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CANADIAN THESES ON MICROFICHE | THÈSES CANADIENNES SUR MICROFICHE

NAME OF AUTHOR/*NOM DE L'AUTEUR* TOMOKI CHIH-SHIH RUO

TITLE OF THESIS/*TITRE DE LA THÈSE* Free Radical Bromination of Several Chiral Molecules

UNIVERSITY/*UNIVERSITÉ* University of Alberta

DEGREE FOR WHICH THESIS WAS PRESENTED/ *GRADE POUR LEQUEL CETTE THÈSE FUT PRÉSENTÉE* Ph D

YEAR THIS DEGREE CONFERRED/*ANNÉE D'OBTENTION DE CE GRADE* 1975

NAME OF SUPERVISOR/*NOM DU DIRECTEUR DE THÈSE* Dr. Dennis D. Tanner

DATED/*DATÉ* July 25/75 SIGNED/*SIGNÉ* Tomoki C. S. Ruo

PERMANENT ADDRESS/*RÉSIDENCE FIXÉ* Dept. of Chem.
Univ. of Alta.
Edmonton, Alberta, Canada

THE UNIVERSITY OF ALBERTA

FREE RADICAL BROMINATION OF SEVERAL CHIRAL MOLECULES

by

TOMOKI CHIH-SHIH RUO

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE

OF

DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

EDMONTON, ALBERTA

Fall, 1975

THE UNIVERSITY OF ALBERTA

FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research for acceptance, a thesis entitled

"FREE RADICAL BROMINATION OF SEVERAL CHIRAL MOLECULES"

submitted by Tomoki Chih-Shih Ruo in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

Dennis D. Tanner
Supervisor

R. S. Brown

M. J. Bolton

Ted T. Tidwell

B. Kratochvil

Frederick D. Greene
External Examiner

July 7, 1975
Date

TO MY PARENTS

A B S T R A C T

The photobromination of the optically active (+)-1-cyano-2-methylbutane, (+)-2-methylbutyl acetate, and (-)-(R)-2-bromobutane with molecular bromine or mixtures of bromine and N-bromosuccinimide (NBS) as well as the bromination of 2-bromobutane with isotopically enriched molecular bromine-81 have been studied.

The bromination of (±)-1-cyano-2-methylbutane with molecular bromine, under varying conditions, yields a mixture of three monobrominated products: 1-Cyano-1-bromo-2-methylbutane (relative yield 78-95%), 1-cyano-3-bromo-2-methylbutane (relative yield 1-5%), and 1-cyano-2-bromo-2-methylbutane (relative yield 4-17%). The major product monobromide is proposed to arise by an acid catalyzed ionic reaction. When the bromination of (+)-1-cyano-2-methylbutane was carried out in the presence of solid N-bromosuccinimide as well as molecular bromine, the three monobrominated products were formed in relative yields that reflected a free radical bromination reaction: (+)-1-Cyano-1-bromo-2-methylbutane (5-14%), (±)-1-cyano-2-bromo-2-methylbutane (68-85%), and (+)-1-cyano-3-bromo-2-methylbutane (10-19%). The inability to obtain active 1-cyano-2-bromo-2-methylbutane from these bromination reactions may not be due to the fundamental nature of the bromination of a substrate at a chiral center but to the

instability of this particular tertiary bromide.

The reaction of (+)-2-methylbutyl acetate with a Br_2-NBS mixture in Freon 11 yields an inactive product, (±)-2-bromo-2-methylbutyl acetate (91%), and minor amounts of erythro- and threo-3-bromo-2-methylbutyl acetate (3.4%) and erythro- and threo-2,3-dibromo-2-methylbutyl acetate (1.8%). Under these reaction conditions the recovered unbrominated acetate was not racemized (at 11% conversion of starting acetate). In contrast to these results the bromination of (+)-2-methylbutyl acetate with molecular bromine was reported to yield extensively racemized recovered acetate. The results provide evidence for the importance of the reversal of the intermediate radical in the presence of hydrogen bromide.

