Anal. Calcd for $C_{10}H_8ClNO$: C, 62.03; H, 4.16; Cl, 18.31; N, 7.23. Found: C, 62.11; H, 4.19; Cl, 18.31; N, 7.40.

7-Bromo-8-methoxyquinoline was prepared in 56% yield in the same manner as the chloro analog, mp 79.5–80.5°. The analytical sample (aqueous ethanol) melted at 80–81°.

Anal. Calcd for $C_{10}H_8BrNO$: C, 50.45; H, 3.39; Br, 33.56; N, 5.88. Found: C, 50.45; H, 3.38; Br, 33.57; N, 5.83.

7-Iodo-8-methoxyquinoline was prepared in 88% yield in the same manner as the chloro analog, mp 112–113°. The analytical sample (aqueous ethanol) melted at 113°.

Anal. Calcd for $C_{10}H_8INO$: C, 42.13; H, 2.85; I, 44.52; N, 4.91. Found: C, 42.34; H, 2.79; I, 44.24; N, 5.07.

2-Acetamido-4-bromophenyl Acetate.—A mixture of 2-acetamidophenyl acetate[8] (32.7 g, 0.3 mol), NBS (53.4 g, 0.3 mol), and 1000 ml of chloroform was heated under reflux with stirring until a clear solution was formed. After cooling, the chloroform solution was washed several times with a dilute $NaHSO_3$ solution, and the chloroform was removed by flash evaporation. The product (31.5 g, 56%) was recrystallized from benzene twice and melted at 148–150°.[9]

Anal. Calcd for $C_{10}H_{10}BrNO_3$: C, 44.14; H, 3.70; Br, 29.37; N, 5.15. Found: C, 44.02; H, 3.75; Br, 29.31; N, 5.22.

6-Bromo-8-quinolinol.—A mixture of 2-acetamido-4-bromophenyl acetate (39 g, 0.14 mol), 30 ml of concentrated sulfuric acid, arsenic oxide (30 g, 0.13 mol), and glycerol (50 g, 0.54 mol) was heated under reflux for 3 hr. After cooling, it was diluted with H_2O and adjusted to pH 6 with concentrated NH_4OH. The suspension was steam distilled and yielded 10.5 g (33%) of product, mp 143–145° (lit.[10a] mp 138–139°).

5,6,7-Tribromo-8-quinolinol.—6-Bromo-8-quinolinol (2.24 g, 0.01 mol) was dissolved in 50 ml of acetic acid. A solution of 3.3 g (0.02 mol) of bromine in 25 ml of acetic acid was added dropwise with stirring. The reaction was complete when the color of the bromine persisted for 10 min. The solution was poured into 1000 ml of H_2O, decolorized with $NaHSO_3$, and brought to pH 7 with Na_2CO_3, and $NaHCO_3$. The product was removed by filtration and washed with H_2O. A yield of 3.5 g (92%) of compound, mp 182–185°, was obtained. Recrystallization from aqueous alcohol raised the melting point to 188–190° (lit.[10b] mp 192°).

Registry No.—8-Methoxyquinoline, 938-33-0; 7-chloro-8-methoxyquinoline, 36748-98-8; 7-bromo-8-methoxyquinoline, 36748-99-9; 7-iodo-8-methoxyquinoline, 36749-00-5; 2-acetamido-4-bromophenyl acetate, 36749-01-6; *N*-chlorosuccinimide, 128-09-6; *N*-bromosuccinimide, 128-08-5; *N*-iodosuccinimide, 516-12-1; 5-Cl-8-MeOx, 17012-44-1; 5,7-Cl_2-8-MeOx, 17012-48-5; 5-Br-8-MeOx, 10522-47-1; 5,7-Br_2-8-MeOx, 17012-49-6; 5-I-8-MeOx, 17012-46-3; 5,7-I_2-8-MeOx, 17012-50-9.

(8) W. Theilacker, *Chem. Ber.*, **71**, 2065 (1938).

