Stereoelectronic Effects in the Brominations of Cyclopropylarenes and 9-Alkylanthracenes

by

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(ABSTRACT)

The free radical bromination of several cyclopropylarenes has been studied. The abstraction of a cyclopropyl hydrogen by bromine atom, which to date has been an unrecognized process, is demonstrated in this study. Specifically, when a cyclopropyl group is attached to the 9-position of an anthracene, an unprecedented hydrogen abstraction product, the corresponding cyclopropyl bromide, is obtained. This is believed to be due to stereoelectronic effects. Molecular mechanics calculations and X-ray crystallography have been used to demonstrate that 9-cyclopropylanthracene, unlike other cyclopropylarenes, is effectively locked in a conformation which places the α-cyclopropyl C-H bond in alignment with the p-orbitals of the aromatic system. This proper alignment activates the α-cyclopropyl hydrogen for abstraction by bromine atom. The relative reactivities of several 9-alkylanthracenes towards bromine atom are established, namely: 9-methyl- > 9-cyclopropyl- > 9-ethyl- >> 9-isopropylanthracene. Semi-empirical molecular orbital theory and molecular mechanics calculations have been utilized to demonstrate that the relative reactivities are not a function of bond dissociation energies but rather a function of the size of the dihedral angle between the α-C-H bonds and the plane of the central ring of the various 9-alkylanthracenes in their lowest energy conformations. The absolute rate constants for the abstraction of hydrogen by bromine atom from 9-methyl-, 9-cyclopropyl-, and 9-ethylanthracene are estimated to be 1.1×10^8 M^{-1} sec^{-1}, 3.8×10^7 M^{-1} sec^{-1} and 7.2×10^6 M^{-1} sec^{-1} respectively. The value for the primary hydrogen/deuterium isotope effect for the abstraction of hydrogen by bromine atom from 9-cyclopropylanthracene is determined to be 2.6. All of the above observations lend support to the importance of stereoelectronic effects in the free radical bromination of the cyclopropylarenes and 9-alkylanthracenes.

Dedication

The author wishes to dedicate this work to his dearest wife, , and their soon to be born first child.

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I am deeply grateful to Dr. James M. Tanko for his understanding, encouragement and guidance in the completion of this dissertation.

A special thanks goes to Dr. Joseph S. Merola and for providing me with the ORTEP drawings of the X-ray crystal structures.

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To , I extend my appreciation for his friendly support and stimulating discussions during the course of this research work.

I would like to express my gratitude to for her help in typing this dissertation.

Finally, I wish to affectionately remember my late parents, , and to acknowledge my dearest sister, , and brothers, and , for their confidence, sacrifice and love which spells the difference between success and failure.

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Chapter 1. Free Radical Bromination of Cyclopropylarenes

Literature Review

The nature of the reaction between a free radical and a cyclopropane derivative is strongly dependent on the identity and reactivity of the attacking radical (X·). Generally, two competing processes are observed (Figure 1): ring opening and hydrogen abstraction. Due to the unusually high dissociation energy of a cyclopropyl C-H bond (106 kcal/mole[1] vs. 98 and 95 kcal/mole for normal 1° and 2° hydrogens, respectively[2]), the hydrogen abstraction process is observed only for extremely reactive radicals, namely chlorine atom,[3,4] t-butoxy,[4] and imidyl.[5,6] For less reactive radicals, specifically bromine atom,[7,8] only the ring opening process is observed.

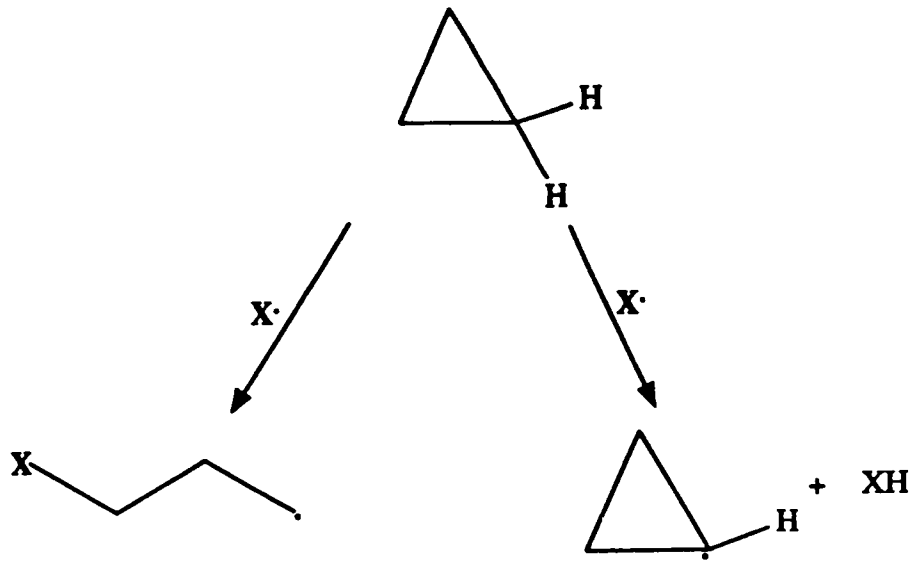


Figure 1. Reactions of cyclopropane with free radicals: ring opening and hydrogen abstraction

A review of the literature pertaining to the free radical bromination of alkyl- and arylcyclopropanes is given below.

The Free Radical Bromination of Alkylcyclopropanes

The free radical bromination of alkylcyclopropanes is a reaction which has been studied in detail. The reaction is rapid and proceeds exclusively via a ring opening process, yielding only the corresponding 1,3-dibromoalkane. Figure 2 depicts the generally accepted mechanism for the propagation steps. The key step involves the attack of Br· at the least-hindered carbon, giving rise to the most stable classical 1-bromo-3-alkyl radical. This radical in turn rapidly abstracts a bromine atom from Br_2 to both produce the 1,3-dibromide and regenerate a Br· which continues the chain reaction. Overall, the reaction can be simply

regarded as a formal 1,3-addition of Br_2 to an alkylcyclopropane to produce the ring-opened product, 1,3- dibromide.

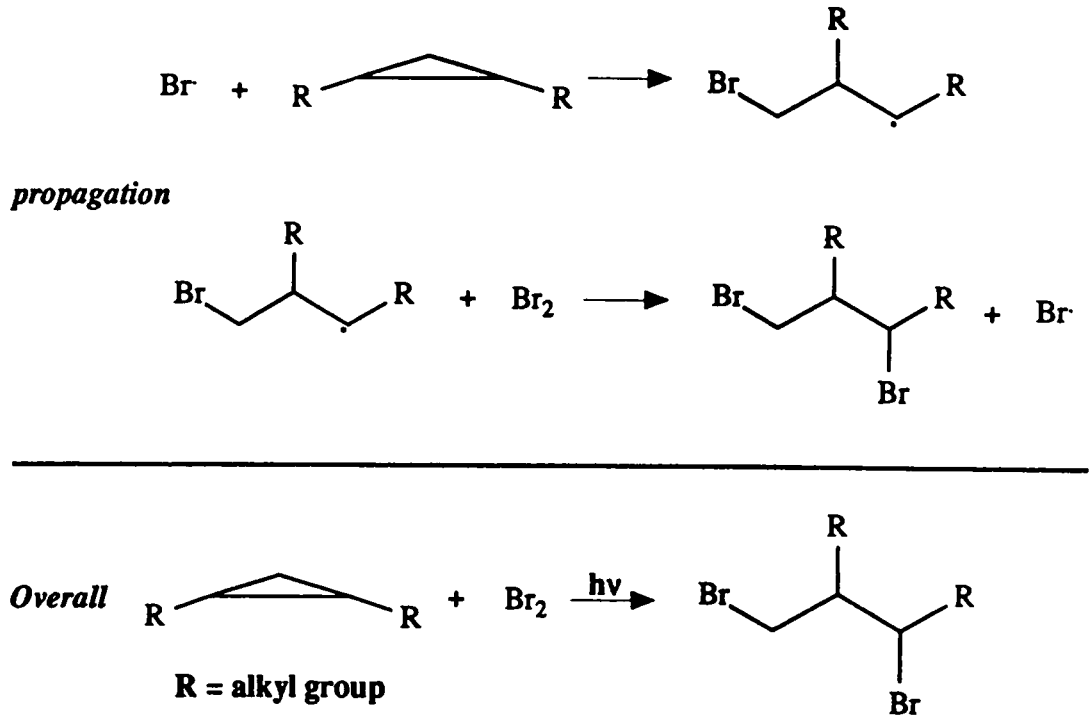
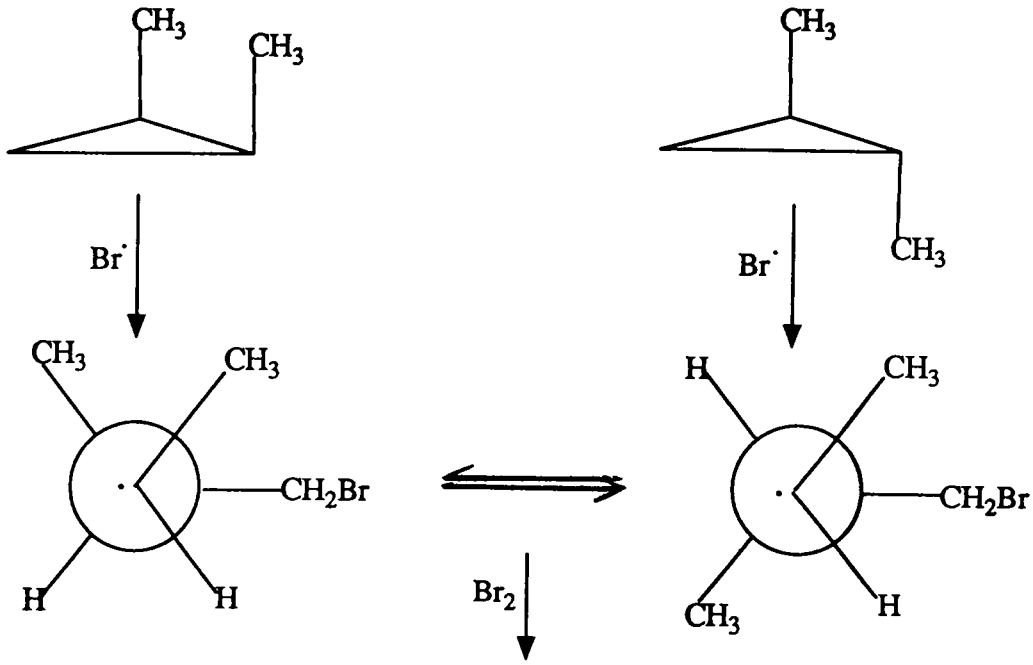


Figure 2. Mechanism for free radical bromination of alkylcyclopropanes

For example, the free radical bromination of cis- and trans-1,2- dimethylcyclopropane was reported to yield a 50:50 mixture of two diastereomers (erythro and threo) of 1,3-dibromo-2-methylbutane (**Eq. 1**).[8] The reaction was quantitative and free of ionic complications.[9] The fact that a 50:50 mixture of erythro- and threo-1,3-dibromo-2-methylbutane was obtained can be explained if the initial attack by Br· occurs at the methylene group accompanied by ring cleavage to a secondary alkyl radical which equilibrates by rotation before being trapped by Br_2. Loss of the stereochemical relationship between carbon atom 1 and 2 in the parent cyclopropane is expected to occur if a classical 1- bromo-3-alkyl radical

is the intermediate. On the other hand, if the initial attack by Br· had occurred at the more substituted carbon, 2,4-dibromopentane would have been the expected product, none of which was observed.

Eq.1



50:50 mixture of erythro- and threo-1,3-dibromo-2-methylbutanes

From a series of competition experiments, the relative reactivities of several alkylcyclopropanes towards Br· have been compared and the results are depicted in Table 1. As a point of interest, we note that an electronegative substituent decreases the rate of reaction relative to cyclopropane. For instance, when solutions of Br_2 and bromocyclopropane were photolyzed at -78 °C for 3 hr, no appreciable amount of reaction was detected; whereas under identical photolytic conditions, bromine color was completely discharged in less than

10 min from a solution of Br_2 and methylcyclopropane, producing exclusively 1,3-dibromobutane. Alkyl substituents, on the other hand, increase reactivity toward bromine atoms. The introduction of the first methyl group causes a 390-fold increase in rate. An additional 20- to 47-fold increase in rate is observed when the second substituent is introduced. The introduction of the third methyl group results in only an additional 3- to 7-fold increase in rate. This saturation effect on successive introduction of methyl substituents is reminiscent of similar effects, such as in the additions of bromine to olefins.[10]

Table 1. Relative Rates of Reaction of Alkylcyclopropanes with Bromine Atoms at -78°C[a]

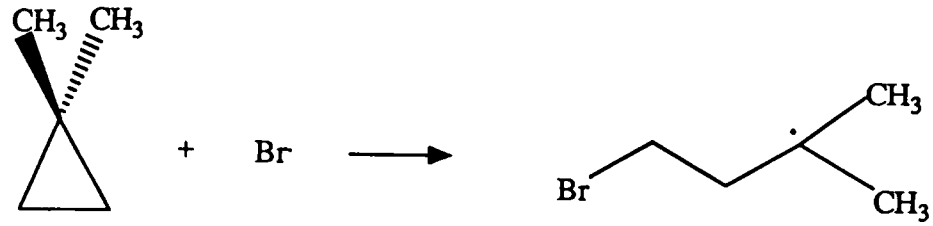
Compound	k_{rel}[b]	k_{rel}/CH_2[c]
Bromocyclopropane	Very slow	-
Cyclopropane	1	1
Methylcyclopropane	390	585
trans-1,2-Dimethylcyclopropane	8650	26,000
1,1-Dimethylcyclopropane	18,500	27,600
1,1,2-Trimethylcyclopropane	61,000	183,000

[a]Cited in reference 8. [b]Cyclopropane was arbitrarily chosen as unity. [c]Relative reactivity divided by the number of unsubstituted methylene groups.

Since Br· preferentially attacks the methylene group when one is available (because it is the least-hindered group), the reactivities of cyclopropanes should be compared after a statistical correction for the number of methylene groups. This comparison has a puzzling feature: the relative reactivities increase with increasing number of alkyl groups attached to the cyclopropane, but not simply correlated to the stability of the radical produced when the ring is opened. If the relative reactivities were dependent solely on the stability of the radical produced, then it would have been expected that 1,1-dimethylcyclopropane and 1,1,2-trimethylcyclopropane would show similar rates since both give rise to tertiary radicals. This is certainly not the case. The relative rates are 27,600 and 183,000 for 1,1-dimethylcyclopropane and 1,1,2- trimethylcyclopropane, respectively. Further, 1,1-dimethylcyclopropane is only 1.06x more reactive towards Br· than 1,2-dimethylcyclopropane.

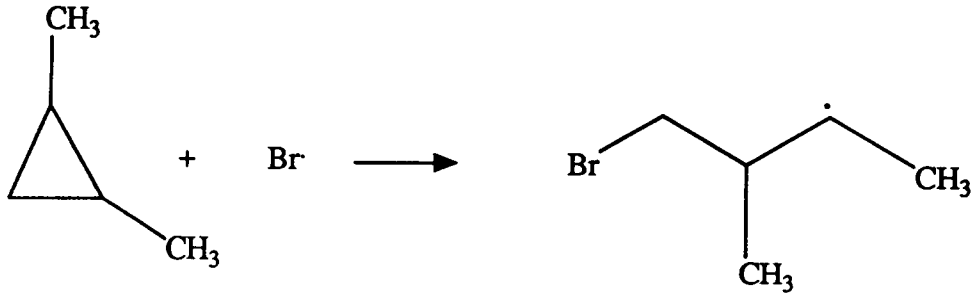
This result is also puzzling because 1,1-dimethylcyclopropane can form a tertiary radical (**Eq. 2**), whereas the 1,2-derivative can only form a secondary radical (**Eq. 3**).

Eq.2



tertiary radical

Eq.3



secondary radical

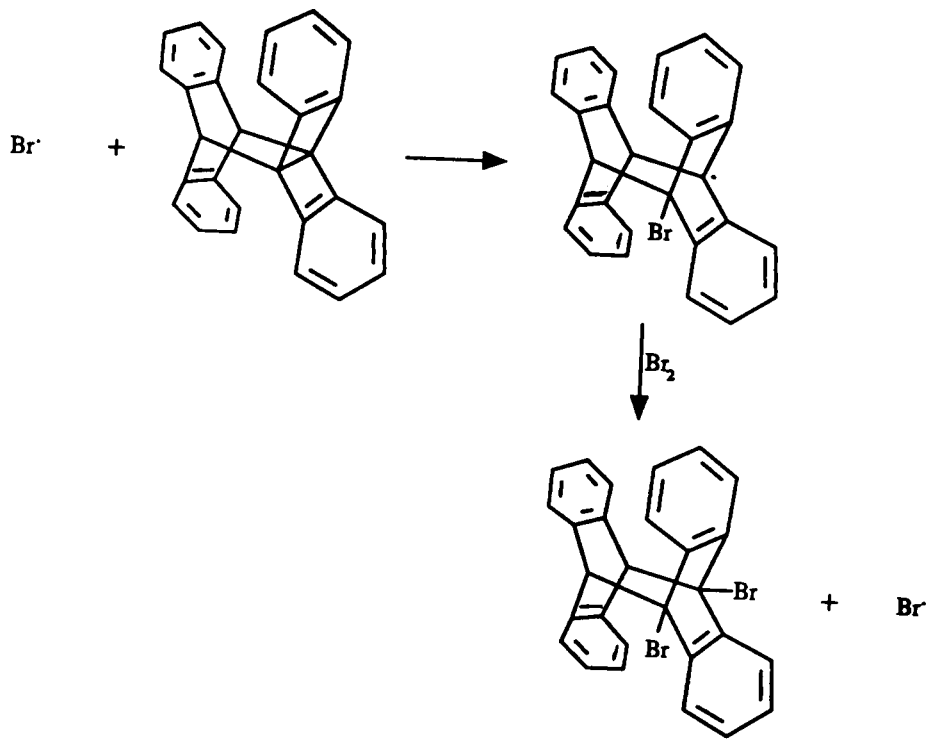
Stereochemistry of Ring Opening by Bromine Atom

One of the most common reaction pathways available for free radicals involves the attack on an atom of a molecule by an incoming radical to bring about the displacement of a fragment originally bound to the atom (i.e. substitution). This process is referred to by the symbols S_H2 (substitution, homolytic, bimolecular). Examples of S_H2 displacements at multivalent atoms are well documented, and has been reviewed by Ingold and Roberts.[11] The only examples of S_H2 displacements at saturated carbon involve the reactions of radicals with

the strained carbon-carbon bonds of cycloalkanes. Since one such radical is Br, a brief review of ring opening reactions induced by Br will be subsequently considered.

Applequist and Searle demonstrated that the free radical bromination of 9,10-dehydrodianthracene (strained Dewar form of anthracene) occurs with inversion at both carbon centers (**Eq. 4**).[12] However, this experiment does not delineate the preferred stereochemistry of S_H2 reaction at saturated carbon since attack with retention is sterically restricted.

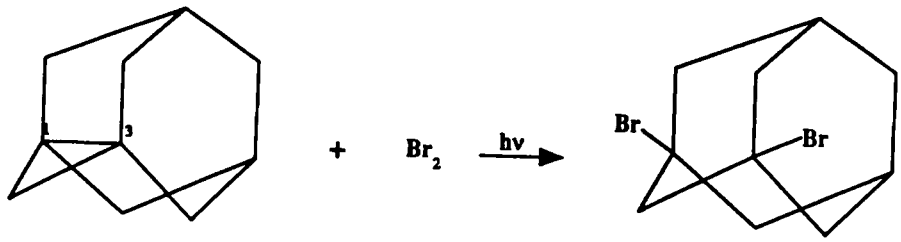
Eq.4



Pincock and Torupka reported that the formal addition of Br_2 across the internal bond of 1,3-dehydroadamantane occurs readily, with inversion of configuration at both carbon atoms 1 and 3, to yield 1,3-dibromoadamantane (**Eq. 5**).[13] The great activity of 1,3-dehydroadamantane is undoubtedly due to its highly constrained structure and its relaxtion to strainless adamantane as the internal 1,3 bond is broken. Hence, the ease of the radical-chain bromination reaction may be due less to the presence of a cyclopropyl ring than to the

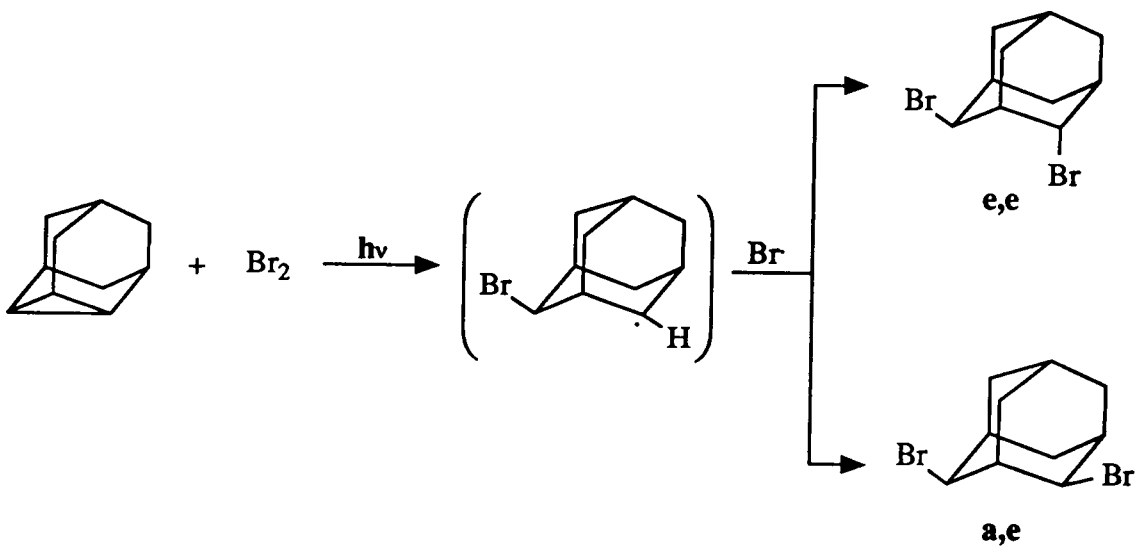
fact that all four bonds at carbon atoms 1 and 3 are extended almost from one side of these atoms.

Eq.5

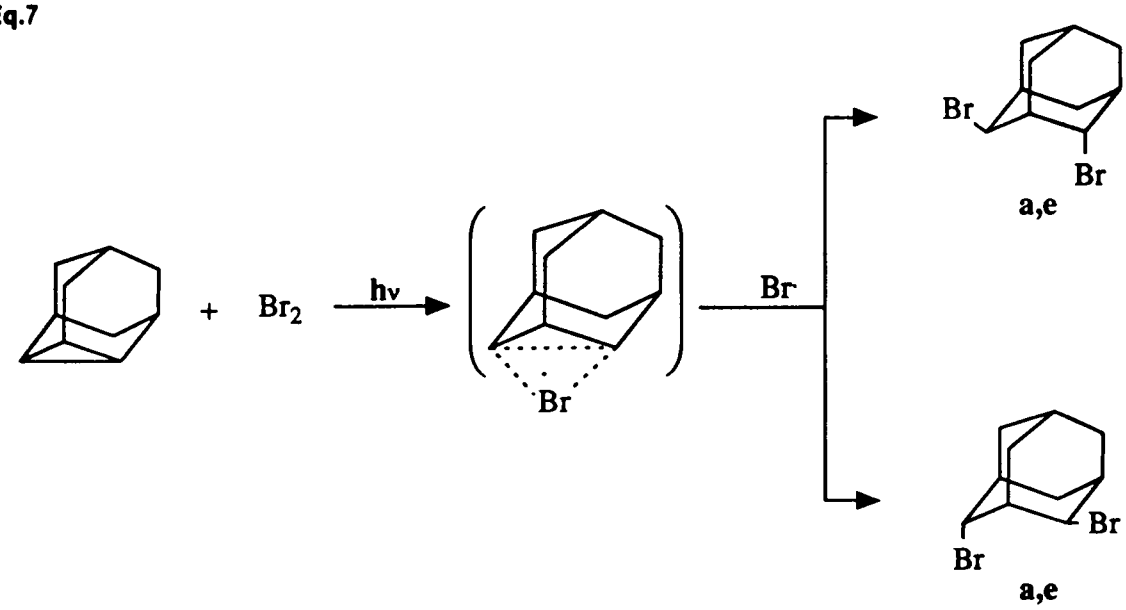


A slightly better representation for an S_H2 process was reported by Shea and Skell.[8] The free radical bromination of 2,4-dehydroadamantane occurs with inversion at one center and randomly at the other, yielding a mixture of (a,e)- and (e,e)-2,4-dibromoadamantane (**Eq.** 6). It is worthwhile to note that this experiment excludes an interpretation involving a 2,4-bridged radical since such bridging would have specified that the product be exclusively a,e (**Eq.** 7).

Eq.6



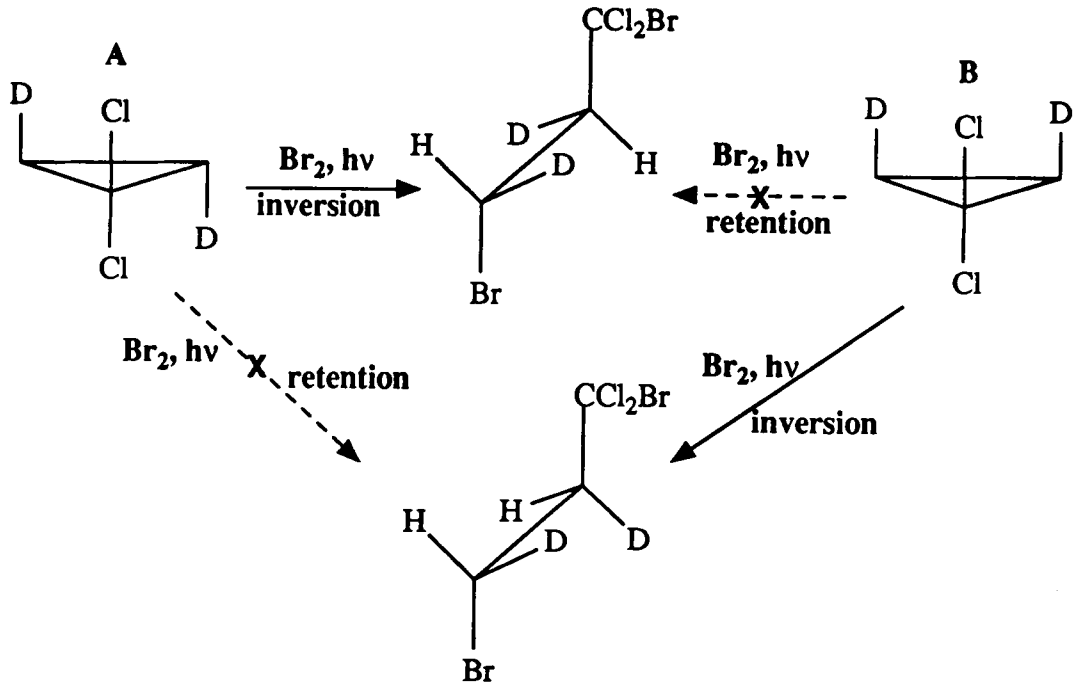
Eq.7



In the above examples, the cyclopropane ring is part of a structurally more complex polycyclic system, and since these molecules suffer some degree of steric and electronic bias, the ring opening process may not be stereochemically indicative of a monocyclic system. Unfortunately, there are only a few studies that actually examined the stereochemistry of the reaction between monocyclic cyclopropyl derivatives and bromine atom.

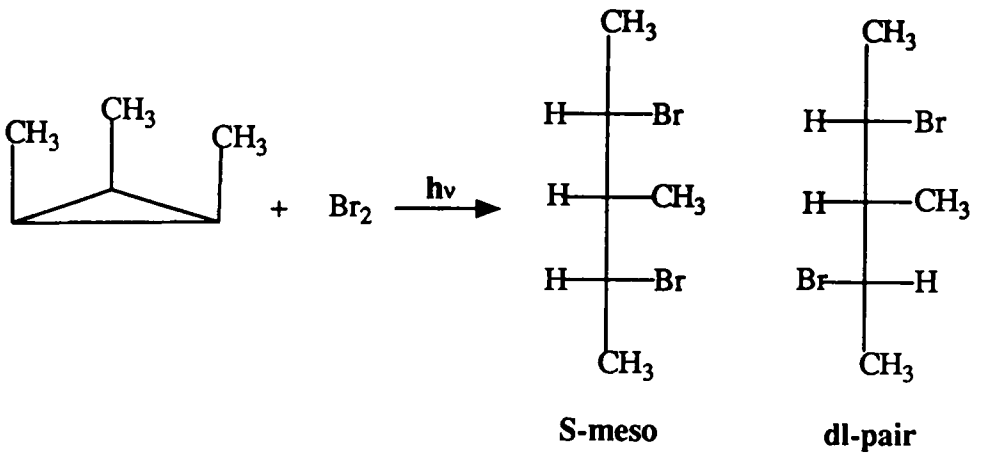
In 1972, Incremona and Upton reported the first example wherein the stereochemistry of the ring opening of a monocyclic cyclopropane was determined: the reaction of chlorine atom with 1,1-dichlorocyclopropane proceeds with >96% inversion of configuration.[14] Four years later (1976), they published a detailed study on the photochlorination and photobromination of deuterated 1,1-dichlorocyclopropanes.[15] Only the results of the free radical bromination will be described. The stereochemical possibilities for the products derived from the photobromination of the trans- and cis-1,1-dichoro-2,3-dideuteriocyclopropanes (**A** and **B**) are outlined in **Eq. 8**. Radical bromination of **A** gave exclusively the erythro-1,3- dibromo-1,1-dichloropropane-2,3-d_2, whereas **B** gave exclusively the threo isomer. This means that only products resulting from complete inversion of configuration at the initial reaction site (attack by Br) were obtained from both **A** and **B**. Furthermore, a Raman spectrum of recovered **B** revealed no evidence of any isomerization.

Eq.8



While the work of Incremona and Upton (vide supra) was in progress, the stereochemistry of the free radical bromination of cis- and trans-1,2,3-trimethylcyclopropane was investigated by Maynes and Applequist (1973).[16] They found that the cis isomer gave equal amounts of (S)-meso- and (dl)-3-methyl-2,4-dibromopentane (**Eq.** 9), while the trans isomer gave a mixture of the (R)-meso, (S)-meso, and (dl) products (**Eq.** 10). The absence of the R-meso form from the bromination products of the cis isomer indicates that the reaction is stereospecific at one center, and the presence of equal amounts of (dl) pair and S-meso form indicates that the reaction is random at the other center.

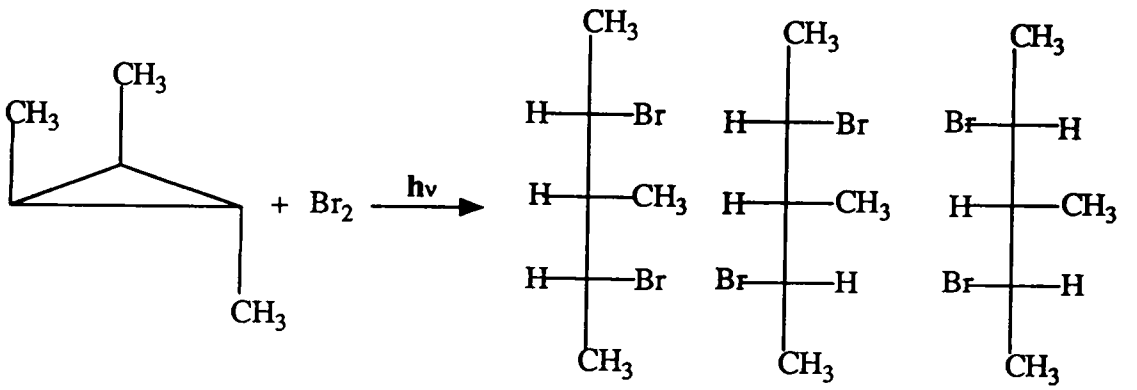
Eq.9



S-meso dl-pair

50:50 mixture

Eq.10



S-meso dl-pair R-meso

Thus, based on the work of Incremona and Upton and the work of Mayes and Applequist, it is reasonable to conclude that the reaction of monocyclic cyclopropyl derivatives with bromine atom proceeds with inversion of configuration at the initial reaction site (i.e. an S_H2 process) and does not involve a bridged radical species. This is illustrated by Figure 3, wherein the initial attack of Br· occurs at the minor lobe of C_2-C_1 hybrid orbital with concomitant breakage of the C_2-C_1 bond, leading directly to the ring-opened radical.

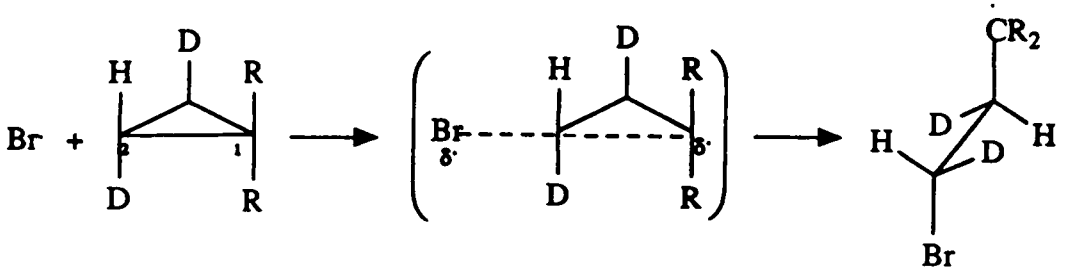


Figure 3. S_H2 mechanism

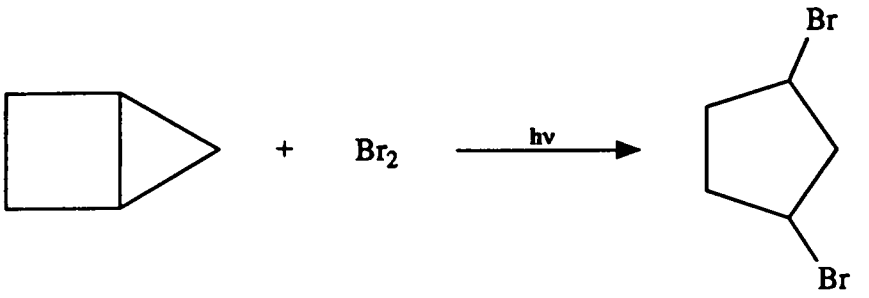
Regiochemistry of Ring Opening by Bromine Atom

The free radical brominations of alkyl-substituted cyclopropanes usually show a consistent pattern of behavior: cleavage of the ring between the least and most substituted carbon atoms. For a 1,2-dialkylcyclopropane, this means that the 1,3 bond is broken.

A variation in the regiochemistry of Br_2 addition has been observed for highly strained derivatives. The transformation of 1,3-dehydroadamantane to 1,3-dibromoadamantane by the addition of Br_2 (vide supra) is an example wherein the initial attack of Br occurs at the more substituted carbon rather than at the less-hindered cyclopropyl methylene carbon. Relief of strain has been postulated to account for this result.[13] Similarly, Ingold and Walton reported that the free radical bromination of bicyclo[2.1.0]pentane results in the exclusive formation of 1,3- dibromocyclopentane, a product derived from the breakage of the internal carbon-carbon bond (**Eq. 11**).[17] The fact that the initial attack by Br does not occur at the methylene group of the cyclopropane is attributed to relief of ring strain. Specifically, attack at the cyclopropylmethylene carbon would lead to loss of the cyclopropane ring strain energy (ca. 27.5 kcal/mol) but retention of the cyclobutane ring strain energy (ca. 26.5 kcal/mol). On the other hand, S_H2 attack at any of the bridgehead carbon leads to relief of both the

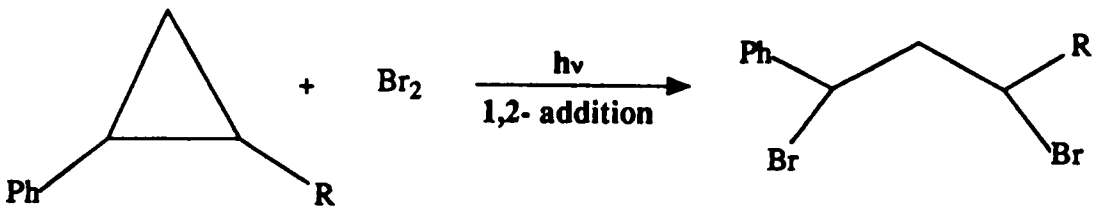
cyclopropane and cyclobutane ring strain energies with only the much smaller cyclopentyl radical strain energy (<6.5 kcal/mol) remaining.

Eq.11



The Free Radical Bromination of Arylcyclopropanes

The mechanism, stereo- and regiochemistry of the free radical bromination of arylcyclopropanes has not been studied in nearly as much detail as for alkylcyclopropanes. While the overall reaction involves the formal addition of Br_2 to a cyclopropyl C-C bond, the regiochemistry of the reaction differs from that of alkylcyclopropanes. For example, radical-chain bromination of cyclopropanes consisting of 1,2-diaryl substituents or 1-aryl and 2-alkyl substituents, results in a 1,2-addition (Figure 4), compared to the 1,3-addition generally associated with 1,2- disubstituted alkylcyclopropanes.



R = aryl or alkyl group

Figure 4. The regiochemistry of free radical bromination of arylcyclopropanes

In 1955, Kuivila and co-workers reported that the free radical bromination of both 1-phenyl-2-isopropylcyclopropane and 1-phenyl-2-ethylcyclopropane give only products resulting from the cleavage of 1,2-bonds.[18] In 1972, LaLonde and co-workers reported that the brominations (electrophilic and free radical) of cis- and trans-1,2-diphenylcyclopropanes produce only 1,2-bond cleaved products.[19] In 1973, Shea and Skell agreed with this 1,2 bond cleavage pattern. They found that the free radical bromination of 1-methyl-2-phenylcyclopropane followed by reduction of the dibromide products with tri-n-butyltin hydride (n-Bu_3SnH) afforded only n-butylbenzene in a 96% yield.[8]

Apart from the observed 1,2-bond cleavage pattern, there is little known about the mechanism of the free radical bromination of arylcylopropanes. Shea and Skell have proposed that the initial $Br^{\cdot}$ attack occurs on the aromatic nucleus, placing the $Br^{\cdot}$ closest to the cyclopropane ring atom bearing the aryl group, and that the stereochemistry is being controlled at the aryl bearing carbon rather than at the alkyl bearer (Figure 5).[8] However, there has not been any experiment reported which tests the validity of this hypothesis.

