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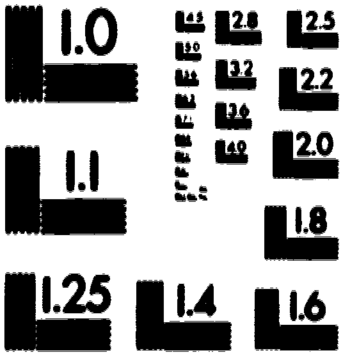

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Reactive Intermediates in Electrophilic Halogenation

BY

Richard Wayne Nagorski ©

A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

DEPARTMENT OF CHEMISTRY

Edmonton, Alberta

Spring, 1994

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UNIVERSITY OF ALBERTA

FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research for acceptance, a thesis entitled Reactive Intermediates in Electrophilic Halogenation submitted by Richard Wayne Nagorski in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

Supervisor

R.S. Brown

Martin Cowie

M. Cowie

R.J. Crawford

E.E. Knaus

E.E. Knaus

Karl R. Kopecky

K.R. Kopecky

External Examiner

D.R. Arnold

Date: December 6, 1993

DEDICATION

To my parents:

They taught me that education was not a punishment to be endured, but a privilege to be embraced.

THANK YOU!

ABSTRACT

The product ratios for the bromination of cyclopentene, cyclohexene, tetramethylethylene, and styrene, with Br_2 and NBS, have been investigated in MeOH at varying $[N_3^-]$ and $[Br^-]$, in order to obtain information about the lifetimes of the bromonium ion intermediates. Assuming that N_3^- attacks with the diffusion limited rate constant of 10^{10} $M^{-1}s^{-1}$, the respective lifetimes of the ions produced from the bromination of the four olefins are 5.9×10^{-10}, 5.0×10^{-10}, 9.3×10^{-10}, and 2.7×10^{-10} s. Product studies of the reaction of cyclohexene with either Br_2 or NBS in MeOH, in the presence of varying $[Br^-]$, indicate that the trans dibromide to *trans*-1-bromo-2-methoxycyclohexane ratio tends to zero as $[Br^-]$ approaches zero. This indicates that in MeOH the trans dibromide is not formed from ion pair collapse. Product studies of the solvolysis of *trans*-2-bromocyclohexyl trifluoromethanesulfonate in MeOH containing N_3^- and Br^- indicate that significantly less trans bromo azide and trans dibromide are produced relative to the products formed from electrophilic addition of Br_2 and NBS to cyclohexene under comparable conditions. This suggests that the bromonium ions produced in the two cases are not identical. The reactions of I_2 and Br_2 with adamantylideneadamantane (**7**) and bicyclo[3.3.1]non-9-ylidenebicyclo[3.3.1]non-9'-ane (**29**) were investigated in order to prepare the corresponding halonium ions. The crystal structure of admantylideneadamantane iodonium ion triflate was obtained by X-ray diffraction. The ^{13}C NMR resonances of the iodonium ions of **7** and **29**, and the bromonium ion of **29**, all with triflate counterion, were investigated in CD_2Cl_2 at -80°C as a function of added parent olefin. The second-order rate constants for I^+ exchange between iodonium ion and added parent olefin were found to be 7.6×10^6 $M^{-1}s^{-1}$, and 4.2×10^6 $M^{-1}s^{-1}$ for **7**-I^+/OTf^- and **29**-I^+/OTf^-, respectively. The kinetics of bromination of 7-norbornylidene-7'-norbornane L_{20} (where L is D or H) were investigated in HOAc and MeOH at various $[Br^-]$ and constant ionic strength. The products of bromination were the corresponding 1,2-dibromide or 1,2-bromosolvate. The kinetics of Br_2 addition in MeOH show a k_D/k_H of

$\sim$1.8 over the entire range of [Br$^-$] investigated, whereas in AcOH the k_D/k_H varies from 1.53 at zero added Br$^-$ to 2.75 at 0.05 M Br$^-$. These results are discussed in terms of a prominent steric secondary deuterium kinetic isotope effect on the partitioning of a reversibly formed bromonium ion intermediate.

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LIST OF ABBREVIATIONS

CTC	charge transfer complex
MeOH	methanol
AcOH	acetic acid
$[Br_2]$	bromine concentration
TBAT	tetrabutylammonium tribromide
TBAB	tetrabutylammonium bromide
σ^+	Hammett substituent constant indicating the substituent's ability to stabilize positive charge by resonance
ρ^+	slope of Hammett plot for system involving positive charge and correlating with σ^+ values
NMR	nuclear magnetic resonance
MeOTf	methyl trifluoromethanesulfonate
OTf^-	trifluoromethanesulfonate
TIBE	tetra*iso*butylethylene
kie	kinetic isotope effects
Dkie	deuterium kinetic isotope effect
S_N1	first-order nucleophilic substitution
OBs^-	4-bromophenylsulfonate
N_DI	internal nucleophilic displacement
NSA	nucleophilic solvent assistance
HOTf	trifluoromethanesulfonic acid
ole	olefin
S_N2	second-order nucleophilic substitution
iip	intimate ion pair

NBS	**N-bromosuccimide**

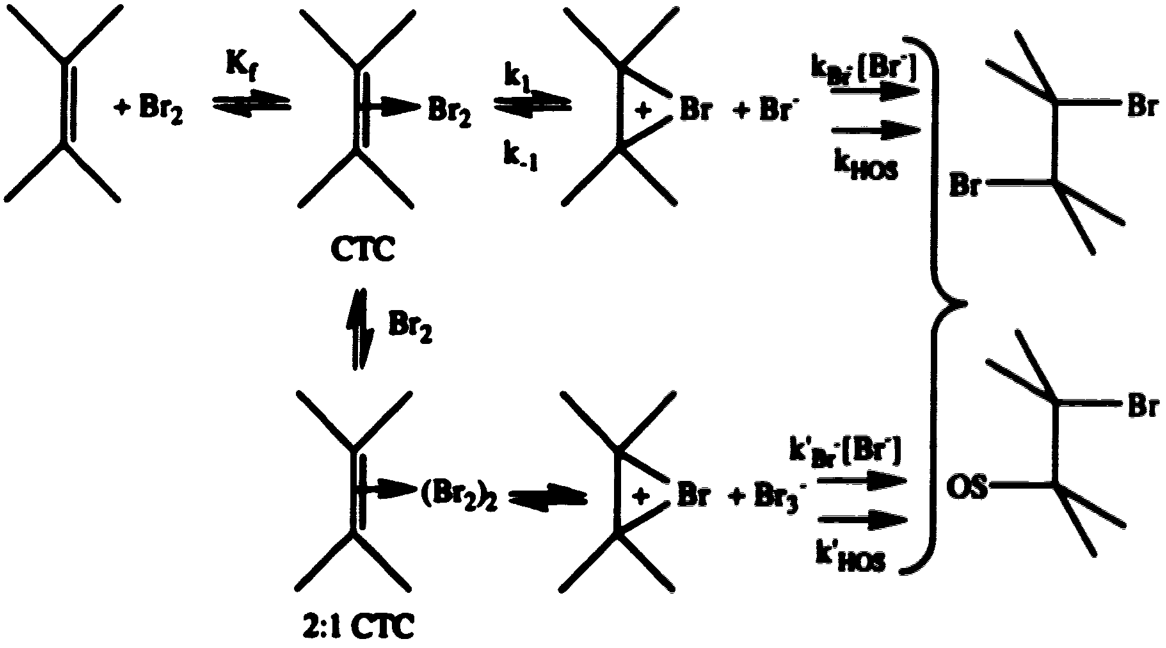
INTRODUCTION

a) General

Often cited as one of the simplest ionic addition reactions of olefins, electrophilic bromination is not fully understood. Generally, it is known that; 1) bromine adds in a 1,2-type addition to olefins, 2) where able to determine, the bromine adds in a trans fashion (with symmetrical olefins). There are exceptions to both general observations.

In 1937, Roberts and Kimball[1] first proposed the existence of a cyclic three-membered bromonium ion as an intermediate on the reaction pathway to explain stereochemical data in the literature. Since then, considerable effort has been expended to study this "simple" reaction[2] in order to gain a greater understanding of how Br_2 ionically adds to olefins. The generally accepted mechanism[2] for Br_2 addition to olefins is shown in **Scheme 1**.

Scheme 1



In **Scheme 1**, the initially formed charge transfer complex (CTC)[3] ionizes in protic solvents such as water (H_2O), methanol (MeOH), and acetic acid (AcOH, at low Br_2

concentration) to form a cyclic, three-membered bromonium ion intermediate. The ionic intermediate can then be nucleophilically attacked by solvent, Br^-, or other nucleophiles present in solution, and thus form the 1,2-addition products. The rate law for Br_2 addition given in equation **1** is a simple second-order expression, first-order in both Br_2 and olefin at low $[Br_2]$ and in ionizing solvents.

(1)

$$\frac{-d[Br_2]}{dt} = k_2\,[ole]\,[Br_2]$$

At high $[Br_2]$ or in solvents that are not highly ionizing the rate law can be expressed as in equation **2**.

(2)

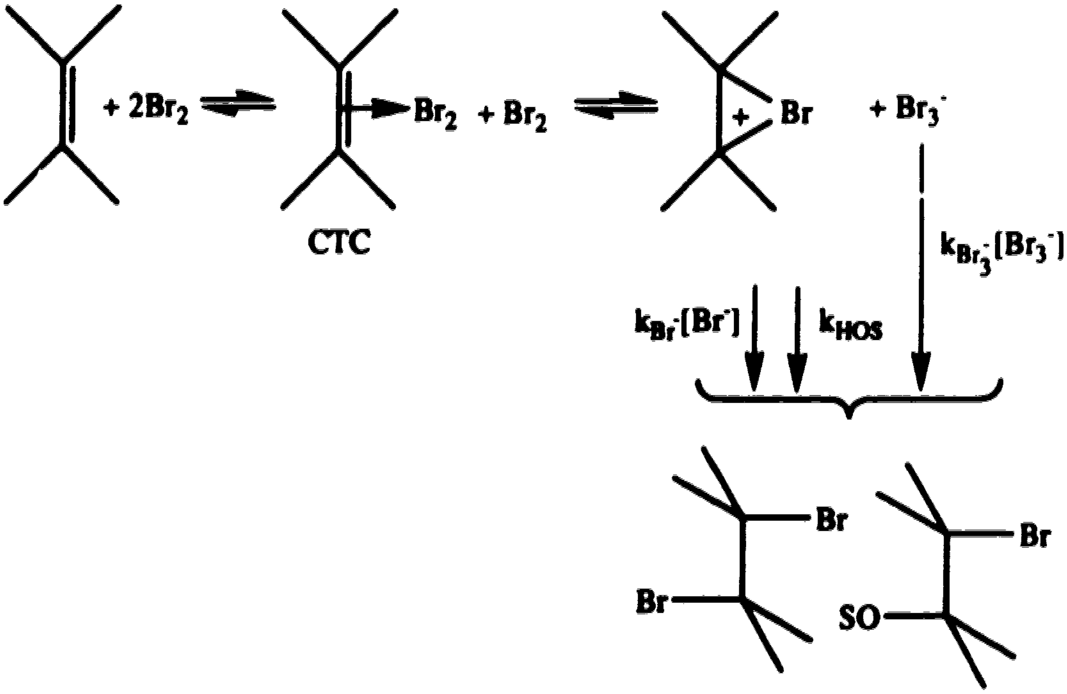
$$\frac{-d[Br_2]}{dt} = k_3\,[ole]\,[Br_2]^2$$

In AcOH at high $[Br_2]$ and in less ionizing solvents (halogenated solvents), a second molecule of bromine is involved in the addition of Br_2 to olefins. There are two possible mechanisms[2c] proposed for the second-order addition of Br_2 to an olefin and these are shown in **Schemes 2** and **3**.

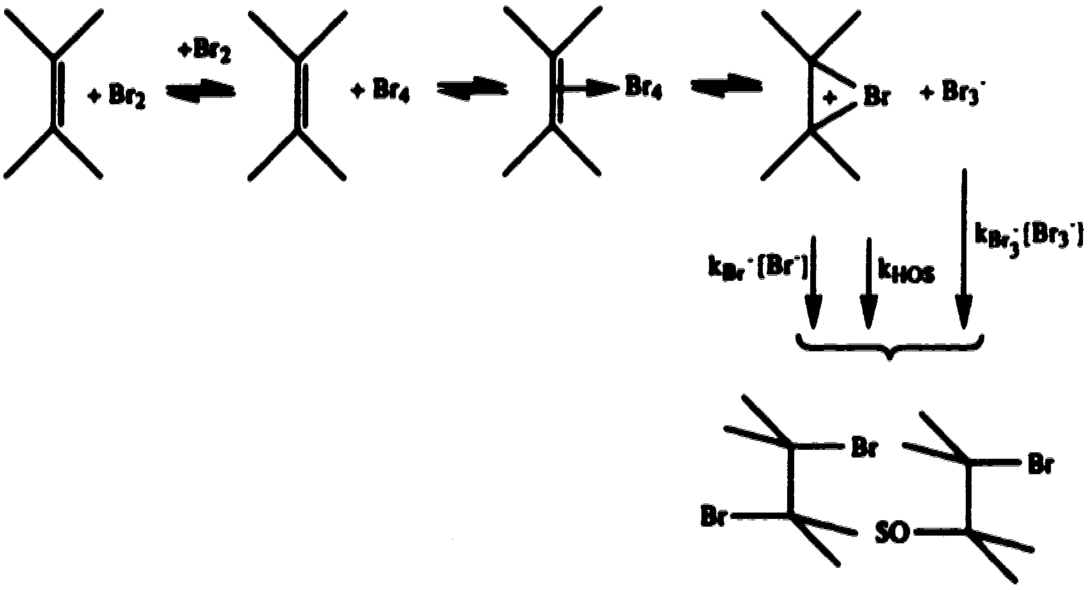
In **Scheme 2**, the initially formed CTC ionizes with the assistance of the second molecule of Br_2 to form the bromonium ion and a Br_3^- counterion. Once the bromonium ion has been formed it is susceptible to nucleophilic attack to form the 1,2-addition products.

In **Scheme 3**, the two molecules of Br_2 come together to form a Br_4 species which complexes the olefin and then ionizes to form the bromonium ion with a tribromide counterion. The processes shown in **Schemes 2 and 3** are kinetically equivalent and, therefore, it is not possible to differentiate between the two using kinetic information. However, it is not surprising that in solvents of low ionizing power a second molecule of Br_2 is needed to assist in the ionization that forms the bromonium ion and tribromide counterion .

Scheme 2



Scheme 3



As the majority of the topics discussed within this work will deal with kinetics performed under pseudo first-order conditions, a discussion of kinetic expressions that are of higher order in [Br_2] would serve little purpose. Therefore, we will concentrate on the discussion of processes that are first-order in [Br_2].

A full discussion of the history of bromination would require many volumes of this size, so the topics discussed in the introduction will be limited to those that are of current research interest. These topics include; 1) Br_3^- mechanism,[4d,5,6] 2) cases where stable bromonium ions exist,[7,8,9] 3) reversibility of bromonium ions,[10] 4) nucleophilic solvent assistance.[2a,2b,10g,10e,11]

b) Br_3^- Reaction

It has long been known that Br_3^- or its kinetic equivalent (Br_2 + Br^-) contributes to the kinetics observed for the bromination of olefins.[2,4] Therefore, any medium that contains Br^- will have the kinetics complicated by the equilibrium in equation 3.

(3)

$$Br_2 + Br^- \underset{k_-}{\overset{k_+}{\rightleftharpoons}} Br_3^-$$

The establishment of the Br_3^- equilibrium is very fast (see **Table 1**), and K_{eq} values are solvent dependent. The establishment of the equilibrium is faster than the rate of Br_2 addition to olefins.

Table 1 : Equilibrium Constants for Halogen/Trihalide Reaction and Individual Rate Constants for the Forward and Reverse Processes of the Equilibrium at 25°C in Various Solvents

X	Solvent	K_{eq}, M^{-1}	k_+,^{a,b} $M^{-1}s^{-1}$	k_-,^{a,b} s^{-1}
I	H_2O	710[d]	5.6×10^9	7.5×10^6
	MeOH	2.3×10^4 [e]	8.7×10^9	6.2×10^5
Br	H_2O	17[d]	1.5×10^9 [c]	5×10^7 [c]
	MeOH	177[f]	2.5×10^9	1×10^7
	EtOH	400[g]	3×10^9 [c]	8×10^6 [c]
	AcOH	92[h]	1×10^9 [c]	1×10^7 [c]
Cl	H_2O	0.2[d]		

a Reference 12.

b Error ±5% unless otherwise noted.

c Error ±25%.

d Reference 13.

e Reference 14.

f Reference 4b.

g Reference 15.

h Reference 16.

In chlorinated hydrocarbons, such as $CHCl_3$ and $ClCH_2CH_2Cl$, K_{eq} for the Br_3^- is even greater than in hydroxylic solvents due to the lower ionizing power of the chlorinated solvents ($K_{eq} = 1.2 \times 10^5$ M^{-1} in $CHCl_3$[17] and $K_{eq} \geq 2 \times 10^7$ M^{-1} in $(ClCH_2)_2$[18]).

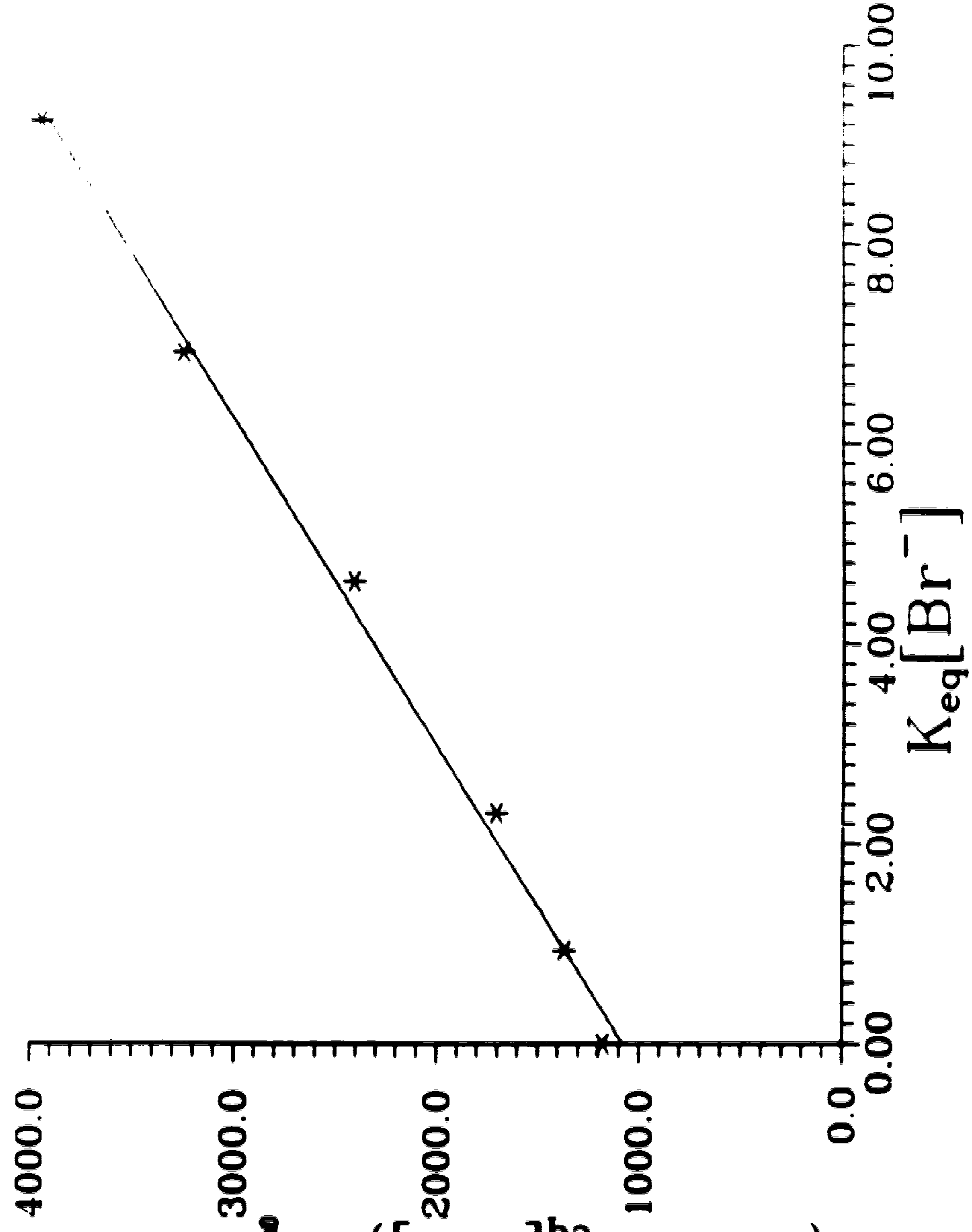
(4)

$$Br_2 + Br^- \overset{K_{eq}}{\rightleftharpoons} Br_3^-$$

$$k_g(1 + K_{eq}[Br^-]) = k_{Br_2} + k_{Br_3^-} K_{eq}[Br^-]$$

The rate constants for the bromination of olefins in the presence of Br^- generally has the form shown in equation 4 where k_g is the observed rate constant, and k_{Br_2} and $k_{Br_3^-}$ are the second-order rate constants for the reaction of the olefin with Br_2 and Br_3^-.[2,3] Plots

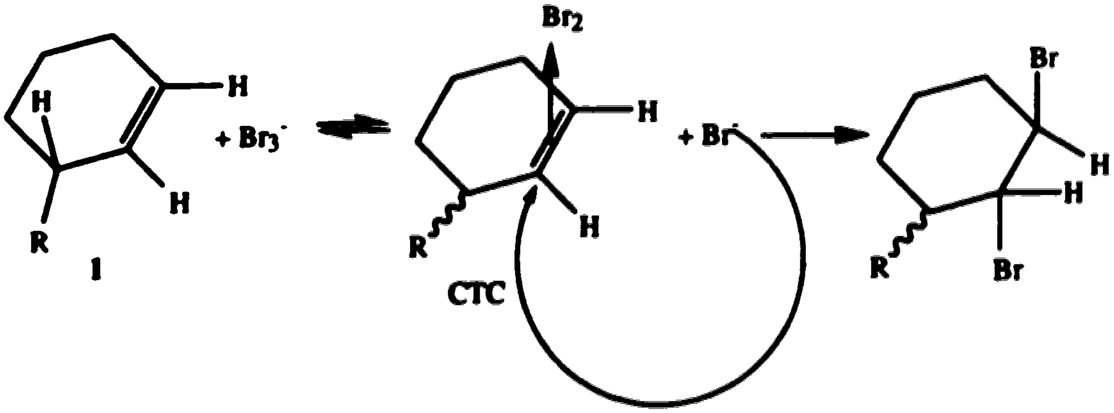
Figure 1 : Plot of $k_g(1 + K_{eq}[Br^-])$ vs $K_{eq}[Br^-]$ for Bromination of Cyclohexene in AcOH at 25°C, $\mu = 0.1$ ($LiClO_4$)[6]



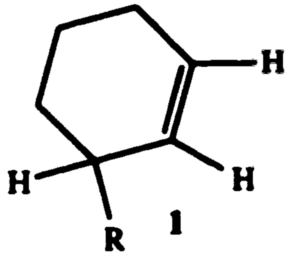
of $k_g(1 + K_{eq}[Br^-])$ vs $K_{eq}[Br^-]$ give straight lines from which k_{Br_2} and $k_{Br_3^-}$ can be determined from the intercept and slope, respectively (see **Figure 1**).

The existence of Br_3^- [2,4] is undisputed, however the mechanism by which Br_3^- adds to olefins is still unclear. Bellucci et al.[5] have provided important experimental evidence as to the mechanism of Br_3^- addition. They concluded that Br^- attack on the CTC is rate limiting in chlorinated solvents (see **Scheme 4**).

Scheme 4



They studied the bromination of a variety of 3-substituted cyclohexenes (**1**) without added Br^- and found the observed rates obeyed a rate expression that was second-order in Br_2. However, when the reactions were conducted with tetrabutylammonium tribromide (TBAT, a solid form of tribromide) the rate data indicated that Br_3^- was the brominating agent. After studying the rate constants and product ratios of these reactions several conclusions were made. The data in **Table 2** show that there are differences in both the rate constant of addition and product ratios that depend upon the brominating agent.



1

Compound	R	Compound	R
1a	Me	**1e**	C_6H_5COO
1b	*t*-Bu	**1f**	*p*-$CH_3C_6H_4COO$
1c	Br	**1g**	*p*-$CH_3OC_6H_4COO$
1d	Cl	**1h**	*p*-$NO_2C_6H_4COO$

Table 2 : Third-Order and Second-Order Rate Constants for Bromination of 3-Substituted Cyclohexenes and Product Ratios of the Reaction at 25°C with Molecular Br_2 and TBAT[a,b]

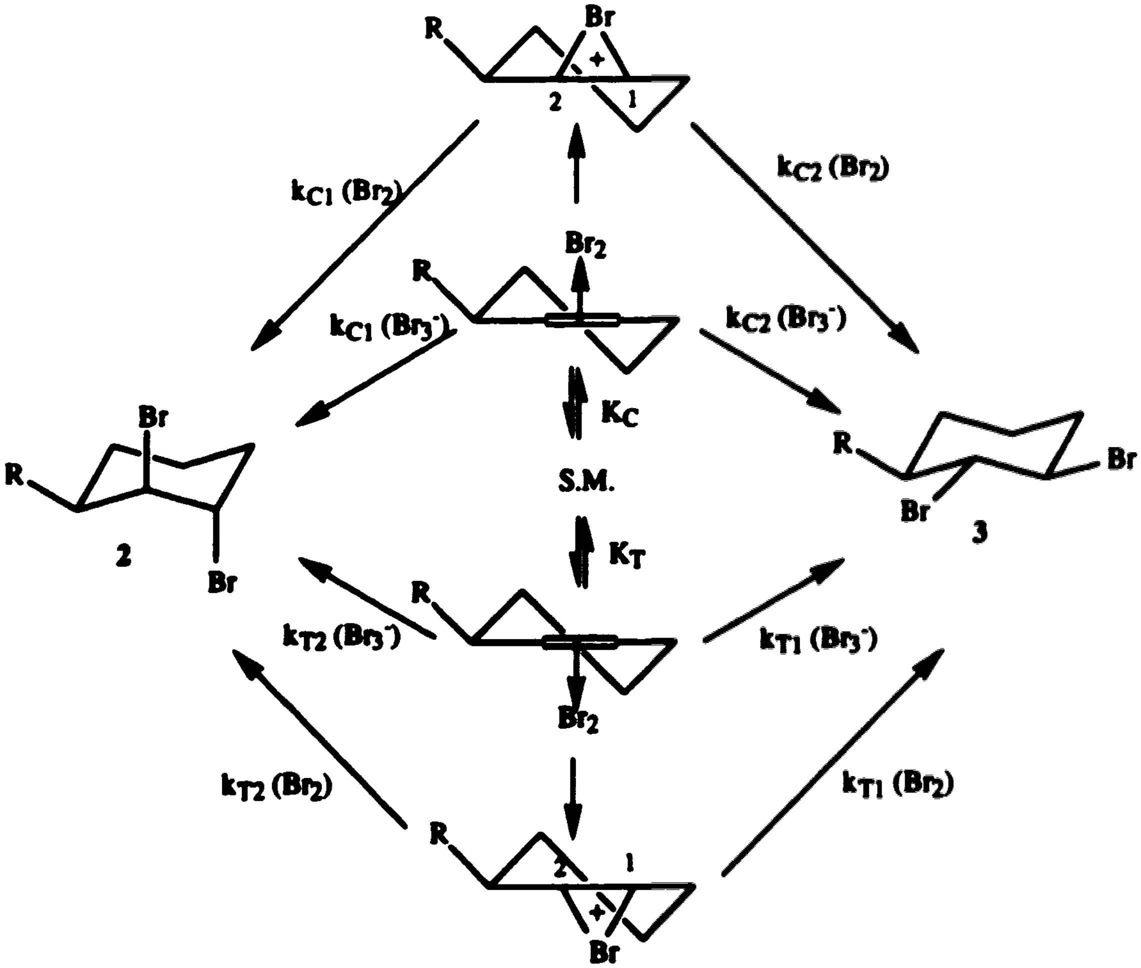
	k_{Br_2} (M^{-2} s^{-1})		$k_{Br_3^-}$ (M^{-1} s^{-1})		Br_2	Products 2:3	
R	$(CH_2Cl)_2$	$CHCl_3$	$(CH_2Cl)_2$	$CHCl_3$	Source	$(CH_2Cl)_2$	$CHCl_3$
H	2.4×10^5	5.8×10^3	7.2×10^{-1}	13.41	Br_2		
1a	3.0×10^5	1.2×10^4			Br_2	76:24	77:23
			4.4×10^{-1}	7.72	TBAT	86:14	90:10
1b	3.7×10^4	1.8×10^3			Br_2	45:55	44:56
			2.1×10^{-2}	3.9×10^{-1}	TBAT	70:30	67:33
1c	1.64	1.2×10^{-1}			Br_2	27:73	26:74
			9.8×10^{-4}	7.4×10^{-3}	TBAT	73:27	71:29
1d	8.8×10^{-1}	6.6×10^{-2}			Br_2	47:53	48:52
			1.3×10^{-3}	1.2×10^{-2}	TBAT	77:23	83:17
1e			4.2×10^{-3}	2.7×10^{-2}	TBAT	78:22	83:17
1f			4.5×10^{-3}		TBAT	81:19	81:19
1g			5.7×10^{-3}		TBAT	75:25	82:18
1h			4.1×10^{-3}		TBAT	74:26	68:32

a Reference 5.

b Tetrabutylammonium tribromide (TBAT).

Shown in **Scheme 5** is the suggested[5] mechanism for the two methods of bromination, where k_{C1}, k_{C2}, k_{T1}, and k_{T2} indicate cis or trans orientation of Br^+ to the R group and nucleophilic attack occurring at C_1 or C_2 of the intermediate ion or CTC. For the Br_3^- mechanism there is an equilibrium formation of the CTC, followed by rate limiting attack of Br^- (**Scheme 4**). When Br_2 is the brominating agent, the equilibrium formation of the CTC is followed by rate limiting Br_2 assisted ionization to form the bromonium ion and Br_3^- counterion which then collapse to form products. In **Table 2**, there is a general reduction in the k_{Br_2} term on moving from 1,2-dichloroethane (ε 10.7) to chloroform (ε 4.6), however the $k_{Br_3^-}$ term shows a general increase in magnitude.

Scheme 5



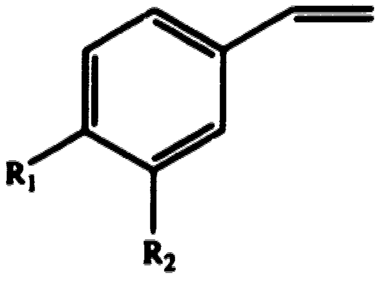
The decrease in k_{Br_2}, upon moving to a less polar solvent, is a result of the Br_2 assisted ionization of the CTC becoming more difficult in the less ionizing solvent. The general increase observed for $k_{Br_3^-}$ is explained as a solvation effect. As the CTC is formed, the solvent hydrogen bonds to the newly formed Br^- ($CHCl_3$ is known to hydrogen bond to halides)[5a] and assists in its transfer to the opposite face of the olefin.

From the data in **Table 2** another trend is observed wherein the k_{Br_2} term decreases (~1.8 times decrease) when changes to the allyl substituent are made (Br to Cl). This decrease suggests that, with stronger electron withdrawing substituents, ionization to form the bromonium ion becomes more difficult. However, the same substituent change causes an increase in the $k_{Br_3^-}$ term (0.70 times increase) suggesting this process does not produce a great deal of charge in its rate determining step.

The most overwhelming evidence for the tribromide mechanism involving attack of the CTC by Br^- was the observation that only 1,2-dibromides were found when brominating **1g-h** with TBAT. However, with Br_2 as the brominating agent both 1,2- and 1,3-dibromides were obtained. This indicates that the reaction of Br_2 with **1g-h** must form a reactive intermediate that allows for the rearrangement of the ester functionality to the 2-position. This same intermediate is not formed with Br_3^- because no 1,3-dibromides were ever observed.

Although much more work on the Br_3^- mechanism has been done in hydroxylic solvents, there is no single mechanism that fits all the experimental data. The three most cited possibilities[4] are; i) a nucleophilic reaction, similar to that shown in **Scheme 4**, where the Br^- captures the CTC, or some other intermediate having the same stoichiometry, e.g. bromonium/bromide ion pair, ii) a salt effect that influences the polarity of the solvent and therefore the medium's ability to support the charge developing in the transition state, iii) a process where Br_3^- acts as an electrophile to yield the bromonium ion and two Br^- ions.

Rolston et al.[4d] investigated the bromination of a variety of substituted styrenes (**4**) in AcOH and obtained the $k_{Br_3^-}/k_{Br_2}$ ratios. These ratios were found to increase as the reactivity of the olefin decreased (see **Table 3**). A similar observation has been made in MeOH[4f], and seems inconsistent with a process where Br_3^- acts as an electrophile.



4

Compound	R_1	R_2
4a	H	H
4b	F	H
4c	Cl	H
4d	Br	H
4e	H	Cl
4f	Cl	Cl
4g	H	NO_2
4h	NO_2	H

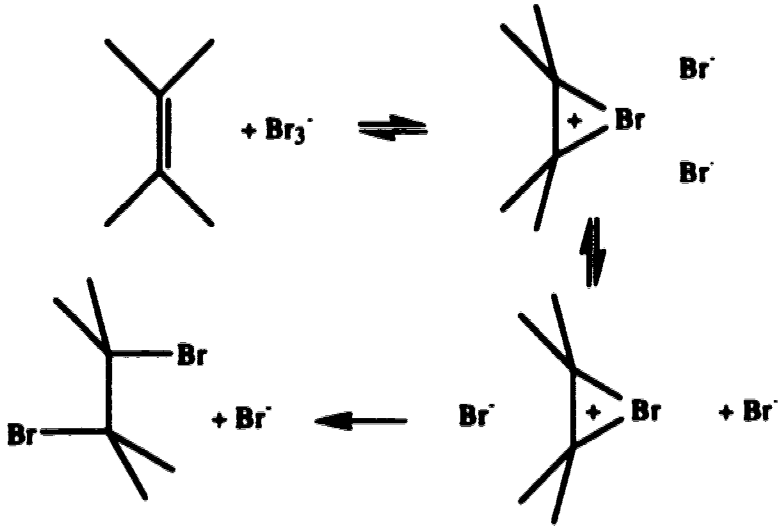
Table 3 : The Rate Constants and Ratios for Br_2 and Br_3^- Addition to Various Substituted Styrenes in Acetic Acid at 25°C and $\mu = 0.1$ ($LiClO_4$)[a]

	4b	4a	4c	4d	4e	4f	4g	4h
k_{Br_2} (M^{-1} s^{-1})	108	77	15.6	13.7	1.3	0.65	0.067	0.031
$k_{Br_3^-}$ (M^{-1} s^{-1})	4.1	3.8	1.95	2.40	0.619	0.420	0.147	0.087
$k_{Br_3^-}/k_{Br_2}$	0.038	0.049	0.125	0.175	0.476	0.646	2.19	2.81

a Reference 4d.

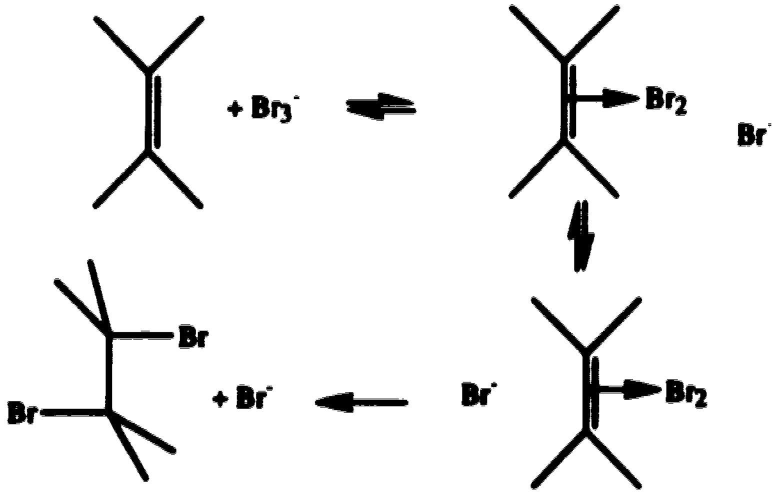
One would anticipate Br_3^- to be a poorer electrophile than Br_2 and, therefore, predict that as the reactivity of the olefin decreases, the $k_{Br_3^-}/k_{Br_2}$ ratio should also decrease. Clearly this is not observed and, therefore, Br_3^- acting as a electrophile does not seem to be plausible on the basis of that expectation. Also, the generation of Br^+ and two Br^- in close proximity (as in **Scheme 6**) seems intuitively unreasonable.

