Reactions of Alkylcyclopropanes with Bromine and with Hydrogen Bromide

Philip S. Skell,* James C. Day, and Kenneth J. Shea

Contribution from the Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802. *Received June 11, 1975*

Abstract: Dark brominations of alkylcyclopropanes rarely produce 1,3-dibromoalkanes as major products. The reactions are sluggish, and the products are a mixture of isomeric mono-, di-, and tribromoalkanes; the latter is often the major product. This is the result of competitive bromination, hydrobromination, dehydrobromination, and extensive rearrangements. Conditions are described for isolating the bromination and hydrobromination processes; the latter is the faster. The reagents are bromine and *N*-bromosuccinimide for studying bromination and hydrogen bromide and bromine for studying hydrobromination. The mechanism of reaction is one of backside attack by bromine to produce a free carbonium ion which is involved in a competition between rearrangements, loss of a proton, and collapse with bromide ion. Similar considerations apply to hydrobromination of cyclopropanes.

Introduction

For a number of years it has been nearly uniform practice to teach a remarkably incorrect description of the reactions of cyclopropanes with bromine.[1,2] But, cyclopropane and bromine do not react in the dark in the absence of Lewis acid catalysts, such as $AlCl_3$;[3] methylcyclopropane and ethylcyclopropane react very slowly (3 days at room temperature) and produce 7 and 12 products, respectively, large proportions of which are tribromides, the purported 1,3-dibromoalkanes being minor products. Perhaps even more puzzling is the formation of substantial amounts of 2,3-dibromobutanes and 2,3-dibromopentanes, respectively, products for which there is no reasonable mechanistic path involving attack by bromine.[4]

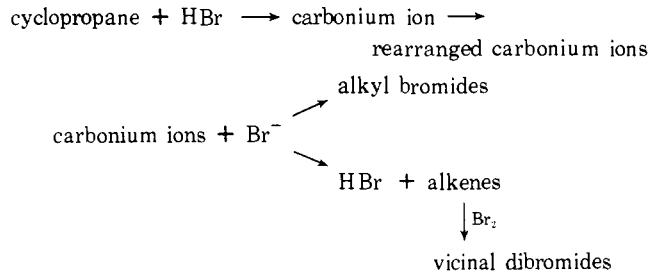
On the other hand, the radical chain reactions of cyclopropanes with bromine are rapid, clean reactions, even at −78°, leading exclusively to 1,3-dibromides.[5]

A simple set of observations provided a basis from which an understanding of the dark reactions could be developed. An olefin reacts with Br_2 exclusively when treated with a mixture of HBr and Br_2 in a nonpolar solvent (CH_2Cl_2, CCl_4, etc.). With this same reagent mixture, a cyclopropane reacts rapidly with the hydrogen bromide (see Table I).

The reactions of a cyclopropane with hydrogen bromide can appear complex, apparently because carbonium ions are intermediates which either react to form bromides or lose a proton to make an olefin, the olefin reacting further either with hydrogen bromide, or by condensation, etc.[6] The reaction of the cyclopropane–hydrogen bromide system is readily understood in detail if a mixture of HBr and Br_2 is used, since the Br_2 converts the olefins to stable dibromides. Examined in this way, the products are monobromides and dibromides; tribromides are absent. For the main, the monobromide is that predicted by a Markownikoff-type opening of the ring, accompanied by easily rationalized rearrangement products; the dibromides are all vicinal and can be explained as Br_2 adducts to the olefins expected from the carbonium ions needed to explain the monobromide products. Since cyclopropanes react more rapidly with hydrogen bromide than with bromine, it follows that the formation of hydrogen bromide in the reactions of cyclopropanes with bromine must result in the production of dibromides from several pathways, thus accounting for the confusion (see Scheme I).

A clear picture of the dark reaction of bromine with cyclopropanes could be obtained only if the hydrogen bromide was efficiently scavenged. For the monoalkyl-, 1,2-dialkyl-, and 1,2,3-trialkylcyclopropanes this could be done by using *N*-bromosuccinimide in methylene chloride solvent as the scavenger system. Rapid scavenging occurs in this system because NBS is moderately soluble (0.25 M), and it reacts rapidly and irreversibly with hydrogen bromide.[7] Study of

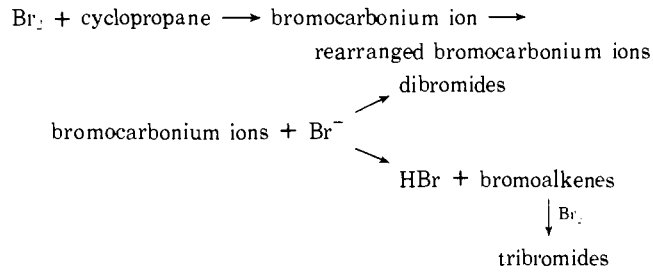
Scheme I



$$HBr + NBS \rightarrow \text{succinimide} + Br_2$$

the dark reactions of cyclopropanes with Br_2–NBS reagent in methylene chloride leads to dibromides and tribromides; the monobromides and dibromides characteristic of HBr attack are conspicuously absent. The initial process is an opening of the ring to make a bromocarbonium ion of structure predicted by Markownikoff-type considerations (Scheme II).

Scheme II



With the Br_2–NBS reagent, ratios of tribromides to dibromides are greater than 1.0 in some cases, indicating the large contribution that would have been made by HBr if it had not been scavenged. The usual reaction mixture of a cyclopropane + Br_2 can thus be recognized as a complex system because ring opening occurs 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 monobromides and another set of dibrominated alkanes. Thus, although these products from cyclopropanes + Br_2 are shown in Table I, they are not useful in understanding the details of the reactions.

Table I. Bromination and Hydrobromination of Alkylcyclopropanes

Reagent	Time	Temp, (°C)	% Yield	% Yield	% Yield[a]	%
Methylcyclopropane			Monobromide	Dibromide	Tribromide	
Br_2	48 hr.	-78	1.5	5	0.39	79
HBr,Br_2	10 min.	-78	50	10	0	-
NBS,Br_2[b]	43 hr.	0	tr.	51	1.02	62
Ethylcyclopropane			Monobromide	Dibromide	Tribromide	
Br_2	48 hr.	-78	2.5	8.5	0.45(5 gc peaks)	
Br_2	72 hr.	25	23	48	1.32(5 gc peaks)	
HBr,Br_2	10 min.	-78	30	7	0	
HBr,Br_2	5 min.	25	19	23	0	
NBS,Br_2[b]	20 hr.	25	tr.	22	1.32(5 gc peaks)	
n-Butylcyclopropane				Dibromide		
NBS,Br_2[b]	5 hr.	25		7		
cis-1,2-Dimethylcyclopropane			Monobromide	Dibromide	Tribromide	
Br_2	48 hr	-78	10	51	0.23(6 gc peaks)	
Br_2	18 hr	-42	d	d		
HBr,Br_2	10 min.	-78	76	11	0	
NBS,Br_2[b]	5 hr.	25	tr.	44	1.38(6 gc peaks)	
trans-1,2-Dimethylcyclopropane						
Br_2	48 hr.	-78	7.5	47	0.22(6 gc peaks)	
Br_2	18 hr.	-42	9	33		
HBr,Br_2	10 min	-78	89		0	
NBS,Br_2[b]	5 hr.	25	tr.	57	1.07(6 gc peaks)	

Reagent	Time	Temp, (°C)	Monobromide					Dibromide							Tribromide
cis-1,2-Dimethylcyclopropane															
Br_2	48 hr	-78	10	19[c]	41	41	1	51	1	55	1	3	2	39	0.23(6 gc peaks)
Br_2	18 hr	-42	d	19[c]	77		4	d	5	45	2	8	4	36	
HBr,Br_2	10 min.	-78	76	12[c]	40	45	3	11	10	0	15	33	38	0	0
NBS,Br_2[b]	5 hr.	25	tr.					44	1	54	1	7	tr	37	1.38(6 gc peaks)
trans-1,2-Dimethylcyclopropane															
Br_2	48 hr.	-78	7.5	9[c]	83	8	0	47	tr	24	0	7	2.5	66.5	0.22(6 gc peaks)
Br_2	18 hr.	-42	9					33	2	14	0	12	tr	72	
HBr,Br_2	10 min	-78	89	18[c]	75	7	0		11	0	9	62	19	0	0
NBS,Br_2[b]	5 hr.	25	tr.					57	tr.	22	0	19	1	58	1.07(6 gc peaks)

[a] Numbers given are ratios of tribromide/dibromide peak areas. [b] Generally, 0.5-1.0M alkylcyclopropane in CH_2Cl_2, 80% of theoretical amt. of both Br_2 and NBS. [c] Correction applied for partial decomposition on g.c. column. [d] Normalized yield: 22% monobromide, 78% dibromide. [e] threo-2,3-Dibromopentane and 1,2-dibromo-3-methylbutane not g.c. separable.

I. Dark Reactions of Cyclopropanes with Bromine (Br_2–NBS)

1. General. Reactions of cyclopropanes with the Br_2–NBS reagent were carried out in the dark to avoid the rapid radical-chain ring opening to produce 1,3-dibromides; contributions from this source could be minimized by chain inhibition with alkyl nitrites, but with careful exclusion of light (Al-foil wrapping), there was evidently little contribution from this source since the products obtained in radical reactions were often minor.