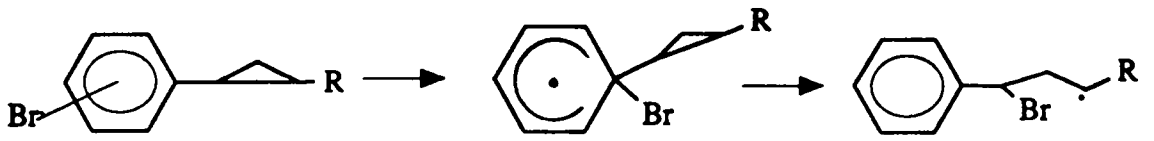
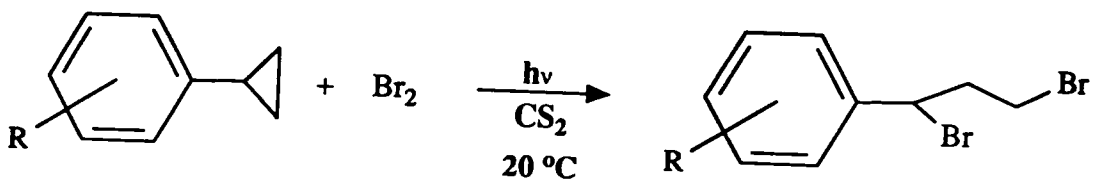


Figure 5. Benzylic attack mechanism

Applequist and McKenzie reported that the competitive photobromination of substituted phenylcyclopropanes in carbon disulfide at 20 °C (**Eq.** 12) gave linear Hammett plots with σ^+ (ρ = -1.84, correlation coefficient - 0.996) or with σ (ρ = -2.16, correlation coefficient - 0.982).[20] The substituent effect is similar to that found in homolytic bromination of toluenes.[21,22] To account for the negative ρ and good correlation with σ^+, Applequist and McKenzie suggested that the transition state for cyclopropane brominolysis has some charge separation (Figure 6). Although this is in accord with the substituent effect observed and tends to suggest β-attack, further experiments are needed to exclude the benzylic attack (see Figure 5). In other words, the transition state suggested by Applequist and McKenzie does not fully explain the regiospecificity of the addition of bromine to phenylcyclopropanes.

Eq.12



a, R = p-phenyl
b. R = p-phenyl
c, R = p-Br
d, R = m-Br
e, R = p-I
f, R = p-CN
g, R = NO_2

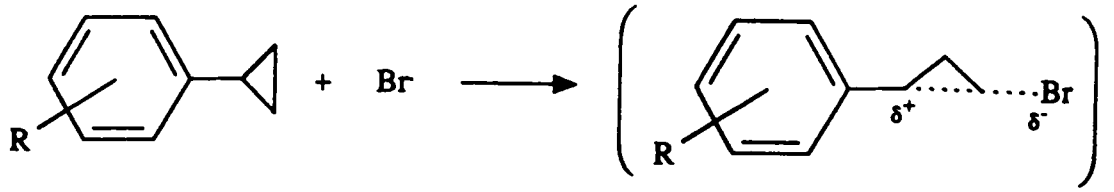


Figure 6. β-attack mechanism

The work of LaLonde and co-workers[19] raises questions regarding the distinction between electrophilic and free radical brominations of arylcyclopropanes. For example, the reaction of Br_2 with phenylcyclopropane (in the presence and absence of light) gave a mixture of brominated products, arising from cyclopropyl ring opening and aromatic substitution processes. It is likely that the nucleus substituted product is a result of electrophilic addition of Br_2 to the arylcyclopropane, while the cyclopropyl ring-opened product may arise from either or both free radical and electrophilic pathways.

A group of Russian researchers have carried out a study on the competition of radical and nonradical mechanisms in the dark low-temperature (160-300 K) bromination of phenylcyclopropane.[23] Their reported results reflect the following: (1) radical bromination with cyclopropane ring cleavage (favored at higher temperatures and higher Br_2 concentrations), (2) nonradical bromination with cyclopropane ring cleavage (favored below 200 K), and (3) nonradical bromination of the aromatic ring (favored at low temperatures but above 200 K). These findings suggest that the reaction between Br_2 and arylcyclopropane is characterized not only by products resulting from cyclopropyl ring opening (via radical and nonradical mechanisms) but also by products resulting from electrophilic aromatic substitution.

In view of the above, a more thorough investigation than the work of LaLonde and co-workers is needed to clearly distinguish or take into account the degree of contributions

from both the free radical and electrophilic processes in reactions involving Br_2 and arylcyclopropanes.

Kuivila and co-workers utilized N-bromosuccinimide (NBS) to brominate 1-phenyl-2-alkylcyclopropanes and reportedly obtained only cyclopropyl cleavage products; the possible presence of other products was not ascertained. Contrary to this report, arylcyclopropanes are reported by other research groups to be "inert" to NBS even in the presence of radical initiators.[24,25] Therefore, the use of NBS in free radical bromination of arylcyclopropanes also needs a more judicious investigation.

Hydrogen Abstraction versus Ring Opening Processes

One of the major factors influencing reactivity of radical reactions is the strength of the bonds being broken and formed. Bond dissociation energies provide information for predicting the feasibility of radical reaction (thermodynamics) and are a source of insight into reactivities (kinetics). Data pertaining to bond energies have been obtained by a variety of techniques and are available with varying reliability for an increasingly large number of compounds.[26-29]

Although theoretical treatments attempting to predict activation energies in terms of the dissociation energies of the bonds involved are generally too inaccurate to be useful in making detailed kinetic predictions, the Polanyi equation[30] ($E = \alpha[H + C]$, where α and C are positive valued constants), which predicts a linear relation between activation energy and enthalpy of related reactions, has been demonstrated to hold for several radical reactions[31] including hydrogen abstraction by bromine atom.[32] Therefore, whether or not bond energies can be used to make effective quantitative predictions of activation energies, a prediction of simply the exothermic or endothermic nature of a reaction is in itself of great importance, since the activation energy of an endothermic reaction must be at least as large as the

enthalpy of the reaction. This means that a reaction step which is strongly endothermic must have a high activation energy, while an exothermic step may require little activation energy.

A possible explanation as to why the abstraction of a cyclopropyl hydrogen by Br· has never been reported in the free radical bromination of any cyclopropane derivative, can be derived by considering the enthalpy of the ring opening and hydrogen abstraction processes. Using the bond dissociation energies of the selected molecules given in Table 2, we can show that the ring opening reaction is exothermic while the hydrogen abstraction reaction is strongly endothermic, $\Delta H^{\circ} = -8$ and $+18$ kcal/mole, respectively. Therefore, it is likely that the hydrogen abstraction process has a very high activation energy whereas the ring opening process has a considerably low activation energy. Apparently, the hydrogen abstraction process is disfavored and the ring opening process favored to such an extent that it completely dominates the nature of the reaction of cyclopropanes with Br·.

Table 2. Bond Dissociation Energies of Selected Molecules

Bond	BDE at 298 K (kcal/mole)	Refs.
C-C (of c-C_3H_6)	61	33
C-H (of c-C_3H_6)	106	1
Br-H	88	34
C-Br (of $CH_3CH_2CH_2$-Br)[a]	69	34

[a]As a close opproximation for the dissociation energy of Br-C bond of the 1-bromoalkyl radical.

Research Objectives

As discussed in the preceding literature review, abstraction of a cyclopropyl hydrogen by Br has never been observed. Using simple thermodynamic arguments, this fact is readily rationalized. Nonetheless, we believed that all the factors contributing to the relative reactivity of the C-H and C-C bonds in cyclopropyl compounds had not fully been explored. Using fundamental concepts of chemical reactivity, our objective in this research was to design suitable cyclopropane-containing compounds for which the hydrogen abstraction by Br would be more prevalent. If successful, this might lead to a better understanding of the factors relating to C-H and C-C bond reactivity in general.

With the understanding that Br is inherently a low energy radical, a careful selection of a suitable cyclopropyl derivative may be the key to observing the abstraction of a cyclopropyl hydrogen by Br. It is not unreasonable to suppose that the presence of an appropriate R-group (substituent on the three-membered ring) may activate the adjacent cyclopropylmethine hydrogen to such an extent that it can be readily abstracted by an attacking Br, and therefore giving a chance for the hydrogen abstraction process to compete with the ring opening process. The question is, what type of an R-group would provide the desirable effects ?

Since free radical brominations of alkylcyclopropanes has been thoroughly studied, and in all reported cases only the ring-opened products (1,3-dibromides) were obtained, an alkyl substituent seems unlikely as a suitable choice for the R-group. On the other hand, not as much is known about the free radical brominations of arylcyclopropanes. Furthermore, a hydrogen which is adjacent to an aromatic ring system (e.g. a side-chain hydrogen of toluene or methylanthracene) is known to be readily abstracted by Br. This is because the p-orbitals of an aromatic ring can activate an adjacent C-H bond, and provide direct stabilization to a developing radical center. In view of these, an appropriate aryl substituent may just be the right choice for the R-group with the desirable effects.

Another factor which may prove to be important in preferentially activating the C-H bond relative to the C-C bond, is the preferred conformation of the cyclopropyl moiety in the cyclopropylarene derivatives: the cyclopropyl C-H bond must be properly aligned with the adjacent p-orbitals in order for it to be strongly activated (Figure 7). In other words, the C-H bond must be coplanar with the p-orbitals to fully realize the "driving force" of the π-system which may be the key factor in enabling a $Br^{\cdot}$ to abstract the cyclopropyl hydrogen. Our research will also explore this issue.

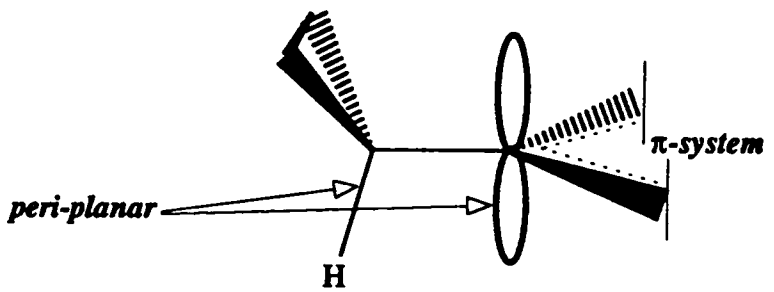
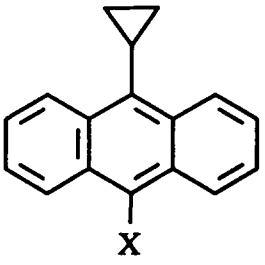


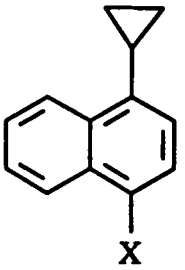
Figure 7. **Ideal conformation for a cyclopropyl C-H bond to be fully activated by an adjacent π-system**

Results and Discussion

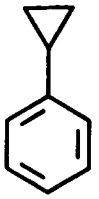
The results of the free radical and electrophilic brominations of 9-cyclopropylanthracene system (**1**, X = H, Br, and Cl), 1-bromo-4-cyclopropylnaphthalene (**2**, X = Br),[35] and phenylcyclopropane (**3**) under a variety of conditions are summarized in Table 3.



1a, X = H
1b, X = Br
1c, X = Cl



2, X = Br



3

It can be seen in each instance shown in Table 3 that under the conditions employed for the bromination of the various cyclopropylarenes, there is a distinct difference between the free radical and ionic reactions. For example, comparing expts. 10 with 11, or 14 with 15, we see that 100% of the corresponding ring-opened products were obtained in expts. 10 and 14 versus no product obtained in expts. 11 and 15. All experiments were carried out under similar conditions with the only difference being that expts. 10 and 14 were performed in degassed solutions in the presence of light, which serves as an initiator for the free radical reaction. In constrast, expts. 11 and 15 were performed in the dark in non-degassed solutions. In these non-degassed solutions, dissolved oxygen inhibits the free radical reaction. Furthermore, for the 9-cyclopropylanthracene system, the dark reaction is not only comparatively slow but also gives rise to a completely different product than that obtained from the light-initiated reaction.

Table 3. Bromination of Cyclopropylarenes under a Variety of Conditions.

Expt.[1]	c-Arenes[2]	Brominating agent reaction conditions[3]	Temp. (° C)	Results[3]	Type of Process
1	1a	Br_2/light/CH_2Cl_2 (5 min)	-78	AnCHBrCH_2CH_2Br (90%)	Radical
2	1a	Br_2/dark/CH_2Cl_2 (5 min)[4]	-78	1b (5%)[5]	Ionic
3	1a	NBS-Br_2/dark/CCl_4 (1 hr)	15	1b (100%)	Ionic
4	1a	NBS/Bz_2/CCl_4(40 min)	80	An-c-CBr$(CH_2)_2$(100%)	Radical
5	1a	Br_2/light/CCl_4 (45 min)[6]	77	An-c-CBr$(CH_2)_2$ (70%)	Radical
6	1b	Br_2/light/CCl_4 (5 min)	15	An*-c-CBr$(CH_2)_2$ (95%)	Radical
7	1c	Br_2/light/CCl_4 (5 min)	15	An**-c-CBr$(CH_2)_2$ (95%)	Radical
8	1b	Br_2/dark/CCl_4 (1 hr)	15	An*-CHBrCH_2CH_2Br (100%)	Ionic
9	1c	Br_2/dark/CCl_4 (1 hr)	15	An**-CHBrCH_2CH_2Br (100%)	Ionic
10	2	Br_2/light/CCl_4 (15 min)	15	Br$C_{10}H_6$CHBrCH_2CH_2Br (100%)	Radical
11	2	Br_2/dark/CCl_4 (15 min)[4]	15	No reaction[7]	Ionic
12	2	NBS/Bz_2O_2/CCl_4 (1 hr)	80	No reaction[7]	-
13 i	3	Br_2/light/CCl_4 (5 min)	0	C_6H_5CHBrCH_2CH_2Br (100%)	Radical
13 ii	3	Br_2/light/CCl_4 (5 min)	15	C_6H_5CHBrCH_2CH_2Br (100%)	Radical
14 i	3	Br_2/light/CH_2Cl_2 (5 min)	-78	C_6H_5CHBrCH_2CH_2Br (100%)	Radical
14 ii	3	Br_2/light/CH_2Cl_2 (5 min)	15	C_6H_5CHBrCH_2CH_2Br (100%)	Radical
15 i	3	Br_2/dark/CH_2Cl_2 (5 min)[4]	-78	No reaction[7]	Ionic
15 ii	3	Br_2/dark/CH_2Cl_2 (5 min)[4]	0	No reaction[7]	Ionic
15 iii	3	Br_2/dark/CH_2Cl_2 (5 min)[4]	15	No reaction[7]	Ionic
16	3	NBS/Bz_2O_2/CCl_4 (1.5 hr)	80	No reaction[7]	-

[1]In all experiments, a 1:1 molar ratio of cyclopropylarene:brominating agent was utilized.

[2] **1a** = 9-cyclopropylanthracene; **1b** = 9-bromo-10-cyclopropylanthracene; **1c** = 9-chloro-10-cyclopropylanthracene; **2** = 1-bromo-4-cyclopropylnaphthalene; **3** = phenylcyclopropane

[3]Key: **light** = irradiated with a 400W medium pressure Hg arc lamp at a distance of 1-2 ft. through at least two layers of Pyrex; **dark** = non-degassed solution, excluded from light; **NBS** = N-bromosuccinimide; **Bz_2O_2** = benzoyl peroxide (2-3 mole-%); **An** = 9-substituted anthracene moiety; **An*** = 9-bromo-10-substituted anthracene moiety; **An**** = 9-chloro-10-substituted anthracene moiety;
Values in parentheses denote yield of products which were determined by proton NMR spectroscopy using appropriate internal standards.

[4]Excess Br_2 was quenched with a suitable olefin before analysis.

[5]95% of the substrate (1a) was recovered.

[6]Br_2 was conducted into solution by means of a gentle stream of nitrogen with concurrent irradiation.

[7]100% of the substrate (corresponding cyclopropylarene) was recovered.

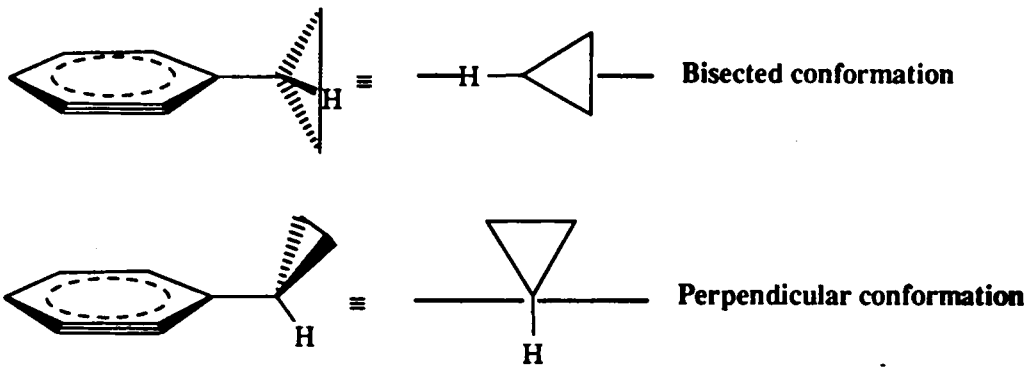
As noted in expts. 1 and 2, respectively, the photobromination of 9-cyclopropylanthracene at -78 °C yields over 90% of 1,3-dibromo-1-anthrylpropane in 5 min while the dark bromination gives rise to 9-bromo-10-cyclopropylanthracene in only 5% yield. This distinction is also seen when comparing expts. 6 with 8, and expts. 7 and 9. The photobromination of 9-bromo- and 9-chloro-10-cyclopropylanthracene at 15 °C produces 95% of the hydrogen abstraction products (9-bromo- and 9-chloro-10-{α-bromocyclopropyl}anthracenes, respectively) in 5 min whereas the dark bromination produces exclusively the ring-opened products (1,3-dibromo-1-{9-bromoanthryl}propane and 1,3-dibromo-1-{9-chloroanthryl}propane, respectively) in 1 hr. Therefore, we can conclude that under the conditions employed, the reaction proceeding via ionic process is comparatively slow and does not contribute to the product obtained from the free radical chain process.

However, at room temperature (see expt. 3), the electrophilic aromatic substitution becomes a significantly important competing reaction in the photobromination of 9-cyclopropylanthracene using Br_2. To overcome this problem, it was necessary to use NBS as the brominating agent in carbon tetrachloride solvent (see expt. 4). We will return to this point later in our discussion.

When the free-radical brominations of the various cyclopropylarenes are compared, it can be noted that the nature of the reaction (ring opening or hydrogen abstraction) depends on the identity of the aryl moiety and the reaction conditions. When the cyclopropyl group is attached to the central ring of an anthracene system, the free radical bromination using molecular bromine produced predominantly an unprecedented hydrogen abstraction product at room temperature (see expts. 6 and 7), while at a low temperature, -78 °C, the ring-opened product predominated (see expt. 1). In contrast, when the cyclopropyl group is attached to a naphthyl or phenyl system only the ring-opened product was obtained at all temperatures (see expts. 10, 13 and 14). In addition, the 9-cyclopropylanthracene system was the only cyclopropylarene that was reactive towards NBS in carbon tetrachloride solvent, yielding exclusively the hydrogen abstraction product, 9-(α-bromocyclopropyl)anthracene (see expts. 4, 12 and 16).

The observed chemoselectivity (ring opening versus hydrogen abstraction) can be explained by considering the conformational preferences of the cyclopropylarenes.

For phenylcyclopropane, it has been demonstrated by ^{1}H NMR studies that the **bisected** conformation is favored over the **perpendicular** conformation by about 1.4 kcal/mole.[36] This conformational preference of a cyclopropyl attached to a π-system is general, and is usually ascribed to the conjugative interaction between the C-C bond of the cyclopropyl group and the p-orbitals of the adjacent π-system.[37]



A plausible explanation for the nature of the conjugative interaction can be derived by considering the Walsh model for cyclopropane.[38-40] According to this model, three sp^2-hybridized -CH_2- groups with their associated p and sp^2 orbitals (Figure 8) are combined (in such a manner that the sp^2 hybrids are oriented radially in a plane toward the center) to form the 3-membered ring.

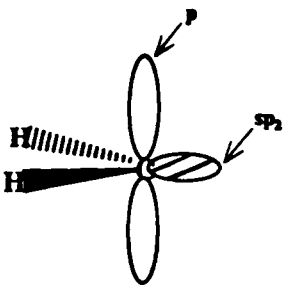


Figure 8. p and sp^2-hybridized orbitals of a -CH_2- group

The molecular orbital diagram depicted in Figure 9 results from the combination and normalization (energy minimization) of this basis set.[41] Strictly speaking, Ψ_2 looks more like a normal C-C σ bond and Ψ_3 looks more like a π bond.

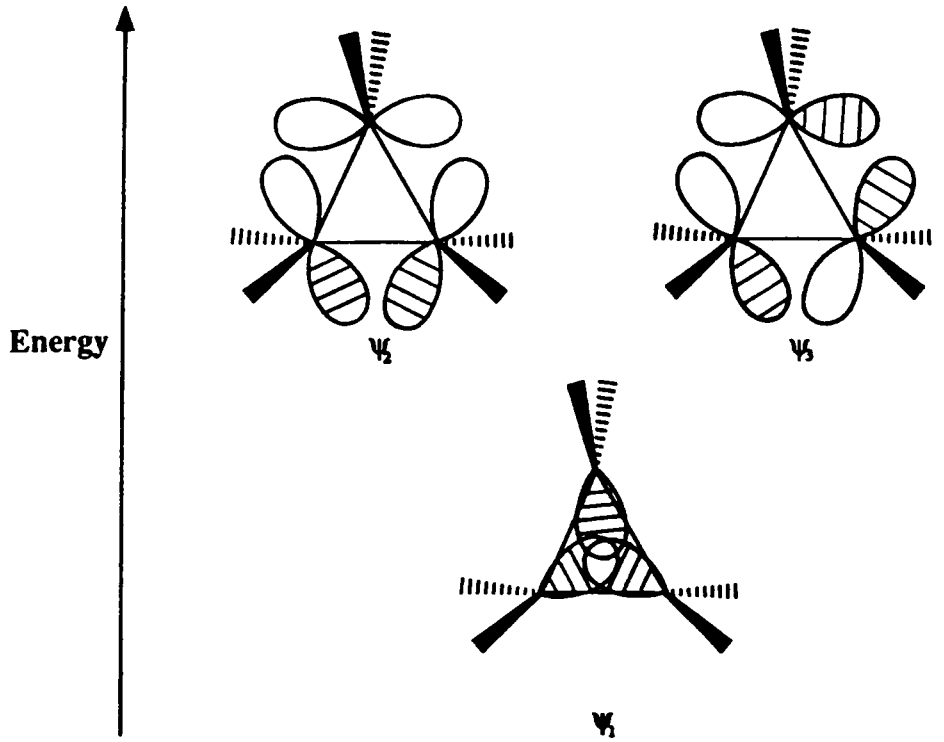
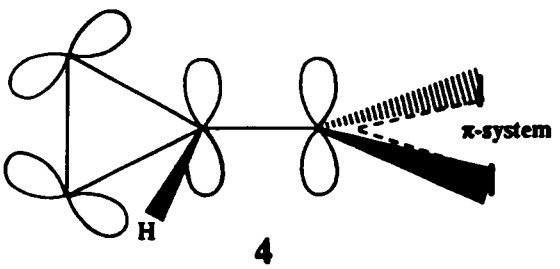


Figure 9. The Walsh model for cyclopropane

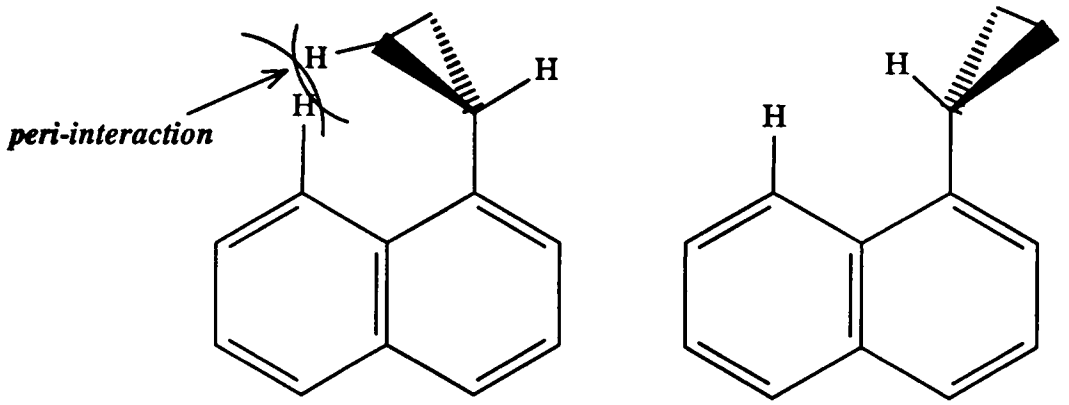
Now consider the symmetry of the orbitals involved in a system such as 4.



4

The bisected conformation allows maximum overlap of the "p-orbital" on the cyclopropyl carbon with the p-orbital on the adjacent π-system, whereas the symmetric conformation does not allow this interaction since the corresponding p-orbitals are orthogonal to each other. It is the favorable overlap or interaction (conjugative interaction) of these orbitals that favors the bisected over the perpendicular conformation.

For the α-naphthyl derivative, there are two non-degenerate bisected conformations, **BI-SYN** and **BI-ANTI**. It is likely that due to the peri-interaction (steric interaction between the cis-methylene hydrogens of the cyclopropyl and the hydrogen at position 8 of the naphthyl moiety), the **BI-SYN** conformation is disfavored.



BI-SYN **BI-ANTI**

For the 9-cyclopropylanthracene system, it is reasonable to expect that the peri-interaction (steric interaction between the cis-methylene hydrogens of the cyclopropyl and the hydrogen at position 1 or 8 of the anthryl moiety) destabilize the bisected conformation (Figure 10). This destabilization is perhaps to such a degree that the perpendicular conformation is preferred at the expense of the conjugative interaction present in the bisected conformation.

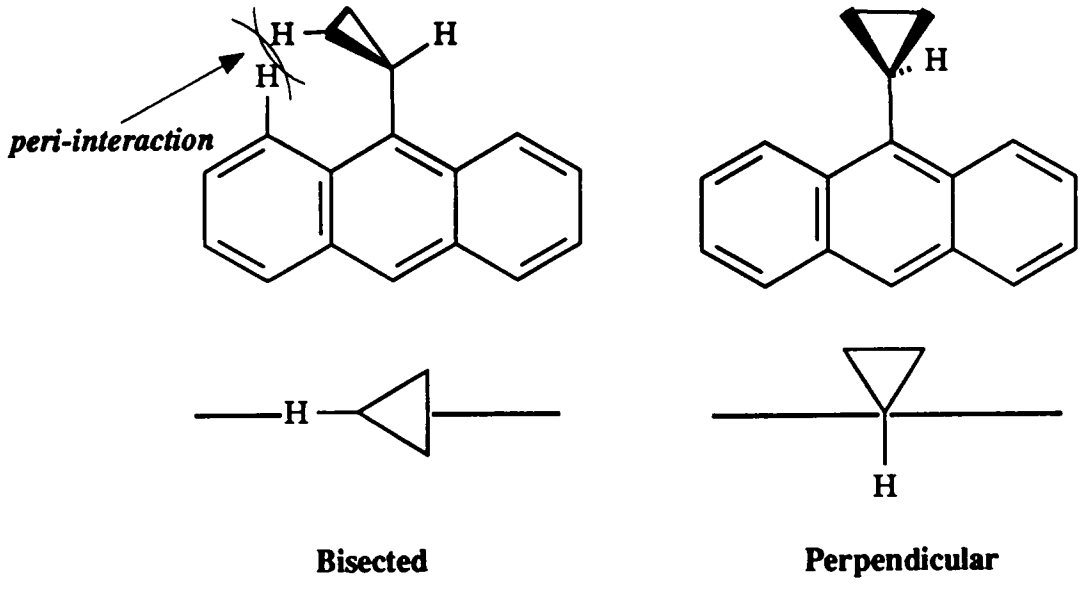


Figure 10. Bisected and perpendicular conformations of 9-cyclopropylanthracene

The expected conformational preferences discussed above are supported by molecular mechanics calculations[43] performed on the cyclopropylarenes. A summary of these calculations is presented in Table 4. A cyclopropyl group attached to a phenyl ring is fairly free to rotate within a 360° framework (rotational barrier being only about 1.3 kcal/mole), and has a slight preference for the bisected conformation. When attached to an α-position of a naphthalene system, the cyclopropyl group disfavors the **BI-SYN** conformation over both the **BI-ANTI** and perpendicular conformations. The perpendicular conformation has the lowest energy. However, the cyclopropyl group can readily attain the **BI-ANTI** conformation because the rotational barrier between the perpendicular and the **BI-ANTI** conformations is only about 1.4 kcal/mole (i.e. the cyclopropyl is fairly free to rotate within a 180° framework). In the case of 9-cyclopropylanthracene, there is a significant difference in energy, 8.0 kcal/mole, between the bisected and the perpendicular conformations, with the latter being the lower energy

conformation. Since the barrier to interconvert these two conformations is large, 12.0 kcal/mole, it is reasonable to suppose that the molecule is essentially locked in the perpendicular conformation. This point is illustrated in Figure 11.

Table 4. Conformational Equilibria in Cyclopropylarenes

Aryl group	Conformational equilibria[1]	ΔE^{o} (kcal/mol)[2]	ΔE_a (kcal/mol)[2]
Phenyl	BISECTED ⇋ PERPENDICULAR	1.2	1.3
Naphthyl	PERPENDICULAR ⇋ BISECTED-ANTI	1.3	1.4
	PERPENDICULAR ⇋ BISECTED-SYN	5.2	8 - 9
Anthryl	PERPENDICULAR ⇋ BISECTED	8.0	12.0

[1]Lowest energy conformation on left side of equilibrium [2]Calculated (molecular mechanics, QCPE 395/QCPE 318)[43]

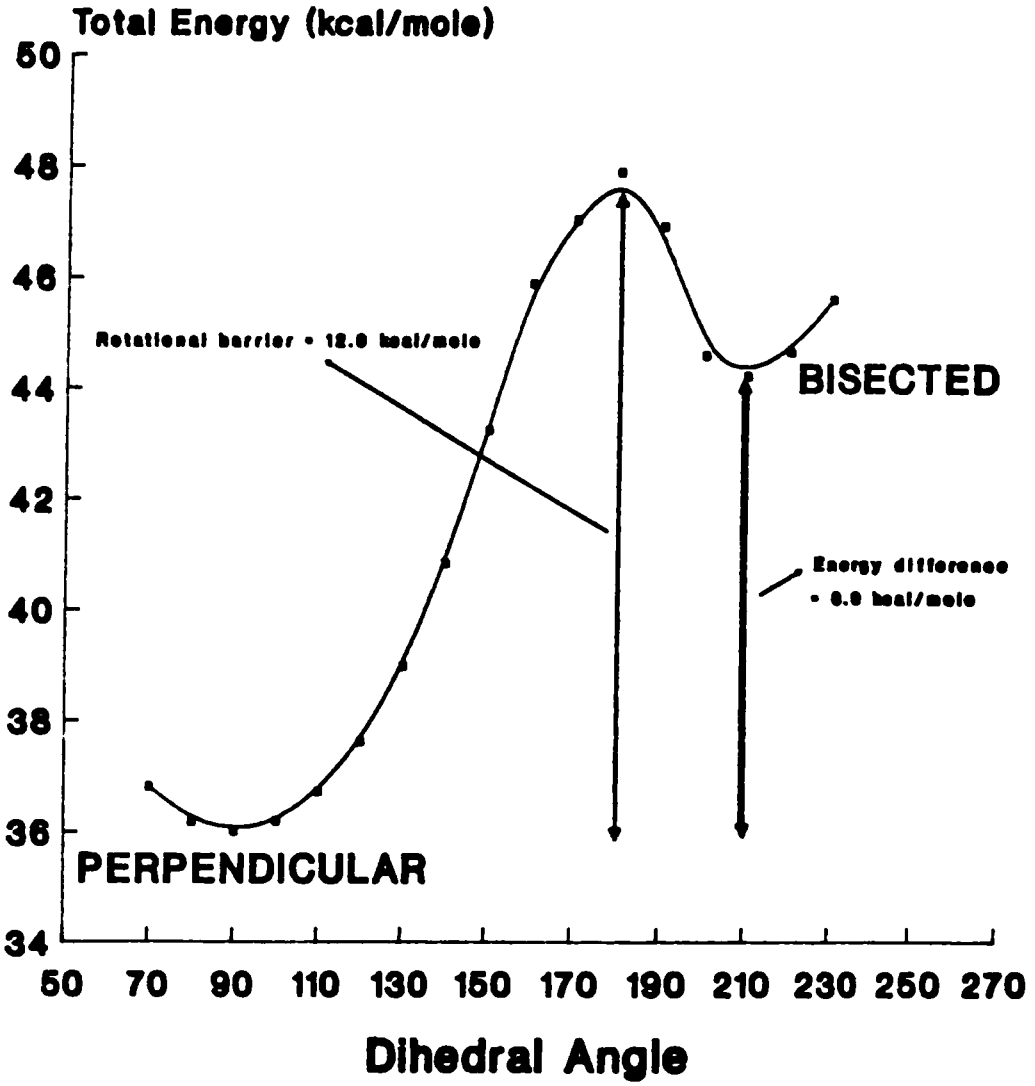


Figure 11. A profile of the relative total energies of several conformations of 9-cyclopropylanthracene

The results of the molecular mechanics calculations are in agreement with the X-ray crystal structures of solid derivatives of the cyclopropylarenes; namely, 2,4-dinitrophenylhydrazine derivative of p-cyclopropylacetophenone, 4-cyclopropyl-1 -naphthalene carboxylic acid and 9-chloro-10-cyclopropylanthracene.[44] The latter exists in the perpendicular conformation (Figure 12), the 4-cyclopropyl-1-naphthalene carboxylic acid exists in the conformation that is in between the perpendicular and **BI-ANTI** conformations (Figure 13), and the 2,4- dinitrophenylhydrazine derivative of p-cyclopropylacetophenone exists in the bisected conformation (Figure 14). Recently, De Boer and co-workers reported that phenylcyclopropane itself exists in the bisected conformation in the solid state (the X-ray crystal structure of this compound was determined at -30 °C).[45]

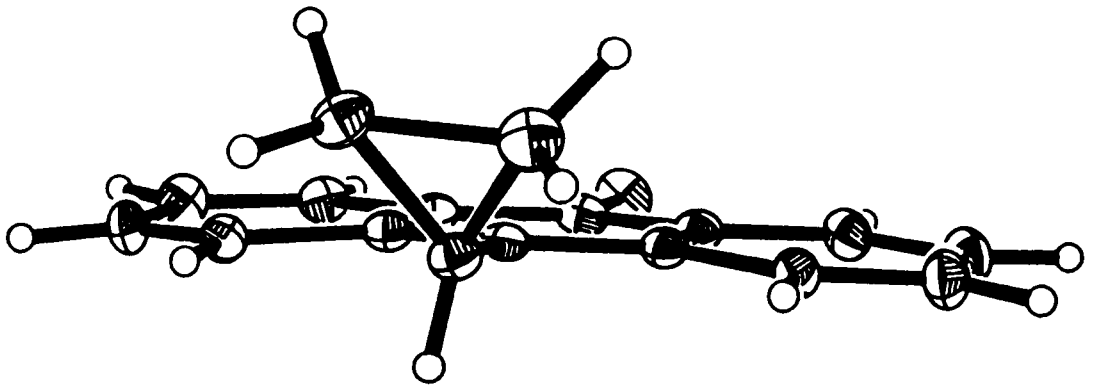


Figure 12. An ORTEP drawing of the X-ray crystal structure of 9-chloro-10-cyclopropylanthracene

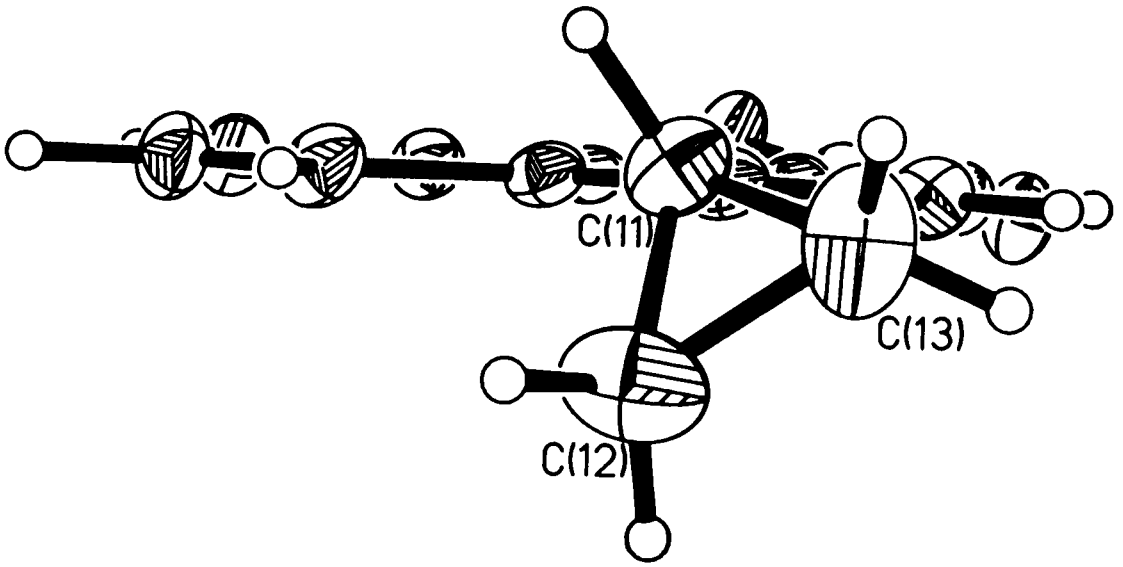


Figure 13. An ORTEP drawing of the X-ray crystal structure of para-cyclopropylnaphthalene carboxylic acid

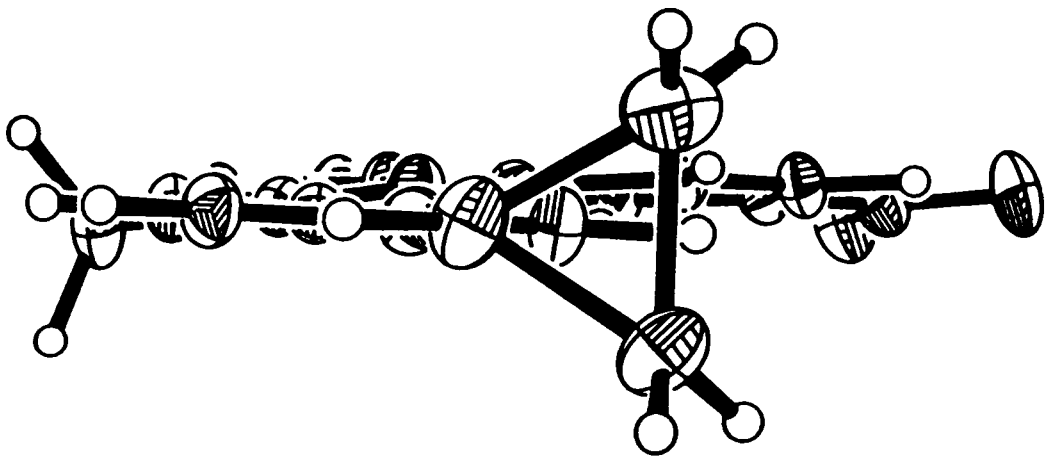


Figure 14. An ORTEP drawing of the X-ray crystal structure of 2,4-dinitrophenylhydrazine derivatives of para-cyclopropylacetophenone

Consider phenylcyclopropane: since it can readily adopt the bisected conformation in a solution, the C-C bond of the cyclopropyl group can attain proper alignment with the p-orbitals of the phenyl ring. Thus when Br· attacks the cyclopropyl group, the p-orbitals of the phenyl ring can furnish benzylic stabilization to the transition state of the normally observed ring opening reaction (Figure 15).

