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Yu-sun Lee

Louisiana State University and Agricultural & Mechanical College

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RADICAL BROMINATIONS OF ALKANIC POSITIONS BY
BROMINE AND BY N-BROMOSUCCINIMIDE

A Dissertation

Submitted to the Graduate Faculty of the
Louisiana State University and
Agricultural and Mechanical College
in partial fulfillment of the
requirements for the degree of

Doctor of Philosophy

in

The Department of Chemistry

by

Yu-Sun Lee

B.S., Chung Yuan Christian College of Science and Engineering, 1965

May, 1974

To my parents

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ABSTRACT

During the past decade, the details of mechanism of radical brominations of alkanes, and in particular the influence of a bromo substituent on the selectivity in the hydrogen-abstraction step, have been studied and debated by several groups of investigators. Central to the controversy is the mechanism of bromination by N-bromosuccinimide (NBS), for some of the proposals are supported almost solely by the presumed sameness of bromination mechanism for both molecular bromine and NBS reagents. That sameness was established for brominations of benzylic positions by kinetic studies and has been assumed for other systems. Some earlier data in the literature on bromocyclohexane halogenations indicate that the isomer distribution obtained with NBS reagent is closer to that obtained with chlorine than to that with bromine, even though the data were presented from the viewpoint that bromine and NBS brominations involve the same hydrogen-abstracting and bromine-transfer species.

Our study suggests that a different mechanism is involved when bromination occurs on alcanic positions. That is, the hydrogen-abstracting agent is different when molecular bromine is used than when NBS is used. Both by intermolecular competition experiments (butyl bromide vs. cyclohexane and cyclohexane vs. cyclopentane) and by reactions with single substrates (cyclopropane and norbornane), the two brominating reagents have been shown to be different. With cyclopropane, the identities of the radicals which attack the substrate are shown to be different from the two reagents, and with norbornane, the identities of the bromine-transfer reagents which react with the alkyl radical are shown to be different.

I. INTRODUCTION

A. Evidence of bridging by neighboring bromine in free-radical reactions

There have been several studies of the influence of an electronegative substituent on the attack of halogen atoms at different positions in an aliphatic system. Two factors, polar effects and C-H bond strengths, generally influence the relative reactivities of the different sites toward halogen atoms; in other words, they determine the distribution of possible radical intermediates and thereby determine the isomeric distribution of halide products.

The reactivity of α -hydrogen with halogen atoms is increased by the electronegative substituent which tends to lower the C-H bond energy of the α -position. However, the inductive effect of this electronegative substituent deactivates the hydrogens in other positions since the halogen atoms are electrophilic. Therefore, the further the position is removed from the substituent, the more reactive it is. These two factors are observed in gas phase free-radical chlorination¹ and bromination² of alkyl halides. For example, the gas phase chlorinations of butane, 1-chlorobutane, and 2-chlorobutane¹ (Table I) show deactivation of the β -position. The gas phase brominations of electronegatively

Table I

Relative reactivities in gas phase chlorination at 35°

$\text{C} - \text{C} - \text{C} - \text{C}$				
1.0	3.9	3.9	1.0	
$\text{Cl} - \text{C} - \text{C} - \text{C} - \text{C}$				
0.7	2.2	4.2	1.0	
$\begin{array}{c} \text{Cl} \\ \\ \text{C} - \text{C} - \text{C} - \text{C} \end{array}$				
0.2	3.2	3.1	0.8	

substituted 1-butanes also give minor substitutions at β -carbon (Table II).³ The reactivity of the α -position depends on the combination of

Table II

Selectivities in gas phase bromination at 160°

	α	β	γ	δ
$X-\text{C}-\text{C}-\text{C}-\text{C}$				
CF_3	1	7	90	1
F	9	7	90	1
CH_3OCO	19	29	73	1

these two competing factors, the polar effect and the lower C-H bond energy. The β and γ positions are both secondary and should have the nearly equal C-H bond strength. Thus, the ratio of relative reactivities of β and γ hydrogens is used to measure the polar effect.

In liquid phase halogenation, Thaler⁴ observed the same results for chlorination and bromination of 1-chlorobutane and chlorination of 1-bromobutane (Table III). However, he also observed that

Table III

Relative reactivities in liquid phase
halogenation of 1-halobutane
at 60°

	$X\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_3$			
Butyl chloride				
Cl_2	0.158	0.478	1.00	0.397
Br_2	0.439	0.488	1.00	-----
Butyl bromide				
Cl_2	0.093	0.434	1.00	0.455
Br_2	0.062	5.78	1.00	-----

1,2-dibromobutane is the major product in bromination of 1-bromobutane (Table III). The reactivity at carbon-2 was 5.78 times that of carbon-1.

Bromination of bromocyclohexane gave 94% of trans-1,2-dibromocyclohexane, while the bromination of chlorocyclohexane gave only about 10% of the vicinal dihalide. A similar result was found for bromination of bromocyclopentane, which gave 90% of trans-1,2-dibromocyclopentane. Likewise, the radical bromination of 2-bromobutane gave 84% of 2,3-dibromobutane, while the bromination of 2-chlorobutane gave only 8% of the 2,3-dihalide. Thaler interpreted this activation of the β -position in bromination of alkyl bromides in terms of neighboring group participation (anchimeric assistance), which was well-documented⁵ in carbocationic reactions but unprecedented in radical reactions.*

The rate determining step for these radical reactions is the hydrogen abstraction step. The larger and more polarizable bromide substituent can assist this β -hydrogen abstraction more effectively than can chlorine.[†] Hydrogen abstraction by chlorine atom shows little selectivity and has little bond breaking at the transition state. There is little chance for anchimeric assistance to occur. In contrast, abstraction by bromine atom, with greater bond breaking, would involve the neighboring substituent, which would delocalize the unpaired electron and lower the energy of transition state (1). In keeping with this expectation, the major product is vicinal dibromide.

* The concept of bridging and anchimeric assistance was proposed in 1952 for radical reactions,⁶ however, these proposals were retracted later.

† Chlorine participation was also reported by Traynham and Hines.⁷

The bromo substituent participates in forming a bridged transition state (1); however, this bridging does not dictate the structure of the intermediate β -bromoalkyl radical as a bridged (3) or nonbridged (2) species. Since the rate determining step is the hydrogen abstraction step, and if there is no reversal reaction, the analysis of the product distribution serves to indicate the relative reactivities of different hydrogens. Thus, the observation of 1,2-dibromide as major product, contrasting with the expected polar effect of the substituent, indicates anchimeric assistance.

However, the reversibility of the reactions of atomic bromine with alkanes is well-documented.⁸⁻¹⁰ To avoid the possibility of this reversibility of alkyl radical and hydrogen bromide, bromostasis has been used for the bromination. Bromostasis is a method for carrying out a bromine substitution reaction at constant bromine concentration. The reaction of N-bromosuccinimide (NBS) with hydrogen bromide is found to be instantaneous.^{11,12} Thus, the hydrogen bromide that is generated by abstraction of hydrogen by bromine atom can be scavenged by NBS, and bromine is regenerated. By this means, one can

avoid the possibility of HBr reversal. Recently, Skell, et al., reported^{12,13} results obtained from the competition photobromination of a series of halogenated alkanes vs. their unsubstituted analogs under bromostasis conditions. In all cases, the bromoalkanes were substituted faster than their corresponding alkanes. The investigators proposed that neighboring bromine assisted in the transition state for hydrogen abstraction by the bromine atom.

Similarly, Traynham and Hines⁷ reported that the radical monobromination of 1-bromomethyl-4-methylcyclohexane with bromine gave exclusively substitution at the position β to the bromine substituent (eq 3).

Lewis and Kozuka¹⁴ observed that the isotope effects in the radical addition of HBr (or TBr) to a series of terminal olefins are small and show no maximum (Table IV). If the intermediate radical is a classical

Table IV

Isotope effect in the radical addition of HBr to $\text{RCH}=\text{CH}_2$ at 0°

<u>R</u>	<u>$k_{\text{H}}/k_{\text{T}}$</u>
p-Tolyl	1.04, 1.03
Phenyl	1.46, 1.47
p-Chlorophenyl	1.55, 1.62
<u>tert</u> -Butyl	1.99, 1.99
<u>n</u> -Hexyl	2.07, 2.07
Br	2.83
H	4.14, 4.25

radical, then the $R = \text{phenyl}$ should give the maximum isotope effect, and the magnitude is calculated to be $49.5-3.2$ ($v_H^\ddagger = 0-1200 \text{ cm}^{-1}$) at 0° by use of Melander's equation.¹⁵ The benzylic carbon-hydrogen bond and the HBr bond have about the same energies (ca. 87 Kcal/mole);¹⁶ therefore, the cases of $R = \text{aryl}$ would appear to be those with the least zero-point stretching vibration. The observation that the isotope effect of $R = \text{phenyl}$ is not a maximum, and as little as 1.46 can be explained by the participation of the β -bromine, which stabilizes the radicals and weakens the C-H bond. Thus, the maximum in the isotope effect will not come at $R = \text{aryl}$, but should come farther down the table (Table IV).

The anchimeric assistance requires a trans arrangement of hydrogen and bromine. For example, the bromination of isomeric 4-tert-butylcyclohexyl bromides would give a mixture of dibromides if there were no neighboring group assistance. Substitution should occur at various positions and decrease in the order of $4 > 3 > 1 > 2$ for both isomers. However, this prediction was not fulfilled in the bromination of cis-4-tert-butylcyclohexyl bromide, which yielded a single product, trans-1,2-dibromo-cis-4-tert-butylcyclohexane (Eq 4).¹⁷ Photobromination

of the trans-isomer gave a mixture of dibromides. Further, the competitive photobromination showed the cis-isomer to be ≥ 15 more reactive than the trans-isomer. These different results can be explained by the trans arrangement of bromine and hydrogen in the more stable chair form for the cis-isomer (4) but only in the less stable boat form for the trans-isomer (5). Competitive photobrominations of cis-4-tert-butylcyclohexyl bromide

vs. cyclohexane showed 1045 fold anchimeric assistance.¹² This increase was attributed to the locked-in configuration ideal for neighboring group to participation. The small anchimeric effect, 26 fold, was observed in substitution of the β -hydrogen in butyl bromide; the anchimeric effect was considered operable only in the less stable conformation (6).¹²

Huyser and Feng¹⁸ reported that a threo β -substituted alcohol, 3-bromo-2-butanol, reacted faster with tert-butoxy radical than did the erythro isomer (Table V). With chlorine as substituent, the isomeric

Table V

Competition reactions of stereoisomeric 3-halo- and 3-methylthio-2-butanols

<u>X</u>	k_t/k_e
Cl	1.02
Br	1.44
SCH ₃	1.26

alcohols were about equal in reactivity. The greater relative reactivity of the threo isomer with a bromine substituent was attributed to a preferred conformation in the transition state to permit the β -bromine participation. The erythro isomer would have eclipsed methyl groups in a transition state involving bridging.