The products were identified by comparison of GC retention times with authentic samples, separately and by mixed GC. Except for very minor products, further identification was made by isolation of pure GC components and comparison of NMR spectra with those of knowns. Products and yields are given in Table I. Except for the tribromides, yields were calculated by the usual methods, employing internal standards.

In the initial account of this work,[4] there were substantial disagreements with a prior report[8] on the bromination products of *cis*- and *trans*-1,2-dimethylcyclopropanes. Happily, a full resolution has been effected as a result of much correspondence and further work, an account of which will appear shortly.[9]

2. Orientation of Ring Opening. Without exception, if there is an unsubstituted methylene group in the cyclopropane, the products all reflect initial attack at this least-substituted position by having a $BrCH_2$ group in the product molecules. All the products can be rationalized by assuming that this is the initial attack, accompanied by ring opening to the most stable 1-bromo-3-cation intermediate, the remaining events occurring at the cation sites, leaving the $BrCH_2$ group untouched. Thus, the slow step in this sequence can be described as a Markownikoff-type ring opening.

Non-Markownikoff ring opening has been claimed for the strained cyclopropane rings of bicyclo[2.1.0]pentane[10b] and -[3.1.0]hexane;[10a] relief of strain appears to be the dominating factor in these cases. However, these experiments should be examined further in the light of the present results, since the earlier studies were carried out without control of hydrogen bromide, and without control of the radical-chain reactions.[5]

3. Rates of Reaction. While the broad outlines of this subject are clear, there are problems which make one hesitate to invest the effort required for a precise treatment. There are, as with halogenations of olefins, low-concentration domains where the kinetic term is $[Br_2]^1$; at higher concentrations (>1.0 M, see Experimental Section), the reaction is at least second order in $[Br_2]$. We have examined, in the low Br_2 concentration domain (0.25-0.5 M), the relative rates of Br_2–NBS brominations of cyclopropanes by analyzing for the loss of cyclopropanes only. In addition, an absolute rate constant for reaction of ethylcyclopropane with bromine was obtained from straight-line plots of concentrations vs. time data using the integrated form of the kinetic equation for a second-order reaction (first order each in cyclopropane and bromine). Using the absolute rate constant and the relative rate data, absolute rate constants

Table II. Competitive Brominations of Alkylcyclopropanes[a]

	k_{rel}	k_{abs}, l./mol s
	~0	
	~1.0	~4.9×10^{-4}
	(1.0)	$4.9 \pm 0.5 \times 10^{-4}$ [d]
	4.3 ± 0.4[b]	$2.1 \pm 0.3 \times 10^{-3}$
	10.8 ± 0.1[b]	$5.2 \pm 0.5 \times 10^{-3}$
	20.8 ± 0.3[c]	$1.0 \pm 0.1 \times 10^{-2}$
	23.8 ± 2.2[c]	$1.2 \pm 0.1 \times 10^{-2}$
	~10^2	~4.9×10^{-2}
	>10^3	>4.9×10^{-1}

[a] Br_2–NBS, dark, 25°, 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.

for each of the alkylcyclopropanes studied were calculated. These results are summarized in Table II.

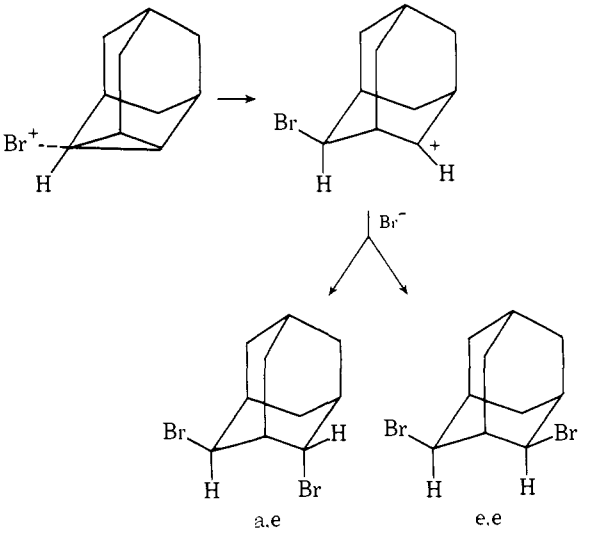
Introduction of a single alkyl substituent generally accelerates the dark reaction with bromine, consistent with formation of a secondary bromo cation rather than the primary carbonium ion that would be formed from reaction of cyclopropane. Introduction of further alkyl groups at the unsubstituted position results in a further modest increase of reactivity. The differences 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; there is more relief of strain if alkyl groups are cis than if trans.

The increase of reactivity with *gem*-dialkylcyclopropanes is attributed to the formation of the more stable tertiary bromocarbonium ion.

Quite substantial increases of rates have been reported for strained systems such as bicyclo[3.1.0]hexane,[10a] which apparently reacts completely in less than 5 min at −30 to −50°, and dehydroadamantane, which reacts rapidly even at −78°.[5]

4. Stereochemistry of Ring-Opening Process. To examine the stereochemistry of the ring-opening process, a 1,2,3-trisubstituted cyclopropane must be used. The 1,2,3-trimethylcyclopropanes were unsuitable substrates;[11] dehydroadamantane was suitable because it reacted rapidly and formed only two products. The dark bromination of dehydroadamantane with bromine is highly susceptible to adventitious radical initiation.[5] Since the dark rate is substantially reduced in the presence of isoamyl nitrite, under these conditions the nonradical pathway is, at least in part, evident. The products are exclusively 2,6-dibromoadamantanes, (a,e)- (59%) and (e,e)- (41%). Since all aspects of dark brominations of cyclopropanes point to formation of a 1-bromo-3-carbonium ion, it is reasonable to attribute to the second step, the reaction with bromide ion, the proportioning between axial and equatorial approach. Had the initial attack occurred with axial orientation, the (a,a)-dibromide would have been among the products. Thus, the equatorial bromine was introduced in the initial attack, indicating that ring opening occurs with inversion at the reaction center (see Scheme III).

Scheme III

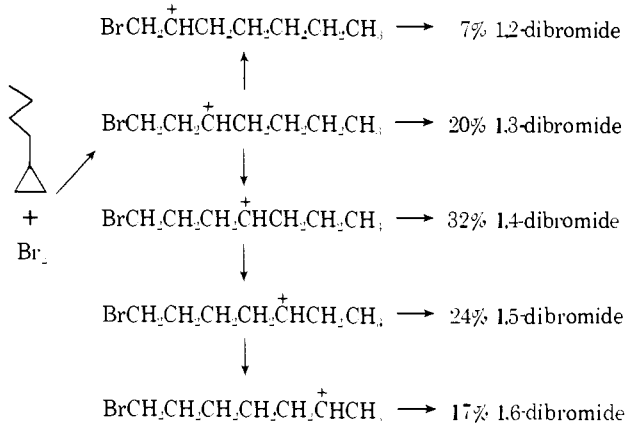


While it may be questionable to use dehydroadamantane as a stereochemical model for simpler alkylcyclopropanes, the rate data, vide supra, suggest it is reasonable to do so. Successive introductions of alkyl groups into the cyclopropane ring result in increase of reactivity *as long as there is an unsubstituted* position on the ring; thus, the 1,2,3-trimethylcyclopropanes are not more reactive than the 1,2-dimethylcyclopropanes. This can be explained by backside attack by Br_2, retarded by substitution at the reaction center.

There are other reports of inversion of configuration in the first step of bromine attack on cyclopropanes,[12] but also a report of retention of configuration in the first step.[13] Other electrophilic substitutions on cyclopropanes offer up a bewildering variety of stereochemical pathways, the details thoroughly reported by DePuy.[14]

5. Rearrangements. An aspect of the dark brominations of cyclopropanes is the variety and extent of rearrangements which occur. A striking example is the bromination of *n*-butylcyclopropane which leads to 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 (Scheme IV).

Scheme IV

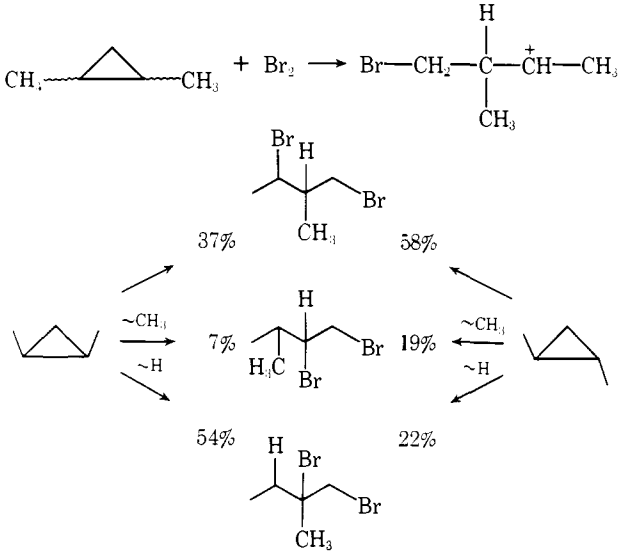


It is significant that the dibromides expected from the most stable carbonium ion, the 1,2-bromonium ion, is obtained in lowest yield; the cationic site moves away from the bromine substituent in the bromocarbonium ion. This is behavior characteristic of free carbonium ions rather than encumbered ones.[15] The rearrangement moves the charged

site away from the positive end of the Br-C dipole, in competition with hot pursuit by the Br^- which ultimately encumbers and traps the carbonium ion.