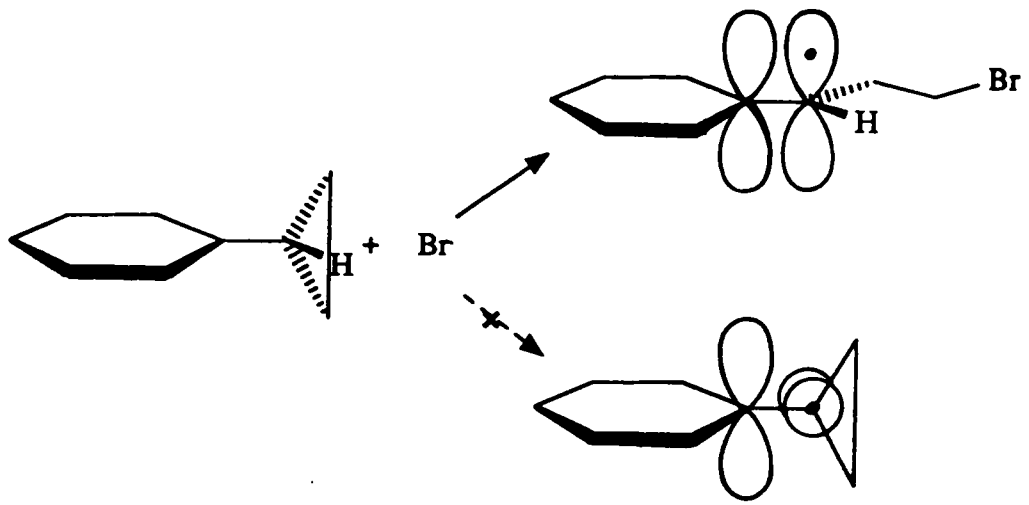


Figure 15. Stereoelectronic effects in the free radical bromination of phenylcyclopropane

A different situation arises when a cyclopropyl group is attached to the central ring of an anthracene system. In this case, the cyclopropyl group is locked in the perpendicular conformation, and therefore the C-H bond, instead of the C-C bond of the cyclopropyl group, is in parallel alignment with the p-orbitals of the adjacent π-system. This proper alignment activates the cyclopropylmethine hydrogen for abstraction by Br· relative to the C-C bond. In other words, when Br· attacks the cyclopropyl group, the p-orbitals of the adjacent anthryl system provides direct stabilization to the developing radical center in the transition state (Figure 16). Since this favorable stereoelectronic effect is not realized in the ring opening process, it is, therefore, comparatively disfavored. In addition, since the p-orbitals are

orthogonal to the C-C bond of the cyclopropyl group the resonance effect is "turned-off". Consequently, the 9-anthryl system might deactivate the cyclopropyl C-C bond because aryl group is known to be electron withdrawing inductively.[46] Thus, the fact that free radical bromination of 9-cyclopropylanthracene system gives rise to unprecedented hydrogen abstraction products is attributable not only to the enhanced reactivity of the cyclopropylmethine C-H bond but probably also to the reduced reactivity of the C-C bond of the cyclopropyl group.

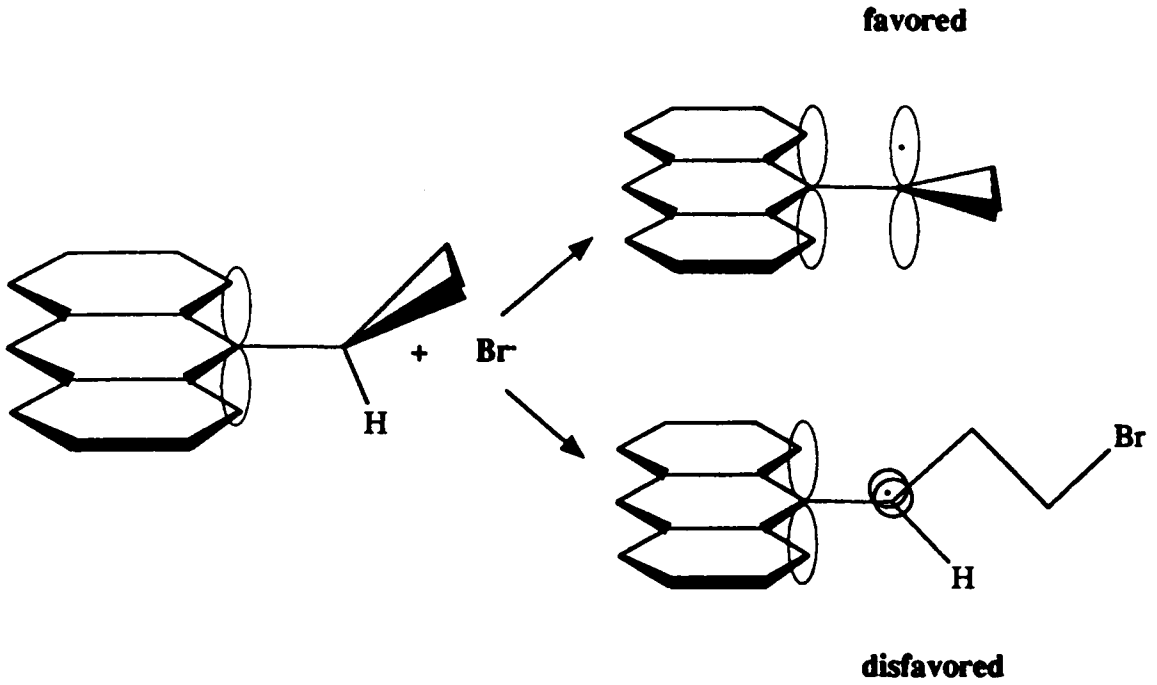


Figure 16. Stereoelectronic effects in the free radical bromination of 9-cyclopropylanthracene

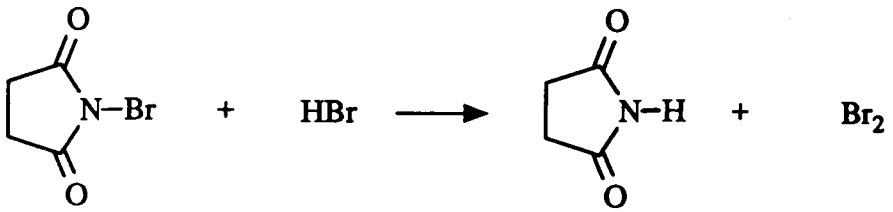
For the α-cyclopropylnaphthalene system, since the cyclopropyl group is not locked in the perpendicular conformation, the p- orbitals of the naphthyl ring are not properly aligned to activate the cyclopropylmethine hydrogen for abstraction by Br. Furthermore, the reactivity of the cyclopropyl C-C bond is not strongly affected (reduced) since the resonance effect on this bond is not completely "turned-off". Thus, because the ideal stereoelectronic effects

requirement for hydrogen abstraction is not present in the α-cyclopropylnaphthalene system, the reaction of Br· with this system proceeds only via the normal cyclopropyl ring opening pathway.

As mentioned earlier, to overcome the competing ionic bromination in the photobromination of 9-cyclopropylanthracene at high temperature it was necessary to use NBS as the brominating agent in carbon tetrachloride solvent. This can be readily explained by considering the mechanism for the radical-chain bromination using NBS. The Goldfinger mechanism (proposed by Goldfinger[47] in 1953) given below is the currently accepted mechanism.[21,48-50] Br· is the chain carrier while NBS acts simply as an HBr scavenger and therefore, as a reservoir capable of sustaining a low steady-state concentration of Br_2 during the reaction. This very low concentration of Br_2 is the reason why radical-chain bromination using NBS is free from any complication due to the competing ionic reaction. It is important to note that the crucial factor in precluding imidyl chain reaction is the use of carbon tetrachloride as the solvent (Ziegler conditions[51]) because both NBS and succinimide are insoluble in this solvent.

Goldfinger Mechanism

$$Br\cdot + R\text{-}H \longrightarrow R\cdot + HBr$$

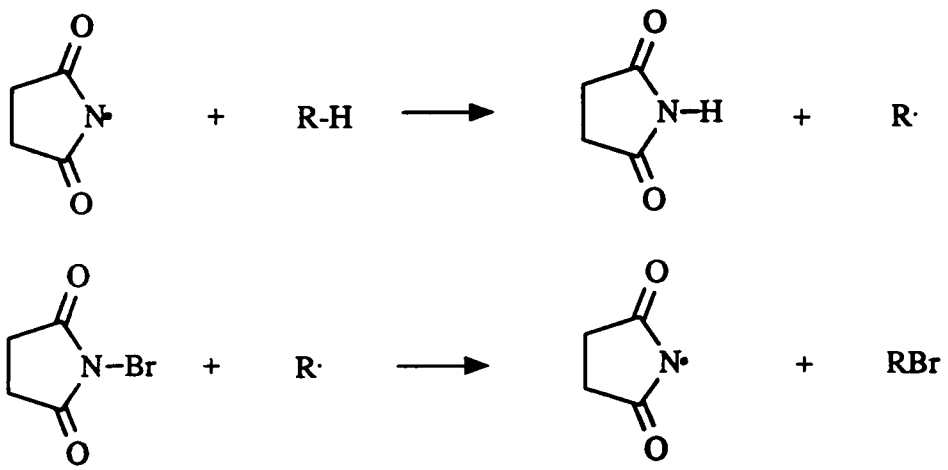


$$R\cdot + Br_2 \longrightarrow RBr + Br\cdot$$

The first evidence that bromination with Br_2 in low concentration mimicks an NBS bromination was presented in 1958 by Sixma and Riem.[64] They observed that the slow introduction of Br_2 by a gentle stream of nitrogen into a refluxing solution of cyclohexene in carbon tetrachloride irradiated with a mercury lamp resulted in an 84% yield of 3-bromocyclohexene. Similar observations of allylic substitution with low-concentration of Br_2 were reported in 1961 by McGrath and Tedder.[65] If the slow introduction of Br_2 in the presence of light can allow allylic bromination to occur at the expense of Br_2 adduct formation with a double bond, then under similar experimental conditions involving 9-cyclopropylanthracene, it should also be possible to produce side-chain bromination at the expense of aromatic substitution. This was indeed the case (see expt. 5 in Table 3). Introduction of Br_2 by a mild but steady stream of dry nitrogen into a reaction vessel containing 9-cyclopropylanthracene in refluxing carbon tetrachloride with concurrent irradiation resulted in a 70% yield of 9-(α-bromocyclopropyl)anthracene. The result of this experiment also supports the Goldfinger mechanism.

An alternate mechanism suggested by Bloomfield[52] in 1944 (known as the Bloomfield Mechanism), which was widely accepted for some time, involves succinimidyl radicals in the chain propagating steps.

Bloomfield Mechanism



Quite recently (1985), Skell and Luning have reviewed the procedures for observing imidyl radical chains in reactions of N-bromoimides.[53] These authors pointed out that if a solvent, such as acetonitrile or dichloromethane, is used in which a given N-bromoimide has a higher solubility, chemistry attributable to imidyl radical can be observed. To examine the reaction of an imidyl radical with 9-cyclopropylanthracene, we carried out the photoinitiated reaction of 9-cyclopropylanthracene with 3,3-dimethyl-N-bromoglutarimide (33DMNBG) in degassed dichloromethane (conditions conducive to imidyl radical chains). Analysis of the resulting mixture with a combination of GC and ^{1}H NMR techniques revealed that only a product arising from the addition of glutarimidyl radical to the aromatic nucleus was formed with no indication of any hydrogen abstraction product. The result of this experiment differs from that obtained in the reaction of 9-cyclopropylanthracene with NBS in carbon tetrachloride (i.e, in the latter reaction the hydrogen abstraction product, 9-{α-bromocyclopropyl}anthracene was readily and exclusively obtained). Thus, the Bloomfield mechanism can be ruled out as a possible mechanism in our system as well.

As stated earlier, only the anthryl system with a cyclopropyl group attached to the central ring of the anthracene nucleus could be brominated by NBS in carbon tetrachloride. In retrospect, this result is not surprising since under Ziegler conditions (NBS/CCl_4), $Br^{\cdot}$ is the chain carrier and NBS serves as an HBr scavenger yielding Br_2 and succinimide (i.e., the Goldfinger mechanism). For the phenyl and naphthyl systems, hydrogen abstraction did not occur. That means no HBr was formed which was needed to maintain (by reacting with NBS) a low steady-state concentration of Br_2. Thus, no reaction was observed.

There is no clear explanation as to why the photobromination of 9-cyclopropylanthracene using molecular bromine at -78 °C gives rise to predominantly (>90%) the cyclopropyl ring-opened product, 1,3- dibromo-1-anthrylpropane. It is interesting to note, however, that a similar temperature dependence in the free radical chlorination of cyclopropane has been reported by Walling and Fredricks.[4] As an explanation for this phenomenon, these authors suggested that the ring opening process has a lower activation

energy, but a smaller probability (i.e., a more favorable Arrhenius pre-exponential factor for the hydrogen abstraction process).

We attempted to determine the rate of ring opening versus hydrogen abstraction processes, k_{RO}/k_{HA} (Figure 17), in the photobromination of 9-bromo-10-cyclopropylanthracene using molecular bromine at several temperatures. Unfortunately, due to the instability of the ring-opened product we were unable to make precise quantitative measurements of this product. Also, the dark reaction (**Eq. 13**) contributed significantly to the formation of the ring-opened product (Table 5), thus adding to the difficulty in accurately measuring the amount of this product.

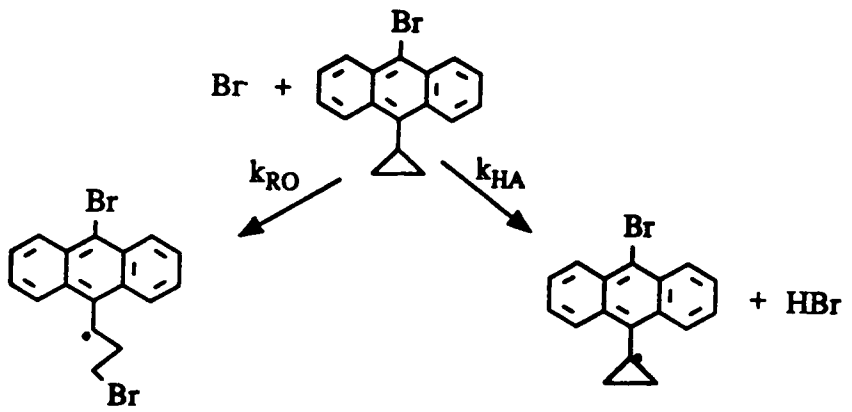


Figure 17. Ring opening versus hydrogen abstraction in the free radical bromination of 9-bromo-10-cyclopropylanthracene

Eq. 13

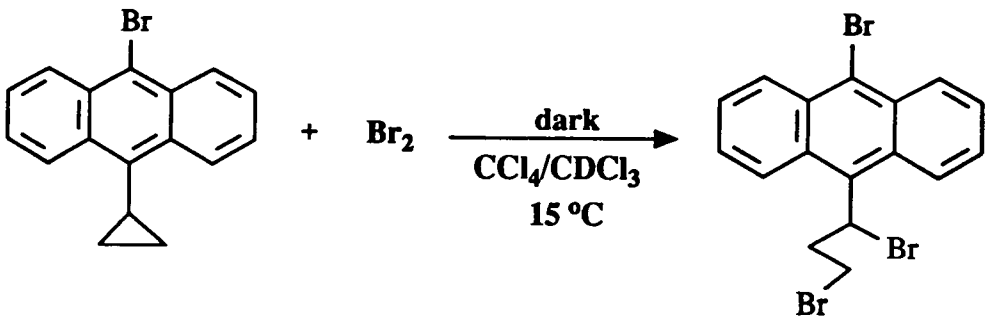


Table 5. Brominations of 9-Bromo-10-Cyclopropylanthracene at Different Temperatures

Expt.	Reaction Conditions	Temp. (°C)	% ABr[a]	% BBr_2[b]
1	Br_2/light/CCl_4 (5 min)	18.0	95	5
2	Br_2/dark/CCl_4 (5 min)	18.0	0	10-15
3	Br_2/light/CH_2Cl_2 (5 min)	0.0	90	10
4	Br_2/dark/CH_2Cl_2 (5 min)	0.0	0	5-10
5	Br_2/light/CH_2Cl_2 (5 min)	-12.0	80	20
6	Br_2/dark/CH_2Cl_2 (5 min)	-12.0	0	5-10

[a]ABr = 9-bromo-10-(α-bromocyclopropyl)anthracene
[b]BBr_2 = 1,3-dibromo-1-(9-bromoanthryl)propane

Chapter 2. Electrophilic Bromination of Cyclopropylarenes

In order to distinguish between the free radical and electrophilic brominations of cyclopropylarenes, it was necessary also to examine the electrophilic process in detail. This chapter describes the results of these experiments.

Literature Review

Electrophilic Addition of Bromine to Alkylcyclopropanes

Photobrominations of cyclopropane and its alkyl derivatives, are rapid, clean reactions, even at -78 °C, yielding exclusively 1,3-dibromoalkanes via a free radical chain process.[8] In stark contrast, when the free radical process is suppressed, cyclopropane and bromine do not react in the dark except in the presence of Lewis acid catalyst, such as

$AlCl_3$;[9] alkylcyclopropanes react sluggishly but rarely produce 1,3-dibromoalkanes as major products.[56,57] A solution of an alkylcyclopropane and bromine in the dark usually results in a mixture of isomeric mono-, di-, and tribromoalkanes; the latter is often the major product (Figure 18). The presence of mono- and vicinal dibromoalkanes can not be explained by any reasonable mechanistic path involving the initial attack of molecular bromine on the alkylcyclopropane.

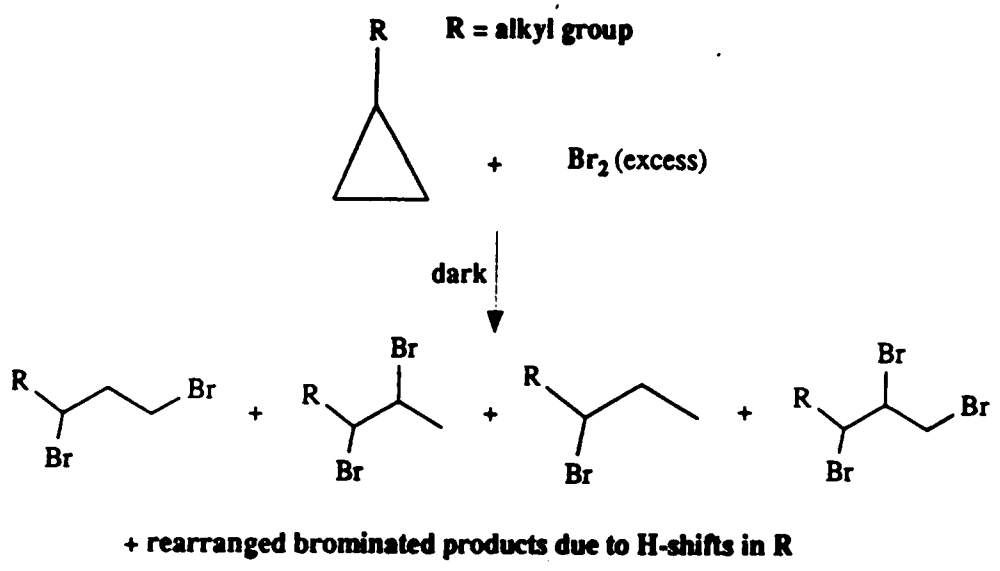


Figure 18. Products obtained from reaction of alkylcyclopropanes and Br_2 in the dark (electrophilic bromination)

Remarkably enough, as early as 1900, Gustavson had the key to resolving the difficulties in understanding the dark bromination of alkylcyclopropanes when he reported that cyclopropanes reacted more rapidly with hydrogen bromide than with bromine.[58] However, not until the reports from two research groups, one headed by Skell[57,59] and the other by Lambert,[60,61] were published about 15 years ago that the dark reaction of bromine with alkylcyclopropanes was clearly resolved.

To assess the relative rates of the reaction of alkylcyclopropanes with HBr and Br_2, Skell and co-workers combined a 1:1 mixture of HBr and Br_2 with a one-half stoichiometric amount of various alkylcyclopropanes in methylene chloride solvent. They found that addition

of the HBr was the primary reaction of the alkylcyclopropanes at -78 °C. This behavior contrasts with that of olefins, since olefins reacted rapidly and exclusively with Br_2 under similar conditions. From this simple set of observations, they proposed that a clear picture of the dark reaction of Br_2 with alkylcyclopropanes in general could be obtained if the HBr formed during the reaction could be rapidly removed. Indeed, by carrying out the reaction in the presence of an efficient HBr scavenger, N-bromosuccinimide (NBS), in methylene chloride solvent, they reportedly obtained only the di- and tribromoalkanes characteristic of Br_2 attack (Figure 19); while the mono- and dibromoalkanes characteristic of HBr attack (Figure 20) were conspicuously absent.

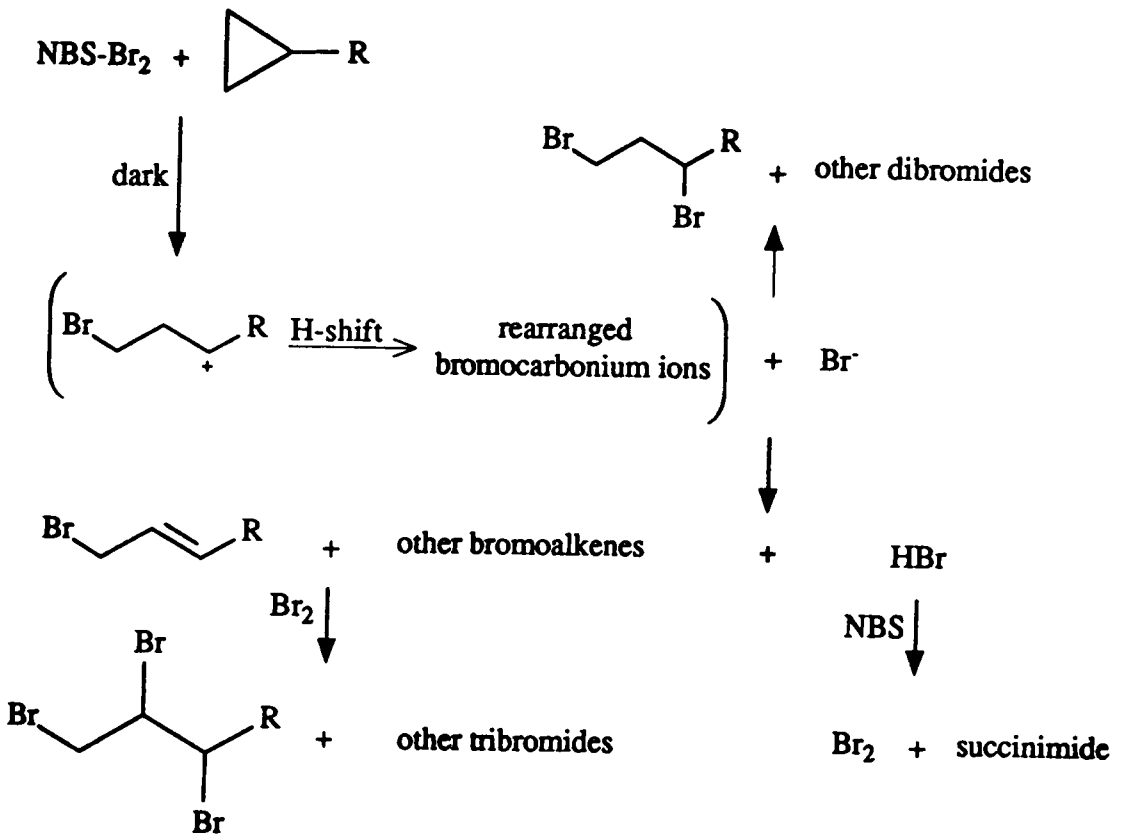


Figure 19. Electrophilic bromination of alkylcyclopropanes in the presence of an efficient HBr scavenger, N-bromosuccinimide

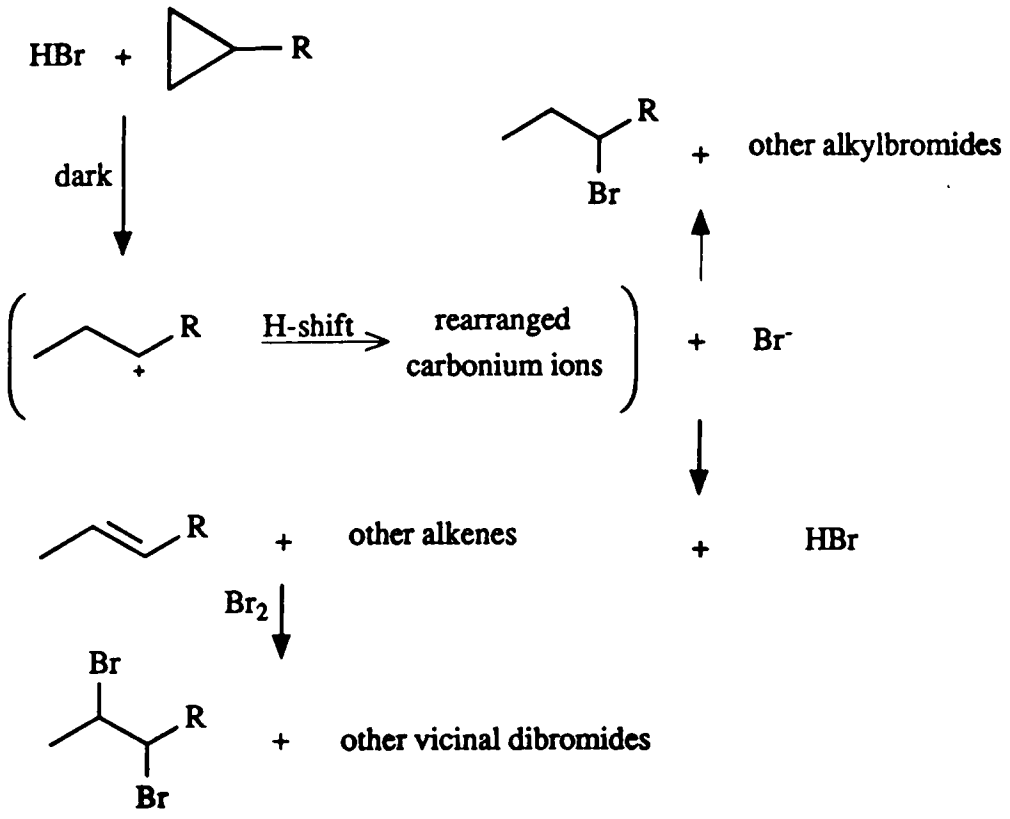


Figure 20. Reaction of alkylcyclopropanes with HBr in the dark

Lambert and co-workers investigated the electrophilic bromination of cis- and trans-1,2-dimethylcyclopropane in order to establish the reaction mechanism of the addition of Br_2 to alkylcyclopropanes. Initially, there were substantial disagreements between their results[60] and those reported by Skell and co-workers.[57] However, the results of Lambert and coworker's second report,[61] wherein they used NBS to remove HBr, are in accord with those reported by Skell and co-workers.[59] Note that (see Figure 19) rapid scavenging occurs because NBS is moderately soluble in methylene chloride (0.25 M in a saturated solution) and reacts rapidly with HBr via an ionic process in the dark, producing Br_2 and the highly insoluble succinimide.[62]

Thus, the reason why a solution of alkylcyclopropane and Br_2 in the dark usually results in the formation of a complex mixture of products is because ring opening occurs, with subsequent rearrangements, by two distinct pathways: a slow reaction with Br_2 which leads to a set of di- and tribrominated alkanes and HBr, and a fast reaction of HBr leading to mono- and another set of dibrominated alkanes.

Formation of the tribromides are presumed to be the result of the addition of Br_2 to bromoolefins formed by loss of a proton from the initial and rearranged bromocarbonium ions. For example, the tribromides produced from the reaction of methylcyclopropane with Br_2-NBS are 1,2,4-tribromobutane, and the threo- and erythro- of 1,2,3-tribromobutane. These products are Br_2 adducts of 4-bromo-1-butene and 1-bromo-2-butene; intermediates that would result from loss of a proton from the 1-bromo-2- and 3-butyl cations (Figure 21). From the report of Skell and co-workers,[57] the yields of the various products of the reaction of methylcyclopropane with Br_2 (NBS, dark, 66% conversion in 3 hr at 0 °C) are 1,2-dibromobutane (13%), 1,3-dibromobutane (37%), and tribromobutanes (48%), identified as a mixture of 1,2,4- and erythro- and threo-1,2,3-tribromobutanes.

In general, at room temperature the tribromides are the major products (50-60% yields are not uncommon) whereas at low temperatures (-78 °C) the 1,3-dibromides are the major products. Presumably the energy of activation for the elimination is greater than the collapse to dibromide, thus accounting for the effect of temperature on tribromide yields.[59]

The extent of rearrangement in electrophilic brominations of alkylcyclopropanes is striking. As a case in point, the bromination of n-butylcyclopropane produces all the 1,x-dibromoheptanes, with the exception of the 1,1- and the 1,7- dibromides; the yields of 1,4- and 1,5-dibromides are greater than that of 1,3-, and the 1,6- is only slightly smaller (Figure 22). It is interesting to note that the dibromides expected from the likely most stable carbonium ion, bridged 1,2-bromonium ion, is produced in lowest yield. Instead, the rearrangement moves the positive charged site away from the first bromine substituent, in competition with hot pursuit by the Br^- which ultimately encumbers and traps the carbonium ion to form the dibromide.

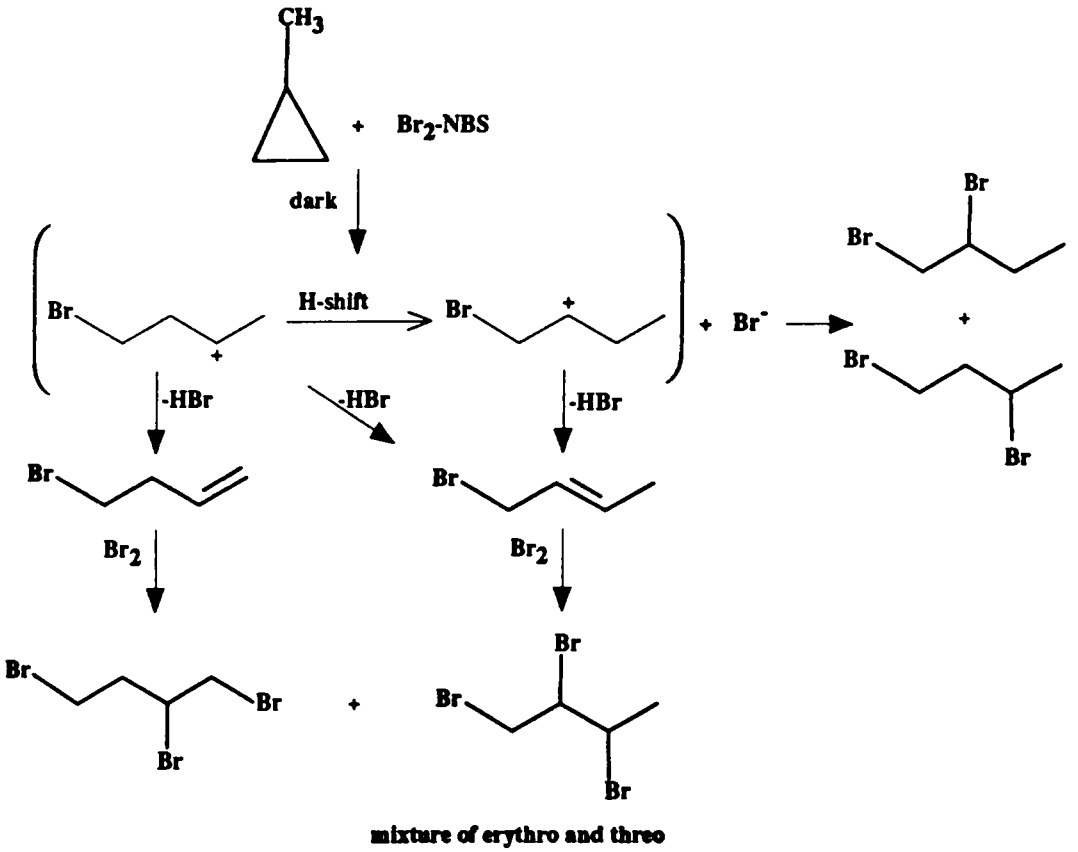


Figure 21. Electrophilic bromination of methylcyclopropane in the presence of N-bromosuccinimide

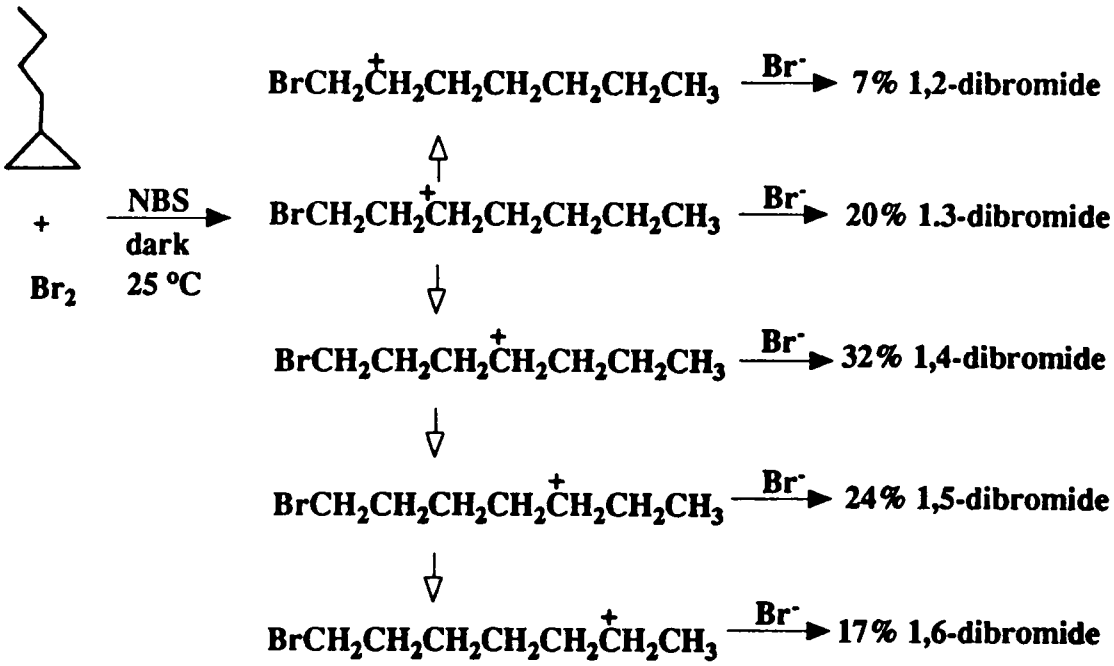


Figure 22. Electrophilic bromination of n-butylcyclopropane in the presence of N-bromosuccinimide

The rate of dark bromination of alkylcyclopropanes generally increases with increasing number of alkyl substituents (Table 6). Introduction of a single alkyl substituent accelerates the dark reaction with Br_2. In other words, it causes the dark reaction to occur even without the presence of a Lewis acid catalyst (recall that cyclopropane and Br_2 do not react in the dark except in the presence of a Lewis acid catalyst such as $AlCl_3$). This is consistent with the formation of a secondary bromo cation rather than the primary carbonium ion that would be formed from reaction of cyclopropane. Introduction of further alkyl substituents at the unsubstituted position results in further moderate increase of reactivity. The fact that cis-alkylcyclopropanes are more reactive than trans-alkylcyclopropanes is attributed to the more relief of strain if the alkyl groups are cis than if they are trans. The difference in rate between the vicinal substituted di- and trialkylcyclopropanes can be rationalized with steric interactions inherent in an attack with inversion: a methylene group is more reactive than a methine group. The substantial increase of reactivity if alkyl groups are geminal rather than vicinal is attributed to the formation of the more stable tertiary bromocarbonium ion.

Table 6. Competitive Dark Brominations of Alkylcyclopropanes[a]

Compound	k_{rel}	k_{abs}, $M^{-1}s^{-1}$
Cyclopropane, Bromocyclopropane	~0	-
Methylcyclopropane	~1.0	$\sim 4.9 \times 10^{-4}$
Ethylcyclopropane	(1.0)	$4.9 \pm 0.5 \times 10^{-4}$[d]
trans-1,2,3-Trimethylcyclopropane	4.3 ± 0.4[b]	$2.1 \pm 0.3 \times 10^{-3}$
trans-1,2-Dimethylcyclopropane	10.8 ± 0.1[b]	$5.2 \pm 0.5 \times 10^{-3}$
cis-1,2-Dimethylcyclopropane	20.8 ± 0.3[c]	$1.0 \pm 0.1 \times 10^{-2}$
cis-1,2,3-Trimethylcyclopropane	23.8 ± 2.2[c]	$1.2 \pm 0.1 \times 10^{-2}$
1,1-Dimethylcyclopropane	$\sim 10^2$	$\sim 4.9 \times 10^{-2}$
1,1,2,2-Tetramethylcyclopropane	$>10^3$	$>4.9 \times 10^{-1}$

[a]Cited in reference 59; Br_2-NBS, dark, 25 °C, CH_2Cl_2 solvent. [b]Experimental relative rates. [c]Calculated relative rates using the following experimental relative rates: k_{cis}/k_{trans}(1,2-dimethylcyclopropane) = 1.9 ± 0.1; k_{cis}/k_{trans}(1,2,3-trimethylcyclopropane) = 5.5 ± 0.2. [d]Average of two independent determinations.

In summary, the dark reaction between alkylcyclopropanes and bromine proceeds with the initial addition of Br_2 to the least-hindered site, with inversion of configuration, to produce a bromocarbonium ion - bromide ion-pair which undergoes extensive sequential rearrangements, uncharacteristic of solvolysis-type intermediates (i.e., intimate or solvent-separated ion-pairs), but characteristic of the nonrelaxed or free carbonium ion-anion pairs.[59,61] It is worthwhile to note that if there is an unsubstituted methylene group in an alkylcyclopropane, the initial attack by Br_2 occurs at this group (because it is the least-hindered site) to form a $BrCH_2$ group and a cationic site, and the remaining events proceed at the cation site leaving the $BrCH_2$ group untouched. The formulation proposed by Skell and coworkers[59] shown in Figure 23, depicting the attack by Br_2 with inversion of configuration, would be consistent with the mechanism of the electrophilic bromination of alkylcyclopropanes.