The observation of anchimeric assistance does not indicate that the structure of the intermediate will be a bridged (7) or nonbridged (8) species. The C-C bond can rotate in nonbridged radical, and the trapping agent can approach from either side of the trivalent carbon atom. In

contrast, the bridged structure correlates with a large barrier to rotation about the C-C bond, and the trapping agent has to approach to the back-side of Br. Although much evidence has been found for the bridged intermediate,^{17,18-21} such evidence does not bear directly on the question of anchimeric assistance in the hydrogen abstraction step of alkane brominations. Because the existence of the intermediate is of some interest here, however, I shall cite three examples of the evidence for illustration. First, Skell, *et al.*, observed different ratios of meso/d,l dibromides by photoinitiated bromination of 2-bromobutane, erythro-3-²H-2-bromobutane, and threo-3-²H-2-bromobutane under bromostasis conditions (Table VI).²¹ If a classical open chain radical were the intermediate,

Table VI

Ratio of diastereomeric 2,3-dibromobutanes from the photobromination of 2-bromobutanes

<u>Starting material</u>	<u>meso/d,l</u>
2-bromobutane	2.5
<u>erythro-(3-²H)-2-bromobutane</u>	0.61
<u>threo-(3-²H)-2-bromobutane</u>	6.50

the same meso/d,l ratio should be obtained for each of the compounds. The large variation in this ratio observed indicates that there are more than a single intermediate in the reaction. The variation in product ratio can be explained with two isomeric bridged intermediates, (9) and (10), formed

in different ratios as a result of the different reactivities of H and D in the abstraction step (Eqs 5 and 6).

Second, bromination of 3-bromopentane- ^{82}Br with ordinary bromine by bromostasis produced a mixture of erythro- and threo-2,3-dibromopentanes (Eq 7).²¹ Dehydrobromination by base of the threo-

RMA = relative molar radioactivity: (counts/mole)/(counts/mole)_{std}

dibromide obtained from above bromination reveals that the original radioactive bromine atom is evenly distributed between the 2- and 3-positions (Eq 8).²¹ (The bromoolefins obtained from dehydrobromination of the

erythro diastereomer could not be separated.) These results also suggest the bridged intermediate for the bromination of 3-bromopentane. Other evidence for control of stereochemistry by neighboring bromine is cited in a review by Skell and Shea.²²

Lyons and Symons²³ studied the esr spectrum of β -bromoalkyl radicals and concluded that the radical existed in a locked conformation with the bromine atom in the plane of the unpaired electron orbital.

B. Evidence against bridging by neighboring bromine in free-radical reactions

As the evidence accumulated to give indications that anchimeric assistance does exist, the contrary argument also developed. Central to the controversy is the mechanism of bromination by NBS, for some of the proposals²⁴ that speak against anchimeric assistance are supported almost solely by the presumed sameness of bromination mechanism for both molecular bromine and NBS reagents.

NBS has been recognized as an effective allylic (and benzylic) bromination agent without addition to double bond since Ziegler, et al.²⁵ first reported the reaction. In 1944, Hey²⁶ and Bloomfield²⁷ suggested a radical mechanism for NBS bromination. Bloomfield also proposed the succinimidyl radical as the allylic hydrogen abstractor, and NBS as the bromine transfer species (Eqs 9 and 10). This "Bloomfield mechanism"

gained popular acceptance for 20 years. However, Goldfinger, et al.,²⁸ proposed that NBS behaves like N-chlorosuccinimide, which was proved to serve as a source of Cl_2 in low concentration. Bromine atoms, which were made possible by the presence of a trace of bromine in the reaction system, were suggested to be the hydrogen-abstracting species instead of succinimidyl radicals. NBS supplies a low steady-state concentration of bromine by reaction with hydrogen bromide (Eq 13). To explain the

specificity for allylic substitution, Goldfinger proposed that the abstraction of allylic hydrogen by bromine atom is irreversible because the hydrogen bromide generated is immediately scavenged by NBS, but the addition of bromine atom to double bond is reversible. At very low concentration of bromine in the system, the rate of reverse of β -bromoalkyl radical back to olefin and bromine atom is faster than the trapping of β -bromoalkyl radical by bromine. With these bases, it is easy to understand why allylic bromination is observed in bromination by NBS. This "Goldfinger mechanism" became more popular than the "Bloomfield mechanism" because of several items of evidence outlined below.

Sixma and Rejm²⁹ observed that photobromination by the slow introduction of bromine into a refluxing solution of cyclohexene in carbon tetrachloride yielded 84% of 3-bromocyclohexene. McGrath and

Tedder³⁰ observed not only the allylic substitution with low concentration of bromine but also the indirect evidence for the reverse of β -bromoalkyl radical back to olefin and bromine atom by obtaining a rapid isomerization of cis-3-hexene to the trans isomer during the reaction of the olefin with NBS.

Sixma and Reim²⁸ also observed the same relative reactivity for the competitive bromination of toluene and *p*-nitrotoluene with both brominating reagents (Br_2 and NBS). Wiberg⁸ observed essentially the same deuterium isotope effect in bromination of toluene and toluene- α - $^2\text{H}_3$ with both brominating reagents. These results of same reactivity and same kinetic isotope effect also suggested the same hydrogen abstraction species.

Kooyman, et al.,³¹ reported that bromination of substituted toluenes using bromine and NBS at 80° gave ρ values of -1.05 and -1.55, respectively. Therefore, both reactions could not be proceeding by the same mechanism. However, Pearson and Martin³² observed identical ρ values (-1.36 at 80°, -1.76 at 19°) for both bromine and NBS. They also demonstrated that HBr was responsible for the different ρ values obtained by Kooyman. Kooyman's $\rho = -1.05$ could be duplicated at lower ratios of Br_2/HBr and hence was being perturbed by reversibility of the abstraction step. Walling, et al.,¹⁰ also observed that the relative reactivities of substituted toluenes toward NBS correlated well with σ^+ and yielded $\rho = -1.38$. This value agrees well with the value obtained by Pearson and Martin.

Identical reactivities for benzylic hydrogens with bromine and NBS have been demonstrated by the data of aralkyl hydrocarbons reported by Russell³³ and Walling.¹⁰ This identity led to the conclusion of the same mechanism for bromine and NBS.

Even though the quantitative data which I have discussed do not give any indication of succinimidyl radical participation in the NBS bromination chain, the authors cited were careful to say that the conclusion of the same mechanism for bromine and NBS applied to benzylic or allylic systems only. Chemists generally seem to have extended the identity to all systems. For example, Poutsma said: "From an experimental point of view, it now seems that a good method of measuring bromine atom selectivities is the use of NBS to avoid reversal of abstraction."³⁴ An illustration of such an extension to alkanic hydrogen has been reported by Tanner, et al.²⁴

Tanner and coworkers have challenged the idea of kinetic assistance by the neighboring bromo substituent in the hydrogen-abstraction step. They reinvestigated the photobromination of 1-bromobutane with molecular bromine⁴ and reported that the product mixtures formed consisted mainly of 1,3-dibromobutane at less than 18% conversion, and that the ratio of 1,2 to 1,3-dibromides increased with the extent of the reaction (Table VII), until the final product mixture consisted of 88% 1,2-dibromobutane.^{24a} Therefore, they argued that the apparent activating effect of the bromo substituent must be attributed to a difference in the rate of reaction of a bromoalkyl radical with HBr and with bromine at positions vicinal to and more remote from the bromo substituent in the bromoalkyl radical. As bromination proceeded, HBr accumulated in the mixture, and the reversal of the radical-forming step

Table VII

Isomer distribution for the bromination of butyl bromide
with molecular bromine at 40°

Reaction %	Dibromobutanes distribution			
	1,1	1,2	1,3	1,4
2	0.52	0.53	1.00	---
18	0.43	0.67	1.00	---
29	0.26	1.10	1.00	---
95	Trace	7.30	1.00	---

(Eq 16) was presumed to be faster than the reaction of alkyl radical

with bromine. Also, the reversal of (12) is faster than that of (11) because (11) is more polar and is expected to react slower with the polar agent HBr. They also proposed that in the NBS reaction, NBS would remove the HBr formed, allowing the reaction to give mainly the kinetically controlled product, 1,3-dibromobutane. However, they failed to obtain trans-1,2-dibromocyclohexane as a minor product in the bromination of cyclohexyl bromide by molecular bromine, even at 1.3% conversion.^{24b} In other words, the HBr effect on the bromine reaction of butyl bromide could not be obtained with the cyclohexyl bromide system. Nevertheless, these authors still considered the NBS reaction data to be the true data for kinetic control in the bromine reaction, since the NBS reaction could give a minimum of interference from the reversible reaction of the alkyl radicals and the hydrogen bromide produced. They observed that trans-1,2-dibromocyclohexane (no cis isomer detected) was the minor

product for the reaction at less than 64% conversion in the AIBN-initiated NBS reaction. Therefore, they concluded that no evidence of anchimeric assistance by the neighboring bromine atom could be found (Table VIII).

Table VIII

Isomer distribution for AIBN initiated
bromination of bromocyclohexane with NBS

Reaction %	-----Peck ratio-----					
	1,1	<u>trans</u> 1,2	<u>trans</u> 1,3	<u>cis</u> 1,4	<u>cis</u> 1,3	<u>trans</u> 1,4
2	0.51	0.22	1.0	0.72	0.71	0.50
64	0.50	0.97	1.0	0.60	0.71	0.60
84	0.55	1.21	1.0	0.62	0.71	0.54
96	0.46	1.57	1.0	0.62	0.70	0.60

After part³⁵ of the work of this Dissertation and related work by others¹³ were published, Tanner and coworkers retracted their early report that at 18% or less reaction the 1,3-dibromobutane is the major product from bromination of butyl bromide.^{24d} In this same article as the retraction, the interpretation of the slow reaction of β -bromoalkyl radical with hydrogen bromide persists, now based on new data reported for reactions in liquid bromine solvent.

Experimentally, Tanner and coauthors said,^{24d} the reversal of HBr with alkyl radical can be made noncompetitive by two means: (1) remove HBr by NBS; (2) carry out the bromination with a large excess of bromine so that essentially all the alkyl radicals produced can be trapped by molecular bromine.

Tanner, et al.,^{24d} observed that the different relative rates of brominations of a number of alkanes and substituted alkanes with bromine and NBS disappeared when the brominations with bromine were carried out in liquid bromine solvent (Table IX).

Table IX

Competitive brominations of butyl bromide and cyclohexane			
-----Substrate-----		Bromination agents and conditions	k_{R_1H}/k_{R_2H}
R_1H	R_2H		
butyl bromide	cyclo- hexane	NBS	0.58 ± 0.10
		$R_1H:R_2H:Br_2 = 1:1:100$	0.52 ± 0.02

The purpose of this work was to resolve the controversy over bridging by a neighboring bromine in the transition state for free-radical hydrogen abstraction, and to investigate the possibility of different mechanisms for radical brominations of alkanic positions by bromine and by NBS. The photobrominations of butyl bromine^{4,24a} were reinvestigated. Some earlier data in the literature on bromocyclohexane halogenation^{24b} indicated that the isomer distribution obtained with NBS reagent is closer to that obtained with chlorine than to that with bromine. We began to suspect that with alkanic hydrogen, bromine and NBS might be reacting by different mechanisms, involving different hydrogen-abstracting radicals with different selectivities. Competitive reaction data were used to establish the identity of bromine and NBS mechanisms for benzylic systems. Therefore, we investigated the competitive reactions, butyl bromide vs. cyclohexane and cyclopentane vs. cyclohexane. We also investigated the reactions with single substrates, cyclopropane and norbornane, which can form in particularly informative ways different products by competitive processes.