Brominations of the 1,2-dimethylcyclopropanes give further insight into the rearrangements. Unfortunately, the products from the 1,2-dimethylcyclopropanes were not fully identifiable by gas chromatography because *threo*-2,3-dibromopentane and 1,2-dibromo-3-methylbutane fall under the same GC envelope. However, since from neither cyclopropane is a significant amount of *erythro*-2,3-dibromopentane obtained, it is assumed that the threo isomer is also absent, and that the total peak area can be attributed to the product from methyl rearrangement, 1,2-dibromo-3-methylbutane. This product and the hydrogen rearrangement product, 1,2-dibromo-2-methylbutane, account for 40-60% of the dibromides (see Scheme V).

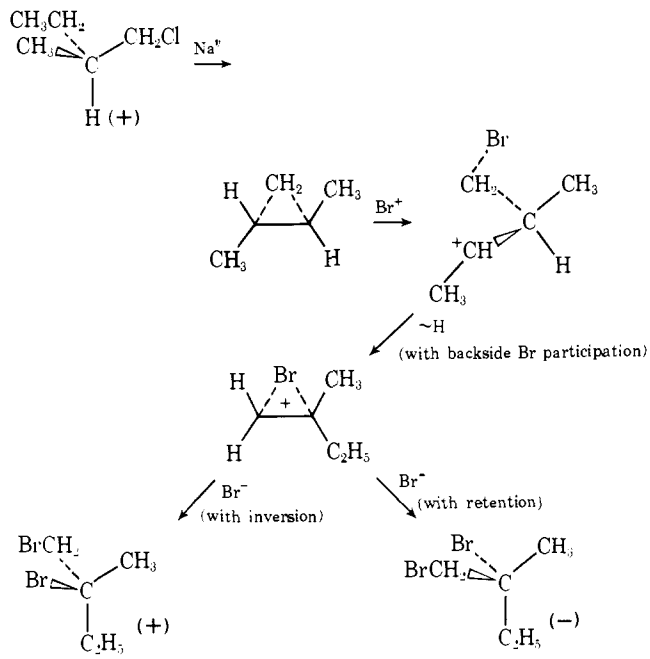
Scheme V



It is clear that the initial bromocarbonium ion products are not the same from the two isomeric cyclopropanes, since the quantitative separation into the different reaction paths is not the same for these isomeric cyclopropanes. Unfortunately, a quantitative description of the various pathways is not feasible because the carbonium ion precursors of the above products are also precursors of the six tribromides via the bromoalkenes by loss of a proton.

It is noteworthy that the rearrangement is strongly directed toward formation of 1,2-dibromoalkanes, while the ethyl- and *n*-butylcyclopropanes, the major rearrangement reactions resulted in separating the two bromine substituents. The large amount of 1,2-dibromide formation made it desirable to examine the possibility that the rearrangement was directed and/or assisted by neighboring group interactions in the rearrangement transition state, leading directly to the 1,2-bromonium ions. If incipient formation of the bromonium ion were involved in the rearrangement transition state, then a stereochemically unique course would be expected. This possibility was tested by use of optically active *trans*-1,2-dimethylcyclopropane;[23] configurations and rotations of the cyclopropane and one of the rearrangement products, 1,2-dibromo-2-methylbutane,[16] was known from other work. If formation of a 1,2-bromonium ion accompanied rearrangement of the hydrogen atom, the dibromide product would have had a rotation of $[\alpha]D \pm 3.85°$, starting with the 2-methyl-1-chlorobutane (88% optical purity) from the (+)-2-methyl-1-butanol (see Scheme VI). The rotation of the dibromide obtained is $[\alpha]^{23}D +0.4°$; this is 10% optical purity.

Scheme VI



This result indicates either (a) an accidental equivalence of rates for the rearrangement with inversion and with retention or, more likely (b) that the initial rearrangement product is an unbridged carbonium ion. This result and the failure to make the most stable rearranged carbonium ion (1,2-bromonium) in the *n*-butylcyclopropane case can be readily interpreted by assuming no assistance by the neighboring bromine in the rearrangement step. If bromonium ions are intermediates, they must be formed after the rearrangement and then with only slightly unequal rates for the formation of the antipodes.

6. Formation of Tribromides. Although there are some indications that tribromides were recognized to be products obtained from the reactions of cyclopropanes with bromine, the full importance of this phenomenon may not have been appreciated. At room temperature, the tribromides can be the major products; 50-60% yields are not uncommon. At low temperatures (−78°), the yields are 10-15%.

The structure of the tribromides from the methylcyclopropane-Br_2 (NBS) reaction are

$$CH_2BrCH_2CHBrCH_2Br$$

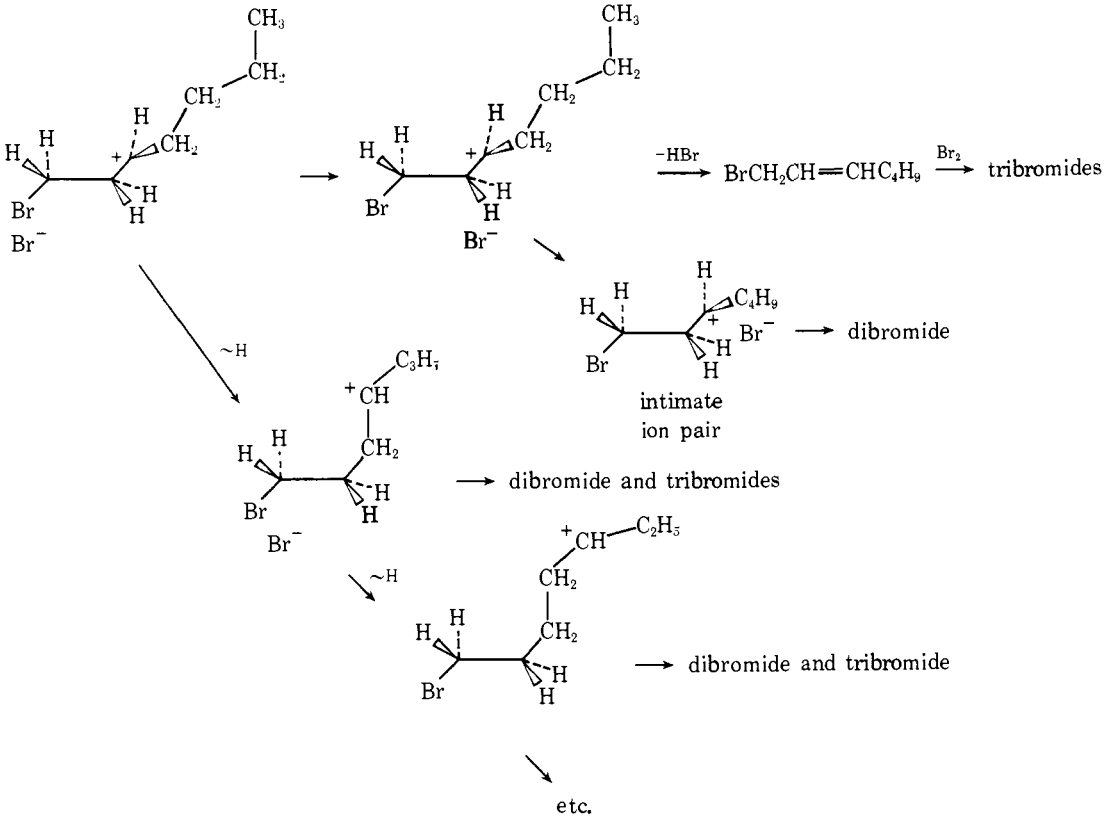
$$CH_3CHBrCHBrCH_2Br \text{ (}erythro\text{ and }threo\text{)}$$

These products are readily explained as Br_2 adducts of the bromoalkenes 1-bromo-2-butene and 4-bromo-1-butene; these in turn are the intermediates that would result from loss of a proton from the 1-bromo-2- and 3-butyl cations. The transfer of a proton from these cations to a nearby bromide ion would yield the bromoolefins and hydrogen bromide, a reaction which competes with collapse of the ion pair to dibromide. Presumably the E_{acl} for the elimination is greater than that for collapse to dibromide, thus accounting for the effect of temperature on tribromide yields.

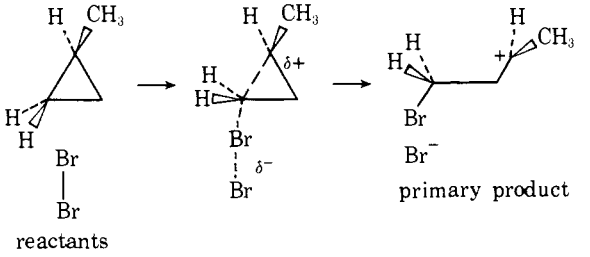
With other cyclopropanes, structures of tribromides were not determined, but in all cases the number of tribromide peaks in the GC approaches the number of tribromides predicted by this mechanism.

