl}\bullet$$

Unlike chlorinations, selectivities observed in free radical brominations are generally independent of solvent. In earlier work examining the importance of solvent pressure effects in halogenations of cyclopropanes,[13,14] slightly distorted results for brominations conducted in CS$_2$ were observed, and we began to suspect the involvement of a Br$^\bullet$/CS$_2$ complex in analogy to Cl$^\bullet$/CS$_2$. We were especially interested in possible complexation effects in this particular solvent because CS$_2$ and CO$_2$ are isolectronic, and supercritical CO$_2$ has proven an effective solvent for conducting free radical brominations.[15]

Br$^\bullet$ is considerably less reactive and more selective in hydrogen abstractions compared to Cl$^\bullet$. The relative reactivities of 3°, 2°, and 1° hydrogens toward Br$^\bullet$ are 25000:700:1.00 (27 °C),[16] compared to 4.2:3.5:1.00 for Cl$^\bullet$ (25 °C).[17] While hydrogen abstractions from alkanes by Cl$^\bullet$ are nearly diffusion-controlled,[4] the corresponding rate constants for Br$^\bullet$ are less than 10^5 M^{-1} s^{-1}.[17] As a result, in order to detect whether Br$^\bullet$ selectivities were altered by complexation with CS$_2$, it was deemed necessary to examine substrates considerably more reactive toward Br$^\bullet$, where the observed selectivities would be smaller and changes in selectivity with solvent would be more easily detected. In this paper, we report the effect of CS$_2$ solvent on selectivities in the free radical brominations of alkyl aromatics.

Results and Discussion

Toluene/Ethylbenzene Competitions. Relative reactivities of the 2° and 1° benzylic hydrogens of ethylbenzene and toluene toward Br$^\bullet$ (r(2°/1°)) were determined by competition kinetics. In a typical experiment, Br$_2$ was allowed to react with an equimolar mixture of toluene and ethylbenzene ([PhCH$_3$]$_i$, [PhCH$_2$CH$_3$]$_i \gg 10 \times$ [Br$_2$]$_i$). 1,2-Epoxybutane was present as an HBr scavenger.[18] Relative reactivities were calculated from

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Table 1. Effect of Solvent on Br$^\bullet$ Selectivity (Ethylbenzene/toluene competitions, 17 °C)

solvent	r(2°/1°)
CCl_4	50 ± 5
$CFCl_2CF_2Cl$	49.6 ± 0.5
$ClCH_2CH_2Cl$	40.0 ± 0.4
CH_2Cl_2	35.0 ± 1.1
PhH	47 ± 3
CS_2	86 ± 4

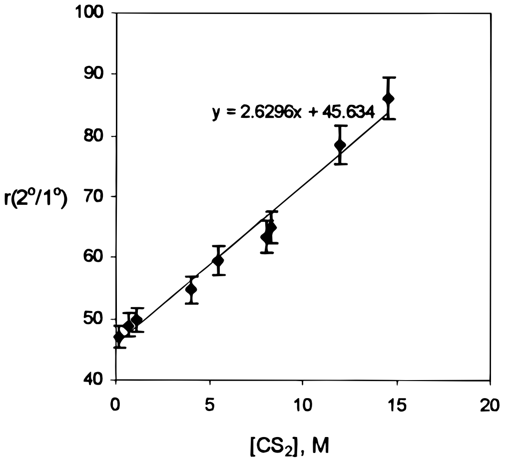


Figure 1. Effect of CS_2 concentration on Br$^\bullet$ selectivity (ethylbenzene/toluene competitions, 17 °C).

product yields (determined by GC analysis) according to eq 1, and the results are summarized in Table 1.

$$r(2°/1°) = \frac{\text{yield of PhCHBrCH}_3}{\text{yield of PhCH}_2\text{Br}} \times \frac{[\text{PhCH}_3]_i}{[\text{PhCH}_2\text{CH}_3]_i} \times \frac{3}{2} \quad (1)$$

The observed selectivity in benzene was indistinguishable from that observed in chlorinated solvents. In light of the fact that Br$^\bullet$/PhH complexes have been characterized spectrocopically,[3] this observation suggests that either the Br$^\bullet$/PhH complex has the same selectivity as free Br$^\bullet$ or that the complex is sufficiently unreactive (or present in low concentrations) so that it does not contribute appreciably to the observed selectivity.

In contrast, the selectivities observed in CS_2 were markedly higher than found for any other solvent examined. The selectivity was found to be *dependent* on CS_2 concentration (Figure 1) but *independent* of the concentration of [$PhCH_3$] and [$PhCH_2CH_3$] at all CS_2 concentrations (Table 2).