II. RESULTS AND DISCUSSION

The deactivating polar effect of a chloro substituent toward radical halogenation of an alkyl chain is well-established.^{3e} When the liquid-phase bromination of alkyl bromides (including butyl bromide and cyclohexyl bromide) led to the formation predominantly (85% or more) of vicinal dibromides, these contrasting results were taken as strong evidence for kinetic assistance by the neighboring bromo substituent in the hydrogen-abstraction step. However, Tanner and coworkers proposed that the selective HBr reversal was responsible for the preferential formation of 1,2-dibromides by molecular bromine because it was strongly and directly tied to the observation of the predominant formation of nonvicinal dibromides at less than 18% reaction of butyl bromide with bromine and in the radical reactions of NBS with butyl bromide and with cyclohexyl bromide.²⁴ The hydrogen-abstracting agent was assumed to be the same ($\text{Br}\cdot$) in both the molecular bromine and the NBS reactions, and the NBS was presumed to consume HBr as rapidly as it was generated.

In our laboratory, we tried to reproduce Tanner's results of 1,3-dibromobutane as major product with less than 18% reaction of butyl bromide with bromine. In spite of repeated, meticulous efforts, we could not reproduce these results. We obtained the 1,2-dibromobutane as major product for extents of reaction ranging from less than 1% to 100%.

If Tanner's HBr reversal theory is correct, then the reversal of bromoalkyl radical with HBr has to be faster than the trapping of bromoalkyl radical by bromine. Although the separate kinetic data do not appear to be available, for other alkyl and haloalkyl radicals for

which data are reported, "The rate of reaction of alkyl radical with bromine is considerably more rapid than the corresponding reaction with HBr."³⁷ Our results of failure to obtain 1,3-dibromobutane as the major product, even early in the reaction with little HBr generated, speak strongly against the HBr reversal proposal. The brominations of butyl bromide were run at $4 \pm 1^\circ$, $25 \pm 1^\circ$, and $60.7 \pm 1.5^\circ$ and the results are summarized in Table X. The product ratio of 1,2-dibromobutane

Table X

Isomeric product distributions obtained from brominations of butyl bromide with molecular bromine.

Time min.	% con- version	Rel amounts of isomeric dibromobutanes ^a			Av dev, %
		1,1	1,2	1,3	
-----25 ± 1°; BuBr:Br ₂ = 6.8:1 ^c -----					
2	1.37		7.3	1.0	1.1
4	2.95		7.3	1.0	2.1
8	6.41	0.1	7.6	1.0	1.5
16	10.5	0.1	7.5	1.0	1.4
32	22.1	0.1	7.3	1.0	1.3
64	43.5	0.1	7.3	1.0	0.98
128	75.4	0.1	8.9	1.0	1.2
-----60.7 ± 1.5°; BuBr:Br ₂ = 7.5:1 ^c -----					
1	1.74	0.1	4.5	1.0	2.0
3	22.5	0.09	4.5	1.0	2.4
10	71.5	0.10	5.2	1.0	0.65
25	89.8	0.11	5.7	1.0	0.94
40	99.8	0.11	6.1	1.0 ^b	1.1
-----4 ± 1°; BuBr:Br ₂ = 5.9:1 ^c -----					
4	1.01	0.1	11	1.0	0.39
10	2.12	0.1	11	1.0	0.52
25	3.42	0.1	11	1.0	1.5
63	13.05	0.1	11	1.0	1.6

a. Each line of data is the average from two to three gc injections; the average deviations are given in the last column. b. The distribution in this line, equivalent to the ratios 1,1:1,2:1,3 = 1.4:84.7:13.9, is nearly identical, within the deviation limits specified, to that reported by Thaler. c. Mol ratio of reactants.

to 1,3-dibromide remains the same for reactions up to approximately 50% conversion. In reactions of higher conversions, the 1,2/1,3 ratio increases slightly, but not to the extent reported at first by Tanner.^{24a} No 1,4-dibromobutane was detected in any of these product mixtures. The $60.7 \pm 1.5^\circ$ reaction gave the identical product distribution as that reported by Thaler⁴ in 1963 within the experimental error. The product ratios of 1,2-dibromobutane to 1,3-dibromobutane decreased as the temperature increased. This agrees with the early report³⁸ that the chlorination of alkyl chlorides at higher temperature gives progressively less vicinal product with increasing temperature. This phenomenon is called the "vicinal effect" and has been attributed to the instability of β -chloroalkyl radicals in high temperature. The data in Table X show the same trend and are attributed to the instability of β -bromo radical derived from butyl bromide and less neighboring bromine assistance at the higher temperature.

Tanner's data for photoinitiated bromination of butyl bromide with NBS in acetonitrile show no 1,4-dibromobutane in the product mixture throughout the course of reaction^{24a} (Table XI); however, the data

Table XI

Isomer distribution in the photoinitiated bromination of butyl bromide with NBS in acetonitrile

Total yields of dibromides, %	-----Isomer distribution-----			
	1,1	1,2	1,3	1,4
5.5	0.19	0.29	1.00	---
22.6	0.24	0.95	1.00	---
23.4	0.21	1.15	1.00	---
105.0	Trace	5.51	1.00	---

for the similar reaction initiated with azoisobutyronitrile (AIBN) indicate 1,4-dibromobutane as a product in reaction mixture after 51%

conversion^{24b} (Table XII). The authors did not provide any reason for this variation. Our data obtained from photoinitiated NBS bromination

Table XII

Isomer distribution in the AIBN-initiated bromination of butyl bromide with NBS in acetonitrile

Reaction %	-----Isomer distribution-----			
	1,1	1,2	1,3	1,4
9	0.27	0.30	1.00	---
37	0.28	0.84	1.00	---
51	0.34	1.36	1.00	Trace
55	0.38	1.25	1.00	0.08
57	0.33	1.37	1.00	0.08

of butyl bromide in acetonitrile show 1,4-dibromobutane is the product in the reaction mixture throughout the reaction (Table XIII). These

Table XIII

Isomeric product distributions obtained from photoinitiated NBS bromination of butyl bromide in acetonitrile at $60 \pm 1^\circ$ (Mol ratio NBS:BuBr:CH₃CN = 1:5.9:27)

Time, Min.	% NBS consumed	---Rel amounts of isomeric dibromides---			
		1,1	1,2	1,3	1,4
4	5.4	0.29	0.30	1.0	0.17
30	35.7	0.27	0.53	1.0	0.12
62	58.1	0.24	0.89	1.0	0.08
105	80.5	0.20	1.16	1.0	0.06
165	93.5	0.20	1.10	1.0	0.06
230	95.9	0.23	1.13	1.0	0.06

data are very different from those obtained in reaction with molecular bromine. Even in the reaction with 96% conversion of NBS, the 1,2/1,3 ratio is only 1.13, as compared with a value of 6.1 obtained from the reaction with molecular bromine after 99.8% conversion.

Tanner, et al, also obtained different product distribution from cyclohexyl bromide and NBS with photoinitiation and with AIBN initiation.^{24b} They reported that a bromine color developed during the more rapid photoinitiated reaction and suggested that a portion of the bromination was attributable to utilization of the molecular bromine. Since the color developed early when plenty of NBS was available for reaction with HBr - a reaction reported to be near-instantaneous^{11,12} - this explanation seems tantamount to acknowledging different selectivities and different attacking radicals for the NBS and bromine reactions.

These data were published in 1972³⁵ along with those of another group who also reported that 1,2-dibromobutane is the major product.¹³ Tanner, et al.,^{24d} later published another paper in which they retracted their early report that at 18% or less reaction the 1,3-dibromobutane was the major product. In that same article, however, the HBr reversal theory remains, based now on new data reported for some competitive reactions in liquid bromine solvent. The authors suggested that essentially all of the alkyl radicals generated could be trapped by molecular bromine by carrying out the bromination with a large excess of bromine. However, an alkyl bromide alone probably provides, by internal competition, a better test of the importance of hydrogen bromide reversal than does the competition between different substrates in bromine solvent. With butyl bromide, the ratio 1,2-C₄H₈Br₂:1,3-C₄H₈Br₂, did not decrease when we changed from 0.1 mol equivalent of bromine to 100 mol equivalent of bromine and interrupted the reaction after less than 3% of the butyl bromide reactant had been converted. Polybromination does not occur under these conditions. Were hydrogen bromide reversal important and faster with less polar radicals (bromo substituent more remote from radical center)

than with more polar ones,²⁴ and were excess bromine able to override that reaction as claimed,^{24d} higher proportions of 1,3-dibromobutane would be expected with large excesses of bromine than with 0.1 mol equiv. Since we do not obtain that result, hydrogen bromide reversal must play little or no role in the proportions of dibromobutanes formed.*

Therefore, we believe that the interpretation²⁴ of the butyl bromide-bromine reaction which emphasizes reversal of the initial alkyl radical formation is erroneous and that the earlier interpretation⁴ in terms of kinetic assistance by neighboring bromine is supported by the present data.

Some earlier data in the literature on bromocyclohexane halogenations^{24b} indicate that the isomer distribution obtained with NBS reagent is closer to that obtained with chlorine than to that with bromine. High selectivity by the attacking radical (substantial bond breaking and radical character development in the transition state) is essential for neighboring bromine participation. If the attacking radical in NBS brominations of alkanes is not bromine atom and is lower in selectivity than is bromine atom, the difference in product distributions for NBS and bromine brominations of alkyl bromides is comprehensible, and the apparent relevance of the NBS reactions to the actual

* By private communication, Professor P. S. Skell and J. C. Day (Pennsylvania State University) have informed us that they have confirmed these observations with butyl bromide, and have extended the investigation to 1-bromoheptane, which likewise gives essentially unvarying proportions of (five) isomeric dibromoheptanes over widely differing substrate: bromine ratios (10:1 to 1:100), with and without NBS present.

mechanism of molecular bromine brominations is lost. Therefore, several alkanic systems were selected for study because of their potential for revealing the identity or difference in mechanism for the two brominating reagents. The results of these studies are summarized and discussed in the following sections.

Butyl bromide vs. cyclohexane. An equimolar mixture of butyl bromide and cyclohexane was brominated with a 0.1 mol equiv of molecular bromine or of NBS. With bromine, the product ratio was approximately 11 times the ratio obtained with NBS. Butyl bromide reacts faster than cyclohexane with bromine ($\text{BuBr}:\text{C}_6\text{H}_{12} = 2.3:1$), but slower than cyclohexane with NBS ($\text{BuBr}:\text{C}_6\text{H}_{12} = 0.20:1$). With both reagents, the dibromobutane isomer distribution was the same as that obtained under the same conditions with butyl bromide substrate alone.