Scheme 6

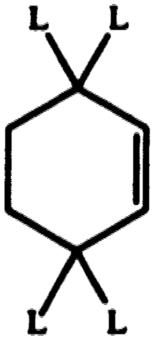


The Hammett plots of the kinetic values for the bromination of the substituted styrenes given in **Table** 3 have ρ^+ values of -4.21 and -2.02 for k_{Br_2} and $k_{Br_3^-}$, respectively. These values indicate that there is less positive charge developed on the α carbon of styrene during the Br_3^- reaction. This is consistent with an asymmetric transition state where the Br^- attacks the α carbon of the CTC, or its kinetic equivalent (ion pair) wherein there is less positive charge development on the olefin carbons than in the Br_2 reaction. Therefore, it seems probable that Br_3^- and olefin interact to form the CTC and nascent Br^-; the latter can translocate and nucleophilically attack the CTC (see **Scheme** 7).

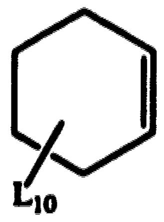
Scheme 7



The electrophilic bromination of compounds **5** and **6**[6] has also been studied and sheds further light on the tribromide reaction mechanism. The bromination of compounds **5a** and **5b** show no difference in k_{Br_2} values which indicates that there is no kinetic effect on the bromination of the olefin upon replacement of the allylic hydrogens with deuterium. However, when cyclohexene-L_{10} (L = H, D) is brominated there are significant differences in k_{Br_2} (k_D/k_H = 1.89 ± 0.19) and $k_{Br_3^-}$ (k_D/k_H = 1.29) between the deuterated and protonated compounds. The inverse valueof k_D/k_H for the k_{Br_2} term is consistent with a process involving significant rehybridization of the olefinic carbons in the rate determining step. The smaller, but still inverse Dkie for the $k_{Br_3^-}$ term, indicates much less rehybridization in the rate determining step for this process. Therefore, if Br_3^- mechanism does involve rate limiting Br^- attack on the CTC, then less rehybridization would be expected relative to a process involving the formation of a bromonium ion.



5a (L = H)
5b (L = D)



6 (L = D)

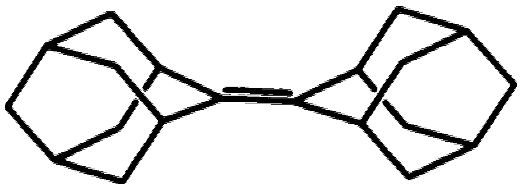
For the three most cited possibilities for the Br_3^- process described above; i) if the mechanism involves Br^- attack on the CTC, one expects a secondary deuterium kinetic isotope effect that is smaller than that observed for the Br_2 mechanism where a bromonium ion is proposed, ii) if the effect were one of ionic strength only, there would be no kinetic isotope effect expected for the bromination of cyclohexene (5a, 6), and this is clearly not what is observed, iii) if Br_3^- were acting as an electrophile, the kinetic isotope effect for the Br_3^- process should be similar to that observed for the Br_2 mechanism because the transition state leading to the intermediate should be similar in terms of rehybridization of the olefinic carbons. Therefore, the kinetic data seem to support a mechanism for the tribromide reaction in which the CTC is nucleophilically captured by Br^-.

c) Electrophilic Br_2 Addition

The generally accepted mechanism for ionic addition of Br_2 to olefins, shown in **Scheme 1**, involves the reversible formation of a CTC[1,2,4] which then ionizes to form the bromonium ion that subsequently undergoes nucleophilic attack to form products. When looking at this scheme several questions come to mind; 1) Are bromonium ions real intermediates that have a lifetime?, 2) Are the bromonium ions reversibly formed? These are questions that have been addressed in part in the current literature.

i) Bromonium Ions:

That a bromonium ion lies on the reaction pathway for electrophilic bromination of olefins is a generally undisputed. However, there is some question as to the exact nature of the ion in the case of unsymmetrical olefins, such as the styrene derivatives studied by Rolston and Yates,[4d] that is, whether it is an open carbocation or a partially bridged halonium ion. For these compounds the attacking nucleophile always substitutes at the α carbon, indicating that one of the carbons of the ion must have greater positive charge than the other. With symmetrical olefins trans addition is generally observed.[1,2,4]



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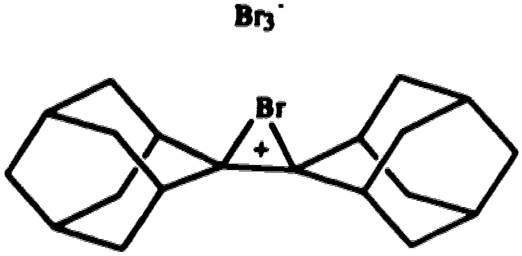


8

The isolation and characterization of a stable bromonium ion, to prove the existence of such, seemed to be an ellusive goal until Wynberg et al. reported that adamantylideneadamantane (7), when brominated in chlorinated solvents, gave a yellow precipitate.[19] This same precipitate, when exposed to high vacuum, reformed 7. Also, when the precipitate was placed in nonchlorinated solvents, 7 was recovered and bromine was released. Wynberg concluded that this behavior was consistent with that expected for the bromonium ion of 7.

That 7 does not add Br_2 in a normal fashion results from the backside of the bromonium ion being very hindered. This hindrance does not allow a nucleophile access to the carbons of the bromonium ion. The protons of the methylene units overlooking the double bond in 7 are in close proximity and after formation of the bromonium ion these protons are pushed even closer together. This feature hinders the approach to the backside of the ion and allows the bromonium ion tribromide (8) to exist as a stable compound.

The nature of 8 makes it difficult to study. For example, whenever 8 is placed in solution there is instantaneous establishment of an equilibrium between ion, CTC, and free bromine. The solution behavior of the 7-Br_2 system in 1,2-dichloroethane at 25°C has been investigated[10b] and it has been shown that the system involves four different species in equilibrium (see Scheme 8). The values of K_{11}, K_{12}, and K_{13} are 2.89×10^2 M^{-1}, 3.23×10^5 M^{-2}, and 7.23×10^6 M^{-3} respectively. This complex behavior makes it difficult to obtain information concerning any one species in solution.

Scheme 8

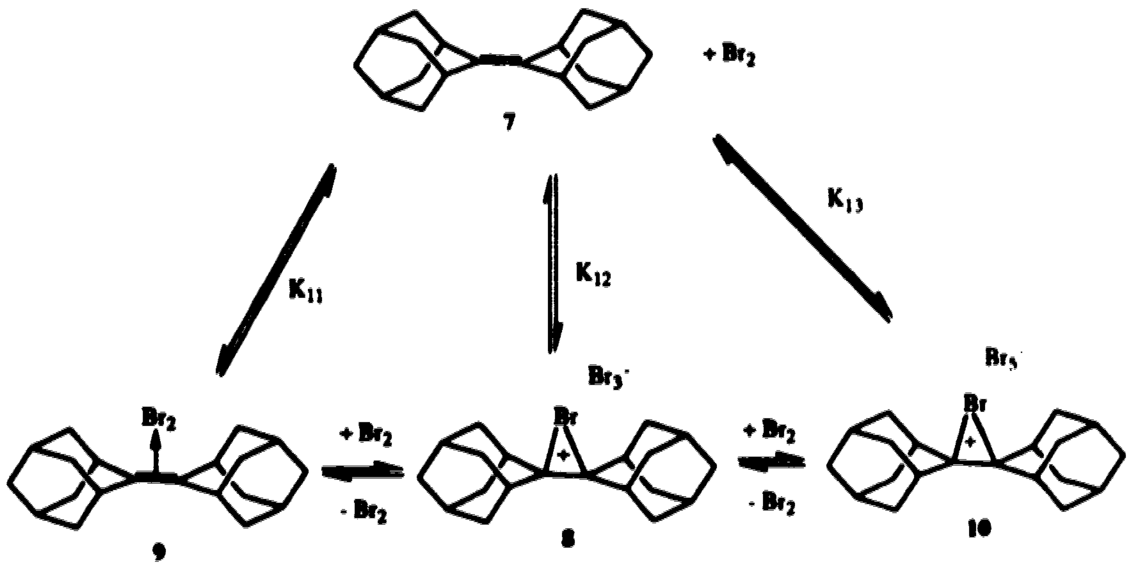
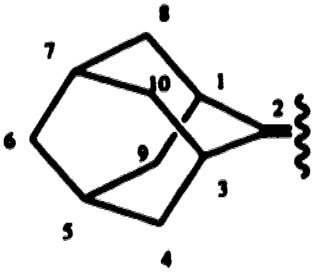


Table 4 :^{13}C NMR Resonances for Adamantylideneadamantane and its Bromonium Ion in Various Solvents[a,b]



Compd	Solvent[c]	$C_{2,2'}$	$C_{1,1',3,3'}$	$C_{4,4',9,9'}$	$C_{8,8',10,10'}$	$C_{5,5',7,7'}$	$C_{6,6'}$
7	C_6H_6	131.6	32.2	39.6	39.6	28.9	37.5
7-Br	Br_2	158.6	39.8	45.0	42.9	29.3	38.8
7-Br	SO_2ClF[d]	157.6	39.7	44.8	42.3	29.0	39.1
7-Br[e]	CD_2Cl_2	156.24	36.99	42.69	40.31	26.57, 26.54	36.18

a Reference 7 with ^{13}C resonances expressed in ppm.

b Numbering scheme used in Reference 7.

c Temperature 30-35°C unless otherwise stated.

d -40°C probe temperature.

e Reference 8 with OTf⁻ counterion at -80°C.

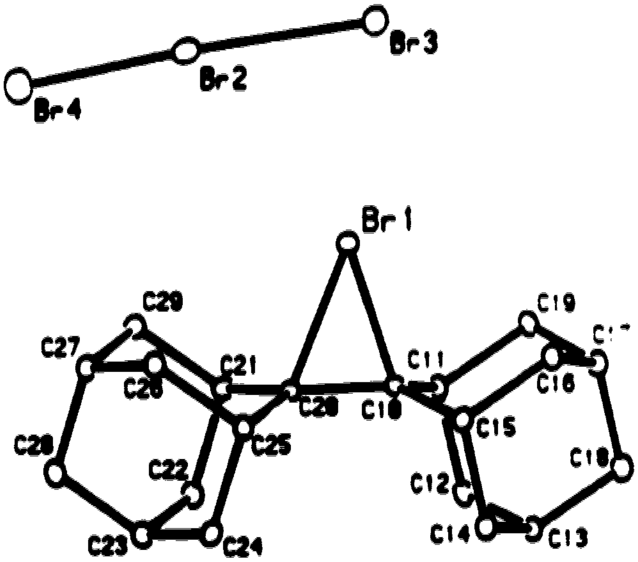
Olah et al.[7] studied the ^{13}C NMR properties of 7-Br^+ in Br_2 and SO_2ClF and obtained a good spectrum for this complex (see **Table 4** for experimental results). They found a significant downfield shift of the olefinic carbon resonances that would be consistent with charge development upon formation of the bromonium ion. The data also suggest that there is a difference between the two faces of the olefin, that is, $C_{4,4',9,9'}$ are not equivalent to $C_{8,8',10,10'}$.

The study performed by Olah et al.[7] shows the NMR characteristics of these ions, but the solvents used were not the organic media normally used for bromination of olefins. Bennet et al.[8] replaced the Br_3^- counterion with trifluoromethanesulfonate (triflate, OTf^-). The reaction of one equivalent of methyl trifluoromethanesulfonate (MeOTf) in solution with 8 produces methyl bromide, Br_2, and OTf^- which replaces Br_3^- as the counterion for the bromonium ion and makes it possible to study the ion in CD_2Cl_2 (see **Table 4** for NMR results). The results obtained by Bennet et al. are similar to those of Olah et al., although the former's results show separation of $C_{5,5'}$ and $C_{7,7'}$.

Bennet et al.[8] also studied the transfer of Br^+ from 7-Br^+/OTf^- to cyclohexene-d_{10}. At -90°C, only the C_6D_{10} resonances could be observed; however upon warming the solution to -50°C there was the slow disappearance of the signals attributable to C_6D_{10} and a new species was formed that was identified as *trans*-2-bromocyclohexyl trifluoromethanesulfonate-d_{10}. This study shows that Br^+ can be transferred between olefins, and that even non-nucleophilic counterions, such as triflate, will attack a bromonium ion if there are no other nucleophiles present.

All the work described here assumes that 8 is the bromonium ion and not some other undefined species. Slebocka-Tilk et al.[9] were the first to obtain X-ray diffraction evidence as to the exact crystal structure of 8. The results indicate that the crystal form of 8 involves a bromonium ion with the tribromide counterion above the Br^+ and parallel to the axis of the double bond (see **Figure 2**). The bond lengths of the bromonium ion were 2.116 Å and 2.194 Å for the C-Br^+ bond lengths and 1.497 Å for the C-C bond. The central Br of the Br_3^- is not directly over the Br^+ of the bromonium ion, and it is the positioning of the Br_3^- that causes the Br^+ to be in an unsymmetrical position.

Figure 2 : Perspective View of **8** Showing the Relative Positioning of the Br_3^- [9]

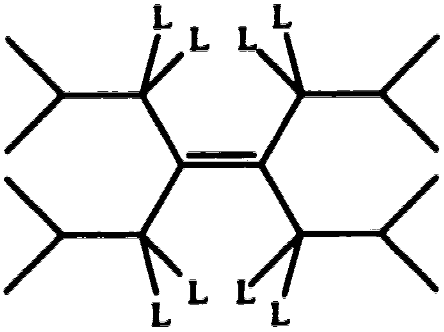


ii) <u>Reversibility of Bromonium Ion Formation</u>:

The question of whether the bromonium ion is reversibly formed is one that has been a matter of some contention. The work with adamantylideneadamantane[8,19,20] has shown that the olefin can be reformed from the ion. However it has been argued[2b] that this compound is atypical because it can not form products and that in highly ionizing solvents reversibility of the formation of normal bromonium ions would be very slow in comparison to product formation. Therefore, cases of reversibility must be found with olefins that can form products.

It has also been pointed out[10b] that the reversible or irreversible formation of the bromonium ion can not be revealed by simple kinetic measurements as the ultimate fate of the reformed Br_2 is to rereact with olefin. Therefore, there must be some feature of the reaction that makes the reverse step detectable.

As a result of the study of **7**, it was postulated that steric hindrance may slow the formation of products to such a point that evidence for reversibility could be obtained. A molecule that exhibits such properties is tetra*iso*butylethylene (**11**, TIBE).[10f]



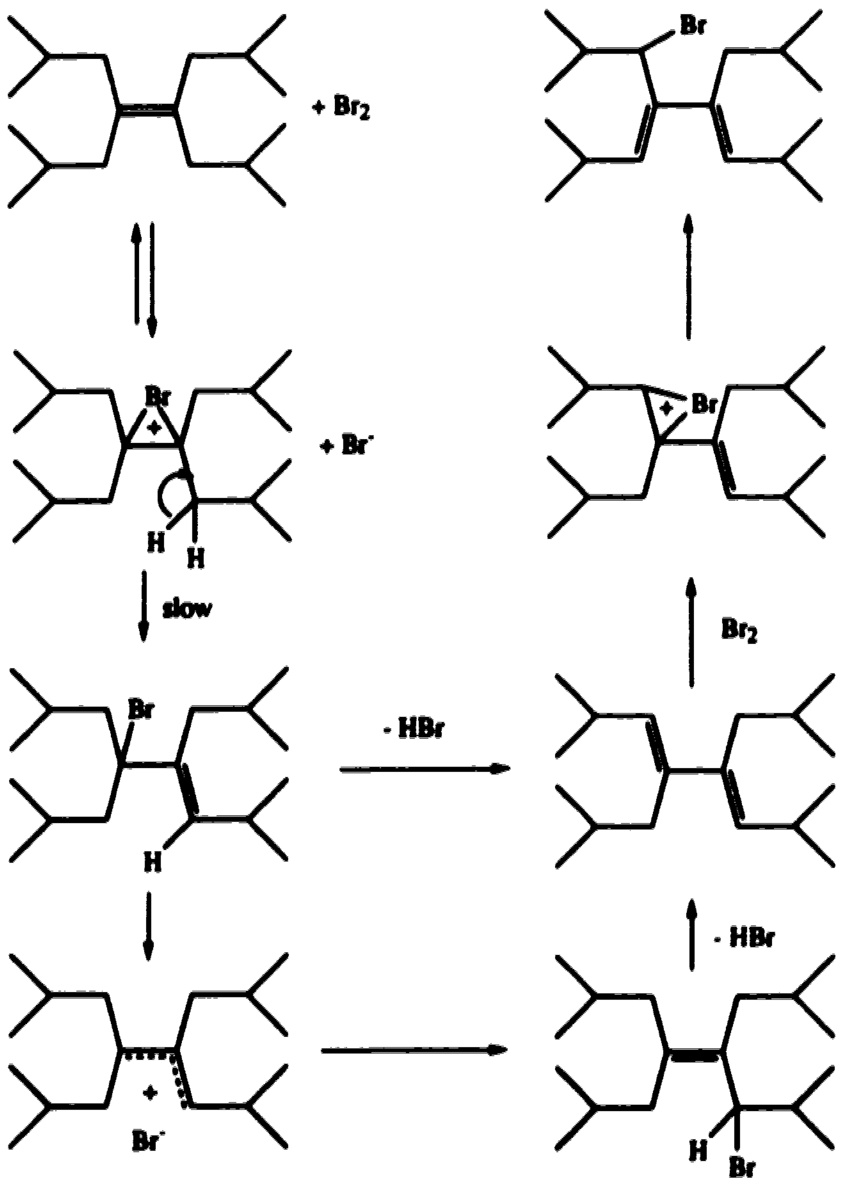
11a L=H

11b L=D

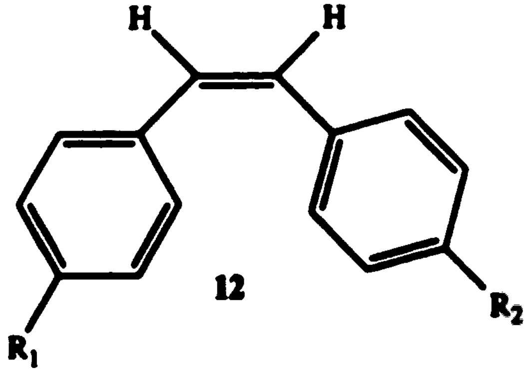
The initial product of the reaction of **11a** with Br_2 is not the normal 1,2-dibromide addition product, but a double bond rearranged allylic bromide. The kinetics of the addition of Br_2 correspond to a clean second-order process (first-order in both Br_2 and olefin) which does not require an induction period. Also, the rate constants for reactions monitored at 480 nm by UV/Vis spectrophotometry using cells that were maintained in the light beam of the spectrophotometer were experimentally the same as the rate constants obtained from cells alternated in and out of the light beam during the course of data collection. These results suggest that the process is an ionic, rather than a radical, addition.

The proposed pathway for the formation of double bond rearranged allylic bromide is shown in **Scheme 9**. Because of the bulky side groups, the nucleophile is restricted from approaching the carbons of the bromonium ion to form normal addition products. Therefore, a lower energy pathway is followed whereby a proton is removed and the double bond rearranged allylic bromide results. These findings, while interesting, do not give information about the potential reversibility of the bromonium ion. Therefore, **11b** was also brominated in AcOH at 25°C and a Dkie of $k_H/k_D = 2.3$ was observed. The observation of a primary Dkie indicates that the rate limiting step must involve proton abstraction with all preceeding steps, including bromonium ion formation, being reversible.

Scheme 9



Cis and *trans*-stilbene (**12a**, **13a**) comprise another set of compounds that has been carefully studied in order to provide some evidence for reversiblity of bromonium ions. It has long been known that Br_2 addition to stilbenes in nonpolar solvents (dielectric constant 2-3) is 90-100% trans[23]. However, as the dielectric constant increases the stereoselectivity of the addition decreases.[23] In solvents of dielectric constant of 35 and higher, the addition becomes essentially nonstereoselective (see Table 5). This is explained by the intermediate cyclic bromonium ion opening to a carbocation in which rotation around the central C-C bond can occur before the ion recloses. The driving force for rotation about the bond of *cis*-stilbene is relief of the compression between the sterically demanding phenyl groups. This compression strain is also invoked to explain the difference in the rates of bromination (k_{cis}/k_{trans} = 2.96 in acetic acid at 25°C)[24]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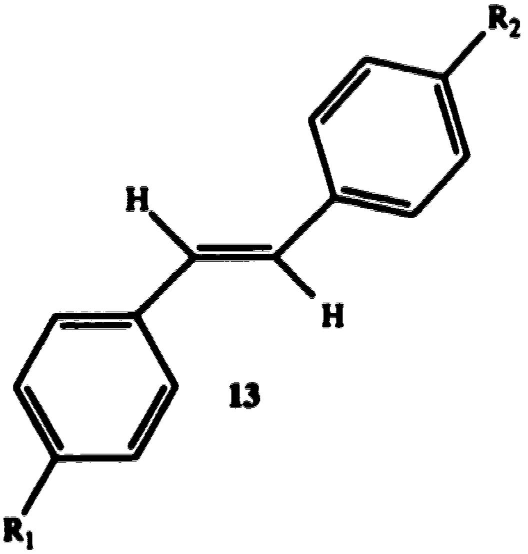

13

a $R_1 = R_2 = H$
b $R_1 = H$, $R_2 = CH_3$
c $R_1 = CF_3$, $R_2 = H$
d $R_1 = R_2 = CF_3$

Table 5 : Fractions of *meso*-α,α'-Dibromobibenzyl as compared to Total Dibromide Product Found from Br_2 Addition to *cis*-Stilbene[a]

Solvent	D[b]	No Br^-	Br^- Added	Solvent	D[b]	No Br^-	Br^- Added
Heptane	1.9	0	-	*t*-BuOH	10.9	0.3[c,d]	-
C_6H_{12}	2.0	0	-	BuCN	17.4	0.4	-
CCl_4	2.2	0	-	C_6H_5CN	25.2	0.6[c]	-
C_6H_6	2.3	0.1	-	$C_6H_5NO_2$	34.8	0.9	0.5
CS_2	2.6	0.1	-	CH_3NO_2	35.9	0.9	-
C_6H_5Cl	5.7	0.4	-	CH_3CN	37.5	0.7	0
CH_3CO_2H	6.2	0.5[c]	-	H_2O[e]	78.5	-	0
CH_2Cl_2	9.1	0.5	0	H_2O[f]	78.5	0.8	0.4
$(CH_2Cl)_2$	10.7	0.4	0				

a Reference 23.

b Dielectric constant; values obtained from reference 25.

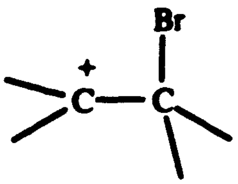
c Experiments with *trans*-stilbene in this solvent gave *meso*-dibromide in each case, but an unidentified impurity other than *d,l*-dibromide or *trans*-stilbene was consistently present. The same type of impurity was presumably a contaminant in the products produced from *cis*-stilbene, but its presence was less apparent.(Ref. 23)

d Experiments with *cis*-stilbene in *tert*-butyl alcohol gave erratic results with the fraction of *meso*-dibromide varying from 0.1 to 0.4.

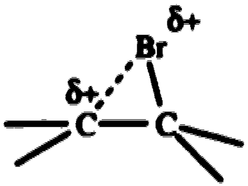
e The water contained cetyltrimethylammonium bromide and sodium bromide.

f The water contained sodium dodecyl sulfate.

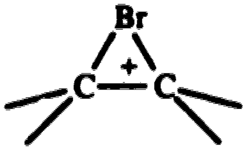
The exact form of the ion produced from stilbenes is undetermined, but in solvents of low ionizing power the ion is probably best represented as **14c** because the Br_2 addition is *trans* and there is little or no rotation about the double bond. As the ionizing power of the solvent increases, the ability of the solvent to stabilize positive charge increases and the ion may resemble the partially bridged **14b**. This ion (**14b**) would have restricted rotation, that is the ion can open to **14a** and have rotation about the central C-C bond before reclosing to **14b**. Therefore, 100% trans addition is not observed. When the reaction is performed in water the addition becomes nonstereospecific and so the ion could resemble the β-bromo carbocation **14a** which may be in equilibrium with **14b**.



14a

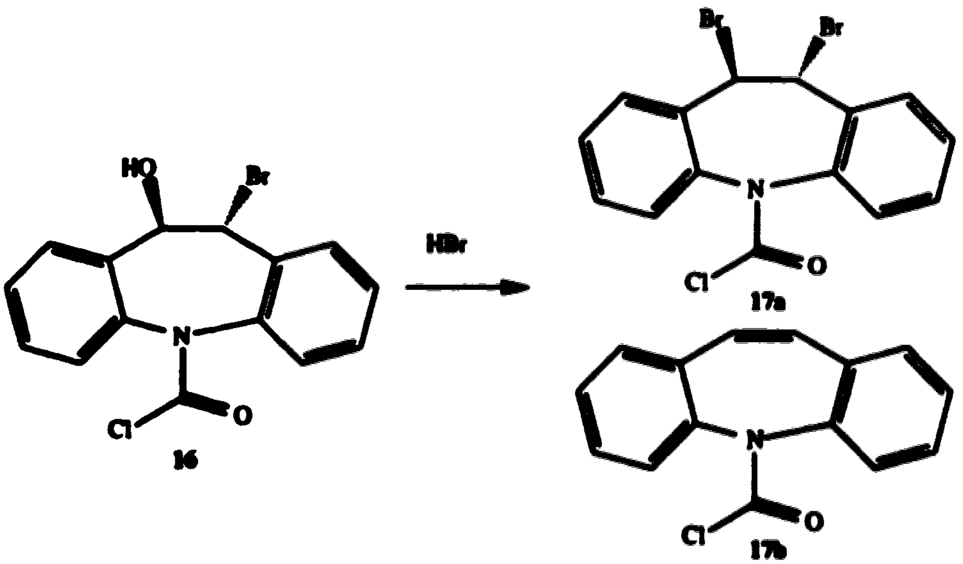


14b



14c

The addition of Br_2 to the stilbenes has been studied very carefully in terms of reaction rates and product ratios,[23,24] but it was a study by Bellucci et al.[10b,26] that showed reversal from the ionic intermediate to olefin. They generated the bromonium-bromide ion pair by reacting *erythro* and *threo*-2-bromo-1,2-diphenylethanol (**15a** and **15b** respectively) with gaseous HBr in 1,2-dichloroethane and chloroform and found that substantial amounts of *trans*-stilbene was generated. Bellucci et al.[10c] also carried out the same type of study on *trans*-10-bromo-10,11-dihydro-11-hydroxy-5*H*-dibenz[*b,f*]azepine-5-carbonyl chloride (**16**) and found products **17a** and **17b**. The products are produced through the generation of the bromonium ion/bromide pair which then further reacts to produce either the dibromide or olefin. The ratios of **17a**:**17b** found were 7:3 in 1,2-dichloroethane and 3:7 in CCl_4. Bellucci's interpretation was that the olefin resulted from Br^- capture of the bromonium ion on Br^+.



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17a

17b

If the ions that were formed in these studies[10b,10c] were indeed the bromonium ions, then it should be possible to detect reversal that occurs during the bromination of *cis*-stilbene (**12a**) by determining the presence of *trans*-stilbene in the reaction mixture.

The composition of the reaction mixture of *cis*-stilbene with Br_2 as a function of time is given in **Table 6** and shows the production of *trans*-stilbene. It was suggested that the *trans*-stilbene was generated by a process much like that shown in **Scheme 10** where the bromonium ion can be nucleophilically attacked to form the *d,l*-dibromide or open to form the carbocation. Once the carbocation is formed there can be rotation about the bond and reclosure to form the bromonium ion of *trans*-stilbene. This bromonium ion can then be nucleophilically attacked at carbon to form the *meso*-dibromide or on Br^+ to form *trans*-stilbene and Br_2. The data give no information as to whether there is reversal from the bromonium ion of *cis*-stilbene.

Scheme 10

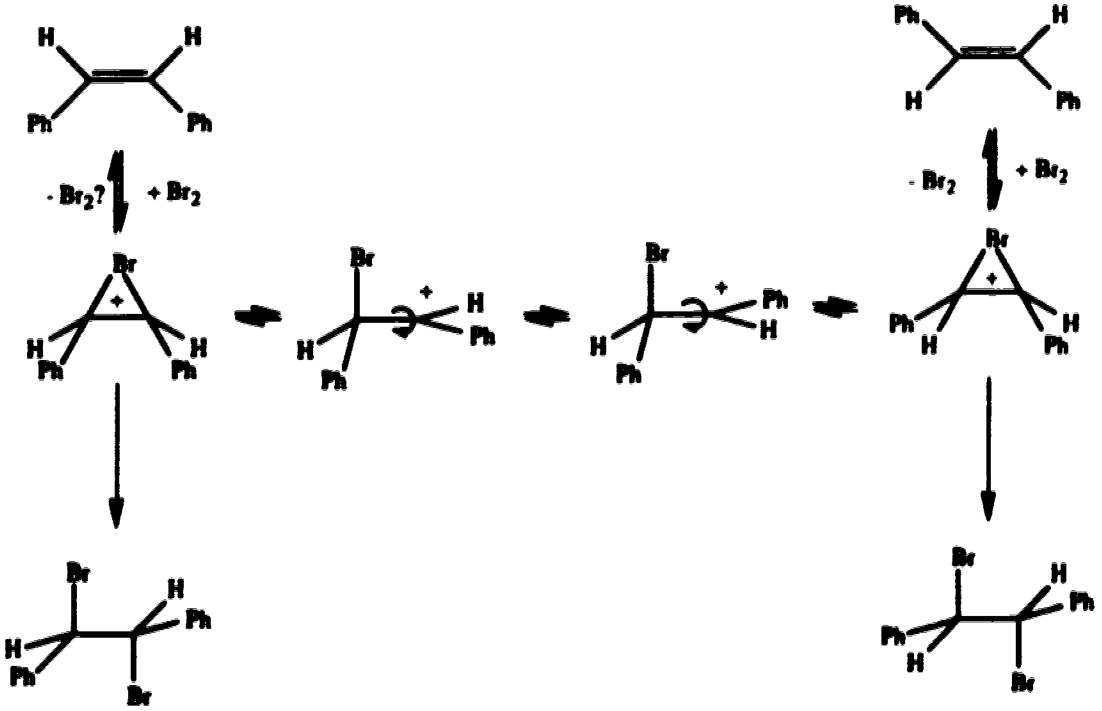


Table 6 : Observed Product Distribution as a Function of Time for the Reaction of 2.5 x 10^{-3} M of both [Br_2] and [*cis*-Stilbene] in 1,2-Dichloroethane at 25°C[a]

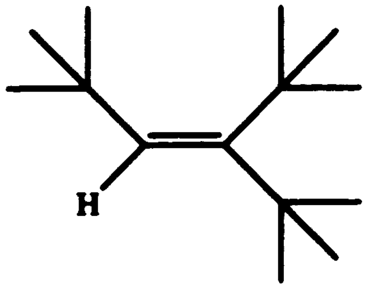
	Products %[b]			
time, min.	*meso*-dibromide	*d,l*-dibromide	*trans*-stilbene	*cis*-stilbene
0	-	-	-	100
16	30	23	4	43
28	34.5	27	5	33.5
53	40	31	5.5	23.5
101	45	34	6.5	14.5
249	47	39	5	9

a Reference 10b.

b Average of three measurements. Errors are ±2% of the quoted values.

In a continuation of this study, Bellucci et al.[26] studied the product ratios for Br_2 addition to 12 and 13 in 1,2-dichloroethane. They concluded that the extent of reversibility is affected by remote substituents that can modify the charge distribution between the bromine and carbons. That is, when electron donating groups were substitued for H there was little or no *trans*-stilbene derivatives produced. One would anticipate that an electron donating group would stabilize a positive charge and the formation of an open β-bromocation, such as 14a, could occur. However, when electron withdrawing groups are substituted on the phenyl ring, the observed *trans*-stilbene increased dramatically. With this in mind, the results showed that β-bromocarbocations did not appear to reverse, whereas the symmetrical bromonium ions were the most prone to have observable reversal.

In the cases reported above, the olefins possessed either internal strain (*cis*-stilbene) or were sterically demanding (adamantylideneadamantane, TIBE). There is other kinetic evidence that sterically hindered olefins such as tri-*tert*-butylethylene[27] (18) and 3-acetoxy-2-cholestene[28] (19) undergo reversal of the bromonium ions back to starting materials.



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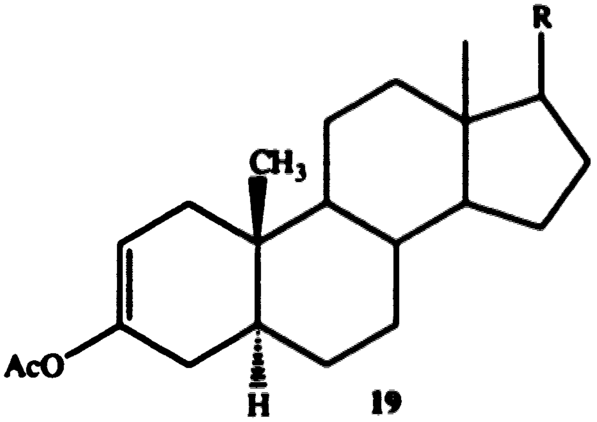
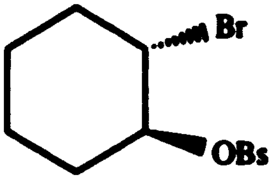


19

For olefins **18** and **19** a straight line for the plot of $k_g(1 + K_{eq}[Br^-])$ vs. $K_{eq}[Br^-]$, as in **Figure 1**, is not observed. The plot gives a line with a downward curve that looks very much like one resulting from a common ion rate depression. This has been interpreted[27,28] in terms of a competitive process involving Br^- capture of the bromonium ion at either the Br^+ or the carbons. The former process leads back to starting material and the latter to dibromide product. For sterically demanding olefins such as **18** and **19**, product formation should be retarded so that capture on Br^+ is prominent.