The brominations of (-)-(R)-2-bromobutane have been studied using both molecular bromine and Br_2-NBS as the brominating agents. The products formed, 2,3-dibromobutane (dl-fraction) and 2,2,3-tribromobutane, were found to have partial activity. The results of the bromination of 2-bromobutane with isotopically enriched bromine-81 indicated that a major pathway, which exchanges the bromine substituent with the bromine pool, is an important factor in the racemization of the 2,3-dibromobutane formed. The major contributing factor to the exchange reaction was demonstrated to be an elimination-readdition mechanism. The combined results can be accommodated by a mechanism

involving a classical radical, the 3-bromo-2-butyl radical, as the initially formed intermediate, which is either captured by transfer with molecular bromine or undergoes β-scission to give 2-butene and hence optically inactive product. Since not all of the racemization has been accounted for by a detailed study of the reaction, some of the racemization must be attributed to processes which do not lead to bromine-81 exchange (i.e. cage elimination-readdition or rearrangement).

A C K N O W L E D G E M E N T S

I would like to thank my supervisor, Dr. Dennis D. Tanner, for his guidance, encouragement and supervision of this work. His enthusiasm and interest were a constant source of inspiration.

My thanks go to my colleagues whose suggestions have been of great assistance. Special thanks go to Dr. Ernie McGoran who has read and corrected many parts of this manuscript.

A special acknowledgement is owed to my wife, Mitsuei, for her constant encouragement.

The competent assistance of the technical staff in the Spectroscopy and Microanalytical Laboratories is gratefully acknowledged.

I wish to thank Lavine Braitenbach for typing this thesis.

To the Chemistry Department and the National Research Council of Canada I am indebted for financial support during the course of this work.

Tomoki C.S. Ruo

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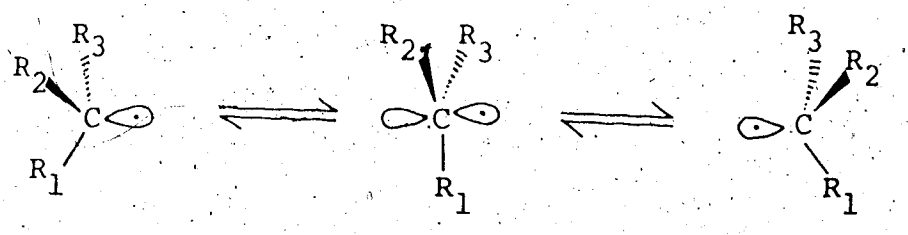
INTRODUCTION

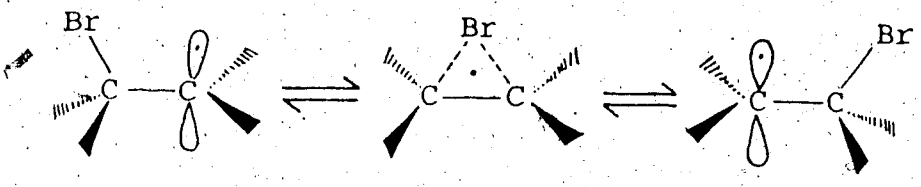
The stereochemistry of the reactions of free radicals and the question of their geometry have been the subject of a large number of recent investigations [1-9]. The question of whether the radical has a pyramidal structure, 1 or 3, and is undergoing rapid interconversion from one form to another (1 ⇌ 3) or whether it is a planar structure, 2, is a difficult one to answer; the situation is further complicated since 2 would be a transition state in the interconversion process. To determine whether 2 is



1 2 3

a transition state or a true intermediate is a difficult question to answer chemically. By analogy with carbonium ion chemistry it has been suggested that the stereochemistry of the free radical can be controlled by interaction with a group situated on the carbon β to the radical center. The most widely studied and controversial example of neighbouring group participation is the β-bromoalkyl radical, where experimental distinction between the clas-

sical radical 4 or 6 and the bromine-bridged radical 5 is very difficult, the difficulty being compounded by the possibility of an equilibrium between the three forms or between 4 and 6, 5 being only a transition state of the bromine migration between two carbons.



4 5 6

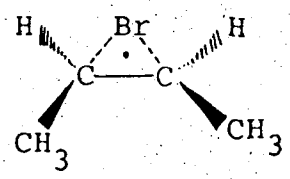
It is well known that planarity is not an essential characteristic of free radicals, since bridge-head radicals which cannot be planar, like the 1-norbornyl [10], the 9-triptycyl [11], and the apocamphyl [12] radicals and other radicals of rigid structure (e.g. cyclopropyl [13,14] and 7-norbornyl [15]) are produced under comparatively mild conditions.