The intermediate radicals, $\dot{\text{C}}_4\text{H}_9\text{Br}$ and $\text{C}_6\text{H}_{11}\dot{\text{r}}$, are formed by competitive hydrogen abstractions and react competitively with the source of substituent bromine. If reversal of the hydrogen abstraction is unimportant, the product ratio, $\text{C}_4\text{H}_9\text{Br}_2:\text{C}_6\text{H}_{11}\text{Br}$, is concordant with the relative rates of hydrogen abstraction from the two substrates. The reversal reaction may occur to substantially different extents with the two intermediate radicals, however, because of the possibility of unfavorable interactions between the bromobutyl radical (more polar than the unsubstituted cyclohexyl radical) and polar HBr .^{24d} This kind of difference in reaction of radical intermediates with HBr would lead to a bromination product which indicates a higher relative rate of substitution into butyl bromide than that which would be indicated in the absence of HBr reversal. Thus, the difference in relative rates of bromination of the two substrates by molecular bromine and by NBS is

consistent with different mechanisms but, in the absence of other data, is not compelling evidence for them.

I find that irradiation of an equimolar butyl bromide-cyclohexane mixture in a large excess (100 mol equiv) of bromine does produce a product mixture indicative of a substantially increased relative reactivity of cyclohexane ($C_4H_9Br:C_6H_{12} = 1:3.1$ at 60°). Some trans-1,2-dibromocyclohexane is also formed (no isomers detected), and the dibromobutane isomer distribution is the same as that obtained with 0.1 mole-equivalent of bromine.

I cannot now account to my own satisfaction for the fact that the change from a brominating mixture which is largely hydrocarbon to one which is largely bromine changes cyclohexane from a less reactive to a more reactive competitor with butyl bromide. One reasonable rationalization lies in the possible complexation of bromine atom with bromine molecule ($Br_3^\cdot$), similar to the well-known anion, Br_3^- . Chlorine atom complexes with aromatic solvents to give radicals different in reactivity from $Cl^\cdot$.^{38a} It may be that $Br_3^\cdot$ is the chain-carrying species in bromine solvent and has reactivity-selectivity quite different from $Br^\cdot$ (or $Br^\cdot$ complexes with RBr). We have no data to support (or refute) this proposal. The overall results, however, (viz., cyclohexyl bromide faster than cyclohexane, and the essentially unchanged dibromide isomer distribution) do not fit or support the interpretation^{24d} that selective hydrogen bromide reversal (reduced or eliminated in excess bromine) is enhancing the apparent reactivity of the alkyl bromide with respect to the cyclohexane.

Cyclohexane vs. cyclopentane. Cyclohexane and cyclopentane undergo chlorinations at different relative rates ($k_{C_5H_{10}}/k_{C_6H_{12}} =$

0.85 at 68°).³⁹ In radical brominations, these two substrates yield intermediate cycloalkyl radicals, both of which are unsubstituted and are expected to show little if any difference in reactivity toward HBr. Competitive brominations of this pair of hydrocarbons at 60° with molecular bromine give relative reactivity ratios of $C_5H_{10}:C_6H_{12} = 6.8$ ($RH:R'H:Br_2 = 10:10:1$) and 8.0 ($RH:R'H:Br_2 = 1:1:100$) and some trans-1,2-dibromocyclopentane; with NBS the relative reactivity ratio is 1.6, and dibromide is formed. The change from hydrocarbon to bromine solvent does affect the $C_5H_{10}:C_6H_{12}$ reactivity ratio slightly, but the change is an increase; the ratio is clearly not reduced^{24d} to that obtained with NBS.

The similarity of the chlorination rates was attributed to the small extent of bond breaking at the transition state (small extent of eclipsing strain relief).³⁹ The substantially different rates for bromination by molecular bromine are consistent with the greater extent of bond breaking expected at the transition state for hydrogen abstraction by $Br\cdot$ than by $Cl\cdot$. It is difficult to rationalize these data with any mechanism which specifies that the hydrogen-abstracting species is the same for Br_2 and NBS reagents.

Cyclopropane. Cyclopropane undergoes liquid phase radical halogenations to give substitution product (cyclopropyl halide) and ring-opening product (1,3-dihalopropane). The proportions of these competitively-formed products depend on the identity of the halogenation reagent. With chlorine as reagent ($Cl\cdot$ chain), the ratio of cyclopropyl chloride:1,3-dichloropropane is about 1:4 at 0° and about 1.5:1 at 68°. ⁴⁰ With tert-butyl hypochlorite (t-BuO $\cdot$ chain) however, the

ratio is at least 17:1 at both 0° and 68°. ⁴⁰ In an early study which established the radical character of the reaction between cyclopropane and bromine (Br• chain), 1,3-dibromopropane, the only product identified, was obtained in high yield. ⁴¹ Under the same conditions, hydrogen bromide (Br• chain) also gave only ring-opening product (propyl bromide). ⁴¹ It is clear and unsurprising that different radical reagents (Cl•, *t*-BuO•, and Br•) give quite differing proportions of hydrogen abstraction and ring-opening processes with cyclopropane.

When we carried out photoinitiated brominations of cyclopropane (C₃H₆:Br₂ = 10:1 mol ratio) in methylene chloride solution at 0°, only 1,3-dibromopropane was obtained; no cyclopropyl bromide was detected by gas chromatography. (There was no reaction under these conditions in the dark). Even with an irradiated solution of cyclopropane in liquid bromine (approximately 0.1 mol equiv of C₃H₆), 1,3-dibromopropane was the sole product detected. When we used NBS (C₃H₆:NBS = 10:1 mol ratio) in acetonitrile solution, however, > 98% of the product mixture was cyclopropyl bromide. These completely opposite ratios of products from Br₂ and NBS reactions must mean that different chain-carrying radicals (Br• and presumably succinimidyl) are generated from the two reagents.

One ($\text{Br}\cdot$) reacts exclusively by attack on carbon (to give ring-opening), but the other, like tert-butoxy radical, abstracts hydrogen predominantly. The relative energies of the alternative pairs of bonds formed and broken (X-C/C-C vs. X-H/H-C) undoubtedly determine the alternative pathways for reaction,* but the data required for a "prediction" when $\text{X} = \text{succinimidyl}$ are not available to us.

Norbornane. Norbornane undergoes chlorination with a variety of chlorinating reagents to give mainly a mixture of exo- and endo-2-chloronorbornanes whose composition is dependent on the identity of the chlorine-transfer agent which reacts with the 2-norbornyl radical intermediate.⁴² Although the exo/endo ratio is related to the size of the chlorine transfer reagent, the order of probable steric requirements of these reagents does not coincide with the order of exo/endo ratios.

*The difference of bond energies between C-Br and C-I in methyl halides is 13.7 Kcal/mole.¹⁶ Benson^{41a} has estimated the activation energy for the ring opening by iodine atom as 17.5 Kcal/mole. Therefore, the activation energy for ring opening by bromine atom may be about 3.8 Kcal/mole. The bond energy for C-H in methane is 104 Kcal/mole and that in cyclopropane is 101 Kcal/mole.¹⁶ Since the activation energy for hydrogen abstraction from methane by bromine atom is 18.3 Kcal/mole,¹⁶ the activation energy for hydrogen abstraction by bromine atom in cyclopropane may be about 15.3 Kcal/mole. Therefore, the preference for cyclopropane ring opening over hydrogen abstraction by bromine atom is readily apparent.

The important aspect for our present consideration, however, is that the exo/endo ratio is different for different halogen-transfer reagents and is unaffected by any reversal of the radical-forming step. No matter how substantial or little is the reversal reaction with HBr, it is difficult to see how that reaction can have any effect on the exo/endo product ratio obtained from brominations. If the bromine-transfer species are the same, the same stereoisomeric product ratio will be obtained. Conversely, if different exo/endo product ratios are obtained with different brominating reagents, the bromine-transfer species must be different.

Kooyman and Vegter^{43a} reported the bromination of norbornane with bromine in boiling carbon tetrachloride (80°) gave an exo/endo product ratio of 3 (only the exo product was actually determined), that use of BrCCl₃ (AIBN initiation) gave an exo/endo product ratio of 5.3 and the use of NBS (AIBN initiation) gave a low conversion to impure product for which an exo/endo ratio could not be determined.

When photo-brominating norbornane with molecular bromine (0.14 mol equiv in Freon 113 solution), no 1-bromonorbornane was detected in the product mixture, and the exo/endo ratio of 2-bromonorbornanes was 2.1. When I used NBS as brominating reagent (0.15 mol equiv in methylene dichloride solution), some 1-bromonorbornane (8.0%) was

found in the product mixture, and the exo/endo ratio of 2-bromonorbornanes was 3.7. When 2-bromonorbornane was prepared by the Kochi reaction⁴³ (2-norbornanecarboxylic acid, lead tetraacetate, sodium bromide), the exo/endo of 2-bromonorbornanes formed from the 2-norbornyl radical intermediate was 1.8.

With bromine, a small amount of a mixture of isomeric dibromides was formed, along with the monobromides, but the product distribution pattern (gc) was quite different from that obtained by reaction of bromine with norbornene.⁴⁴ I did not attempt to determine the absolute or even relative yields of all these isomeric dibromonorbornanes, because such data would have required a substantial amount of experimental work that would have made no contribution to the issue of bromine vs. NBS mechanisms. It seems rather certain then that these dibromides are formed by radical substitution into the monobromides rather than by an HBr elimination-Br₂ addition sequence. When a mixture of 2-bromonorbornanes (exo/endo = 1.8) was brominated with Br₂ (0.067 mol equiv), the bromine was consumed faster than it was with norbornane under the same conditions, and the same mixture of dibromides was formed. The exo/endo ratio of reactants remained constant, however, within the precision of the gc measurements, throughout the course of the bromination. Thus, the exo/endo product ratio obtained from norbornane and Br₂ is reliable and unaffected by the small amount of dibromination which occurred.

These results establish that brominations of norbornane by Br₂ and by NBS involve different bromine-transfer species, different mechanisms. I believe that the original reagent is the bromine-transfer agent with both molecular bromine and NBS and that all available information favors this conclusion for other alkanic systems.

Discussion. The single publication that attacks the mechanism of alkanic bromination by NBS seems to be that by Skell, et al.⁴⁵ They observed that a 500-fold change in concentration of NBS for bromination of (+)-1-bromo-2-methylbutane produced only a small change, from -0.25° to -0.30° , in the rotation of the final product (Table XIV). This leads

Table XI

Bromination of (+)-1-bromo-2-methylbutane by NBS			
Solvent	Temp., ($^{\circ}\text{C}$)	Solubility of NBS (mol/l)	α_{obsd} (temp., $^{\circ}\text{C}$)
CFCl_3	25	0.0006	-0.25 (28)
CH_2Cl_3	40	0.29	-0.30 (25)
CCl_4	76	0.006	-0.06 (35)

to the conclusion that "the alkyl radical intermediate is not brominated by NBS, but presumably by molecular bromine present in steady low concentration." These authors attributed the low optical rotation (-0.06°) in carbon tetrachloride solvent (concentration of NBS 10 times higher than in CFCl_3) to the effect of temperature, also observed in the reaction of (+)-1-bromo-2-methylbutane with molecular bromine (Table XV).¹⁹

Table XV

Bromination of (+)-1-bromo-2-methylbutane by bromine

Temp. ($^{\circ}\text{C}$)	α_{obsd} (27°C)
-40 and +40	-2.86°
72-80	-2.33°

This explanation assumes that both NBS and bromine reactions have the same mechanism and therefore the same temperature effect, even though the temperature effect observed for the bromine reaction is much smaller than that for NBS reaction. This greater dependence of the α value on temperature change in the NBS reaction compared with that in the bromine

reaction may suggest that NBS is actually the bromine transfer species. Because NBS is a positive halogen compound (13), the transfer of bromine

to an alkyl radical should be slower than from molecular bromine. Therefore, the lifetime of the radical intermediate for the NBS reaction is longer, and more racemization can be observed. A larger temperature effect might be expected for the longer intermediate lifetime, thus a larger increasing racemization could be obtained by changing the temperature from 25° to 76°, even though the concentration of NBS was increased 10 times. Had the 500-fold concentration of NBS (methylene chloride solution) been run at 25° instead of 40°, the α value may have been larger than -0.30°. In other words, a temperature effect may exist in the NBS reaction for a change from 25° to 40°, although no temperature effect has been found for the bromine reaction over this temperature range. Therefore, an increase in the α value expected for a 500-fold increase in NBS concentration may be partially cancelled by the temperature effect. It is hard to distinguish between Skell's proposal and this explanation by the results reported in Tables XIV and XV without further experiments.