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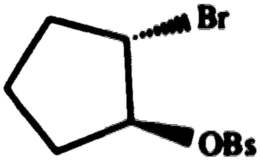

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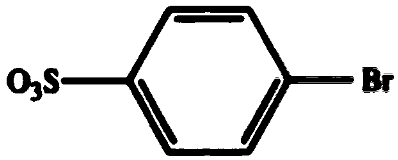
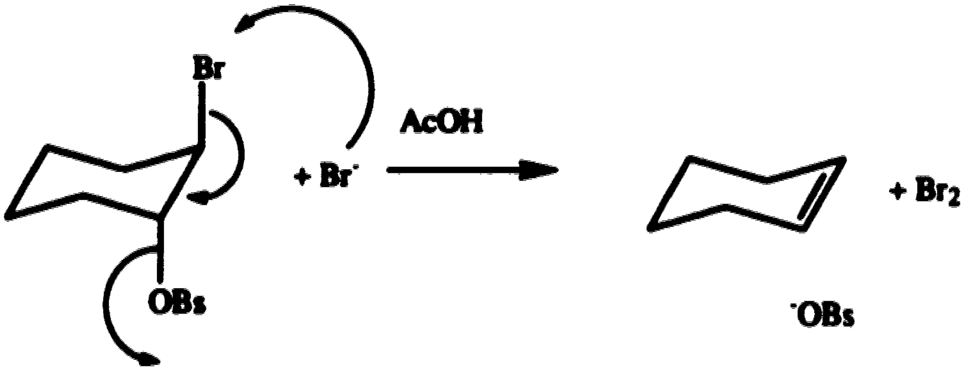
OBs =



Experimental evidence for reversal of the bromonium ions of less sterically demanding olefins, such as cyclohexene, has also been obtained. A study was performed by Brown et al.[10a] in which *trans*-2-bromo-1-[((4-bromophenyl)sulfonyl)oxy]cyclohexane and *trans*-2-bromo-1-[((4-bromophenyl)sulfonyl)oxy]cyclopentane (**20** and **21**) were solvolyzed at 75°C in acetic acid in the presence of Br^- and a scavenger olefin (cyclopentene for **20** and cyclohexene for **21**) that was added to react with any Br_2 that was generated. The results for the solvolysis of **20** in the presence of added Br^- show that there is a substantial amount of cyclopentene addition product (5-10% of total products). This was interpreted as Br^- capture at Br^+ of the solvolytically formed bromonium ion to form Br_2 and olefin. This regenerated Br_2 can then react with another olefin (cyclopentene) faster than Br_2 can recombine with the small amount of cyclohexene. Cyclopentene is known to react faster with Br_2 than cyclohexene.[29]

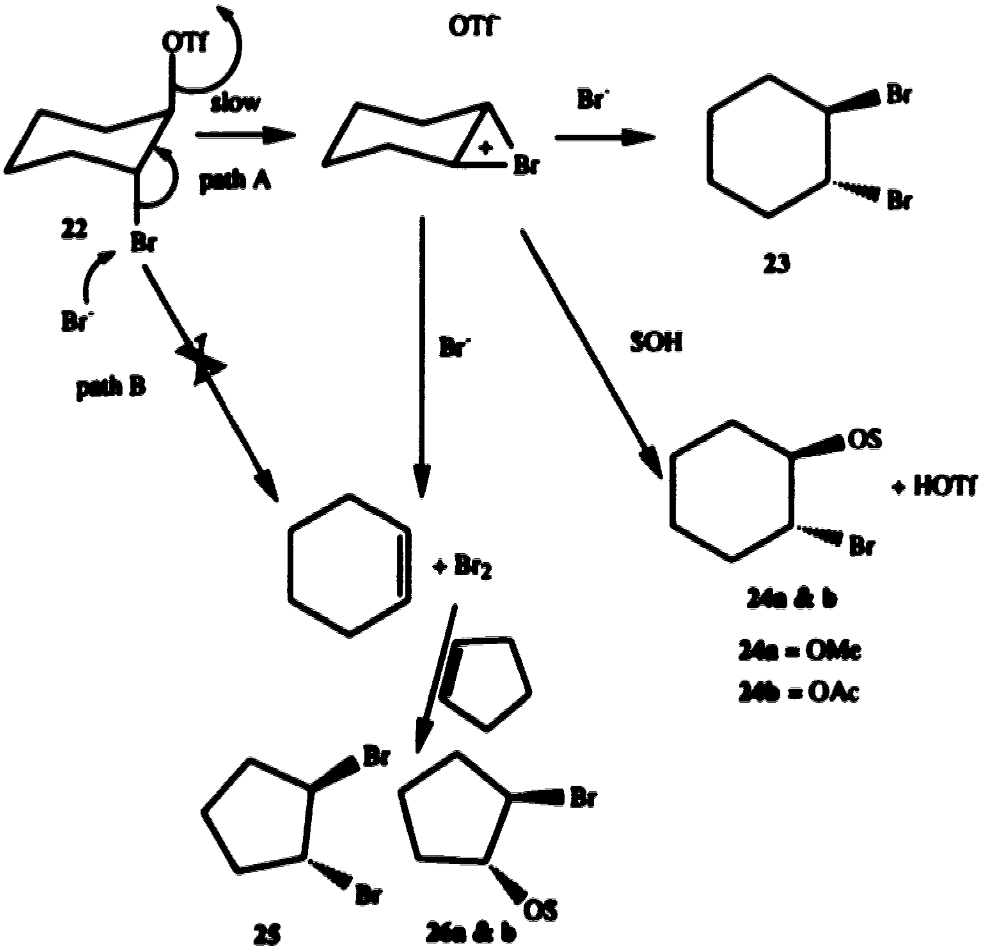
There were several difficulties with this study; 1) the solvolysis required high temperature (75°C) in order to proceed at a reasonable rate, 2) the KBr added was not completely soluble in the media and an accurate determination of $[Br^-]$ was not possible, 3) although there is no question that free bromine was generated, there is uncertainty about how it was formed. As shown in **Scheme 11**, Br_2 may be generated by Br^- attack on Br to produce Br_2, OBs^-, and cyclohexene.

Scheme 11



In a continuation of the work outlined above, these difficulties were addressed. Zheng et al.[30] studied the solvolysis of *trans*-2-bromocyclohexane trifluoromethanesulfonate (**22**). This compound has the advantage of solvolyzing quickly in MeOH at room temperature and, therefore, does not require the elevated temperatures necessary in the previous study.[10a] A potential mechanism for this reaction is shown in Scheme 12. In path A, the bromine effects an internal nucleophilic displacement (N_DI) of OTf^- to form the bromonium ion. Once the bromonium ion is formed, solvent capture forms *trans*-bromosolvate (**24**), and Br^- capture at carbon leads to dibromide (**23**). If bromide captures at Br^+, cyclohexene and Br_2 are generated and the Br_2 can then react with cyclopentene. If the solvolysis occurs by path B, then Br^- nucleophilically attacks at the bromine of **22** and forms Br_2, cyclohexene, and OTf^-.

Scheme 12



It was found that the rate of solvolysis in both MeOH and AcOH is independent of [Br⁻]. This indicates that Br⁻ does not appear in the rate limiting step, and therefore path B is not a kinetically important process.

Shown in **Tables** 7 and 8 are the product ratios of the solvolysis of 22 in MeOH and AcOH at varying [Br⁻] in the presence of the scavenger olefin, cyclopentene. The presence of addition products of cyclopentene indicates that Br_2 is generated during the course of the solvolysis.

Table 7 : Percentages of Dibromocyclohexane (23), Dibromocyclopentane (25), *trans*-1-Acetoxy-2-bromocyclohexane (24b), and *trans*-1-Acetoxy-2-bromocyclopentane (26b) Obtained from the Solvolysis of 22 in AcOH Containing 0.5 M Cyclopentene and Varying [Br⁻], $\mu = 0.1$ ($LiClO_4$)[a,b,c]

[LiBr] (M)	%25	%26b	%23	%24b	(25+ 26b)/23
0	0	0	0	100	
0.025	9.7	3.1	5.4	81.7	2.4
0.05	17.4	3.7	8.4	70.5	2.5
0.075	22.4	3.2	10.8	63.6	2.4
0.10	26.4	2.2	12.8	58.7	2.2

a Reference 30.

b Ambient temperature (22-26°C); [22] = 0.015 M.

c Averages of triplicate determination; estimated error ± 0.4%.

Table 8 : Percentages of Dibromocyclohexane (23), Dibromocyclopentane (25), *trans*-1-Methoxy-2-bromocyclohexane (24a), and *trans*-1-Methoxy-2-bromocyclopentane (26a) Obtained from the Solvolysis of 22 in MeOH Containing 0.5 M Cyclopentene and Varying [Br$^-$], μ = 0.3 (LiClO$_4$)[a,b,c]

[LiBr] (M)	%25	%26a	%23	%24a	(25+26a)/23[d]
0	0	0	0	100	
0.1	3.2	9.7	1.2	84.9	10.8±4.2
0.2	9.9	14.2	2.0	73.0	12.0±2.5
0.3	18.9	17.1	2.5	60.5	14.4±2.2

a Reference 30.

b Ambient temperature (22-26°C); [22] = 0.015 M.

c Averages of duplicate determination; estimated error ± 0.3%.

d Errors computed on the basis of estimated errors in percentage of 23, 25, and 26a.

The dibromide/bromosolvate product ratios for the addition of Br$_2$ to cyclopentene in MeOH and AcOH at varying [Br$^-$] were determined and compared to those ratios of cyclopentyl products produced during the solvolysis of 22 under the same conditions. The cyclopentyl product ratios observed for the solvolysis of 22 were the same as for the reaction of cyclopentene with Br$_2$. This result indicates that it must be free Br$_2$ that reacts with cyclopentene. Without added Br$^-$, there are no cyclopentyl addition products observed. This indicates that transfer of Br$^+$ from the cyclohexene bromonium ion to cyclopentene in AcOH or MeOH does not appear to be important under the solvolysis conditions.

The most important information contained in Tables 7 and 8 are the ratios (25+26b)/23 and (25+26a)/23 which stay relatively constant over the entire [Br$^-$] range. In AcOH the ratio (25+26b)/23 is 2.0 to 2.5 and in MeOH the ratio (25+26a)/23 is 10.8 to 14.4 which means that in both solvents there is a greater propensity for Br$^-$ to capture at Br$^+$ than at carbon. The relative invariance of these ratios to [Br$^-$] indicates that the three species arise from Br$^-$ capture of a common intermediate.

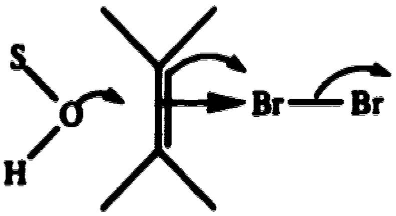
The finding that the solvolytically produced bromonium ion of cyclohexene is captured by Br^- at Br^+ 25 times more often than at carbon in a highly ionizing solvent such as MeOH is surprising. This evidence suggests that reversibility of the bromonium ions produced during electrophilic bromination of olefins may be more general than was once thought.

iii) Solvent Effects

It has been shown by *ab initio* calculations[31] that more than 60 kcal mol^{-1} would be required to form the bromonium ion and bromide counterion of ethylene in the gas phase, whereas the same reaction in water[32] has an activation free energy of less than 10 kcal mol^{-1}. This tremendous difference in energies is due to solvation stabilization of a reaction intermediate which in turn lowers the energy required for the reaction to proceed.

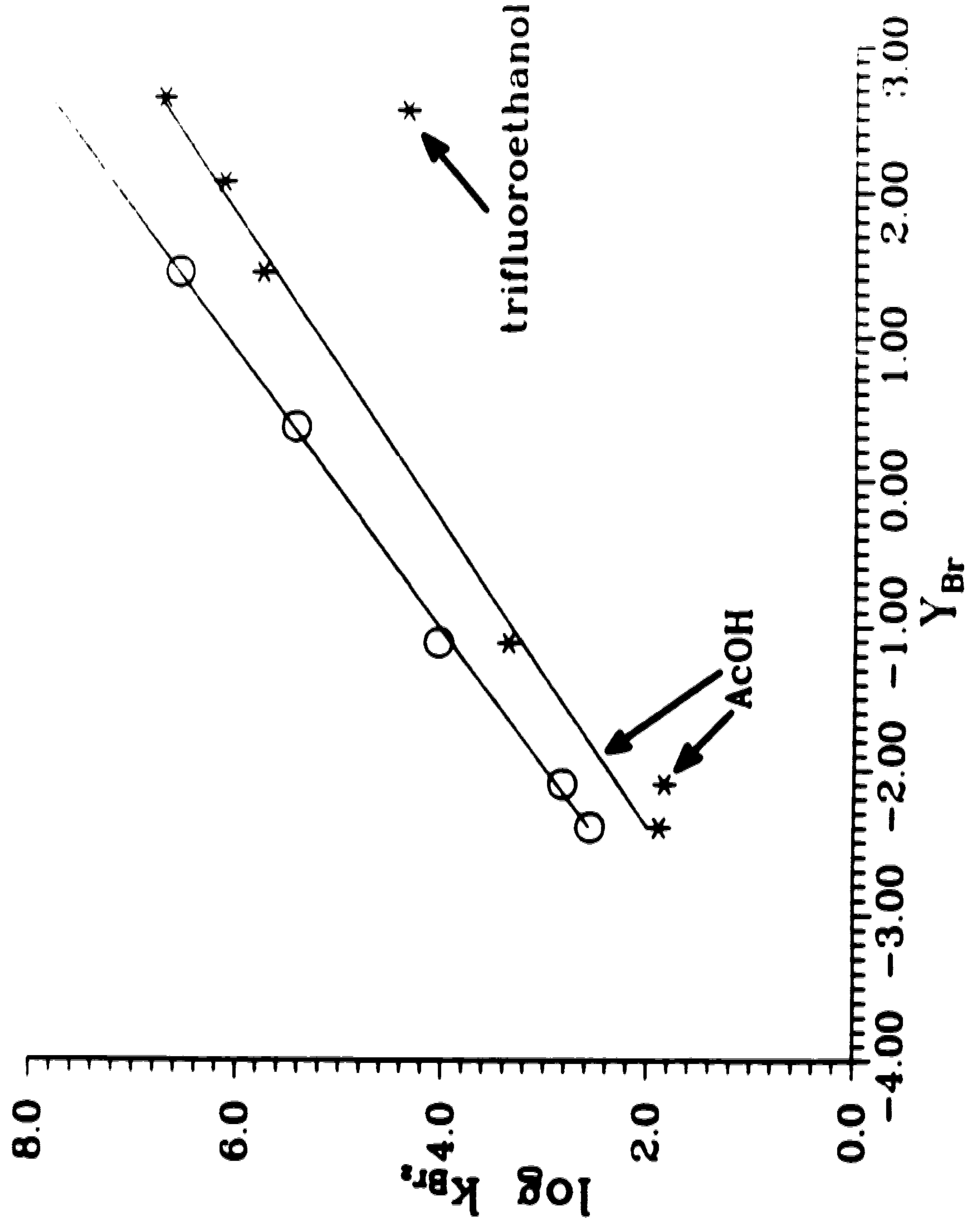
In protic solvents, such as methanol[33,34] and acetic acid,[35] the solvent kinetic isotope effects have been determined for the bromination of several alkenes and interpreted in terms of stabilization of a fully developed bromide ion. It seems reasonable that a protic solvent should solvate a developing negatively charged ion.

Scheme 13



It has also been suggested that there is some nucleophilic solvent assistance (NSA) of ionization of the CTC to form the bromonium ion (see **Scheme 13**).[2a,2b,10g,10e,11] The suggested form of NSA shown in **Scheme 13** is reminiscent of the proposed tribromide mechanism where Br^- nucleophilically attacks the CTC. The evidence to support this form of assistance comes from Winstein-Grunwald plots ($\log k = m\,Y$) of the $\log k_{Br_2}$ vs Y: the latter represents the ionizing power of the solvent. The plots shown in **Figure 3** were

Figure 3 : log k_{Br_2} vs Y_{Br} Plots for Bromination of Pent-1-ene (*) and *cis*-Methyl-*tert*-butylethylene (O) in Ethanol, Methanol, and Their Aqueous Mixtures and also AcOH and Trifluoroethanol.[37]



obtained using Y_{Br} parameters derived from 1-bromoadamantane solvolysis,[36] a reaction which cannot involve NSA and where the leaving group is a bromide ion as in bromination. The m_{Br} values for free bromine addition to alkenes are all close to unity (m_{Br} varies from 0.8 to 1.1).[2a] The important aspect of **Figure 3** is the displacement from the line of the AcOH and trifluoroethanol points for 1-pentene, whereas for the more sterically hindered *cis*-methyl-*tert*-butylethylene the AcOH point falls on the line. This has been interpreted as evidence that there is a solvent assistance for bromination of a nonsterically hindered olefin in ethanol, methanol and their aqueous mixtures that is not present in solvents that are less nucleophilic but of similar ionizing power. However, as the olefin becomes more sterically hindered the solvent cannot closely approach the olefinic bond. As a result the points for both nucleophilic and nonnucleophilic solvents fall on the same line because NSA can no longer occur.

Because of experimental limitations, the modified Winstein-Grunwald equation (($\log k_S/k_{S_O} = m\,Y + l\,N$) where l represents the substrate's sensitivity to solvent nucleophilicity and N is solvent nucleophilicity) could not be employed. Consequently, the magnitude of NSA has been estimated by direct comparison of the rate constants for bromination in solvents of similar ionizing power but different nucleophilicities. Shown in **Table 9** is a comparison of these values for different olefins.

Table 9 : Nucleophilic Solvent Assistance in Alkene Bromination Estimated by R, the Rate Ratios in Two Solvents of Different Nucleophilicity but Similar Ionizing Power

Alkene	(k_{60EtOH}/k_{AcOH})	$(k_{60MeOH}/k_{TFE})^{a}$
Allylbenzene[b]	8.3	8.7
1-Pentene[c]	6.2	7.6
Ad=CH_2[d]	0.9	-
t-Bu-*i*-PrC=CH_2[c]	1.4	-
DPE[e]	2.6	-
4-MeO-DPE[e]	1.5	-

a This ratio is given only for weakly reactive alkenes because the bromination rates in trifluoroethanol (TFE) are generally too fast for kinetic measurement.

b Ref. 10g.

c Ref. 37a.

d Ref. 33.

e DPE = 1,1-diphenylethylene; Ref. 38.

The ratios in **Table 9** show that as the steric hindrance increases R drops to 1 which indicates a lack of NSA. However, for the less hindered molecules, R increases to a value of 8. It appears that there is some form of assistance by the solvent to the unhindered molecules that causes an increase in the rate constant for Br_2 addition. This effect is not present for the more sterically hindered olefins. The observed effect is small but undeniably present. The exact nature of this assistance may be as shown in **Scheme 13** or be of some other unspecified nature.

Current literature has provided abundant intimate detail concerning the subtleties of electrophilic bromination, but several areas remain to be investigated. In what follows, we will present new results obtained from the investigation of three aspects of electrophilic halogenation. These are; 1) lifetimes of bromonium ions in MeOH solution, 2) studies of the stable bromonium ion and iodonium ions of **8** and bicyclo[3.3.1]non-9-ylidenebicyclo[3.3.1]non-9'-ane, 3) the use of secondary deuterium kie's in the study of the kinetics of bromination of a sterically hindered olefin, 7-norbornylidene-7'-norbornane.

CHAPTER 1

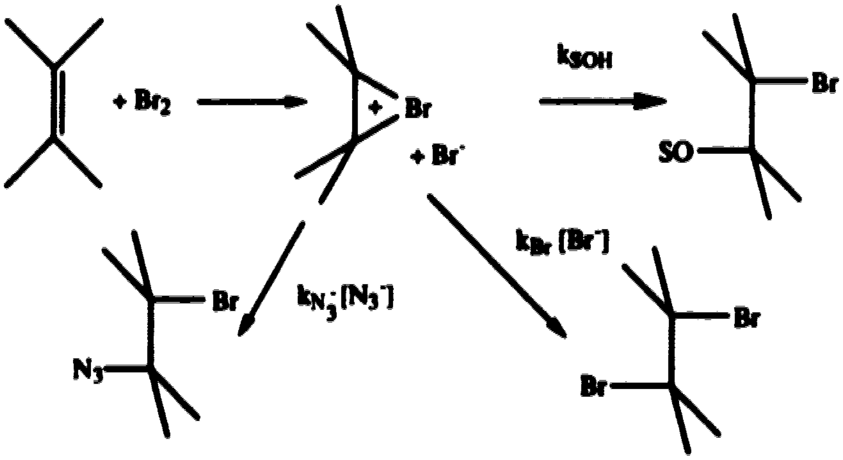
Lifetimes of the Bromonium Ions of Common Olefins

a) Introduction

Due to the general instability of the ions of less hindered olefins toward nucleophilic attack, there is very little information about the properties of these ions in solution. For example, there exist no data concerning the lifetime of bromonium ions in solution other than the experimentally observable fact that the ion must exist long enough for the nucleophile (Br^-) to translocate from where it is formed to a position where it can nucleophilically attack to generate trans product.

We sought to determine whether information about the lifetime of the bromonium ion in solution can be obtained using the azide "clock" methodology developed by Jencks and co-workers.[40,41] Using this method, the partitioning of a cationic intermediate between capture by solvent or added nucleophile (N_3^-) is determined. The nucleophile (N_3^-) is assumed to react with the carbocation at the diffusion limit and quantitative assessment of product ratios as a function of added nucleophile (N_3^-) are determined. Reported here is the application of this method to the bromonium ion problem by consideration of the competing product forming steps shown in **Scheme 14**.

Scheme 14



The bromonium ions of cyclohexene (**5a**), cyclopentene (**27**), tetramethylethylene (**28**), and the intermediate ion of styrene (**4a**) were studied in MeOH . Evidence will be provided which shows that collapse of the intimate ion pair or solvent separated ion pair is not an important route for product formation in MeOH for **5a**. Also studied was the solvolysis of *trans*-2-Bromocyclohexyl trifluoromethanesulfonate (**22**) in MeOH containing added N_3^- and Br^-. The solvolysis of **22** is believed to be a N_DI^{10a} process where the intermediate formed should be a bromonium ion. Therefore, the product ratios from the solvolysis of **22** were compared to those obtained from brominating **5a** under comparable conditions.

b) Experimental

i) General

Routine NMR and IR spectra were obtained with Bruker WP-80 NMR and Nicolet SX-20 FTIR spectrometers. The 200 MHz NMR spectra were obtained with a Bruker WP-200 spectrometer. HPLC analysis of the product mixtures was performed using a Hewlett-Packard 1081A HPLC with a Waters Differential Refractometer R401 detector and utilizing a Waters RCM 8 x 10 radial compression module containing a Waters 10 cm C-18 μ Bondapak 8 mm x 100 mm column. The eluent was 70:30 methanol:H_2O for all systems except tetramethylethylene where the eluent was 55:45 methanol:H_2O. GLPC analysis of the product mixtures from solvolysis experiments were completed with a Hewlett-Packard 5830A gas chromatograph using a 6' x 1/8" 10% DEGS on 80-100 mesh Chromosorb W column. Temp. 1 = 100°C for 3 min., programmed at ΔT = 9°C/min. to 180°C; He flow = 38 mL/min.

ii) Materials

trans-1,2-Dibromocyclohexane,[42] *trans*-1,2-dibromocyclopentane,[42] 2,3-dibromo-2,3-dimethylbutane,[43] and 1,2-dibromo-1-phenylethane[44] were prepared and purified as described in the literature. *trans*-1-Bromo-2-methoxycyclohexane,[44] and *trans*-1-bromo-2-methoxycyclopentane[45] were prepared by a method outlined by Erickson and Kim[46] and purified by vacuum distillation. 2-Bromo-3-methoxy-2,3-dimethylbutane[47] was prepared analogously[46] and purified by spinning band distillation using a water aspirator (bp 49°C, ~20 Torr, lit.[47] 52°C, 17 Torr). 2-Bromo-1-methoxy-1-phenylethane[48] was prepared[46] and purified by vacuum distillation (bp 50°C, 0.05 Torr; lit.[48] 52°C, 0.05 Torr).

All bromoazides were prepared by a general procedure described by Van Ende and Krief.[49] The crude materials were purified by column chromatography using silica gel (70-230 mesh) and an eluent of petroleum ether. The last traces of hydrocarbon solvent were removed from the pure compound by freeze-thaw cycles under 0.5 Torr vacuum. So prepared were *trans*-1-azido-2-bromocyclohexane,[50] and *trans*-1-azido-2-bromocyclopentane; ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 4.11 (m, 2H), 2.40-1.60 (m, 6H); FTIR (neat) 2104 cm^{-1} (-N_3). Exact mass calculated for $C_5H_8BrN_3$; 188.9901, found 188.9900. Also, 2-azido-3-bromo-2,3-dimethylbutane[51] was prepared in this manner; ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 1.79 (s, 6H), 1.49 (s, 6H). Exact mass calculated for $C_6H_{12}Br$ (M^+ -N_3); 165.0102, 163.0122, found; 165.0102, 163.0107. Microanalysis calculated for $C_6H_{12}BrN_3$: C, 34.97; H, 5.87; N, 20.39; Br, 38.77. Found: C, 34.95; H, 5.94; N, 20.31; Br, 38.70.

2-Azido-1-bromo-1-phenylethane and 1-azido-2-bromo-1-phenylethane were prepared[49] as a mixture and purified by column chromatography as an inseparable 8:5 mixture (by ^{1}H-NMR) of the respective isomers. Exact mass calculated for $C_8H_8{}^{81}BrN_3$; 226.9881, found 226.9882. Microanalysis calculated for $C_8H_8BrN_3$: C, 42.50; H, 3.57; N, 18.59. Found: C, 42.64; H, 3.45; H, 18.68. The identities of the two regioisomers and their relative ratios were ascertained by comparison with ^{1}H-NMR data obtained by Boerwinkle and Hassner.[52] 2-Azido-1-bromo-1-phenylethane, ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 7.40 (m, 5H), 5.00 (t, 1H, J = 7.6 Hz), 3.88 (d, 2H, J = 7.6 Hz). 1-Azido-2-

bromo-1-phenylethane, ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 7.40 (m, 5H), 4.76 (t, 1H, J = 7.6 Hz), 3.55 (d, 2H, J = 7.6 Hz).

trans-2-Bromocyclohexyl trifluoromethanesulfonate (22) was prepared from the corresponding *trans*-2-bromocyclohexanol[53] (1-2g) in dry CH_2Cl_2 (10 mL) containing equimolar pyridine and cooled to 0°C in an ice bath.[54] To this solution was added dropwise a 10-20% excess of neat trifluoromethanesulfonic anhydride (Aldrich) at such a rate that the temperature of the reaction mixture did not exceed 5°C. Immediately after the addition, the reaction mixture was washed with 2 x 2 mL aliquots of ice cold 0.01 N HCl, and then the CH_2Cl_2 layer was dried over $MgSO_4$. During these manipulations the solution was cooled in an ice bath. The CH_2Cl_2 solution was then filtered through glass wool into a flask, immediately stoppered, and placed in a dry ice chest. At this temperature (-78°C) the material solidifies and can be purified further by the removal of solvent with a pipette and recrystallization of the residue from fresh, dry CH_2Cl_2 at -78°C. The material is stable at -78°C for several days, but becomes discolored when kept above 0°C for prolonged periods. ^{1}H-NMR (CD_2Cl_2) δ 5.0-4.8 (m, 1H), 4.2-4.0 (m, 1H), 2.5-2.3 (m, 2H), 2.0-1.6 (m, 4H), 1.5-1.2 (m, 2H).[8,30] The material so produced is ~90% pure by ^{1}H-NMR, the remaining 10% being the 2-bromocyclohexanol (by ^{1}H NMR) that probably is formed by hydrolysis of 22 during the aqueous workup.

iii) Bromination

Reagent grade methanol (Mallinckrodt) was purified by distillation from CaH_2 under argon and was used within 24 hours. Bromine (Fluka), cyclohexene (BDH), 2,3-dimethyl-2-butene (Aldrich) and styrene (Fischer) were used as supplied. Cyclopentene was prepared by the dehydration[55] of cyclopentanol and purified by distillation (bp 44°C, ambient pressure). N-Bromosuccimide (NBS) (MCB) was recrystallized from water and stored in the dark in a sealed bottle at 5°C.

A typical bromination was conducted under conditions where the olefin and brominating agent were maintained at as low a concentration as possible. A solution of NaN_3 (0.03-0.4 M) in MeOH, (minimum volume of 70 mL), was placed in a three necked flask equipped with a magnetic stirbar. Two addition funnels, one containing olefin (3.5×10^{-4} - 9.7×10^{-3} moles) in 1.5 - 3.0 mL of MeOH and the other containing an equimolar amount of Br_2 or NBS in a similar volume of MeOH. (The relative concentrations of olefin and azide were chosen such that $[N_3^-] \geq 10[ole]$, and for purposes of calculation the $[N_3^-]$ was determined at the final volume which included all added MeOH.) The mixture was vigorously stirred (product ratios were independent of stirring process used) and both the olefin and Br_2 solutions were added dropwise over a period of several minutes at such a rate that the Br_2 color was discharged before the next drops were added. All reactions were conducted at ambient temperature (22 ± 2°C). Control experiments at temperatures of 15.5°C and 27.5°C established that the dibromide/methoxybromide/bromoazide product ratios for cyclohexene and styrene were invariant over this temperature range ($[NaBr] = [NaN_3] = 0.1$ M).

After completion of the addition, the reaction mixture was poured into approximately 800 mL of water and then extracted with 4 x 75 mL of CH_2Cl_2. The CH_2Cl_2 solution was dried over $MgSO_4$, and after filtration, the solvent was removed by rotary evaporation. The residue was diluted with a small amount of the HPLC solvent (70:30, methanol:H_2O) or CH_2Cl_2 to give a final concentration of 0.01-0.7 M in total products. This mixture was analyzed in 5-7 separate HPLC injections and the values of the integrated areas averaged for the final computations.

In the case of 2,3-dimethyl-2-butene, the above extraction procedure proved to give non-reproducible product recovery ratios, so an alternative workup procedure was employed. Following the bromination (as above) the reaction mixture was poured into saturated NaCl solution, (300-500mL) and further solid NaCl was added to saturate the MeOH. This mixture was then extracted with hexane (5 x 50 mL), and the combined hexane extracts were dried over $CaCO_3$. The hexane was removed by distillation through a 20 cm Vigreux column, and the last traces of hexanes were "chased" by co-distillation with added CH_2Cl_2.

HPLC and GLPC analyses were calibrated using known amounts of the authentic materials to determine the response factors of the detectors. For each series of reactions, the extraction procedure was tested using known amounts of the authentic products expected in MeOH, and subjecting this mixture to the workup procedure. In all cases, the products were recovered in amounts that agreed with the initial ratios. In the case of the bromoazides of styrene, only 1-azido-2-bromo-1-phenylethane was ever detected from the bromination in MeOH.

iv) Solvolysis of *trans*-2-bromocyclohexyl trifluoromethanesulfonate (22)

The solvolyses were conducted by adding a small aliquot of 22 in CH_2Cl_2 (1.5-2.5 mL containing 3.5×10^{-4} to 9.5×10^{-3} moles) dropwise, at ambient temperature, to 100 mL MeOH solutions containing 0.0 - 0.3 M NaN_3 or NaBr. The solution was vigorously stirred for 10 min., after which time the products were isolated in the same fashion as in the bromination experiments. Analysis of the products for solvolyses in the presence of N_3^- were conducted using the same HPLC protocol as described above. For the solvolyses in the presence of Br^-, the analysis were conducted by GLPC.

v) UV Studies

To ascertain the presence of new species formed from N_3^- and Br_2 or NBS, qualitative UV experiments in MeOH (purified by distillation from Br_2 as described by Dubois et al[4c]) were undertaken. With Br_2 (1.2×10^{-3} M) and NaN_3 (5.3×10^{-2} M) a very rapid formation of a new species having a λ_{max} at 312 nm was observed with subsequent decomposition ($k_{obsd} = 1.5 \times 10^{-2}$ s^{-1}) to generate a faint rose colored solution that was unreactive toward subsequently added cyclohexene. With NBS ($3\text{-}6 \times 10^{-3}$ M) and NaN_3

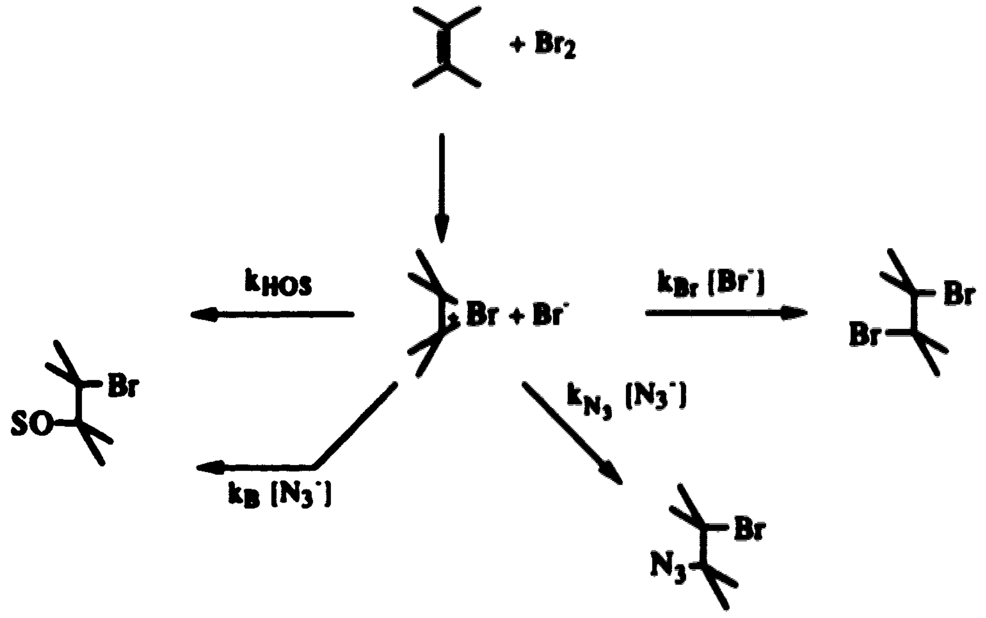
(3.5-5.3×10^{-2} M) a slower buildup of the 312 nm transient absorbance was observed (approximate $k_2 = 0.1$ M^{-1} s^{-1}), followed by its decomposition ($k_{obsd} = 1.5 \times 10^{-2}$ s^{-1}). The nature of the 312 nm species is unknown, but can be surmised to be BrN_3.[56]

When a MeOH solution of 3.3×10^{-3} M NBS and 0.10 M NaBr was monitored by UV-Vis spectroscopy the slow buildup (approximately 10 min.) of an absorbance at 280 nm was observed ($k_2 = 0.064$ M^{-1} s^{-1}). The resulting solution was stable for several hours and addition of cyclohexene immediately discharged the color thus suggesting that the 280 nm absorbance was attributable to Br_3^-.

c) Results

In Scheme 15 is presented a simplified working model for the various fates of the ion formed at low [Br_2] in MeOH in the presence of added N_3^- and/or Br^-. Subsequently, we will show that azide performs a dual role of nucleophile and a general base for delivery of solvent to the ion.

Scheme 15[a]



[a] k_{HOS} incorporates the solvent concentration

The fraction of bromo azide product (f_{az}) is given as:

(5)

$$f_{az} = \frac{k_{N_3^-}[N_3^-]}{k_{Br}[Br^-] + k_{HOS} + k_{N_3^-}[N_3^-] + k_B[N_3^-]}$$

which can then be rewritten as:

(6)

$$\frac{1}{f_{az}} = \frac{k_{N_3^-} + k_B}{k_{N_3^-}} + \frac{k_{Br}[Br^-] + k_{HOS}}{k_{N_3^-}} \quad \frac{1}{[N_3^-]}$$

From a plot of $1/f_{az}$ vs $1/[N_3^-]$ we obtain the slope and intercept given in equation 6. It should be noted that if the base term for azide (k_B) is non-existent then the y-intercept should be equal to 1 with the rest of the equation being unaffected (see equation 6).

Shown in **Figure** 4 is the plot of $1/f_{az}$ vs $1/[N_3^-]$ for the bromination of cyclohexene at ambient temperature in MeOH containing varying $[N_3^-]$. Similar plots for cyclopentene, tetramethylethylene, and styrene are shown in **Figures 5-7**, respectively. The primary data used to construct these plots are given as supplementary material (**Tables S1-S6**). The atypical experimental protocol adopted for bromination (see experimental) was followed because it has been shown[8] that intermolecular transfer of Br^+ between the bromonium ion and olefins have remarkably large rate constants in CD_2Cl_2. Therefore, by keeping the [ole] low, we had hoped to make the transfer process less important in these experiments. However, in retrospect, this is probably of little consequence since intermolecular transfer of Br^+ between ion and olefin has since been shown to be insignificant in the solvolysis of 22 under conditions comparable to those used here.[30] As an additional precaution, since even "innocent" anions such as triflate[57a] and perchlorate[57b] have been shown to capture bromonium ions, the addition of electrolytes to maintain

Figure 4 : Plot of $1/f_{az}$ vs $1/[N_3^-]$ for the Bromination of Cyclohexene in MeOH, T = 22 ± 2 °C. *, Br_2 Data; Open Circles, NBS Data. Slope, 2.05×10^{-1} (0.031×10^{-1}); Intercept, 1.36 (0.06).