(9) R. K. Smalley and H. Suschitzky, *J. Chem. Soc.*, 5571 (1963). This compound was mentioned but not characterized.

(10) (a) A. R. Pinnington, Ph.D. Thesis, Oxford, 1954, in R. G. W. Hollingshead, "Oxine and Its Derivatives," Vol. III, Butterworths, London, 1956, p 674; (b) p 751.

The Electrophilic Addition of Bromine to *cis*- and *trans*-1,2-Dimethylcyclopropane

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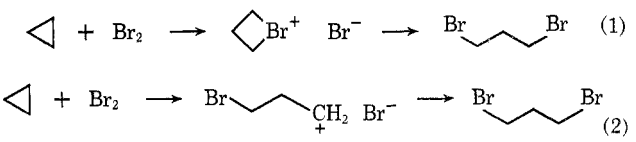
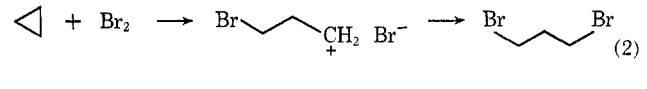
Under polar conditions, the major pathway for bromination of both *cis*- and *trans*-1,2-dimethylcyclopropane opens the less substituted carbon–carbon bond nonstereospecifically. Addition to the more substituted bond, also nonstereospecific, occurs to the extent of about 8% in both cases. A major component of the cis, but not the trans, reaction mixture is the hydride-shift product, 1,2-dibromo-2-methylbutane. The intermediates responsible for product formation are best described as nonbridged, secondary carbonium ions, because of the nonstereospecific nature of the reaction. The distribution of products is discussed in terms of steric and stereoelectronic effects.

Stereochemistry[2,3] and regiochemistry[4] have only recently been brought to bear on the mechanistic problems offered by the addition of electrophiles to cyclopropane rings. The bulk of the work to date has consisted in the addition of electrophiles to polycyclic compounds that contain a three-membered ring, and examination of the diastereomeric products in order to deduce the stereochemistry of the reaction. No single preferred stereochemical path has emerged from these studies, although individual cases have been thoroughly examined. No simple monocyclic cyclopropane has yet been studied with the view of determining the stereochemistry of the reaction.[5] To this end, we have studied the bromination of *cis*- and *trans*-1,2-dimethylcyclopropane. The products of this reaction offer a simple handle on the stereochemistry of the halogen addition. This study supplies the cyclopropane analog of the bromination of *cis*- and *trans*-2-butene. Conformational constraints on the conceivable acyclic carbonium ion intermediates produced from these monocyclic systems are much less important than those on the ions produced from the previously studied polycyclic compounds,[2,3] since the residual rings present in these latter ions prohibit free rotation. The structure of the monocyclic systems therefore has little bias on the stereochemical outcome. Furthermore, the availability of both the cis and the trans isomers enables the reaction to be studied from two diastereomeric directions. Such a comparison is not possible in polycyclic systems without using trans-fused rings.

The primary objective of these stereochemical studies is to distinguish between mechanistic pathways that involve cyclic bromonium ions (eq 1, analogous to



(1)



(2)

(1) This work was supported by the Petroleum Research Fund, administered by the American Chemical Society (Grant 2970-AC4,5) and by the National Science Foundation (Grant GP-22942).

(2) S. J. Cristol, W. Y. Lim, and A. R. Dahl, *J. Amer. Chem. Soc.*, **92**, 4013 (1970); S. J. Cristol, J. K. Harrington, T. C. Morrill, and B. E. Greenwald, *J. Org. Chem.*, **36**, 2773 (1971), and references cited therein.

(3) J. B. Lambert, R. D. H. Black, J. H. Shaw, and J. J. Papay, *J. Org. Chem.*, **35**, 3214 (1970), and references cited therein.