A group of French workers⁴⁶ reported the isolation of sizable quantities of adducts of olefins with NBS. One might consider this addition of NBS to olefins as an ionic reaction. However, Zalkow and Kennedy⁴⁷ observed that NBS reacted (benzoyl peroxide initiation) with

bicyclo[2.2.1]hept-5-ene-endo-cis-2,3-dicarboxylic anhydride in carbon tetrachloride to give exo-5-bromo-exo-6-succinimidobicyclo[2.2.1]-heptane-endo-cis-2,3-dicarboxylic anhydride (14). This exo-cis addition

of NBS to the double bond appears to rule out the possibility of addition by an ionic mechanism, because ionic reaction would be expected to give a trans adduct by way of an intermediate bridged bromonium ion. The by-product of this reaction is β -bromopropionyl isocyanate.

The rearrangement of NBS to β -bromopropionyl isocyanate was first observed independently by Johnson and Bubilitz⁴⁸ and Bartlett and Martin.⁴⁹ The rearrangement proceeds by β -scission of succinimidyl radical. The observation of this rearrangement strongly suggests that, during a bromination by NBS, succinimidyl radical may be present.

Tanner, et al., tried to show that the reactivity observed in the NBS reactions was not due to a carbon-centered radical [(16), arising from β -scission of a succinimidyl radical] by comparing the NBS reactivity

with that of three other N-bromo amides, viz., 1,3-dibromo-5,5-dimethylhydantoin (17), 1-bromo-3,5,5-trimethylhydantoin (18), and tetramethyl-N-bromosuccinimide (19). They concluded that all four N-bromo brominating agents showed the same reactivity, even though a three-fold range of reactivities was actually reported (Table XVI)^{24d}

Table XVI

Relative rates of competitive brominations of chlorocyclohexane (R_1H) and cyclohexane (R_2H)

Brominating agents	k_{R_1H}/k_{R_2H}
(15)	0.43 ± 0.01
NBS	0.23 ± 0.02
(16)	0.18 ± 0.02
(17)	0.14 ± 0.02

for the chlorocyclohexane:cyclohexane competition (the one for which the data are most precise). Contrary to their claim that bromine atoms are the hydrogen abstractors in each case, the data actually support a proposal that different chain carrying species are involved. Earlier, Walling and Rieger⁵⁰ obtained "quite similar" relative reactivities (Table XVII) for NBS and three other N-bromo amides [viz., 1-bromo-5-

Table XVII

Relative rates of competitive brominations of ethylbenzene (R_1H) and toluene (R_2H)

Brominating agent	k_{R_1H}/k_{R_2H}
NBS	15.8
(20)	11 ± 4.5
(21)	8.44
(22)	6.2 ± 0.3

isobutyl-5-methylhydantoin (20), 3-bromo-1,5,5-trimethylhydantoin (21),

and 1-bromo-3,5,5-trimethylhydantoin (22) reacting competitively with ethylbenzene and toluene. The published data, however, do show as big as a 2.5-fold range. Again, the data may support a proposal that four different imidyl radicals, four different chain carrying species, are obtained from different N-bromo amides. These authors also reported⁽⁴⁾ the relative reactivities toward alkanic positions vs. toluene (Table XVIII). From the data, they concluded: "Data

Table XVIII

Relative rates of alkanic positions vs. toluene toward N-bromo amides

<u>Substrate</u>	<u>NBS</u>	<u>(20)</u>
Toluene	1.00	1.00
2,3-Dimethylbutane	0.07	0.10
Methylcyclohexane	0.027	0.06
<u>n</u> -Octane	0.022	0.017
Cyclohexane	0.012	0.017

for saturated hydrocarbons are subject to considerable uncertainty and may represent merely orders of magnitude. In any case, the results again support the hypothesis of a common bromine atom chain as the major reaction path." In my opinion, the data equally strongly suggest that bromine atoms are not the common hydrogen-abstraction species for NBS and (20).

Our data for competitive reactants and for two single substrates, which were brominated by molecular bromine and by NBS, demonstrate that radical brominations of alkanic positions by bromine and by NBS proceed by different mechanisms. Yet the evidence that the same mechanism ($\text{Br}^\bullet$ chain) occurs with benzylic positions^{*} is equally

* NBS bromination of ethylbenzene was investigated; the gc spectrum showed a trace amount of β -bromoethylbenzene, which could not be detected by nmr

compelling.^{49,52,53a} How can we reconcile these results?

The transition state for hydrogen abstraction by a bromine atom involves considerably more bond-breaking (and a higher activation energy) than the one for hydrogen abstraction by chlorine atom.⁵¹ The reactivity ratio for toluene:cyclohexane at 80° is 60 for bromination but 0.091 for chlorination.⁵¹ For bromination, but not for chlorination, the C-H bond breaking with toluene is sufficient to allow substantial stabilization of the transition state by benzylic resonance, compared with the alkanic system, cyclohexane. The electronic effect of gem-phenyl actually slows hydrogen abstraction by chlorine atom.

NBS dissociation can potentially initiate either a bromine atom or succinimidyl radical chain. With alkanic systems (at least the

spectroscopy. This trace amount of β -bromoethylbenzene suggested that the succinimidyl radicals at least competed with bromine atoms for hydrogen abstraction.

ones we have examined, without exception), the succinimidyl chain appears to have the lower activation energy and is the one which occurs. The selectivity patterns indicate that, as with $\text{Cl}^\bullet$, little C-H bond breaking has occurred at the transition state for succinimidyl attack, and little resonance stabilization of the transition state from benzylic systems is to be expected. As is true for chlorine atom, then, succinimidyl radical will, we believe, react less readily with benzylic systems than with alkanic ones. With benzylic systems, the alternate, bromine atom chain becomes favored, because of stabilization in the transition state.

Photodissociation of NBS under our conditions (tungsten lamp) is far slower and less efficient than is photodissociation of bromine. Therefore, in mixtures containing both bromine and NBS, bromine atom generation will far exceed succinimidyl radical generation. These mixtures give alkanic product distributions substantially the same as those obtained with bromine alone rather than those obtained with NBS alone.³⁵ In a mixture of bromine and NBS, the bromine atom chain does not diminish the concentration of bromine nor the efficiency of generation of bromine atoms.

III. EXPERIMENTAL

A. General

All small glass ampoules used for bromination reactions were cleaned first with cleaning solution, second with concentrated aqueous ammonia. They were then rinsed with distilled water and dried in an oven.

The reagents used in all syntheses were reagent grade commercial chemicals. They were used without further treatment unless otherwise indicated.

Ultraviolet (uv) spectra and visible (vis) spectra were obtained with a Cary 14 recording spectrophotometer. Infrared (ir) spectra were obtained with a Perkin-Elmer 137 infrared spectrophotometer. Liquid samples were examined as thin film on sodium chloride plates. Proton nuclear magnetic resonance (nmr) spectra were obtained with a Varian Associates Model A60A, or a Perkin-Elmer R12 nuclear magnetic resonance spectrometer. Samples were examined as 10-20% solution in carbon tetrachloride with tetramethylsilane (TMS) as internal reference. Chemical shifts are reported relative to TMS in δ units, and coupling constants are recorded in Hertz (Hz). The following abbreviations are used to describe the splitting patterns: s = singlet, d = doublet, t = triplet, and m = multiplet.

Gas chromatographic (gc) data were obtained with a Hewlett-Packard Model 700 instrument equipped with a hydrogen flame ionization detector and 0.125 in., Teflon-lined aluminum columns packed with 10% Carbowax 20M or 10% QF-1 on 60/80 mesh Chromosorb P (acid washed). Preparative gc separations were accomplished with a Varian Aerograph

Model 90-P instrument equipped with a 5 ft. x 0.25 in. column packed with 10% Carbowax 20M on 60/80 mesh Chromosorb W (acid washed).

B. Syntheses

1. Preparation of 1,1-dibromobutane

1,1-Dibromobutane was obtained by a Hunsdiecker degradation from 2-bromopentanoic acid by a described procedure.⁵²

a. 2-Bromopentanoic acid⁵³

Pentanoic acid (115 g, 1.08 moles) and red phosphorus powder (4.5 g) were placed in a 250-ml 3-necked flask equipped with a thermometer, a reflux condenser carrying a gas exit through a calcium chloride-tube, an addition funnel having a pressure-equalizing side arm, and a magnetic stirring bar. Bromine (180 g, 1.1 moles) was dropped slowly from the addition funnel into the reaction mixture whereby the temperature rose to 60°. Hydrogen bromide gas was generated profusely and was trapped with 3M sodium hydroxide solution. When the addition of bromine was completed, the flask was heated with a heating mantle to keep the temperature at 65°. More hydrogen bromide was liberated while the brown bromine color of the mixture slowly lightened. After 3 hours, the escape of hydrogen bromide stopped. Excess bromine was removed under aspirator suction at 65° leaving an orange solution with brownish thick oil at the bottom. The solution was decanted into a 200-ml round bottom flask. Vacuum distillation gave 95 g (52.4%) of the colorless 2-bromopentanoic acid; bp 105-106° (4 mm) [lit⁵⁴ bp 123-124° (15 mm)]; nmr (CCl₄) δ 12.8 (s, 1, COOH), 4.42 (t, 1, J = 7.2 Hz, CHBrCOOH), 2.1 (m, 2, CH₂CB_r), 1.8 (m, 2, CH₃CH₂), 1.0 (t, 3, J = 7.0 Hz, CH₃).

b. Silver 2-bromopentanoate⁵²

All the operations in this silver salt preparation were conducted at 0°.