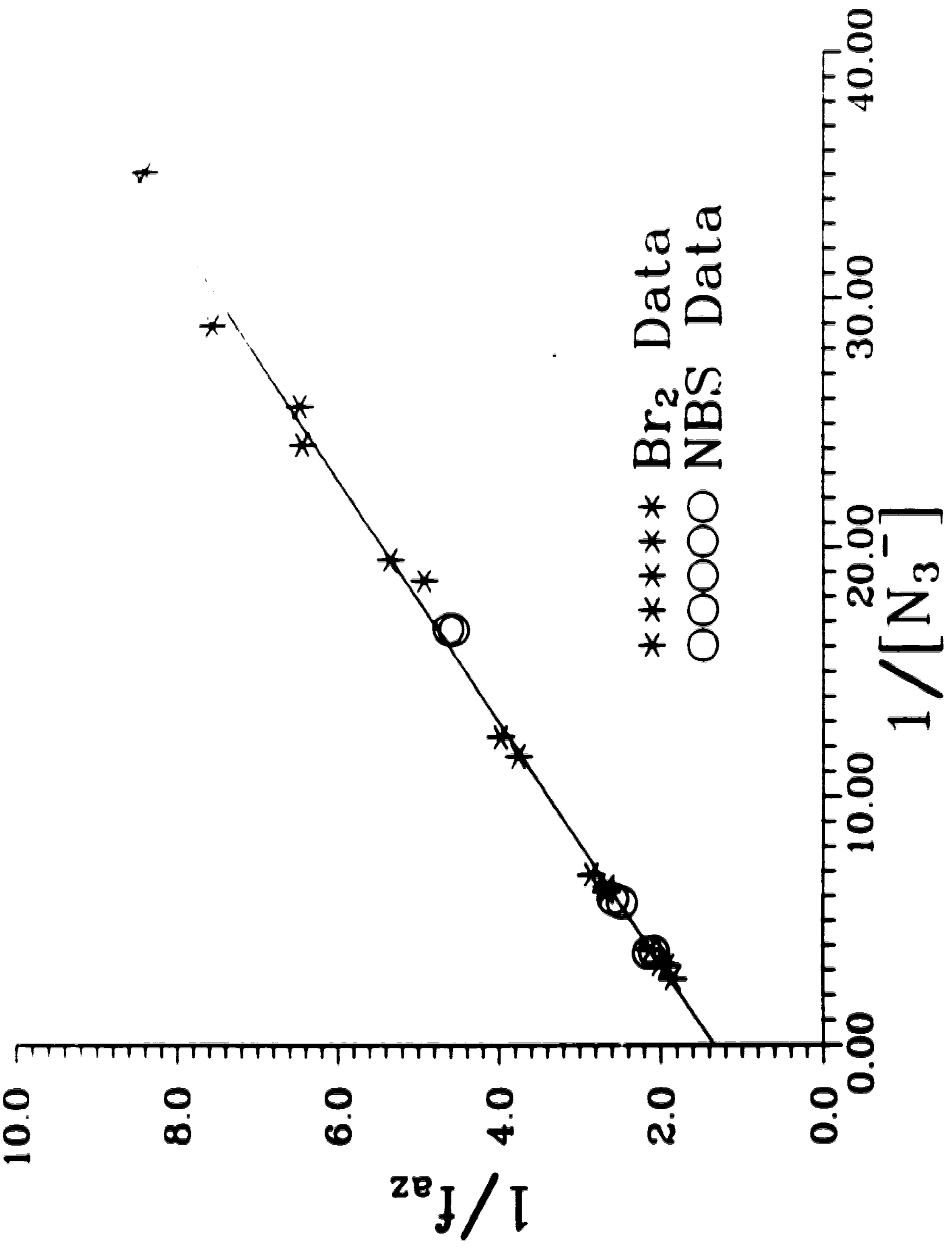


Figure 5 : Plot of $1/f_{az}$ vs $1/[N_3^-]$ for the Bromination of Cyclopentene in MeOH. T = 22 ± 2 °C. Slope, $1.69 \times 10^{-1} \pm (6.97 \times 10^{-3})$; Intercept, 1.64 ± (0.12).

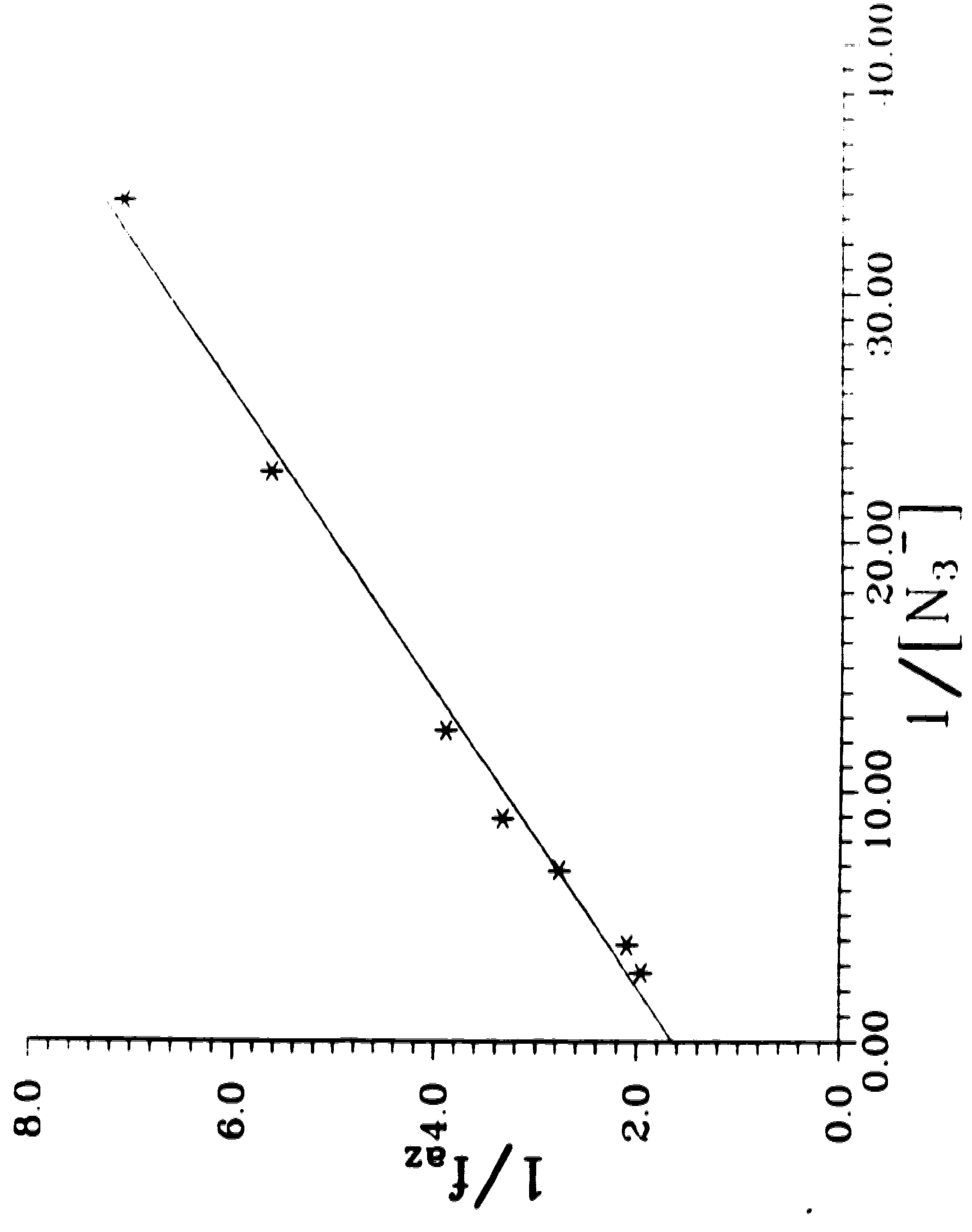


Figure 6 : Plot of $1/f_{az}$ vs $1/[N_3^-]$ for the Bromination of 2,3-Dimethyl-2-butene in MeOH. T = 22 ± 2 °C. *, Br_2 Data; Open Circles, NBS Data. Slope, $1.08 \times 10^{-1} \pm (8.39 \times 10^{-3})$; Intercept, $1.96 \pm (0.10)$.

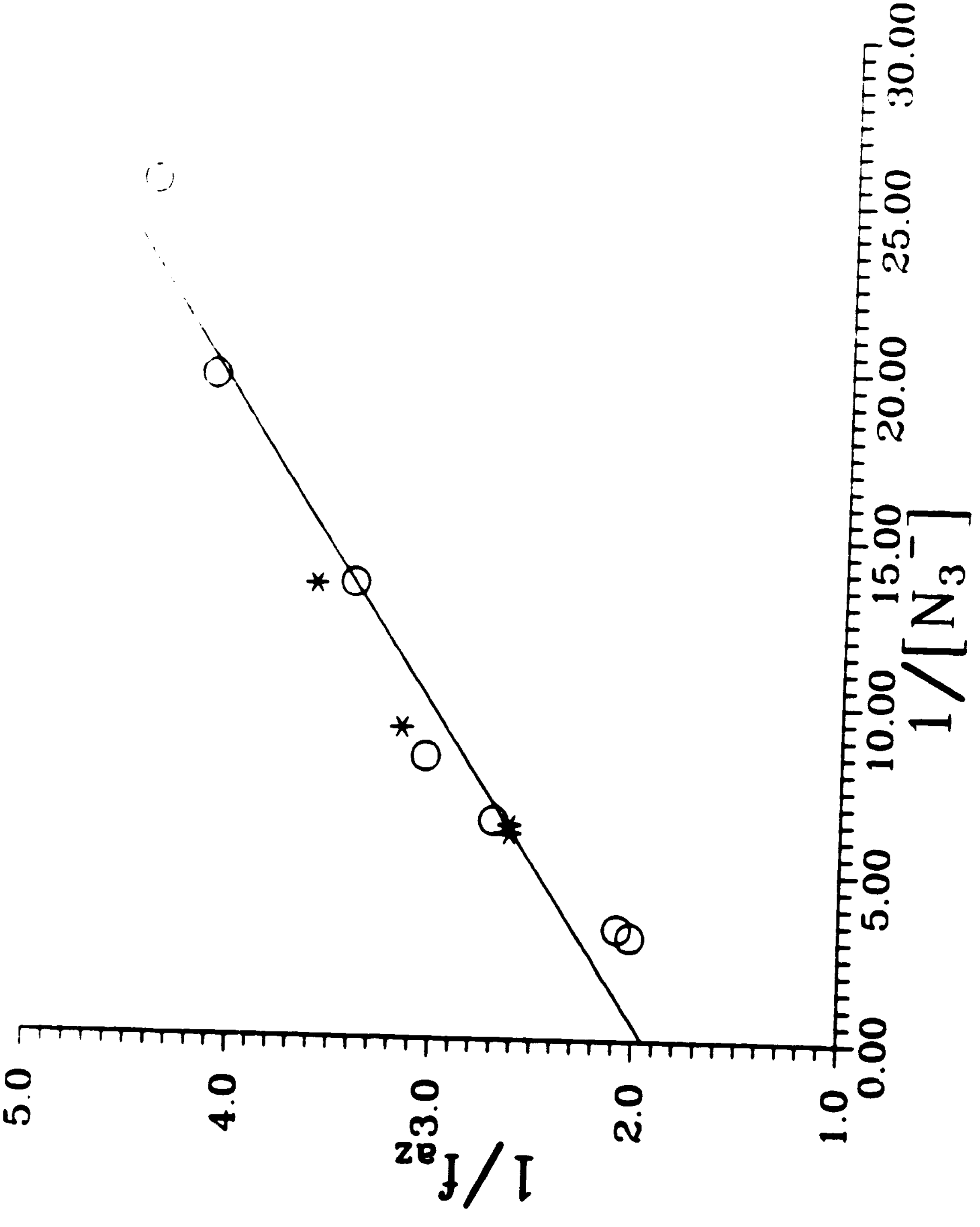
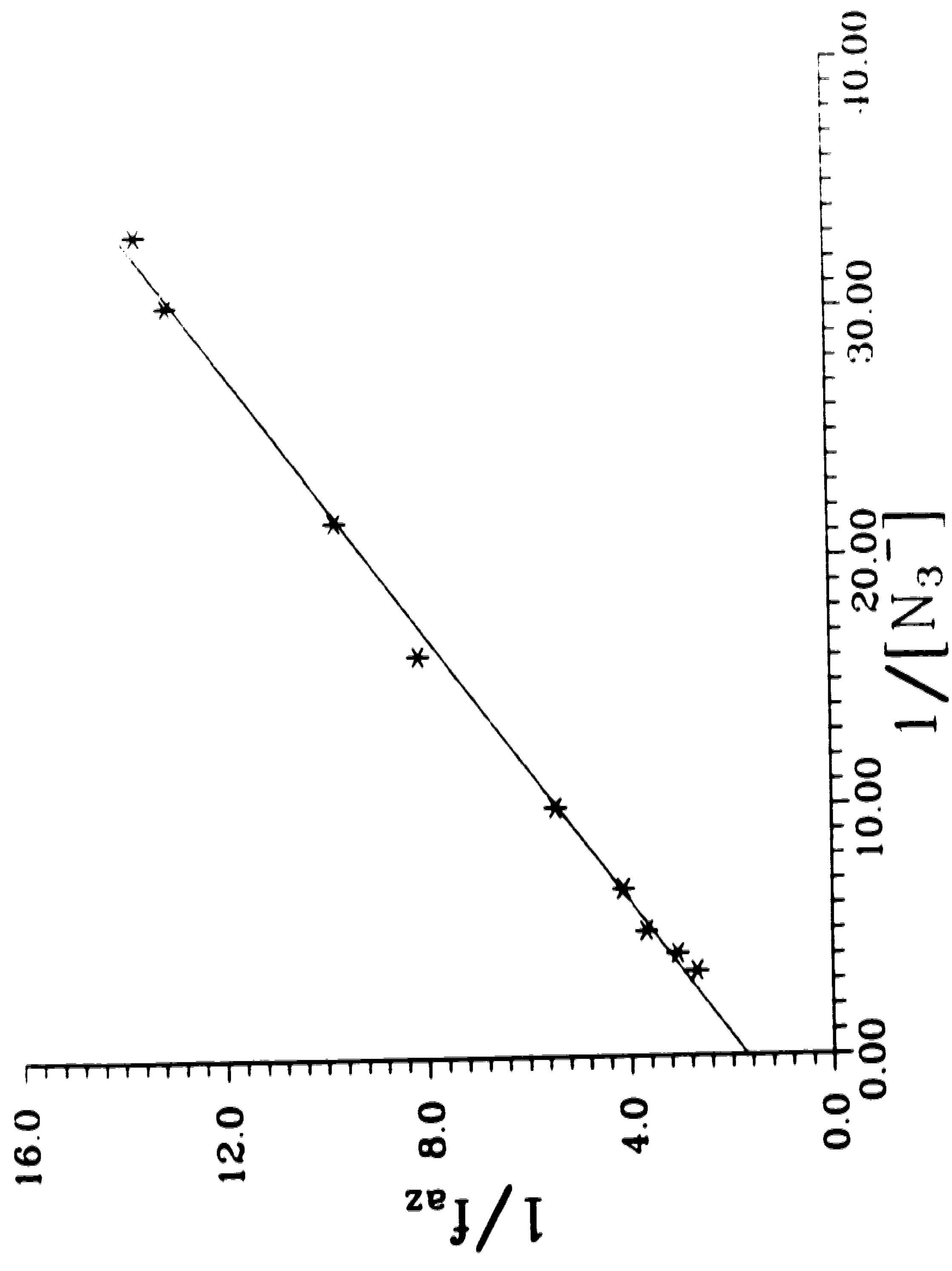


Figure 7 : Plot of $1/f_{az}$ vs $1/[N_3^-]$ for the Bromination of Styrene in MeOH. T = 22 ± 2 °C. Slope, $3.73 \times 10^{-1} \pm (2.84 \times 10^{-3})$; Intercept, $1.71 \pm (0.14)$.



constant ionic strength was avoided to eliminate possible complications in product analysis. Thus, the slopes of **Figures 4-7** also incorporate effects of ionic strength changes. Also, to simplify the analysis, only data for the methoxybromides (Br,OCH_3) and bromoazides (Br,N_3) were used to construct the plots. This can be done because the [Br^-] is usually very low and there are not significant amounts of dibromide products produced. Under these conditions equation **6** simplifies to:

(7)

$$\frac{1}{f_{az}} = \frac{k_{N_3^-} + k_B}{k_{N_3^-}} + \frac{k_{SOH}}{k_{N_3^-}} \frac{1}{[N_3^-]}$$

For none of the plots of the olefins (**Figures 4-7**) is the intercept unity, which is required if there is only a nucleophilic role for the azide (see equation **6** and **7**). One possible explanation for the nonunity intercepts is that N_3^- has a dual role where it also assists in the delivery of HOS (MeOH) to the ion. This sort of behavior has been observed in the past and similarly interpreted for bisulfite reactions with oxocarbonium ions produced from the acid catalyzed cleavage of substituted acetophenone acetals.[58] In the present case, N_3^- should be relatively basic since the pKa of HN_3 is 4.72.[59] Given in **Table 10** are the partitioning rate constant ratios for the reaction of N_3^- and MeOH with the bromonium ions generated in MeOH. Also in **Table 10** are the intercepts of the plots of $1/f_{az}$ vs $1/[N_3^-]$ which are interpreted as $(k_{N_3^-} + k_B) / (k_{N_3^-})$, and the $k_{N_3^-}/k_B$ ratio which reflects the ratio of the nucleophilicity to basicity of N_3^- under these conditions.

Table 10 : Partitioning Rate Constant Ratios for the Reactions of Azide and MeOH with Various Bromonium Ions Formed from Electrophilic Addition of Br^+ to Olefins in MeOH ($T = 22\text{-}25^{o}C$)[a]

olefin	k_{N_3}/k_{SOH} (M^{-1})[b]	$(k_{N_3} + k_B)/k_{N_3}$	k_{N_3}/k_B
cyclohexene	4.9	1.4	2.5
cyclopentene	5.9	1.6	1.7
tetramethylethylene	9.3	2.0	1.0
styrene	2.7	1.7	1.4

[a] Errors ± 5% of quoted number, except for tetramethylethylene for which errors are ± 10%.

[b] Calculated taking k_{SOH} as a first-order rate constant.

Competition experiments were undertaken to determine whether N_3^-, Br^-, and MeOH all capture the same intermediate. Given in **Table 11** are the product ratios observed for bromination of cyclohexene in MeOH using NBS or Br_2 and varying amounts of added Br^- and/or N_3^-. The product ratios are controlled by the concentrations of the two added nucleophiles, and less so by salt effects: no attempt was made to account for the latter.

Table 11 : Relative Product Ratios Observed for Bromination of Cyclohexene in MeOH, (T = 22-25°C), Using NBS or Br_2 in Presence of Added Br^- and N_3^-.[a]

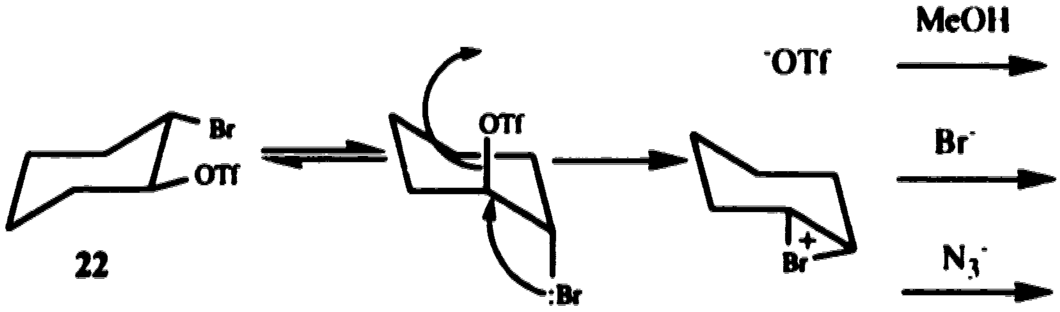
Run #	[NaBr] (M)	[NaN_3] (M)	Brominating Agent	Relative Product Ratio[b] Br,OCH_3	Br,Br	Br,N_3
1	-	-	NBS	1.0	-	-
2	0.075	-	NBS	1.0	0.33	-
3	0.15	-	NBS	1.0	0.63	-
4	0.154	-	NBS	1.0	0.70	-
5	0.156	-	NBS	1.0	0.70	-
6	-	0.06	NBS	1.0	-	0.28
7	-	0.17	NBS	1.0	-	0.63
8	-	0.27	NBS	1.0	-	0.86
9	0.03	0.10	NBS	1.0	0.12	0.42
10	0.10	0.10	NBS	1.0	0.36	0.40
11	0.10	0.23	NBS	1.0	0.30	0.67
12	0.15	0.10	NBS	1.0	0.58	0.37
13	0.16	0.17	NBS	1.0	0.58	0.60
14	0.05	-	Br_2	1.0	0.22	-
15	0.105	-	Br_2	1.0	0.46	-
16	0.11	-	Br_2	1.0	0.44	-
17	0.15	-	Br_2	1.0	0.58	-
18	0.18	-	Br_2	1.0	0.71	-
19	0.20	-	Br_2	1.0	0.77	-
20	0.035	0.10	Br_2	1.0	0.13	0.40
21	0.11	0.10	Br_2	1.0	0.41	0.33
22	0.11	0.20	Br_2	1.0	0.36	0.66
23	0.21	0.11	Br_2	1.0	0.74	0.34

a [NBS] = [ole]= 3×10^{-3} M - 2×10^{-3} M; NBS in 3.0 mL of MeOH added to solution of cyclohexene in 100 mL MeOH containing salts. Concentrations refer to final volume.

b Relative to Br,OCH_3 product: errors ± 5% of quoted number.

From the data in **Table 11**, a general trend exists where added Br^- at constant [N_3^-] leads to more dibromide, but does not effect the Br,OCH_3/Br,N_3 ratios to any great extent (e.g., runs 7,13; 9,10,12; 20,21,23). There is a small drop in the observed ratios which may be attributable to non-constant ionic strength effects. In the cases where $[N_3^-]$ is varied at constant $[Br^-]$, the amount of Br,N_3 increases as expected, and this is coupled to an increase in the Br,OCH_3/Br,Br product ratio (runs 3, 4, 5, 12, 13; 10, 11; 15, 16, 21,22) as would be required if N_3^- acts both as a nucleophile and as a base that assists in the delivery of MeOH to the ion as in **Scheme 15**.

Scheme 16



22

Finally, analysis of the products formed from a series of solvolysis experiments of *trans*-2-bromocyclohexyl trifluoromethanesulfonate (**22**, **Scheme 16**) in MeOH containing Br^- or N_3^- was undertaken in order to compare the solvolytic product ratios with those obtained from electrophilic addition of Br_2 and NBS to cyclohexene under similar conditions. The products arising from MeOH or Br^- capture were always trans. For N_3^-, the bulk of the azide product was trans, however, an additional azide containing product (by GCIR and GC mass spectral analysis) was produced that, we believe, arises from S_N2 displacement of the triflate to produce *cis*-1-azido-2-bromocyclohexane.[60] This material did not interfere with the analysis, which compares the ratios of the *trans* bromo/azido and *trans*bromo/methoxy compounds which must have arisen from capture of a common bromonium ion intermediate.[10a] Given in **Table 12** are the ratios of the trans products formed from the solvolysis of **22** in MeOH containing varying $[Br^-]$ and $[N_3^-]$. The salient feature is that for a given concentration of N_3^- or Br^-, roughly $^1/_4$-$^1/_6$ as much *trans* bromo/azido or dibromo product was formed from the solvolysis as was formed from electrophilic addition of Br_2 or NBS to cyclohexene.

Table 12 : Relative Product Ratios Observed for Solvolysis of *trans*-2-Bromocyclohexyl trifluoromethanesulfonate (22) in MeOH (T = 22-25°C) Containing Added Br^- or N_3^-.[a]

Run #	[NaBr] (M)	[NaN_3] (M)	Relative Product Ratio[b]		
			Br,OCH_3	Br,Br	Br,N_3
1	-	0.10	1.0	-	0.04
2	-	0.16	1.0	-	0.07
3	-	0.21	1.0	-	0.09
4	-	0.23	1.0	-	0.12
5	-	0.26	1.0	-	0.12
6	-	0.31	1.0	-	0.12
7	0.10	-	1.0	0.09	-
8	0.15	-	1.0	0.13	-
9	0.20	-	1.0	0.19	-
10	0.25	-	1.0	0.25	-
11	0.30	-	1.0	0.31	-

a Concentrations of salts at the final volume.

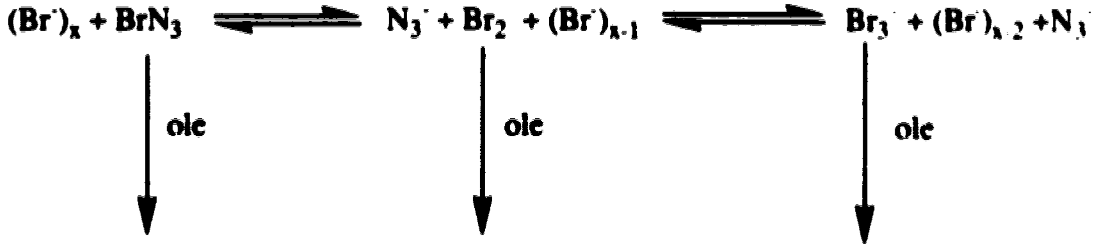
b Relative to Br,OCH_3 product: estimated errors ±5% of quoted numbers.

d) Discussion:

i) Nature of the Brominating Agent:

Bromination in MeOH with added Br^- and N_3^- is potentially a complex process involving a number of competing equilibria (**Scheme 17**) that can possibly generate different brominating agents. In addition, there exists uncertainty about the importance of intimate ion pairs, solvent separated ions and free ions in the generation of products in MeOH.[2] However, we are concerned with the fate of the bromonium ions after their formation, and whether the reaction of the ions is influenced by how they were formed. We deal first with the potential brominating species that are produced in the reaction mixture.

Scheme 17



A well-known complication of the kinetic analysis of olefin bromination is the tribromide (Br_3^-) equilibrium (K_{MeOH} = 177 M^{-1}).[4c,4j] The equilibrium in MeOH is established nearly at the diffusion limit (k_f = 2.5 x 10^9 M^{-1} s^{-1}).[12,61] Both Br_2 and Br_3^- are brominating agents, however, in general, Br_2 is more effective than Br_3^- ($Q = k_{Br_2} / k_{Br_3^-}$; depending on the olefin, Q commonly varies from 2-30)[4f,4j,62] In the present set of experiments the relative importance of Br_2 or Br_3^- in the addition is uncertain and could vary since Br^- is continually generated due to solvent or azide capture of the bromonium ion. Nevertheless, when Br_2 was used with no added Br^-, the maximum [Br_3^-] could be no more than 3 x 10^{-5} M while the maximum [Br_2] was ~1 x 10^{-4} M.[63]

The control experiments established that Br_2 in MeOH containing N_3^- and no olefin resulted in the formation (too rapid to follow by conventional spectrophotometry) of a new species (λ_{max} 312 nm) which decays with a $t_{1/2}$ of ~45 sec. It is likely that the new species is BrN_3, and that this is the brominating agent when Br_2 is added to a solution containing N_3^-. The new species at 312 nm disappears immediately upon the addition of cyclohexene, and the degradation of this new species is likely to be oxidation of MeOH.

A similar transient species was produced more slowly when NBS was added to a solution of NaN_3 in MeOH. This species is again likely to be BrN_3, a material originally shown by Hassner and coworkers to be capable of ionic electrophilic addition to a variety of olefins,[52,56c,56d] and subsequently shown by Van Ende and Krief[49] to be generated in situ (at least as its Br^+/N_3^- constituents) by the action of NBS and NaN_3 in aqueous DME.

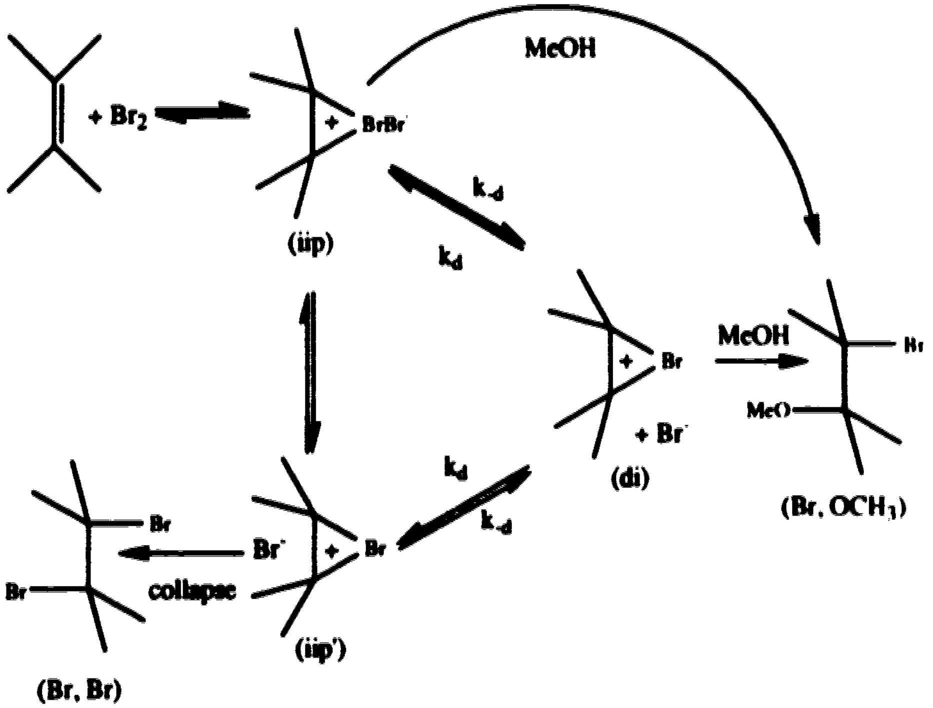
Potentially BrN_3 as well as NBS are the brominating agents in the present set of experiments due to the slower formation of the BrN_3 with NBS. In the absence of N_3^-, NBS alone is likely the brominating agent, and not Br_2 or Br_3^-, because even when NBS and significant amounts of NaBr are used, the observed rate of formation of Br_2/Br_3^- under the present conditions appears to be too slow to account for all the products being formed from only these brominating species.

ii) How is dibromide formed?

Shown in **Scheme 18** is a detailed pathway for Br_2 addition to olefins in MeOH that depicts various fates for the proposed ionic intermediates. Ionization of the CTC (formed in equilibrium with ole + Br_2) must initially form an intimate ion pair (iip) in which the Br^- and bromonium ion Br^+ are in close proximity. This ion (iip) has several possible fates, namely; 1) reversal to the CTC, 2) rapid backside capture by solvent to yield Br,OCH_3 products, 3) translocation of the Br^-/bromonium ions to form the trans disposed intimate ion pair (iip') which perhaps involves solvent separated ions, 4) diffusional separation of the intimate ion pairs to solvent separated ion pairs, and then free ions.

This scheme indicates that at zero added Br^-, if the iip's undergo diffusional separation, the Br^- should be sufficiently diluted that the major product from the free ions will be solvent incorporated (Br,OCH_3). Therefore, at zero added Br^-, the only way to produce significant amounts of dibromide will be from translocation of the ions of iip to form iip' and then collapse to form the dibromide. Solvent incorporated product can arise from MeOH attack on the iip, or on the free/solvent separated ions (di). The rate constants for diffusional separation of a bromonium-bromide ion pair (k_{-d}) cannot be established with any certainty, but may be surmised from consideration of the association constants for the ions in solution.[40a] In H_2O and hydroxylic solvents of high dielectric constant, the

Scheme 18 ((iip) and (iip') are intimate ion pairs; (di) is dissociated ion)



association constants for ions are small ($K_{ass} = k_d/k_{-d} \le 1\ M^{-1}$)[64a] but might be expected to increase somewhat in moving from H_2O to MeOH. Since k_d, the rate constant for formation of the ion pairs can be assumed to be diffusion limited at $5 \times 10^9 - 1 \times 10^{10}\ M^{-1}\ s^{-1}$ (the larger value accommodating the reduced viscosity of MeOH relative to H_2O),[64b] k_{-d} can be computed to have a value $\ge 10^{10}\ s^{-1}$.

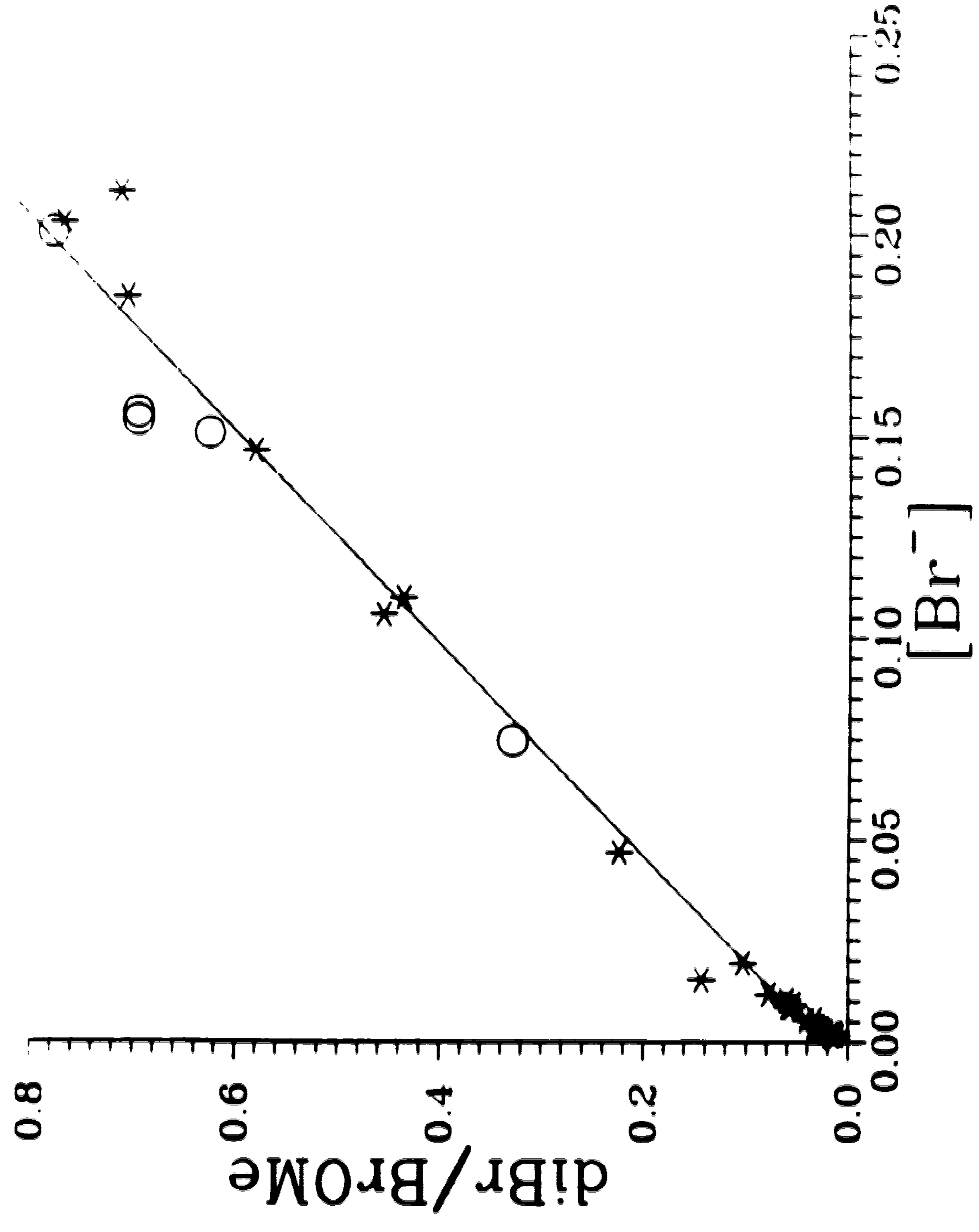
Shown in **Figure 8** is a plot of the dibromide/methoxy bromide ratio for the bromination of cyclohexene as a function of added $[Br^-]$. Some of the points (depicted as O on the plot) use NBS as the source of Br^+, otherwise Br_2 was used as the source of electrophilic bromine. Two features are readily apparent from the plot. First, that all the data fall, within respectable limits, on the same line, suggests that all possible pathways for product formation lead through a common intermediate. This is likely to be the free bromonium ion, or a bromonium ion that is not perturbed by the presence of a counterion (nascent Br^- or succimide) as there seems to be no effect on the product ratios upon changing the brominating agent. Second, the intercept of the plot tends to zero (intercept = 2.60 (0.87) x 10^{-2}), which indicates that significant amounts of dibromide cannot be formed without the presence of external Br^-. This in turn suggests that the conversion of iip to iip' (**Scheme 18**) followed by collapse of the ion pair must be slower than solvent capture of the first formed intimate ion pair, or diffusional separation followed by solvent capture of the free ion. If collapse of the iip' were an important process, then a non-zero intercept would be expected and this value would give an estimate of the relative importance of ion pair collapse versus solvent capture of iip or free ion. For example, the bromination of cyclohexene in AcOH at zero added Br^- leads to the formation of ~30% dibromide product.[6] This indicates that in the less polar solvent, AcOH, intimate ion pair collapse is a significant pathway to product formation. Although we cannot rule out solvent capture of the intimate ion pair in bromination, this has recently been shown to be an unimportant pathway for product formation from the reactive carbocation produced from the S_N1 aqueous solvolysis reaction of 1-(4-methoxyphenyl)-2,2,2-trifluoroethyl bromide.[65]

iii) Azide Capture

I) Assumption of Diffusion Limited Capture:

The critical assumption made in using the azide capture methodology to infer the lifetimes of the bromonium ions is that N_3^- reacts with the ions at the diffusion limit in MeOH. Ritchie et al.[66] have provided seminal stopped-flow evidence concerning the relative nucleophilicities of anions with different electrophiles in a variety of solvents including H_2O, MeOH, and DMSO. For the strong nucleophiles, such as N_3^- and PhS^-, the rate constants for capture of a series of substituted aryl diazonium ions ($XC_6H_4N_2^+$) in DMSO[66a] or MeOH[66d] approached a maximal value of ~10^{10} M^{-1} s^{-1}. This value can be set as the diffusion rate constant for the attack of good nucleophiles on unstable cations. Importantly, the nucleophilic selectivity of N_3^- relative to MeOH (defined by Ritchie[66] as $N^+ = \log k_{N_3^-} - \log k_{MeOH}$) for an activation-limited nucleophilic capture of a relatively unstable cation is 8.5.[66]

Figure 8 : Plot of the Ratio of Dibromide/Methoxybromide Products Formed from the Bromination of Cyclohexene in MeOH, T = 22 ± 2 °C, as a Function of [Br^-]. * Br_2 Data Open Circles, NBS Data. Slope, 3.80 ± (0.09); Intercept, 2.60 x 10^{-2} ± (0.87 x 10^{-2}).