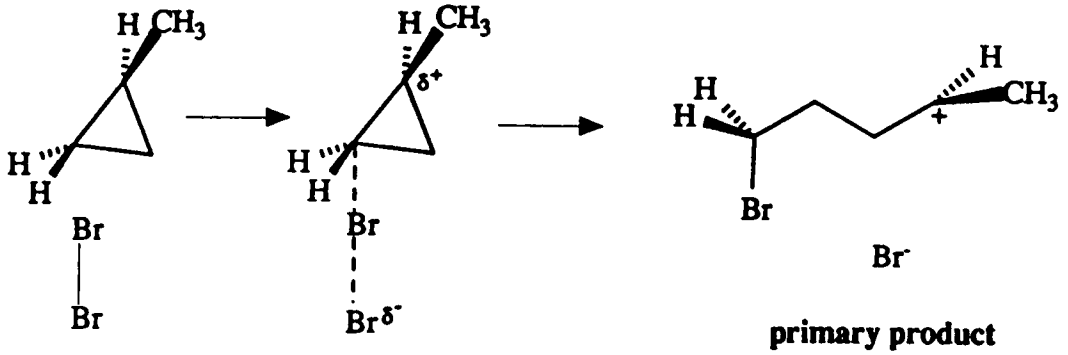


Figure 23. A proposed mechanism for the dark bromination of alkylcyclopropanes

However, there are reports with both retention and inversion of configuration in the first step of electrophilic bromination of alkylcyclopropanes.[63,64] Furthermore, the parent hydrocarbon, cyclopropane itself, is an exceptional case in which complexed or protonated cyclopropanes are the intermediates. Other electrophilic substitutions on alkylcyclopropanes with a bewildering variety of stereochemical pathways has been reported by DePuy.[65]

Electrophilic Addition of Bromine to Arylcyclopropanes

There is little known about the dark reaction of bromine with arylcyclopropanes. LaLonde and co-workers reported that the dark brominations of cis- and trans-1,2-diphenylcyclopropane at 20 °C yields exclusively cyclopropyl ring-opened products (1,3-dibromides), while phenylcyclopropane produces a mixture of products arising from addition and aromatic substitution.[19] However, they also noted in the same report that the dark bromination of phenylcyclopropane at 25 °C affords only the addition product. Their reported results may be obscured by radical-chain bromination; that is, the nature of the brominations

(electrophilic or radical-chain) was not clear. Sergeev and co-workers examined the competition of the nonradical (dark) low-temperature brominations of phenylcyclopropane, and concluded that cyclopropyl ring opening is favored below -73 °C while the aromatic substitution is favored at low temperature but above -73 °C.[23] Since these authors did not state whether they carried out the experiments in the presence of an efficient HBr scavenger, their conclusion is questionable. This is because cyclopropyl ring opening can result not only from the attack of Br_2 but also from the attack of HBr.

It is apparent, however, the dark reaction of Br_2 with phenylcyclopropane and its derivatives occurs by two distinct pathways: aromatic substitution and cyclopropyl ring opening. The question remains whether the addition of Br_2 to the cyclopropyl moieties of arylcyclopropanes may lead to the formation of other products, resulting from competitive brominations, dehydrobromination, hydrobromination, and rearrangements; similar to those commonly found in the dark bromination of alkylcyclopropanes.

Research Objectives

In chapter one, we observed that aromatic substitution is an important competing side reaction in the photobromination of 9-cyclopropylanthracene with molecular bromine, except under conditions where the anthryl moiety is deactivated (halogen substituted) or the bromine concentration is kept very low (for example, using NBS as a source of Br_2). In view of this, and since there is no documentation on the dark reaction of Br_2 with 9-cyclopropylanthracene or its derivatives, we have examined the electrophilic bromination of 9-cyclopropylanthracene and 9-halo-10-cyclopropylanthracenes. The electrophilic bromination of phenylcyclopropane was also examined since the available information on this reaction is ambiguous.

It was also shown in chapter one that the free radical brominations of 9-cyclopropylanthracene and phenylcyclopropane yield products arising from two different processes; the former produces an unprecedented cyclopropyl hydrogen abstraction product, while the latter affords only an expected cyclopropyl ring-opened product. We believe the formation of the hydrogen abstraction product is a consequence of the conformational preference of the cyclopropyl moiety of the 9-cyclopropylanthracene, and hence, due to stereoelectronic effects. That is to say, because the cyclopropyl group of the 9-cyclopropylanthracene is essentially locked in the perpendicular conformation, proper alignment with the adjacent π-system activates the cyclopropylmethine C-H bond to an extent that the hydrogen abstraction process is favored over the ring opening (see Figure 16, page 33).

However, an alternate explanation is that the result is due to steric inhibition of resonance in the products radical, that is, the radical resulting from the hydrogen abstraction is favored over that arising from cyclopropyl ring opening because of the unfavorable peri-interaction presence in the latter (Figure 24).

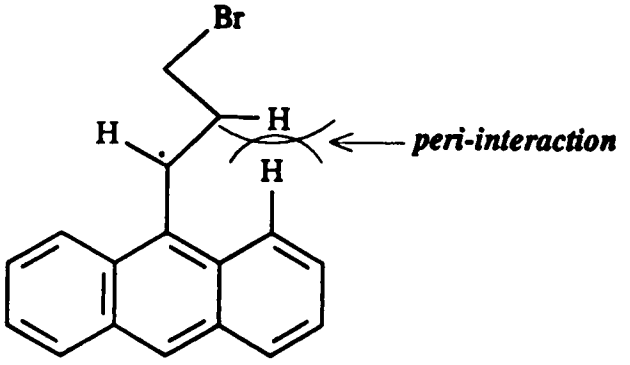


Figure 24. Cyclopropyl ring-opened radical of 9-cyclopropylanthracene

The ring-opened radical is structurally similar to the ring-opened carbonium ion that would form from the addition of molecular bromine to the cyclopropyl moiety of 9-cyclopropylanthracene (Figure 25).

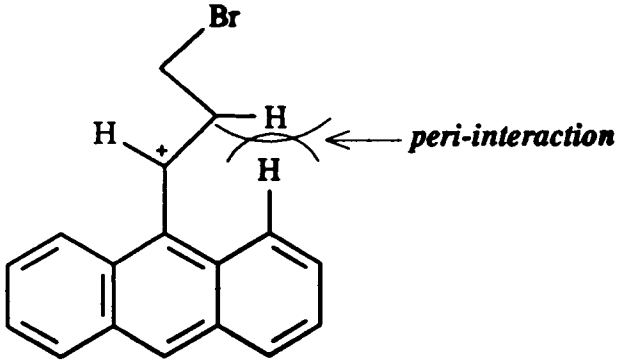


Figure 25. Cyclopropyl ring-opened carbonium ion of 9-cyclopropylanthracene

Therefore, the electrophilic bromination reaction may also be subject to stereoelectronic constraints analogous to the free radical reaction. Consequently, one of the goals of this chapter was to explore this possibility.

Results

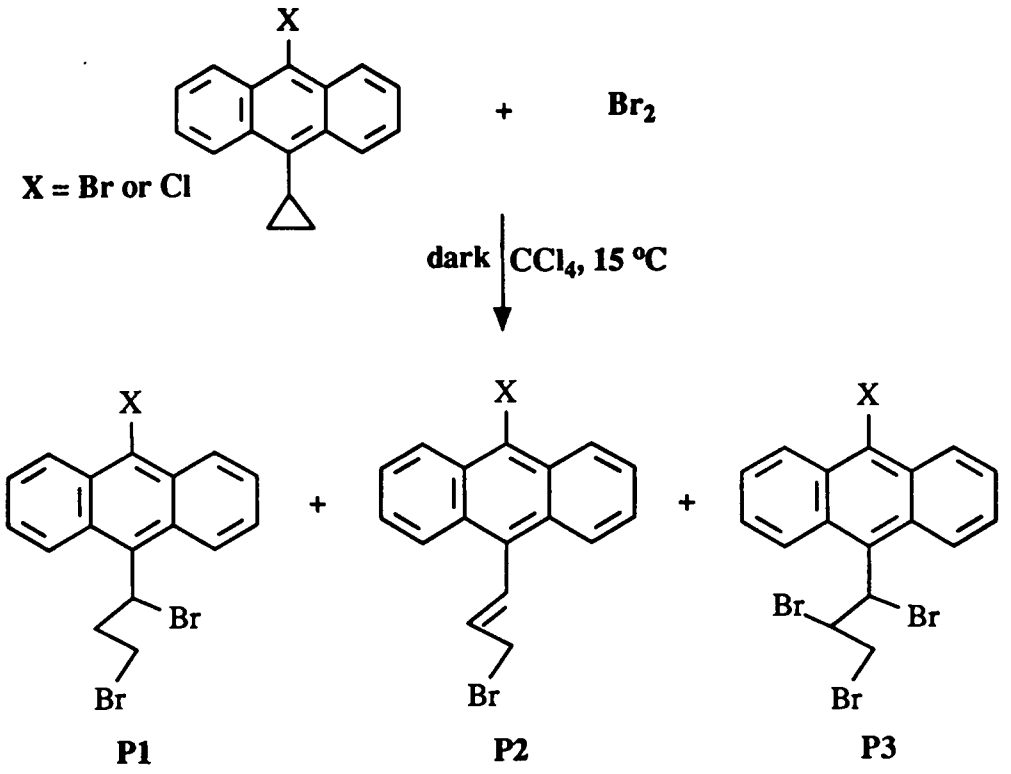
The Dark Reaction of Bromine with 9-Cyclopropylanthracene and its Derivatives

Reaction of a 1:1 mixture of Br_2-NBS with 9-cyclopropylanthracene in the dark at ambient temperature (15-20 °C) resulted in a quantitative yield of 9-bromo-10-cyclopropylanthracene. On the other hand, a 2:1 mixture of Br_2-NBS and 9-cyclopropylanthracene produced several products, apparently resulting from aromatic substitution, cyclopropyl ring opening, and aromatic substitution with subsequent cyclopropyl ring opening.

To circumvent the aforementioned problem, we isolated 9-bromo-10-cyclopropylanthracene and then reacted it with a stoichiometric amount of Br_2 in the dark. Additionally, the dark reaction between 9-chloro-10-cyclopropylanthracene and Br_2 was also examined. All the products of the ionic brominations were identified, characterized and quantitated by ^1H NMR spectroscopy. Attempts to quantitate reaction products by Gas Chromatography (GC) techniques were not successful because the polybrominated products, decompose readily at elevated temperatures. Nonetheless, further indirect characterization was achieved by reducing the brominated products with tri-n-butyltin hydride to the corresponding hydrocarbons, and analyzing the resulting mixture by GC techniques. The structures of the products obtained from the dark reaction of Br_2 with 9-bromo- and 9-chloro-10-cyclopropylanthracene are depicted in **Eq. 14**.

The dark reaction between 9-chloro-10-cyclopropylanthracene and Br_2 was carefully monitored by ^1H NMR spectroscopy and the relative yields of the corresponding brominated products at several time intervals are presented in Table 7. The experiment was performed in triplicate.

Eq. 14



Referring to Table 7, it can be seen that only the dibromide (**P1**) was formed after 1 hr. The presence of the alkene (**P2**) and the tribromide (**P3**) was detected after 5 hr. The relative percentage ratio of dibromide:alkene:tribromide at 5 hr was 90:6:4. After 30 hr, while the relative amount of the tribromide remained at 4%, the relative amount of the alkene increased to 26% and that of the dibromide decreased to 70%. Further increase in the relative concentration of the alkene to 52% and decrease in the relative concentration of the dibromide to 44% was observed after 70 hr. The relative concentration of the tribromide, however, remained unchanged at about 4%.

Table 7. Relative Yields (%) of Products from the Dark Bromination of 9-Chloro-10-Cyclopropylanthracene at Different Time Intervals.[a,b]

Product[c]	1hr	5hr	30hr	70hr
P1	100	90	70	44
P2	—	6	26	52
P3	—	4	4	4

[a]A 1:1.04 mixture of reactants was utilized, and the reaction conducted at 15 °C in a 50:50 mixture of CCl_4 and $CDCl_3$ as solvent; [b]Quantitation was done by ^1H NMR spectroscopy. [c] **P1** = 1,3-dibromo-1-(9-chloroanthryl)propane; **P2** = 3-bromo-1-(9-chloroanthryl)propene; **P3** = 1,2,3-tribromo-1-(9-chloroanthryl)propane.

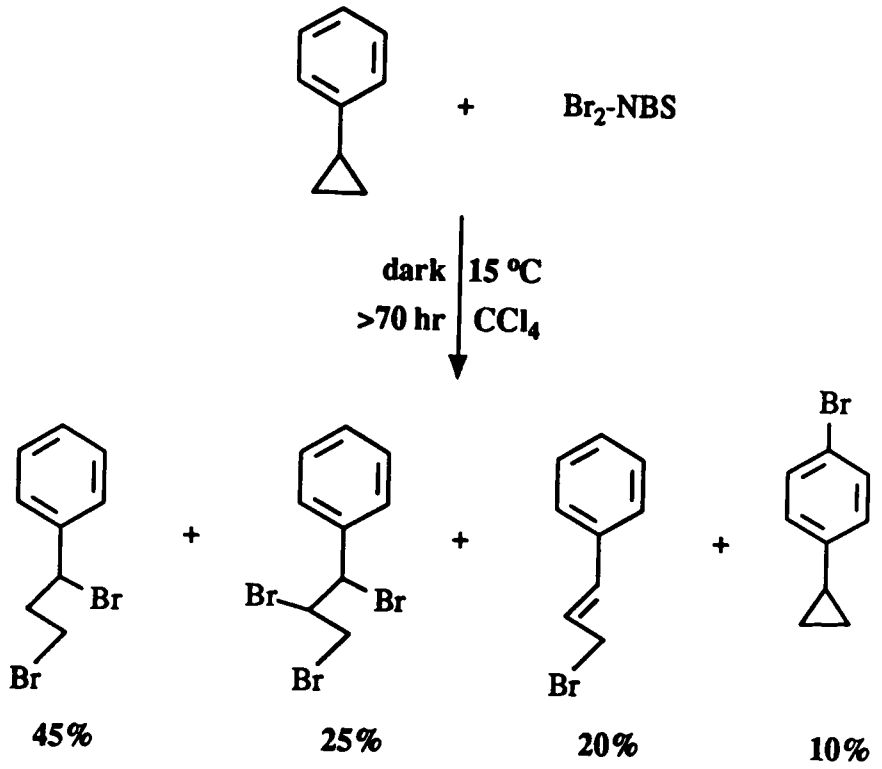
It is worthwhile to mention here that direct analysis by ^1H NMR spectroscopy is a convenient method for monitoring the progress of the dark bromination of 9-halo-10-cyclopropylanthracene because the side-chain protons of the starting material and the products (**P1**, **P2** and **P3**) have different chemical shifts and splitting patterns. For example, using the chemical shift of the protons of tetramethylsilane at $\delta = 0.00$ ppm as an internal reference, the chemical shift values of each of the side-chain protons of the starting material and products are as follows: for 9-chloro-10-cyclopropylanthracene, the cyclopropylmethine proton is at 2.47 ppm (m, 1H), the cis- and trans-cyclopropylmethylene protons are at 0.79 ppm (m, 2H) and 1.47 ppm (m, 2H), respectively; for **P1**, the chiral methine proton is at 6.82 (dd, 1H, -CHBr-), one of the diastereotopic protons of the $-CH_2Br$ group is at 3.66 ppm (m, 1H) and the other overlaps with one of the diastereotopic protons of the $-CH_2-$ group in the region 3.49 - 3.38 ppm (mm, 2H), while the other diastereotopic proton of the $-CH_2-$ group is at 2.77 ppm (m, 1H); for **P2**, the alkenic proton adjacent to the anthryl moiety is at 7.33 (d, 1H, J = 15.8 Hz, -CH=), the central alkenic proton is at 6.20 ppm (m, 1H, =CH-), and the protons of the $-CH_2Br$ group are at 4.33 ppm (d, 2H, J = 7.7 Hz); and finally for **P3**, the chiral methine proton adjacent to the anthryl moiety is at 6.93 ppm (d, 1H, J = 11.3 Hz), the chiral methine proton of the central -CHBr- group is at 5.66 ppm (m, 1H), and the diastereotopic protons of the $-CH_2Br$ group are at 4.66 ppm (dd, 1H) and 4.15 ppm (dd, 1H).

The fact that there were only three different products was ascertained by adding an excess amount of Br_2 to a reaction mixture which had been set aside for 70 hr, and immediately obtaining a ^1H NMR spectrum of the resulting solution. The addition of the excess Br_2 caused all resonances of the protons of the alkene to vanish. Only the resonances of the protons of the dibromide and tribromide remained, and with no indication of the presence of any other product.

The Dark Reaction of Bromine with Phenylcyclopropane

The reaction of Br_2-NBS and phenylcyclopropane (1:1 mixture) in the dark at 15 °C occurred very slowly; total discharge of bromine was observed only after 3 days. The structures of the various products of the dark bromination of phenylcyclopropane are shown in **Eq. 15**. The aromatic substituted product, para-bromophenylcyclopropane, was 10% of the total products formed. The remaining 90% was comprised of cyclopropyl ring-opened products: 1,3-dibromo-1-phenylpropane (45%), 3-bromo-1-phenylpropene (20%), and 1,2,3-tribromo-1-phenylpropane (25%).

Eq. 15



Competitive Dark Bromination of Phenylcyclopropane versus 9-Bromo-10-Cyclopropylanthracene

The rate constant ratio, k_A/k_B (Figure 26), for the dark bromination of 9-bromo-10-cyclopropylanthracene with respect to phenylcyclopropane at 15 °C was determined to be 18.6. Note that this value is just an approximation of the lower limit of the reactivity of 9-bromo-10-cyclopropylanthracene with respect to phenylcyclopropane towards Br_2 because the latter was also partly lost via aromatic substitution (ca. 10%, see Eq. 15).

Therefore, it is reasonable to say that 9-bromo-10-cyclopropylanthracene is at least 18 times more reactive than phenylcyclopropane towards Br_2 in the dark at 15 °C.

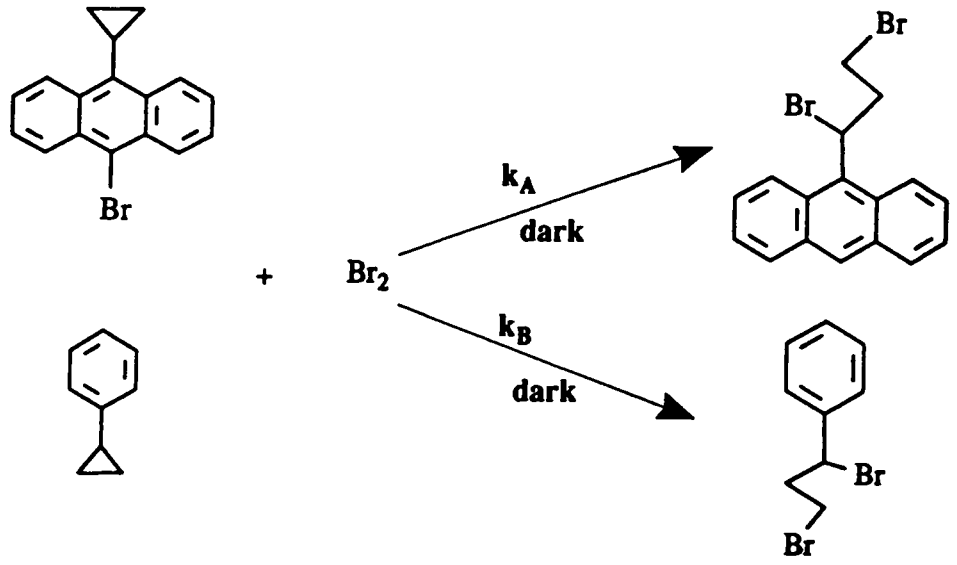


Figure 26. Competitive bromination of 9-bromo-10-cyclopropylanthracene versus phenylcyclopropane

A better comparison might be to measure the relative rate of electrophilic bromination of 9-cyclopropylanthracene versus phenylcyclopropane, or 9-bromo-10-cyclopropylanthracene versus para-bromophenylcyclopropane. Unfortunately, the former combination has an unavoidable drawback because 9-cyclopropylanthracene is readily susceptible to electrophilic aromatic substitution. The latter combination is also not practical because, compared to 9-bromo-10-cyclopropylanthracene, para-bromophenylcyclopropane is virtually inert to bromine in the dark. This is consistent with the report of Quellette and co-workers which demonstrated that the presence of an electron withdrawing group, namely a halogen, at the para-position of a phenylcyclopropane retards the rate of electrophilic cleavage of the phenylcyclopropane.[66] For example, the rate of cleavage of para-chlorophenylcyclopropane

($k = 4.7 \times 10^{-5}\ M^{-1}\ sec^{-1}$) by mercuric acetate in acetic acid at 25 °C is only about 0.3 times as fast as the rate of cleavage of phenylcyclopropane ($k = 1.6 \times 10^{-3}\ M^{-1}\ sec^{-1}$).

In view of the above, the rate of cleavage of the cyclopropyl moiety of 9-cyclopropylanthracene by Br_2 in the dark should be faster than the rate of cleavage of the cyclopropyl moiety of 9-bromo-10-cyclopropylanthracene. Since phenylcyclopropane is at least 18 times less reactive than 9-bromo-10-cyclopropylanthracene towards Br_2 in the dark, it is not unreasonable to say that the rate of cleavage of the cyclopropyl moiety of 9-cyclopropylanthracene by Br_2 in the dark is 18 times faster than that of phenylcyclopropane. The significance of this result will be elaborated upon later in the discussion section.

Discussion

The dark reaction of Br_2 with the cyclopropyl moiety of either 9- bromo or 9-chloro-10-cyclopropylanthracene at 15 °C produces only three products (see **Eq. 14**). A plausible mechanism for this reaction is given by Figure 27. The initial addition of Br_2 leads to the formation of 1-bromo-3-carbonium ion which collapses to produce the dibromide (**P1**). It is possible that a loss of proton from the 1-bromo-3-carbonium ion to a nearby bromide ion would produce the alkene (**P2**). However, this was not the case here since the presence of the alkene was not detected until the starting material had been essentially converted to the dibromide. The formation of the alkene then must have resulted from the elimination of HBr from the dibromide. This is a comparatively slow process because as soon as the alkene is formed, it will be rapidly attacked by any unreacted Br_2 in the solution, producing the tribromide (**P3**). In fact, the presence of the tribromide can be safely regarded as an indication that the solution was completely depleted of Br_2.

The fact that the relative concentration of the tribromide remained virtually at about 4% throughout the entire reaction time recorded (see Table 7) adds support to the notion that the alkene did not form until the starting material had been consumed by Br_2 (initial concentration ratio of 9-chloro-10- cyclopropylanthracene:Br_2 was set at 1:1.04), producing exclusively the dibromide. If the alkene had formed during the progress of the dark reaction, then the relative concentration of the tribromide would have been considerably more than 4%. Another interesting feature that can be noted from Table 7 is that the increase in the relative concentration of the alkene from 6% at 5 hr to 26% at 30 hr to 52% at 70 hr is proportional to the decrease in the relative concentration of the dibromide from 90% at 5 hr to 70% at 30 hr to 44% at 70 hr. This means that the alkene was being produced from the dibromide (i.e., **P1** - HBr → **P2**). Therefore, it is reasonable to say that the electrophilic bromination of 9-halo-10-cyclopropylanthracene is fairly rapid and clean if care is taken to avoid long reaction times.

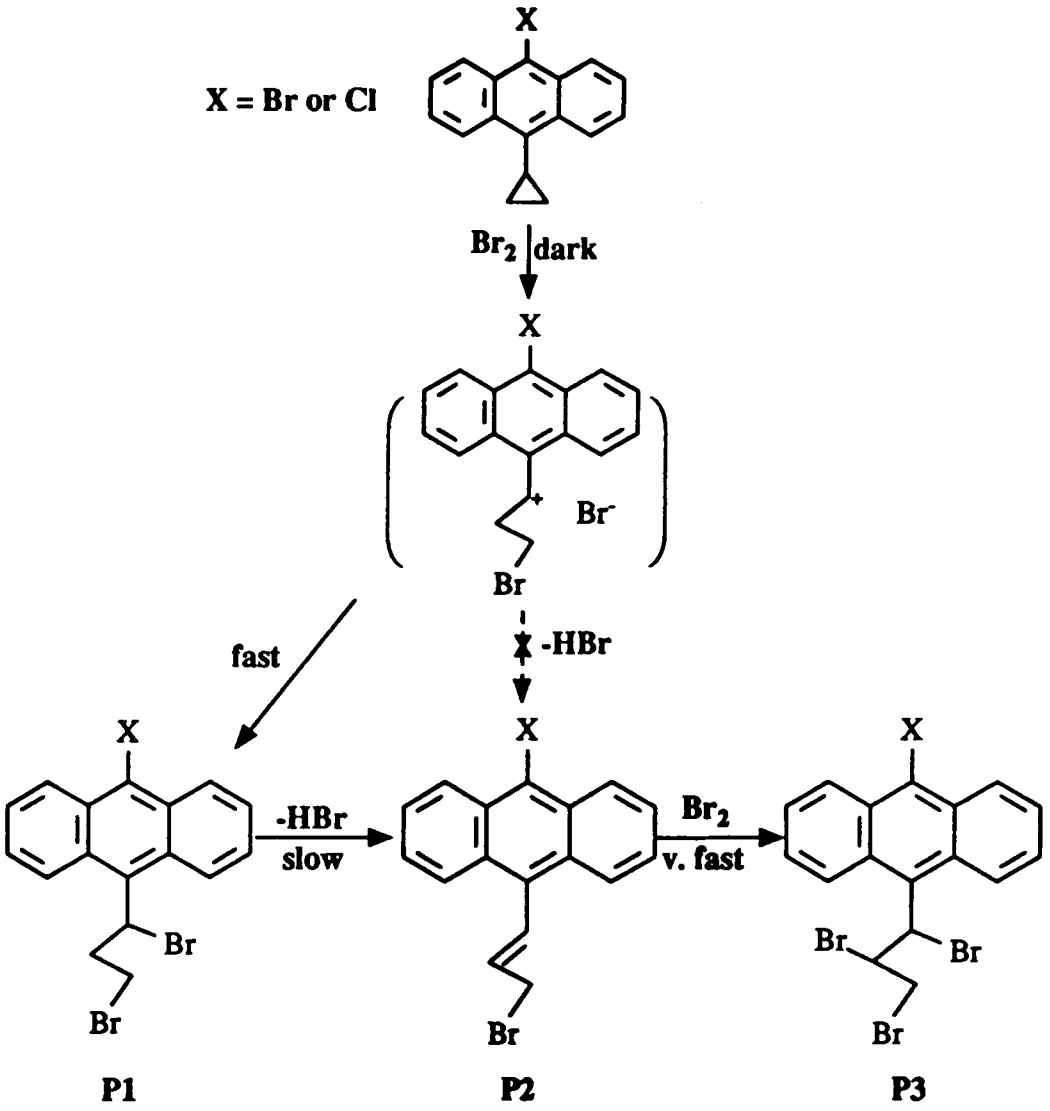


Figure 27. A plausible mechanism for the electrophilic bromination of 9-halo-10-cyclopropylanthracene

Furthermore, unlike what is usually obtained from a mixture of Br_2 and alkylcyclopropane in the dark, there is no detectable evidence of any product arising from the addition of HBr to the cyclopropyl moiety of either 9-bromo- or 9-chloro-10-cyclopropylanthracene. This is not surprising because HBr was formed (based on the presence of the alkene, **P2**) only after the starting material had been essentially consumed by Br_2.

Compared to 9-cyclopropylanthracene, phenylcyclopropane does not readily undergo aromatic substitution when subjected to bromine in the dark at 15 °C; reaction of a 1:1 mixture of NBS-Br_2 with 9-cyclopropylanthracene yields quantitatively 9-bromo-10-cyclopropylanthracene, while a 1:1 mixture of NBS-Br_2 and phenylcyclopropane produces only about 10% para-bromophenylcyclopropane, with the remaining 90% comprised of cyclopropyl ring-opened products. The formation of the cyclopropyl ring-opened products can be rationalized as follows: the 1,3-dibromo-1-phenylpropane was produced from the direct attack of Br_2 on the cyclopropyl moiety, the 3-bromo-1-phenylpropene may have resulted from the discharge of HBr from both 1,3-dibromo-1-phenylpropane and 3-bromo-1-phenylpropyl cation, and the 1,2,3-tribromo-1-phenylpropane was the product of rebromination (i.e., addition of Br_2 to 3-bromo-1-phenylpropene). Note that the relative concentration of 1,2,3-tribromo-1-phenylpropane was fairly large (25%). Presumably, the dehydrobromination process leading to the formation of 3-bromo-1- phenylpropene was taking place while the reaction of Br_2 and phenylcyclopropane was still in progress.

The absence of rearranged products from the dark reaction of Br_2 with the cyclopropyl moieties of 9-cyclopropylanthracene and phenylcyclopropane strongly suggests that the initial attack of Br_2 on the cyclopropyl moieties of both aryl systems leads to the formation of resonance-stabilized carbonium ions. If rearrangements were to take place, such as a shift of one of the hydrides from the adjacent methylene carbon to the cation site, the stabilization due to resonance from the aryl moieties would be destroyed, and therefore, would result in less stable carbonium ions. In other words, there is no driving force for rearrangement to occur.

The fact that Br_2 is at least 18 times more reactive towards the cyclopropyl moiety of 9-cyclopropylanthracene than towards that of phenylcyclopropane can be attributed to the greater delocalization of charge by the larger anthryl system. This means that although the carbonium ion resulting from 9-cyclopropylanthracene may suffer some steric inhibition of resonance (see Figure 25, page 51) and may be slightly distorted from planarity, the p-orbitals of the anthracene system are able to effectively delocalize the positive charge and hence, stabilize the cationic center. Thus, it can be inferred that the p-orbitals of the anthracene system should also be able to resonance-stabilize the product radical derived from the cyclopropyl ring opening process (see Figure 24, page 51). It appears then, the fact that free radical bromination of 9-cyclopropylanthracene yields an unprecedented hydrogen abstraction product is likely to be due to stereoelectronic effects (i.e., proper orbitals overlap in the ground state), and not to steric inhibition of resonance in the product radical.

Chapter 3. Competitive Bromination of 9-Alkylanthracenes

Background

The individual steps of a free radical bromination can be divided into three categories: initiation (**Eq.** 16a or **Eq.**16b), propagation (**Eq.** 17 and **Eq.** 18) and termination (**Eq.** 19 and **Eq.** 20).

Eq. 16a $Br_2 + M \rightleftharpoons 2Br^{\cdot} + M$

Eq. 16b $Br_2 + h\nu \longrightarrow 2Br^{\cdot}$

Eq. 17 $Br^{\cdot} + RH \rightleftharpoons R^{\cdot} + HBr$

Eq. 18 $R\cdot + Br_2 \rightleftharpoons RBr + Br\cdot$

Eq. 19 $Br\cdot + R\cdot \longrightarrow RBr$

Eq. 20 $2R\cdot \longrightarrow RR$

The initiation step is the dissociation of molecular bromine into bromine atoms. This can be accomplished by thermolysis, photolysis, ionizing radiation, or chemical free-radical initiators. The symbol M in **Eq.** 16a is commonly used to indicate the involment of a third body which is required for the transfer of energy in the dissociation of bromine molecules and in the recombination of bromine atoms. The symbol $h\nu$ in **Eq.** 16b refers to one quantum of radiation energy needed to dissociate bromine molecules into bromine atoms. Photoinitiation has the advantage of being relatively temperature independent, and it is the most commonly used method of initiating brominations at low temperatures where thermal initiation would not be efficient. However, in certain circumstances photoinitiation may cause undesirable cleavage of the bonds of reactants and reaction products, giving rise to a complex mixture of compounds.[34] The energy E of a quantum of light required to dissociate Br_2 into $2Br\cdot$ must be equal to or greater than the energy of the Br-Br bond. Since the dissociation energy of a Br-Br bond is about 46 kcal/mole, visible light of wavelengths below 6000 Å, as well as ultraviolet light (<4000 Å), should be effective in initiating free-radical brominations. In practice, ordinary incandescent light bulbs and sun lamps, as well as high- and medium-pressure mercury arc lamps, are effective and can be used in conjunction with ordinary Pyrex equipment, which cuts off below 3000 Å.

The propagation steps involve the exchange of one radical for another. The formation of the hydrocarbon radical ($R\cdot$) by the transfer of a hydrogen from the hydrocarbon (RH) to a bromine atom, in the first propagation step, is often reversible, and consequently the HBr that is generated in this step must be removed (by employing an appropriate HBr scavenger) in

order to achieve efficient bromination.[67-69] The second propagation step, wherein a bromine atom is transferred to R· from Br_2 with regeneration of the chain-propagating bromine atom is generally irreversible, and occurs at a diffusion-controlled rate.

All the steps that lead to the distruction of radicals generated in the initiation and propagation steps can be considered as the termination steps. The reactions described by **Eq. 19** and **Eq. 20**, as well as the backward reaction of **Eq. 16a**, are possible termination steps.

Rate Expressions

If the kinetic chain length of the bromination is greater than 10, that is, if more than 10 molecules of product are formed for each initiating event, the initiation and the other termination steps do not contribute significantly to the stoichiometry of the reaction (i.e., the stoichiometry is equal to the sum of the propagation steps in the reaction). The rate of the hydrogen abstraction step (RH + Br· → R· + HBr) reflects the reactivity of the C-H bond towards Br·. Direct measurement of this absolute rate constant is not trivial as R· is very reactive and therefore present in very small (steady-state) concentration.[70]

As an alternate method, frequently employed by physical organic chemists for the purpose of obtaining rate data sufficient for the correlation of structure with reactivity, involves the determination of the relative reactivity of different C-H bonds towards bromine atoms by means of competitive brominations. This method provides the ratio of the absolute rate constants for the abstraction of hydrogen from various compounds, and is not influenced by the mode of initiation, termination, or even the presence of trace impurities such as oxygen, which can plague rate measurements in radical chain reactions. In addition, this method is elegantly simple as the desired information is obtained from analysis of the ratio of products or the quantity of starting materials consumed.

Consider, for example, two hypothetical substrates R-H and R′-H that will be competing for Br· in the same reaction vessel. If the reaction is performed under conditions

in which the reverse of the reactions given by the following **Eq. 21** and **Eq. 22** is not significant, then R· and R'· are converted to R-Br and R'-Br, respectively, by the subsequent reaction of these radicals with Br_2.

Eq. 21

$$R\text{-}H + Br\cdot \xrightarrow{k_R} R\cdot + HBr$$

Eq. 22

$$R'\text{-}H + Br\cdot \xrightarrow{k_{R'}} R'\cdot + HBr$$

The rate of bromination of each of these two substrates can be expressed as:

Eq. 23

$$-d(RH)/dt = k_R(RH)(Br\cdot)$$

Eq. 24

$$-d(R'H)/dt = k_{R'}(R'H)(Br\cdot)$$

At any particular time during the reaction period, each substrate will experience the same concentration of Br·. Therefore, **Eq. 23** and **Eq. 24** can be rearranged in terms of (Br·)dt and equated to give

Eq. 25

$$d(RH)/k_R(R'H) = d(R'H)/k_{R'}(R'H)$$

Stoichiometry requires -d(RH)/dt = d(RBr)/dt and -d(R'H)/dt = d(R'Br)/dt, therefore we have

Eq. 26

$$d(RBr)/k_R(RH) = d(R'Br)/k_{R'}(R'H)$$

Further, since both sides of **Eq. 25** are in the integrable form du/u, integrating between limits of initial and final concentrations and rearranging gives **Eq. 27** which is commonly used

for determining relatives reactivities by measuring the consumption of the substrates RH and R'H.

Eq. 27

$$k_R/k_{R'} = \frac{\ln (RH_f/RH_o)}{\ln (R'H_f/R'H_o)}$$

Note that any unit of measure which is proportional to both the initial (RH_o, $R'H_o$) and final (RH_f, $R'H_f$) quantities of the substrates is acceptable for the purpose of getting the ratios of the final/initial concentrations.

Eq. 27 can also be used for the determination of relative reactivities without having to measure accurately the quantities of reactants if one measures (by means of GC or ^{1}H NMR techniques) the concentration ratio of each reactant with respect to an inert internal standard before and after the completion of the reaction of interest. For example, using GC as the method of analysis, if two substrates, RH and R'H, are placed in the reaction flask along with an inert internal standard (S), the ratio of the peak heights or areas, RH_o/S and $R'H_o/S$, which is essentially the ratio of initial concentration of each substrate with respect to the concentration of internal standard, can be measured. If less than a stoichiometric quantity of bromine is then added, and when the reaction is complete, the ratios of the GC peaks, RH_f/S and $R'H_f/S$, can again be measured. Dividing RH_f/S by RH_o/S gives RH_f/RH_o. The value of $R'H_f/R'H_o$ can be calculated in similar manner. Thus, sufficient information is available for determining the the relative reactivity of RH and R'H.

Although it is convenient to just measure the amount of substrates before and after reaction, this procedure is restricted to competitions between different compounds and can not be used to determine reactivities for different C-H bonds on the same compound. Furthermore, it is limited to competitions between substrates of similar reactivity. If one of the substrates, say RH, is very reactive and is completely consumed in the reaction, then $(R'H)_f/(R'H)_o$ approaches zero and $K_R/k_{R'}$ approaches infinity.

An alternate expression that can be used can be derived from **Eq.** 26, and it requires the measuring of the relative amounts of brominated products formed. By assuming that $RH_f = RH_o - RBr$ and $R'H_f = R'H_o - R'Br$ hold, and intergrating **Eq.** 26 between the limits of the initial and final concentration of bromide products gives the alternate expression for computing relative rate constant ratio:

Eq. 28

$$k_R/k_{R'} = \frac{\ln \dfrac{RH_o - RBr}{RH_o}}{\ln \dfrac{R'H_o - R'Br}{R'H_o}}$$

If the conversion of substrates to corresponding brominated products is low, ln (1 - RBr/RH_o) and ln (1 - $R'Br/R'H_o$) can be approximated by $-(RBr/RH_o)$ and $-(R'Br/R'H_o)$, respectively, and **Eq.** 28 simplifies to

Eq. 29

$$k_R/k_{R'} = (RBr/R'Br)(R'H_o/RH_o)$$

where (RBr/R'Br) is the ratio of products and $(R'H_o/RH_o)$ is the ratio of the initial concentrations of the two substrates.

It should be pointed out that since the reactivity is determined from reactant or product ratios in competitive kinetic procedures, the rate constants are not time-resolved. However, if the absolute rate constant for any one of the processes is known (or can be determined) then the absolute rate constant values for all the reactions in the series can be evaluated.

Relative Reactivities of 1°, 2° and 3° Hydrogen Atoms of Alkanes and Alkylbenzenes toward Bromine atom

Table 8 lists the bond dissociation energies and relative reactivities toward bromine atom of 1°, 2° and 3° C-H bonds of alkanes and their corresponding benzylic analogs. It is evident from this table that the relative reactivities of the hydrocarbons increase regularly with decrease in strength of the C-H bond being attacked.