7. Detailed Mechanism. The dark reaction of bromine with alkylcyclopropanes occurs at the least substituted position, with inversion, to produce a bromocarbonium ion-bromide pair which undergoes extensive sequential rearrangements, uncharacteristic of solvolysis-type intermediates (intimate or solvent separated ion pairs), but characteristic

Scheme VII



of the nonrelaxed or free carbonium ion-anion pairs. This is consistent with the following formulation, showing the attack by Br^+ with inversion.



The relaxation of the "free" ion pair to the encumbered state of an intimate ion pair would require 10^{-9}-10^{-11} s. During this time interval, free carbonium ions had been found earlier to undergo as many as four to five successive hydride shifts.[15] While the Br^- moves toward the positive center, hydride shifts occur; these rapid events terminate when the carbonium ions and Br^- either reach the positions characteristic of an intimate ion pair, followed by collapse, or a hydrogen β- to the cation site is abstracted to make HBr and a bromoalkene. Some of the possible configurations leading to these products from *n*-butylcyclopropane are illustrated in Scheme VII. The results obtained in the Br_2-*n*-butylcyclopropane case suggest that all of these competing processes are occurring with similar rates.

II. Dark Reactions of Cyclopropanes with Hydrogen Bromide (HBr-Br_2)

The reaction of cyclopropanes with hydrogen bromide showed such puzzling aspects that mechanisms of reaction have not been on a firm footing.[17] Remarkably, Gustavson[1] (1900) had the key to the difficulties in his recognition that cyclopropanes reacted more rapidly with hydrogen bromide than with bromine.

We have found that with cyclopropanes, which react very slowly with bromine at −78° in the dark, hydrogen bromide alone reacts much faster, and a mixture of hydrogen bromide and bromine the fastest. The possibility that adventitious initiation of radical chain reactions was occurring had to be examined, since the photoinitiated bromination of cyclopropanes is fast at −78°.[5]

At −78°, a cyclopropane-HBr-Br_2 mixture gives identical absolute yields of 1-bromopropane in the light or dark. In the dark reaction there is no 1,3-dibromopropane product, while in the illuminated system the yield of 1,3-dibromopropane exceeded that of the 1-bromopropane. It follows (1) that the dark reaction is not a radical chain system and (2) that bromine is far more reactive than hydrogen bromide in reaction with the classical 3-bromo-1-propyl radical (there are few instances in which the relative reactivities of radicals with Br_2 and HBr have been examined).

Reactions of all alkylcyclopropanes with hydrogen bromide are rapid at −78°, being complete in a matter of minutes. With cyclopropane (C_3H_6), the reaction is sufficiently slow to make easy the recognition that the ionic dark reaction with hydrogen bromide is considerably accelerated by the presence of bromine, the product being exclusively 1-bromopropane in both circumstances.

The details of the ionic reaction of hydrogen bromide with cyclopropanes are most satisfactorily obtained by use of the HBr-Br_2 reactants because any olefins formed are converted to vicinal dibromides rather than to rearranged monobromides. With this reagent system, the ratio of monobromides to dibromides is a function of temperature, just as with dibromide to tribromide ratios in the bromination of cyclopropanes. At −78° the HBr-Br_2 system yields ~20% dibromides, at room temperature 55% dibromide (from ethylcyclopropane).

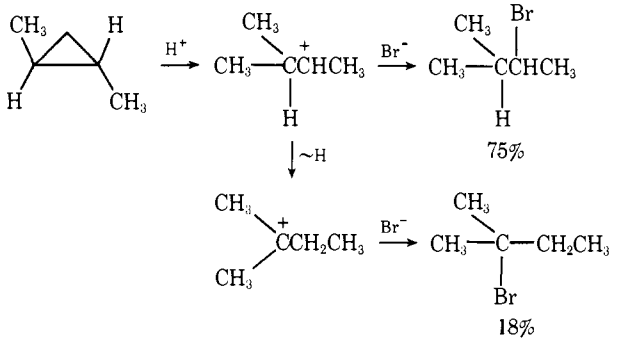
Although there are some claims in the older literature that the orientation of ring opening by hydrogen bromide was of the Markownikoff type, the analytical procedures then available leave some doubt about this point.

Cyclopropane and HBr-Br_2 yield exclusively 1-bromopropane; methylcyclopropane reacts to form 2-bromobu-

tane; ethylcyclopropane is converted to a mixture of 3-bromopentane (9.4–9.6%) and 2-bromopentane (4–6%). While in these instances the addition appears to be exclusively Markownikoff type, a different pattern emerges in the reactions of the 1,2-dimethylcyclopropanes, particularly the cis isomer.

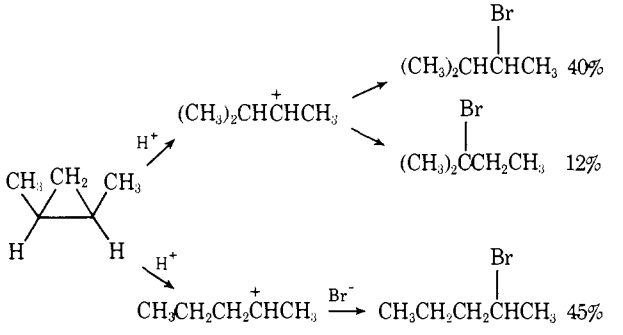
With *trans*-1,2-dimethylcyclopropane, the major monobromide products are obtained from the addition of the proton to the least substituted carbon atom, accounting for 93% of the monobromides (Scheme VIII). Only 7% of the product is 2-bromopentane. (non-Markownikoff process).

Scheme VIII



With *cis*-1,2-dimethylcyclopropane, 2-bromopentane is 45% of the monobromide and 3-bromopentane 3%. Thus, half of the monobromide results from a non-Markownikoff-type addition, with the proton going to the more substituted carbon atom. It seems that two types of ionic hydrobromination might be required (Scheme IX).

Scheme IX



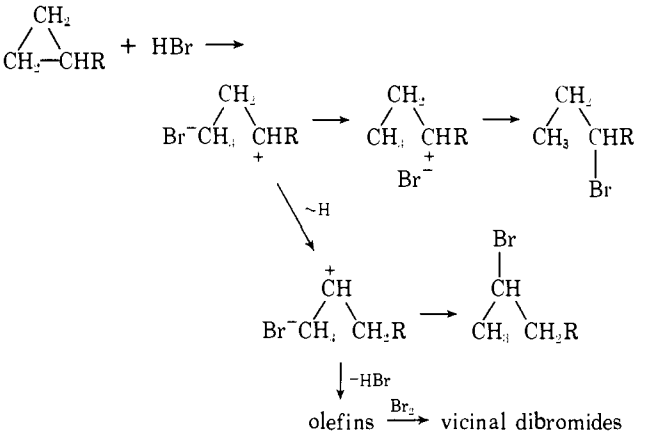
In other work we have shown that HCl has a much higher solubility (smaller Henry's law constant) in cyclopropane than in alkanes.[18] The cyclopropane nucleus is a stronger Lewis base than an alkane. This complex formation precedes product formation since it was possible to recover unchanged cyclopropane after quenching. The faster reaction with HBr–Br_2 reagent than with HBr alone is explained by complexation of HBr with Br_2 to make a stronger protonic acid.

$$HBr + Br_2 \rightleftarrows H^+Br_3^-$$

In the case of the parent hydrocarbon, cyclopropane itself, the complex apparently goes to a protonated cyclopropane in a slow step. The latter has been shown to equilibrate the hydrogens in competition with return to cyclopropane and opening of the ring.[19] This may be the case in reactions of cyclopropane with HBr–Br_2 reagent, since we could show that some exchange of hydrogen for deuterium occurs if DBr–Br_2 is used, and the 1-bromopropane product also has deuterium at positions other than C-3. In addition, the degree of deuterium incorporation in the 1-bromopropane product is the same for the cyclopropane–DBr and cyclopropane–DBr–Br_2 reactions. However, as found in other reactions of alkylcyclopropanes, protonated cyclopropanes, while they may be intermediates, are not required to explain the products.[19]

The reaction of methyl- and ethylcyclopropanes with HBr–Br_2 can be understood with a mechanism similar to that of the bromination reaction, namely, initial formation of the most stable carbonium ion, not encumbered by the simultaneously formed bromide ion. During the relaxation of this pair to the intimate pair, some rearrangement and loss of a β proton can occur, the former accounting for the formation of isomeric monobromides, the latter for olefins which are then converted to vicinal dibromides (Scheme X).

Scheme X



It is worth noting that while the extent of elimination is similar in the bromination and hydrobromination reactions of cyclopropanes, the extents of rearrangement are far greater in the bromination. We attribute this, in part, to the increase of stability of the bromo cation as the positive center moves away from the positive end of the Br–C dipole. In the hydrobromination, the attraction between the Br^- neighbor and the cation site is dominant.

The detail which is still obscure for the hydrobromination reaction is whether the attack by the proton, opening the ring, occurs with inversion or retention of configuration. Experiments in progress may help to clarify this aspect.