On the other hand, as argued by Young and Jencks,[58] in cases where the cations become progressively less stable, the nucleophilic selectivity between a strong nucleophile such as N_3^- or $SO_3^=$ and its host solvent is reduced. In the limit, where the cation reaches such stability that it is just barely able to exist, the nucleophilic selectivity tends to plateau at low values between 1-10. For the capture of the oxocarbonium ion intermediates produced from substituted acetophenone dimethyl ketals,[58] $k_{SO_3^=}/k_{H_2O}$ ratios fell in a range of $1.3 \times 10^1 - 7 \times 10^2$ M^{-1}, and were clearly far less than expected for an activation limited process where $k_{SO_3^=}/k_{H_2O} = 10^{7.9}$ M^{-1}.[66b,66c] Variable, but relatively low selectivities for $k_{N_3^-}/k_{MeOH}$ were observed for capture of a series of substituted phenylethyl cations.[40a,40b] The small ratios observed[58,40a,40b] could be readily explained if reaction of the strong nucleophiles N_3^- or $SO_3^=$, but not H_2O or MeOH, with the intermediate was diffusion limited.

For the bromonium ions generated in this study, the data presented in **Table 12** suggest relatively low nucleophilic selectivities ($k_{N_3^-}/k_{MeOH}$ = 2.7-9.3 M^{-1}). These values are clearly smaller than the $10^{8.5}$ M^{-1} expected for an activation limited process.[66] This can be taken as evidence that whatever intermediate is being attacked, it is a highly unstable species and N_3^- reacts with the intermediate in a diffusion limited process. This would be consistent with the expected behavior of a reactive bromonium ion, but not a neutral CTC.

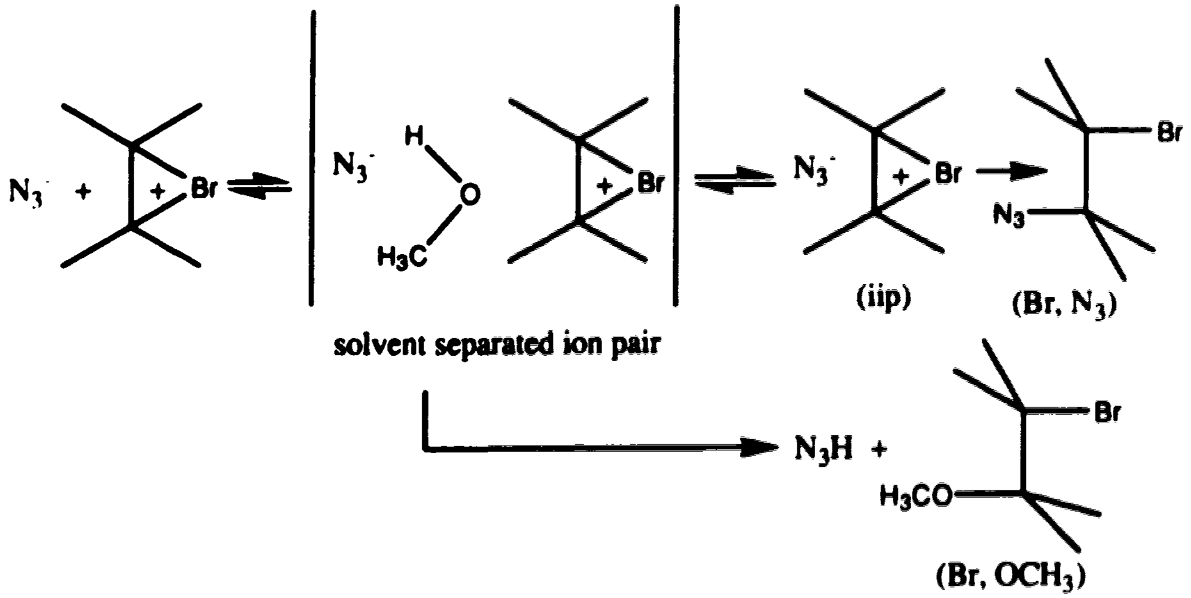
II) Do Br^-, N_3^- and MeOH capture a common intermediate?

It is important to distinguish N_3^- capture of a free bromonium ion from a process where N_3^-, olefin, and brominating agent all appear in a rate limiting step. Normally this would be determined by showing that the solvolysis rate constant was independent of the $[N_3^-]$. If nucleophilic capture is post rate limiting, the rate constant will be independent of $[N_3^-]$. For bromination in MeOH we were unable to perform kinetic measurements since; a) the reactions are too fast for our existing equipment, b) added N_3^- introduces the possibility of a new competitive brominating agent (BrN_3, **Scheme 17**) that can complicate UV-Vis spectrophotometry. Therefore, we have employed a competition method[10c,41] wherein the products of brominating cyclohexene in MeOH containing N_3^- were monitored as a function of [Br^-]. If a third nucleophile (Br^-) competes for the intermediate with N_3^- and MeOH, then the Br,OCH_3/Br,N_3 ratio should be unchanged as a function of [Br^-]. Within acceptable limits, the data in **Table 11** (eg. runs 9,10,12; 7,13; 20,21,23) show the expected trend and suggests that all the nucleophiles capture a common intermediate, which we take to be the bromonium ion. There is some scatter in the data at the highest concentration of salts, but this could arise from non-constant ionic strength effects, or from the proposed dual roles of nucleophile and base for N_3^- and possibly Br^-. It should be noted that these experiments do not specify what the intermediate is, but only that all three nucleophiles are involved in capturing the same intermediate. While it may be argued that this common intermediate is really the CTC, arguments presented above concerning the relatively low capture ratios (k_{N_3}/k_{MeOH}) tend to suggest the capture arises not from any activation limited process, but from attack on a highly unstable intermediate such as the bromonium ion.

The data in **Table 11** also provide evidence for our explanation of the non-unity intercepts in **Figures 4-7**. That is, N_3^- is not only a nucleophile but can also act as a base to promote solvent attack. At a given [Br^-], added azide increases the Br,OCH_3/Br,Br ratio as well as producing larger amounts of Br,N_3 product. This can be explained, as in **Scheme 15**, by a process wherein N_3^- acts as a base in solvent delivery to the bromonium ion in addition to its nucleophilic role. The process is visualized in **Scheme 19** where diffusion of N_3^- from the bulk solvent to the backside of the bromonium ion must first proceed through a solvent separated ion pair. The relatively basic[59] N_3^- could assist in the delivery of solvent in competition with intimate ion pair formation followed by collapse. The k_{N_3}/k_B ratio for these azide dependent processes in the case of cyclohexene is 1.4 (**Table 10**). Using this value and the slopes of the lines of the plots of the dibromide/methoxybromide or bromoazide/methoxybromide ratios vs [Br^-] or [N_3^-]

(**Table 11**, runs 1-7, plots not shown) allows one to determine the partitioning of the bromonium ion between N_3^- and Br^- nucleophilic capture. The value, $k_{Br^-}/k_{N_3^-} = 4.15/(3.4 \times 1.4) = 0.87$, indicates a relative insensitivity of the capture to the two anionic nucleophiles as would be expected for a bromonium ion having little or no activation barrier toward attack.

Scheme 19



III) The question of N_3^-, Br^- and solvent assistance in electrophilic bromination

Ruasse et al.[33,37] have reported studies of the differential effects of solvents on the kinetics of bromination of linear and branched alkenes. These were interpreted[33,37] in terms of a small but significant nucleophilic assistance by solvent in promoting bromination. Additionally, it has been long noted that Br_3^- or its kinetic equivalent Br^- + Br_2 can contribute to the bromination of olefins.[4,10g,12,60,61,62] While an exact interpretation of the Br_3^- mechanism is not presently in hand, a reasonable (but not entirely satisfying[4d,4h,67]) possibility is a Br^- assisted ionization of the CTC.

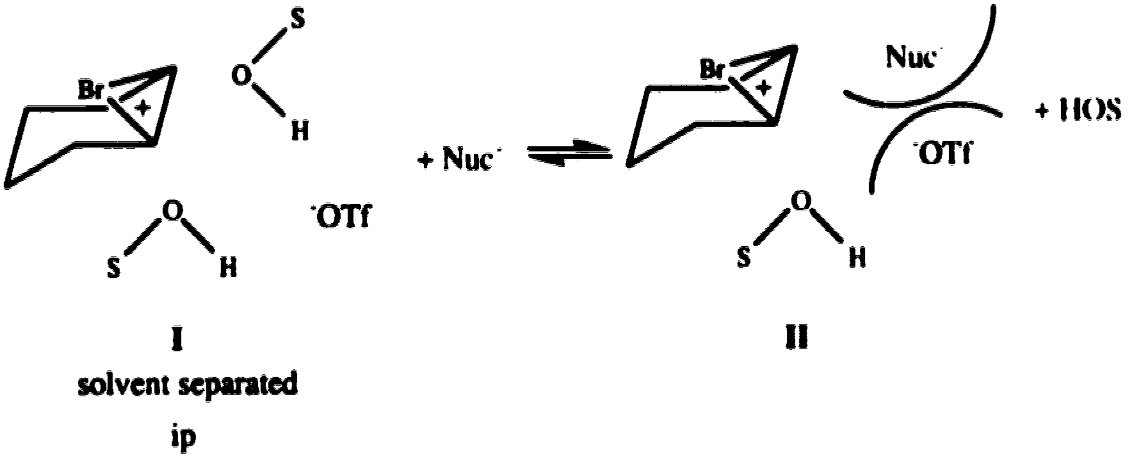
It has been pointed out that there is no nucleophilic assistance by solvent for the S_N1 ionization of 1-(4-methoxyphenyl)ethyl chloride in 50% $MeOH/H_2O$ or the corresponding pentafluorobenzoate in 50% TFE:H_2O.[10c,68] This conclusion was based on the observed rate constants for the S_N1 reactions which were shown to be independent of $[N_3^-]$. In our case, due to the experimental limitations listed earlier, the rate constants for bromination in the presence of added nucleophile were not determined, and we rely on the trapping ratios to provide information about nucleophilic capture of the intermediates. The N_3^-/MeOH trapping ratios provided in **Table 10** indicate that despite its much greater nucleophilicity in an activation limited process,[66] N_3^- is unable to generate the large amount of bromoazide product that would be anticipated if N_3^- assisted significantly in the ionization of the CTC. We conclude, following Jencks and Richard,[68] that if there is little or no assistance by a strong nucleophile such as azide, then substantial assistance by weakly nucleophilic solvent is not expected.[69,70] Similarly, if assistance to ionization occurs in bromination, then a strong dependence on the nature of the departing anion should be expected.[40a] Correspondingly, the absence of an effect of structure or charge of the leaving group on the partitioning of an intermediate suggests that it is a species whose reactivity is independent of the counterion, perhaps behaving as a free ion.[69] With respect to bromination of the olefins studied here, in MeOH containing N_3^-, it is particularly important that the ratio of azide to methoxy capture is independent of whether Br_2 or NBS was used as the brominating agent. This fact, and the plot in **Figure 8** showing that the Br,Br/Br,OCH_3 for bromination of cyclohexene in the presence of Br^- is independent of whether the source of Br^+ is Br_2 or NBS, argue strongly for the capture of an intermediate reacting independently of its leaving group, and against significant nucleophilic involvement of N_3^-, Br^- or solvent in assisting the bromination.

IV) The location of the counterion influences the bromonium ion partitioning

All of the above information suggests that in the electrophilic bromination of cyclohexene, N_3^-, Br^- and solvent capture a highly reactive bromonium ion whose reactivity and partitioning to trans products is insensitive to what brominating agent was used to form the ion. This seems to imply that the ion is completely free from its associated counterion, but does not necessarily exclude capture of a solvent separated ion pair where nucleophilic capture of the bromonium ion occurs on the face opposite to where the counterion is located. Therefore, the associated counterion is sufficiently far away from the attacking (trans) nucleophile that mutual interaction of the two anions is at a minimum. However, we can provide evidence indicating that solvolytically produced bromonium ions may react in ways that are influenced by the nature and location of the anionic counterion.

In an effort to determine whether the ions produced from electrophilic bromination and solvolysis are equivalent, we have determined the products for the solvolysis of *trans*-2-Bromocyclohexyl trifluoromethanesulfonate (**22**) in MeOH containing varying [N_3^-] and [Br^-]. The assisted solvolysis (**Scheme 16**) should generate a bromonium ion/triflate ion pair, the subsequent nucleophilic capture of which generates *trans*-2-bromocyclohexyl adducts. The corresponding product ratios are given in **Table 12**. The main finding of the solvolysis study is that there is less attack of the anionic nucleophiles N_3^- or Br^-, and more solvent incorporated products in the case of the solvolysis of **22**, than is observed during electrophilic bromination of cyclohexene under comparable conditions. This finding requires that one or both of the intermediate bromonium ions retains "knowledge" of its counterion, which in turn affects the partitioning between the various nucleophiles. The ion most likely to discriminate against anionic nucleophiles would be the solvolytically produced one because the nascent OTf^- would occupy the same region of space that the attacking nucleophile must in order to form trans addition products. The observations can be readily explained if the departing OTf^-, when as a solvent separated ion pair (**I**, see **Scheme 20**) preferentially assists in the delivery of MeOH and, by charge repulsion, discriminates against anionic nucleophiles as in **II**. This sort of favored delivery of solvent molecules that are H-bonded to a departing anion has been invoked several times to explain retained configuration of solvent incorporated products arising from S_N1 solvolyses.[71] Also of note in such S_N1 solvolyses is that N_3^- capture proceeds with excess inversion of configuration, probably due to charge repulsion between the anionic nucleophile and leaving group.[72]

Scheme 20



V) Implications for the lifetimes of bromonium ions in MeOH

Using the $k_{N_3^-}/k_S$ partitioning constants given in **Table 10** and the diffusion limited rate constant of $1 \times 10^{10}\ M^{-1}\ s^{-1}$ determined by Ritchie et al.[66] for N_3^- attack on cations in MeOH, allows calculation of lifetimes of 5.0×10^{-10} s, 5.9×10^{-10} s, 9.3×10^{-10} s, and 2.7×10^{-10} s respectively for the ions produced from electrophilic bromination of cyclohexene, cyclopentene, tetramethylethylene, and styrene. The ions produced from the cyclic olefins are undoubtedly of the bromonium type as only trans products are observed. These ions last ~100-fold longer than what would be expected for secondary carbocations, e.g., isopropyl, the lifetime of which is estimated to be 5×10^{-12} s by extrapolation of a σ-constant correlation[71] for cation hydration. The ion formed from bromination of tetramethylethylene is probably of the bromonium ion type, but no stereochemical data are available from the present study to determine whether the additions are trans. For a simple tertiary carbocation in H_2O, the lifetime is estimated[71] to be $\sim 10^{-10}$ s which implies that such an ion is just barely stable enough to be a solvent equilibrated reaction intermediate in dilute aqueous solution. That the lifetime of the ion produced by Br^+ addition to tetramethylethylene is ~10^{-9} s in MeOH suggests the ion has some extra stability possibly attributable to the involvement of a bridged bromonium ion.

The situation with respect to styrene is not as clear, and the extent of bromine bridging in the intermediate ion has been the subject of much debate.[4d,2b,73-75] The ρ^+ determined for Br_2 addition to substituted styrenes in MeOH (-4.3[73]) suggests considerable development of (+)-charge on the benzylic carbon in the rate limiting step. With strong electron donors, some evidence for deviation from a linear free-energy plot was observed and interpreted as a change in the extent of bridging in the transition state.[73-75] Styrene apparently produces an ion having some unspecified, but definite bridging. This bridging imparts kinetic stability to the ion as judged by its longer lifetime (2.7 x 10^{-10} s) relative to the unsubstituted 1-phenylethylcation (1 x 10^{-11}s).[40a]

As a final consideration, it seems surprising that the tetrasubstituted bromonium ion of tetramethylethylene has a lifetime only a factor of two longer than those of cyclohexene or cyclopentene. Based on the compared lifetimes for isopropyl/tertiary butyl cations[72] or $H\text{-}C^+(OR)_2$ / $CH_3C^+(OR)_2$ cations,[76] substitution of CH_3 for H on a cationic site leads to 20-1000-fold increase in lifetime with the lower value pertaining to inherently shorter lived cations.[72] It is well-known that increased substitution on the double bond leads to marked increases in the rate of bromination. For the compounds studied here the reported k_{Br_2} values in MeOH are: styrene,[73] 1.5 x 10^3 M^{-1} s^{-1}; cyclohexene,[29] 1.14 x 10^4 M^{-1} s^{-1}; cyclopentene,[29] 6.25 x 10^4 M^{-1} s^{-1}; and tetramethylethylene,[37] 1.4 x 10^7 M^{-1} s^{-1}. The increase in rate stems from substituent induced (+)-charge stabilization of the transition state leading to the bromonium ion, and implies that considerable charge is developed on the olefinic carbons. Recent theoretical analyses[77-79] have indicated that the bromine atom in the ethylene bromonium ion is nearly neutral, and almost all the (+)-charge is born by the carbons. However, these charges refer to isolated gas phase species and solvent interactions could markedly affect the charge distributions. Nevertheless, how these charges relate to the lifetimes in solution is difficult to assess, particularly since for the symmetrically bridged ions the charge is distributed equally over two carbons and the property of lifetime is a kinetic one that is determined by transition state energies associated with solvent attack. The present available evidence accumulated from the N_3^- trapping experiments described above suggests that these ion lifetimes are rather insensitive to effects in the narrow range of olefins investigated.

CHAPTER 2

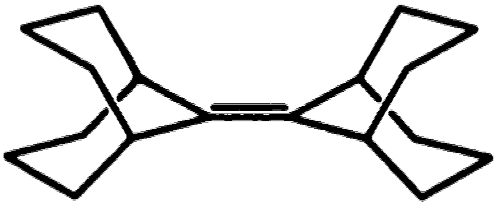
Properties of the Halonium Ions of Sterically Hindered Olefins

a) Introduction

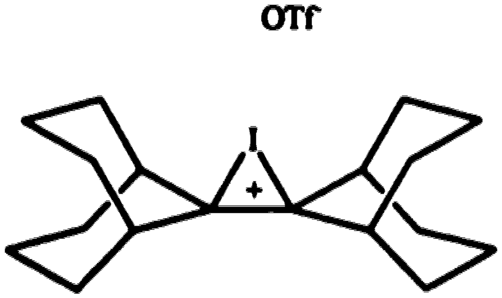
Ever since Wynberg et al.[19] first reported that Br_2 reacted with adamantylideneadamantane (7) in chlorinated solvents to produce a solid, yellow bromonium ion/tribromide salt (8), that system remains as the only known example of a three membered cyclic bromoniun ion.[7,8,9,10d,80] Recently the Br_3^- counterion of 8 has been replaced with trifluoromethanesulfonate[8] (triflate, OTf^-). It was also reported[8] that the bromoniun ion can rapidly transfer Br^+ to residual olefin (eq. 8).

(8)

Therefore, there has been interest in whether other olefins could be found that would generate stable bromonium and possibly other halonium ions. With this goal in mind, bicyclo[3.3.1]non-9-ylidenebicyclo[3.3.1]non-9'-ane (29) was synthesized because of its structural similarity to 7. The bromonium ions and iodonium ions of 7 and 29 were studied by ^{13}C NMR with various counterions and the crystal structure of $7\text{-I}^+/\text{OTf}^-$ (adamantylideneadamantane iodonium ion triflate) was determined.



29



$29\text{-I}^+/\text{OTf}^-$

b) Experimental:

i) General

Routine NMR and IR spectra were obtained with Bruker WP-200 and Nicolet SX-20 FTIR spectrometers. All ^{13}C spectra at low temperature were obtained using a Bruker WH-400 spectrometer unless otherwise stated. All reported probe temperatures were obtained using a Sensotek, BAT-10 external thermocouple which was lowered into the NMR probe and allowed to equilibrate for 15 minutes before the temperature was recorded.

ii) Materials

Adamantylideneadamantane (7) was synthesized[81] from adamantanone (Aldrich), and recrystallized from MeOH with a final purification by sublimation yielding colorless crystals (400 MHz ^{13}C NMR (CD_2Cl_2) as in **Table 14**).

Bicyclo[3.3.1]nonan-9-one[82] was synthesized and then coupled in the same manner as adamantanone to yield bicyclo[3.3.1]non-9-ylidenebicyclo[3.3.1]non-9'-ane (**29**) which was purified by sublimation (gentle warming, 2 Torr) for a 30% overall yield. ^{13}C NMR as in **Table 14** and ^{1}H NMR lit[83] (CCl_4) δ, 2.88 (m, 4H), 1.8 (m, 24H); obs ($CHCl_3$) δ, 2.85 (broad singlet, 4H), 1.4-2.1 (m, 24H). mp uncorrected 143-144°C, lit.[83] 144-146°C.

iii) Preparation of Ions

Adamantylideneadamantane bromonium trifluoromethanesulfonate (triflate) (**7-Br^+/OTf^-**) was synthesized as previously described[8]. Adamantylideneadamantane iodonium triflate (**7-I^+/OTf^-**) was synthesized by the addition of a saturated solution of I_2 in CH_2Cl_2 (BDH, purified[84]) to a CH_2Cl_2 solution containing equimolar amounts of **7** (0.1-0.25g in 15-25 mL) and silver triflate (AgOTf, Aldrich) cooled to 0 ± 5°C. Iodine was added until the purple color persisted, followed by filtration through glass wool lodged in a Pasteur pipette to remove the AgI precipitate. Hexanes (120-190 mL, BDH, purified[84]) were added to the CH_2Cl_2 solution with cooling to -20°C to precipitate 7-I^+/OTf^-. The organic layer was decanted with the remainder of the solvent removed under high vacuum (0.05 Torr, for 5-10 minutes, or until flask had warmed to room temp.). All glassware was oven dried before use. ^{13}C NMR data for 7-Br^+/OTf^- and 7-I^+/OTf^- are listed in **Table 14**.

Adamantylideneadamantane iodonium tetraflouroborate (7-I^+/BF_4^-) was synthesized and isolated in the same manner as 7-I^+/OTf^-, with the AgOTf substituted by silver tetrafluoroborate (Aldrich). ^{13}C NMR data in **Table 14**.

Bicyclo[3.3.1]non-9-ylidenebicyclo[3.3.1]non-9'-ane iodonium triflate (29-I^+/OTf^-) and bicyclo[3.3.1]non-9-ylidenebicyclo[3.3.1]non-9'-ane bromonium triflate (29-Br^+/OTf^-) were synthesized in the same manner as 7-I^+/OTf^-. However for 29-Br^+/OTf^-, Br_2 is substituted for I_2. During all phases of the synthesis and isolation of 29-Br^+/OTf^- the reaction mixture must be kept between -60 and -80°C or decomposition will occur. ^{13}C NMR data for 29-I^+/OTf^- and 29-Br^+/OTf^- are in **Table 14**.

Upon mixing **29** with Br_2 in CH_2Cl_2 at room temperature there is an immediate yellow precipitate. It is possible to isolate the yellow precipitate directly after formation by filtration followed by washing the yellow solid with small aliquots of ice cold CH_2Cl_2. The yellow solid is stable at room temperature for a short period of time, however prolonged periods at this temperature results in the solid fuming and becoming discolored. Following Wynberg,[19] this solid was proposed to be 29-Br^+/Br_3^- and has properties similar to those of 7-Br^+/Br_3^-.[9,19]. Microanalysis calculated for $C_{18}H_{28}Br_4$: C, 38.33; H, 5.00; Br, 56.67; found: C, 37.96; H, 4.89. Mass spectral analysis gave mass ion peak for the olefin $C_{18}H_{28}$; calculated 244.21910, found 244.2189. This mass spectral analysis coincides with what is observed for 7-Br^+/Br_3^-;[19] that is, under high vacuum there is the loss of two molecules of Br_2 and regeneration of the parent olefin.

When 29-Br^+/Br_3^- was stored in CH_2Cl_2 for 24 hours in the dark at room temperature, a brightly colored homogenous solution resulted. This reaction was performed several times and the final color of the solution varied each time, however the products of the reaction were invariant. Mass spectral analysis of the product mixture showed the mass ion peak for the olefin with one hydrogen being replaced by Br. Exact mass calculated for $C_{18}H_{27}Br$ 324.12756, 322.12960 found 324.1283, 322.1301 and for $C_{18}H_{26}Br_2$ calculated; 404.0360, 402.0380, 400.0401; found; 404.0369, 402.0386, 400.0395. When one equivalent of Br_2 was added to a CH_2Cl_2 solution containing **29** the main isolated product was $C_{18}H_{27}Br$ (**30**). ^{13}C NMR (300 MHz, CD_2Cl_2) δ 137.79, 126.00 (olefinic carbons), 50.18 C-Br. Identification by APT and ^{13}C data for similar molecules show results similar to those obtained above; 4(e)-bromoadamantylideneadmantane[86] ^{13}C NMR ($CDCl_3$) δ 136.9, 131.0, 63.8; 4(e)-chloro[3.3.1]non-9-ylidenebicyclo[3.3.1]non-9'-ane[86] ^{13}C NMR ($CDCl_3$) δ 136.8, 129.7, 66.0.

Adamantylideneadamantane silver triflate complex (7-Ag^+/OTf^-) and the silver complex of **29** (**29**-Ag^+/OTf^-) were formed by mixing equimolar amounts of the olefin and AgOTf in CD_2Cl_2. The silver complexes were stable and did not decompose at room temperature, however to observe complete separation of the top and bottom faces of the ion, the NMR probe had to be cooled to -80°C. At higher temperatures, the two faces of the olefin were equivalent. ^{13}C NMR data are listed in **Table 14**.

iv) X-Ray Diffraction

Crystals of 7-I^+/OTf^- suitable for X-ray diffraction were grown in sealed Pasteur pipettes having a constriction separating the tubes into upper and lower chambers. A solution of 7-I^+/OTf^- (2×10^{-2} - 3×10^{-3}M) in CH_2Cl_2 with a slight excess of I_2 was placed in the lower chamber and dry hexanes in the upper chamber. The tubes were then capped with a septum and stored at -15 to -20°C until crystals of suitable size had developed at the constriction.

X-Ray data collection was performed on a colorless crystal (see **Table 13** for experimental details) mounted in a glass capillary, and optically centered in the X-ray beam of an Enraf-Nonius CAD4 automated diffractometer.[87,88] The crystal was cooled to -50°C, using a cold N_2 stream apparatus and all measurements were made at this temperature.

Table 13 Experimental Details for X-ray Structure of 7-I^+/OTf^-

A. Crystal Data

$C_{21}H_{30}F_3IO_4S$; FW = 562.43
Crystal dimensions: 0.40 x 0.37 x 0.30 mm
orthorhombic space group $P2_12_12_1$ (No. 19)
$a = 11.199$ (2)Å, $b = 12.674$ (4)Å, $c = 15.093$ (2) Å
$V = 2142.2$ Å^3; $Z = 4$; ρ(calcd)= 1.744 g cm^{-3}; $\mu = 16.21$ cm^{-1}
no. of reflections used for unit cell determinations (2θ range) = 24 (16.8-29.9°)

B. Intensity Measurements

Diffractometer	Enraf-Nonius CAD4
Temperature	-50°C
Radiation:	Mo K_α ($\lambda = 0.71073$ A)
Take-off angle:	3.0°
Detector aperture:	(3.00 + tanθ) mm horiz x 4.00 mm vert
Crystal-to-detector distance:	173 mm
Scan type:	θ - 2θ
Scan rate:	6.71 - 1.56° min^{-1}
Scan width:	0.60 + 0.344tanθ°
Data collection 2θ limit:	56.0°
Data collection index range:	$0 \le h \le 14$, $0 \le k \le 16$, $0 \le l \le 19$
Reflections measured:	2933 total; 2282 with $I > 3\sigma(I)$

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SHELXS-86)[a]
Refinement[b]	Full-matrix least-squares
Function Minimized	$\Sigma w(\|F_o\|-\|F_c\|)^2$
Weighting Factor w	$4F_o^2/\sigma^2(F_o^2)$
Range of Transmission Factors[c]	0.7906-1.1239
No. of Observations (NO)	2282 ($I \ge 3\,\sigma(I)$)
No. of Variables (NV)	271
R_1[d]	0.032

R_2^e	0.039
GOF^f	1.260

a Ref.89a

b The diffractometer programs used include the Enraf-Nonius Structure Determination Package, Version 3 (1985, Delft, The Netherlands) adapted for a Sun Microsystems 3/160 computer, and several locally written programs by R.G. Ball.

c Differential absorption correction: DIFABS (Ref 89b).

d $R_1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$.

e $R_2 = [(\Sigma w(|F_o|-|F_c|)^2/(\Sigma w F_o^2)]^{1/2}$.

f $\mathrm{GOF} = [\Sigma w(|F_o|-|F_c|)^2/(\mathrm{NO}-\mathrm{NV})]^{1/2}$.

v) NMR Experiments

In order to determine the dynamic exchange of X^+ between the ion and excess parent olefin, the following experimental protocol was followed for all ions for which exchange was studied.

A solution of the ion (20-25 mg in 0.3-0.4 mL CD_2Cl_2, purified[84]) was filtered through a glass wool plug in a Pasteur pipette into a 0.5 mm diameter NMR tube with teflon insert. The sample was then placed into the probe which was cooled to approximately -80°C and after 15 minutes the spectrum was collected. The tube was removed, opened, and a measured aliquot of the parent olefin in CH_2Cl_2 (0.69 mM for 7-I^+/OTf^- and 21 mM for 29-I^+/OTf^-) was added. The tube was then recapped, and reinserted into the probe and allowed to equilibrate for 15 minutes before the next spectrum was collected. The rate constants for the iodonium ion/olefin exchange were determined by analysis of the ^{13}C NMR line shapes of the $C_{8,8',10,10'}$ and $C_{4,4',9,9'}$ resonances.

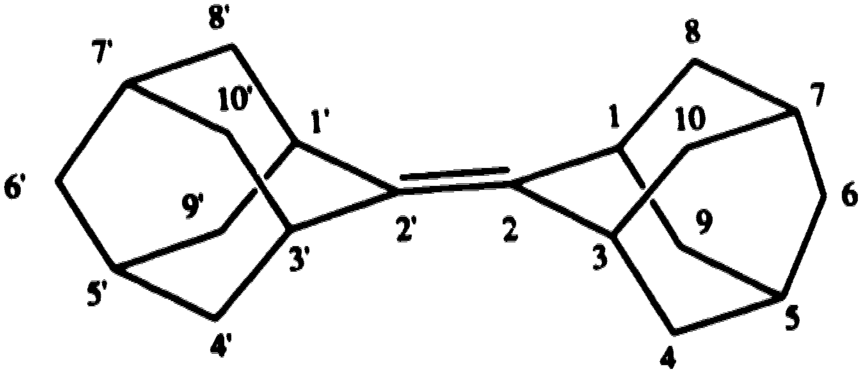
The freshly synthesized solutions of the ions, with one exception, always had excess olefin present and, when first observed, the ions were already at the fast exchange limit. For the exchange study to be performed, the excess olefin had to be removed from the system. Triflic acid was added to solutions of 7-I$^+$/OTf$^-$ to protonate the excess olefin[8] thereby inhibiting the exchange process.

However, the addition of triflic acid to solutions containing the ions of **29** did not protonate the excess olefin as had been observed for **7**. Therefore, the sample was filtered (at -78°C) through a Pasteur pipette containing glass wool that had been impregnated with AgOTf (5-15 mg) in order complex the excess olefin.

c) Results and Discussion:

i) ^{13}C NMR data for the ions:

Shown in **Table 14** are the ^{13}C NMR data for the various ions studied. To understand the numbering scheme see below (please note that **29** does not contain carbons 6 and 6').