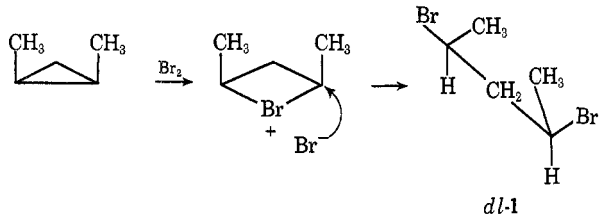
(4) N. C. Deno and W. E. Billups, *Chem. Commun.*, 1387 (1970).

(5) Since the preparation of this manuscript, the addition of bromine to the 1,2-diphenylcyclopropanes has been described; see R. T. LaLonde, P. B. Ferrara, and A. D. Debboli, Jr., *J. Org. Chem.*, **37**, 1094 (1972).

bromination of ethylenes) and pathways that involve open-chain carbonium ions (eq 2). Protonated cyclopropane rings, which are related to the bridged bromonium ion of eq 2, have been implicated in the addition of HX to the parent unsubstituted system[6a] and to some substituted cyclopropanes.[4,6b] Exclusively open-chain carbonium ions, however, have been indicated in the bromination of bicyclo[3.1.0]hexane.[3] Scheme I illus-

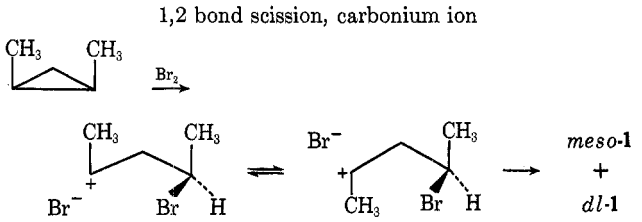
Scheme I

1,2 bond scission, bromonium ion

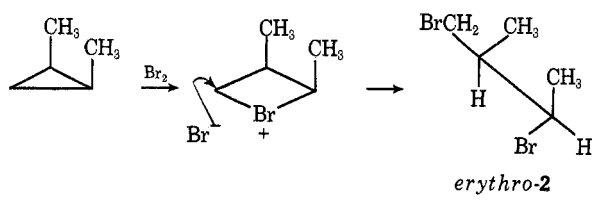


dl-1

1,2 bond scission, carbonium ion

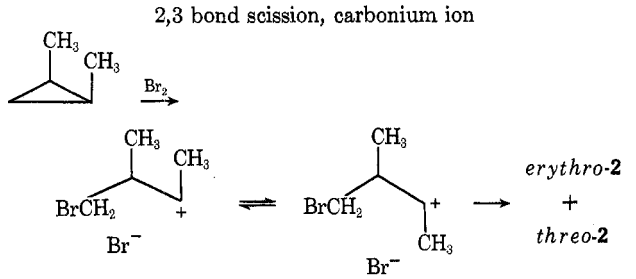


2,3 bond scission, bromonium ion



erythro-2

2,3 bond scission, carbonium ion

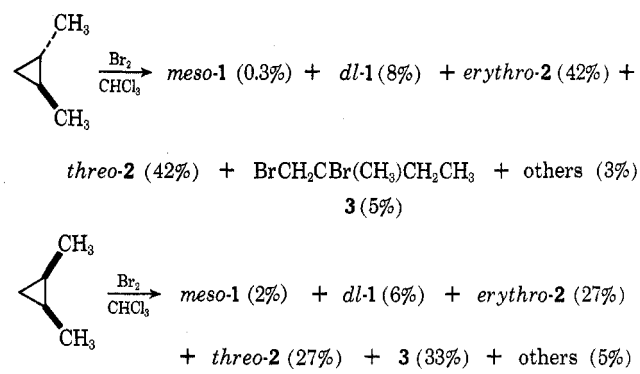


trates the various reaction pathways for the addition of bromine to *cis*-1,2-dimethylcyclopropane. Electrophilic addition can occur on either the more substituted 1,2 bond or on the less substituted 2,3 bond. According to the bromonium ion mechanism,[7] the cis compound would give entirely *dl*-2,4-dibromopentane (*dl*-1) from 1,2 bond scission and entirely *erythro*-1,3-dibromo-2-methylbutane (*erythro*-2) from 2,3 bond scission (Scheme I). The trans compound, on the other hand, would give *meso*-1 and *threo*-2 by these routes, respectively. According to the open-chain carbonium ion mechanism, with free rotation about carbon–carbon bonds, the cis compound would give both *meso*- and *dl*-1 from 1,2 bond scission and both *erythro*- and *threo*-2 from 2,3 bond scission. The trans compound would give a similar mixture. The procedure we followed in this study was to allow the substrates to react with bromine under polar conditions, to identify the products, and to draw mechanistic conclusions from comparisons with the expectations illustrated in Scheme I.

Results

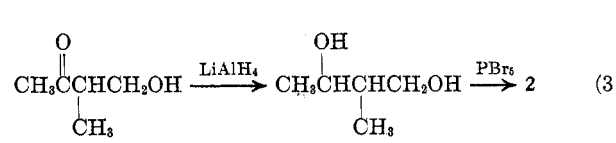
The polar addition of molecular bromine to the dimethylcyclopropanes was carried out at −60° in chloroform with the exclusion of light. The reaction mixtures were concentrated and the excess bromine was removed without altering the product composition (see Experimental Section). Each component of the reaction mixture was collected and compared with authentic material that had been independently synthesized. The product distributions, rounded off to the nearest percentage point, are given in Scheme II as the mean