These observations are interpreted according to the mechanism summarized in Scheme 2 which recognizes the contributions of two hydrogen abstractors in this system, free and CS_2-complexed bromine atom, to the observed selectivity. A simple kinetic analysis based upon Scheme 2 reveals that r(2°/1°) is expected to vary with [CS_2] and the concentrations of toluene and ethylbenzene according to eq 2.

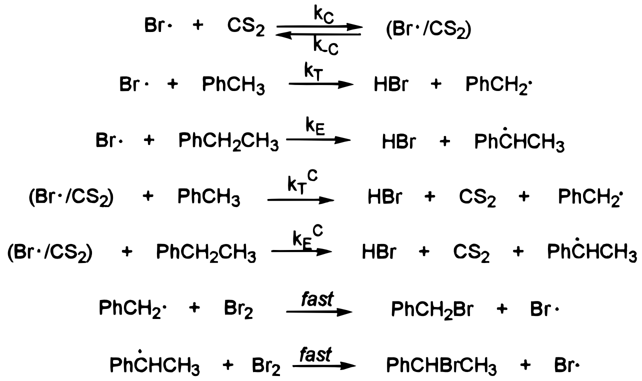
$$r(2°/1°) = \frac{\dfrac{k_E}{k_T} + \dfrac{k_C}{k_T}[\text{CS}_2]\left(\dfrac{k_E^C}{k_{-C} + k_T^C[\text{PhCH}_3] + k_E^C[\text{PhCH}_2\text{CH}_3]}\right)}{1 + \dfrac{k_C}{k_T}[\text{CS}_2]\left(\dfrac{k_T^C}{k_{-C} + k_T^C[\text{PhCH}_3] + k_E^C[\text{PhCH}_2\text{CH}_3]}\right)} \times \frac{3}{2} \quad (2)$$

Table 2. Effect of Hydrocarbon Concentration on Br$^\bullet$ Selectivity (Ethylbenzene/toluene competitions, 17 °C)[a]

[RH], M	r(2°/1°)
[CS_2] = 4.0 M	
2.8	53.6 ± 1.2
2.1	51.6 ± 1.1
1.1	53.6 ± 1.7
0.70	54.3 ± 1.0
0.33	56.0 ± 1.4
0.13	56.8 ± 1.6
0.08	57.0 ± 1.6
0.058	55.6 ± 2.6
[CS_2] = 8.0 M	
1.7	64.4 ± 1.9
0.90	64.0 ± 1.8
0.19	62.1 ± 1.4
0.10	64.1 ± 1.3
0.06	63.3 ± 2.0
[CS_2] = 12.0 M	
1.0	76.9 ± 0.7
0.84	73.3 ± 1.9
0.79	78.4 ± 2.3
0.36	76.3 ± 1.1
0.13	77.9 ± 2.4
0.12	87.6 ± 2.8
0.087	78.6 ± 2.6
0.046	88.6 ± 3.8

[a] CCl_4 solvent was utilized as a diluent.

Scheme 2



The fact that the experimentally observed selectivity is independent of [$PhCH_3$] and [$PhCH_2CH_3$] suggests that $k_{-C} \gg k^C{}_T[PhCH_3] + k^C{}_E[PhCH_2CH_3]$ and that eq 2 can be reduced to eq 3. The important point which emerges from this analysis is that the Br$^\bullet$/CS_2 complex decomposes to free Br$^\bullet$ + CS_2 *faster* than it abstracts hydrogen from the alkyl aromatics (i.e., CS_2/Br$^\bullet$ and free Br$^\bullet$ are at equilibrium).

$$r(2°/1°) = \frac{\dfrac{k_E}{k_T} + K_C\dfrac{k_E^C}{k_T}[\text{CS}_2]}{1 + K_C\dfrac{k_T^C}{k_T}[\text{CS}_2]} \times \frac{3}{2} \quad (3)$$

Equation 3 also predicts that as [CS_2] → ∞, the selectivity should reach a plateau value corresponding to $^3/_2(k^C{}_E/k^C{}_T)$, the selectivity of the Br$^\bullet$/CS_2 complex. However, within the range of concentrations accessible, 0 → 14.5 M (neat) CS_2, no curvature in the r(2°/1°) vs [CS_2] plot is discernible within experimental error.