An aqueous solution of ammonia (50 ml of concentrated aqueous ammonia in 50 ml of distilled water) was added to the stirred 2-bromopentanoic acid (12.2 g, 0.0674 mole) in an Erlenmeyer flask until the pH was 7. Then an aqueous solution of silver nitrate (11.45 g, 0.0674 mole, in 50 ml of distilled water) was added, and a white precipitate formed immediately. Rapid filtration gave the crude product, which was washed with 150 ml of distilled water, 100 ml of ethyl alcohol, and 150 ml of ethyl ether (all at 0°). The precipitate was then transferred to a 100 ml round bottom flask and dried in vacuo for 24 hours. In the subsequent reaction, the salt was used directly from the bottle after large lumps were broken up with a spatula.

c. 1,1-Dibromobutane⁵²

All apparatus used were dried overnight in the oven. Bromine was dried over phosphorus pentoxide, then distilled. Carbon tetrachloride was dried by distillation and standing over Drierite. Bromine (10.8 g, 0.0674 mole) and 100 ml carbon tetrachloride were placed in a 250-ml 3-necked round bottom flask equipped with a reflux condenser and a mechanical stirrer. In order to remove any remaining water from the apparatus, the solution was boiled, with no cooling water going through the condenser, until 2 ml had distilled out the top of the condenser. A calcium chloride drying tube was then fitted into the top of the condenser, the source heat was removed, and the cooling water was turned on. The bottle (kept at 0°) containing the silver salt was attached to

a third neck of the reaction flask by means of a flexible rubber coupling. The red bromine solution was cooled to 0° . The silver salt was introduced in small portions with good stirring. Carbon dioxide was liberated, and the rate was measured by a bubble counter which was connected to the drying tube. A rate of 5-10 bubbles per second was maintained. At the end of the addition, the reaction mixture was allowed to stir for 30 minutes and to warm to room temperature. The solution was orange after 30 minutes stirring at room temperature. A cold aqueous sodium bisulfite solution was added slowly until the solution became colorless. Silver bromide was then filtered off and washed with carbon tetrachloride. The combined organic layer was washed with three 20-ml portions of aqueous sodium carbonate solution and three times with water and dried over Drierite. Carbon tetrachloride was removed by rotary evaporation. Vacuum distillation gave 4.8 g (33%) of the colorless 1,1-dibromobutane; bp $65-66^{\circ}$ (20 mm) [lit⁵² bp $90.5-92^{\circ}$ (101 mm)]; nmr (CCl_4) δ 5.70 (t, 1, $J = 6.2$ Hz, CHBr_2), 2.37 (m, 2, CH_2CBr_2), 1.60 (m, 2, CH_3CH_2), 0.98 (m, 3, CH_3).

2. Preparation of trans-1,2-dibromocyclopentane

Cyclopentene (6.0 g, 88 mmol) was placed in a 50 ml 3-necked flask covered with aluminum foil and equipped with condenser, magnetic stirrer, thermometer, and additional funnel and cooled to 0° by an ice bath. A mixture of 14.7 g (92 mmol) of bromine in 15 ml of carbon tetrachloride was added dropwise from the addition funnel while the temperature was maintained below 2° . At the end of addition, the reaction mixture was allowed to stir further for 10 minutes at 0° and then allowed to warm to room temperature. The solution was orange. Cold 10%

aqueous sodium thiosulfate solution (1 ml) was added to destroy the excess bromine. This reaction mixture was washed with three 5 ml portions of water, dried over calcium chloride, and distilled to give 17.1 g (85%) of the colorless trans-1,2-dibromocyclopentane; bp 85-87° (23 mm); [lit⁵⁵ bp 75-76° (15 mm)].

3. Preparation of exo-2-bromonorbornane⁵⁶

3. Preparation of exo-2-bromonorbornane⁵⁶ed 5.0 g (0.053 mole) of norbornene and 18 g (excess) of 48% hydrobromic acid was equipped with condenser and magnetic stirrer. The mixture was stirred and heated at 50-65° for 2.5 hours. The organic layer was separated, and the aqueous layer was extracted with three 10-ml portions of ethyl ether. The ethyl ether extracts were combined with the organic layer and washed with 10 ml of water, 10 ml of aqueous sodium bicarbonate, and two 10-ml portions of water. After the organic material had been dried over anhydrous magnesium sulfate, the solvent was removed with rotary evaporation. Distillation gave 6.0 g (64%) of colorless exo-2-bromonorbornane, bp 86-87° (31 mm); [lit⁵⁶ bp 84-87° (31 mm); 80-81° (25 mm)]; nmr (CCl₄) δ 3.9 (m, 1, CHBr), 2.65-0.84 (m, 10).

4. Preparation of endo-2-bromonorbornane⁵⁸

A dry 100-ml, 3-necked, round bottom flask was equipped with a condenser which connected to a nitrogen outlet, a pressure-equalizing dropping funnel which connected to a nitrogen inlet, a thermometer, and a magnetic stirrer. The system was flushed with nitrogen and then maintained with a positive nitrogen pressure. A mixture of 5.64 g (0.060 mole) of norbornene and 10 ml of dry tetrahydrofuran (THF, dried over calcium hydride and distilled before use) was added to the flask and

cooled to 0° with an ice-water bath. Borane in THF (21 ml of a 1M solution) was added dropwise. The solution was stirred for 30 minutes at 20°, the nitrogen flow was disconnected, and 1 ml of methanol was added to destroy the excess borane. The condenser was replaced by another dropping funnel. One dropping funnel was charged with bromine (9.6 g, 0.060 mole) and the other with a solution of sodium methoxide in methanol (17.2 ml of a 3.84 M solution, 0.066 mole of sodium methoxide). The bromine and base were added simultaneously at a rate such that the reaction mixture was always slightly yellow and the reaction temperature was 20-25°. The reaction mixture was allowed to stir further for 20 minutes at room temperature. Water (10 ml) and pentane (25 ml) were added to the reaction mixture, the layers were separated, and the aqueous layer was extracted with three 10-ml portions of pentane. The combined organic solution was washed with 20 ml of water, with 10 ml of saturated aqueous sodium chloride and with two 20-ml portions of water. After being dried with potassium carbonate, the pentane was removed by a rotary evaporator. The crude product was allowed to react with 80% aqueous ethanol at 55° for 17 hours to hydrolyze any exo-bromide.⁵⁸ The mixture was extracted with three 20-ml portions of methylene chloride, and the combined organic material was washed with three 10-ml portions of water. After being dried with anhydrous magnesium sulfate, the methylene chloride was removed on a rotary evaporator. Distillation gave 3.2 g of a fraction, bp 69-71° (15.5 mm) [lit⁵⁹ bp 69-70° (15.5 mm)] Gc analysis showed no exo-2-bromonorbornane but did reveal other unidentified impurities. Therefore, pure endo-2-bromonorbornane was separated and collected by preparative gc; nmr (CCl₄) δ 4.21 (m, 1, CHBr), 2.60-0.9 (m, 10).

5. Preparation of 1-bromonorbornane

a. exo-2-Norbornyl formate⁶⁰

Formic acid (88%, 31.5 g, 0.61 mole) was added to 14.0 g (0.149 mole) of norbornene in a 500-ml round-bottom flask equipped with a condenser, and the mixture was boiled under reflux for 4 hours. The dark solution was cooled, and the condenser was arranged for distillation. The excess formic acid was removed under reduced pressure; bp 26-31° (22 mm). Distillation of the residue gave 16.3 g (78%) of colorless exo-2-norbornyl formate, bp 65-67° (15 mm) [lit⁶⁰ 65-67° (14-16 mm)]; nmr (CCl₄) δ 7.9 (s, 1, HCOO), 4.7 (m, 1, CHOCO), 2.5-0.9 (m, 10).

b. 2-Norbornanone⁶⁰

A solution of 15.3 g (0.109 mole) of exo-2-norbornyl formate in 45 ml of reagent grade acetone was contained in a 300-ml 3-necked round bottom flask equipped with a thermometer, stirrer, and dropping funnel. A chromic acid solution, made by dissolving 16.02 g of chromium trioxide in ice water, adding 13.32 ml of concentrated sulfuric acid, and diluting the solution to 60 ml with water, was placed in the dropping funnel. The flask was cooled with an ice bath, and the oxidant was added to the stirred solution at a rate to maintain the temperature at 20-30°. The solution was stirred overnight at room temperature. Solid sodium bisulfite was added in portions to reduce the excess oxidant. The reaction mixture was decanted into a separatory funnel, washed with three 10-ml portions of saturated aqueous potassium carbonate solution, and dried over anhydrous potassium carbonate. The acetone was removed by distillation, and 5 ml of benzene was added to remove water

by azeotropic distillation. When the distillation of solvent was completed and the considerably hotter vapors of product began to ascend the column, the condenser was replaced by an adapter and a collection flask immersed in ice water. The adapter was heated and maintained above 100° by a free flame until the product began to distill. Colorless 2-norbornanone (7.6 g, 63.2%) was collected at $170-173^{\circ}$ (lit⁵⁹ $170-173^{\circ}$). It crystallized immediately in the collection flask and melted at $89-91^{\circ}$ (lit⁶⁰ $90-91^{\circ}$); nmr (CCl_4) δ 2.67 (m, 2, $\alpha\text{-H}$), 1.75 (m, 8).

c. Phosphorus pentabromide⁶¹

A 100-ml, 3-necked, round bottom flask was equipped with a stirring bar, a condenser, and an addition funnel. A solution 14.4 g (90 mmoles) of bromine in 60 ml of petroleum ether was charged to the flask and stirred vigorously. While the flask was chilled by an ice-bath, 24.4 g (90 mmoles) of phosphorus tribromide was added to the solution dropwise. A precipitate formed immediately. When the addition was completed, the reaction mixture was stirred at room temperature for 20 minutes. The solvent was decanted, and the phosphorus pentabromide was washed by decantation with three 20-ml portions of fresh petroleum ether. It was used to prepare 2,2-dibromonorbornane without further purification.

d. 2,2-Dibromonorbornane⁶²

The 100-ml, 3-necked flask which contained the phosphorus pentabromide was fitted with thermometer, a reflux condenser, and a stirring rod. When 2-norbornanone (6.6 g, 0.060 mole) was added to this flask, the mixture liquified and the temperature rose. The mixture was heated at 70° for 1 hour and then gradually poured into water

at 60-70° with stirring. After 20 minutes stirring, the mixture was extracted with two 25 ml portions of dichloromethane. The extracts were combined, washed with 10 ml of 2M aqueous sodium hydroxide and with two 10 ml portions of water, and dried over magnesium sulfate. Solvent was removed by rotary evaporation. Distillation gave 11.0 g of colorless 2,2-dibromonorbornane, bp 76-80° (1.5 mm). The ir spectrum included absorption at 1750 cm⁻¹ which indicated the unreacted starting ketone. Redistillation failed to remove this starting ketone. The product mixture was then washed with cold concentrated sulfuric acid until no yellow color showed in the sulfuric acid layer. The organic layer was then washed with 10 ml of water with 10 ml of 10% sodium carbonate, and with two 10-ml portions of water and then dried over magnesium sulfate. Distillation gave 7.6 g (50.7%) of product without carbonyl group in absorption; bp 71-73° (2.2 mm); nmr (CCl₄) δ 3.5-0.9 (m, all peaks). Anal. Calcd. for C₇H₁₀Br₂: C, 33.07; H, 3.97. Found: C, 33.18; H, 3.91.

e. 1-Bromonorbornane

The procedure paralleled one published for the preparation of 1-chloronorbornane from 2,2-dichloronorbornane.⁶³

A solution was prepared by mixing 6.0 g (23.6 mmols) of 2,2-dibromonorbornane, 5 ml of isopentane, and 17 ml of pentane. (Both pentanes were purified by being stirred with anhydrous aluminum bromide and then distilled before use.) While the solution was stirred in a 100-ml, 3-necked, round bottom flask equipped with a reflux condenser, powdered anhydrous aluminum bromide (2.76 g, 10.3 mmols) was added in small portions as rapidly as the hydrogen bromide evolution would permit.