Scheme II



of 25 measurements on a total of three independent brominations. The mean deviation is roughly 3–5% of each given value.

An authentic sample of 1,2-dibromo-2-methylbutane (**3**) was readily prepared by the addition of bromine to 2-methyl-1-butene. The major product, 1,3-dibromo-2-methylbutane (**2**), was obtained as a 50:50 mixture of erythro and threo stereoisomers by the method of eq 3. No attempt was made to identify the isomers

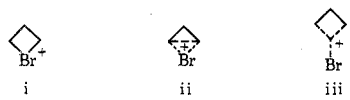


(3)

separately, because the reaction mixtures contained nearly equal amounts of each. The minor product, 2,4-dibromopentane (**1**), was obtained by bromination of the corresponding diol. Since the product mixtures from the halogenations of the dimethylcyclopropanes contained unequal amounts of the stereoisomeric meso and *dl* forms of **1**, an unambiguous isomeric assignment was necessary. The protons on the 3 carbon are chemically nonequivalent in the meso form (the AB portion of an ABX_2 spectrum), whereas those in the *dl* form are

(6) (a) C. J. Collins, *Chem. Rev.*, **69**, 543 (1969); (b) J. Mockus, Ph.D. Dissertation, Pennsylvania State University, 1971.

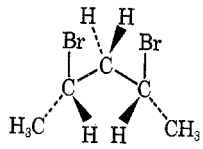
(7) We have chosen to represent the bromonium ions by structure i, although ii and iii are legitimate alternative representations. The differences have been discussed elsewhere.[8]



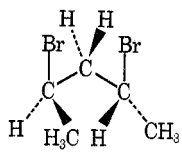
i ii iii

(8) G. A. Olah, J. M. Bollinger, Y. K. Mo, and J. M. Brinich, *J. Amer. Chem. Soc.*, **94**, 1164 (1972).

chemically equivalent (the AA′ portion of an AA′XX′ spectrum). The complexity of the 3-proton resonance



meso-1



dl-1

therefore serves as an indicator of the isomeric identity. The spectra of the 2,4-dichloropentanes have been fully analyzed in this manner.[9] Our spectra of the dibromopentanes closely resembled those of the dichloropentanes; so a parallel assignment could be made. The *dl*/meso product distributions given in Scheme II follow from the AB pattern for the 3-protons in the meso isomer and the AA′ pattern (not A_2) for the 3-protons in the *dl* isomer. Over 95% of the product mixture has therefore been identified. The remaining 3–5% was present as several short retention time products.