Experimental Section

A. General. NMR spectra were obtained on a Varian A-60-A spectrometer. Chemical shifts are reported on the δ scale relative to Me_4Si as an external standard. GC analyses were performed on a Perkin-Elmer F-11 hydrogen-flame instrument and/or a Varian 1400 flame-ionization detector gas chromatograph. Unless otherwise indicated, all mono-, di-, and tribromide analyses were performed on a $\frac{1}{8}$ in. × 15 ft 7% SE-30 on 80–100 Gas Chromosorb R-Z column. Yields for mono- and dibromides were obtained from GC analyses using an internal standard, applying appropriate recorder response factors for internal standard vs. product determined from known mixtures of both. Products were identified by comparison of GC retention times and spectra with those of authentic materials.

Optical rotations were obtained on a Rudolph Model 200 photoelectric polarimeter using a 100-μl capacity cell.

B. Materials. Methylene chloride was purified by successive washings with concentrated sulfuric acid, aqueous sodium carbonate, aqueous sodium bicarbonate, and water. After drying over $CaCl_2$, the methylene chloride was distilled from P_2O_5.

Hydrogen bromide (Matheson), bromine (Baker), and *N*-bromosuccinimide (Aldrich) were used without purification.

The alkylcyclopropanes used in this study were obtained commercially. Purity was checked by GC and/or NMR prior to use. Excessive olefin contaminant was removed by treating the alkylcyclopropane dropwise with bromine in subdued light until a bromine color persisted. A considerably higher boiling olefin (e.g., dode-

cene) was then added to remove excess bromine and the alkylcyclopropane distilled. Samples of *cis*- and *trans*-1,2,3-trimethylcyclopropanes were kindly supplied by D. E. Applequist, University of Illinois.

C. Alkylcyclopropanes and Bromine. Electrophilic bromination of alkylcyclopropanes were carried out in the dark to eliminate competing light-initiated free-radical ring-opening reactions.[5] Generally, the alkylcyclopropane and 80% of the theoretical amount of bromine were stirred magnetically in methylene chloride in an aluminum-foil-wrapped flask at the desired temperature for varying periods of time. The reaction was quenched by shaking with aqueous sodium bisulfite, neutralizing with aqueous $NaHCO_3$, and drying with Na_2SO_4.

A series of low-temperature brominations of methyl-, ethyl-, and *cis*-, and *trans*-1,2-dimethylcyclopropanes were carried out under identical reaction conditions. In these experiments, the alkylcyclopropane (5 mmol) was condensed into a mixture of bromine (4.2 mmol) in 10 ml of methylene chloride. The mixture was warmed to −78° in a dry ice dewar and stirred magnetically for 48 h in the dark. The reaction mixture was then worked up as indicated above.

Outlined below are the product identification procedures used for the various alkylcyclopropanes studied. All yield and product composition data for brominations of alkylcyclopropanes are given in Table I.

Methylcyclopropane. Methylcyclopropane (5 mmol) was condensed from a vacuum line into a mixture of bromine (4.2 mmol) in 10 ml of methylene chloride in an aluminum-foil-wrapped flask. The mixture was maintained at −78° for 48 h. Work-up and GC analysis at 85° revealed a low-boiling product, with a retention time identical with that of 2-bromobutane, and four dibromides, identified on the basis of retention time comparisons with authentic samples as *meso*- and *d,l*-2,3-dibromobutanes, 1,2-dibromobutane, and 1,3-dibromobutane. Product composition data are given in Table I.

At a higher column temperature (145°), two further product peaks were noted. These were suspected to be tribromobutanes. An authentic sample of diastereomeric 1,2,3-tribromobutanes was prepared by bromine addition to a commercial mixture of crotyl bromide and 3-bromo-1-butene: NMR (CCl_4) δ 2.02 and 2.06 (overlapping doublets, 3 H), 3.9–4.3 (m, 2 H), 4.3–4.9 (m, 2 H). The GC retention time of this material (diastereomers not resolved) is identical with that of the first tribromide product noted above.

An authentic sample of 1,2,4-dibromobutane was prepared by heating a commercial sample of 1,4-dibromo-2-butanol with phosphorus tribromide in benzene at steam-bath temperatures in a sealed tube. The retention time of this tribromide matches that of the second tribromobutane product.

Ethylcyclopropane. Ethylcyclopropane (4.8 mmol) and bromine (4.3 mmol) in 15 ml of methylene chloride were stirred in the dark at −42° for 3 h. After the mixture was quenched ($NaHSO_3$), GC analysis at 85° revealed a low-boiling product with a retention time identical with that of 3-bromopentane. Five dibromides were observed with the product composition indicated in Table I. Products were identified on the basis of retention time comparisons with authentic samples. They are, in order of increasing retention times, *erythro*- and *threo*-2,3-dibromopentanes (products 1 and 2 respectively), 1,2-, 1,3-, and 1,4-dibromopentanes (products 3, 4, and 5, respectively). In addition, the suspected 2,3-dibromopentanes and 1,4-dibromopentane were isolated by preparative GC and their NMR spectra compared with those of authentic dibromides.

Product 1: NMR (CCl_4) δ 1.11 (t, 3 H), 1.91 (d) and 1.8–2.3 (m) 5 H total, 4.12 (m, 2 H). The spectrum is consistent with the proposed *erythro*-2,3-dibromopentane structure.

Product 2: NMR δ 1.11 (t, 3 H), 1.75 (d) and 1.6–2.4 (m, 5 H total), 3.9–4.6 (m, 2 H). This spectrum is identical with that of *threo*-2,3-dibromopentane obtained from bromine addition to *cis*-2-pentene.

Product 5: NMR δ 1.75 (d) and 1.9–2.3 (m, 7 H total), 3.3–3.6 (m, 2 H), 4.12 (6 line multiplet, 1 H). This spectrum is identical with that of authentic 1,4-dibromopentane.

GC analysis of the mixture at a higher column temperature (145°) revealed five products. By analogy with the methylcyclopropane case, these were assumed to be tribromopentanes. No attempt was made to determine the structures of these products.

A second experiment was performed using ethylcyclopropane (4.8 mmol) and bromine (2.2 mmol) in 5 ml of methylene chloride at room temperature. The bromine color slowly disappeared over a 72-h period.

In a third experiment, ethylcyclopropane (15 mmol) and bromine (7.5 mmol) in 15 ml of methylene chloride at room temperature gave the products already described. The low-boiling product was isolated by preparative GC. NMR (CCl_4) δ 1.0 (t, 6 H), 1.8 (m, 4 H), 3.82 (pentuplet, 1 H). The spectrum is identical with that of authentic 3-bromopentane.

***trans*-1,2-Dimethylcyclopropane.** A mixture of *trans*-1,2-dimethylcyclopropane (4.8 mmol) and bromine (4.3 mmol) in 10 ml of methylene chloride was stirred in the dark at −42° for 18 h. Work-up and GC analysis at 85° revealed three low-boiling product peaks with retention times comparable to those for C-5 monobromides. Three major dibromides were noted, and at a higher column temperature (145°) six product peaks appeared. These were considered to be tribromopentanes, and no attempt was made to determine their structures.

The three major dibromides, listed in order of increasing retention times, were isolated by preparative GC on a ¼ in. × 20 ft 7.5% SE-30 on 60–80 Gas Chromosorb Z column at 90–100°.

Product 1: NMR (CCl_4) δ 1.05 (t, 3 H), 1.8 (s) and 1.9 (q, 5 H total), 3.76 (s, 2 H). The spectrum is identical with that of 1,2-dibromo-2-methylbutane prepared by photobromination of 1-bromo-2-methylbutane.

Product 2: 0.96 and 1.11 (overlapping doublets, 6 H), 2.0–2.8 (m, 1 H), 3.4–4.4 (m, 3 H). The spectrum matches that for the product of bromine addition to 3-methyl-1-butene, 1,2-dibromo-3-methylbutane.

Product 3: 1.22 and 1.29 (overlapping doublets, 3 H), 1.96 (d) and 2.26 (m, 4 H total), 3.47–3.70 (5-line multiplet, 2 H), 4.1–4.8 (complex multiplet, 1 H). The spectrum is identical with that of a sample of 1,3-dibromo-2-methylbutanes prepared by treatment of 2-methyl-1,3-butanediols with triphenylphosphine dibromide in DMF.[5] The overlapping doublets in the NMR spectrum of the product are assigned to the 2-methyl groups in the diastereomeric pair. Triangulation of the doublets in a 100-Hz sweep-width NMR spectrum gave a diastereomer composition of 71 and 29%. No attempt was made to assign structures to the diastereomers.

In addition to the three major dibromides described, several minor ones were observed. These were identified as 2,3-dibromo-2-methylbutane and 1,2-dibromopentane on the basis of retention time comparisons with authentic samples prepared by bromine addition to the appropriate olefins.

An attempt was made to determine if 2,4-dibromopentanes were reaction products in bromination of *trans*-1,2-dimethylcyclopropane. A mixture of *meso*- and *d,l*-2,4-dibromopentanes was prepared by treating 2,4-pentanediol with phosphorus pentabromide. The diastereomers were isolated by preparative GC and identified by comparing their NMR spectra with those reported for *meso*- and *d,l*-2,4-dichloropentanes.[20] A portion of the GC-collected *d,l*-2,4-dibromopentane was added to the dibromide mixture from *trans*-1,2-dimethylcyclopropane bromination and GC analyzed on a ⅛ in. × 6 ft 30% Carbowax 20M on Chromosorb R column at 85°. A new peak appeared where none had been present in the GC spectrum of the bromination product mixture on the same column. On this basis, *d,l*-2,4-dibromopentane was excluded as a reaction product.