Table 8. Bond Dissociation Energies and Relative Reactivities of 1°, 2° and 3° Hydrogen Atoms of Alkanes and Alkylbenzenes

Hydrocarbon	BDE(kcal/mole)[a]	$k_{rel}(Br)$[b]
CH_3-H	103.8	0.0007
CH_3CH_2-H	98.0	1.00[c]
$(CH_3)_2CH$-H	94.5	220
$(CH_3)_3C$-H	91.0	19,000
$C_6H_5CH_2$-H	88.0	64,000
$C_6H_5CH(CH_3)$-H	85.4	1,600,000
$C_6H_5C(CH_3)_2$-H	84.4	3,800,000

[a]Obtained from references 34 and 1. [b]Relative reactivity towards Br, obtained from reference 71. [c]Arbitrary standard

Consider first the relative reactivities of the different alkane hydrogens toward bromine atom. We see that the differences in relative reactivity between 1°, 2° and 3° hydrogens toward bromine atom are obviously quite large. This is due to the differences in stability of the alkyl radicals which are formed in the transition state (tertiary alkyl radical is more stable than a secondary alkyl radical, and which in turn is much more stable than a primary alkyl radical), and may be considered to stem from the participation of the methyl substituents in stabilizing the unpaired electron by inductive effects. It has been pointed out by Evans and Polanyi[30] that there is a good correlation between activation energy and the

dissociation energy of the bond in question. This point is demonstrated in Table 9. It is, therefore, reasonable to say that replacement of a hydrogen by a methyl group lowers the α-C-H bonds energy, and thereby activates the α-hydrogens towards attack by bromine atom. Replacement by additional methyl groups increases activation further, but a "saturation effect" occurs and the addition of a second or third substituent does not produce as large an activation as the addition of the first substituent. In general, addition of a methyl substituent has less of an effect as the hydrogen in question becomes more highly activated.

Table 9. Relationship between Activation Energies and Bond Dissociation Energies for the Reaction of Bromine Atoms with Alkanes

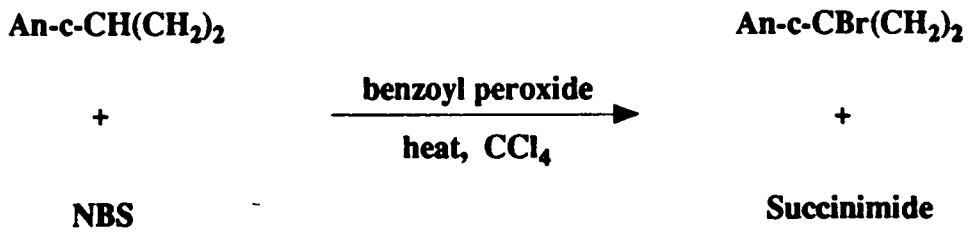
Alkyl-H	D(C-H)	E_a,(Expts)[a]	E_a,(Cald)[b]
Methyl-H	103.8	18.3	18.3
Ethyl-H	98.0	13.4	13.3
Isopropyl-H	94.5	10.1	10.3
t-Butyl-H	91.0	7.5	7.3

[a]Obtained from reference 34; numerical values are in kcal/mole. [b]Calculated using the Polanyi relationship $E_a = 0.86[D(C\text{-}H) - 82.5]$, where D(C-H) is the dissociation energy of the aliphatic bond in question.

Now consider the relative reactivities of the alkylbenzenes toward bromine atom. Due to the "saturation effect" noted above, there is a relatively small (compared to alkyl systems) but a clearly noticeable increase in relative reactivities in the order of $1^\circ < 2^\circ < 3^\circ$ benzylic hydrogens toward bromine atom (i.e., ethylbenzene is 25 times more reactive than toluene while cumene is only about twice as reactive as ethylbenzene). However, a notable fact is that a phenyl substituent lowers the α-C-H bonds energy more than a corresponding methyl substituent (by about 10 kcal/mole more). This is because the resulting benzylic radicals are stabilized by the delocalization of the unpaired electron in the π-cloud of the benzene ring, thus making the benzylic hydrogens much more reactive than the corresponding hydrogens of alkane. As shown in Table 8, the primary benzylic hydrogens of toluene are 64,000 times more reactive than the corresponding hydrogens of ethane towards bromine atom.

Research Objectives

In chapter one, it was shown that the free radical bromination of 9-cyclopropylanthracene (An-c-CH{CH_2}$_2$), using N-bromosuccinimide (NBS) in carbon tetrachloride as a reservoir for Br_2, yields exclusively a novel hydrogen abstraction product (An-c-CBr{CH_2}$_2$):



This result clearly indicates that the cyclopropylmethine C-H bond is more reactive towards Br· than the C-C bond of the cyclopropyl ring. We believe this is due to stereoelectronic effects - proper alignment of the cyclopropylmethine C-H bond with the p-orbitals of the adjacent anthracene nucleus activates the cyclopropylmethine hydrogen for abstraction by Br· (see Figure 16, page 33). However, an alternative explanation is that the result is due to steric inhibition of resonance in the ring-opened radical. Thus, formation of the hydrogen abstraction product is favored over the corresponding ring-opened product because the radical resulting from the ring opening process is destabilized (see Figure 24, page 51).

In chapter two, in an attempt to show that the p-orbitals of the anthracene system can participate in stabilizing an adjacent cationic center which is formed on the side-chain group, we have carried out a number of competitive ionic brominations of 9-bromo-10-cyclopropylanthracene versus phenylcyclopropane. The rate of ring opening of the cyclopropyl moiety of the anthracene system is found to be at least 18 times that of the phenylcyclopropane. It appears then, despite unfavorable peri-interaction, the cationic site

formed from the attack of Br_2 on the cyclopropyl moiety can be effectively stabilized by the adjacent π-cloud of the anthracene system. By inference, the p-orbitals of the anthracene system should also be able to effectively resonance-stabilized the ring-opened radical arising from reaction of 9-cyclopropylanthracene with bromine atom. The fact that the hydrogen abstraction product is preferentially formed (rather than the cyclopropyl ring-opened product) tends to support our contention that the abnormally high reactivity of the cyclopropylmethine hydrogen of 9-cyclopropylanthracene towards $Br^{\cdot}$ is a result of favorable overlap of the corresponding cyclopropyl C-H bond with the π-cloud of the anthracene moiety (i.e. stereoelectronic effects) rather than steric inhibition of resonance in the product radical.

In this chapter, we have determined the relative reactivity of several 9-alkylanthracenes towards bromine atom (via a series of competitive brominations using NBS as the brominating agent). The specific 9-alkylanthracenes to be employed in this study are 9-methyl-, 9-ethyl-, 9-isopropyl, and 9-cyclopropylanthracene. Additionally, the dissociation energies of the α-C-H bonds of these compounds have been calculated using semi-empirical molecular orbital theory[72,73] and the values are summarized in Table 10. It is evident from this table that the cyclopropylmethine C-H of 9-cyclopropylanthracene is the strongest bond (BDE = 85.9 kcal/mole) compared to the α-C-H bonds of the other 9-alkylanthracenes. This is reasonable considering the severe angular strain inherent in a cyclopropyl radical[74] which may cause it to be comparatively less stable than an acyclic side-chain 9-alkylanthracene radical. For example, the dissociation energy of a cyclopropane C-H bond is 106 kcal/mole while the dissociation energy of a C-H bond of an unstrained $-CH_2-$ group is generally 96 kcal/mole. 9-isopropylanthracene has the weakest α-C-H bond (BDE = 78.8 kcal/mole), and that an α-C-H bond of 9-ethylanthracene (BDE = 83.2 kcal/mole) is weaker than an α-C-H bond of 9-methylanthracene (BDE = 84.7 kcal/mole). This is consistent with the normal trend observed for alkanes (D{C-H}- primary, 98.0 kcal/mole > secondary, 94.5 kcal/mole > tertiary, 91.0 kcal/mole)[34] and alkylaromatics (D{C-H}-toluene, 88.0 kcal/mole > ethylbenzene, 85.9 kcal/mole > cumene, 84.4 kcal/mole).[1] Based on the notion that the rate of abstraction of hydrogens by bromine atom increases with decreasing bond strength of the C-H bonds being

attacked,[34,71,75] one might anticipate a relative reactivity order of 9-isopropylanthracene > 9-ethylanthracene > 9-methylanthracene > 9-cyclopropylanthracene for the abstraction of the α-hydrogens of these compounds by bromine atom.

Table 10. Dissociation Energies of the α-C-H Bonds of 9-Alkylanthracenes

9-Alkylanthracene	BDE (kcal/mole)[a]
An-c-$C(CH_2)_2$-H	85.9
$AnCH_2$-H	84.7[b]
$AnCH(CH_3)$-H	83.2
$AnC(CH_3)_2$-H	78.8

[a]Calculated using semi-empirical molecular orbital theory.[73] [b]Experimental 81.4 kcal/mole.[1]

Since the absolute rate for the abstraction of primary benzylic hydrogens of toluene by bromine atom is known, and if the relative reactivity between an appropriate alkylbenzene (relative reactivity data for alkylbenzenes is in the literature[76]) and one of the 9-alkylanthracenes of interest could be determined, it should be possible to estimate the absolute rates for the abstraction of the α-hydrogens by bromine atom from all of the 9-alkylanthracenes.

Finally, because of the novelty of the abstraction of the cyclopropyl hydrogen of 9-cyclopropylanthracene by bromine atom, we have also determined the magnitude of the primary (H/D) isotope effect associated with this process.

Results and Discussion

The relative reactivities of the α-hydrogens of the 9-alkylanthracenes of interest toward bromine atom (obtained from a number of competitive NBS brominations) at various temperatures are presented in Table 11.

Table 11. Relative Reactivities of 9-Alkylanthracenes toward Bromine Atom at Different Temperatures[a]

9-Alkyl-Anthracene	Relative Reactivities[b] as a function of temperature, °C					
	(12.0°)	(40.0°)	(60.0°)	(80.0°)	(100.0°)	(120.0°)
$AnCH_2$-H	1.00	1.00	1.00	1.00	1.00	1.00
An-c-$C(CH_2)_2$-H	0.15	0.21	0.27	0.33	0.43	0.53
$AnCH(CH_3)$-H	0.047	0.051	0.055	0.063	0.069	0.099
$AnC(CH_3)_2$-H	Virtually unreactive (<0.0001)					

[a]Bromination using NBS in carbon tetrachloride; benzoyl peroxide was used as an initiator at all temperatures except at 12.0 °C, which was irradiated (initiated) with a 400W medium pressure Hg arc lamp. [b]per-hydrogen, with 9-methylanthracene as an arbitrary standard

Statistical corrections were made using 9-methylanthracene as an arbitrary standard, based on the assumption that the three α-hydrogens of this molecule are equally reactive toward bromine atom. For example, consider the competitive reaction of Br· with 9-methylanthracene and 9-cyclopropylanthracene:

$$Br\cdot + An\text{-}CH_2H \xrightarrow{k_{MA}} An\text{-}\dot{C}H_2 + HBr$$

$$Br\cdot + An\text{-c-}C(CH_2)_2\text{-}H \xrightarrow{k_{CA}} An\text{-c-}\dot{C}(CH_2)_2 + HBr$$

At a temperature of, say 80 °C, the rate of hydrogen abstraction from 9-methylanthracene relative to 9-cyclopropylanthracene (k_{MA}/k_{CA}) on a per-molecule basis was determined to be 9.20. Since 9-methylanthracene has three α-hydrogens whereas 9-cyclopropylanthracene has only one, and assuming that all the three α-hydrogens of 9-methylanthracene are equally reactive toward the attacking Br·, the k_{MA}/k_{CA} on a per-hydrogen basis for this reaction is therefore 3.07. For convenience, the rate of hydrogen abstraction by Br· from 9-methylanthracene was arbitarily assigned a value of 1.00, thus making the rate of hydrogen abstraction from 9-cyclopropylanthracene with respect to 9-methylanthracene equal to 0.33 per-hydrogen (i.e., k_{CA}/k_{MA} = 1/3.07 = 0.33 per-hydrogen). Similar calculations were done for this reaction at different temperatures and also for the other 9-alkylanthracenes.

As revealed in Table 11, the α-methyl hydrogens of 9-methylanthracene are the most reactive, followed by the cyclopropylmethine hydrogen of 9-cyclopropylanthracene, and which in turn is more reactive than the α-methylene hydrogens of 9-ethylanthracene, toward bromine atom. The α-methine hydrogen of 9-isopropylanthracene is virtualy unreactive towards bromine atom. For instance, when an equimolar mixture of 9-ethylanthracene and 9-isopropylanthracene was subjected to slightly less than a stoichiometeric amount of NBS in refluxing carbon tetrachloride (in the presence of benzoyl peroxide as a radical initiator for 2 hr) only 9-ethylanthracene reacted to form the corresponding α-hydrogen abstracted product, 9-(α-bromoethyl)anthracene, while 9-isopropylanthracene remained virtually unreacted. Thus, the order of the relative reactivities of the α-hydrogens of the four 9-alkylanthracenes toward bromine atom, at all temperatures, is

$$\text{An-CH}_3 > \text{An-c-CH(CH}_2)_2 > \text{An-CH}_2\text{CH}_3 >> \text{An-CH(CH}_3)_2$$

The order of these relative reactivities is in marked contrast to that normally associated with radical chain processes involving bromine atom (i.e., in all known cases, the order of primary < secondary < tertiary hydrogens is clearly observed).[71] Consider, for

example, the reaction of a series of alkylbenzenes with Br as represented in the following equation.

$$C_6H_5\text{-}R + Br \rightarrow C_6H_5\text{-}R(\text{-}H) + HBr$$

If R represents $-CH_3$, $-CH_2CH_3$, and $-CH(CH_3)_2$, the rate of abstraction of the tertiary benzylic hydrogen of cumene and the secondary benzylic hydrogens of ethylbenzene are reported to be about 57 and 25 times (per hydrogen), respectively, the rate of abstraction of the primary benzylic hydrogens of toluene.[76]

Further, phenylcyclopropane reacts with bromine atom to yield exclusively the ring-opened product, 1,3-dibromo-1-phenylpropane. For the purpose of assessing the reactivity of the cyclopropyl moiety of phenylcyclopropane relative to that of the side-chain hydrogens of toluene towards bromine atom, we carried out a number of competitive photobrominations (using molecular bromine) of phenylcyclopropane versus toluene in carbon tetrachloride at 40.0 °C. From the results of these experiments, the rate of ring opening of the cyclopropyl moiety of phenylcyclopropane was determined to be 1.6 times the rate of abstraction of one of the primary benzylic hydrogens of toluene. Thus, the order of relative reactivities of alkylbenzenes toward bromine atom can be presented as

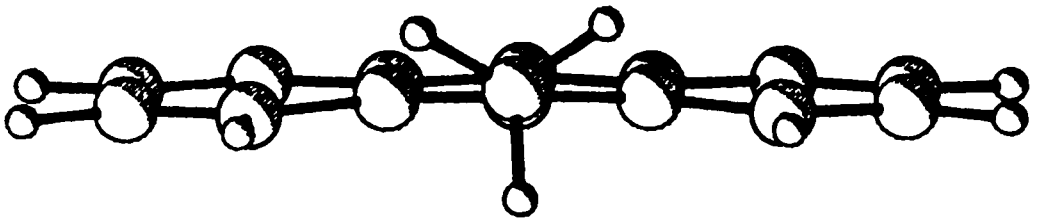
$$Ph\text{-}CH_3 < Ph\text{-}c\text{-}CH(CH_2)_2 < Ph\text{-}CH_2CH_3 < Ph\text{-}CH(CH_3)_2$$

Obviously, replacement of the phenyl by the anthryl system not only alters the mode of the reaction between bromine atom and the side-chain groups (compare the nature of the reactions of phenylcyclopropane and 9-cyclopropylanthracene with bromine atom), but also causes a complete reversal of the order of reactivities of the α-hydrogens of the side-chain groups. This is not what was expected based on the dissociation energies of the α-C-H bonds of the 9-alkylanthracenes in question (see Table 10, page 73). Clearly, the commonly accepted notion - the weaker the bond the more reactive it is towards bromine atom - does not hold in

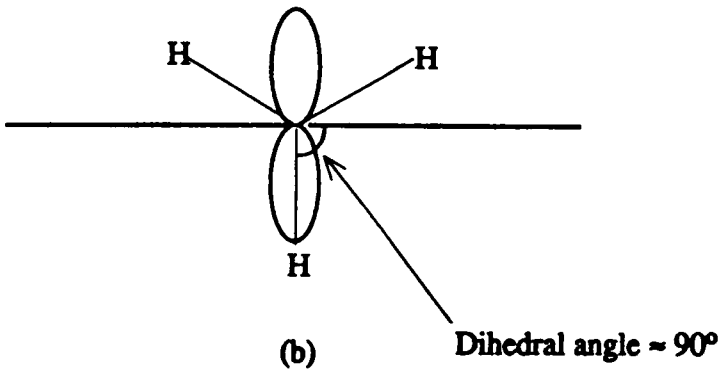
this case. In other words, the order of relative reactivities of the α-C-H bonds toward bromine atom is not a function of the stability of the 9-alkylanthracene radicals.

A plausible explanation for the unusual trend of relative reactivities can be derived by considering the conformational preferences of each of the 9-alkylanthracenes. The preferred conformation of each of the 9-alkylanthracenes as determined by molecular mechanics calculations[43] will now be briefly described.

For 9-methylanthracene, there are three degenerate low-energy conformations, each having an α-C-H in parallel arrangement with the p-orbitals of the adjacent anthracene nucleus. The dihedral angle between one of the α-C-H bonds and the plane of the central ring of the anthracene nucleus in the lowest energy conformation is determined to be 90° (Figure 28). The energy barrier to interconvert the position of an α-hydrogen with another by rotating the methyl moiety is only about 0.5 kcal/mole. This implies that any one of the α-C-H bonds can readily assume proper alignment with the p-orbitals of the anthracene nucleus.



(a)



(b)

Figure 28. **The lowest energy conformation of 9-methylanthracene:**
(a) PLUTO plot of the structure obtained from molecular mechanics calculations
(b) Schematic drawing of the structure

As discussed in chapter one, the cyclopropyl moiety of 9-cyclopropylanthracene is essentially locked in the perpendicular conformation (Figure 29), placing the cyclopropylmethine C-H bond in proper alignment with the adjacent π-system. The dihedral angle between this C-H bond and the plane of the central ring of the anthracene nucleus is determined to be 89°.

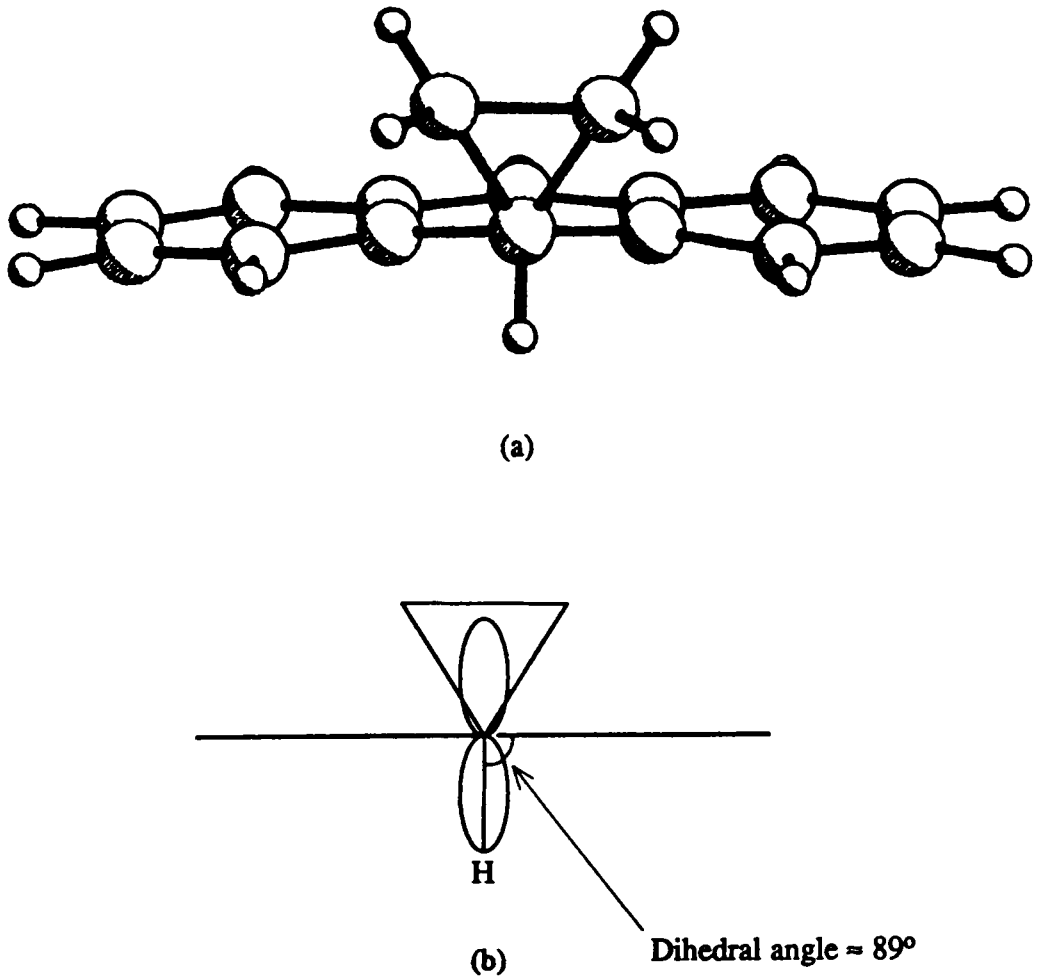
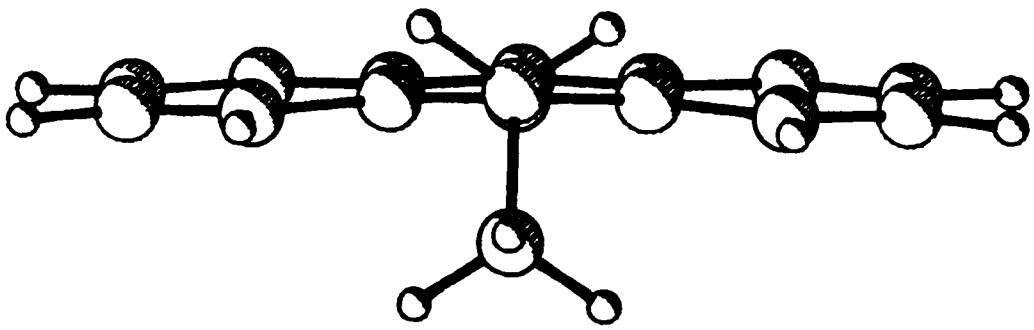
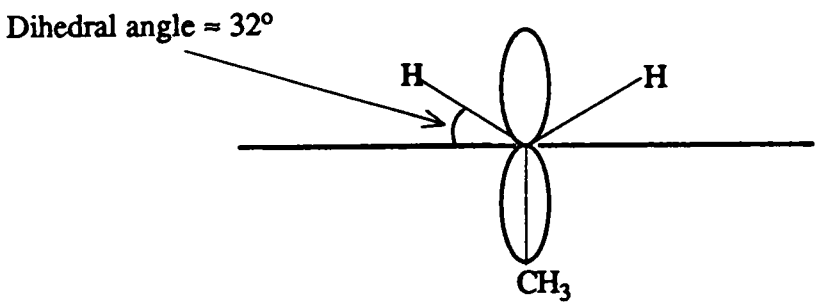


Figure 29. The lowest energy conformation of 9-cyclopropylanthracene:
(a) PLUTO plot of the structure obtained from molecular mechanics calculations
(b) Schematic drawing of the structure

For 9-ethylanthracene, there is only one stable conformation (Figure 30). The dihedral angle between either one of the α-methylene C-H bonds and the plane of the central ring of the anthracene nucleus is determined to be about 32°. Any other conformation is disfavored because of the increase in peri-interaction between the methyl hydrogens of the ethyl group and the hydrogens at positions 1 and 8 of the anthracene nucleus.



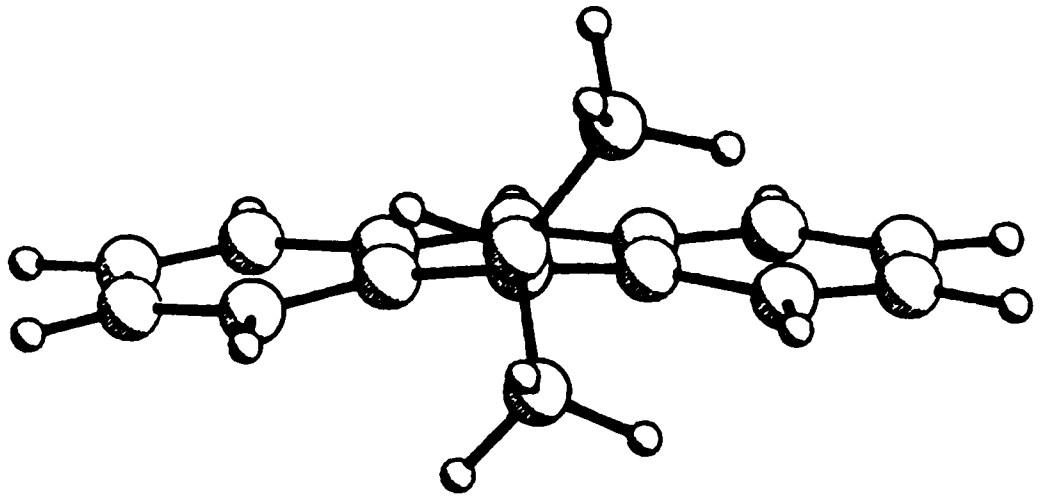
(a)



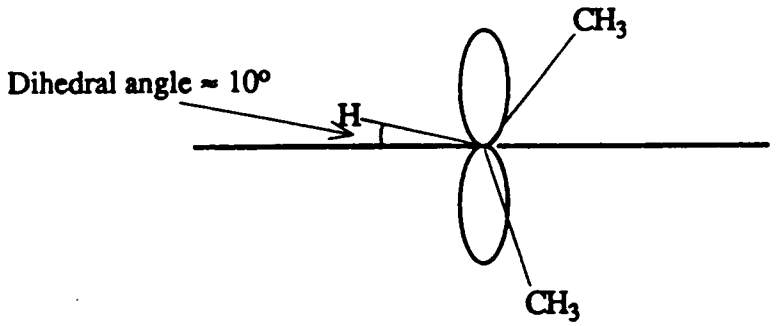
(b)

Figure 30. **The lowest energy conformation of 9-ethylanthracene:**
(a) PLUTO plot of the structure obtained from molecular mechanics calculations
(b) Schematic drawing of the structure

In the case of 9-isopropylanthracene, the preferred conformation has the methyl groups of the isopropyl moiety on the opposite sides of the plane of the anthracene nucleus (Figure 31). The dihedral angle between the α-methine C-H bond and the plane of the central ring of the anthracene nucleus is only about 10°. It is worthwhile to mention here that, if the isopropyl moiety is rotated through 270° and the total energy for a given conformation at every 10° is calculated, no other conformation, aside from the preferred conformation depicted by Figure 31, is found in a valley of minimum energy. Furthermore, it requires about 15 kcal/mole to rotate a methyl group of the isopropyl moiety and pass it by one peri-hydrogen (H-1 or H-8). Therefore, the isopropyl moiety is essentially locked in this conformation. Harvey and co-workers have examined the structures of several 9,10-dialkyl-9,10-dihydroanthracenes by ^{1}H NMR techniques (NOE experiments),[77] and they concluded that a bulky alkyl substituent with an α-hydrogen, such as an isopropyl group, exists in a conformation whereby the α-C-H bond is directed toward the peri-hydrogens. This is in accord with the results obtained using molecular mechanics calculations.[43]



(a)



(b)

Figure 31. **The lowest energy conformation of 9-isopropylanthracene:**
(a) PLUTO plot of the structure obtained from molecular mechanics calculations
(b) Schematic drawing of the structure

The bond dissociation energies and the relative reactivities of the corresponding α-C-H bonds toward bromine atom at 80.0 °C are retabulated in Table 12, along with the dihedral angles between the α-C-H bonds and the plane of the central ring of the various 9-alkylanthracenes that were obtained from the molecular mechanics calculations on the lowest energy conformations. We can see from this table that, although there is no correlation between the relative reactivities and bond dissociation energies, the relative reactivities are a function of the size of the dihedral angles. In other words, proper alignment of the α-C-H bonds with the p-orbitals of the corresponding anthracene system is the dominant factor in the reactivity of the α-hydrogens toward bromine atom.

Table 12. Bond Dissociation Energies[a], Relative Reactivities[b], and Dihedral Angles[c] of α-C-H Bonds of Different 9-Alkylanthracenes.

9-alkylanthracene	BDE (kcal/mole)	k_{rel}	Dihedral Angle H-C-C(Ar)-C(Ar)
$AnCH_2$-H	84.7	1.00[d]	90° ± 1
$AnC(CH_2)_2$-H	85.9	0.33 ± 0.02	89° ± 3
$AnCH(CH_3)$-H	83.2	0.063 ± 0.005	32° ± 2
$AnC(CH_3)_2$-H	78.8	<0.0001	10° ± 5

[a]Obtained from semi-empirical molecular orbital calculations.[73] [b]per-hydrogen towards $Br^{\cdot}$ at 80.0 °C. [c]Obtained from molecular mechanics calculation on lowest energy conformation.[43] [d]9-methylanthracene was chosen as an arbitary standard.

Consider 9-methylanthracene, since any one of the α-methyl C-H bonds can readily adopt parallel alignment with the p-orbitals of the anthracene nucleus (recall that the rotational barrier being only 0.5 kcal/mole), all the α-methyl hydrogens are fully activated for abstraction by bromine atom.

In the case of 9-cyclopropylanthracene, the cyclopropyl moiety is locked in the perpendicular conformation and therefore demands that the α-cyclopropyl C-H bond to be in proper alignment with the p-orbitals of the anthracene nucleus. Thus, the cyclopropyl hydrogen is strongly activated for abstraction by bromine atom. This is reflected by the fact

that, despite having higher bond strength (BDE = 85.9 kcal/mole), the α- cyclopropyl C-H bond of 9-cyclopropylanthracene is only 3 times less reactive than the α-methyl C-H bonds (BDE = 84.7 kcal/mole) of 9-methylanthracene.

For 9-ethylanthracene, the α-methylene hydrogens are not fully activated for abstraction by bromine atom because the dihedral angle between the α-methylene C-H bonds and the plane of the central ring of the anthracene nucleus is only 32°. Consequently, despite having lower bond strength (BDE = 83.2 kcal/mole), the α-methylene C-H bonds of 9-ethylanthracene are less reactive than the α-C-H bonds of both 9-methylanthracene and 9-cyclopropylanthracene.

The lack of reactivity of the α-methine C-H bond of 9-isopropylanthracene towards bromine atom compared to the α-C-H bonds of the other 9-alkylanthracenes is because it is almost orthogonal to the p-orbitals of the anthracene nucleus, and therefore, is not activated. In addition, since the α-methine C-H bond is directed towards the peri-hydrogen at position 1 or 8 8) of the anthracene moiety, there is likely to be a steric hindrance to approach by the Br (Figure 32).

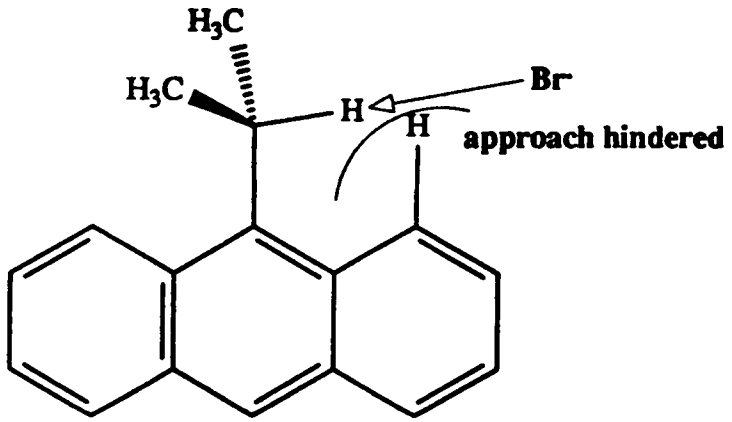
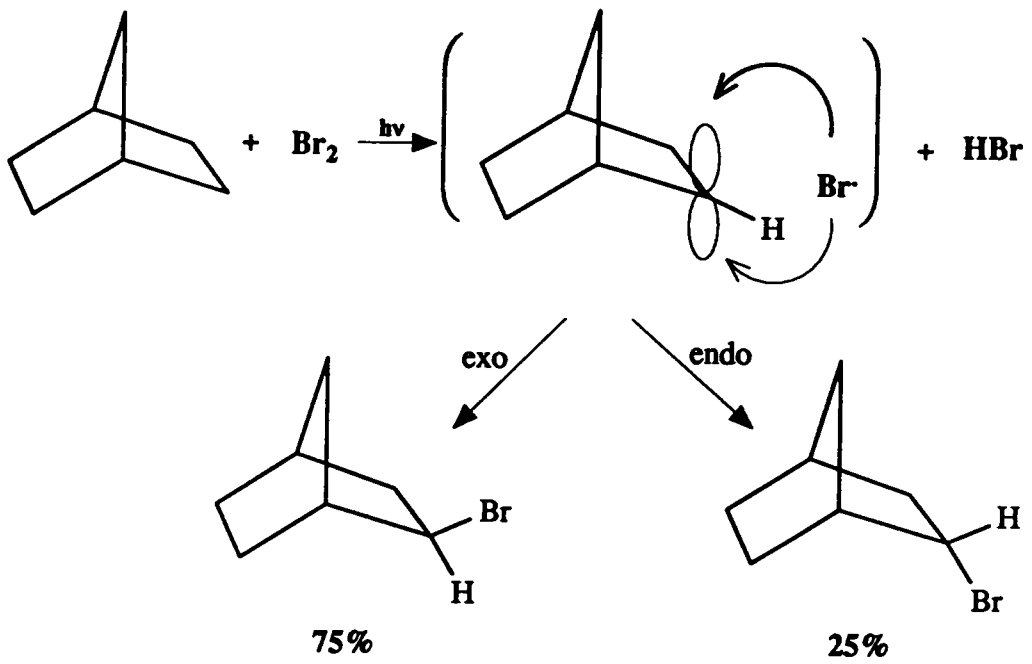


Figure 32. Steric hindrance to approach by Br· to the α-hydrogen of 9-isopropylanthracene

This may also contribute to lowering the ability of the Br· to abstract the α-methine hydrogen. The rate of attack of halogen atoms on carbon-hydrogen bonds has been known to decrease due to steric hindrance to approach. For example, the preference for the exo-2-bromide (75%) over the endo-2-bromide in the photobromination of norbornane was reported to be due to steric hindrance to approach, that is, the bulky Br· atom favors the less hindered exo approach (Eq. 30).[78]

Eq. 30



Another example, is the reaction of chlorine atom with 2,2,4,4-tetramethylpentane: due to steric hindrance to approach the tertiary hydrogen atom is 3 times less reactive than the secondary hydrogen atoms towards Cl· (Figure 33).[79]

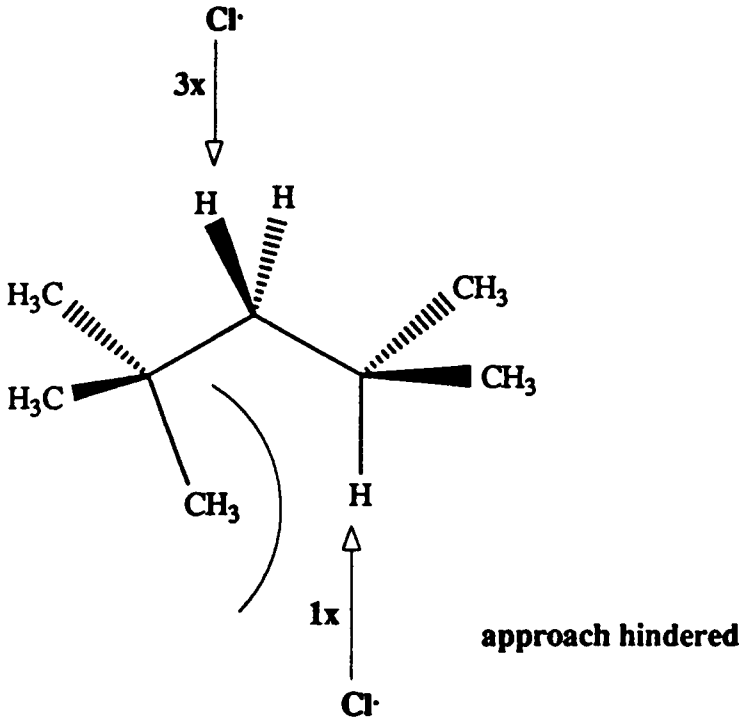


Figure 33. Reverse relative reactivities of the 2° and 3° hydrogen atoms of 2,2,4,4-tetramethylpentane toward Cl· at 40 °C due to steric hindrance to approach

Estimated Absolute Rate Constants

A number of competitive brominations of 9-methylanthracene and cumene using NBS were carried out in carbon tetrachloride at 40.0 °C. From the results of these experiments, the rate of hydrogen abstraction by bromine atoms from 9-methylanthracene with respect to cumene was determined to be 18.7 (per molecule). Since 9-methylanthracene has three α-hydrogen atoms whereas cumene has only one, and assuming that all of the three α-hydrogen atoms of 9-methylanthracene are equally reactive toward the attacking bromine

atom, the relative rate of hydrogen abstraction from 9-methylanthracene versus cumene on a per-hydrogen atom basis can be calculated to be 6.23. It has been reported that the rate of hydrogen abstraction by bromine atom from cumene on per hydrogen atom basis is 57.5 times faster than that of hydrogen abstraction from toluene.[76] Therefore, the rate of hydrogen abstraction by bromine atom from 9-methylanthracene with respect to toluene can be calculated to be 358.2. Using this value, and since the relative rates of the reaction of bromine atom with 9-cyclopropylanthracene and 9-ethylanthracene versus 9-methylanthracene have been determined, the relative rates of hydrogen abstraction by bromine atom from 9-cyclopropylanthracene and 9-ethylanthracene with respect to toluene can also be calculated. The reactivities of the compounds of interest toward bromine atom with respect to toluene are presented in the first column of Table 13.

The absolute rate of the abstraction of primary benzylic hydrogen from toluene by bromine atom at 40.0 °C is reported[71] to be 3.2×10^5 M^{-1} sec^{-1}. Using this value, the absolute rates of hydrogen abstraction by bromine atom from the other alkylarenes were estimated and the results are given in the second column of Table 13.

Table 13. Relative Reactivities and Estimated Absolute Reactivities of α-Hydrogens of Various Aralkanes towards Bromine Atom

Aralalkane	k_{rel}	k_{abs} M^{-1} sec^{-1}
$PhCH_2$-H	1.00[a]	3.2×10^5[b]
$PhCH(CH_3)$-H	25.2	8.2×10^6
$PhC(CH_3)_2$-H	57.5	1.8×10^7
$AnCH_2$-H	358.2	1.1×10^8
$AnC(CH_2)_2$-H	118.2	3.8×10^7
$AnCH(CH_3)$-H	22.6	7.2×10^6

[a]Arbitrary standard. [b]Obtained from reference 71.

Referring to Table 13, we see that the estimated absolute rate constants of the reaction of bromine atom with 9-cyclopropylanthracene and 9-methylanthracene are in the order of 10^7 and 10^8, respectively. These are extremely fast reactions, and are approaching the diffusion-controlled limit (generally in the order of 10^9 $M^{-1}sec^{-1}$ in carbon tetrachloride solvent).[70] The significance of this high reactivities of the α-C-H bonds of 9-methylanthracene and, particularly, 9-cyclopropylanthracene towards bromine atom will be elaborated upon later in our discussion.