Discussion

Three conclusions may be drawn from the observed product distributions. (1) Both the major (2) and minor (1) "1,3"-dibromides are formed in a nonstereospecific fashion from both the cis and the trans substrates. (2) The major path of ring opening involves scission of the less substituted carbon–carbon bond. (3) The major difference between the cis and trans reaction product mixtures is the large amount of 1,2-dibromide observed in the former case. In the folllowing discussion, we will endeavor to draw mechanistic conclusions from these three observations.

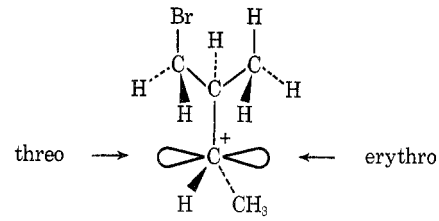
Stereochemistry.—The bromonium ion mechanism (Scheme I) requires that the cis substrate form exclusively *dl*-1 and *erythro*-2, and that the trans substrate form *meso*-1 and *threo*-2. In fact, both *cis*- and *trans*-1,2-dimethylcyclopropane form similar mixtures of **1** (with a large predominance of the *dl* form) and of **2** (with almost equal amounts of the diastereomers). These observations are consistent with the open carbonium ion mechanism, and rule out the bromonium ion mechanism in the product-forming step. The question as to whether a bromonium ion precedes the open carbonium ion will be discussed later.

The *dl*/meso and erythro/threo ratios may be explained if it is assumed that the first-formed open carbonium ion from either the cis or the trans starting materials proceeds rapidly to the most stable conformational form. Scheme III depicts the most stable conformational form for both 2,3 and 1,2 bond scission. In the best conformer obtained by scission of the less substituted (2,3) bond, the two faces of the carbonium ion experience approximately equivalent amounts of steric crowding. The bromide ion may therefore enter equally well from either direction to form similar amounts of the erythro and threo products. In the best conformer formed from scission of the more substituted (1,2) bond, the bromine atom shields the face that would produce the meso product. As a result, there is a predominance of *dl*-1. This latter conclusion is based on the assumption that the nonbonded interactions of the bromine atom are less than those of the methyl

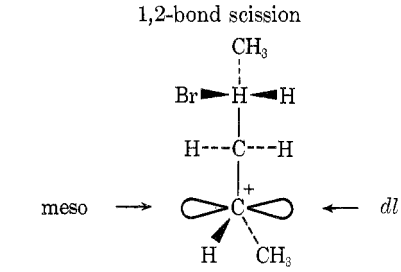
(9) P. E. McMahon and W. C. Tincher, *J. Mol. Spectrosc.*, **15**, 180 (1965).

SCHEME III

2,3 bond scission



1,2-bond scission



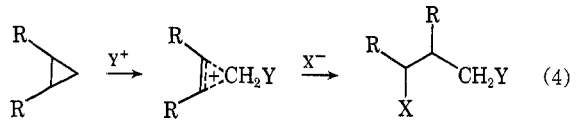
group. If the reverse were true, the methyl group would shield the side of the carbonium ion that produces the *dl* isomer, and the meso form would predominate. The larger size of the methyl group has been well documented in both cyclohexyl and acyclic systems (*cf.* the *A* value of 1.8 for methyl *vs.* 0.5 for bromine).

Regiochemistry.—The addition of electrophiles to substituted cyclopropane rings has a regiochemical complication not present in additions to substituted ethylenes. According to the Markovnikov rule for addition to unsymmetrically substituted double bonds, the electrophile adds to the less substituted carbon atom to form the more stable carbonium ion. Cyclopropane rings substituted at only one carbon atom would follow a similar rule. Electrophilic addition to cyclopropane rings with two substituted carbon atoms, however, can occur by two distinct modes to produce a secondary carbonium ion, as illustrated in Scheme I for the present system (1,2 and 2,3 bond scission). Ring opening of the 1,2-dimethylcyclopropanes occurs predominantly by cleavage of the less substituted (2,3) cyclopropane bond. Deno and Mockus[6] have also observed that addition of HX usually occurs between the most and the least substituted bond in cyclopropanes bearing several alkyl substituents.