On the ⅛ in. × 15 ft 7% SE-30 column, the *meso*-2,4-dibromopentane overlaps with 1,2-dibromo-3-methylbutane. The NMR of the latter material, already described, contains no peaks which might be attributable to the presence of *meso*-2,4-dibromopentane.

Diastereomeric 2,3-dibromopentanes were prepared by bromine addition to *cis*- and *trans*-2-pentenes. *threo*-2,3-Dibromobutane was found to have the same retention time as both 1,2-dibromo-3-methylbutane and *meso*-2,4-dibromopentane. The erythro isomer has a retention time between those of 1,2-dibromo-2-methylbutane and 1,2-dibromo-3-methylbutane.

Preparation of Optically Active *trans*-1,2-Dimethylcyclopropane. Optically active 2-methyl-1-butanol[21] was converted to active 2-methyl-1-chlorobutane with thionyl chloride in pyridine, following the procedure of Brown and Groot:[22] $[\alpha]^{21}D$ +1.46° (neat), 88% of reported value of +1.66°.[23]

The active chloride (45.5 g, 0.43 mol) was added to sodium

metal (9.9 g, 0.43 mol) in cyclohexane (60 ml) at a rate to maintain gentle reflux, using an overhead motor stirrer. Volatile products were passed into a dry ice trap. Low-boiling olefin product (primarily 2-methyl-1-butene) was removed by addition of Br_2 in the dark, followed by addition of the higher boiling olefin 5-methyl-1-hexene. The product mixture, consisting of *cis*- and *trans*-1,2-dimethylcyclopropane, ethylcyclopropane, and isopentane was then separated from cyclohexane solvent and 5-methyl-1-hexene by trap-to-trap distillation on a vacuum line. Finally, a portion of optically active *trans*-1,2-dimethylcyclopropane, diluted with isopentane, was preparatively gas chromatographed on a ¼ in. × 15 ft SE30 column at 25°. A total of 5.5 ml of a solution of dimethylcyclopropane (10%) and isopentane (90%) was obtained.

Bromination of Optically Active *trans*-1,2-Dimethylcyclopropane. A mixture of optically active *trans*-1,2-dimethylcyclopropane and isopentane, containing 0.34 g of the former (4.8 mmol), was condensed from a vacuum line into a solution of Br_2 (4.3 mmol) in CH_2Cl_2 (10 ml). The mixture was warmed to −42° in an acetonitrile–liquid nitrogen slush bath and maintained at this temperature with magnetic stirring for 18 h. The reaction was then quenched with aqueous $NaHSO_3$, washed with H_2O, and dried (Na_2SO_4).

The three major dibromide products were preparatively gas chromatographed on a ¼ in. × 15 ft SE 30 column at 90°, 50 ml/min He flow. Product 1: 1,3-dibromo-2-methylbutane, 175 mg, $[\alpha]^{19}D$ +12.6° (88 g/100 ml of soln, CCl_4). Product 2: 1,2-dibromo-3-methylbutane, 42 mg, $[\alpha]^{21}D$ +0.6° (21 g/100 ml of soln, CCl_4). Product 3: 1,2-dibromo-2-methylbutane, 38 mg, $[\alpha]^{23}D$ +0.4° (20 g/100 ml of soln, CCl_4).

A sample of (−)1,2-dibromo-2-methylbutane was prepared according to the method of Readio,[16] α_{obsd} 1.43°, 59% optical purity, $[\alpha]^{18}D$ −2.56° (23.8 g/100 ml of soln, CCl_4) (for optically pure dibromide, $[\alpha]^{18}D$ −4.41°).

***cis*-1,2-Dimethylcyclopropane.** *cis*-1,2-Dimethylcyclopropane (5 mmol) and bromine (4.2 mmol) in 10 ml of methylene chloride were allowed to react in the dark at −42° for 21 h. Work-up and GC analysis, as before, revealed three low-boiling products (C-5 monobromides), six dibromides, and six tribromopentanes. Product composition data appear in Table I. The only product from this bromination which was not observed in the trans case is *erythro*-2,3-dibromopentane.

Dehydroadamantane and Bromine. A solution of Br_2 (0.48 mmol) in CH_2Cl_2 (1 ml) was condensed into a mixture of dehydroadamantane (0.1 g, 0.7 mmol), prepared as described previously,[5] in CH_2Cl_2 (4 ml). The mixture was warmed to −78° and stirred for 5 min in the dark. Tetramethylethylene was then condensed into the mixture to scavenge excess Br_2. After stirring an additional 1.5 min at −78°, the mixture was warmed to room temperature. GC analysis on a ¼ in. × 6 ft 10% SE 30 column at 200° revealed the presence of (a,e)- and (e,e)-2,6-dibromoadamantanes. No product was observed with a retention time of that of an authentic sample of (a,a)-dibromide.[24]

Use of isoamyl nitrite as a radical inhibitor gave the same dibromide products; no diaxial product was found.

D. Alkylcyclopropanes with Hydrogen Bromide and Bromine. Reactions with alkylcyclopropanes with hydrogen bromide were carried out in methylene chloride in the dark at −78° in the presence of sufficient bromine to convert olefinic products to dibromides. Generally, HBr (1 mmol) was condensed from a vacuum line into a mixture of alkylcyclopropane (0.5 mmol) and bromine (1 mmol) in 4 ml of methylene chloride. The mixture was warmed to −78° in acetone–dry ice and maintained at that temperature for 10 min with manual shaking. The reaction was then quenched with aqueous K_2CO_3. The organic layer was washed with water and dried (Na_2SO_4). GC analyses were performed under the same conditions as those outlined for brominations. Yield and product composition data for these reactions are presented in Table I.

In one experiment, a mixture of 0.1 mol each of DBr, Br_2, and cyclopropane (no solvent) in a sealed, thick-walled Pyrex pressure tube was gently warmed above −78°. A moderate explosion occurred, injuring several workers. The high exothermicity of the HBr–cyclopropane reaction in the presence of Br_2 was believed to be responsible for a rapid buildup of pressure, exceeding the limits of the reaction vessel. Experiments of this sort should therefore always be performed in a solvent and at a temperature not exceeding −78°.

a. Cyclopropane. Light Reaction. Cyclopropane (16.4 mmol), HBr (2.0 mmol), and Br_2 (2.0 mmol) were condensed into degassed CH_2Cl_2 (5.0 ml) in a Pyrex glass pressure tube. The mixture was warmed to −78° and photolyzed with a G.E. A-H6 high-pressure mercury arc lamp for 40 min. The mixture was then cooled to −196°, excess 1-butene condensed in, and the mixture rewarmed to −78° to remove Br_2. Trap-to-trap distillation of the reaction mixture on a vacuum line allowed separation of mono- and dibromide product from excess cyclopropane. The products consisted of 1-bromopropane (0.55 mmol, 28% yield), 1,3-dibromopropane (0.66 mmol, 33% yield), and 1,2-dibromopropane (0.03 mmol, 1.5% yield).

Dark Reaction. A dark reaction of a mixture of HBr, Br_2, and cyclopropane was performed exactly as indicated for the light reaction. After 46 min, the excess Br_2 was removed with 1-butene. The only product obtained was 1-bromopropane (0.56 mmol, 28% yield).

Reaction with DBr. Cyclopropane (23.0 mmol) and DBr (24.0 mmol) were distilled into a Pyrex glass pressure tube fitted with a Fischer–Porter valve (25 ml vol) and stirred at room temperature behind a safety shield. Over a 25-h period, an approximate 80% drop in pressure was noted (followed monometrically at −78°). Trap-to-trap distillation of the products on a vacuum line allowed isolation of 1-bromopropane (2.5 g, 20 mmol, 86% yield) and recovery of unreacted cyclopropane. Mass spectral analysis (70 eV) of the 1-bromopropane indicated 35% d_0, 50.5% d_1, and 14.5% d_2 material (corrected for ^{13}C natural abundance). A 2:2:2.8 ratio for the integrations of the NMR peaks of the protons at carbons 1, 2, and 3, respectively, was obtained.

An ir spectrum of the recovered cyclopropane contained C–D stretching bands at ~4.4 μ. The amount of deuterium incorporation was determined by mass spectral analysis (14 eV): 55% d_0, 34.5% d_1, 7.5% d_2, 2.5% d_3, and 0.5% d_4 (corrected for ^{13}C natural abundance).

Reaction with DBr–Br_2. Deuterium bromide (55.0 mmol) and cyclopropane (55.0 mmol) were condensed into a mixture of Br_2 (100 mmol) in an aluminum foil-wrapped Pyrex glass pressure tube. The mixture was warmed to −78° and maintained at that temperature for 15 min with manual shaking. The tube was then opened and the contents added to ice-cold aqueous K_2CO_3. The organic layer was separated, washed with water, and dried (Na_2SO_4). The monobromide product was exclusively 1-bromopropane (2.0 g, 30% yield). No 2-bromopropane was detected by GC analysis. Mass spectral analysis (70 eV) indicated 27% d_0, 56% d_1, and 17% d_2 (corrected for ^{13}C natural abundance). Integration of the NMR bands for the protons at carbon 1, 2, and 3 gave a ratio of 2:2:2.75.

b. *cis*-1,2-Dimethylcyclopropane. For the purpose of identifying the monobromide products obtained in the HBr reactions of *cis*- and *trans*-1,2-dimethylcyclopropanes, the following experiment with *cis*-1,2-dimethylcyclopropane and HBr in the absence of bromine was performed.