Cumene/Ethylbenzene Competitions. Competitions pitting cumene vs ethylbenzene were performed in order to assess the relative reactivity of the 3° benzylic hydrogens of cumene to the 2° benzylic hydrogens of

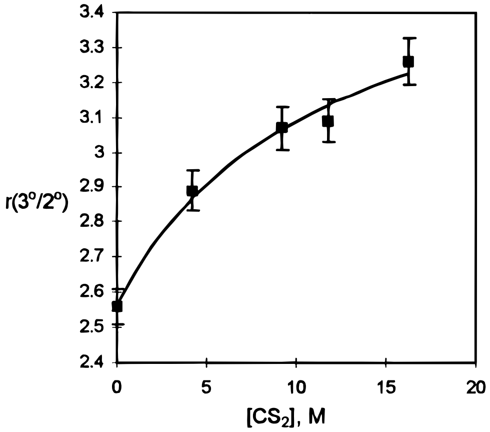


Figure 2. Effect of CS_2 concentration on $Br^{\bullet}$ selectivity (cumene/ethylbenzene competitions, 17 °C).

ethylbenzene toward $Br^{\bullet}$ (r(3°/2°)) in CS_2 solvent. These experiments were conducted in a manner similar to the ethylbenzene/toluene competitions with the following exception: Because the product arising from bromination of cumene (cumyl bromide) undergoes facile elimination in the GC injector port, it was necessary to determine r(3°/2°) on the basis of consumed starting materials (eq 4).

$$r(3°/2°) = \frac{\log\left(\frac{[PhCH(CH_3)_2]_i}{[PhCH(CH_3)_2]_f}\right)}{\log\left(\frac{[PhCH_2CH_3]_i}{[PhCH_2CH_3]_f}\right)} \times 2 \qquad (4)$$

As with the ethylbenzene/toluene competitions, selectivity was found to vary with CS_2 concentration (Figure 2). However, curvature was observed at high CS_2 concentrations.

Assuming a mechanism analogous to that depicted in Scheme 2 and letting k_{CU} and k^{C}_{CU} represent the rate constants for hydrogen abstraction by free and CS_2-complexed $Br^{\bullet}$, respectively, r(3°/2°) can be expressed according to eq 5. Nonlinear regression analysis of the results according to eq 5 leads to $k_{CU}/k_E = 1.28 \pm 0.02$, $K_C(k^{C}_{CU}/k_E) = 0.16 \pm 0.07$, and $K_C(k^{C}_{E}/k_E) = 0.088 \pm 0.041$. (From this analysis, the r(3°/2°) is ascertained to be 2.56 and 3.7 for free and CS_2-complexed $Br^{\bullet}$, respectively.)

$$r(3°/2°) = \frac{\frac{k_{CU}}{k_E} + K_C\frac{k^{C}_{CU}}{k_E}[CS_2]}{1 + K_C\frac{k^{C}_{E}}{k_E}[CS_2]} \times 2 \qquad (5)$$

Laser Flash Photolysis (LFP) Results. Complexes of $Cl^{\bullet}$ and $I^{\bullet}$ with CS_2 have been characterized by UV/vis spectroscopy. For $Cl^{\bullet}/CS_2$, $\lambda_{max} = 370$ nm with a shoulder at 490 nm.[19] For $I^{\bullet}/CS_2$, $\lambda_{max} = 485$ nm.[20] In an attempt to spectroscopically detect the $Br^{\bullet}/CS_2$ complex and to gain information on the kinetics of its reactions, laser flash photolysis experiments were performed. Initially, molecular bromine was used as a bromine atom source (excitation at 532 nm) in the presence of varying concentrations of CS_2. However, because of overlapping Br_2 and CS_2 absorptions, detection was limited to a narrow range of wavelengths (ca. 380 nm and between 500 and 600 nm). In this region, no transients were observed which could be attributed to a $Br^{\bullet}/CS_2$ complex.

Subsequently, $Br^{\bullet}$ was generated from α-bromoacetophenone[21,22] with a 355 nm laser pulse. In the presence of benzene, a transient corresponding to the $Br^{\bullet}$/PhH complex was observed ($\lambda_{max} = 490$ nm), thereby confirming $Br^{\bullet}$ formation under these conditions. Using α-bromoacetophenone, $Br^{\bullet}$ was generated in the presence of varying concentrations of CS_2 in CCl_4. However, no transient was observed in the region 350−550 nm suggesting either (a) the $Br^{\bullet}/CS_2$ complex was invisible in this region or (b) the concentration of complex is too low to be detected, presumably because of a short lifetime. Therefore, it was not possible to detect this complex spectroscopically or to obtain a rate constant for its formation.