Three explanations for the observed regiochemistry in the electrophilic ring-opening of disubstituted cyclopropanes are possible. (1) For steric reasons, the electrophile always attacks the least substituted carbon atom, by analogy with nucleophilic opening of substituted epoxides. Such steric effects have been established in the electrophilic cleavage of organomercurials.[10] Attack at the least substituted atom would result in cleavage of the bond to the most substituted neighbor in order to produce the most stable carbonium ion. Without knowing the stereochemistry of the initial addition,[2] we cannot assess this possibility. (2) Addition might be favored at the less substituted ring atom because this atom in fact is more nucleophilic. In order for the more substituted atom to be less nucleophilic, the methyl groups would have to be electron withdrawing. Again, this explanation cannot be tested

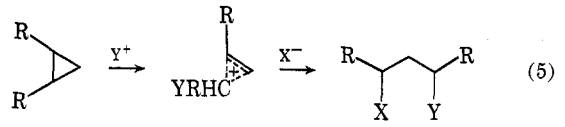
(10) F. R. Jensen and B. Rickborn, "Electrophilic Substitution of Organomercurials," McGraw-Hill, New York, N. Y., 1968, Chapters 3 and 4.

by the present experiments. (3) Mockus[6b] has suggested that the observed orientation of HX addition arises because it produces the most stable corner-protonated carbonium ion (Y = H in eq 4). Initial



(4)

addition to either of the more substituted carbon atoms, it is suggested,[6b] would produce a less stable corner-protonated species (eq 5). If the corner-

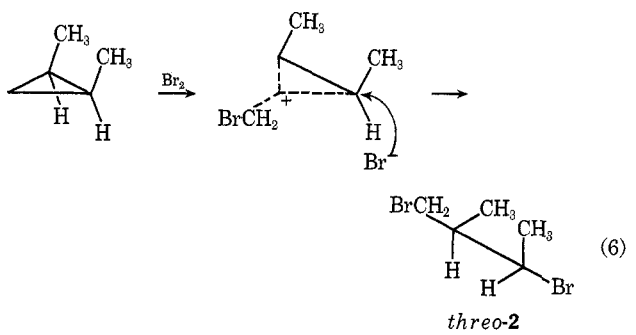


(5)

protonated ions in eq 4 and 5, however, are written with three-center bonds like that in structure iii of ref 7, there is no obvious advantage of one over the other; **4** contains a methyl and two secondary centers, **5** one

4 **5**

secondary and two primary centers. We therefore do not believe that the observed regiochemistry can be offered as evidence for corner-halogenated intermediates. Corner-halogenated ions can be firmly rejected as the product-forming intermediate. The observed regiochemistry requires that the initial attack of halogen occur at the least substituted position. The resulting species should decompose stereospecifically, with the cis starting material giving *threo*-**2**, and the trans giving *erythro*-**2** (eq 6). The observed nonstereospecificity of the reaction rules out such a process.

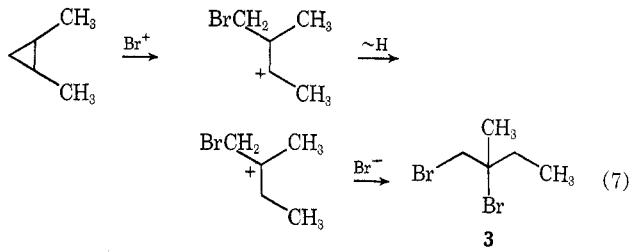


(6)

threo-**2**

Addition of bromine to bicyclo[3.1.0]hexane occurs with predominant opening of the more substituted carbon–carbon bond,[8] in contrast to these monocyclic systems. It may be that an additional effect that can alter the regiochemistry is present in polycyclic systems containing strained single bonds. In monocyclic systems, we favor either the steric or electronic effects described above, although no decision can be made until more subtle stereochemical experiments are performed.