Primary Hydrogen/Deuterium Isotope Effect

The term primary hydrogen/deuterium isotope effect refers to the change in the rate of a given reaction when a hydrogen of a reactant molecule is replaced by deuterium, and is commonly expressed by the ratio k_H/k_D. This effect is observed only if the bond-breaking occurs in the rate-determining step. The replacement of a hydrogen by a deuterium is presumed not to alter the overall potential energy surface or the electronic structure of the reactant molecule. Therefore, the change in reaction rate can be attributed solely to the difference in the zero-point vibrational energy between the C-H bond and that of the corresponding C-D bond of the reactant molecule. The zero-point energy of a bond depends on the mass of the atoms constituting the bond and is lower when the reduced mass is higher. Since the reduced mass of a C-D bond is higher, dissociation of a C-D bond requires more energy than that of a corresponding C-H bond in the same environment (Figure 34).[80]

The zero-point energy difference associated with bending and stretching vibrational modes of C-H and C-D bonds can be calculated to be about 1.5 kcal/mole.[71] A portion of this energy difference can be lost in the transition state in which these bonds are ruptured. If only the stretching vibration is lost and the transition state is symmetrical, a primary deuterium isotope effect of approximately 7 is expected. However, if the transition state is asymmetrical, for example, if it possesses little bond breaking or extensive bond making, the stretching

vibration will only be partially lost and a greatly reduced isotope effect will result. Thus, the magnitude of the primary hydrogen/deuterium isotope effect provides an insight into the structure of the transition state of the reaction of interest.

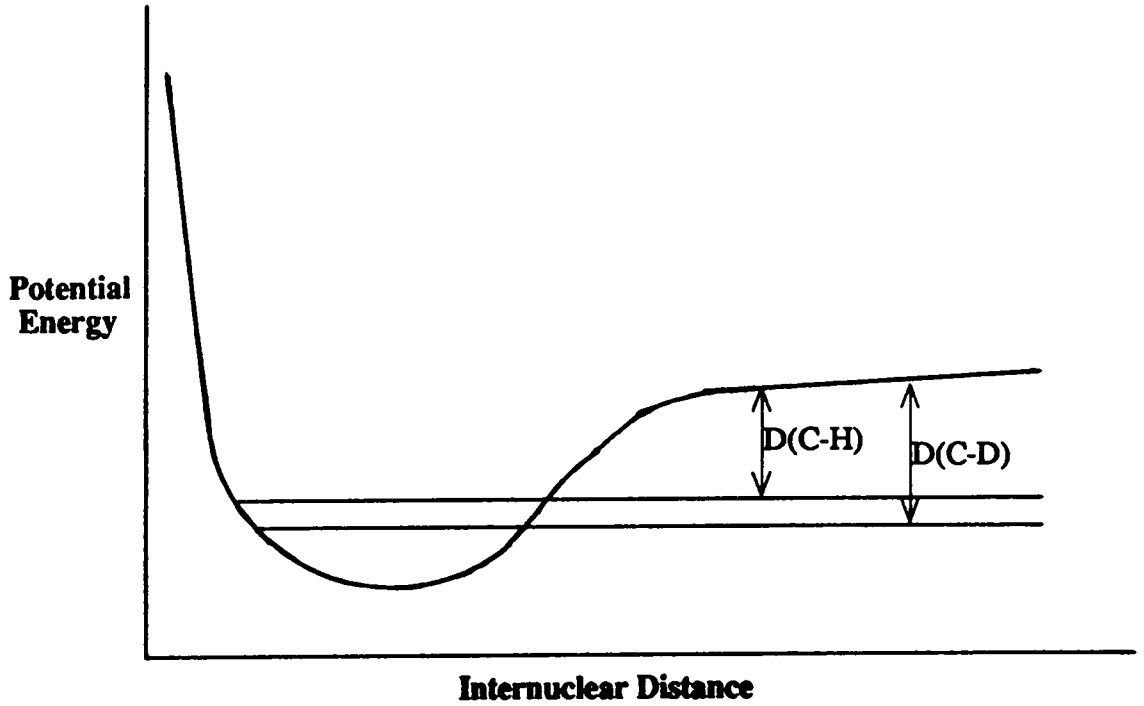


Figure 34. **Schematic representation of the zero-point energies of C-H and C-D bonds:** a C-D bond has lower zero-point energy than the corresponding C-H bond, thus the dissociation energy of a C-D bond is higher

Hanzlik and co-workers have recently reported a value of 6.37 for the k_H/k_D of the abstraction of hydrogen by Br· from toluene ($C_6H_5CH_2$-H{D} + Br· → $C_6H_5CH_2$· + H{D}-Br) using NBS as the brominating agent in carbon tetrachloride at 105 °C.[81] This high primary hydrogen/deuterium isotope effect value indicates that the transition state of this reaction is fairly symmetrical and involves extensive C-H bond-breaking. This is illustrated in Figure 35. Note that since the amount of energy required for the formation of an H-Br bond, ca. 88 kcal/mole, is approximately the same as that required for the dissociation of an α-C-H bond

of toluene, ca. 88 kcal/mole, the structure of toluene and the corresponding fully developed benzylic radical is drawn at about the same energy level.

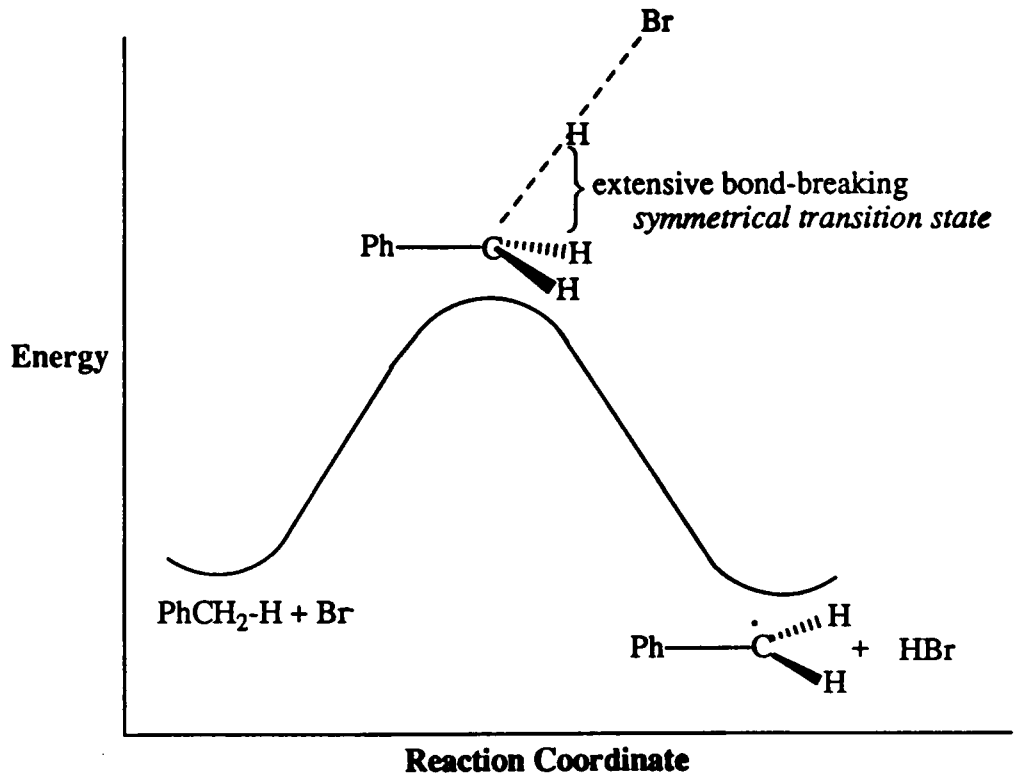
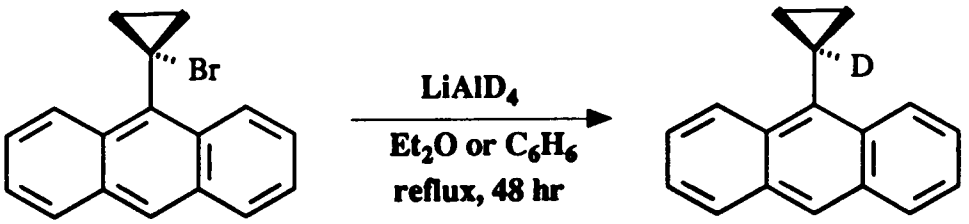


Figure 35. A reaction coordinate diagram for the abstraction of hydrogen by Br· from toluene

In order to determine whether the abstraction of the cyclopropylmethine hydrogen of 9-cyclopropylanthracene exhibits primary hydrogen/deuterium isotope effect, we have to first synthesize the α-deuterium analog of 9-cyclopropylanthracene. Fortunately, this was readily accomplished by reducing the α-brominated 9-cyclopropylanthracene with lithium aluminum deuteride in refluxing diethyl ether or benzene (**Eq. 31**).

Eq. 31



We then carried out the competitive bromination between 9-methylanthracene and the α-deuterium analog of 9-cyclopropylanthracene using NBS in carbon tetrachloride at 80.0 °C. From this experiment, the rate of hydrogen abstraction by bromine atom from 9-methylanthracene is determined to be 23.6 times faster than that of the abstraction of deuterium from the α-deuterium analog of 9-cyclopropylanthracene. Since the relative rate of hydrogen abstraction by bromine atom from 9-methylanthracene versus 9-cyclopropylanthracene is found to be 9.2, the k_H/k_D value for the abstraction of cyclopropylmethine hydrogen of 9-cyclopropylanthracene by bromine atom can be calculated to be 2.6. The small primary hydrogen/deuterium isotope effect value suggests that this reaction involves an asymmetrical and early transition state (i.e, with little bond breaking). This is illustrated in Figure 36. Note that the reaction of Br· with 9-cyclopropylanthracene is an exothermic reaction because the bond dissociation energy of the cyclopropylmethine C-H, ca. 86 kcal/mole, is lower than the bond formation energy of H-Br, ca. 88 kcal/mole.

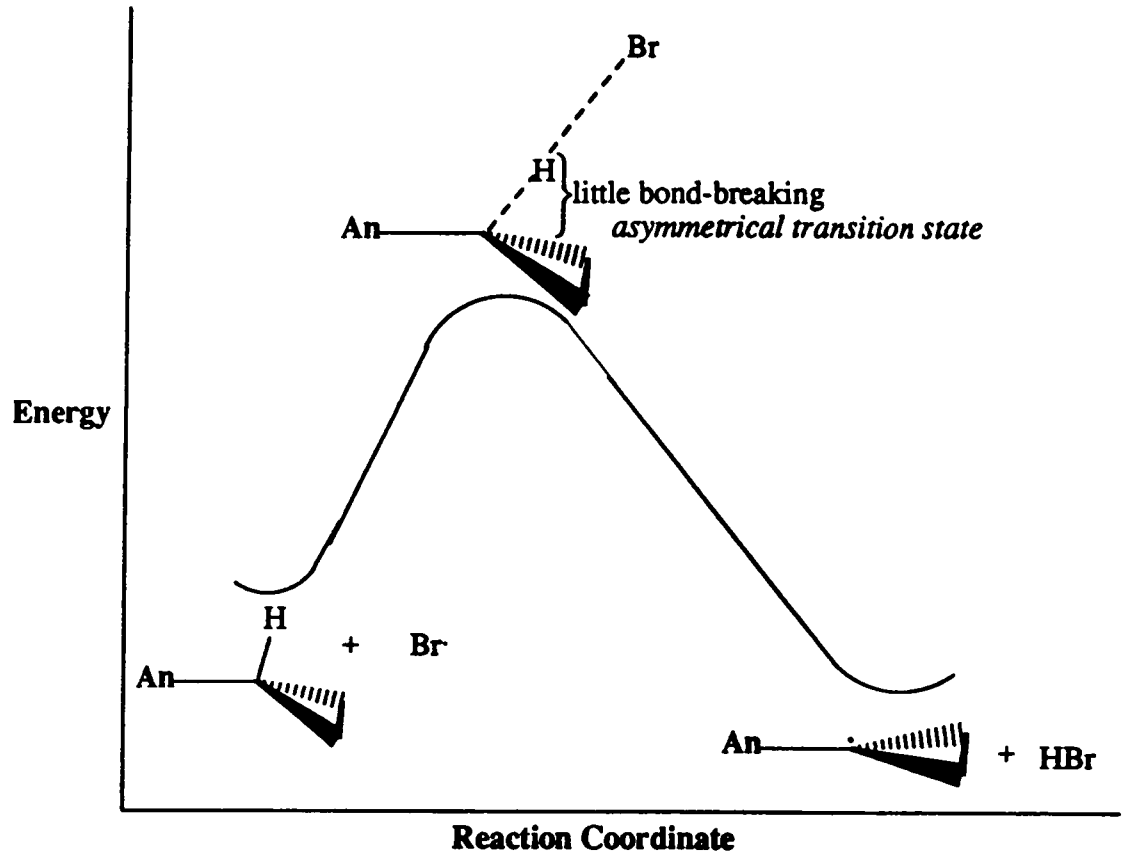


Figure 36. A reaction coordinate diagram for the abstraction of hydrogen by Br· from 9-cyclopropylanthracene

In the previous section, we have shown that 9-cyclopropylanthracene is much more reactive than toluene towards bromine atom (i.e., the absolute rate of hydrogen abstraction by Br· from 9-cyclopropylanthracene and toluene are 3.8×10^7 M^{-1} sec^{-1} and 3.2×10^5 M^{-1} sec^{-1}, respectively). This result supports the smaller value of primary hydrogen/deuterium isotope effect for the reaction of bromine atom with 9-cyclopropylanthracene than with toluene. Therefore, it is reasonable to conclude that the transition state of the abstraction of hydrogen by bromine atom from 9-cyclopropylanthracene is more reactant-like. From this we can infer that the conformational preference (perpendicular conformation) of the

9-cyclopropylanthracene plays a dominant role in the reactivity of the cyclopropylmethine hydrogen.

Chapter 4. Conclusions

We have examined the free radical bromination of several cyclopropylarenes (9-cyclopropylanthracene, 9-bromo-10-cyclopropylanthracene, 9-chloro-10-cyclopropyl-anthracene, 1-bromo-4-cyclopropylnaphthalene and phenylcyclopropane) and found that the nature of the reaction is critically dependent on the identity of the aryl system. For phenyl or α-naphthyl system, only the cyclopropyl ring-opened product is observed. In contrast, when the cyclopropyl group is attached to the central ring of an anthryl system, the results obtained are temperature-dependent. At 0°C and above, an unprecedented cyclopropyl hydrogen abstraction product predominates (>90%), but at -78°C, only the "expected" ring opening product is observed. The hitherto unrecognized process - the abstraction of a cyclopropyl hydrogen by bromine atom - is believed to arise from stereoelectronic effects. Molecular mechanics calculations and X-ray crystallography have been used to demonstrate that 9-cyclopropylanthracene, unlike other cyclopropylarenes, is effectively locked in a conformation which places the α-cyclopropyl C-H bond in alignment with the p-orbitals of the aromatic system. This orbital alignment favors the hydrogen abstraction process at the expense of cyclopropyl ring opening.

The electrophilic bromination of phenylcyclopropane and 9-cyclopropylanthracene has also been examined. Aromatic substitution and cyclopropyl ring-opened products were

obtained from both systems. The rate of ring opening of the cyclopropyl moiety of the anthryl system by molecular bromine is found to be 18 times faster relative to that of the phenyl. This can be attributed to greater delocalization of charge by the larger anthryl system. Thus, steric factors do not inhibit stabilization due to resonance. From this it can be inferred that the reason why the free radical bromination of 9-cyclopropylanthracene yields an unprecedented hydrogen abstraction product is due to the favorable alignment of the cyclopropyl C-H bond with the π-cloud of the anthryl system in the ground state (i.e., stereoelectronic effects), and not to steric inhibition to resonance in the product radical.

The relative rates of hydrogen abstraction from 9-methyl-, 9-cyclopropyl-, 9-ethyl-, and 9-isopropylanthracene by bromine atom are determined to be in the order of: 9-methylanthracene > 9-cyclopropylanthracene > 9-ethylanthracene >> 9-isopropylanthracene. These relative reactivities are drastically different from those normally associated with radical chain processes (i.e., the normal reactivity trend of $1° < 2° < 3°$ hydrogen atoms toward free radical is not obeyed). Semi-empirical molecular orbital theory and molecular mechanics calculations have been utilized to demonstrate that the relative reactivities are not a function of bond dissociation energies but rather a function of the dihedral angle between the α-C-H bonds and the plane of the central ring of the various 9-alkylanthracenes in their lowest energy conformations.

The absolute rate constants for reactions of the α-primary hydrogens of 9-methylanthracene, α-cyclopropyl hydrogen of 9-cyclopropylanthracene and the α-secondary hydrogens of 9-ethylanthracene toward bromine atom are estimated to be 1.1×10^8 M^{-1} sec^{-1}, 3.8×10^7 M^{-1} sec^{-1} and 7.2×10^6 M^{-1} sec^{-1} respectively. The value of the primary hydrogen/deuterium isotope effect for the abstraction of hydrogen by bromine atom from 9-cyclopropylanthracene is determined to be 2.6, suggesting an asymmetrical transition state with little bond breaking. The high absolute reactivities of 9-methylanthracene and 9-cyclopropylanthracene and the small isotopic effect for the abstraction of hydrogen by bromine atom from 9-cyclopropylanthracene provide additional support to the importance of stereoelectronic effects in the brominations of cyclopropylarenes and 9-alkylanthracenes.

Chapter 5. Experimental

General Considerations.

Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. Elemental analyses were submitted to and obtained from Multichem Laboratories Inc., Lowell, Ma. Nuclear magnetic resonance (^1H and ^{13}C) spectra were obtained on a 270 MHz Bruker FT NMR spectrometer. All chemical shift values are reported in δ units relative to Me_4Si (δ 0.00 ppm). Infrared spectra were recorded on a Perkin-Elmer model 710B spectrometer. IR bands were calibrated with the 1601.8 cm^{-1} band of polystyrene and are reported in cm^{-1}. Samples were prepared as KBr pellets. Ultraviolet spectra were obtained on Hitachi Perkin Elmer 100-60 spectrometer and are given as λ in nm (ε). Gas chromatographic analyses were performed on a Hewlett-Packard HP 5890A instrument equipped with both FID and TCD detectors, and an HP 3393A reporting integrator. Analyses were accomplished either on Alltech RSL-200 (nonpolar) capillary column (30m x 0.25mm) or on HP-1 (Methyl Silicone Gum) Instrument Test column (5m x 0.53mm). Mass spectra data were obtained from a Varian MAT 112 magnetic instrument operating at either 10eV or 70eV.

Materials

The following materials (99% gold label or HPLC grade) were purchased from Aldrich Chemical Company and used as received (unless otherwise noted): anthrone, hexamethyldisiloxane, chlorobenzene, benzyl chloride, benzyl bromide, 1,1,2,2-tetrachloroethane, methyl bromide, ethyl bromide, propyl bromide, isopropyl bromide, cyclopropyl bromide, magnesium ribbon, methylcyclohexene, 1,1,2-trichloroethene, diphenyl ether, phenylcyclopropane, benzoyl peroxide, cumene, iodine, bromine, deuterated chloroform with and without added tetramethylsilane, lithium aluminium deuteride, tri-n-butyltin hydride, anhydrous potassium carbonate, anhydrous sodium sulfate, sodium bicarbonate, sodium thiosulfate, anhydrous magnesium sulfate, anhydrous sodium bisulfite, neutral alumina, acetonitrile and ethanol. N-bromosuccinimide (NBS) was recrystallized from water and dried extensively in vacuo. 3,3-dimethyl-N-bromoglutarimide (33DMNBG) was prepared according to a published procedure.[82] Carbon tetrachloride and dichloromethane were slurried with potassium hydroxide for 24 hr, decanted and fractionally distilled from phosphorus pentoxide. The middle portion of each solvent was stored over molecular sieves. Tetrahydrofuran, benzene and toluene were distilled fresh from sodium or potassium metal (using benzophenone as an indicator) while diethyl ether was distilled fresh from lithium aluminum hydride before use.

Chlorine (Matheson, UHP) was transferred to a glass pressure tube, degassed, and stored at 0 °C.

General Procedure for the Synthesis of 9-Alkylanthracenes

All of the 9-alkylanthracenes utilized in this research were prepared according to a modified version of the procedures reported by Mosnaim *et al*[83] and by Bauld *et al*[37]

Grignard reagents were prepared by mixing appropriate alkyl bromides with magnesium ribbon in the presence of catalytic amount of iodine. All glassware was flame-dried and kept under dry nitrogen just prior to conducting the experiment. Typically, a measured amount of anthrone (5-10 g) was dissolved in tetrahydrofuran (1 g of anthrone per 20 mL of THF) and the solution added dropwise to an appropriate Grignard reagent (5-10% mole excess compared to the amount of anthrone used). The reaction mixture was refluxed for 2-3 hr. After cooling to room temperature and chilling in an ice-bath for 10 min, the resulting reaction mixture was gradualy acidified with concentrated HCl. The acidified mixture was extracted twice with dichloromethane (two 50-75 mL portions), and the combined extracts were washed with saturated solution of sodium bisulfite (30-40 mL) and dried over anhydrous sodium sulfate. Crude product was obtained by evaporating the solvent with a rotary evaporator. Preliminary purification was done by percolating the product through a column of neutral alumina with large amount of hexane-dichloromethane (95:5 mixture). Pure product was obtained by recrystallization from either ethanol or acetonitrile. Typical yield of pure product samples ranged from 40% to 70%.

Representative products:

9-cyclopropylanthracene: mp 134-135 °C (lit.[37] 133 - 135 °C); **Elem. Anal.** for $C_{17}H_{14}$, calculated %C 93.58 %H 6.42, found %C 93.23 %H 6.56; **^{1}H NMR** ($CDCl_3$) δ 0.84 (m, 2H, cis-cyclopropylmethylene hydrogens), 1.47 (m, 2H, trans-cyclopropylmethylene hydrogens), 2.49 (m, H, cyclopropylmethine hydrogen), 7.44-7.56 (m, 4H, 2-,3-,6- and 7-H anthryl hydrogens), 8.00 (m, 2H, 4- and 5-H anthryl hydrogens), 8.37 (s, H, 10-H anthryl hydrogen), 8.77 (m, 2H, 1-

and 8-H anthryl hydrogens); **^{13}C NMR** ($CDCl_3$) d 9.18 and 10.47 (cyclopropyl carbons), 124.74, 124.94, 125.92, 126.38, 128.86, 131.58, 131.72 and 134.68 (anthryl carbons); **IR** 3077, 3059, 3050, 3033, 3025, 3016, 3000, 2978, 2971, 2372, 2332, 1622, 1440, 1424, 1316, 1059, 1035, 1018, 1004, 891, 851, 830, 808, 796, 787, 734, 628, 612, 563; **UV** (CH_3CH_2OH) 387 (7,993), 367 (8,211), 349 (3,997), 336 (1,090), 256 (149,690); **MS** (EI, 70eV) m/e (relative intensity) 218 (100, M^+), 217 (72), 215 (33), 203 (82), 202 (70), 189 (24), 101 (11); **MS** (EI, 10eV) m/e (relative intensity) 220 (1.5), 219 (17.9), 218 (100, M^+), 217 (56.4), 216 (10.9), 215 (33.5), 204 (9.9), 203 (59.2), 202 (54.6), 191 (9.9), 190 (5.3), 189 (20.4).

9-propylanthracene: mp. 68-69 °C (lit.[83] 69-70); **Elem. Anal.** for $C_{17}H_{16}$, calculated %C 92.73 %H 7.72, found %C 92.28 %H 7.37; **^{1}H NMR** ($CDCl_3$) δ 1.15 (t, 3H, J = 7.33 Hz, CH_3), 1.86 (m, 2H, central CH_2) and 3.59 (t, 2H, J = 8.00 Hz, CH_2) of α-propyl, 7.53-7.42 (m, 4H, 2-,3-,6- and 7-H), 7.99 (m, 2H, 4- and 5-H), 8.27 (m, 2H, 1- and 8-H) and 8.33 (s, H, 10-H) of anthryl.

9-ethylanthracene: mp. 56-57 °C (lit.[83] 56-57 °C); **^{1}H NMR** ($CDCl_3$) δ 1.44 (t, 3H, J = 7.60 Hz, CH_3), 3.60 (q, 2H, J = 7.60 Hz, CH_2) of α-ethyl, 7.52-7.41 (m, 4H, 2-,3-,6- and 7-H), 7.98 (m, 2H, 4- and 5-H), 8.27 (m, 2H, 1- and 8-H) and 8.31 (s, H, 10-H) of anthryl.

9-methylanthracene: mp. 78-79 °C (lit.[83] 79-80 °C); **^{1}H NMR** ($CDCl_3$) δ 3.10 (s, 3H, CH_3) of α-methyl, 7.52-7.45 (m, 4H, 2-,3-,6-and 7-H), 8.00 (m, 2H, 4- and 5-H), 8.29 (m, 2H, 1- and 8-H) and 8.34 (s, H, 10-H) of anthryl. This compound was later purchased from aldrich chemical company.

9-isopropylanthracene: mp. 75-78 °C (lit.[83] 75-76 °C); **^{1}H NMR** ($CDCl_3$) δ 1.77 (d, 6H, J = 7.37 Hz, 2 x CH_3), 4.58 (h, H, J = 7.36 Hz, CH) of α-isopropyl, 7.51-7.42 (m, 4H, 2-,3-,6- and 7-H), 8.01 (m, 2H, 4- and 5-H), 8.47 (m, 2H, 1- and 8-H) and 8.34 (s, H, 10-H) of anthryl; **^{13}C NMR** ($CDCl_3$) δ 22.93 and 28.32 (isopropyl carbons), 124.51, 124.82, 125.05, 126.30, 129.59, 132.09 and 140.53

(anthryl carbons); **MS** (EI, 70eV) m/e (relative intensity) 220 (50, M^+), 205 (100), 190 (10), 178 (20), 149 (8), 101 (7).

Synthesis of 9-Chloro-10-Cyclopropylanthracene

Chlorine (1.55 mmol) was condensed into a 30-mL pressure tube containing 9-cyclopropylanthracene (0.34 g, 1.55 mmol), anhydrous potassium carbonate (0.22 g, 1.60 mmol) and 5 mL of carbon tetrachloride. The pressure tube was carefully wrapped with aluminum foil and placed in a water-bath maintained at 15 °C. After 1 hour, the reaction mixture was filtered and the resulting filtrate concentrated using a rotary evaporator. A small portion (0.25 mL) of this concentrated solution was combined with $CDCl_3$ (0.25 mL) in an NMR tube. ^1H NMR analysis revealed the presence of only one product which was identified and characterized (with a combination of other techniques, see below) to be 9-chloro-10-cyclopropylanthracene. The remainder of the concentrated solution and the solution in the NMR tube were tranferred to a column containing neutral alumina soaked in hexane. A dual-solvent hexane-dichloromethane (97:3 by volume) was used to elute the product. All eluents containing this compound (as indicated by GC analysis) were combined and the solvent evaporated under reduced pressure. Recrystallization from absolute ethanol gave 0.25 g (65%) of needle-like yellow crystals of 9-chloro-10- cyclopropylanthracene: **mp.** 117-118 °C; **Elem. Anal.** for $C_{13}H_{13}Cl$, calculated %C 80.79 %H 5.15 %Cl 14.06, found %C 80.40 %H 5.19 %Cl 14.88 and %C 80.35 %H 5.26 %Cl 13.41; **^1H NMR** ($CDCl_3/CCl_4$) δ 0.79 (m, 2H, cis-cyclopropylmethylene hydrogens), 1.47 (m, 2H, trans- cyclopropylmethylene hydrogens), 2.47 (m, H, cyclopropylmethine hydrogen), 7.51-7.61 (m, 4H, 2-,3-,6- and 7-H anthryl hydrogens), 8.69 (m, 2H, 1- and 8-H anthryl hydrogens), 8.78 (m, 2H, 4- and 5-H anthryl hydrogens); **^{13}C NMR** ($CDCl_3$) δ 9.64 and 10.67 (cyclopropyl carbons), 121.78, 125.22, 126.29, 128.25, 128.65, 132.25 and 134.56 (anthryl carbons); **MS** (EI, 70eV) m/e (relative intensity) 254 (14, M^+, ^{37}Cl), 252 (40, M^+,

^{35}Cl), 217 (100), 215 (55), 202 (68), 108 (13), 101 (12), 95 (11); an X-ray crystal structure of this compound was also obtained (see Figure 12, page 30).

Synthesis of 9-Bromo-10-Cyclopropylanthracene

A 20 mL carbon tetrachloride solution of bromine (35 uL, 0.69 mmol) was added dropwise using an addition funnel to a mixture of 9-cyclopropylanthracene (0.30 g, 1.38 mmol) and NBS (0.12 g, 0.70 mmol) inside a 100-mL round bottom flask wrapped with aluminum foil and equipped with a magnetic stirring bar. The reaction mixture was maintained at 15 °C in a water bath. After 1 hr, 30 mL aqueous solution of sodium bisulfite was added to quench the reaction. The organic layer was isolated, dried over anhydrous sodium sulfate, filtered and the filtrate evaporated to dryness. The resulting residue was dissolved in 40 mL of hexane, chilled in an ice-bath and filtered to further remove any unreacted NBS and the corresponding succinimide that formed. A portion (5.0 mL) of the filtrate was removed and evaporated to dryness under reduced pressure. ^1H NMR ($CDCl_3$) analysis of the residue revealed that only one product (see below) was formed. After column chromatography, using neutral alumina soaked in hexane as a stationary phase and a dual-solvent benzene-hexane (1: 30 by volume) as a mobile phase, 0.35 mg (85% yield) of 9-bromo-10- cyclopropylanthracene was isolated. Recrystallization from ethanol afforded yellow crystals: **mp.** 113-114 °C; **^1H NMR** ($CDCl_3/CCl_4$) δ 0.78 (m, 2H, cis-cyclopropylmethylene hydrogens), 1.48 (m, 2H, trans-cyclopropylmethylene hydrogens), 2.46 (m, H, cyclopropylmethine hydrogen), 7.50-7.61 (m, 4H, 2-,3-,6- and 7-H anthryl hydrogens), 8.56 (m, 2H, 1- and 8-H anthryl hydrogens), 8.78 (m, 2H, 4- and 5-H anthryl hydrogens); **IR** 2996, 2987, 1438, 1361, 1310, 1274, 1254, 1029, 1007, 954, 907, 865, 846, 817, 797, 757, 750, 699, 655, 612, 597, 578, 523; **UV** (CH_3CH_2OH) 399 (10,243), 378 (10,392), 359 (6,176), 341 (1,900), 257 (135,683); **MS** (EI, 70eV) m/e (relative intensity) 298 (11.8, M^+, ^{81}Br), 296 (12.0, M^+, ^{79}Br), 217 (100), 215 (55), 202 (54), 189 (18), 176 (10), 108 (18).

Bromination of 9-Cyclopropylanthracene with N-bromosuccinimide (NBS)

9-cyclopropylanthracene (0.47 g, 2.16 mmol), NBS (0.77 g, 4.32 mmol), benzoyl peroxide (0.0030 g, 0.022 mmol) and 30 mL of anhydrous carbon tetrachloride were placed in a 100-mL round bottom flask equipped with a Teflon-coated magnetic stirring bar, nitrogen inlet and a refluxing condenser. The reaction mixture was bubbled with dry nitrogen for 15 min and then refluxed for 1 hr. After cooling to 15 °C, succinimide and excess NBS were filtered off and the filtrate concentrated by evaporating most of the carbon tetrachloride under reduced pressure at room temperature (15-20 °C). The resulting viscous brown liquid was dissolved in 50 mL of hexane. The hexane solution was chilled in an ice-bath and filtered. The filtrate was washed with 15 mL of saturated solution of sodium bicarbonate and 15 mL of saturated solution of sodium thiosulfate, consecutively, and dried over anhydrous sodium sulfate. The hexane solution was then concentrated and chilled in an ice-bath. After about 30 min, 0.58 g (90% yield) of 9-(α-bromocyclopropyl)anthracene was isolated: **mp.** 113-115 °C; **Elem. Anal.** for $C_{17}H_{13}Br$, calculated %C 68.71 %H 4.38 %Br 26.91, found %C 68.34 %H 4.49 %Br 25.63; **^{1}H NMR** ($CDCl_3/CCl_4$) δ 1.48 (m, 2H, cis-cyclopropylmethylene hydrogens), 2.06 (m, 2H, trans-cyclopropylmethylene hydrogens), 7.49 (m, 2H, 3- and 6-H anthryl hydrogens), 7.64 (m, 2H, 2- and 7-H anthryl hydrogens), 8.02 (m, 2H, 4- and 5-H anthryl hydrogens), 8.47 (s, H, 10-H anthryl hydrogen), 8.78 (m, 2H, 1- and 8-H anthryl hydrogens); **^{13}C NMR** ($CDCl_3$) δ 20.31 and 27.90 (cyclopropyl carbons), 125.37, 126.11, 128.93, 128.99, 129.78, 130.17, 131.73, 133.30 and 134.20 (anthryl carbons), see the ^{1}H NMR (Figure 37) and ^{13}C NMR (Figure 38) spectra for direct comparison between this compound and 9-cyclopropylanthracene; **IR** 3084, 3075, 3053, 3031, 2998, 1623, 1521, 1443, 1413, 1291, 1261, 1158, 1135, 1049, 1018, 893, 848, 826, 803, 790, 734, 686, 615, 575, 543; **MS** (EI, 70eV) m/e (relative intensity) 298 (21.5, M^+, ^{81}Br), 296 (22.0, M^+, ^{79}Br), 217 (100), 215 (77), 202 (82), 189 (40), 176 (15), 163 (18), 150 (10), 108 (15), see Figure 39; In

addition, reduction of this compound with tri-n-butyltin hydride (n-Bu_3SnH) gave back the correponding hydrocarbon, 9- cyclopropylanthracene (vide infra).

Comments:

The above experiment was repeated several times with a 1:1 molar ratio of NBS and 9-cyclopropylanthracene rather than using NBS in excess. In each case, direct analysis of the reaction mixture by ^1H NMR indicated that 9-(α-bromocyclopropyl)anthracene was produced in essentially 100% yield (quantitated using either or a combination of both hexamethyldisiloxane and benzyl chloride as internal standards).

However, if the reaction mixtures were irradiated with a 400-W medium pressure mercury arc lamp varying amounts of 9-(α-bromocyclopropyl)anthracene were obtained, depending on the length of time of irradiation (see Table 14). The mercury arc lamp was placed at a distance of 2 ft from the reaction mixture and the radiation had to pass through two layers of Pyrex.

Table 14. Relative Distributions of 9-(α-bromocyclopropyl)anthracene from the Reaction[a] of 9-Cyclopropylanthracene with NBS in CCl_4 at 12.0 °C

Time (min)	Relative Distribution (%)[b]	Extent of Reaction (%)[c]
20	99	46
30	97	57
90	85	80
120	<70	>95

[a]Irradiated with a 400-W medium presure mercury arc lamp through two Pyrex layers at a distance of 2 ft. [b]Relative distributions were determined by ^1H NMR using benzyl bromide and/or hexamethyldisiloxane as internal standard(s). [c]Extent of reactions were determined based on the amount 9-cyclopropylanthracene and NBS recovered.

The results depicted in Table 14 can be attributed to the decomposition of 9-(α-bromocyclopropyl)anthracene once it was formed. 9-cyclopropylanthracene itself was stable under similar conditions (i.e., when a CCl_4 solution of only 9- cyclopropylanthracene

was irradiated with a 400-W medium pressure mercury arc lamp through two Pyrex layers at a distance of 2 ft for 2 hr, 100% of 9-cyclopropylanthracene was recovered). On the other hand, pure sample of 9-(α-bromocyclopropyl)anthracene decomposed significantly under similar conditions.

Reduction of 9-(α-bromocyclopropyl)anthracene with Tri-n-butyltin Hydride, n-Bu_3SnH

A sample of 9-(α-bromocyclopropyl)anthracene (50.0 mg, 0.17 mmol) was dissolved in 6 mL of anhydrous benzene inside a 25-mL Erlenmeyer flask, and the solution was analyzed by GC analytical techniques to ascertain the absence of 9-cyclopropylanthracene. The solution was then poured into a 30-mL pressure tube equipped with a Teflon-coated magnetic stirring bar and an O-ringed Teflon needle valve. After charging with n-Bu_3SnH (100.0 mg, 0.34 mmol) and benzoyl peroxide (0.60 mg, 0.0025 mmol), the reaction mixture was degassed 4 times by freeze-pump-thaw procedure (see below) and then heated to 80 °C for 3 hr. GC analysis of the resulting solution using diphenyl ether as an internal standard revealed the presence of 9-cyclopropylanthracene in quantitative yield.

[**Note**: The freeze-pump-thaw procedure was carried out as follows: With the valve closed, the pressure tube was placed in liquid nitrogen (ca. -196°C). The valve was opened and the pressure in the tube was reduced to about 10 millitorr. Then the valve was closed again and the reaction mixture thawed by running cold tap water over the tube. The entire process was repeated 4 times.]