Finally, in an attempt to obtain kinetic information regarding the $Br^{\bullet}/CS_2$ complex, the "probe" method was employed. This method takes advantage of the properties of parallel first- or pseudo-first-order reactions (Scheme 3) wherein the rate constant obtained by monitoring formation of *one* of the products from a common intermediate (e.g., $Br_2^{\bullet -}$ formed by reaction of $Br^{\bullet}$ with Br^-) is actually the *sum* of all rate constants involving the intermediate (i.e., $k_{obs} = k_o + k_C[CS_2] + k_{Br}[Br^-]$). The $Br^{\bullet}/Br^-$ reaction has been well-characterized kinetically and used as a probe to obtain absolute rate constants for reactions involving $Br^{\bullet}$ which do not lead to spectroscopically observable products.[22]

Scheme 3

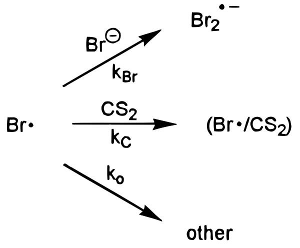


Table 3. Observed Pseudo-First-Order Rate Constant for $Br^{\bullet} + Br^- \rightarrow Br_2^{\bullet -}$ in the Presence of Varying Concentrations of CS_2[a]

$[CS_2]$, M	k_{obs}, s^{-1}
1.0	2×10^8
0.7	2×10^8
0.5	4×10^8
0.1	2×10^8
0.0	0.9×10^8

[a] Room temperature in CH_3CN; $[Bu_4NBr] = 0.003$ M; $k_{obs} = k_{Br}[Br^-]$.

In our experiments, tetra-*n*-butylammonium bromide was used as the Br^- source, and $Br^{\bullet}$ was generated from α-bromoacetophenone (as above) in CH_3CN solvent in the presence of various concentrations of CS_2. Within experimental error, k_{obs} was found to be independent of $[CS_2]$ (Table 3).

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Conclusions

LFP experiments fail to detect any transient corresponding to $Br^•/CS_2$. Moreover, the apparent rate constant for the reaction $Br^• + Br^- \rightarrow Br_2^{•-}$ (obtained by monitoring the buildup of $Br^{•-}$) is unaffected by concentrations of CS_2 up to 1 M, suggesting either that no kinetically discrete $Br^•/CS_2$ complex exists or that if it does exist, it is fully equilibrated with free $Br^•$ during the time scale of the experiment.[23] This proposition is not unreasonable. To the extent that a weak association of $Br^•$ with CS_2 occurs without significant structural alteration (e.g., as a donor−acceptor complex), it is reasonable to suspect that k_C is near-diffusion-controlled and that $k_{-C} > k_{Br}[Br^-]$ at the concentrations of Br^- used in these experiments.

The increased selectivities observed for free radical brominations conducted in CS_2 solvent clearly argue for stabilization of $Br^•$ in this medium. To the extent that an actual $Br^•/CS_2$ complex is formed, the fact that selectivities are not altered by hydrocarbon concentration is also consistent with the proposal that this complex is fully equilibrated with free $Br^•$. Thus, it appears that the interaction between bromine atom and CS_2 is extremely weak, perhaps simple solvation rather than formation of a strong covalent or π-complex. The apparent weakness of this interaction is consistent with the relatively small changes in selectivity observed when radical brominations are conducted in CS_2. These results are in contrast to free radical chlorinations conducted in CS_2 where a significantly stronger complex is formed ($K_{eq} = 1.9 \times 10^3$ M^{-1}) and where dramatic increases in selectivity are observed.

Experimental Section

General. Gas chromatographic analyses were performed on a Hewlett-Packard HP 5890 A instrument equipped with an FID detector and an HP 3393A reporting integrator using a 30 m SE-54 capillary column (0.25 mm diameter). The following materials were obtained from Aldrich (carbon disulfide, cumene, ethylbenzene, and 1,1,2-trichlorotrifluoroethane), Fisher (benzene, chlorobenzene, ethylene dichloride, dichloromethane, and toluene), and EM Science (acetonitrile and carbon tetrachloride) and used as received. α-Bromoacetonitrile (Aldrich) was recrystallized from hexane prior to use.

Laser flash photolysis experiments were performed on a nanosecond laser system. The system consists of a continuum Q-switched NY81-10 Nd/YAG excitation source (8 ns) using doubling (532 nm) and tripling (355 nm) crystals. The source for the transient absorbance spectroscopy was an Oriel 1000 W xenon arc lamp which passes through two monochromators, one prior to and one after the sample. The excitation beam and probe beam intersect at a 90° angle with the probe beam being focused to be contained within the excitation beam. The probe beam intensity was detected using a Hamamatsu R928 instrument with a modified socket designed for higher light intensity. The signals for all of the experiments were digitized by a LeCroy 6880B fast digitizer (operating at 1.3 Gs/s) and transferred to a 486-50 MS-DOS computer for data handling and analysis.

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[23] $Br_2^{•-}$ may be formed by reaction of $Br^•/CS_2$ with Br^-. Presumably the complex is less reactive than free $Br^•$, and it would be reasonable to suspect that the rate constant for this reaction would be less than that for involving free $Br^•$. However, it is possible that these two reactions are “leveled” in solution (i.e., both are diffusion-controlled).