Hydride Shift.—The final point that warrants consideration is the relative amount of the 1,2-dibromide (**3**) found in the cis and trans reaction mixtures. Whereas the cis compound produces 33% of this material on bromination, the trans compound produces only 5%. Because the 1,2 compound is formed at the expense of 1,3-dibromo-2-methylbutane (**2**), rather than of 2,4-dibromopentane (**1**), it is presumed to be a by-product of the 2,3-bond scission path (Scheme I). A simple mechanism for its production involves a hydride shift from the first-formed carbonium ion (eq 7). The

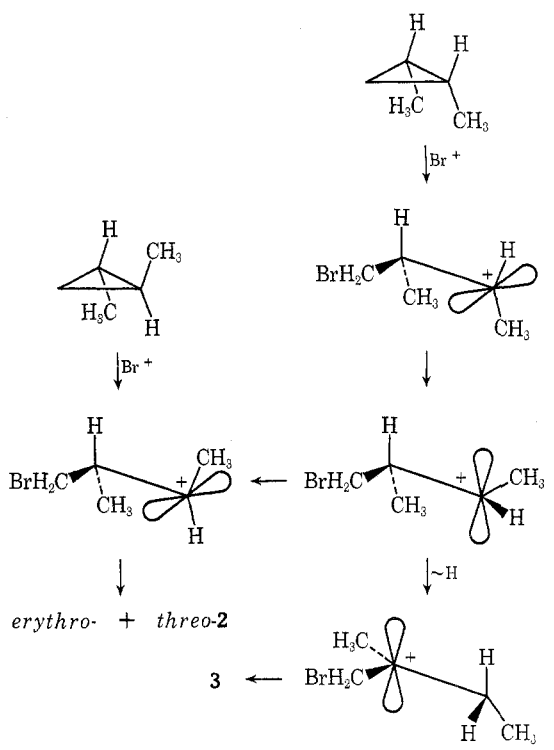


(7)

3

question remains as to why the hydride shift occurs more easily in the carbonium ion formed from the cis compound than that from the trans compound. Halogenation of the trans compound produces a carbonium ion that is very close to the most stable conformation depicted in Scheme III. The hydride shift must occur when the carbon–hydrogen bond is parallel to the empty p lobe. The carbonium ion that is initially formed from the trans compound would have to be converted into a much less favorable conformation in order to permit the hydride shift (Scheme IV). The

Scheme IV



cis compound, on the other hand, produces a carbonium ion that must undergo rotation about the bond connecting the methyl-substituted carbon atoms before achieving the most stable conformation. As it undergoes this rotation, the ion passes through the geometry that is most favorable for the hydride shift (Scheme IV). Therefore, part of the first-formed cis carbonium ion is shunted to the more stable tertiary carbonium ion by a hydride shift (eq 7) before it can achieve the best conformation that eventually would lead to the erythro/

threo mixture of compound **2**. The argument illustrated in Scheme IV is not dependent on the stereochemistry of the initial electrophilic addition.

Summary.—*cis*- and *trans*-1,2-dimethylcyclopropane add bromine under polar conditions to form a mixture of 2,4-dibromopentane (**1**), 1,3-dibromo-2-methylbutane (**2**), and 1,2-dibromo-2-methylbutane (**3**). The major product (**2**) is formed in a 1:1 mixture of the erythro and threo isomers, and the minor product (**1**) is formed with an excess of *dl* over meso for both the cis and trans starting materials. The nonstereospecificity of the reaction precludes bridged bromonium ions from being the product-forming intermediate. The erythro/threo and *dl*/meso ratios can be readily explained in terms of steric effects on the approach of the nucleophile to the intermediate open carbonium ion. The preference for 2,3 ring scission over 1,2 ring scission is not fully explained, but can arise from steric or electronic effects during the initial electrophilic attack. The significant amount of hydride-shift product found in the cis, but not the trans, reaction mixture arises because the initially formed open carbonium ion in the cis case must rotate through a conformation favorable to hydride shift before it arrives at the conformationally more stable form that gives the 1,3 products. The initially formed ion from the trans compound is already very close to the stablest (product-forming) conformation.