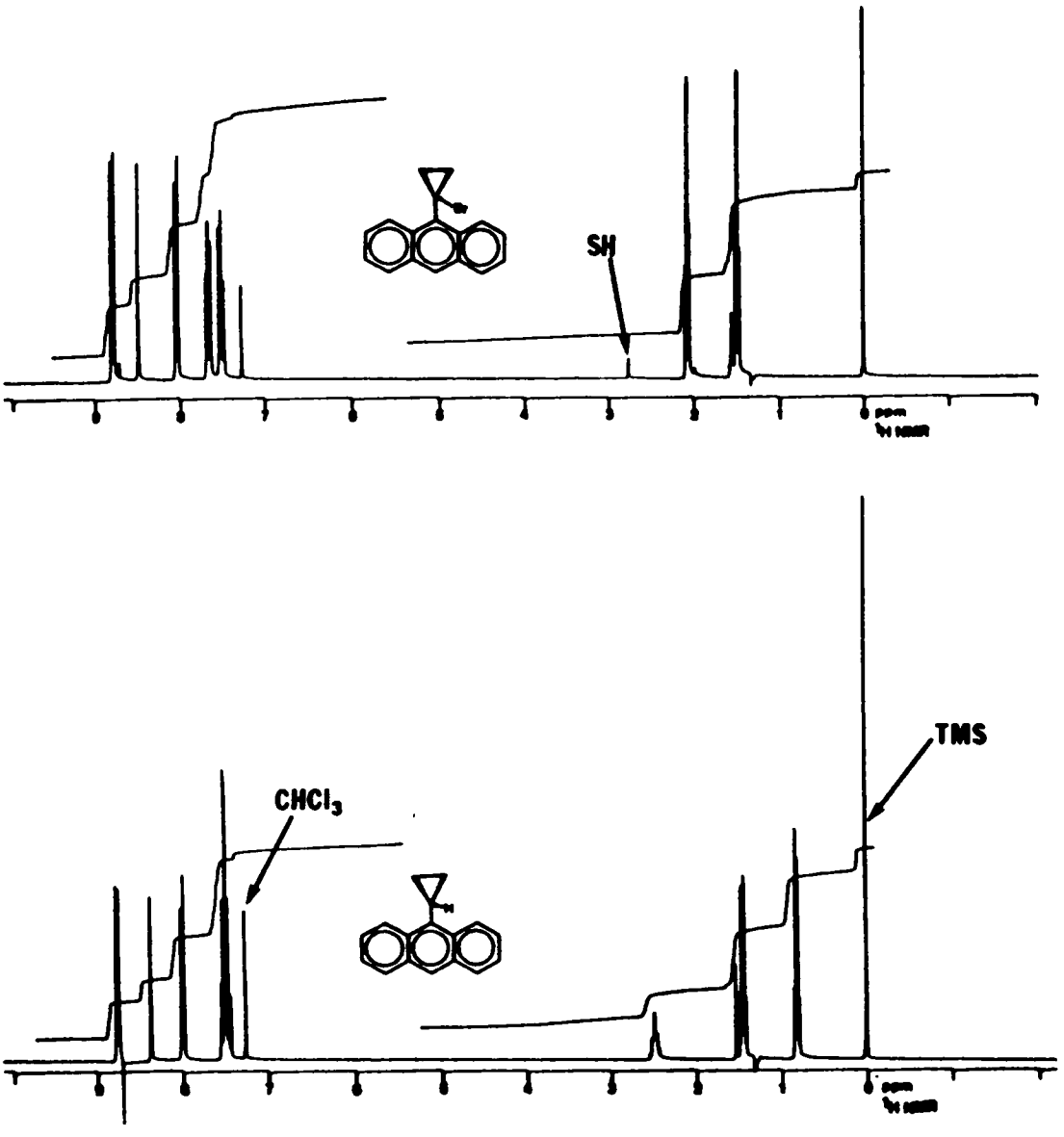


Figure 37. ^1H NMR spectra of 9-cyclopropylanthracene and 9-(α-bromocyclopropyl)anthracene

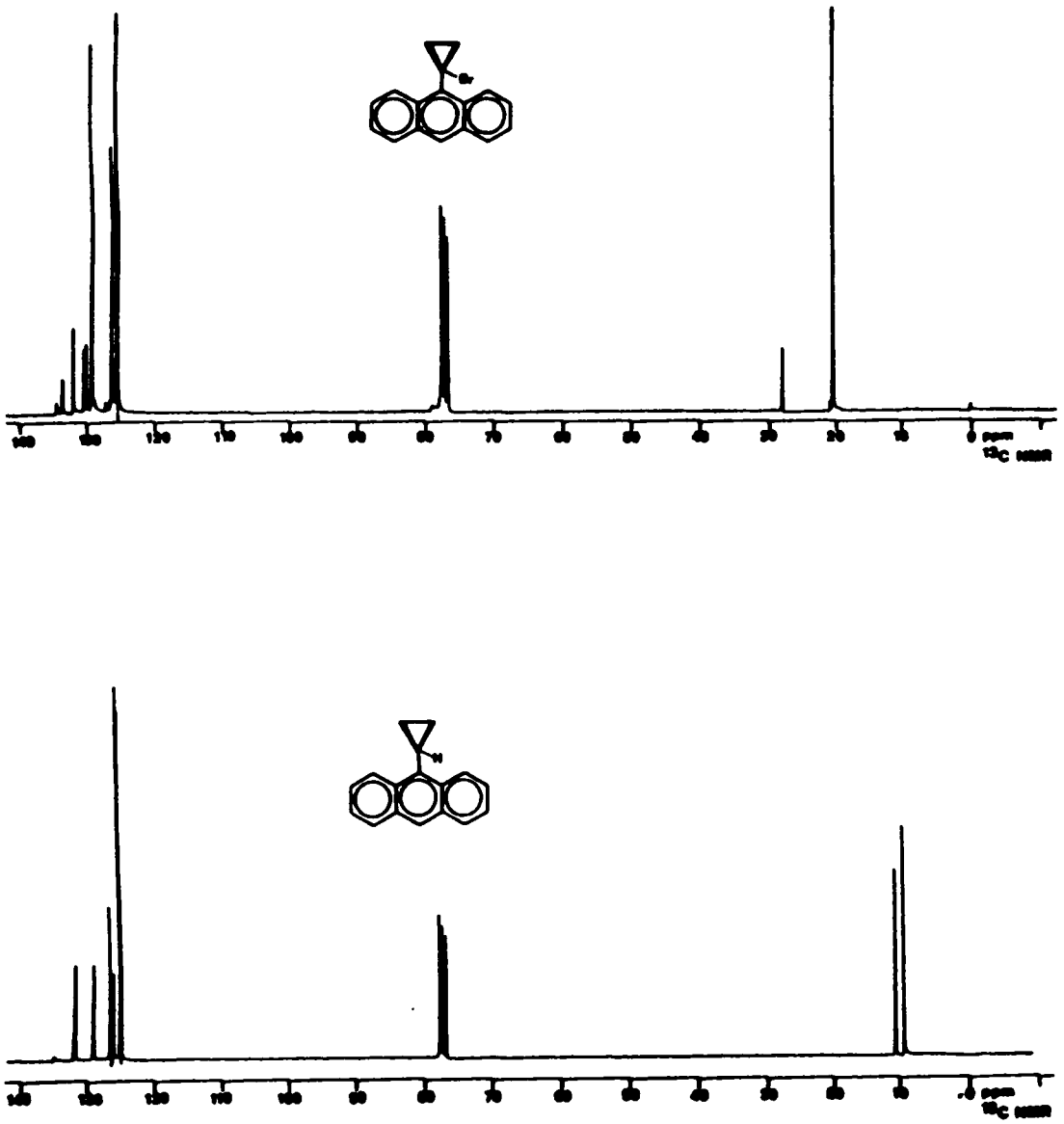


Figure 38. ^{13}C NMR spectra of 9-cyclopropylanthracene and 9-(α-bromocyclopropyl)anthracene

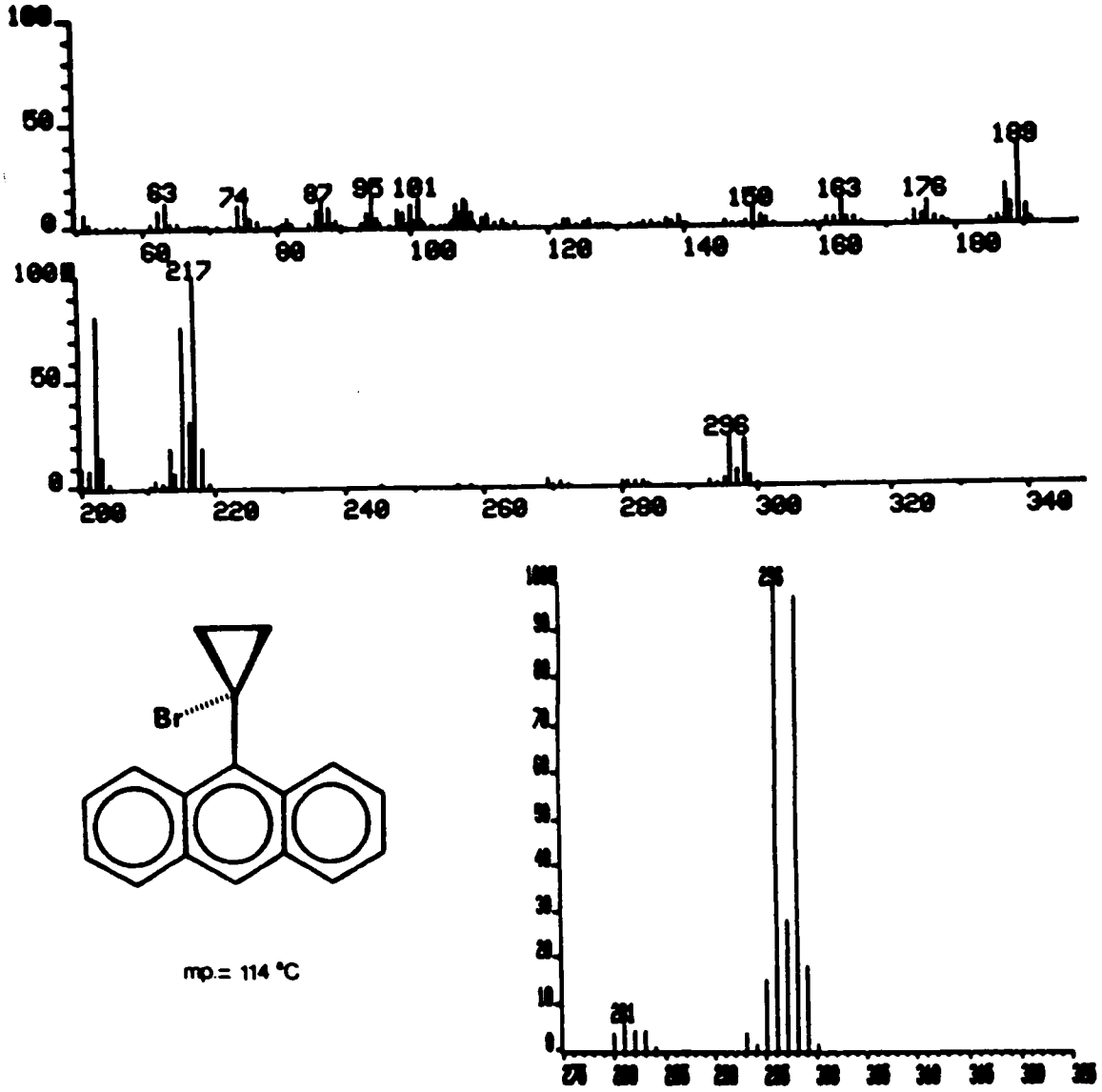


Figure 39. Mass spectrum (EI, 70 eV) of 9-(α-bromocyclopropyl)anthracene

Direct Reduction of a Reaction Mixture with n-Bu$_3$SnH

A reaction mixture, obtained from the reaction of NBS (54.0 mg, 0.30 mmol) with 9-cyclopropylanthracene (33.0 mg, 0.15 mmol) initiated by benzoyl peroxide (0.30 mg, 0.0012 mmol) in refluxing carbon tetrachloride (5 mL) for 1 hr, was cooled to room temperature and filtered. GC analysis of the filtrate indicated that 9-cyclopropylanthracene had been completely consumed and there was no higher molecular weight compound than 9-(α-bromocyclopropyl)anthracene. The filtrate was evaporated to dryness under reduced pressure, and the resulting residue was dissolved in 5 mL of anhydrous benzene. The solution was transferred to a pressure tube and charged with n-Bu$_3$SnH (140.6 mg, 0.48 mmol) and benzoyl peroxide (0.40 mg, 0.0017 mmol). The content of the pressure tube was degassed 4 times by freeze-pump- thaw method and heated in an oil bath (80-85 °C) for 4 hr. GC analysis of the resulting mixture (using retention times of authentic samples for comparison) showed the presence of only 9- cyclopropylanthracene (99%) and 9-propylanthracene (<1%). No 9-isopropylanthracene could be detected.

Photoinitiated Reaction of 9-Cyclopropylanthracene with N-bromo-3,3-dimethylglutarimide (33DMNBG)

9-cyclopropylanthracene (150.0 mg, 0.688 mmol) and 33DMNBG (160.0 mg, 0.727 mmol) were dissolved in 5 mL of dichloromethane inside a 30-mL pressure tube (sealed with an O-ringed Teflon needle valve). The solution was degassed 4 times by freeze-pump-thaw method, placed in a 20 °C water-bath, and then irradiated with a 400-W medium pressure mercury arc lamp (through two layers of Pyrex at a distance of 1.5 ft) for 1 hr. The irradiated

solution was evaporated to dryness under reduced pressure. The residue obtained was dissolved in 0.5 mL of deuterated chloroform and the resulting solution filtered through glass wool into an NMR tube. Measured amount of benzyl bromide (internal standard) was added and several ^{1}H NMR spectra of the solution were obtained. Examination of these ^{1}H NMR spectra showed that 40% of 33DMNBG was consumed in the reaction. However, there was no evidence of the formation 9-(α-bromocyclopropyl)anthracene (i.e., hydrogen abstraction did not take place and the cyclopropyl moiety remained intact). This was confirmed by GC analysis utilizing the retention time of an authentic sample for comparison. Scrutinization of the region of the aromatic protons revealed that substitution had occurred, apparently 3,3-dimethylglutarimidyl radicals added preferentially to the anthryl moiety. The exact structure of this product was not determined.

Photoinitiated Reaction of 9-Chloro-10-Cyclopropylanthracene with 33DMNBG

This experiment was carried out in a similar manner to the above experiment, except 9-cyclopropylanthracene was replaced with 9-chloro-10-cyclopropylanthracene and the irradiation time was 4 hr. The resulting solution was analyzed by ^{1}H NMR spectroscopy utilizing hexamethyldisiloxane as an internal standard. Although 99% of the 33DMNBG had reacted, there was no evidence of cyclopropyl hydrogen abstraction product (i.e., the cyclopropyl moiety remained clearly unreacted). This was supported by GC analysis utilizing the retention time of an authentic sample (9-{α-bromocyclopropyl}anthracene) for comparison. However, substitution had occurred at the 1 and 8 positions of the anthryl system since the area under the resonances corresponding to these positions (both the 1 and 8 anthryl hydrogens have similar chemical shift, 8.55ppm) was reduced by half compared to the area

under the resonances corresponding to the 4 and 5 positions (both the 4 and 5 anthryl hydrogens have similar chemical shift, 8.78 ppm). The exact structure of this aromatic substituted product was not determined

Comments:

The purpose of reacting 9-cyclopropylanthracene and its derivative with 33DMNBG in dichloromethane, conditions conducive to imidyl radical chains, was to rule out the possibility of hydrogen abstraction by imidyl radical. This was indeed the case, no hydrogen abstraction product was observed. To know this, it was not necessary to determine the exact structure of the aromatic substituted products that formed in the reactions described above. Therefore, no attempt was made to isolate the aromatic substituted products.

"Dilute Bromination"

A three-necked round bottom flask was charged with 11.0 mg (0.050 mmol) of 9-cyclopropylanthracene, 10.0 mg (0.072 mmol) of anhydrous potassium carbonate and 15 mL of carbon tetrachloride. A gentle stream of dry nitrogen was bubbled into the reaction mixture for 20 min while the flask was immersed in a water-bath which was maintained at 15 °C. Liquid Br_2 (8.0 mg, 0.050 mmol) was injected into a container (U-tube) which had been flushed with dry nitrogen and maintained at 0 °C in an ice-bath. Then the Br_2 was conveyed from the 0 °C container by a very mild but steady stream of dry nitrogen into the reaction mixture was irradiated with a 400-W medium pressure mercury arc lamp (placed at a distance of 2.5 ft) and maintained at 77°C. When the Br_2 had been completely transferred (45 min), the light was turned off and 5 uL of methylcyclohexene was introduced into the reaction flask. The reacted mixture was shown by GC analyses (utilizing diphenyl ether as an internal standard) to contain 70% 9-(α-bromocyclopropyl)anthracene. The remainder 30% was composed of a

mixture of products: 9-bromo-10-cyclopropylanthracene, 1,3-dibromo-1-(9-bromoanthryl) propane and some unidentified compounds (which presumably formed from decomposition of the primary brominated compounds due to the 45 min of irradiation time).

Photobromination of 9-Chloro-10-Cyclopropylanthracene

A mixture of 9-chloro-10-cyclopropylanthracene (55.0 mg, 0.22 mmol), anhydrous potassium carbonate (61.0 mg, 0.44 mmol) and 5 mL of carbon tetrachloride in a 30-mL pressure tube (sealed with an O-ringed Teflon needle valve and equipped with a Teflon-coated magnetic stirring bar) was degassed 4 times by freeze-pump-thaw technique. Bromine (11.0 uL, 0.22 mmol) was degassed on the vac-line and distilled directly into the reaction mixture. The mixture was irradiated at 15 °C with a 400-W medium pressure mercury arc lamp (placed at a distance of 2 ft from the pressure tube) through two layers of Pyrex. Bromine was completely consumed (decolorization) in 5 min. An aliquot (0.25 mL) of the reaction mixture was filtered through cotton wool into an NMR tube containing 0.25 mL of deuterated chloroform. ^{1}H NMR analysis of this solution (using hexamethyldisiloxane as internal standard) showed that 9-chloro-10-(α-bromocyclopropyl)anthracene was formed in 95% yield. The remainder 5% was comprised of 1,3- dibromo-1-(9-chloroanthryl)propane (3%) and unidentified products (2%). Spectral data for 9-chloro-10-(α- bromocyclopropyl)anthracene: **^{1}H NMR** ($CDCl_3/CCl_4$) δ 1.45 (m, 2H, cis-cyclopropylmethylene hydrogens), 2.06 (m, 2H, trans-cyclopropylmethylene hydrogens), 7.57-7.71 (m, 4H, 2-,3-,6- and 7-H anthryl hydrogens), 8.56 (m, 2H, 1- and 8-H anthryl hydrogens), 8.81 (m, 2H, 4- and 5-H anthryl hydrogens); **^{13}C NMR** ($CDCl_3$) δ 20.30 and 28.00 (cyclopropyl carbons), 125.00-136.00 (m, anthryl carbons)

Comments:

Repeated attempts to isolate pure sample of 9-chloro-10-(α- bromocyclopropyl)anthracene by column and thin layer chromatography proved to be very difficult and were not successful because the compound decomposes quite readily.

The above experiment was carried out at -78 °C in dichloromethane. Bromine (16.5 uL, 0.32 mmol) was dagassed and distilled via a vac-line into a 30-mL pressure tube containing a degassed mixture of 9-chloro-10-cyclopropylanthracene (81.0 mg, 0.32 mmol), anhydrous potassium carbonate (88.0 mg, 0.64 mol) and 7 mL of dichloromethane. The pressure tube was placed in a dry- ice isopropyl bath (-78 °C) and irradiated with a 400-W medium pressure mercury arc lamp. The reaction mixture turned greenish-brown in 10 min, and remained that color even after 40 min of irradiation. Upon warming (by placing the pressure tube in a water bath), decoloration occurred rapidly (within 1 min). The content of the pressure tube was filtered and evaporated to dryness under reduced pressure at ambient temperature. The resulting residue was dissolved in 0.5 mL of deuterated chloroform and the solution analyzed by ^{1}H NMR spectroscopy (using hexamethyldisiloxane as an internal standard). From this analysis the relative composition of the solution was found to be 80% 1,3-dibromo-1-(9-chloroanthryl)propane, 15% was presumed to be 9-chloro-10-cyclopropyl-anthracene (starting material), and 5% mixture of unidentified cyclopropyl ring-opened products. None of the α-cyclopropyl hydrogen abstration product, 9-chloro-10-(α-bromocyclopropyl)anthracene, was observed.

Photobromination of 9-Bromo-10-Cyclopropylanthracene

This reaction was carried out at 15 °C. The procedure was similar to that described for the photobromination of 9-chloro-10-cyclopropylanthracene. Yield of 9-bromo-10-(α-bromocyclopropyl)anthracene was determined by ^{1}H NMR analysis to be 95%. **^{1}H NMR**

($CDCl_3/CCl_4$) δ 1.47 (m, 2H, cis-cyclopropylmethylene hydrogens), 2.08 (m, 2H, trans-cyclopropylmethylene hydrogens), 7.44-7.69 (m, 4H, 2-,3-,6- and 7-H anthryl hydrogens), 8.61 (m, 2H, 1- and 8-H anthryl hydrogens), 8.81 (m, 2H, 4- and 5-H anthryl hydrogens)

Dark Bromination of 9-Bromo-10-Cyclopropylanthracene

9-bromo-10-cyclopropylanthracene (70.0 mg, 0.23 mmol), NBS (20.5 mg, 0.12 mmol) and 5 mL of CCl_4 were placed in a 30-mL pressure tube which was equipped with a magnetic stirring bar and carefully wrapped with Al-foil. Bromine (5.8 uL, 0.11 mmol) was distilled into the pressure tube via a vac-line. The pressure tube was sealed with an O-ringed Teflon needle valve and submerged in a water-bath maintained at 15 °C. After 1hr, the content of the pressure tube was evaporated to dryness under reduced pressure. Then 0.5 mL of a 1:1 mixture of CCl_4 and $CDCl_3$ was added to the residue, and the resulting solution filtered (through glass wool) directly into an NMR tube. ^{1}H NMR analysis indicated the presence of only one product, 1,3-dibromo-1-(9-bromoanthryl)propane. **^{1}H NMR** ($CCl_4/CDCl_3$): δ 2.8 (m, 1H, one of the hydrogens of the $-CH_2-$ group), 3.4 - 3.5 (m, 2H, one of the hydrogens of the $-CH_2-$ group and one of the hydrogens of the $-CH_2Br$ group), 3.7 (m, 1H, one of the hydrogens of the $-CH_2Br$ group), 7.5 - 7.7 (m, 4H, 2-,3-,6- and 7-H anthryl hydrogens), 8.4 (d, 1H, J = 9 Hz, 4-H anthryl hydrogen), 8.7 (dd, 2H, 1-H and 8-H anthryl hydrogens), 8.8 (d, 1H, J = 10 Hz, 5-H anthryl hydrogen).

Comments: Similar result was obtained when the above experiment was repeated without utilizing NBS. That means the reaction of 9-bromo-10-cyclopropylanthracene with Br_2 in the dark is free from complication due to HBr. Reduction of a reaction residue with an excess amount of n-Bu_3SnH in benzene afforded only 9-propylanthracene. This was determined by GC analysis of the resulting solution using the retention time of an authentic sample.

Dark Bromination of 9-Chloro-10-Cyclopropylanthracene

This experiment was carried out in an analogous manner as the dark bromination of 9-bromo-10-cyclopropylanthracene described above. Only one product, 1,3-dibromo-1-(9-chloroanthryl)propane, was obtained in 1hr of reaction time: **^{1}H NMR** ($CCl_4/CDCl_3$): δ 2.77 (m, 1H, one of the hydrogens of the $-CH_2-$ group), 3.38 - 3.49 (m, 2H, one of the hydrogens of the $-CH_2-$ group and one of the hydrogens of the $-CH_2Br$ group), 3.66 (m, 1H, one of the hydrogens of the $-CH_2Br$ group), 7.65 - 7.54 (m, 4H, 2-,3-,6- and 7-H anthryl hydrogens), 8.36 (d, 1H, J = 8.7 Hz, 4-H anthryl hydrogen), 8.60 (dd, 2H, 1-H and H-8 anthryl hydrogens), 8.79 (d, 1H, J = 9.8 Hz, 5-H anthryl hydrogen). **^{13}C NMR** ($CDCl_3$): δ 31.24, 41.65 and 45.79 (aliphatic carbons), 123.08 - 131.8 (region of aromatic carbons).

For longer reaction time, the reaction was performed in an NMR tube and monitored directly by ^{1}H NMR spectroscopy. A typical procedure is as follows: 9-chloro-10-cyclopropylanthracene (10.0 mg, 0.040 mmol) was dissolved in 0.3 mL $CDCl_3$, and the solution filtered into an NMR tube which was carefully wrapped with Al-foil. Bromine (2.1 uL, 0.041 mmol) was distilled via a vac-line into a thick-walled glass tube that contained 0.3 mL CCl_4. The CCl_4 solution of bromine was transferred (using a glass pipet) into the NMR tube. It is worthwhile to note here that the experiment was conducted with all the lights in the room turned off. The NMR tube was capped with a rubber septum and placed in a water-bath maintained at 15 °C. After 1hr, the NMR tube was temporarily removed from the water-bath and a ^{1}H NMR spectrum of the solution was immediately obtained. This was repeated at 5, 30 and 70 hr of reaction time. Three products were formed. They were identified and characterized as: 1,3-dibromo-1-(9-chloroanthryl)propane, NMR data for this compound has been given above; 3-bromo-1-(9- chloroanthryl)propene, **^{1}H NMR** parameters - δ 4.33 (dd, 2H, J = 0.94 Hz and J = 7.71 Hz, $-CH_2Br$), 6.20 (m, 1H, =CH-), 7.33 (d, 1H, J = 15.8 Hz, -CH=), 7.64 - 7.44 (m, 4H, 2-,3-,6- and 7-H anthryl hydrogens), 8.18 (d, 2H, J = 8.7 Hz, 4- and 5-H anthryl hydrogens), 8.49 (d, 2H, J = 8.7 Hz, 1-H and H-8 anthryl hydrogens);

1,2,3-tribromo-1-(9-chloroanthryl)propane, **^{1}H NMR** ($CDCl_3/CCl_4$) δ 4.15 and 4.66 (dd, 2H, J = 11.6 Hz, $-CH_2Br$), 5.66 (m, 1H, central -CHBr-), 6.93 (d, 1H, J = 11.3 Hz, -CHBr- adjacent to the anthryl moiety), 7.72 - 7.57 (m, 4H, 2-,3-,6- and 7-H anthryl hydrogens), 8.31 (d, 1H, J = 9.0 Hz, 4-H anthryl hydrogen), 8.63 (m, 2H, 1-H and H-8 anthryl hydrogens), 8.70 (d, 1H, J = 10.3 Hz, 5-H anthryl hydrogen). See Table 7, page 54 for yields of these products.

Photobromination of 9-Cyclopropylanthracene -78 °C

Liquid bromine (8.0 uL, 0.156 mmol) was degassed on the vac-line and distilled directly into a 30-mL pressure tube containing a degassed solution of 9-cyclopropylanthracene (65.0 mg, 0.298 mmol) in 6 mL of dichloromethane. The pressure tube was placed in a dry ice isopropyl bath (-78 °C) and irradiated with a 400-W medium pressure Hg arc lamp (through two layers of Pyrex at a distance of 2 ft). The solution was completely discharged of bromine color in 5 min. The solvent was evaporated under reduced pressure at room temperature, and a portion of the resulting oily residue was dissolved in 0.5 mL of deuterated chloroform. The relative composition of this solution was determined by ^{1}H NMR analysis (using hexamethyldisiloxane as an internal standard) to be 43% 1,3-dibromo-1-anthrylpropane, 52% excess 9-cyclopropylanthracene and 7% 9-bromo-10-cyclopropylanthracene. None of the α-cyclopropyl hydrogen abstraction product, 9-(α-bromocyclopropyl)anthracene was detected. In addition, reduction of the oily residue with n-Bu_3SnH gave only 9-propylanthracene and the starting material (9-cyclopropylanthracene), and with no indication of the presence of 9-isopropylanthracene. This was confirmed by GC analysis using the retention times of authentic samples for comparison. **^{1}H NMR** ($CDCl_3$) data for 1,3-dibromo-1- anthrylpropane: δ 2.78 (m, H, one of the protons of the $-CH_2-$ group), 3.49-3.38 (m, 2H, one proton from the $-CH_2-$ group and another from the $-CH_2Br$ group), 3.66 (m, H, one of the protons of the $-CH_2Br$ group) and 6.62 (m, H, -CHBr- group), 7.45 - 8.60 (m, 9H, aromatic hydrogens).

Control experiment:

The above experiment was repeated with the following changes: the reaction mixture was not degassed and the pressure tube was carefully wrapped with Al-foil to exclude light. After 5 min, 20 uL (0.17 mmol) of methylcyclohexene was added. ^{1}H NMR analysis of the resulting solution (using benzyl bromide as an internal standard) indicated the presence of 5% 9-bromo-10-cyclopropylanthracene and 95% 9-cyclopropylanthracene (i.e., the 95% of the starting material remained unreacted). Both of these compounds were isolated by standard column chromatography techniques using neutral alumina as the stationary phase and a dual-solvent hexane-dichloromethane (97:3 by volume) as the mobile phase.

Photobromination of Phenylcyclopropane

Phenylcyclopropane (15 uL, 0.13 mmol), anhydrous potassium carbonate (20.0 mg, 0.14 mmol) and 5.0 mL of dichloromethane were combined in a 30-mL pressure tube (sealed with an O-ringed Teflon needle valve), and the reaction mixture was degassed 4 times by freeze-pump-thaw method. Bromine (6.5 uL, 0.13 mmol) was degassed and distilled via a vac-line into the pressure tube and onto the reaction mixture which was held at -198 °C (liquid nitrogen temperature). The pressure tube was then placed in a dry-ice isopropanol bath (min.78 °C) while the reaction mixture was irradiated with a 400-W medium-pressure Hg arc lamp (placed a distance of 2 ft from the pressure tube). Complete discharge of bromine color occurred in 5 min. The content of the pressure tube was filtered, and the filtrate obtained was evaporated to dryness under reduced pressure at room temperature. The resulting oil was dissolved in 0.5 mL of deuterated chloroform. ^{1}H NMR analysis of this solution (using hexamethyldisiloxane as an internal standard) indicated that 1,3-dibromo-1-phenylpropane

was formed in 100% yield. Furthermore, reduction of the resulting oil with n-Bu_3SnH afforded, as shown by GC analysis, only n-propylbenzene.

The above experiment was repeated several times in the same solvent at 15 °C, and also in carbon tetrachloride at 0 and 15 °C. In each case, 1,3-dibromo-1-phenylpropane was the only product obtained. **^{1}H NMR** ($CDCl_3$) δ 2.59 and 2.78 (m, 2H and 2H, CH_2), 3.44 and 3.56 (m, 2H and 2H, -CH_2Br), 5.19 (m, 1H, CHBr), 7.56-7.08 (dd, 5H, aromatic).

Control experiments:

All experiments (in both solvents at different temperatures) were repeated with the following changes: the pressure tubes were carefully wrapped with Al-foil to exclude light and the reaction mixtures were not degassed. After 5 min, ample amount (>0.26 mmol) of methylcyclohexene or 1,1,2- trichloroethene (0.26 mmol) was added to scavenge bromine and the resulting solution analyzed by GC and ^{1}H NMR techniques. In each case, virtually 100% of phenylcyclopropane (starting material) was recovered.

Dark Bromination of Phenylcyclopropane

The procedure for this experiment is similar to that described for the dark bromination of 9-bromo-10-cyclopropylanthracene. A 1:1 molar ratio of reactants was utilized. Reaction was allowed to proceed for about 72 hr. Products formed were identified as: para-bromophenylcyclopropane, yield 10%, **^{1}H NMR** ($CDCl_3/CCl_4$) δ 0.72 (m, 2H, cis-cyclopropylmethylene hydrogens), 1.00 (m, 2H, trans- cyclopropylmethylene hydrogens), 1.90 (m, 1H, cyclopropylmethine hydrogen), 7.56 - 7.08 (m, 4H, aromatic hydrogens); 1,3-dibromo-1- phenylpropane, yield 45%, **^{1}H NMR** ($CDCl_3/CCl_4$) δ 2.59 and 2.78 (m, 2H, -CH_2-), 3.44 and 3.56 (m, 2H, -CH_2Br), 5.19 (dd, 1H, -CHBr-), 7.56 - 7.08 (m, 5H, aromatic hydrogens); 3-bromo-1- phenylpropene, yield 20%, **^{1}H NMR** ($CDCl_3/CCl_4$) δ 3.96 (m, 2H, -

CH_2Br), 4.76 (m, 1H, =CH-), 5.47 (d, 1H, -CH=), 7.56 - 7.08 (m, 5H, aromatic hydrogens); 1,2,3-tribromo-1-phenylpropane, yield 25%, **^{1}H NMR** ($CDCl_3/CCl_4$) δ 3.75 and 4.27 (dd, 2H, $-CH_2Br$), 4.39 (m, 1H, central -CHBr-), 5.32 (d, 1H, -CHBr- adjacent to the phenyl moiety), 7.56 - 7.08 (m, 5H, aromatic hydrogens).

Attempts to Brominate Phenylcyclopropane using NBS

Several mixtures of phenylcyclopropane (15.0 uL, 0.130 mmol), NBS (23.5 mg, 0.132 mmol) and benzoyl peroxide (1.0 mg, 0.0041 mmol) were throughly degassed by freeze-pump-thaw method. The mixtures were then heated and maintained at 80.0 °C for 40-90 min. GC and ^{1}H NMR analyses of the resulting reaction mixtures revealed no evidence of the addition of bromine atom to phenylcyclopropane (i.e., 100% of phenylcyclopropane remained unreacted). It should be pointed out that substantial amounts of NBS (>90%) were converted to β-bromopropionyl isocyanate (BPI). This was indicated by the presence of two set of triplets with identical coupling constant (J = 6.7 Hz) appearing at δ = 2.79 ppm and δ = 3.61 ppm, corresponding to the α- and β-methylene hydrogens of BPI, respectively. Also, the characteristic odor of isocyanate could be easily noted from the reaction mixtures.

Synthesis of 9-(α-deuteriocyclopropyl)anthracene

9-(α-deuteriocyclopropyl)anthracene (An-c-$CD(CH_2)_2$) was prepared in two steps. The first step involves the bromination of 9-cyclopropylanthracene (An-c-$CH(CH_2)_2$) with NBS to

produce the 9-(α-bromocyclopropyl)anthracene (An- c-CBr(CH_2)$_2$). The second step involves the reduction of this product with $LiAlD_4$ to An-c-CD(CH_2)$_2$.

First step:

A 30-mL pressure tube was charged with An-c-CH(CH_2)$_2$ (242.1 mg, 1.11 mmol), NBS (218.0 mg, 1.22 mmol), benzoyl peroxide (3.0 mg, 0.012 mmol), and 10 mL of carbon tetrachloride. The reaction mixture was degassed 4 times by freeze-pump-thaw method and heated to 80.0 °C in a constant temperature bath for 2 hr. Then the pressure tube was placed in an ice-bath for 5 min. Approximately 10 mL of hexane was added (to completely precipitate excess NBS and succinimide) and the content of the pressure tube was filtered directly into a clean 100-mL round bottom flask. (Note: It would be worthwhile to run a GC analysis on this solution to ascertain that An-c-CH(CH_2)$_2$ had been completely converted, which it should be, to An-c-CBr(CH_2)$_2$ before proceeding to the second step.) The solvent was removed under vacuo (1-2 hr) to give a yellow residue.

Second step:

The round bottom flask containing the product (yellow residue) obtained from the first step was charged with 50 mL of dry benzene (or diethyl ether) and 84.0 mg (2.00 mmol) of $LiAlD_4$. The flask was then equipped with a refluxing condenser, nitrogen inlet, and magnetic stirring bar. The content of the flask was refluxed with continous stirring under nitrogen atmosphere for 48 hr. Then 20-30 mL of cold deionized water was added cautiously to quench the excess $LiAlD_4$. An additional of 25 mL of solvent (benzene or diethyl ether) was also added. The organic layer was isolated and dried over anhydrous magnesium sulfate. Column chromatography over neutral alumina using a 97:3 mixture of hexane-dichloromethane as solvent afforded 130.0 mg (yield 54%) of white powder of An-c-CD(CH_2)$_2$. Recrystallization from ethanol gave crystalline material with a melting point of 132-133. **^{1}H NMR** ($CDCl_3$) δ 0.81 (m, 2H, cis-cyclopropylmethylene hydrogens), 1.48 (m, 2H, trans-cyclopropylmethylene hydrogens), 7.44-7.53 (m, 4H, 2-,3-,6- and 7-H anthryl hydrogens), 8.00 (m, 2H, 4- and 5-H anthryl hydrogens), 8.36 (s, H, 10-H anthryl hydrogen), 8.73 (m, 2H, 1- and 8-H anthryl hydrogens); **^{13}C NMR** ($CDCl_3$) δ 9.10 and 9.86 (cyclopropyl carbons), 124.78, 124.97, 125.96,

126.42, 128.88, 131.66, 131.81 and 134.63 (anthryl carbons); **IR** 3077, 3051, 3000, 1621, 1440, 1366, 1036, 1018, 1005, 892, 867, 847, 823, 795, 771, 734, 697, 624, 562; **MS** (EI, 10eV) m/e (relative intensity) 221 (2.0), 220 (19.0), 219 (100, M^+), 218 (53.4), 217 (13.6), 216 (27.7), 215 (6.9), 205 (7.6), 204 (45.7), 203 (48.6), 202 (14.6), 192 (7.9), 191 (4.2), 190 (13.4), 189 (5.1), 110 (5.1), 109 (5.2), 102 (5.5).

Competitive Experiments

Competitive brominations with NBS were carried out as follows: At temperatures of 40.0 ± 0.5 °C and above, each of the competitors was weighed into a 30-mL pressure tube (equipped with a Teflon-coated magnetic stir bar and an O-ring Teflon needle valve) containing a weighed amount of NBS and benzoyl peroxide (2 mole-%). 5 to 7 mL of CCl_4 was then added. The mixture was degassed 4-5 times by freeze-pump- thaw technique and placed in a controlled temperature bath. When the reaction was completed (1-2 hr), as indicated by the disappearance of NBS from the bottom of the reaction flask, the mixture was chilled in an ice-bath. Weighed quantity (0.100-0.200 mmol) of one or two appropriate internal standards for NMR analysis were added. The internal standards employed were benzyl chloride, benzyl bromide, 1,1,2,2-tetrachloroethane and hexamethyldisiloxane. The selection of an internal standard was based on its suitability for NMR analysis procedure, specifically on the chemical shift values of its proton absorptions. A 0.25 mL sample of the liquid portion of the reaction mixture was then transferred to a thin-walled NMR tube containing 0.25 mL of $CDCl_3$. ^1H NMR analysis of the solution was performed as soon as possible (generally, in less than 10 min) so as to avoid significant degradation or hydrolysis of α-brominated products.

For the competive bromination of 9-cyclopropylanthracene versus cumene, excess 9-cyclopropylanthracene and its corresponding α-brominated product were analyzed by ^1H NMR while excess cumene was analyzed by GC techniques. The internal standard used for

GC analysis was chlorobenzene. This was added to the mixture along with the NMR internal standard (benzyl chloride) after the completion of the reaction.

At a temperature of 12.0 ± 1.0 °C, instead of using benzoyl peroxide, the reaction mixture was irradiated with a 400-W medium pressure mercury arc lamp (at a distance of 2 ft and through two layers of Pyrex) for 20-30 minutes. During this time, about 50-75% of the initial amount of NBS was consumed. Irradiation was not done for a longer period of time because the primary reaction products tend to decompose significantly (see Table 14, page 103).

The competitive bromination of phenylcyclopropane and toluene with Br_2 was carried out using a modification of the above procedure. Briefly, Br_2 was degassed on the vac-line and distilled directly into a degassed solution of toluene and phenylcyclopropane in 5 mL of CCl_4. The reaction mixture was irradiated at 40.0 ± 0.5 °C. Complete discharge of Br_2 took place within 5-10 min. Weighed amount (0.100 - 0.200 mmol) of both NMR and GC internal standards were added, and the resulting reaction mixture was analyzed by both methods.

Quantitation by GC Analysis

The peak areas of excess competitors were converted to millimoles using known number of millimoles of the internal standard and correction factors calculated from the analyses of standard solutions. Analyses were performed in triplicate.

Quantitation by ^1H NMR Analysis

At least four integrations were carried out on selected proton absorptions of α-brominated products, excess competitors and internal standards. Integral amplitudes were maximized to obtain the highest possible accuracy. The average deviation of individual

integrations from the mean was generally on the order of 1%. The average values of integrations of different proton absorptions were then corrected for the number of protons contributing to the absorptions. From these values, and the number of millimoles of internal standards, the number of millimoles of brominated products and excess competitors were calculated (see Appendix for further details).