Hydrogen bromide (10 mmol) was condensed from a vacuum line into 10 ml of methylene chloride, followed by *cis*-1,2-dimethylcyclopropane (4.6 mmol). The mixture was warmed to −78° for a 10-min period. The mixture was then treated with aqueous ammonium hydroxide, washed with water, and dried (Na_2SO_4). Four monobromide products were obtained. The first three of these (in order of increasing retention time) were isolated by preparative GC.

Product 1: NMR (CCl_4) δ 1.05 (t, 3 H), 1.71 (s) and 1.79 (q, 8 H total). The spectrum is that of *tert*-amyl bromide.

Product 2: NMR (CCl_4) 0.90 and 0.92 (overlapping doublets, 6 H), 1.59 (d) and 1.4–1.9 (m, 4 H total), 4.02 (doublet of quartets, 1 H). The compound was assigned the structure 2-bromo-3-methylbutane.

Product 3: NMR (CCl_4) 0.9 (t, 3 H), 1.68 (d, overlapping with 1.2–1.9 multiplet, 7 H total), 4.02 (m, 1 H). The spectrum is identical with that of authentic 2-bromopentane.

The minor fourth product was not isolated, but its retention time was identical with that of 3-bromopentane.

E. Alkylcyclopropanes with Bromine and NBS. Electrophilic brominations of the alkylcyclopropanes in the presence of *N*-bromosuccinimide were carried out in the manner already described for reactions utilizing bromine alone, except that a 1:1 molar ratio of NBS to bromine was used to scavenge HBr. Generally, reaction

temperatures of 0° or room temperature were necessary. At lower temperatures, incomplete HBr scavenging occurs because of the decreased solubility of NBS. The results obtained are given in Table I. Outlined below are product identification procedures followed in several of these experiments.

***trans*-1,2-Dimethylcyclopropane.** A mixture of *trans*-1,2-dimethylcyclopropane (4.8 mmol), bromine (4.0 mmol), and NBS (9.6 mmol) was stirred in the dark at room temperature for 5 h. Work-up and GC analysis gave the results outlined in Table I.

The second major dibromide product was isolated by preparative GC and found to have an NMR spectrum identical with that of authentic 1,2-dibromo-3-methylbutane.

***n*-Butylcyclopropane.** A mixture of *n*-butylcyclopropane (5 mmol), bromine (4 mmol), and NBS (4 mmol) in 10 ml of methylene chloride was stirred in the dark at room temperature for 5 h. Work-up and GC analysis gave the dibromide product composition indicated in Table I. Partial overlap of 1,5- and 1,6-dibromoheptanes occurred on the ⅛ in. × 15 ft 7% SE-30 column. Curve resolution was effected on a Du Pont 310 curve resolver. No attempt was made to analyze the tribromoheptanes.

The same dibromides were formed in photobromination of 1-bromoheptane (5.6 mmol) with Br_2 (5.6 mmol) and NBS (2.8 mmol) in methylene chloride (15 ml) at room temperature. These photobromination products were isolated by preparative GC using a ¼ in. × 6 ft silicon rubber on Gas Chromosorb R at 120°, 80 ml/min He flow. They are listed in order of increasing retention time.

Product 1: NMR (CCl_4) δ 0.98 (t, 3 H), 1.2–2.7 (complex multiplet, 8 H), 3.4–4.5 (overlapping multiplets, 3 H). The spectrum agrees with that for 1,2-dibromoheptane.

Product 2: NMR δ 0.98 (t, 3 H), 1.2–2.5 (m, 8 H), 3.6 (m, 2 H), 3.9–4.3 (m, 1 H). The spectrum is consistent with the proposed 1,3-dibromoheptane structure. In addition, this component has a retention time identical with that of the single dibromide (1,3) formed in photobromination of *n*-butylcyclopropane.

Product 3: NMR δ 0.98 (t, 3 H), 1.5–2.3 (m, 8 H), 3.45 (m, 2 H), 3.7–4.2 (m, 1 H).

Product 4: NMR δ 1.04 (t, 3 H), 1.5–2.2 (m, 8 H), 3.37 (t, 2 H), 3.7–4.3 (m, 1 H).

The NMR data for products 3 and 4 are consistent with proposed 1,4- and 1,5-dibromoheptane structures. Since the SE-30 column separates components according to their boiling point differences, product 3 is identified as 1,4-dibromoheptane and product 4 as 1,5-dibromoheptane.

Product 5: NMR δ 1.72 (d, superimposed on 1.3–2.2 multiplet, 11 H total), 3.4 (t, 2 H), 3.9–4.3 (m, 1 H). The doublet at 1.72 ppm and the absence of a triplet in the 1.0 ppm region are consistent with the proposed 1,6-dibromoheptane structure.

F. Kinetic Experiment. Bromination of Ethylcyclopropane. Ethylcyclopropane (0.14 g, 2.0 mmol) and *n*-heptane (0.2 g, 2.0 mmol) in CH_2Cl_2 (50 ml) were treated with NBS (12.0 mmol) and Br_2 (1.92 g, 12.0 mmol; $[Br_2] \approx 0.23$ M) in the dark at room temperature. Aliquots (1 ml) were removed at various times and added to 1-pentene in CH_2Cl_2. Direct GC analysis was then performed, monitoring disappearance of ethylcyclopropane. Using the following integrated rate equation for a second-order reaction, a linear plot was obtained with a slope of 4.4×10^{-4} l./mol s as the rate constant for the ionic bromination:

$$\frac{2.303}{(a-b)}\left[\log\frac{a-x}{b-x} + \log\frac{b}{a}\right] = k_2 t$$

where $a = [Br_2]_{initial} = 0.23$ M and $b = [\text{ethylcyclopropane}]_{initial} = 0.04$ M. Data for a second experiment using initial concentrations of 0.43 M each for ethylcyclopropane and Br_2 gave a straight line plot with a slope of 5.3×10^{-4} l./mol s.

In a third experiment, a mixture of 2.0 mmol each of ethylcyclopropane and *n*-heptane in CH_2Cl_2 (10 ml) was treated with 12.0 mmol each of NBS and Br_2. After 0.5 h, an aliquot was removed and quenched with 1-pentene. GC analysis revealed that only 4% of the initial amount of ethylcyclopropane remained. The calculated value for the percent of ethylcyclopropane unreacted after 30 min using the average rate constant (4.9×10^{-4} l./mol s) is 41%. Thus at an initial Br_2 concentration >1.0 M, appreciable departure from second-order kinetics occurs.

G. Competition Brominations. Pairs of alkylcyclopropanes were allowed to compete for a deficiency of bromine in methylene chloride at room temperature, using NBS as the HBr scavenger. Disappearance of reactants was monitored by GC with the use of *n*-heptane or 2,3-dimethylbutane as inert internal standards. Alkylcyclopropane analyses were performed using a ⅛ in. × 20 ft 30% propylene carbonate on 80/100 Gas Chromosorb R column at 40°. Mixtures were analyzed before addition of bromine and NBS to obtain initial alkylcyclopropane/internal standard peak area ratios. Aliquots of reaction mixtures were removed at various times and several determinations of relative rate constant ratios made for each competition experiment using the rate relationship

$$\frac{k_{\text{alkylcyclopropane}_1}}{k_{\text{alkylcyclopropane}_2}} = \frac{\ln \dfrac{[\text{alkylcyclopropane}_1]_{final}}{[\text{alkylcyclopropane}_1]_{initial}}}{\ln \dfrac{[\text{alkylcyclopropane}_2]_{final}}{[\text{alkylcyclopropane}_2]_{initial}}}$$

In each case at least 10% of the less reactive alkylcyclopropane had been consumed before calculations were attempted. The average ratios were calculated and results appear in Table II.

In a typical experiment, a mixture of 2.5 mmol each of *trans*-1,2,3-trimethylcyclopropane, ethylcyclopropane, and *n*-heptane in 5 ml of methylene chloride was GC analyzed. After protecting the mixture from light, NBS (2.5 mmol) and bromine (2.5 mmol) were added. The mixture was stirred magnetically at room temperature. After 2 h and 15 min a 1-ml aliquot was removed and added to dodecene (1 mmol) in 0.5 ml of methylene chloride at 0°. Direct GC analysis indicated that 14% of the ethylcyclopropane and 51% of the trimethylcyclopropane had been consumed. A rate constant ratio of $k_{\text{trimethylcyclopropane}}/k_{\text{ethylcyclopropane}} = 4.7$ was calculated using the rate relationship given above.

Several qualitative experiments using considerably more reactive alkylcyclopropanes are outlined below.