At low temperature (-80°C) and in the absence of added olefin, a slow exchange condition is satisfied wherein the ^{13}C spectra provide evidence that the ions 7-Br$^+$/OTf$^-$, 7-I$^+$/OTf$^-$, 29-Br$^+$/OTf$^-$, and 29-I$^+$/OTf$^-$ possess only two perpendicular planes of symmetry. These are, a plane that intersects carbons 2 and 2' and the Br$^+$, and a plane the intersects the Br$^+$ and splits carbons 2 and 2'. The olefinic carbon resonances for both olefins appear at about 133 ppm, but upon formation of the

Table 14 ^{13}C NMR Resonances (ppm) for Various Ions and Parent Olefins for 7 and 29^{a}

	2,2'	1,1',3,3'	8,8',10,10'	4,4',9,9'	7,7'	5,5'	6,6'
29^{b}	132.68	32.44	34.31	34.31	22.70	22.70	-
29-Br^{+}/OTf^{-c}	159.33	37.23	38.33	36.37	20.63	20.63	-
29-I^{+}/OTf^{-c}	151.40	36.63	38.45	36.74	20.06	19.93	-
29-I^{+}/OTf^{-cd}	150.91	36.26	37.23	37.23	19.73	19.73	-
7^{b}	133.66	32.44	40.01	40.01	29.16	29.16	37.76
7-Br^{+}/OTf^{-ce}	156.24	36.99	42.69	40.31	26.57	26.54	36.18
7-Br^{+}/Br$_3^{-fg}$	158.6	39.8	45.0	42.9	29.3	29.3	38.8
7-Br^{+}/Br$_3^{-fh}$	157.6	39.7	44.8	42.3	29.0	29.0	39.1
7-I^{+}/OTf^{-c}	149.57	36.74	42.28	41.88	26.67	26.55	36.59
7-I^{+}/OTf^{-cd}	148.37	36.67	42.02	42.02	26.64	26.64	36.56
7-I^{+}/BF$_4^{-cd}$	151.52	37.90	43.33	43.33	27.63	27.63	37.46
7-I^{+}/CN^{-fi}	153.6	38.4	43.9	43.3	27.9	27.9	37.7
7-Ag^{+}/OTf^{-c}	135.64, 135.46	36.02	40.13	39.19	27.71	26.56	33.02
7-Ag^{+}/BF$_4^{-c}$	138.55, 138.37	35.60	40.58	40.01	27.50	26.44	33.09
29-Ag^{+}/OTf^{-c}	137.49, 137.32	35.77	35.91	33.98	22.67	21.67	-
7-Ag^{+fjl}	143.6	36.7	44.0	44.0	30.2	30.2	38.7
7-Ag^{+fkl}	141.0	34.5	42.5	41.2	28.1	27.8	37.0

a) Referenced to CD_2Cl_2 unless otherwise stated.

b) Ambient temperature.

c) -80°C ± 3.0

d) ^{13}C spectrum fast exchange limit

e) Reference 8

f) Reference 7

g) Br_2 solvent.

h) solvent SO_2ClF (-40°C)

i) solvent SO_2 (-70°C)

j) CH_2Cl_2

k) SO_2, -30°C

l) hexafluoroantimonate counterion

bromonium ion these resonances for 2 and 2' shift downfield to about 158 ppm which would be expected upon formation of bonds with a positive ion. Upon replacement of Br^+ with I^+ there is a smaller downfield shift of carbons 2 and 2' to approximately 150 ppm. If the downfield shift is a measure of the amount of positive charge that carbons 2 and 2' are experiencing, then it follows that the less electronegative I^+ should cause a smaller downfield shift. The ^{13}C resonances for the carbons on the topside of the molecule ($C_{8,8',10,10'}$) adjacent to the X^+ are, in all cases, downfield from their counterparts ($C_{4,4',9,9'}$) on the bottom side. Resonances for $C_{7,7'}$ and $C_{5,5'}$ are similarly behaved for all ions presented in **Table 14**, except **29-Br**

There do not seem to be major differences in the ^{13}C NMR properties of the ions in different solvents. All ^{13}C NMR data in **Table 14** were collected using CD_2Cl_2 at approximately -80°C except those for **7**-Br^+/Br_3^- in Br_2, **7**-Br^+/Br_3^- in SO_2ClF, and **7**-I^+/CN^- in SO_2.[7] Also, Olah et. al.[7] obtained the spectra for **7**-Br^+/Br_3^- in both Br_2 at ambient temperature and SO_2ClF at -40°C.

Variation of the counterion also produced very little change in the spectral characteristics of **7**-I^+ ions. The ions were generated with three different counterions, ^-OTf, $^-BF_4$, and ^-CN[13] and little change in the spectrum of the ion was observed. The most significant difference is the larger separation of $C_{8,8',10,10'}$ and $C_{4,4',9,9'}$ in SO_2 with ^-CN than with OTf^- in CD_2Cl_2.

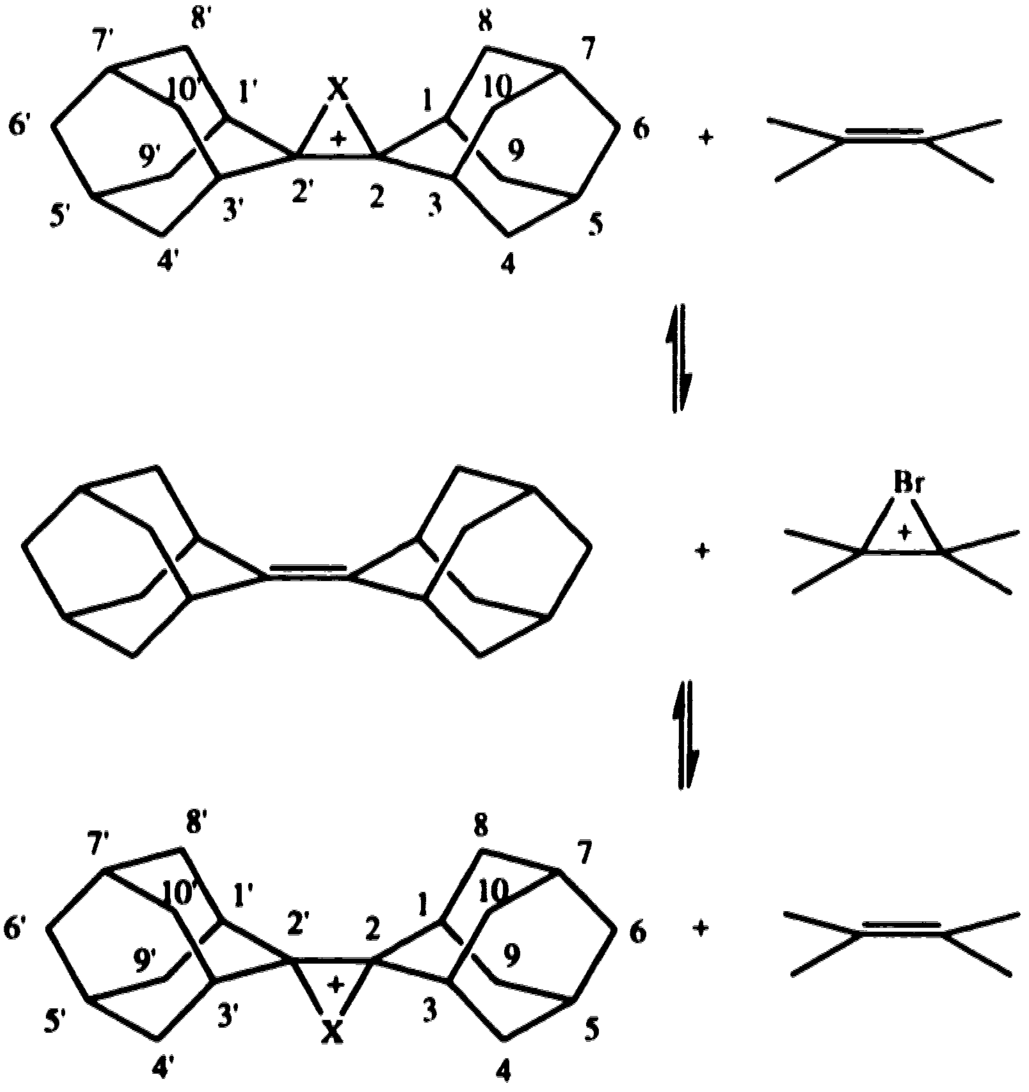
Except for some minor shifts, the data over this range of solvents, temperature and counterion are remarkably similar. This lack of sensitivity to these variables suggests that the general structure and charge distribution of the ions is, generally, unaffected by solvent and counterion.

Additions of small amounts of parent olefin to the NMR solutions containing the ions caused broadening of the resonances attributable to $C_{8,8',10,10'}$ and $C_{4,4',9,9'}$ and those for $C_{7,7'}$ and $C_{5,5'}$. By addition of olefins **7** and **29** to the appropriate solutions of ion and gathering the spectra of coalescing $C_{8,8',10,10'}$ and $C_{4,4',9,9'}$ resonances as a function of added [ole], the observed rate constants for exchange can be determined by line shape analysis of the carbon resonances. At the limit, these pairs coalesce and the spectra arise from species having three perpendicular planes of symmetry. These observations indicate a two step exchange process where X^+ is translocated from the top side of the halonium ion to the bottom side in a process mediated by added olefin (**Scheme 21**). A detailed analysis of this process shows (**Appendix**) that, since [ole] << [Halonium ion], the magnetizations of the olefin carbon nuclei do not contribute significantly to the spectrum, and that the transfer of magnetization between sites $C_{8,8',10,10'}$ and $C_{4,4',9,9'}$ is a pseudo first-order process characterized by the rate constant:

$$k_{obs} = \frac{k}{2}[\mathrm{Ole}]$$

Since the process is dependent upon added [olefin], the transfer must proceed via an olefin:ion complex, and a given halonium ion completely transfers its X^+ to the acceptor olefin prior to once again receiving the X^+ at either of the now equivalent faces of the olefin. The factor of 2 in the rate expression results from only half of the back transfers leading to translocation of Br^+ from the top to the bottom side.

Scheme 21



Line shape analysis of the NMR resonances for $C_{8,8',10,10'}$ and $C_{4,4',9,9'}$ yielded the pseudo first-order rate constants, k_{obs}, for the site exchange listed in **Tables 15** and **16**. The plots of this data are shown in **Figures 9** and **10** and yield the second-order rate constants listed in **Table 17**.

Figure 9 : The Plot of k_{obs} vs [7] Added to Solutions of 7-I$^+$/OTf$^-$ in CD_2Cl_2 at -79°C for Three Separate Experiments.

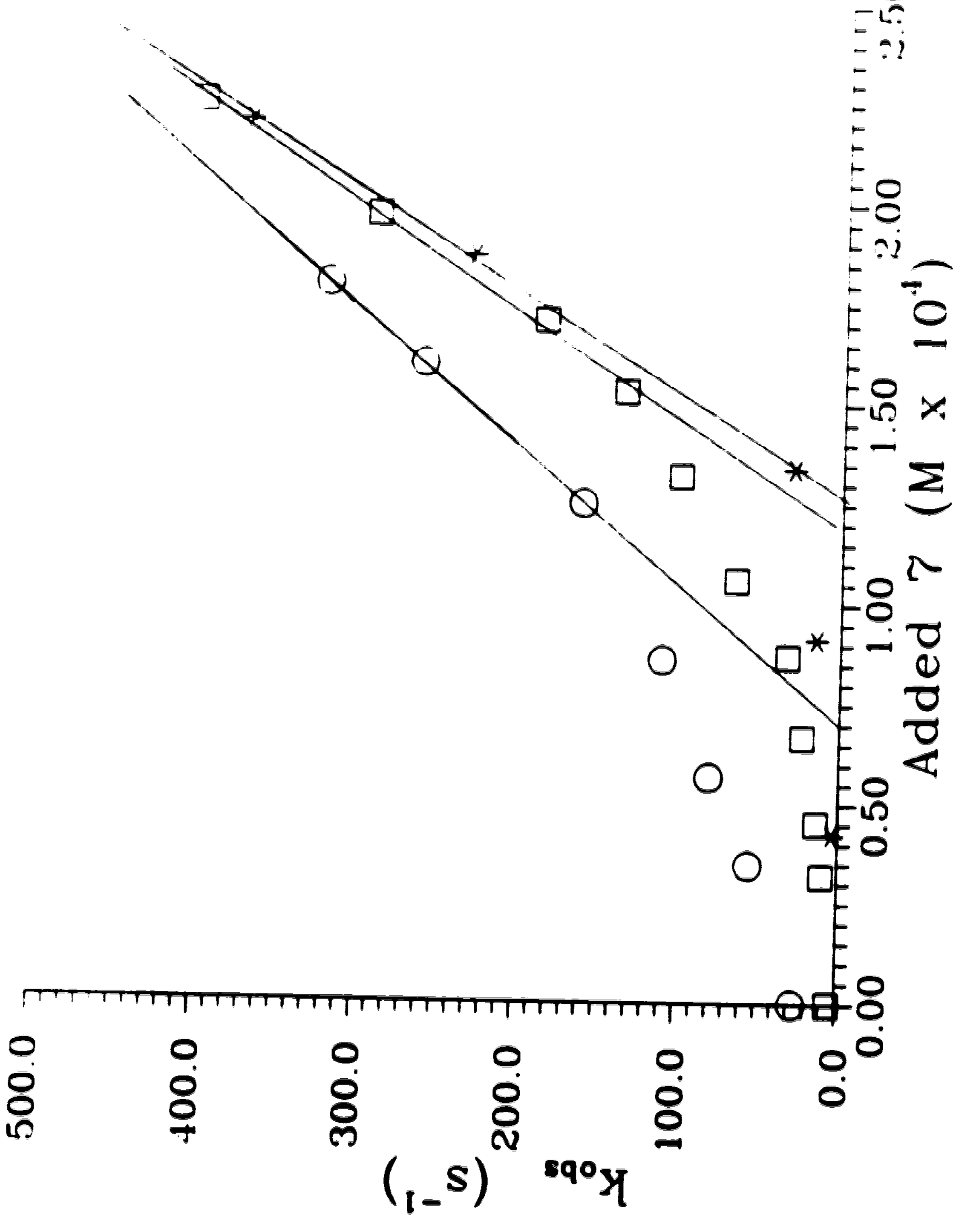


Figure 10 : The Plot of k_{obs} vs [29] Added to Solutions of $29\text{-}1^{+}/OTf^{-}$ in CD_2Cl_2 at -79°C.

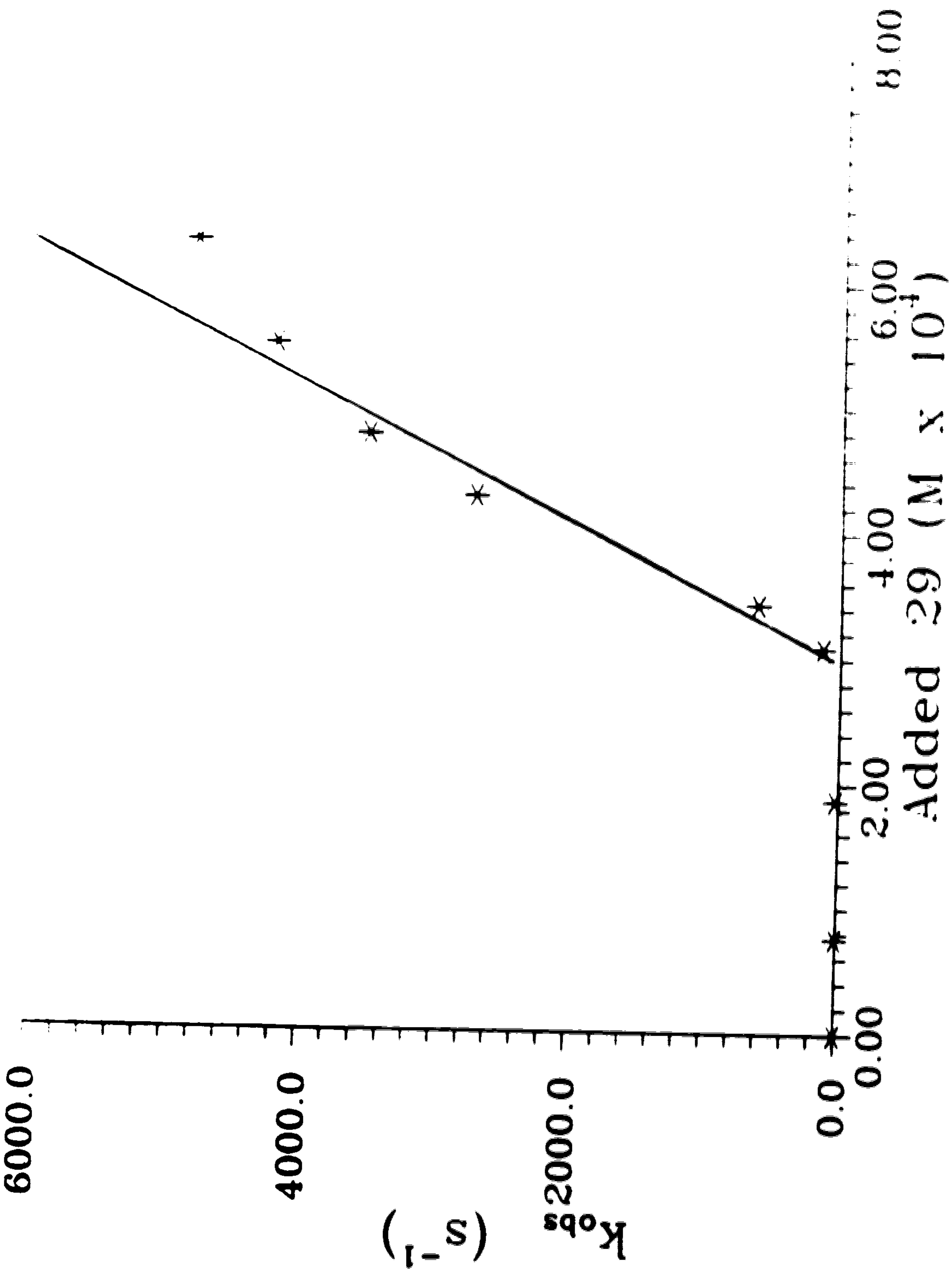


Table 15 : Observed Exchange Rate Constants of I^+ Between 7-I^+/OTf^- and Added 7 in CD_2Cl_2

7 mM[ab]	k_{obs} (s^{-1})	7 mM[ab]	k_{obs} (s^{-1})
0	27	0.106	65
0.0346	55	0.132	140
0.0568	80	0.153	[illegible]
0.0861	110	0.171	[illegible]
0.125	160	0.197	290
0.160	260	0.225	400
0.180	320	0.0424	<10
0	<10	0.0914	15
0.0321	~10	0.134	[illegible]
0.0453	14	0.187	230
0.0669	23	0.220	370
0.0870	33		

a) 6.92 x 10^{-4} M solution of 7

b) Temperatures maintained at -79°C ± 2

Table 16 : Observed Exchange Rates of I^+ Between 29-I^+/OTf^- and Added 29 in CD_2Cl_2

29 (mM)[ab]	k_{obs} (s^{-1})	29 (mM)[ab]	k_{obs} (s^{-1})
0	<10	4.27	2715
0.761	<10	4.76	3515
1.87	25	5.48	4215
3.09	135	6.30	4815
3.43	615		

a) 2.099 x 10^{-2} M solution of 29

b) Temperature of the study was -79°C ± 2

The appearances of the plots in **Figures 9** and **10** should be explained because both have early flat sections where the additions of olefin cause very little change in the observed exchange rate constant, but then further additions cause large increases. These initial flat sections are a result of our inability to prepare the ion in a sufficiently pure state, so that no excess olefin is present. For **7-I$^+$/OTf$^-$**, small amounts of HOTf were added to complex this residual olefin. However, excess acid was added and initial additions of **7** were complexed by this excess acid leading to the initial flat section. Once the excess acid had been exhausted, all olefin that was added participates in the exchange with the ion and large increases in the k_{obs} are observed. The values obtained from three independent exchange experiments for **7-I$^+$/OTf$^-$** (**Figure 9**) are 2.9, 3.7, and 3.9 x 10^6 M^{-1} s^{-1} and give the average adjusted value shown in **Table 17**.

Table 17 : Second Order Rate Constants for X$^+$ Exchange Between Halonium Ions and Their Parent Olefins **7** and **29** at -80^{o}C in CD_2Cl_2.

Ion	Second-Order Rate Constant
7-Br$^+$/OTf$^-$	2.0 (0.2) x 10^6 M^{-1} s^{-1}
7-I$^+$/OTf$^-$	7.6 (0.8) x 10^6 M^{-1} s^{-1}
29-I$^+$/OTf$^-$	4.2 (0.4) x 10^6 M^{-1} s^{-1}

For **29-I$^+$/OTf$^-$**, the addition of HOTf did not complex the olefin and the excess olefin was removed from the solution by filtration of the sample through glass wool that had been impregnated with AgOTf. Therefore, the initial flat section of **Figure 10** was due to the excess AgOTf complexing the small amounts of initially added olefin. The linear portion of **Figure 10** gives the second-order rate constant of 4.0 x 10^6 M^{-1} s^{-1}.

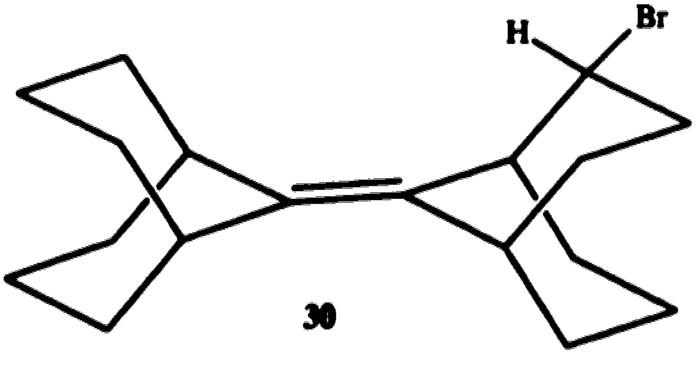
The most striking feature of the data in **Table 17** are the similarities of the transfer rate constants between the olefins, and the independence of X$^+$. Accepting that the olefins are structurally similar, it is somewhat surprising that the rate constants for exchange of Br$^+$ and I$^+$ are so similar. The high numerical values of the rate constants suggests that the rates of X$^+$ exchange may be dominated by the rates of encounter of halonium ion and olefin rather than by energetics. The data for **7-Br$^+$/OTf$^-$** are $\Delta H^{\ddagger} = 1.8 \pm 0.2$ kcal and $\Delta S^{\ddagger} = -21 \pm 1$ cal K^{-1} mol^{-1}.[8,85] The enthalpy of activation is essentially the same as the Arrhenius activation energy (1.7 kcal/mol) for the viscous flow in methylene chloride.[85b] It appears that the exchange of Br^+ between 7-Br^+ and 7, and by inference the exchange of I^+, is largely an entropy driven process which is encounter-limited. The diffusion-controlled encounter rate of two spheres of radii r_A and r_B in medium of viscosity η at temperature T is characterized by a rate constant:[85c]

$$k_{diff} = \frac{2\,RT\,(r_A + r_B)^2}{3000\eta\, r_A r_B}$$

If we assume $r_A = r_B$ and we estimate the viscosity of CD_2Cl_2 to be 0.0919 poise at -80°C by extrapolation of available viscosity data,[85b] the value of k_{diff} is 2.3×10^9 $M^{-1}s^{-1}$. The large difference between k_{diff} and the observed values of k for the halonium/olefin exchange reactions is undoubtedly due to the stringent orientation requirements for reactive encounters.

ii) <u>Properties of 29-Br^+/Br_3^-</u>:

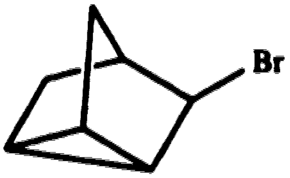
29-Br^+/OTf^- is very unstable which precluded experimental investigation of the exchange rate because any warming of the solution caused degradation of the ion.



30

When 29 was dissolved in CH_2Cl_2 and Br_2 added, there was an immediate yellow precipitate formed that, upon sitting for 24 hours in the dark, disappeared, leaving a brightly colored solution. Product analysis showed that the main product was $C_{18}H_{27}Br$ to which we have assigned the tentative structure **30**. This assignment is based upon the work of Wynberg et. al[86] and also presently obtained ^{13}C NMR data and APT experiments. The proposed mechanism for this abstraction and addition is shown in **Scheme 22**.

The cyclopropyl carbinyl intermediate shown in **Scheme 22** has been proposed for these sorts of reactions in the past.[86,90] The reaction of NBS with bicyclo[2.1.1]heptene (norbornene)[91] in DMSO gives nortricyclene bromide (**31**) as one of the major products.



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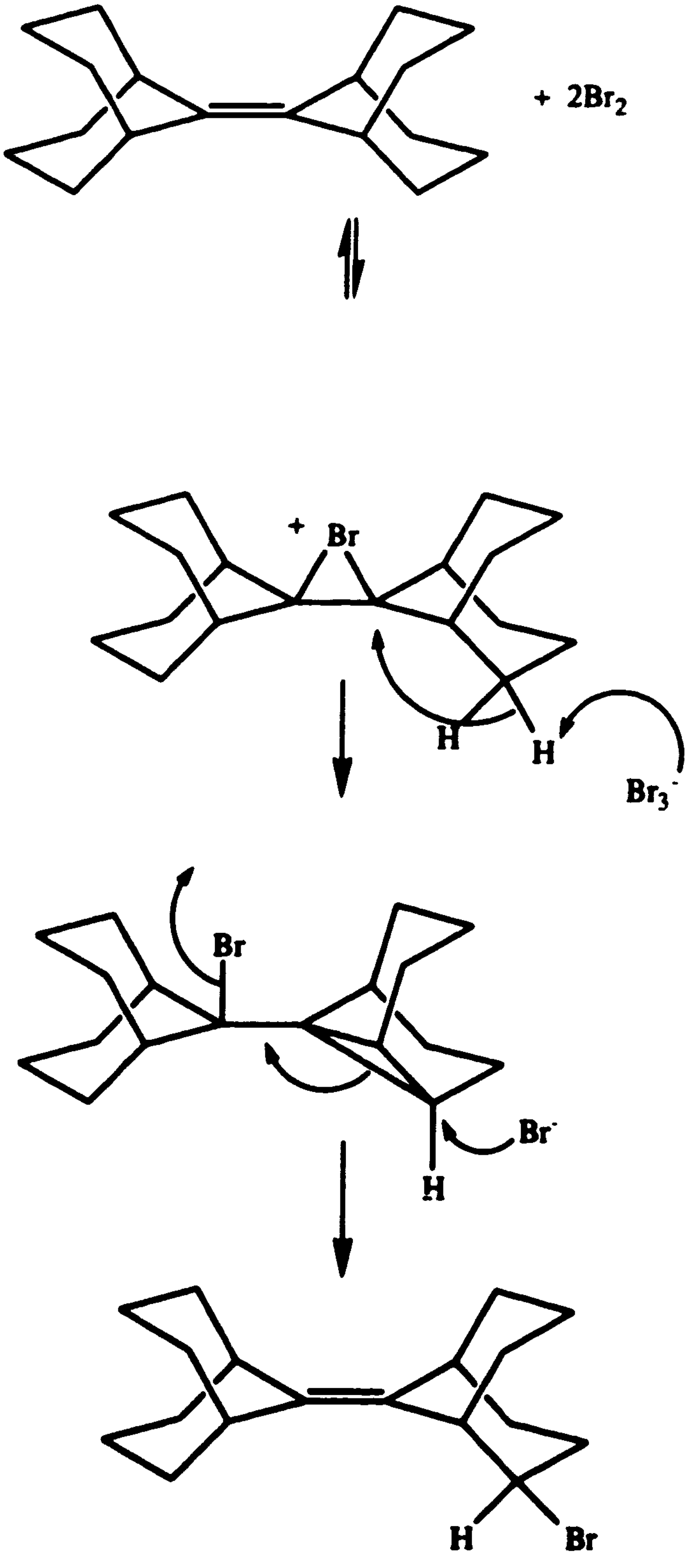
Scheme 22



iii) Silver complexation of 7 and 29:

Because AgOTf was used in the preparation of the halonium ions, it became important to determine if there were silver olefin complexes and what the NMR properties of these complexes were. It is well known that olefins can be separated using silver nitrate impregnated silica gel[92], silver ion impregnated gas chromatograph columns[93], and also HPLC columns that have been impregnated with silver ion.[94]

There has been considerable study, experimental[95] and computational,[96] of silver/olefin complexes. Olah et al.[7] have reported the ^{13}C NMR resonances of 7 complexed by silver hexafluoroantimonate in CH_2Cl_2 and SO_2 (-30°C) (**Table 14**). The surprising result that was observed in our study, but not previously, was coupling of the Ag^+ ion to the olefinic carbons (see **Table 14**). The coupling of approximately 18 hertz is considerably less than the 132 hertz[97] observed when ^{107}Ag and ^{13}C are connected by a sigma bond. The smaller coupling should be expected because the π-complex would have considerably weaker bonding than a sigma complex and therefore coupling should not be as strong. This indicates that future studies relating the J_{Ag}-^{13}C to the strength of π-complexes may be viable.

iv) Structures of 7-Br$^+$/Br$_3^-$, 7-Br$^+$/OTf$^-$, and 7-I$^+$/OTf$^-$:

The iodonium ion, 7-I$^+$/OTf$^-$, crystallizes as a monohydrate (**Figures 11a,b**), the source of the H_2O being adventitious water, or water introduced during the handling of the compound for crystallization. The oxygen of the H_2O is placed 2.630 Å from the I^+, lying roughly along a line connecting the I atom and the center of the C_{10}-C_{20} bond of the iodonium ion. The oxygen of the H_2O is 2.796 and 2.752 Å from the oxygen atoms of two separate triflates (one associated to the indicated iodonium ion, and the other being symmetry related). This is best visualized in the perpendicular view shown in **Figure 11b**, and suggests that the triflate counterions form a chain held together by hydrogen bonds from the bridging H_2O. As for the iodonium ion itself, it is essentially symmetric as is judged from the similarity of the I-C bond lengths and the I-C-C bond angles. Shown in **Tables 18, 19**, and **20** are the selected interatomic bond lengths and bond angles of the crystal structure of 7-I$^+$/OTf$^-$ (see **Figures 11a, b** to understand the numbering system).

Given in **Table 21** is a comparison of selected bond lengths and angles for 7-Br$^+$/OTf$^-$ [98a] and 7-Br$^+$/Br$_3^-$,[9] and 7-I$^+$/OTf$^-$. The two bromonium ions in the unit cell of 7-Br$^+$/OTf$^-$ are essentially the same (**Figures 12, 13**), and the average C-C bond lengths for the adamantane group for the three bromonium ions are the same (7-Br$^+$/OTf$^-$, 1.532 Å; 7-Br$^+$/Br$_3^-$, 1.534 Å). The major structural difference between the two bromonium ions are the two bond lengths between the Br and C of 7-Br$^+$/Br$_3^-$ (**Figure 2**), where the Br is preferentially displaced toward C_{10} from an asymmetrical position. This results in a 0.07 Å longer C_{20}-Br bond than the C_{10}-Br bond, and a larger angle for Br-C_{10}-C_{20} than Br-C_{20}-C_{10}. The pairs of Br-C bonds (Br-C_{10} and Br-C_{20}, Br-C_{30} and Br-C_{40}) in the two bromonium ions in 7-Br$^+$/OTf$^-$ are nearly equivalent, which indicates that these ions are nearly symmetric species as expected, and that the source of the bromonium ion asymmetry observed in 7-Br$^+$/Br$_3^-$ is the placement of the Br$_3^-$.

The major structural difference between the bromonium ions and the iodonium ion is the longer C-I bond (2.35 Å vs. 2.11 Å for C-Br) and a slightly shorter central C_{10}-C_{20} bond (1.45 Å vs. 1.49 Å). See **Table 21** for a comparison of selected interatomic distances and angles in 7-I$^+$/OTf$^-$ with analogous quantities in 7-Br$^+$/Br$_3^-$ and 7-Br$^+$/OTf$^-$.

Table 18 : Table of Selected Interatomic Bond Lengths (in Å) for 7-I$^+$/OTf$^-$[a]

Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance
I	C10	2.362 (6)	C11	C12	1.55 (1)	C21	C22	1.55 (1)
I	C20	2.338 (6)	C11	C19	1.548 (9)	C21	C29	1.554 (9)
S	O1	1.403 (8)	C12	C13	1.51 (1)	C22	C23	1.58 (1)
S	O2	1.45 (1)	C13	C14	1.54 (1)	C23	C24	1.50 (1)
S	O3	1.406 (7)	C13	C18	1.54 (1)	C23	C28	1.532 (9)
S	C1	1.777 (7)	C14	C15	1.538 (9)	C24	C25	1.563 (9)
F1	C1	1.28 (1)	C15	C16	1.536 (9)	C25	C26	1.532 (8)
F2	C1	1.32 (1)	C16	C17	1.53 (1)	C26	C27	1.51 (1)
F3	C1	1.32 (1)	C17	C18	1.54 (1)	C27	C28	1.52 (1)
C10	C11	1.52 (1)	C17	C19	1.52 (1)	C27	C29	1.55 (1)
C10	C15	1.530 (9)	C20	C21	1.53 (1)			
C10	C20	1.454 (6)	C20	C25	1.509 (9)			

[a] Error in brackets represents standard error in the last value of the number it is associated with.

Table 19 : Table of Selected Distances (in Å) Between Non-Bonded Atoms for 7-I$^+$/OTf$^-$[a]

Atom 1	Atom 2	Distance
O4	I	2.630 (4)
O4	O1	2.796 (8)
O4	O3	2.752 (8)

[a] Error in brackets represents standard error in the last value of the number it is associated with.

Table 20 : Table of Selected Interatomic Angles (in degrees) for 7-I$^+$/OTf$^-$[a]

Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle
C10	I	C20	36.0 (1)	C15	C16	C17	109.9 (6)
O1	S	O2	115.3 (6)	C16	C17	C18	109.8 (7)
O1	S	O3	114.7 (6)	C16	C17	C19	109.0 (6)
O1	S	C1	106.0 (4)	C18	C17	C19	109.7 (8)
O2	S	O3	113.8 (7)	C13	C18	C17	109.0 (5)
O2	S	C1	101.6 (5)	C11	C19	C17	110.5 (6)
O3	S	C1	103.4 (4)	I	C20	C10	72.9 (4)
S	C1	F1	116.0 (6)	I	C20	C21	109.6 (4)
S	C1	F2	111.2 (7)	I	C20	C25	109.7 (4)
S	C1	F3	111.3 (6)	C10	C20	C21	121.6 (8)
F1	C1	F2	107.2 (7)	C10	C20	C25	122.1 (7)
F1	C1	F3	109.2 (8)	C21	C20	C25	111.8 (5)
F2	C1	F3	100.7 (7)	C20	C21	C22	107.6 (6)
I	C10	C11	109.2 (5)	C20	C21	C29	111.1 (6)
I	C10	C15	108.8 (5)	C22	C21	C29	107.8 (5)
I	C10	C20	71.1 (4)	C21	C22	C23	108.8 (6)
C11	C10	C15	110.6 (5)	C22	C23	C24	109.1 (5)
C11	C10	C20	123.0 (8)	C22	C23	C28	108.7 (6)
C15	C10	C20	123.4 (7)	C24	C23	C28	110.5 (7)
C10	C11	C12	105.7 (6)	C23	C24	C25	110.9 (6)
C10	C11	C19	111.5 (6)	C20	C25	C24	106.4 (6)
C12	C11	C19	108.1 (6)	C20	C25	C26	111.5 (6)
C11	C12	C13	111.6 (7)	C24	C25	C26	107.4 (5)
C12	C13	C14	108.5 (5)	C25	C26	C27	110.7 (6)
C12	C13	C18	110.2 (7)	C26	C27	C28	110.3 (6)
C14	C13	C18	108.7 (7)	C26	C27	C29	109.7 (5)
C13	C14	C15	110.0 (6)	C28	C27	C29	109.2 (8)
C10	C15	C14	107.3 (6)	C23	C28	C27	109.4 (5)
C10	C15	C16	111.6 (6)	C21	C29	C27	109.2 (6)
C14	C15	C16	108.5 (5)				

[a] Error in brackets represents standard error in the last value of the number it is associated with.

Figure 11a : Perspective View of the $[(C_{10}H_{14})_2I^+][CF_3SO_3]\cdot(H_2O)$ Asymmetric Unit Showing the Atom Labelling Scheme. Atoms are Represented by Gaussian Ellipsoids at the 20% Probability Level Except for Hydrogens, Which are Shown Artificially Small for the Water Molecule and are not Shown at all for the $(C_{10}H_{14})_2I^+$ Unit.