The average chemical shift values (δ in parts per million downfield from TMS) which vary slightly in different mixtures for the various individual aliphatic proton absorptions of the internal standards, competitors and bromide products are as follows: benzyl chloride, 4.6 (s, 2H, CH_2Cl); benzyl bromide, 4.4 (s, 2H, CH_2Br); 1,1,2,2-tetrachloroethane, 5.9 (s, 2H, $\{CHCl_2\}_2$); hexamethyldisiloxane, 0.07 (s, 18H, $(CH_3)_3$ x 2); toluene, 2.4 (s, 3H, CH_3); phenylcyclopropane, 0.7 and 1.0 (m, 2H and 2H, cis- and trans-cyclopropylmethylene, respectively), 1.8 (m, 1H, cyclopropylmethine); 9- methylanthracene, 3.1 (s, 3H, CH_3); 9-ethylanthracene, 1.4 (t, 3H, J = 7.6 Hz, CH_3), 3.6 (q, 2H, J = 7.6 Hz, CH_2); 9-isopropylanthracene, 1.8 (d, 6H, J = 7.4 Hz, 2 x CH_3), 4.6 (h, 1H, J = 7.4 Hz, CH); 9-cyclopropylanthracene, 0.8 (m, 2H, cis-cyclopropylmethylene), 1.5 (m, 2H, trans-cyclopropylmethylene), 2.5 (m, 1H, cyclopropylmethine); 1,3-dibromo-1-phenylpropane, 2.59 and 2.78 (m, 2H, CH_2), 3.44 and 3.56 (m, 2H, CH_2Br), 5.19 (m, 1H, CHBr); 9-(α-bromomethyl)anthracene, 5.5 (s, 2H, CH_2Br); 9-(α-bromoethyl)anthracene, 2.3 (d, 3H, J = 7.3 Hz, CH_3), 6.7 (q, 1H, J = 7.3 Hz, CHBr); 9-ethyleneanthracene, 5.6 and 5.9 (dd, 2H, J = 2.0 Hz and J = 15.6 Hz, cis- and trans-alkenic protons of CH_2), 7.4 (dd, 1H, CH); 9-(α-bromocyclopropyl) anthracene 1.5 (m, 2H, cis-cyclopropylmethylene), 2.1 (m, 2H, trans- cyclopropylmethylene).

All absorptions used in the computations of relative reactivities were clean and well resolved. For examples, see Figure 40 for the spectrum of the resulting solution of the competitive bromination of 9-methylanthracene and 9-cyclopropylanthracene, and Figure 41 for the spectrum of the resulting solution of the competitive bromination of 9-methylanthracene and 9-ethylanthracene with NBS at 80.0 ± 0.5 °C. For most starting materials and bromide products there is more than one absorption on which the quantitative analyses could be based. In such cases, computations based on either absorption gave essentially similar

results. Also, it is worthwhile to note that 1,1,2,2-tetrachloroethane (one of the internal standards used) could be added to a reaction mixture before or after the competitive bromination. In either case, no significant difference in results was observed.

Calculation of Relative Reactivities

Relative reactivities per molecule from individual competition experiments were calculated using the integrated rate equation $k_A/k_B = \ln (A_o/A_f)/ \ln (B_o/B_f)$, where A_o and B_o are the initial and A_f and B_f the final amounts of the two competitors (the derivation of this equation is given in chapter three).

The data and results of several different competition experiments are tabulated in Tables 15 to 19.

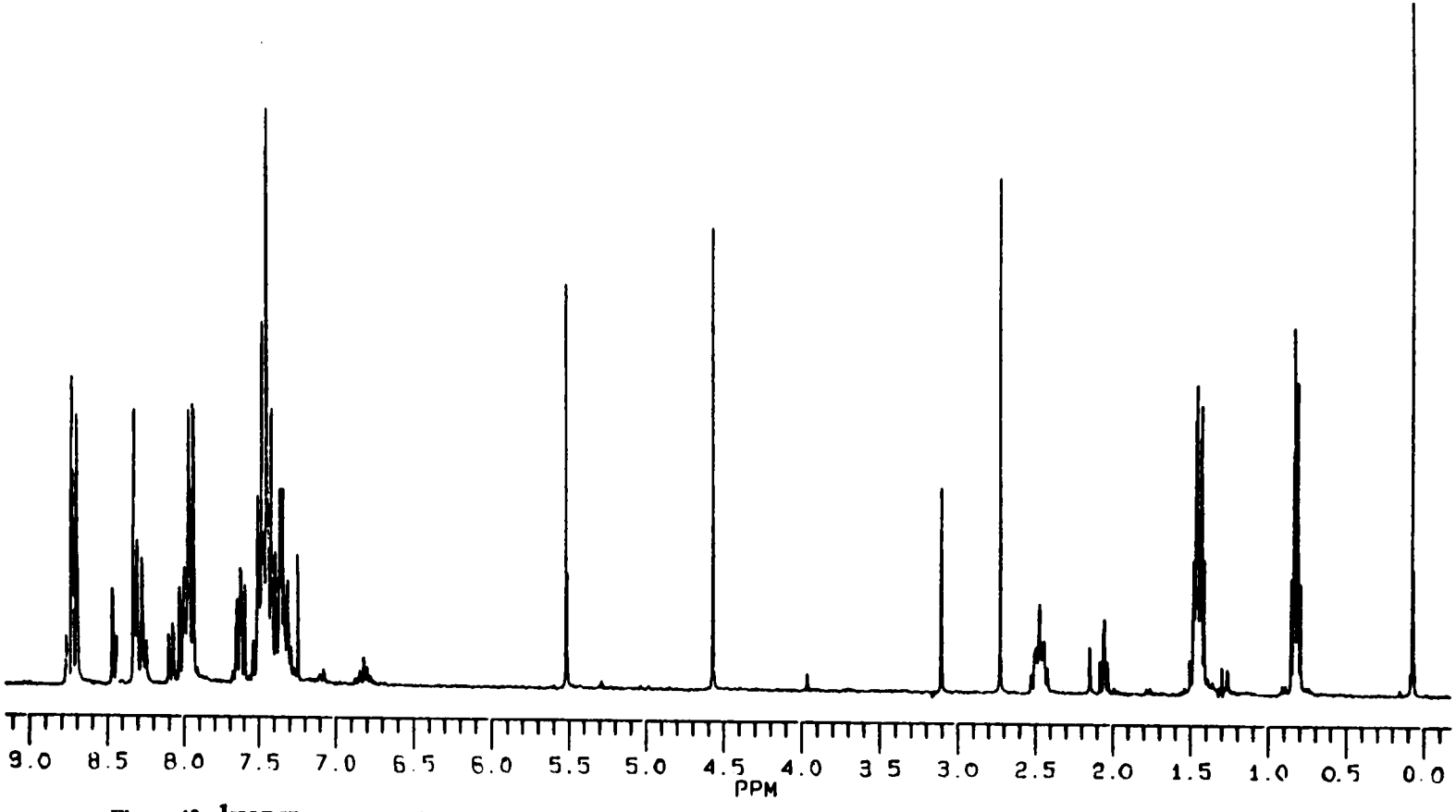


Figure 40. ^{1}H NMR spectrum of the resulting solution of the competitive bromination of 9-methylanthracene and9-cyclopropylanthracene: the competitors and the corresponding bromides (9-{α-bromomethyl}anthracene and 9-{α-bromocyclopropyl}anthracene), and the internal standards (benzyl chloride and hexamethyldisiloxane) are clearly shown.

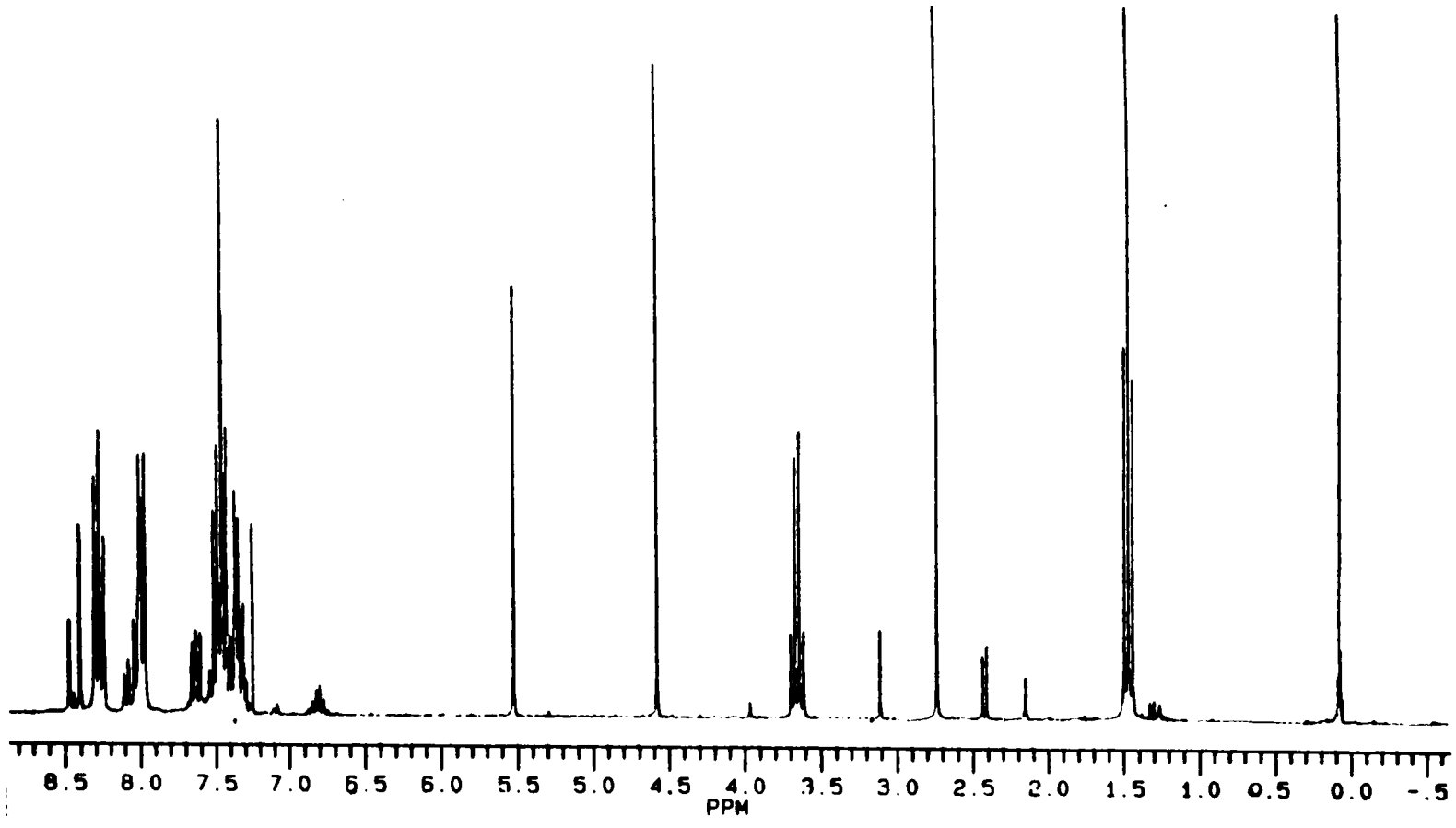


Figure 41. ^{1}H NMR spectrum of the resulting solution of the competitive bromination of 9-methylanthracene and 9-ethylanthracene: the competitors and the corresponding bromides (9-{α-bromomethyl}anthracene and 9-{α-bromoethyl}anthracene), and the internal standards (benzyl chloride and hexamethyldisiloxane) are clearly shown.

Table 15. Competitive Brominations of $AnCH_3$ (A) and An-c-$CH(CH_2)_2$ (B) with NBS in CCl_4 at Different Temperatures[a]

Temp. (°C)	$(A)_o$, mmol	$(A)_f$, mmol	$(B)_o$, mmol	$(B)_f$, mmol	ABr, mmol	BBr mmol	NBS[b] mmol	k_A/k_B[c] per molecule
12.0	0.214	0.123	0.655	0.637	0.0908	0.0170	0.200	19.9
12.0	0.275	0.135	0.286	0.275	0.140	0.00900	0.250	18.1
12.0	0.190	0.113	0.393	0.383	0.0750	0.00930	0.180	20.2
								Av. 19.4 ± 1.14[d]
40.0	0.381	0.0520	0.639	0.557	0.310	0.0770	0.420	14.5
40.0	0.306	0.0992	0.603	0.554	0.200	0.0460	0.270	13.3
40.0	0.367	0.0562	0.612	0.539	0.290	0.0700	0.390	14.8
								Av. 14.2 ± 0.79[d]
60.0	0.371	0.122	0.727	0.655	0.236	0.0690	0.335	10.7
60.0	0.423	0.0885	0.726	0.631	0.320	0.0920	0.430	11.2
								Av. 11.0 ± 0.35[d]
80.0	0.170	0.0488	0.360	0.314	0.123	0.0450	0.171	9.13
80.0	0.236	0.0668	0.562	0.490	0.163	0.0700	0.245	9.21
80.0	0.177	0.0514	0.375	0.328	0.122	0.0451	0.180	9.23
								Av. 9.19 ± 0.05[d]
100.0	0.134	0.0291	0.157	0.125	0.100	0.0310	0.140	6.70
100.0	0.136	0.0349	0.261	0.215	0.098	0.0440	0.150	7.02
100.0	0.149	0.0231	0.264	0.205	0.123	0.0560	0.190	7.37
								Av. 7.03 ± 0.34[d]
120.0	0.154	0.0353	0.232	0.174	0.110	0.0550	0.175	5.12
120.0	0.129	0.0222	0.207	0.156	0.101	0.0500	0.160	6.22
								Av. 5.67 ± 0.78[d]

[a]The competitive reaction was initiated with benzoyl peroxide (2 mole-%) at all temperatures except at 12.0 °C, which was irradiated with a 400-W medium pressure mercury arc lamp; $AnCH_3$ = 9-methylanthracene, An-c-$CH(CH_2)_2$ = 9-cyclopropylanthracene; ABr = 9- (α-bromomethyl)anthracene ($AnCH_2Br$), BBr = 9-(α-bromocyclopropyl)anthracene (An-c-$CBr\{CH_2\}_2$). [b]Initial amount of N-bromosuccinimide. [c]Quantitated by ^1H NMR analysis using hexamethyldisiloxane and either benzyl chloride or benzyl bromide as internal standards. [d]Standard deviation.

Table 16. Competitive Brominations of $AnCH_3$ (A) and $AnCH_2CH_3$ (B) with NBS in CCl_4 at Different Temperatures[a]

Temp. (°C)	$(A)_o$, mmol	$(A)_f$, mmol	$(B)_o$, mmol	$(B)_f$, mmol	ABr mmol	BBr mmol	NBS[b] mmol	k_A/k_B[c] per molecule
12.0	0.160	0.0616	0.856	0.830	0.0950	0.0250	0.160	30.9
12.0	0.183	0.0617	0.407	0.393	0.118	0.0130	0.180	31.1
12.0	0.184	0.0617	0.400	0.387	0.120	0.0130	0.180	33.1
								Av. 31.7 ± 1.22[d]
40.0	0.150	0.0435	0.320	0.307	0.102	0.0123	0.125	29.8
40.0	0.130	0.0370	0.305	0.292	0.0880	0.0120	0.110	28.8
40.0	0.135	0.0394	0.313	0.300	0.0940	0.0120	0.130	29.0
								Av. 29.2 ± 0.53[d]
60.0	0.180	0.0470	0.400	0.381	0.130	0.0180	0.160	27.6
60.0	0.180	0.0488	0.397	0.378	0.127	0.0170	0.160	26.6
								Av. 27.1 ± 0.71[d]
80.0	0.164	0.0329	0.288	0.269	0.130	0.0180	0.155	23.5
80.0	0.174	0.0359	0.309	0.290	0.130	0.0170	0.165	24.9
80.0	0.171	0.0244	0.326	0.300	0.138	0.0240	0.180	23.4
								Av. 23.9 ± 0.84[d]
100.0	0.106	0.0175	0.355	0.326	0.0860	0.0270	0.125	21.1
100.0	0.141	0.0173	0.258	0.235	0.120	0.0220	0.150	22.5
								Av. 21.8 ± 0.99[d]
120.0	0.123	0.0280	0.258	0.232	0.0900	0.0230[e]	0.130	13.9
120.0	0.116	0.0237	0.301	0.273	0.0900	0.0245[e]	0.130	16.3
								Av. 15.1 ± 1.70[d]

[a]The competitive reaction was initiated with benzoyl peroxide (2 mole-%) at all temperatures except at 12.0 °C, which was irradiated with a 400-W medium pressure mercury arc lamp; $AnCH_3$ = 9-methylanthracene, $AnCH_2CH_3$ = 9-ethylanthracene; ABr = 9-(α- bromomethyl)anthracene ($AnCHBrCH_3$), BBr = 9-(α-bromoethyl)anthracene ($AnCHBrCH_3$). [b]Initial amount of N-bromosuccinimide. [c]Quantitated by ^1H NMR analysis using haxamethyldisiloxane and either benzyl chloride or benzyl bromide as internal standards. [d]Standard deviation. [e]The amount of BBr was calculated as the sum of the amount of $AnCH=CH_2$ formed and $AnCHBrCH_3$ remained.

Table 17. Competitive Brominations of $AnCH_3$ (A) and An-c-$CD(CH_2)_2$ (B) with NBS in CCl_4 at 80.0 °C[a]

$(A)_o$, mmol	$(A)_f$, mmol	$(B)_o$, mmol	$(B)_f$, mmol	ABr mmol	BBr mmol	NBS[b] mmol	k_A/k_B[c] per molecule
0.0940	0.0104	0.207	0.188	0.0780	0.0180	0.105	22.9
0.0619	0.00994	0.110	0.102	0.0500	0.00770	0.0620	24.2
							Av. 23.6 ± 0.92[d]

[a]The competitive reaction was initiated with benzoyl peroxide (2 mole-%); $AnCH_3$ = 9-methylanthracene, An-c-$CD(CH_2)_2$ = 9-(α-deuteriocyclopropyl)anthracene; ABr = 9-(α-bromomethyl) anthracene ($AnCH_2Br$), BBr = 9-(α-bromocyclopropyl)anthracene (An-c-$CBr\{CH_2\}_2$). [b]Initial amount of N-bromosuccinimide. [c]Quantitated by ^1H NMR analysis using hexamethyldisiloxane and benzyl chloride as internal standards. [d]Standard deviation.

Table 18. Competitive Brominations of $AnCH_3$ (A) and $C_6H_5CH(CH_3)_2$ (B) with NBS in CCl_4 at 40.0 °C[a]

$(A)_o$, mmol	$(A)_f$[b], mmol	$(B)_o$, mmol	$(B)_f$[c] mmol	ABr[b] mmol	BBr[d] mmol	NBS[e] mmol	k_A/k_B per molecule
0.163	0.0624	0.288	0.273	0.0978	(0.0145)	0.120	17.9
0.114	0.0284	0.144	0.134	0.0840	(0.0103)	0.100	19.3
0.149	0.0285	0.144	0.132	0.116	(0.0122)	0.130	19.0
							Av. 18.7 ± 0.74[f]

[a]The competitive reaction was initiated with benzoyl peroxide (2 mole-%); $AnCH_3$ = 9-methylanthracene, $C_6H_5CH(CH_3)_2$ = cumene; ABr = 9- (α-bromomethyl)anthracene ($AnCH_2Br$), BBr = cumyl bromide ($C_6H_5CBr\{CH_3\}_2$). [b]Quantitated by ^1H NMR analysis using benzyl chloride as an internal standard. [c]Quantitated by GC analysis using chlorobenzene as an internal standard, correction factor for cumene is 0.684. [d]Calculated as $([B]_o - [B]_f)$. [e]Initial amount of N-bromosuccinimide. [f]Standard deviation.

Table 19. Competitive Bromination of Phenylcyclopropane (A) and Toluene (B) with with Br_2 in CCl_4 at 40.0°C[a]

$(A)_o$, mmol	$(A)_f$, mmol	$(B)_o$, mmol	$(B)_f$ mmol	ABr mmol	BBr mmol	Br_2[b] mmol	k_A/k_B per molecule
0.166	0.0839	0.190	0.124	0.0818	0.0660	0.156	1.60[c]
0.176	0.0953	0.208	0.142	0.0802	0.0654	0.156	1.61[c]
0.156	0.0783	0.182	0.117	(0.0777)[d]	(0.0650)[e]	0.156	1.56[f]
0.156	0.0774	0.185	0.121	(0.0786)[d]	(0.0640)[e]	0.156	1.65[f]
							Av. 1.61 ± 0.04[g]

[a]Reaction mixtures were irradiated with a 400-W medium pressure mercury arc lamp; ABr = 1,3-dibromo-1-phenylpropane ($C_6H_5CHBrCH_2CH_2CH_2Br$), BBr = benzyl bromide ($C_6H_5CH_2Br$). [b]Initial amount of Br_2. [c]Quantitated by ^1H NMR analysis using hexamethyldisiloxane as an internal standard. [d]Calculated as $([A]_o - [A]_f)$. [e]Calculated as $([B]_o - [B]_f)$. [f]Quantitated by GC analysis using chlorobenzene as an internal standard, correction factor for phenylcyclopropane is 0.696 and correction factor for toluene is 0.889. [g]Standard deviation.

Competitive Dark Bromination of Phenylcyclopropane versus 9-Bromo-10-Cyclopropylanthracene

Weighed amounts of 9-bromo-10-cyclopropylanthracene, phenylcyclopropane and an internal standard (chlorobenzene) were combined in 5 mL of CCl_4. The solution was analyzed by GC (triplicate determinations). From the millimole ratios and peak area ratios of the competitors against the internal standard, appropriate correction factors were calculated (e.g., the correction factor for phenylcyclopropane is equal to millimole ratio of phenylcyclopropane/chlorobenzene divided by the peak area ratio of phenylcyclopropane/chlorobenzene). The solution was then transferred to a 30-mL pressure tube containing 30-40 mg of anhydrous potassium carbonate. The pressure tube was carefully wrapped with Al-foil and Br_2 was distilled into it via a vac-line. After placing the pressure tube in a 15 °C water-bath for 3 hr, methylcyclohexene (ca. 1.5 times the initial amount of Br_2) was added. The resulting mixture was filtered and the filtrate analyzed by GC (triplicate determinations). From the calculated correction factors and appropriate peak area ratios, the amount of excess competitors were determined. The experiment was performed in triplicate. Experimental data and the result of this competition reaction are summarized in Table 20.

Table 20. Competitive Reaction of 9-Bromo-10-Cyclopropylanthracene (A) and Phenylcyclopropane (B) with Bromine in the Dark at 15 °C[a]

$(A)_o$, mmol	$(A)_f$, mmol	$(B)_o$, mmol	$(B)_f$, mmol	Br_2[b], mmol	k_A/k_B per molecule
0.0333	0.0249	0.0399	0.0392	0.0195	16.4
0.0333	0.0207	0.0399	0.0390	0.0195	20.8
0.0333	0.0228	0.0399	0.0391	0.0195	18.7
					Av. 18.6 ± 2.2[c]

[a]Quantitated by GC analytical technique using chlorobenzene as an internal standard, correction factor for 9-bromo-10-cyclopropane was estimated to be 0.697. [b]Initial concentration of Br_2. [c]Standard deviation.

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Appendix

Quantitative Analysis By ^1H NMR Spectroscopy

The amount of different hydrogen-containing compounds present in a given solution can often be easily and rapidly determined by ^1H NMR spectroscopy. In addition, this technique is nondestructive (compounds that had been analyzed could generally be recovered) and can be utilized to study competitive reactions. Friedrich and co-workers employed this technique to examine the competitive side-chain brominations of α-substituted toluenes with NBS.[76] They were able to make reasonably accurate determinations of both the quantities of unreacted starting materials and the quantities of brominated products in the reaction mixtures. From these determinations they established the relative reactivities of numerous α-substituted toluenes toward bromine atoms.

It should be pointed out that prior to the work of Friedrich and co-workers, the relative reactivities of various α-substituted toluenes toward bromine atoms were generally determined by the application of gas-liquid chromatographic (glc) techniques. The results from different research groups are, however, not in particularly good accord even if allowances are made for the fact that the experimental conditions used were somewhat

different. The discrepancies are believed to be associated with problems encountered in applying the glc techniques; some of the α-substituted toluenes cannot be separated satisfactorily from the product mixtures on the columns used. Also, cross-check analyses for reaction products cannot be made since many of the products are not stable under the glc conditions.

In comparison to α-brominated α-substituted toluenes, α-brominated 9-alkylanthracenes are much more unstable under gas chromatographic conditions. Therefore, ^{1}H NMR analytical technique is required to study the competitive side-chain brominations of 9-alkylanthracenes. An outline of the quantitation procedure using this technique is presented below.

Weighed amounts of benzyl chloride (**W**), cumene (**X**), 9-cyclopropylanthracene (**Y**) and hexamethyldisiloxane (**Z**) were combined in 5 mL of CCl_4 (see column one of Table 21). After thorough mixing, 0.25 mL of this solution was syringed (using a hypodermic syringe) into a thin-walled Pyrex NMR tube containing 0.25 mL of $CDCl_3$. The ^{1}H NMR spectrum of this solution is shown in Figure 42. The chemical shift values for the aliphatic proton resonances of the individual compounds (relative to the TMS, δ 0.0 ppm) are approximately as follows: **W**, 4.6 (s, 2H, CH_2Cl); **X**, 2.9 (h, 1H, J = 7 Hz, CH), 1.3 (d, 6H, J = 7 Hz, $(CH_3)_2$); **Y**, 2.5 (m, ^{1}H, cyclopropylmethine hydrogen), 1.5 (m, 2H, trans-cyclopropylmethylene hydrogens), 0.8 (m, 2H, cis-cyclopropylmethylene hydrogens); **Z**, 0.07 (s, 18H, 2 x $(CH_3)_3$). The aliphatic region was expanded and is represented by Figures 43 and 44. Four integrations were run for each resonance or set of resonances shown in these Figures. The average deviation of individual integrations from the mean is on the order of 1%. Note that the integrals in Figure 44 were drawn on a smaller scale than that in Figure 43. The reason for this will be explained a little later.

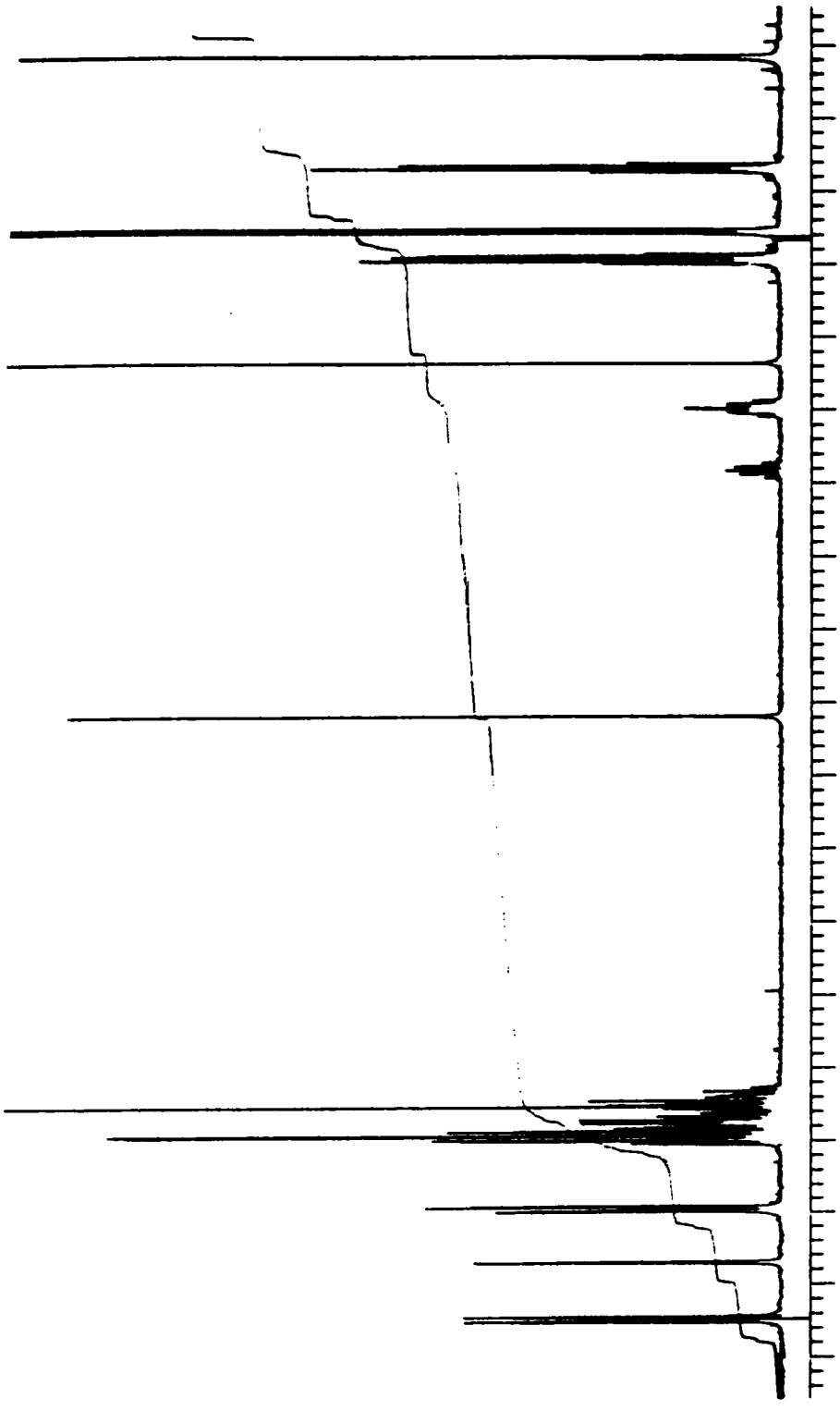

Figure 42. ^{1}H NMR spectrum of a standard mixture of benzyl chloride, cumene, 9-cyclopropylanthracene and benzonitrile/dioxane

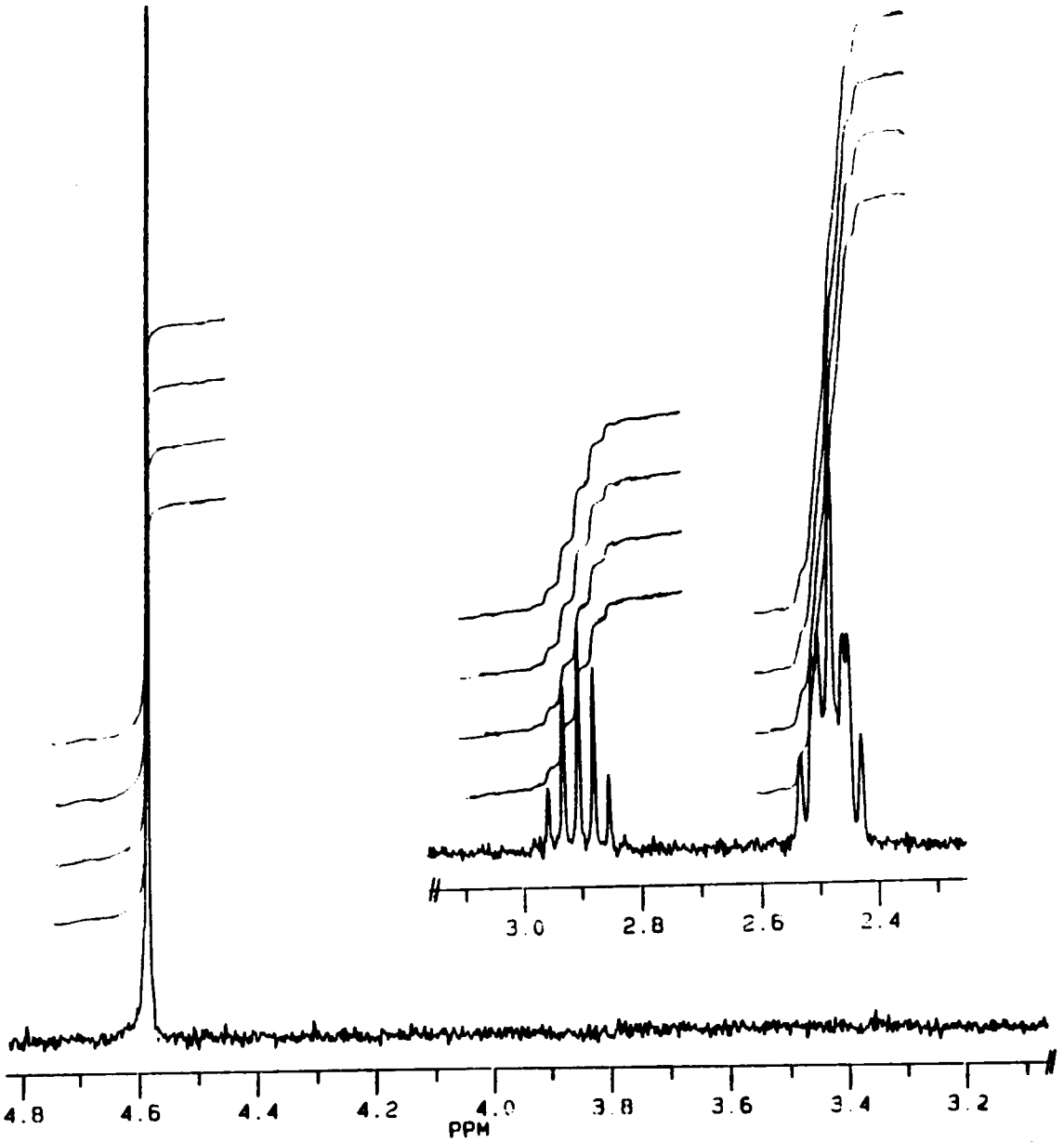

Figure 43. Expanded ^1H NMR spectrum showing the aliphatic proton resonances of benzyl chloride, cumene and 9-cyclopropylanthracene

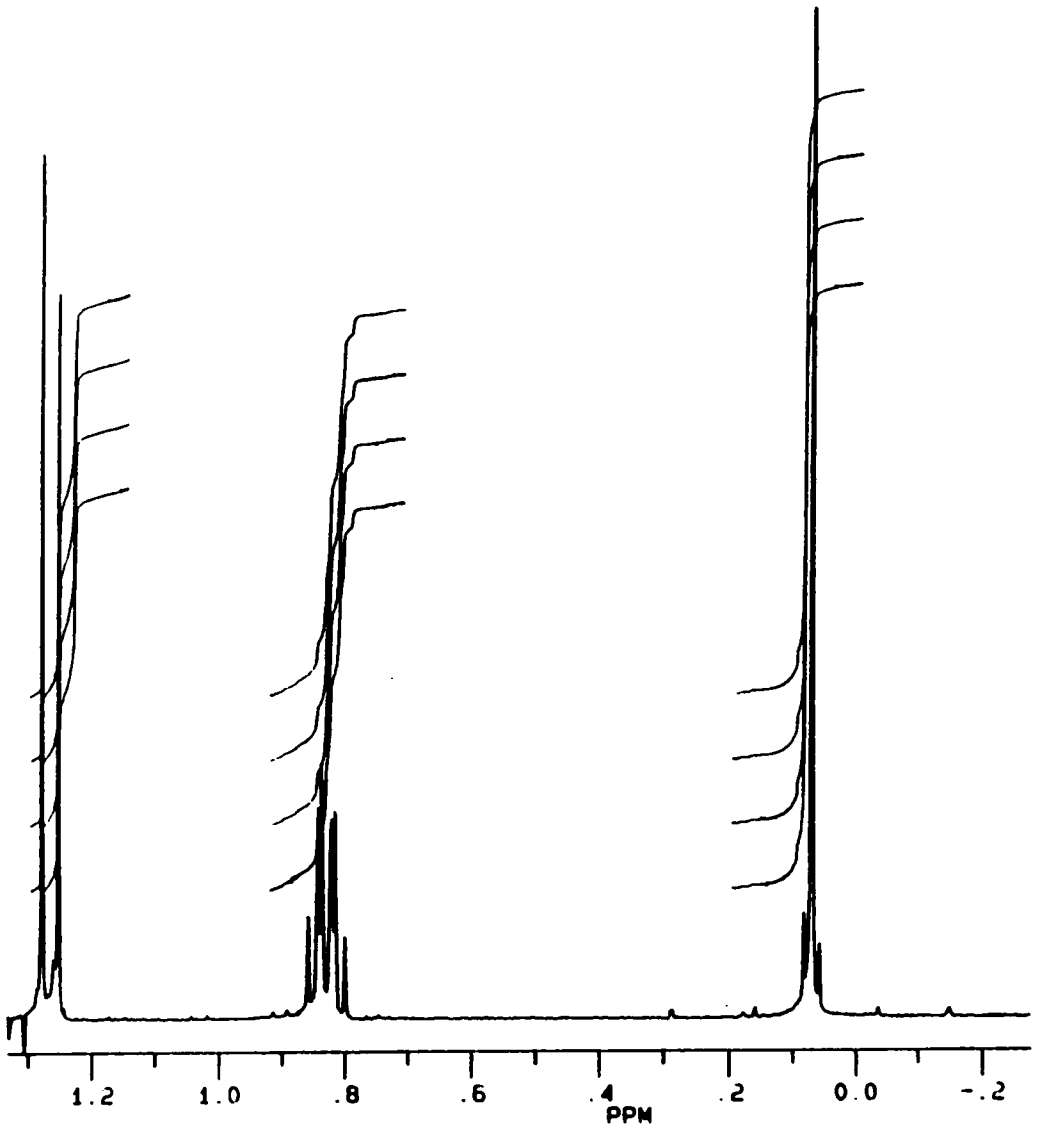

Figure 44. Expanded ^1H NMR spectrum showing the aliphatic proton resonances of cumene, 9-cyclopropylanthracene and hexamethyldisiloxane

Consider Figure 43 wherein only the resonances of the aliphatic protons of **W**, **X** and **Y** are shown. Since the area under a given set of resonances is proportional to the number of moles and the number of protons for a particular compound,[84,85] the relationship between **W**, **X** and **Y** can be represented by **Eq.** 32.

Eq. 32 $$N_W/A_W = N_X/A_X = N_Y/A_Y$$

where N = number of moles of a compound; A = area under a resonance or set of resonances divided by the number of protons in the group associated with the resonance or set of resonances.

Supposing **W** is taken as an internal standard, the number of moles of **X** and **Y** can be calculated using **Eq.** 32 (see column two of Table 21). In order to minimize the error in measuring the area, it is essential to do baseline correction and to maximize integral amplitudes for a given set of resonances. However, when maximizing the size of the smallest integral, the largest integral in the spectrum may become too large to fit into the scale used. In such cases, the spectrum has to be split into two different spectra with a different scale for the integrals depicted in each spectrum. This is the reason why, as mentioned earlier, the spectrum in Figure 44 is recorded on a smaller scale than that in Figure 43, thus making it possible to plot the integrals for the resonance of the protons of **Z**. The resonances and integrals of the protons of **X** and **Y** are also shown in Figure 44. Since the number of moles of **X** and **Y** are known (calculated using **W** as a standard), the number of moles of **Z** can in turn be determined. The value for the number of moles of **Z** shown in the second column of Table 21 was determined based on the number of moles of **Y**. From the third column of Table 21, it is evident that the deviations of the calculated number of moles from the measured number of moles of **X**, **Y** and **Z** are within 6%. This exemplifies that quantitation by ^{1}H NMR techniques can be used to obtain reasonably accurate amounts of the different hydrogen-containing compounds present in a given solution.

Table 21. Quantitation by ^{1}H NMR Analytical Techniques

Compound[a]	Measured (mmol)	Calculated (mmol)	Deviation[b] (%)
W	0.1651	0.1651[c]	-
X	0.1438	0.1400	2.6
Y	0.4430	0.4668	5.4
Z	0.0910	0.0868	4.6

[a]**W** = benzyl chloride; **X** = cumene; **Y** = 9-cyclopropylanthracene; **Z** = hexamethyldisiloxane.
[b]Absolute value of 100% x (measured - calculated)/measured.
[c]Arbitrary standard.

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