The stirring was continued for 6 hours at room temperature. The pentane layer was decanted, and the dark sludge which remained in the flask was washed with four 5-ml portions of purified pentane. The combined pentane solution was washed with 5 ml of water, 5 ml of aqueous sodium bicarbonate solution, and two 5-ml portions of water. After the solution had dried over anhydrous sodium sulfate, the pentanes were removed by rotary evaporation. Distillation gave four fractions: (1) 0.48 g (7%), bp 50-58° (15 mm); (2) 0.5 g (13.5%), bp 58-68° (15 mm); (3) 0.5 g (13.5%), bp 68-88° (15 mm); and (4) 2.1 g (42%), bp 84-87° (1.5 mm). The first three fractions were identified by nmr to be mixtures of 1-bromonorbornane, exo- and endo-2-bromonorbornanes, and the fourth fraction was identified by nmr to be dibromonorbornanes. [Lit⁶⁴ 1-bromonorbornane, bp 56° (18 mm), 57-58° (21 mm).] 1-Bromonorbornane was separated from the monobromonorbornane fractions by preparative gc. All peaks in the nmr spectrum of 1-bromonorbornane were between δ 2.4 and δ 1.0.

C. Brominations

1. Materials

Commercial bromine (reagent grade) was distilled in flame-dried apparatus through a short column at 59° and collected. The initial cut of about 3 ml and final cut of about 3 ml were discarded. The distillation was stored over phosphorus pentoxide and redistilled just before use.

N-Bromosuccinimide (NBS) was recrystallized from hot water and dried in a desiccator (calcium chloride desiccant) protected from light. It was determined to be $99.8 \pm 0.1\%$ pure by titration with aqueous thiosulfate solution.

Commercially available compounds to be brominated and solvents were purified by standard methods as described in "Organic Solvents" by Riddick and Bunger.¹⁵

2. General procedure for bromination

The dried small glass ampoules (inside diameter 8.5 mm, outside diameter 10 mm) were covered with aluminum foil; charged with a mixture of compound(s) to be brominated, brominating reagent, and solvent, if one were used; incorporated into a vacuum line apparatus and degassed by a freeze-thaw method; sealed off; placed in a water bath at the selected reaction temperature; and irradiated with a 300 w incandescent lamp 30 cm from the ampoules. After different times, one by one of the ampoules was removed, immediately frozen in liquid nitrogen, and opened. Except for the experiments in which a large excess of bromine was used, the reaction mixture (1.0 ml) was added to a mixture of about 10 ml of 10% potassium iodide, 1 ml of Freon 113, and about 2 ml of 1M hydrochloric acid. A brown solution showed iodine formation. This brown solution was titrated with standard aqueous sodium thiosulfate until the solution became light yellow. Starch indicator (1 ml) was added, and the solution became blue. Titration was continued until the blue color disappeared. The quantity (mmol) of thiosulfate consumed was equivalent to the quantity (mmol) of bromine or NBS remaining. The organic layer was pipetted into a small sample vial and was analyzed by gc for product distribution. Authentic samples of products were used for gc identifications and standardizations.

a. Bromination of butyl bromide by bromine

Run 1: Four ampoules were each charged with about 2 ml of a mixture of butyl bromide and bromine (mol ratio, 5.9:1.0; no solvent) and irradiated at $4 \pm 1^\circ$. After work-up, the gc analysis showed the product distribution as below.*

Time min.	% Con- version	% of isomeric dibromobutanes		
		1,1	1,2	1,3
4	1.01	0.8 (0.1)	90.9 (11)	8.3 (1.0)
10	2.12	0.8 (0.1)	90.9 (11)	8.3 (1.0)
25	3.42	0.8 (0.1)	90.9 (11)	8.3 (1.0)
63	13.05	0.8 (0.1)	90.9 (11)	8.3 (1.0)

Run 2: Seven ampoules were each charged with about 2 ml of a mixture of butyl bromide and bromine (mole ratio, 6.8:1.0; no solvent) and irradiated at $25 \pm 1^\circ$. After work-up, the gc analysis showed the product distribution as below.

* In each report of product distributions that follow, figures not in parentheses record the relative yield of dibromobutanes in the total product mixture, while those in parentheses show the amounts of dibromobutanes only relative to the 1,3-isomer.

Time min.	% Con- version	% of isomeric dibromobutanes		
		1,1	1,2	1,3
2	1.37	*	88.0 (7.3)	12.0 (1.0)
4	2.95	*	88.0 (7.3)	12.0 (1.0)
8	6.41	1.15 (0.1)	87.4 (7.6)	11.5 (1.0)
16	10.5	1.16 (0.1)	87.2 (7.5)	11.6 (1.0)
32	22.1	1.2 (0.1)	86.9 (7.3)	11.9 (1.0)
64	43.5	1.2 (0.1)	86.9 (7.3)	11.9 (1.0)
128	75.4	1.0 (0.1)	89.0 (8.9)	10.0 (1.0)

* Trace amount; gc recording for this component too noisy to afford good data.

Run 3: Five ampoules were each charged with about 2 ml. of a mixture of butyl bromide and bromine (mole ratio, 7.5:1.0; no solvent) and irradiated at $60.7 \pm 1.5^\circ$. After work-up, the gc analysis showed the product distribution as below.

Time min.	% Con- version	% of isomeric dibromobutanes		
		1,1	1,2	1,3
1	1.74	1.8 (0.1)	80.3 (4.5)	17.9 (1.9)
3	22.5	1.6 (0.09)	80.5 (4.5)	17.9 (1.0)
10	71.5	1.6 (0.10)	82.5 (5.2)	15.9 (1.0)
25	89.8	1.6 (0.11)	83.7 (5.7)	14.7 (1.0)
40	99.8	1.4 (0.11)	84.7 (6.1)	13.9 (1.0)

[Lit⁴ 0.9%:84.5%:14.6% = 1,1:1,2:1,3 for 100% conversion at 60°.]

Run 4: Two ampoules were each charged with a mixture of butyl bromide and bromine (mole ratio, 1:100; no solvent) and were irradiated at $60 \pm 1^\circ$. When each tube was opened, Freon 113 (1 ml) was added to the mixture. A yellow precipitate (sulfur) formed when the excess bromine was destroyed by ice-cold aqueous sodium thiosulfate. This reaction mixture was centrifuged, and the organic layer (Freon 113 layer) was pipetted into a vial. The gc analysis showed the product distribution ($\pm 0.2\%$ max) as below.

Time min.	Reaction %	% of isomeric dibromobutanes		
		1,1	1,2	1,3
10	1	1.6 (0.1)	82.5 (5.2)	15.9 (1.0)
20	3	1.6 (0.1)	82.8 (5.3)	15.6 (1.0)

b. Bromination of butyl bromide by NBS
Bromination of butyl bromide by NBS

Run 5: Six ampoules were each charged with about 2 ml of a mixture of butyl bromide, NBS, and acetonitrile (mole ratio, 1.0:5.9:27) and irradiated at $60 \pm 1^\circ$. After work-up, the gc analysis showed the product distribution as below.

Time min.	% NBS consumed	% of isomeric dibromobutanes			
		1,1	1,2	1,3	1,4
4	5.4	16.5 (0.29)	17.0 (0.30)	56.8 (1.0)	9.7 (0.17)
30	35.7	14.1 (0.27)	27.6 (0.53)	52.0 (1.0)	6.3 (0.12)
62	58.1	10.9 (0.24)	40.3 (0.89)	45.2 (1.0)	3.6 (0.08)
105	80.5	8.3 (0.20)	47.9 (1.16)	41.3 (1.0)	2.5 (0.06)
165	93.5	8.5 (0.20)	46.6 (1.10)	42.4 (1.0)	2.5 (0.06)
230	95.5	9.5 (0.23)	46.7 (1.13)	41.3 (1.0)	2.5 (0.06)

c. Competitive bromination of butyl bromide and cyclohexane by bromine

Run 6: Three ampoules were each charged with about 2 ml of a mixture of butyl bromide, cyclohexane, and bromine (mole ratio, 10:10:1; no solvent) and irradiated at $60 \pm 1^\circ$. After work-up, the gc analysis showed the product distribution ($\pm 0.2\%$ max) as below. The relative reactivity was butyl bromide:cyclohexane = 2.3:1.

Time min.	% con- version	-----% of products-----				
		isomeric 1,1	dibromobutanes 1,2	1,3
2	53.3	1.1 (0.1)	49.9 (4.5)	11.1 (1.0)	37.9	trace
4	87.2	1.0 (0.1)	55.2 (5.5)	10.0 (1.0)	33.8	trace
11	100	0.95 (0.1)	59.3 (6.2)	9.5 (1.0)	30.2	trace

Run 7: Two ampoules were each charged first with a mixture of butyl bromide and cyclohexane (mole ratio, 1:1; no solvent) and then with 100 mole equiv of bromine and were irradiated at $60 \pm 1^\circ$. Freon 113 (1 ml) was added to each opened ampoule. A yellow precipitate (sulfur) formed when the excess bromine was destroyed by ice-cold aqueous sodium thiosulfate. This reaction mixture was centrifuged, and the organic layer (Freon 113 layer) was pipetted into a vial. The gc analysis showed the product distribution ($\pm 0.1\%$ max) as below. The relative reactivity was butyl bromide:cyclohexane = 1:3.1.

Time min.	% of BuBr consumed	-----% of products-----				
		isomeric 1,1	dibromobutanes 1,2	1,3
10	1	trace	20.6 (5.2)	4.0 (1.0)	60.7	14.7
20	3	trace	20.4 (5.2)	3.9 (1.0)	60.7	14.9

d. Competitive bromination of butyl bromide and cyclohexane by NBS

Run 8: Two ampoules were each charged with about 2 ml of a mixture of butyl bromide, cyclohexane, and acetonitrile (mol ratio, 10:10:26.5) saturated with NBS (less than 1 mol equiv),* and irradiated at $60 \pm 1^\circ$. After work-up, the gc analysis showed the product distribution ($\pm 0.3\%$ max) as below. The relative reactivity was butyl bromide: cyclohexane = 0.20:1.