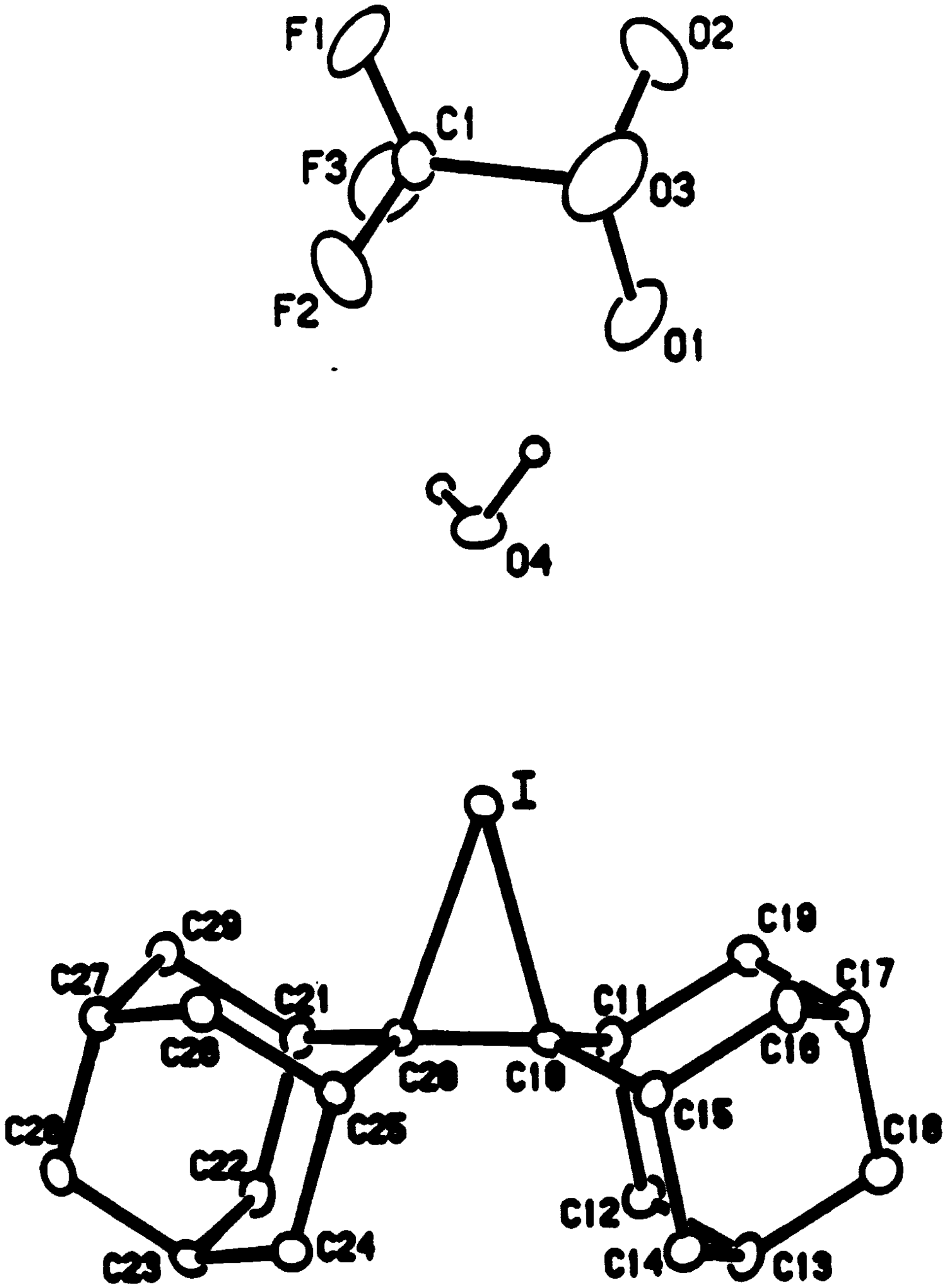


Figure 11b : Alternate View of $[(C_{10}H_{14})_2I^+][CF_3SO_3]\cdot(H_2O)$ Showing the Interactions of the Water Molecule with the $(C_{10}H_{14})_2I^+$ Unit and with Symmetry-Related Triflate Ions.

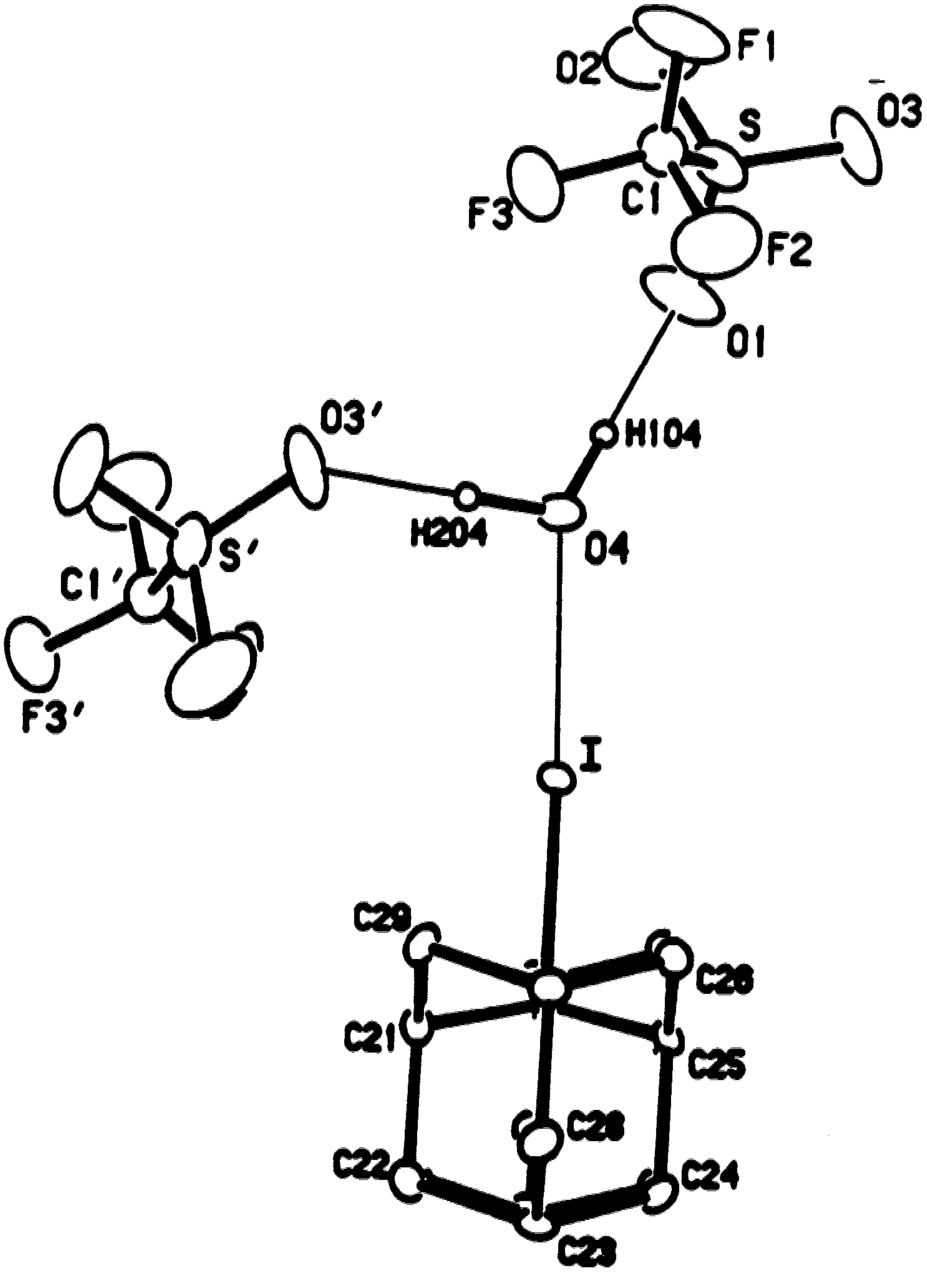


Figure 12 : Perspective View of the Asymmetric Unit of 7-Br$^+$/OTf$^-$ Showing the Atom Labelling Scheme. Atoms are Represented by Guassian Ellipsoids at the 20% Probability Level

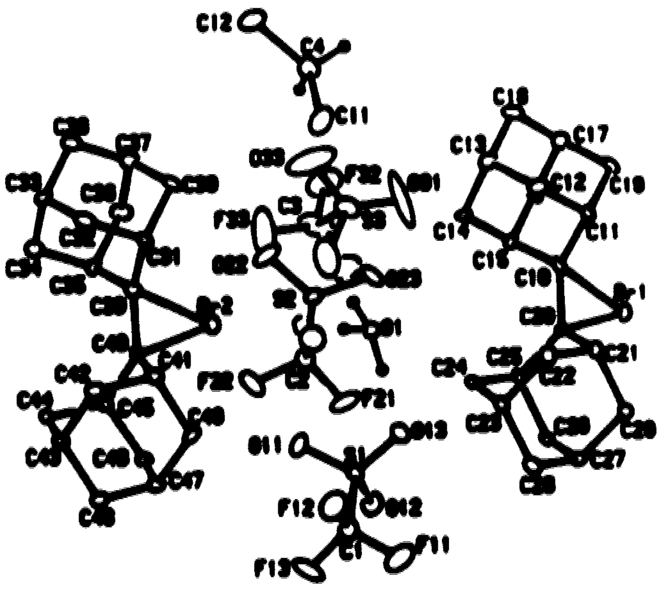


Figure 13 : View of the Asymmetric Unit of 7-Br$^+$/OTf$^-$ Down the Br1-Br2 Axis, Highlighting the Triflate, Hydronium and Dichloromethane Units.

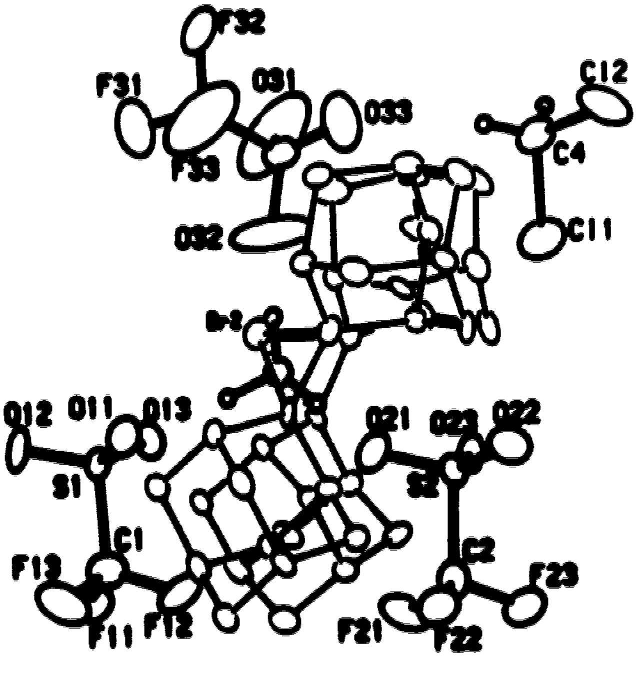


Table 21 : Selected bond lengths and angles for 7-Br^+/OTf^-, 7-Br^+/Br_3^- and 7-I^+/OTf^- determined from X-ray diffraction.[a]

Bond parameter (S.D.) (Å or °)	7-Br^+/Br_3^- [b]	7-Br^+/OTf^- [c]	Calculated[d]
C_{10} - C_{20}	1.497 (8)	1.492 (15)	1.491
(C_{30} - C_{40})		1.491 (14)	
Br - C_{10}	2.116 (6)	2.118 (10)	2.158
(Br - C_{30})		2.089 (10)	
Br - C_{20}	2.194 (6)	2.136 (10)	2.158
(Br - C_{40})		2.114 (20)	
C - C_{10} -C	113.1 (5)	111.2 (8)	111.3
(C - C_{30} -C)		112.1 (5)	
C - C_{20} -C	112.7 (5)	112.9 (9)	111.3
(C - C_{40} - C)		112.7 (5)	
C_{10} - Br - C_{20}	40.6 (2)	41.0 (5)	40.4
(C_{30} - Br - C_{40})		41.6 (4)	
Br - C_{10} - C_{20}	72.5 (3)	70.1 (6)	69.8
(Br - C_{30} - C_{40})		70.2 (6)	
Br - C_{20} - C_{10}	66.9 (3)	68.8 (7)	69.8
(Br - C_{40} - C_{30})		68.3 (6)	

Bond parameter (S.D.) (Å or °)	7-I^+/OTf^-		Calculated
C_{10} - C_{20}	1.454 (6)		1.485
I - C_{10}	2.362 (6)		2.389
I - C_{20}	2.338 (6)		2.389
I - O_4	2.630 (4)		-
O_4 - O_1	2.796 (8)		-
O_4 - $O_{3'}$	2.752 (8)		-
C - C_{10} - C	110.6 (5)		110.9
C - C_{20} - C	111.8 (5)		110.9
C_{10} - I - C_{20}	36.0 (1)		36.2
I - C_{10} - C_{20}	71.1 (4)		71.9
I - C_{20} - C_{10}	72.9 (4)		71.9

a. For atom numbering see Figures 2, 11, 12, and 13.

b. Reference 9.

c. The two sets of data correspond to the two independent bromonium ions found in the unit cell of 7-Br^+/OTf^- (see **Figures 12, 13**)

d. Computed as described in section v

v) Calculation of the structure of adamantylideneadamantane bromonium ion and iodonium ion[98b]

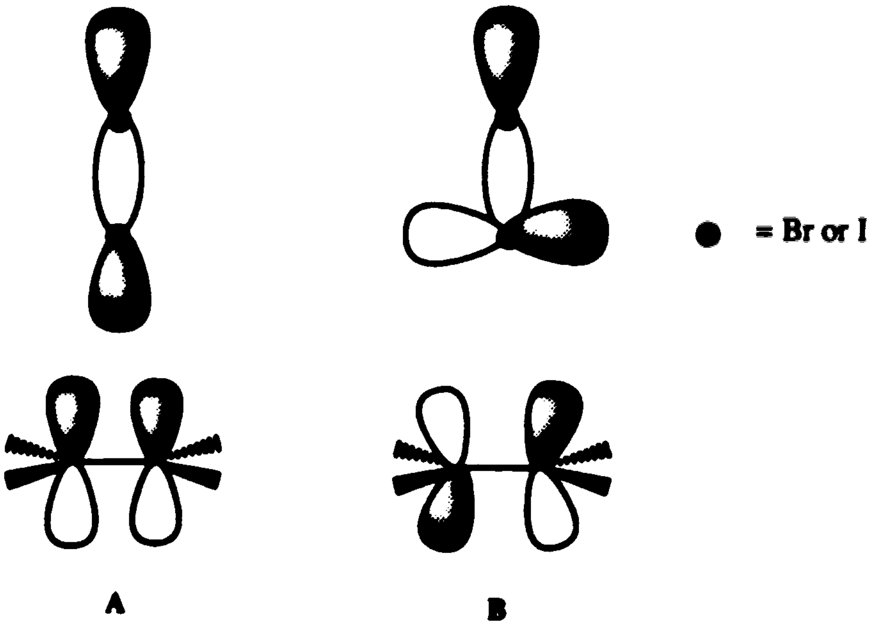
All calculations were performed by Dr. Mariuz Klobukowski[98b] of this department. The results are included here insofar as they pertain to the experimental halonium ion structures. The geometries of the two ions, 7-Br^+ and 7-I^+, were optimized using the gradient techniques incorporated in the GAMESS code.[99] A basis set having a total of 442 molecular basis functions was used. The optimized geometric parameters are collected in **Table 21**, together with the experimental X-ray values. The computed structural parameters of the free 7-X^+ ions agree well with those in the X-ray structure of 7-X^+/OTf^-. The calculated X-C_{10} and C_{10}-C_{20} bond lengths are slightly longer than the experimental ones.

vi) Orbital interactions of the bromonium and iodonium ions with olefins

Many aspects of the reaction of Br_2 with olefins have been discussed, and different mechanisms of addition proposed, but the question of orbital interactions remains. How are the orbitals interacting to form the halonium ions? In **Figure 14**, the interaction of X_2 and olefin orbitals to form the CTC are shown.

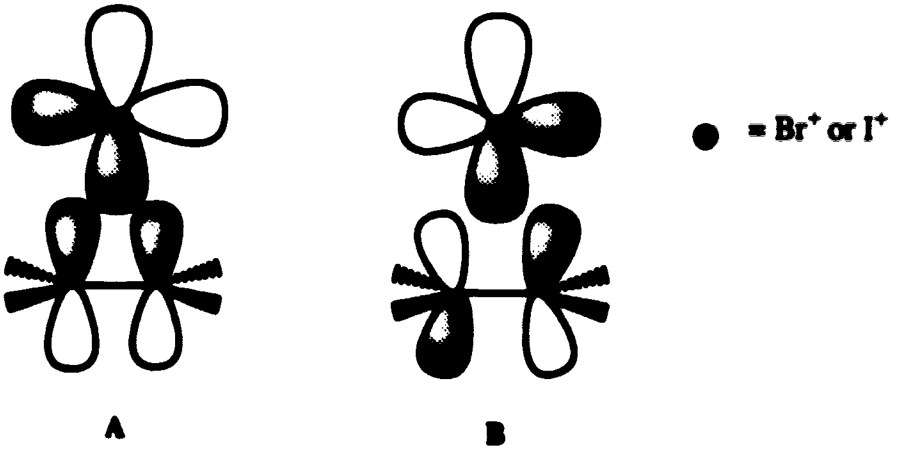
In **Figure 14 A**, there is electron donation from the π-bond of the olefin to the σ^* of X_2. There is also a back donation of electron density from the appropriately oriented 4 or 5p-orbitals of a X atom into the π^* orbitals of the olefin, as shown in **Figure 14 B**. This then represents the interaction of the orbitals at the stage of the CTC. In **Figure 15** are the orbital interactions for the halonium ion itself.

Figure 14



In Figure 15 A, there is electron donation from the π-orbitals of the olefin into the empty 4 or 5p-orbital of the X cation. This is accompanied by back donation from a filled 4 or 5p-orbital of the cation into the π^*-orbitals of the olefin (as in Figure 15 B). This results in the +1 charge of the free X ion being substantially reduced in the halonium ion. The bonding is very similar to that shown for the CTC, and Figures 14 and 15 qualitatively resemble the complexation of silver cation and olefins[96] with 4d-orbitals being involved for silver cation.

Figure 15

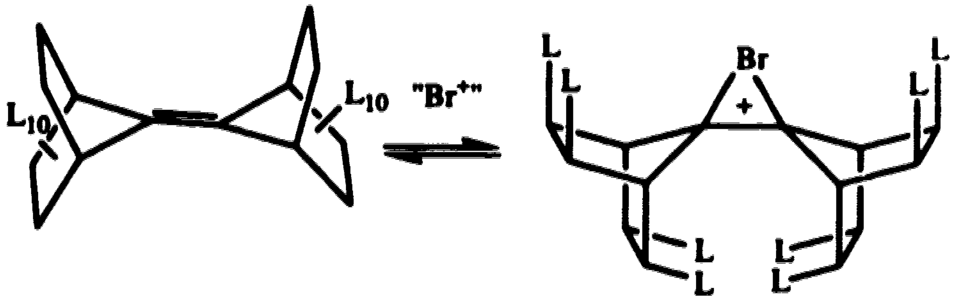


CHAPTER 3

Inverse Secondary Deuterium Kinetic Isotope Effect for Br_2 Addition to Sterically Congested Olefins

a) Introduction

Many sterically demanding olefins have been synthesized and brominated but only two compounds (adamantylideneadamantane (7)[7,8,9,10d,80] and bicyclo[3.3.1]non-9-ylidenebicyclo [3.3.1]non-9'-ane (29)) have yielded bromonium ions that have been isolated and characterized. In an effort to gain further information about the bromination of other sterically demanding olefins of the same type, a study using 7-norbornylidene-7'-norbornane (32) was undertaken.



32a L = H

32b L = D

33a L = H

33b L = D

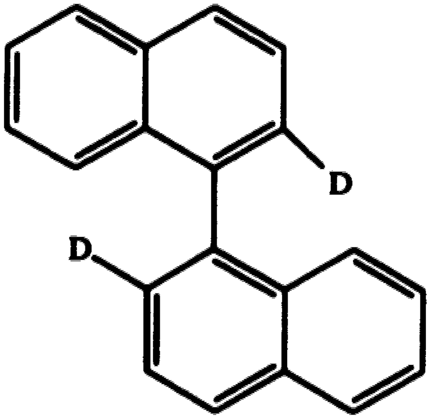
It has been shown[100] that this compound (**32a**), when treated with Br_2 in CCl_4, gives the 1,2-dibromide addition products. There is no stereochemical handle to determine if the addition is trans, but it is assumed to be thus because it is known that compounds of this type do form the bromonium ions.[7,8,9,10d,80] Because of the structural similarity of 32 to 7 and 29, nucleophilic attack on the bromonium ion should be difficult and may even be rate limiting.

If the rate limiting step is indeed nucleophilic attack on the bromonium ion (33), then the reaction should be facilitated if the rear face of the olefin is less sterically encumbered. One method of slightly affecting the steric properties of the molecule would be to replace the hydrogen with deuterium because it has been shown that the C-D bond is shorter than the C-H bond.[101] By replacement of the endo hydrogens with D, the carbons of the bromonium ion should be slightly more accessible and an effect on the rate of bromination may be observed.

Despite limited usage,[102,6,10f] deuterium kinetic isotope effects[20,21] (Dkie) have been valuable in the study of electrophilic bromination. The observations of inverse secondary α-Dkie's for the bromination of stilbene,[102a] styrenes,[102b] and various deuterated cyclohexenes[6] have yielded information about the extent of rehybridization in the rate limiting step. A primary Dkie has been reported for the bromination of a sterically crowded olefin (Tetra*iso*butylethylene, **11**) which gives double bond rearranged products.

Clearly, **33** cannot form double bond rearranged allylic bromides, nor can it exhibit a secondary α-Dkie for electrophilic reaction with Br_2. The effect that should be observed upon replacement of hydrogen with deuterium is mostly one of remote steric effects, perhaps superimposed upon smaller electronic effects.

Steric kinetic isotope effects are not unknown. The largest kinetic effects have been observed in systems such as 1,2'-binaphthyl-2,2'-d_2[103] (**34**) where the isotope effect on the rate of racemization has been observed and measured. The kie for the racemization of **34** in dimethylformamide was measured between 20° and 65°C and found to vary from $k_D/k_H = 1.20$ to 1.14. 9,10-Dihydro-4,5-dimethylphenanthrene (**35**) racemization has also been investigated[104] and an inverse isotope effect of 1.17 (k_D/k_H) in benzene at 23°C was observed.



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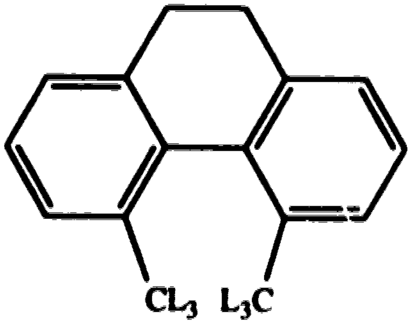

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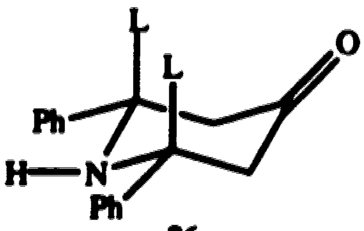
While many other steric isotope effects have been observed for racemization reactions, very few steric kie's have been observed for nucleophilic reactions. The solvolyses of *n*-propyl methanesulphonate and *n*-propyl iodide with the γ positions fully deuterated have been studied[105] in water at 60° and 90°C, respectively, and kinetic isotope effects (k_D/k_H) of 1.06 and 1.08 were found. A similarly small effect of $k_D/k_H = 1.04$[106] was observed for BH_4^- attack on cis-2,6-diphenyl-4-piperidone (36) in water:dioxane (0.01M NaOH). In these cases, approach of the nucleophile to the reaction center appeared to be slightly more hindered for the H derivative, a fact that is consistent with a shorter C-D bond.



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In view of the possibility that 32 and its corresponding bromonium ion contain remote γ-CL bonds that shield the olefinic portion and, even more so, the backside of the three membered ring, the bromination kinetics of **32a** and **32b** in AcOH and MeOH at varying [Br$^-$] were undertaken along with a determination of the reaction products.

b) Experimental

i) General

Routine NMR and IR spectra were obtained with Bruker WP-200 NMR and Nicolet SX-20 FTIR spectrometers. GLPC initial analyses of product mixtures were performed with Hewlett-Packard 5830A gas chromatograph using a 6 ft x 1/8 in. 10% DEGS on 80-100 mesh Chromosorb W column. GCIR determinations were performed using a Hewlett-Packard 5890 GC with an HP5 30 m x 0.24 mm column attached to a Hewlett-Packard 5965A IRD. GCMS were performed using a Varian Vista 6000 GC with a HP5 30 m x 0.24 mm column and 12 psi column head pressure, attached to a VG 7070E low resolution mass spectrometer.

ii) Materials

The synthesis of 7,7-dimethoxy-1,2,3,4-tetrachlorobicyclo[2.2.1]hept-2-ene was attempted as outlined by Gassman and Pape,[107] but little or no product was ever produced by us, when using this method. The optimum conditions, we found, involved preheating the 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene to 150°C (at this temperature the starting material did not decompose) and bubble a mixture of nitrogen and ethylene through the compound for 14 hours. After purification, by distillation, the product was isolated in 75% yield; bp 55-57°C at 0.05 Torr; lit 56°C at 0.05 Torr[108]. The synthesis of 7-norbornanone was then completed as outlined by Gassman and Pape.[107]

7-Norbornanone was coupled as outlined by Bartlett and Ho[100] to produce 7-norbornylidene-7'-norbornane (**32a**). This was recrystallized as outlined by Bartlett,[100] but we did not obtain the pure product as there was an impurity present in roughly a 1:1

ratio (by GC) with the product. The identity of the impurity was not investigated. The two compounds could be separated by preparative GC utilizing an 11 ft x 3/8 in. 20% DEGS on 80-100 mesh Chromosorb W preparative column: Temperature 185°C; He flow = 98 cc/min. Pure **32a** was obtained: microanalysis calcd: C, 89.29; H, 10.70; observed: C, 89.02; H, 10.90; mp 140-141°C (uncorrected); lit. mp[100] 137-138°C.

7-Norbornylidene-7'-norbornane-d_{20} (**32b**) was synthesized[109] as follows: 1,2-Dibromo-1,2-dideuterioethylene was synthesized[110] and reacted with 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene as outlined by Mackenzie[111] to obtain 5,6-dibromo-1,2,3,4-tetrachloro-5,6-dideuterio-7,7-dimethoxybicyclo[2.2.1]hept-2-ene. The synthesis was then carried on to bicyclo[2.2.1]heptan-7-one-d_{10} as outlined by Gassman and Pape,[107] followed by coupling using the McMurray[81] method to obtain 7-norbornylidene-7'-norbornane-d_{20} (**32b**). This compound was purified in the same manner as **32a**. The sample was analyzed by ^{1}H NMR using $CHCl_3$ as an internal standard to determine the extent of deuteration; ^{1}H NMR δ 2.3 (4H) bridgehead shows 6% H; 1.48 (8H) exo shows 8% H; 1.25 (8H) endo shows 9.4% H.

iii) Bromination Kinetics

The kinetics of the disappearance of Br_2 were monitored at 410 nm in purified[10a] AcOH and purified[10d] MeOH with varying [Br^-] at 25°C, $\mu = 0.1$ ($LiClO_4$) and $\mu = 0.3$ ($LiClO_4$), respectively, using a Cary 210 UV/Vis spectrophotometer interfaced to a microcomputer as previously described.[10d]

To a 1 cm cuvette containing 3 mL of olefin (~1 x 10^{-3} M) in AcOH or MeOH was added 100 µl of a bromine (9 x 10^{-5} - 1 x 10^{-4} M final Br_2 concentration) in the same solvent as the olefin. Before bromine addition the cuvette was allowed to equilibrate at 25°C in the thermostated cell holder of the Cary 210 for at least 15 minutes. All reactions were performed in triplicate and the rate constants quoted in Tables 22 and 23 are an average of three runs. Given in **Tables S7 & S8** (supplementary material) are the original rate constants for bromination of **32a** and **32b**.

iv) Product Studies

All solutions used for determining the kinetics at each Br^- concentration in MeOH or AcOH were combined and poured into 100 mL of H_2O. The aqueous mixture was then extracted with 3 x 35 mL CH_2Cl_2. The organic layers were separated from the aqueous layer, combined, and washed with 2 x 100 mL of H_2O (AcOH extracts were also washed with 1 x 100 mL 20% Na_2CO_3 to remove excess AcOH). The organics were dried ($MgSO_4$), filtered, and the solvent removed by rotary evaporation. To the residue was added 1 to 3 drops of CH_2Cl_2 before injection into the GC.

Products were identified using GC mass spectrometry and GCIR. A HP5 30 m x 0.24 mm column was used for both the mass spectrometry and IR analysis with the following conditions: $T_1 = 40^oC$ for 2 min., programmed for $\Delta T = 20^oC$ per min. until $T_2 = 280^oC$; column head pressure 12 psi.

The only addition products observed in MeOH were the dibromide and bromo/methoxy products. In AcOH only dibromide and bromo/acetate were observed. Products of addition in MeOH: $C_{14}H_{20}Br_2$; calcd; 345.99315, 347.99111, 349.98907; obs; 345.4, 347.5, 349.6; $C_{15}H_{23}OBr$; calcd; 298.09322, 300,09657; obs; 297.7, 299.8. Products of addition in AcOH: $C_{14}H_{20}Br_2$; calcd; 345.99315, 347.99111, 349.98907; obs; 346.0, 348.0, 349.9; $C_{16}H_{23}O_2Br$; calcd; 326.08813, 328.08944; obs. 325.9, 328.0. Bartlett and Ho[100] isolated and characterized $C_{14}H_{20}Br_2$; found mp 144-147°C; mass ion 350.

c) Results

i) Bromination

Shown in **Tables 22 and 23** are the kinetic rate constants for bromination of **32a** and **32b** in AcOH and MeOH at varying $[Br^-]$ and constant ionic strength (μ = 0.1 and 0.3 $LiClO_4$, respectively). The kinetics of electrophilic bromine addition to olefins in solvents containing added Br^- are complicated by the rapid establishment[12] of the equilibrium, $Br^- + Br_2 \rightleftharpoons Br_3^-$ as described in the introduction (p 4).[4] In AcOH and MeOH, the accepted values for the tribromide equilibrium constants are K_{eq} = 92 and 177 M^{-1}.[12,4c,4d,4j] Both Br_2 and Br_3^- are brominating agents,[2,4] so the rate of disappearance of total bromine, or $[Br_2]_t$, is as shown in equation **9**.

(9)

$$\frac{-d[Br_2]_t}{dt} = k[Br_2]_t[ole]$$

$$= (k_{Br_2}[Br_2]_f + k_{Br_3^-}[Br_3^-])[ole]$$

$$= (k_{Br_2}[Br_2]_f + k_{Br_3^-}K_{eq}[Br^-][Br_2]_f)[ole]$$

Where k_{Br_2} is the second-order rate constant for addition of Br_2 ($[Br_2]_f$) and k_{Br_3} is the rate constant for addition of Br_3^-, or its kinetic equivalent, $Br^- + Pr_2$. The observed global second-order rate constant for the disappearance of bromine (k_g) can be expressed[2,4] as in equation **10**.

(10)

$$k_g = (k_{Br_2} + k_{Br_3^-}K_{eq}[Br^-])/(1 + K_{eq}[Br^-])$$

Figure 16 : A Plot of k_{obs} vs $[Br^-]$ for the Bromination of **32a** (O) and **32b** (*) in MeOH; $T = 25^{o}C$, $\mu = 0.3$ ($LiClO_4$).

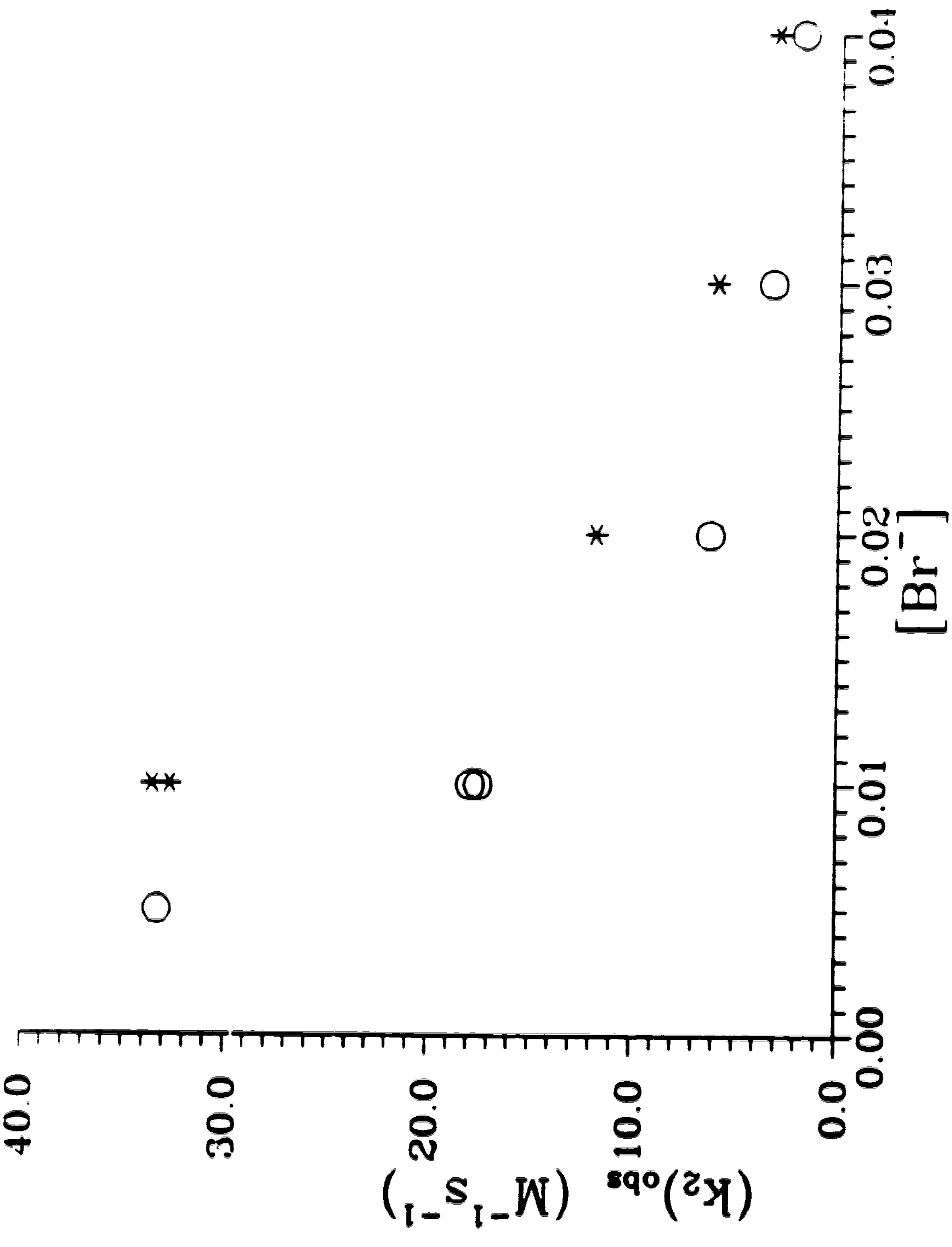
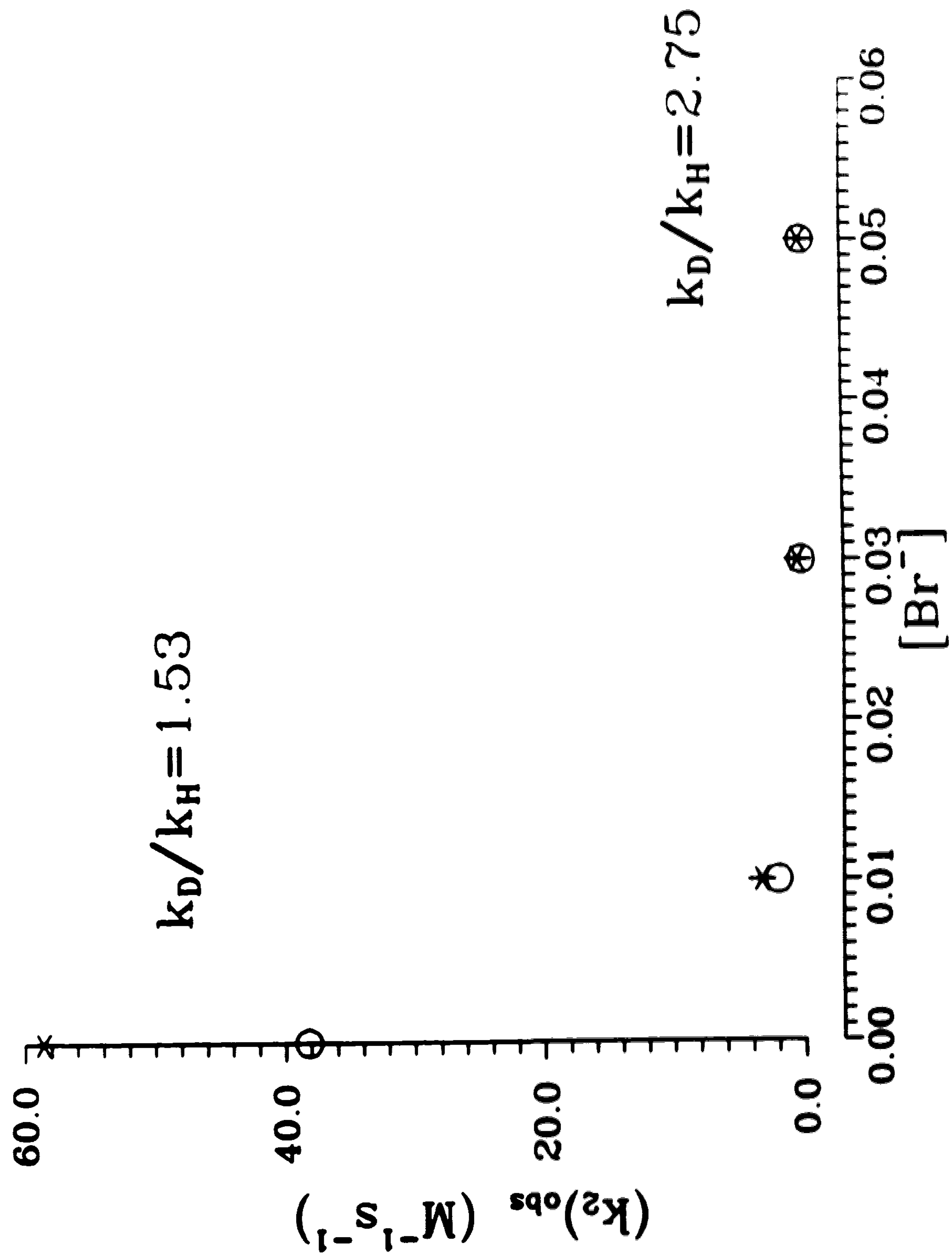


Figure 17 : A Plot of k_{obs} vs [Br⁻] for the Bromination of **32a** (O) and **32b** (*) in AcOH; T = 25°C, μ = 0.1 ($LiClO_4$).