Although our results require open carbonium ions as the product-forming intermediates, we cannot exclude an initial formation of edge- or corner-brominated ions that rapidly decompose to the open carbonium ions. Under conditions favorable to long-lived cations, Olah and coworkers[8] attempted to generate trimethylene halonium ions, analogous to those depicted in Scheme I, from a variety of precursors. In no case were they successful. Four-membered bromonium ions as a class therefore appear to be unstable and might have eluded our experiment. The SbF_5–FSO_3H–SO_2 experiments, however, cannot be brought directly into the context of our experiments, since the 1,3-type products, such as those observed by us, are also not stable in superacid media. Thus 2,4-dibromopentane was observed by Olah, *et al.*, to rearrange to a 1,4 product.[8] It therefore does not follow that because trimethylene bromonium ions are unstable under highly acidic conditions that they would also be unstable under our conditions and therefore be possible initial intermediates. Nonetheless, the early stages of the reaction coordinate of this reaction, particularly the stereochemistry of the initial bromination, merit further investigation.

Experimental Section

Nmr measurements were made on Varian Models T-60 and A-60 spectrometers. Infrared spectra were recorded on a Beckman IR-5 spectrophotometer. Gas chromatographic analyses and separations were carried out on F & M Model 700 instruments, using a 0.25 in. × 6 ft column containing 10% Carbowax 20M on Chromosorb W 60–80.

Brominations.—The reaction was carried out in a dark room with illumination exclusively by a red light. The appropriate 1,2-dimethylcyclopropane (1.4 g, 0.015 mol, Chemical Samples Co.) and 25 ml of $CHCl_3$ were placed in an aluminum foil wrapped 100-ml round-bottomed flask and cooled to −78° with Dry Ice–acetone. A solution of bromine (3.2 g, 0.02 mol) in 25 ml of $CHCl_3$ was placed in a 20-mm test tube with a break seal at the bottom and likewise cooled to −78°. The temperature was allowed to equilibrate to −60°, at which temperature the Br_2–$CHCl_3$ solution was frozen. The test tube was removed from its bath and wiped clean, and the glass seal was broken over the dimethylcyclopropane solution. The bromine solution dropped in slowly as the $CHCl_3$ melted. The reaction occurred rapidly and smoothly. After addition was complete, the flask was warmed first to −30°, then to room temperature. Vpc traces during this procedure showed that the reaction mixture did not change with time. The crude mixture was washed with 10 × 100 ml of H_2O to remove any excess Br_2. The solution was dried overnight ($MgSO_4$), filtered, and stripped of solvent under aspirator pressure. The residue was used directly for analysis and collection of components. The products were stable to reaction conditions.

2,3-Dibromopentane (**1**) was prepared by treatment of 2,4-pentanediol (Aldrich Chemical Co.) with PBr_5 according to the procedure of Pritchard and Vollmer.[11]

1,3-Dibromo-3-methylbutane (**2**).—4-Hydroxy-3-methyl-2-butanone (Aldrich Chemical Co.) was reduced with $LiAlH_4$ by standard procedures, and the resulting 2-methyl-1,3-butanediol was treated with PBr_5 to give a 1:1 mixture of the erythro and threo isomers of **2**, as judged by vpc and nmr analysis.

1,2-Dibromo-2-methylbutane (**3**) was prepared by treatment of 2-methyl-1-butene (Analabs, Inc.) with Br_2 in $CHCl_3$ at 0°.

Registry No.—*cis*-1,2-Dimethylcyclopropane, 930-18-7; *trans*-1,2-dimethylcyclopropane, 2402-06-4.

(11) J. G. Pritchard and R. L. Vollmer, *J. Org. Chem.*, **28**, 1545 (1963).