Time min.	% Con- version	-----% of products-----				
		isomeric 1,1	dibromobutanes 1,2	1,3	1,4	bromocyclo- hexane
2	26.9	1.6 (0.28)	2.8 (0.50)	5.7 (1.0)	trace	89.9
75	97.7	1.5 (0.23)	8.3 (1.25)	6.6 (1.0)	0.5 (0.07)	83.1

e. Competitive bromination of cyclopentane and cyclohexane by bromine

Run 9: Three ampoules were each charged with about 2 ml of a mixture of cyclopentane, cyclohexane, and bromine (mole ratio, 10:10:1;

* It was intended to use a 10:10:1:26.5 mole ratio of butyl bromide:cyclohexane:NBS:acetonitrile; however, the NBS was only partially soluble in the mixture, so this saturated NBS solution at 25° was used.

no solvent) and irradiated at $60 \pm 1^\circ$ until the reaction mixture turned colorless (i.e., 100% conversion). After work-up, the gc analysis revealed the average product distribution: bromocyclopentane ($72.4 \pm 0.4\%$), trans-1,2-dibromocyclopentane ($14.8 \pm 0.5\%$), bromocyclohexane ($12.8 \pm 0.1\%$), and trace amount of trans-1,2-dibromocyclohexane. The relative reactivity was cyclopentane:cyclohexane = 6.8:1.

Run 10: Two ampoules were each charged first with a mixture of cyclopentane and cyclohexane (mole ratio, 1:1; no solvent) and then with 100 mole equiv of bromine and irradiated at $60 \pm 1^\circ$ for 70 seconds. Freon 113 (1 ml) was added to each opened ampoule. When excess bromine was destroyed by ick-cold aqueous sodium thiosulfate, a yellow precipitate (sulfur) formed. This reaction mixture was centrifuged, and the organic layer (Freon 113 layer) was pipetted into a via. The gc analysis revealed that 2.1% of the cyclohexane had been consumed, and the average product distribution: bromocyclopentane ($71.8 \pm 0.3\%$), trans-1,2-dibromocyclopentane ($17.1 \pm 0.3\%$), bromocyclohexane ($10.0 \pm 0.2\%$), and trans-1,2-dibromocyclohexane ($1.1 \pm 0.3\%$). The relative reactivity was cyclopentane:cyclohexane = 8.0:1.

f. Competitive bromination of cyclopentane and cyclohexane by NBS

Run 11: Two ampoules were each charged with about 2 ml of a methylene chloride solution of cyclopentane, cyclohexane and NBS (mole ratio, cyclopentane:cyclohexane:NBS:methylene chloride = 10:10:1:132) and irradiated at $60 \pm 1^\circ$ for one hour. Titration with aqueous sodium thiosulfate showed reaction to be 99% complete. The gc analysis revealed the average product distribution: bromocyclopentane ($62.3 \pm 0.2\%$) and bromocyclohexane ($37.7 \pm 0.2\%$). The relative reactivity was cyclopentane:cyclohexane = 1.6:1.

g. Bromination of cyclopropane by bromine

Run 12: Two ampoules chilled in liquid nitrogen were each charged first with 0.76 g (18 mmol) of cyclopropane and then with a solution of 0.1 ml (1.8 mmol) of bromine in 1 ml of methylene chloride (mole ratio, cyclopropane:bromine:methylene chloride = 10:1:8.6) and irradiated at $0 \pm 1^\circ$ for 6 hours. The reaction mixture changed color from brown to colorless (i.e., 100% conversion). After work-up, the gc analysis of both ampoules showed only 1,3-dibromopropane formed in the reaction mixture.⁴⁶ 1,3-Dibromopropane was identified by comparing the gc retention time with that of a commercial sample.

Run 13: Two ampoules were each charged with 0.027 g (0.65 mmol) of cyclopropane and bromine (4 ml, 65 mmol) and irradiated with the lamp at $0 \pm 1^\circ$, one for 30 minutes and the other for 90 minutes. Freon 113 (1 ml) was added to each opened ampoule. A yellow precipitate (sulfur) formed when the excess bromine was destroyed by ice-cold aqueous sodium thiosulfate. This reaction mixture was centrifuged, and the organic layer (Freon 113 layer) was pipetted into a vial. The gc analysis revealed only 1,3-dibromopropane formed. No cyclopropyl bromide was detected.

h. Bromination of cyclopropane by NBS

Run 14: Two ampoules were each charged with first 1.68 g (40 mmol) of cyclopropane and then with a solution of 0.71 g (4 mmol) of NBS in 2 ml of acetonitrile (mole ratio, cyclopropane:NBS:acetonitrile = 10:1:9.4). Some NBS precipitated, but the solid NBS disappeared during the 10 hours of irradiation at $0 \pm 1^\circ$. Thiosulfate titration showed that all NBS had been consumed. The gc analysis of both ampoules revealed the following product distribution: 1,3-dibromopropane (< 2%),

and bromocyclopropane ($> 98\%$). 1,3-Dibromopropane and bromocyclopropane were identified by comparing the gc retention times with those of commercial samples.

1. 11. Bromination of norbornane by bromine

Run 15: Two ampoules were each charged with a Freon 113 solution of norbornane and bromine (mole ratio, norbornane:bromine: Freon 113 = 6.95:1:16), and irradiated at $60 \pm 1^\circ$ for 4.5 hours. The reaction mixture changed color from brown to colorless (i.e., 100% conversion). The gc analysis revealed the average product distribution: exo-2-bromonorbornane ($67.7 \pm 0.8\%$), endo-2-bromonorbornane ($32.3 \pm 1.0\%$), and small amount of dibromonorbornanes.

j. Bromination of norbornane by NBS

Run 16: Three ampoules were each charged with a methylene chloride solution of norbornane and NBS (mole ratio, norbornane:NBS: methylene chloride = 6.78:1:117) and irradiated at $60 \pm 1^\circ$ for 4.5 hours. Thiosulfate titration showed that all NBS had been consumed. The gc analysis revealed the average product distribution: exo-2-bromonorbornane ($72.3 \pm 0.5\%$), endo-2-bromonorbornane ($19.7 \pm 0.8\%$), and 1-bromonorbornane ($8.0 \pm 0.1\%$).

k. Preparation of exo- and endo-2-bromonorbornanes by Kochi reaction¹⁸

exo-2-Norbornanecarboxylic acid (2.8 g, 0.02 mole, prepared by S. D. Elakovich), 20 ml of benzene, 8.86 g (0.02 mole) of lead tetraacetate, and 2.06 g (0.02 mole) of sodium bromide were placed consecutively in a 50-ml 3-neck round bottom flask fitted with a reflux condenser, a magnetic stirrer, and a nitrogen inlet. The condenser was

protected with a calcium chloride drying tube. The dark red mixture was heated at reflux for four hours. The resultant yellow liquid was separated from the brown precipitate. The filtrate was washed with dilute aqueous perchloric acid-sodium chloride solution, twice with 25-ml portions of sodium carbonate, and thrice with 25-ml portions of distilled water. It was dried over anhydrous magnesium sulfate overnight. The solution was filtered, and the gc analysis revealed the product distribution: exo-2-bromonorbornane (64.3%) and endo-2-bromonorbornane (35.7%).

2. Bromination of ethylbenzene by NBS

Run 17: An ampoule was charged with 2 ml of a solution of NBS in acetonitrile and then with ethylbenzene (mole ratio, NBS: ethylbenzene:acetonitrile = 1:10:19) and irradiated at $60 \pm 1^\circ$ for one hour. The sodium thiosulfate titration indicated 100% conversion. After work-up, the gc analysis showed styrene (formed by dehydrobromination in the gc instrument), α -bromoethylbenzene, and a trace amount of β -bromoethylbenzene. The attempt to detect this β -bromoethylbenzene failed because of the limitation of the sensitivity of the nmr instrument.

D. Miscellaneous Control Experiments

1. Control reaction for bromination of butyl bromide by bromine and by NBS

Analysis of mixtures of butyl bromide and bromine or NBS which were prepared as for Run 1 to Run 5 but not irradiated showed no bromination product.

2. Control reaction for bromination of cyclohexane by NBS

An ampoule was charged with a mixture of cyclohexane, NBS, and acetonitrile [saturated solution obtained by mixing cyclohexane, NBS, and acetonitrile (mole ratio, 10:1:26.5)] and heated at $60 \pm 1^\circ$ for 5 hours but not irradiated. Work-up as described in the General Procedure and gc analysis showed no bromination product.

3. Control reaction for bromination of cyclopropane by bromine

Analysis of a mixture of cyclopropane and bromine which was prepared as for Run 12 but not irradiated showed no 1,3-dibromopropane.

4. Addition of bromine to norbornene

Norbornene (10 g, 0.105 mole) in 20 ml of carbon tetrachloride was placed in a 100-ml 3-neck round bottom flask equipped with a reflux condenser, an addition funnel, and a magnetic stirrer. The mixture was stirred and cooled to -10° with an ice-salt bath. A solution of 14.5 g (0.09 mole) of bromine in 10 ml of carbon tetrachloride was added dropwise with stirring at a rate such that the temperature remained at or just below 0° . After the bromine solution had been added, the persistence of red color and lack of exothermicity indicated that the olefin had been consumed. Bromine was quenched by the addition of 25 ml of an aqueous sodium thiosulfate solution (prepared by adding water to 20 g of pure sodium thiosulfate to make 100 ml of solution. The reaction mixture was filtered to remove sulfur, washed with two 20-ml portions of distilled water, and dried over anhydrous magnesium sulfate overnight. A mixture was obtained; the gc pattern agreed with that reported.⁴⁹

5. Bromination of *exo*- and *endo*-2-bromonorbornanes by bromine

Four ampoules were each charged with about 2 ml of a mixture of 2.8 g (16 mmoles) of *exo*- and *endo*-2-bromonorbornanes (*exo/endo* = 1.8), 0.17 g of bromine (1.06 mmoles), and 14.9 g of Freon 113, and irradiated at $60 \pm 1^\circ$ for different times. Thiosulfate titrations showed the conversions to be 54% (6 min), 79% (13 min), 98% (25 min) and 100% (40 min). After work-up, all of the gc patterns of dibromonorbornanes were the same as that obtained from bromination of norbornane and different from that obtained from the addition of bromine to norbornene. The unreacted bromonorbornanes in these four runs all remained *exo/endo* = 1.8.

6. Control reaction of bromination of *exo*- and *endo*-2-bromonorbornanes by bromine

An ampoule was charged with a mixture of *exo*- and *endo*-2-bromonorbornanes, bromine, and Freon 113, as in control experiment 5, and heated at $60 \pm 1^\circ$ without irradiation for 4 hours. The gc analysis showed no bromination product, and the reactant *exo/endo* ratio remained 1.8.

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APPENDIX

NMR SPECTRA

VITA

Yu-Sun Lee was born on February 6, 1941, in Taipei, Taiwan, China. He completed his elementary and secondary education in Taipei, and entered the Chung Yuan Christian College of Science and Engineering in September 1961. He received the degree of Bachelor of Science in Chemical Engineering in June 1965. Following one year military service in Taiwan, he taught in the Chemistry Department of Fu Jen University (Taipei) for two years. He enrolled in the Graduate School of the University of Missouri, Columbia, Missouri, in September 1968, and transferred to the Graduate School of Louisiana State University in January 1969. He was married to Ya-wen Shih in 1969. He is currently a candidate for the Doctor of Philosophy Degree with a major in Organic Chemistry.

EXAMINATION AND THESIS REPORT

Candidate: Yu-Sun Lee

Major Field: Chemistry

Title of Thesis: Radical Brominations of Alkanic Positions by Bromine and by
N-Bromosuccinimide

Approved:

Major Professor and Chairman

Dean of the Graduate School

EXAMINING COMMITTEE:

Date of Examination:

March 5, 1974