For normal unsaturated species such as cyclohexene, a plot of (1 + $K_{eq}[Br^-])k_g$ vs. $K_{eq}[Br^-]$ gives an intercept of k_{Br_2} with a slope of $k_{Br_3^-}$. However, as seen in **Figures 16** and **17**, the plots for the bromination of **32** are not linear and asymptotically approach the x-axis at higher $[Br^-]$. To our knowledge, this observation has only been made with two other olefins, tri-*tert*-butylethylene[27] (**18**) and 3-acetoxy-2-cholestene[28] (**19**). Because it was not possible to compare k_{Br_2} and $k_{Br_3^-}$ from the **Figures 16** and **17**, except at zero $[Br^-]$ where k_{Br_2} can be compared, the direct comparison of the (1 + $K_{eq}[Br^-])k_g$ values are also shown in **Tables 22** and **23**. The k_D/k_H values in MeOH (from **Table 22**) stay reasonably constant at ~1.8 over the entire range of $[Br^-]$, whereas the k_D/k_H in AcOH (**Table 23**) varies from 1.53 at zero added Br^- to 2.75 at 0.05 M Br^-. The addition of LiBr could not be studied over a larger range because at $[Br^-]$ higher than 0.04 M and 0.05 M in MeOH and AcOH, respectively, the rates of bromination were retarded to the point that competing reactions interfered with the kinetics.

Table 22 : Rate Constants and Product Percentages for Bromination of **32a** and **32b** in MeOH as a Function of Added $[Br^-]$, T = 25°C, μ = 0.3 ($LiClO_4$)[a]

[LiBr] M	**32a** k_g[b] ($M^{-1}s^{-1}$)	**32b** k_g[b] ($M^{-1}s^{-1}$)	K_{eq}[c]$[Br^-]$	$(1+K_{eq}[Br^-])$ x k_g **32a**	$(1+K_{eq}[Br^-])$ x k_g **32b**	k_D/k_H	%[d] diBr	%[d] BrM
0.005	33.30	-	0.885	62.8	-	-	-	100[f]
0.01	17.52 17.90[e]	33.57 32.70[e]	1.77	49.58	90.58	1.83	-	100[f]
0.02	6.23	11.82	3.54	28.28	53.66	1.90	-	-
0.03	3.28	5.98	5.31	17.10	37.73	1.82	7.1	92.9
0.04	1.85	3.115	7.08	14.95	25.17	1.68	-	-

a $[Br_2] = 9 \times 10^{-5} - 1 \times 10^{-4}$ M; [ole] = ~1×10^{-3} M; followed at 410 nm.

b k_g defined as $k_{observed}$/[ole]; ±5%.

c $K_{eq} = 177\ M^{-1}$ [4c,4j] for $Br_2 + Br^- \rightleftharpoons Br_3^-$ in MeOH.

d Isolated as described in the Experimental Section. (diBr = dibromide of **32a**; BrM = bromomethoxy of **32a**)

e Separate set of experiments, so two sets of data resulted.

f No dibromide product could be detected.

Table 23 : Rate Constants and Product Percentages for Bromination of **32a** and **32b** in AcOH as a Function of Added [Br$^-$], T = 25°C, μ = 0.1 (LiClO$_4$)^a

[LiBr] M	**32a** k_g^{b} ($M^{-1}s^{-1}$)	**32b** k_g^{b} ($M^{-1}s^{-1}$)	K_{eq}^{c}[Br$^-$]	(1+K_{eq}[Br$^-$]) x k_g **32a**	(1+K_{eq}[Br$^-$]) x k_g **32b**	k_D/k_H	%^{d} diBr	%^{d} BrA
0.00	38.2	58.6	0.0	38.2	58.6	1.53	-	-
0.01	2.07	3.33	0.92	3.97	6.39	1.61	38.6	61.4
0.03	0.270	0.541	2.76	2.76	2.034	2.00	62.4	37.6
0.05	0.092	0.253	4.6	4.6	1.417	2.75	82.6	17.4

a [Br$_2$] = 9 x 10^{-5} - 1 x 10^{-4} M; [ole] = ~1 x 10^{-3} M; followed at 410 nm.

b k_g defined as $k_{observed}$/[ole]; ±5%.

c K_{eq} = 92 M^{-1} [4d,12] for $Br_2 + Br^- \rightleftharpoons Br_3^-$ in AcOH.

d Isolated as described in the Experimental Section. (diBr = dibromide of **32a**; BrA = bromoacetate of **32a**)

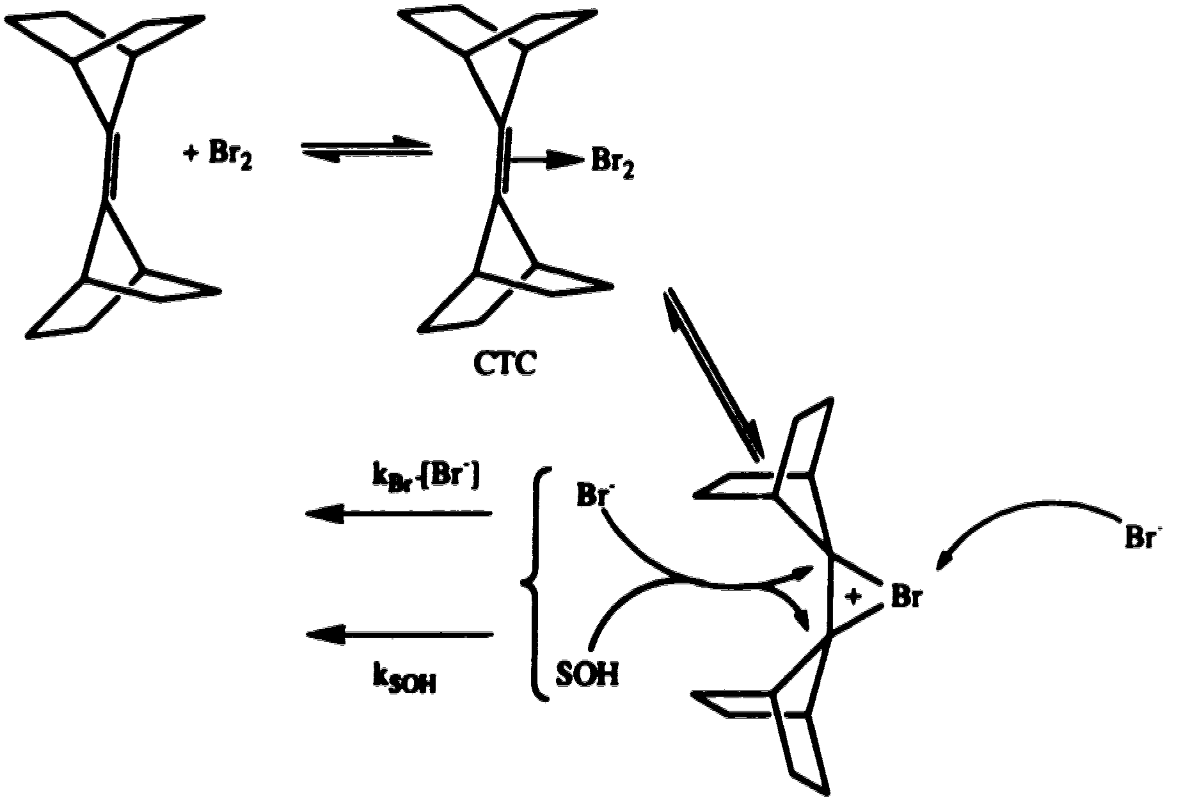
The product ratios shown in **Tables 22** and **23** were determined from the area of the GC traces and represent the percentage of the total addition products. In MeOH there is little or no dibromide product observed even at 0.01 M LiBr, and only 7% at 0.03 M LiBr. However, in AcOH at 0.01 M LiBr there is already 39% dibromide product, and at 0.05 M LiBr the dibromide product constitutes 80% of the total products.

d) Discussion:

i) Br$_2$ Reaction

The data in **Tables 22** and **23** indicate that there are significant differences in the rates of bromination of **32a** and **32b** in both MeOH and AcOH. Shown in **Scheme 23** is the proposed mechanism for the reaction of **32** and Br$_2$.

Scheme 23



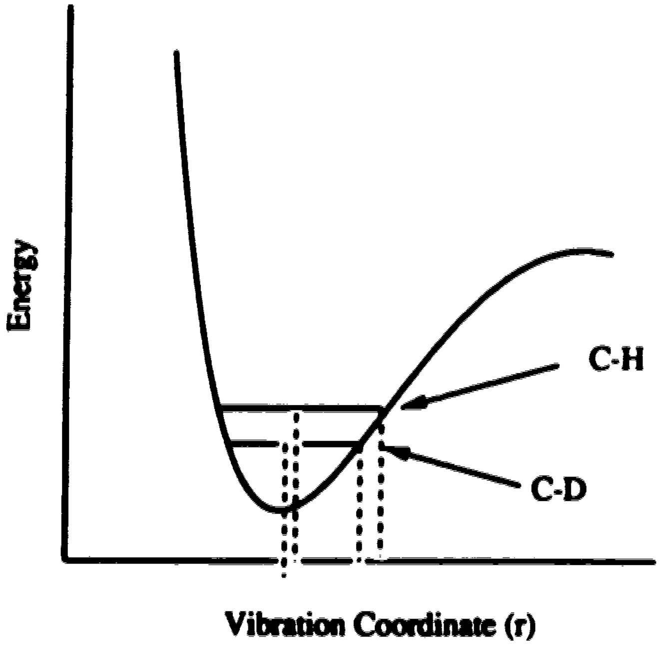
From the scheme, we see that the initially formed CTC ionizes to the bromonium ion. Once the ion has formed, nucleophilic attack by solvent or Br^- on the carbons of the bromonium ion will lead to product formation. However, if Br^- were to capture the bromonium ion on Br^+, it would reform the CTC, and eventually starting materials. It has been shown,[30] that the bromonium ions that are solvolytically produced from *trans*-2-bromocyclohexyl trifluoromethanesulfonate (22) can be captured by Br^- at Br^+ to form cyclohexene and free Br_2 in both MeOH and AcOH. In MeOH there is a 25-fold greater preference for attack by Br^- on Br^+ than on the bromonium ion carbons. In AcOH this drops to a 4-5-fold greater preference for Br^- attack on Br^+. For 33, the backside of the bromonium ion should be hindered by the crowding of the C-L while the ethano groups on the topside of the ion move further apart to accommodate the Br^+. This accompanies rehybridization of the olefinic carbons from sp^2 towards sp^3 during formation of the bromonium ion. This hindrance of the backside of the ion should severely inhibit the approach of a nucleophile and promote capture at Br^+. The plots of $k_g(1 + K_{eq}[Br^-])$ vs. $K_{eq}[Br^-]$ in **Figures 16** and **17** both have a downward curvature that is interpreted as experimental evidence for reversal from the bromonium ion by capture by Br^- on Br^+.[27,28] Thus, the rate limiting step for this reaction is not the formation of the bromonium ion, but nucleophilic capture to yield products.

ii) <u>Deuterium Kinetic Isotope Effect</u>

The observed ratio of the rate constants for bromination of **32a** to **32b** (k_D/k_H) in MeOH varies between 1.7 and 1.9, and in AcOH is 1.53 at zero added bromide and at 0.05 M Br^- increases to 2.75. It has been argued in the case of tetraisobutylethylene[108] (TIBE (**11**)), and demonstrated in the case of cyclohexene[6] (**5** and **6**) that the β-secondary kinetic isotope effects for the bromination of those olefins are $k_D/k_H = 1$. Unlike TIBE (**11**), **32** cannot form double bond rearranged allylic bromides so primary kinetic isotope effects are not expected. Also, since there are no deuterium atoms bonded directly to the olefinic bond, the kie cannot arise from an α-secondary kie. One likely explanation for the inverse Dkie observed for bromination of **32** is that the change from protium to deuterium causes a change in the steric effects within the molecule.

Shown in **Figure 18** is a Morse potential curve for the C-L bond. It is well known[20,21] that the C-D bond has a lower zero-point energy than the C-H bond and a lower vibrational amplitude. This, coupled to the anharmonicity of the potential well, makes the C-D bond effectively shorter than the C-H bond. This is easily visualized as in **Figure 18** which shows that vibrational amplitude for the C-H bond is larger than for the C-D bond with the consequence that the volume filled by all the vibrational modes of the C-H bond is larger than for the C-D bond. The center of the vibration amplitude (indicated by the left set of dotted lines) can be considered the average length of the bond and the C-D bond is shorter than C-H.[112]

Figure 18 : The Zero-Point Energy Differences of the C-H and C-D Bonds as a Source of the Steric Difference Between Protium and Deuterium



Molecules such as adamantylideneadamantane[9,19] (7) and bicyclo[3.3.1]non-9-ylidenebicyclo [3.3.1]non-9'-ane[113] (29) have been shown to form stable halonium ions and cannot form normal products because the back side of the bromonium ion is too sterically hindered to allow nucleophilic attack. A similar explanation accounts for the relatively slow bromination of 32. By substituting each C-H unit with a somewhat smaller C-D unit there should be slightly more access to the carbons of bromonium ion (33). That is, the separation between the endo C-L atoms of the γ positions should be slightly larger for 33b. Since nucleophilic attack on the bromonium ion is rate limiting, the deuterated compound would react more quickly than the protonated one which accounts for the observed $k_D/k_H > 1$.

One must be mindful of small but cumulative, inductive effects that might result from the substitution of twenty C-H bonds with the slightly more inductively donating C-D bonds.[20,21] Nevertheless, even if we allow an inductive effect that contributes 1-2% per

D/H substitution (which is probably an overestimation considering that sixteen of these are γ substitutions[101,104,114,115]), this accounts for a predicted inverse Dkie of k_g (32b/32a) ≤ 1.4. While an inductive effect of this magnitude cannot be ruled out with certainty, it cannot account for all of the observed inverse Dkie, nor can it account for the increasingly inverse value observed as a function of added [Br⁻] in HOAc. We believe, that whatever the electronic contributions are, they are superimposed upon an important steric component.

Previously observed experimental steric Dkie's have been very small for nucleophilic reactions.[105,106] However bromination of **32a/32b** gives rise to inverse secondary Dkie's of $k_D/k_H = 1.5\text{-}2.75$ in AcOH and 1.8 in MeOH. These large values may be the result of several factors; i) the bromonium ion, once formed squeezes the backside of the olefin closed and enhances the steric compression of the four C-L bonds; the same must be true for the transition state leading to and from the ion, ii) the fact that there are four C-H units being replaced by C-D amplifies the observed Dkie over what would be observed for a single C-H to C-D replacement. The effect could be further amplified if the four C-L units proximal to the Br^+ were involved in some compression with it during the nucleophilic attack.

iii) Product Ratios

It seems likely that the rate limiting step for the bromination of **32a,b** is attack of the nucleophile on the carbons of the bromonium ion. However, the source of an increasingly inverse Dkie as the [Br⁻] increases in AcOH has still not been addressed. At zero [Br⁻], the Dkie is $k_D/k_H = 1.53$ and at 0.05 M Br^- the Dkie becomes $k_D/k_H = 2.75$. The product ratios show that as the [Br⁻] increases, in AcOH, the amount of dibromide product also increases. However, in MeOH, this is not observed; that is, at 0.01 M [Br⁻], there is no observable dibromide product. Even at 0.03 M Br^- there is only 7% dibromide produced.

The probable source of the increasingly inverse Dkie observed in HOAc is the change in the nature of the incoming nucleophile. At low [Br⁻] the main attacking nucleophile is AcOH, but as [Br⁻] increases the main product becomes dibromide due to prominent Br⁻ attack (see **Table 23**), and a different value for the Dkie is observed. The fact that the Dkie increases suggests that Br⁻ has greater steric requirements than does HOAc for nucleophilic capture of 33. For bromination of 32 in MeOH, the dibromide never becomes the major product (see **Table 22**), and therefore the observed isotope effect is not greatly affected since the major incoming nucleophile does not change.

iv) Radical Br_2 Addition

The question of whether Br_2 addition to olefins is ionic or follows an electron transfer mechanism is an area that has not been well investigated. Several observations can provide clues that a radical reaction is occurring. These include; 1) observation of anti-Markovnikov addition products, 2) mixtures of cis and trans addition products,[116] 3) observation of allylic bromide products, 4) kinetic results that are non-reproducible. However, certain qualitative observations can be made that suggest we are observing ionic addition in all the studies reported herein.

1) The general observation that, with styrene, no anti-Markovnikov addition products were observed in the lifetime of bromonium ions study, reported earlier (Chapter 1). However, anti-Markovnikov addition has been observed for styrene by Hassner et al.[56c,d] with BrN_3 and this was interpreted as radical addition.

2) The products for the cyclic olefins, studied in the lifetimes of bromonium ions investigation, were always trans and product ratios did not change when reactions were performed in the dark.

3) The presence of allylic bromide products resulting from hydrogen abstraction was not detected for any of the olefins in the lifetime of bromonium ions study.

4) The clean, reproducible pseudo first-order kinetics for **11a** and **32a** and **b** seem to indicate an ionic rather than a radical mechanism. Also, the kinetics of bromination of **11a**[10f] did not vary when samples were cycled in and out of the light beam, or allowed to stay in the beam of the spectrometer for the entire kinetic investigation. This suggests that the spectrophotometer is not initiating the reaction.

These observations lead us to conclude that we are observing a ionic rather than radical addition mechanism for the olefins studied in this publication.

e) Conclusions

We have presented an example of an olefin where reversibility of the bromonium ion is a very important process (see **Figures 16** and **17**). When the ion is formed the steric bulk of the molecule inhibits nucleophilic attack on the carbons of the bromonium ion. Because attack on the carbons is inhibited, Br^- captures predominantly at Br^+ and a common ion rate depression is observed.

Isotopic substitution of hydrogen with deuterium gives a k_D/k_H of 1.7-1.9 in MeOH and 1.5-2.75 in AcOH suggesting that substitution with the shorter C-D bond increases the availability of the carbons of the bromonium ion to nucleophilic attack. The increasingly inverse value of the isotope effect as a function of $[Br^-]$ in AcOH also suggests that there is a rate difference in attack of acetate as compared to Br^-. This conclusion is based on the observation of an increasing amount of dibromide product (see **Table 23**) as the $[Br^-]$ increases. However, a similar observation is not made for the reaction in MeOH. The major product is always bromosolvate, and the dibromide never becomes a major product as in AcOH. This indicates that the sterics of the molecule can cause selectivity of one nucleophile over another on the basis of the steric requires of the nucleophile. This leaves open the possibility that **32a**, **b** and their specifically deuterated analogues will be important for testing the steric demands of the transition states for other reactions of, and leading to, the double bond.

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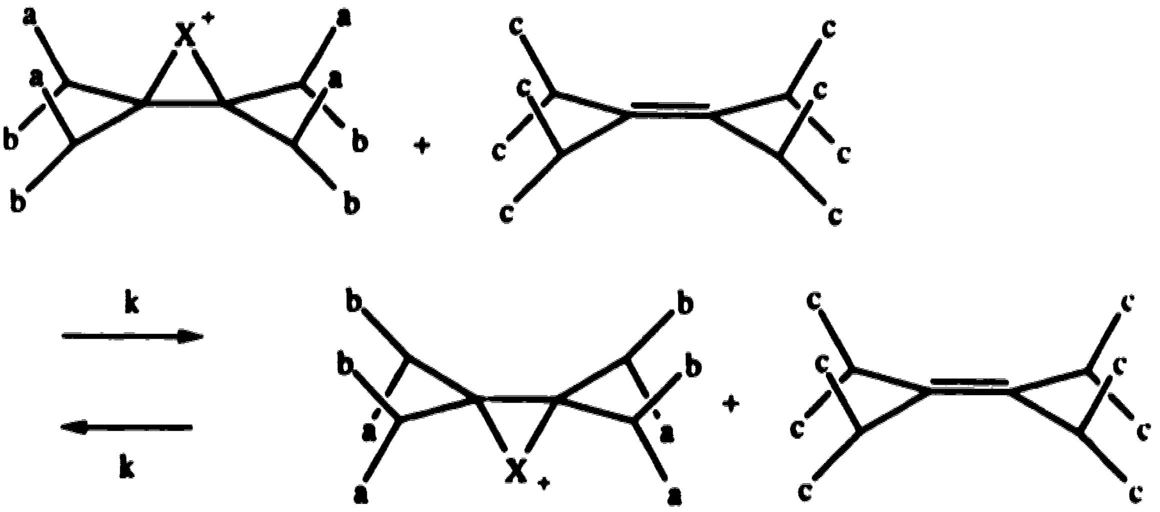
Appendix

Derivation of Rate Expression for X^+ Exchange[117]

The exchange reaction in a solution of $AdAdX^+$ containing a very small amount of 7 is most clearly described by;



where carbon atoms labeled "a" are on the top side of the halonium ion, those labeled "b" are on the bottom side, and those labeled "c" are the corresponding carbon atoms of the parent olefin. In the forward reaction, carbon atoms "a" and "b" are all converted to "c" carbon atoms, and carbon atoms "c" are converted to "a" or "b" atoms with equal probability. Hence magnetization is exchanged between sites a, b, and c according to the rate laws;

$$\frac{dM_a}{dt} = -k[7]M_a + \frac{k}{2}[7\text{-}X^+]\,M_c$$

$$\frac{dM_b}{dt} = -k[7]M_b + \frac{k}{2}[7\text{-}X^+]\,M_c$$

$$\frac{dM_c}{dt} = -k[7\text{-}X^+]M_c + k[7]\,(M_a + M_b)$$

where M_a, M_b, and M_c are the magnetizations at sites a, b, and c. The exchange-modified Bloch equations for this process are therefore:

$$\frac{d\mathcal{M}_a}{dt} = \{-\Lambda_a - k[7]\}\mathcal{M}_a + \frac{k}{2}[7\text{-}X^+]\mathcal{M}_c$$

$$\frac{d\mathcal{M}_b}{dt} = \{-\Lambda_b - k[7]\}\mathcal{M}_b + \frac{k}{2}[7\text{-}X^+]\mathcal{M}_c$$

$$\frac{d\mathcal{M}_c}{dt} = \{-\Lambda_c - k[7\text{-}X^+]\}\mathcal{M}_c + k[7](\mathcal{M}_a + \mathcal{M}_b)$$

where

$$\Lambda_a = \frac{1}{T_{2a}} + i(\omega_a - \omega)$$

$$\Lambda_b = \frac{1}{T_{2b}} + i(\omega_b - \omega)$$

$$\Lambda_a = \frac{1}{T_{2c}} + i(\omega_c - \omega)$$

and $\mathcal{M}_a$, $\mathcal{M}_b$, and $\mathcal{M}_c$ are the complex transverse magnetizations for the sites at time t.

Since the concentrations of olefin, 7, in the solution is much smaller than the concentration of halonium ion, 7-X$^+$,

$$\mathcal{M}_c \ll \mathcal{M}_a, \mathcal{M}_b$$

and

$$\frac{d\mathcal{M}_c}{dt} << \frac{d\mathcal{M}_a}{dt}, \frac{d\mathcal{M}_b}{dt}$$

We make the approximation that

$$\frac{d\mathcal{M}_c}{dt} \sim 0$$

and

$$k[7\text{-}X^+] >> |\Lambda_c|$$

so that

$$\mathcal{M}_c \sim \frac{[7]}{[7\text{-}X^+]}(\mathcal{M}_a + \mathcal{M}_b)$$

Therefore the equations of motion for $\mathcal{M}_a$ and $\mathcal{M}_b$ may be written in the form

$$\frac{d\mathcal{M}_a}{dt} = \left(-\Lambda_a-\frac{k[7]}{2}\right)\mathcal{M}_a + \frac{k[7]}{2}\mathcal{M}_b$$

$$\frac{d\mathcal{M}_b}{dt} = \left(-\Lambda_b-\frac{k[7]}{2}\right)\mathcal{M}_b + \frac{k[7]}{2}\mathcal{M}_a$$

These equations are identical to the exchange-modified Bloch equations for exchange between 2 equally populated sites with rate constant k/2.

SUPPLEMENTARY MATERIAL

Table S1 : Experimental Product Ratios for the Bromination of Cyclohexene with Br_2 in the presence of varying $[N_3^-]$ in MeOH[e]

$[N_3^-]$	$1/[N_3^-]$	BrM[a]	BrN_3[b]	diBr[c]	f_{az}[d]	$f_{az}/[N_3^-]$[d]	$1/f_{az}$[d]
0.0284	35.174	1	0.14	0.011	0.12	4.17	8.43
0.0345	28.960	1	0.15	0.022	0.13	3.82	7.58
0.0389	25.727	1	0.18	0.027	0.15	3.96	6.49
0.0413	24.196	1	0.19	0.015	0.15	3.75	6.46
0.0512	19.516	1	0.23	0.024	0.19	3.64	5.36
0.0536	18.674	1	0.25	0.027	0.20	3.78	4.94
0.0806	12.401	1	0.34	0.042	0.25	3.11	3.99
0.0859	11.636	1	0.36	0.050	0.27	3.09	3.77
0.146	6.854	1	0.54	0.077	0.35	2.39	2.86
0.157	6.361	1	0.60	0.056	0.37	2.39	2.67
0.162	6.181	1	0.60	0.062	0.37	2.31	2.68
0.262	3.820	1	0.88	0.094	0.47	1.79	2.13
0.307	3.263	1	0.99	0.084	0.50	1.62	2.01
0.314	3.182	1	1.08	0.057	0.52	1.65	1.92
0.378	2.647	1	1.17	0.086	0.54	1.43	1.85

[a] trans-1-bromo-2-methoxycyclohexane

[b] trans-1-azido-2-bromocyclohexane

[c] trans-1,2-dibromocyclohexane

[d] does not include the dibromide data

[e] all product amounts are shown as a ratio of the bromomethoxy product

Table S2 : Experimental Product Ratios for the Bromination of Cyclohexene using NBS in the presence of varying $[N_3^-]$ in MeOH[a]

$[NaN_3]$	BrM[b]	BrAz[c]	diBr[d]	f_{az}	$f_{az}/[N_3^-]$	$1/[N_3^-]$	$1/f_{az}$
0.174	1	0.67	0	0.40	2.30	5.724	2.48
0.267	1	0.92	0	0.48	1.80	3.745	2.08
0.0599	1	0.28	0	0.21	3.60	16.697	4.63

[a] No dibromide was ever observed

[b] *trans*-1-bromo-2-methoxycyclohexane

[c] *trans*-1-azido-2-bromocyclohexane

d *trans*-1,2-dibromocyclohexane

Table S3 : Experimental Product Ratios for the Bromination of Cyclopentene with Br_2 in the presence of varying $[N_3^-]$ in MeOH

$[NaN_3]$	$1/[N_3^-]$	BrM[a]	BrAz[b]	diBr[c]	f_{az}[d]	$f_{az}/[N_3^-]$[d]	$1/f_{az}$[d]
0.113	8.818	1	0.43	0.029	0.30	2.64	3.33
0.0298	33.512	1	0.16	0.026	0.14	4.70	7.12
0.37	2.703	1	1.04	0.048	0.51	1.38	1.96
0.264	3.779	1	0.91	0.062	0.48	1.80	2.10
0.0808	12.372	1	0.35	0.030	0.26	3.17	3.90
0.0441	22.691	1	0.22	0.030	0.18	4.02	5.65
0.148	6.748	1	0.56	0.043	0.36	2.44	2.77

[a] *trans*-1-bromo-2-methoxycyclopentane

[b] *trans*-1-azido-2-bromocyclopentane

[c] *trans*-1,2-dibromocyclopentane

[d] without dibromide data

Table S4 : Experimental Product Ratios for the Bromination with Br_2 of Tetramethylethylene in the presence of varying $[N_3^-]$ in MeOH[ab]

$[NaN_3]$	BrM[c]	BrAz[d]	$1/[N_3^-]$	f_{az}	$f_{az}/[N_3^-]$	$1/f_{az}$
0.163	1	0.62	6.138	0.38	2.34	2.62
0.0741	1	0.38	13.500	0.28	3.75	3.60
0.157	1	0.62	6.378	0.38	2.43	2.62
0.108	1	0.46	9.242	0.32	2.92	3.16

[a] using Br_2 as the source of Br^+

[b] dibromide was always too low in concentration to get an accurate measurement

[c] 2-bromo-3-methoxy-2,3-dimethylbutane

[d] 2-azido-3-bromo-2,3-dimethylbutane

Table S5 : Experimental Product Ratios for NBS Addition to Tetramethylethylene at varying [N_3^-] in MeOH[ab]

[NaN_3]	1/[N_3^-]	BrM[c]	BrN_3[d]	f_{az}	f_{az}/[N_3^-]	1/f_{az}
0.0738	13.557	1	0.41	0.29	4.00	3.41
0.153	6.517	1	0.59	0.37	2.41	2.70
0.119	8.394	1	0.49	0.33	2.76	3.04
0.325	3.078	1	0.98	0.50	1.53	2.02
0.301	3.325	1	0.92	0.48	1.60	2.08
0.0393	25.450	1	0.29	0.23	5.73	4.44
0.0508	19.689	1	0.32	0.24	4.77	4.13

[a] all brominations completed with NBS

[b] dibromide was always in too low a concentration to get an accurate measurement

[c] 2-bromo-3-methoxy-2,3-dimethylbutane

[d] 2-azido-3-bromo-2,3-dimethylbutane

Table S6 : Experimental Product Ratios for the Bromination of Styrene in the presence of varying [N_3^-] in MeOH[ab]

[NaN_3]	1/[N_3^-]	BM[c]	BA[d]	f_{az}	1/f_{az}	f_{az}/[N_3^-]
0.202	4.946	1	0.37	0.27	3.68	1.34
0.0622	16.080	1	0.14	0.12	8.14	1.98
0.151	6.629	1	0.32	0.24	4.13	1.60
0.299	3.338	1	0.59	0.37	2.68	1.25
0.0303	33.003	1	0.079	0.073	13.65	2.42
0.0332	30.120	1	0.083	0.077	13.05	2.31
0.0466	21.440	1	0.11	0.10	9.76	2.20
0.248	4.038	1	0.48	0.33	3.07	1.32
0.101	9.942	1	0.22	0.18	5.46	1.82

[a] all reactions completed at 25°C with Br_2

[b] dibromide was present but in too low a concentration to measure

[c] 2-bromo-1-methoxy-1-phenylethane

[d] 1-azido-2-bromo-1-phenylethane

Table S7 : **Observed Rate Constants for the Bromination of 32a and 32b in MeOH with Br_2, T = 25°C, μ = 0.3 ($LiClO_4$)**

	32a		**32b**	
[LiBr]	**k_{obs} (s^{-1})**	**[ole] (M)**	**k_{obs} (s^{-1})**	**[ole] (M)**
0.005	$3.56\pm0.05 \times 10^{-2}$	1.060×10^{-3}		
	$3.46\pm0.04 \times 10^{-2}$			
	$3.57\pm0.04 \times 10^{-2}$			
0.01	$1.85\pm0.01 \times 10^{-2}$	1.067×10^{-3}	$3.80\pm0.03 \times 10^{-2}$	1.108×10^{-3}
	$1.89\pm0.02 \times 10^{-2}$		$3.64\pm0.03 \times 10^{-2}$	
	$1.85\pm0.02 \times 10^{-2}$	1.056×10^{-3}	$3.54\pm0.05 \times 10^{-2}$	1.110×10^{-3}
	$1.93\pm0.02 \times 10^{-2}$		$3.72\pm0.02 \times 10^{-2}$	
0.02	$7.21\pm0.09 \times 10^{-3}$	1.148×10^{-3}	$1.24\pm0.02 \times 10^{-2}$	1.108×10^{-3}
	$7.18\pm0.05 \times 10^{-3}$		$1.31\pm0.01 \times 10^{-2}$	
	$7.09\pm0.06 \times 10^{-3}$		$1.38\pm0.02 \times 10^{-2}$	
0.03	$2.58\pm0.11 \times 10^{-3}$	1.045×10^{-3}	$6.36\pm0.07 \times 10^{-3}$	1.058×10^{-3}
	$2.46\pm0.10 \times 10^{-3}$		$6.30\pm0.06 \times 10^{-3}$	
	$2.71\pm0.03 \times 10^{-3}$			
0.04	$2.05\pm0.03 \times 10^{-3}$	1.106×10^{-3}	$3.22\pm0.04 \times 10^{-3}$	1.053×10^{-3}
	$2.03\pm0.03 \times 10^{-3}$		$3.28\pm0.04 \times 10^{-3}$	
	$2.06\pm0.03 \times 10^{-3}$		$3.34\pm0.04 \times 10^{-3}$	

Table S8 : **Observed Rate Constants for the Bromination of 32a and 32b in AcOH with Br_2, T = 25°C, μ = 0.1 ($LiClO_4$)**

	32a		**32b**	
[LiBr]	**k_{obs} (s^{-1})**	**[ole] (M)**	**k_{obs} (s^{-1})**	**[ole] (M)**
0.00	$4.62\pm0.12 \times 10^{-2}$	1.236×10^{-3}	$6.48\pm0.12 \times 10^{-2}$	1.106×10^{-3}
	$4.52\pm0.08 \times 10^{-2}$		$6.05\pm0.10 \times 10^{-2}$	
			$6.28\pm0.07 \times 10^{-2}$	
0.01	$2.37\pm0.02 \times 10^{-3}$	1.139×10^{-3}	$3.90\pm0.03 \times 10^{-3}$	1.1725×10^{-3}
	$2.36\pm0.03 \times 10^{-3}$		$3.91\pm0.03 \times 10^{-3}$	
0.03	$3.40\pm0.03 \times 10^{-4}$	1.257×10^{-3}	$6.46\pm0.03 \times 10^{-4}$	1.194×10^{-3}
	$3.39\pm0.03 \times 10^{-4}$		$6.47\pm0.04 \times 10^{-4}$	
0.05	$1.58\pm0.01 \times 10^{-4}$	1.139×10^{-3}	$3.01\pm0.04 \times 10^{-4}$	1.169×10^{-3}
	$1.01\pm0.01 \times 10^{-4}$		$2.90\pm0.03 \times 10^{-4}$	
	$1.09\pm0.02 \times 10^{-4}$			