1,1-Dimethylcyclopropane and *trans*-1,2-Dimethylcyclopropane. *trans*-1,2-Dimethylcyclopropane (5 mmol) and 1,1-dimethylcyclopropane (1 mmol) were condensed from a vacuum line into a mixture of *n*-hexane (2 mmol) and NBS (6 mmol) in 3 ml of methylene chloride. The mixture was GC analyzed to obtain alkylcyclopropane/internal standard peak area ratios. The mixture was protected from light with aluminum foil and cooled to −63°. A precooled mixture of bromine (6 mmol) in 2 ml of methylene chloride was added at once. The mixture was stirred magnetically. A 1-ml aliquot was removed after 15 min and quenched with dodecene (1.5 mmol) in methylene chloride. GC analysis revealed that 97% of 1,1-dimethylcyclopropane had reacted, while 30% of the *trans*-1,2-dimethylcyclopropane had disappeared. These data lead to a $k_{1,1\text{-dimethylcyclopropane}}/k_{1,2\text{-dimethylcyclopropane}}$ ratio of *at least* 10. Owing to the nearly complete conversion of 1,1-dimethylcyclopropane to bromination product, the rate ratio could not be determined with reasonable accuracy.

1,1-Dimethylcyclopropane and 1,1,2,2-Tetramethylcyclopropane. 1,1-Dimethylcyclopropane (1 mmol) was condensed into a mixture of 1,1,2,2-tetramethylcyclopropane (1 mmol), 2,3-dimethylbutane (2 mmol), and NBS (4 mmol) in 25 ml of methylene chloride. The mixture was GC analyzed, then protected from light and cooled to 0°. Bromine (4 mmol) in 5 ml of methylene chloride at 0° was added at once. The mixture was stirred magnetically for 45 s. Dodecene (3 mmol) in 5 ml of methylene chloride was then added to remove unreacted bromine. Direct GC analysis indicated that complete reaction of the tetramethylcyclopropane had occurred, while about 10% of the 1,1-dimethylcyclopropane had been consumed.

Acknowledgment. Financial assistance from the Air Force Office of Scientific Research (Grant No. AFOSR-75-2748) is acknowledged with gratitude.

References and Notes

(1) The earliest work involving the cyclopropane–Br_2 dark reaction under a variety of conditions was carried out by G. Gustavson, *J. Prakt. Chem.*, **62**, 273 (1900).
(2) For a discussion of some of the common misconceptions of the halogen–cyclopropane reaction as an addition to yield exclusively 1,3-dihalide, see A. J. Gordon, *J. Chem. Educ.*, **44**, 461 (1967).
(3) N. C. Deno and D. N. Lincoln, *J. Am. Chem. Soc.*, **88**, 5357 (1966).
(4) J. C. Day, K. J. Shea, and P. S. Skell, *J. Am. Chem. Soc.*, **95**, 5089 (1973).
(5) K. J. Shea and P. S. Skell, *J. Am. Chem. Soc.*, **95**, 6728 (1973).

(6) G. Gustavson, *J. Prakt. Chem.*, **62**, 270 (1900).
(7) K. J. Shea, D. C. Lewis, and P. S. Skell, *J. Am. Chem. Soc.*, **95**, 7768 (1973).
(8) J. B. Lambert and B. A. Iwanetz, *J. Org. Chem.*, **37**, 4082 (1972).
(9) J. B. Lambert and K. Kobayashi, *J. Org. Chem.*, in press.
(10) (a) J. B. Lambert, R. D. H. Black, J. H. Shaw, and J. J. Papay, *J. Org. Chem.*, **35**, 3214 (1970); (b) R. T. La Londe, *J. Am. Chem. Soc.*, **87**, 4217 (1965).
(11) G. G. Maynes and D. E. Applequist, *J. Am. Chem. Soc.*, **95**, 856 (1973).
(12) S. J. Cristol and R. T. La Londe, *J. Am. Chem. Soc.*, **80**, 4355 (1958); C. H. DePuy, W. C. Arney, Jr., and D. H. Gibson, *ibid.*, **90**, 1830 (1968).
(13) S. J. Cristol, W. Y. Lin, and A. R. Dahl, *J. Am. Chem. Soc.*, **92**, 4013 (1970).
(14) C. H. DePuy, *Fortschr. Chem. Forsch.*, **40**, 73 (1973).
(15) P. S. Skell and J. Keating in "Carbonium Ions", Vol. II, G. A. Olah and P. v. R. Schleyer, Ed., Wiley-Interscience, New York, N.Y., 1970, pp 573–653.
(16) P. S. Skell and P. D. Readio, *J. Am. Chem. Soc.*, **85**, 2849 (1963).
(17) M. S. Karasch, M. Z. Fineman, and F. R. Mayo, *J. Am. Chem. Soc.*, **81**, 2139 (1939).
(18) S. C. Stodola, Ph.D. Thesis, The Pennsylvania State University, 1972.
(19) N. C. Deno in "Isotopes in Organic Chemistry", Vol. I, E. Buncel and C. C. Lee, Ed., Elsevier, Amsterdam, in press.
(20) P. E. McMahon and W. C. Tincher, *J. Mol. Spectrosc.*, **15**, 180 (1965).
(21) Supplied by the Chemical Engineering Department, The Pennsylvania State University.
(22) H. C. Brown and C. Groot, *J. Am. Chem. Soc.*, **64**, 2563 (1942).
(23) W. von E. Doering and W. Kirmse, *Tetrahedron*, **11**, 272 (1960).
(24) A sample of (a,a)-2,4-dibromoadamantane was kindly supplied by Professor M. A. McKervey, The Queens University, Belfast.

Bromomalonates as Synthetic Reagents. Transfer Alkylations[1]

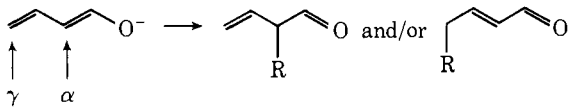
Barry M. Trost*[2] and Lawrence S. Melvin, Jr.

Contribution from the Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706. *Received June 27, 1975*

Abstract: A procedure for site selectivity in the alkylation of polyenolates is developed. The substrates examined, alkylidene succinates, were prepared by an Emmons–Wadsworth–Horner modification of the Stobbe condensation. The "alkylating" agents were bromomalonates of which cyclic isopropylidene 2-bromo-2-methylmalonate was the most useful. It can also serve as a general source of Br^+ toward carbanions. Reaction of the enolates of the alkylidene succinates with the bromomalonates leads initially to bromine transfer and malonate anion. Recombination of the two parts by conjugate addition–elimination leads to the product of remote alkylation. The regioselectivity of the reaction with polyenolates is discussed.

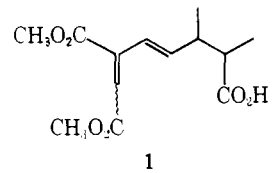
Introduction

The position of alkylation of a polyenolate is an intriguing and important problem. Normally, it is expected and observed that reaction occurs at the α position, at least in a kinetic process.[3,4] In several instances, the initial product

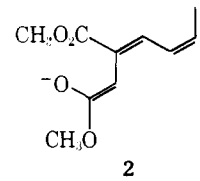


arising by alkylation at the α position has been rearranged to isomers which correspond to a net γ attack.[5,6] Direct attack at the γ (or more remote position) has been observed in a few cases. For example, allylation of a copper enolate of an α,β-unsaturated ester has led to an approximately 1:1 mixture of the α and γ alkylation products.[7] The alkylation of the dianion of 2-butynoic acid gives a 2.2:1 ratio of γ vs. α attack.[8] Alkylation of β-dialkylamine α,β-unsaturated ketones apparently gives only products of γ attack.[9]

In conjunction with a problem in sesquiterpene synthesis we developed a need for large quantities of acid **1**. One approach involves the alkylation of the polyenolate **2** at the ϵ

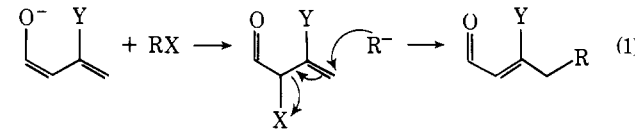


1



2

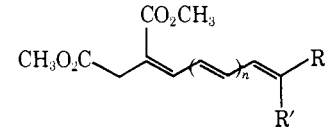
position. A potential solution to this problem takes advantage of the intrinsic preference for reaction at the α position by choosing an "alkylating" agent, RX, that reacts at the X group rather than at carbon. Recombination of the thus-formed R^- in a SN2′-type process with **3** would yield the product of net γ or ϵ, etc., attack (see eq 1). This process will be aided by the presence of polarizing groups on the enolate (e.g., Y in **3**) which will facilitate SN2′ attack. Con-



(1)

3

sidering our interest in the synthesis of **1**, we restricted our study to an examination of alkylidene succinates of general formula **4**. As a result of this investigation, we have uncov-



4

ered a new positive brominating agent, *O,O*-isopropylidene 2-bromo-2-methylmalonate, which serves as an excellent reagent for bromination of anions.

The need for such a route was underscored by the failure of a conceptually more direct path to **1**. Alkylation of the bromoester **5** with *tert*-butyl 2-lithiopropionate would be expected to give the *tert*-butyl ester of the desired carboxylic acid. Instead, it underwent reaction by a net SN2″ alkylation to give **6**, presumably by a Michael addition followed by elimination.[10]

Preparation of Alkylidenesuccinates

The Stobbe condensation is the most direct approach to alkylidene succinates; however, the yields in this reaction with aldehyde partners are generally low.[11] Considering the