Elucidation of the structures of these intermediates poses challenging problems to experimental and theoretical chemistry because these short-lived radicals cannot be isolated and subjected to conventional methods of structure determination. Many attempts have been made to overcome these problems, either by the direct detection of the radicals by spectroscopic means, by kinetic studies of reaction rates, or by stereochemical studies.

Theoretical treatments based on molecular orbital

energy levels tend to suggest that simple alkyl radicals are pyramidal [16-18]. However, esr [13,19-23], UV [24-26], as well as IR [27] spectral investigations suggest that the structure of simple alkyl radicals is planar or near planar. More refined quantum mechanical calculations are also compatible with the concept of planar radicals [28-30].

Electron spin resonance investigation of β-haloalkyl radicals has received considerable attention in the recent literature. Abell and Piette [31] studied the esr spectra for the intermediate β-bromoalkyl radicals resulting from the photolysis of hydrogen bromide (or deuterium bromide) and 2-butene at 77°K. The observed spectra from both cis- and trans-2-butene showed identical seven line patterns with 10.8 and 12.6 gauss splitting respectively. The authors concluded that these observations were consistent with an intermediate bromoalkyl radical in which the bromine was located equally on both C_2 and C_3, and strongly suggested a cyclic intermediate, a bromine-bridged radical 7 and 8 respectively.



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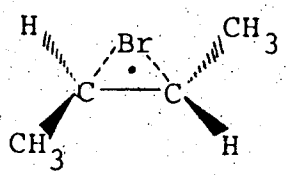

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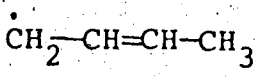


9

However, Symons [32] later reported that the photoaddition of hydrogen bromide to 2-butene led to the formation

of 2-butenyl radicals, 9, instead of 3-bromo-2-butyl radicals, 7 and 8. Symons' conclusions were reinforced by the observation [33-34] that the reactions of hydrogen atoms with 1,3-butadiene at 77°K results in the formation of 2-butenyl radicals, 9; the observed esr spectrum was very similar to that reported by Abell and Piette [31] in the photolysis of hydrogen bromide and trans-2-butene.

The effect of a neighbouring halogen on the conformation of alkyl radicals have been recently investigated by several laboratories by esr spectroscopy. It has been shown that a chlorine atom located in the β-position of the radical has a profound effect on the alkyl radicals[9,35-46]. On the basis of the small β-proton hyperfine splittings (see Table I) and the absence of any selective line broadening with changing temperature, it was suggested that the β-chloroethyl radical is essentially locked in a conformation with the chlorine atom eclipsing the odd electron orbital [9,35-41], 10. A β-chlorine hyperfine coupling constant of the magnitude of 17 G is also diagnostic of such a conformation (see Table I). Hyperfine splitting constants appear usually to arise from interaction between the odd electron of a radical and neighbouring atoms possessing nuclear magnetic moments. It thus gives information about the extent of delocalization of the unpaired electron and the electronic structure of the radical. When the isotropic coupling was used to estimate an approximate spin density

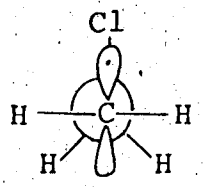
Table I

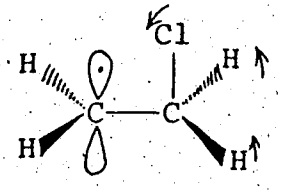
The Hyperfine Coupling Constants of Some β-Substituted Alkyl Radicals, $\dot{C}H_2CH_2$-X.

X	Temp, °C	Hyperfine Coupling Constants (G) a_α^H	a_β^H	a_β^X	Ref.
H	-180	22.38	26.87	--	37
CH_3	-130	22.10	31.12	0.27	37
F	-120	22.15	27.92	45.44	37
F	- 60	--	27.4	47.8	42
F	- 60	22.3	26.9	47.1	40
Cl	-120	21.75	10.20	18.78 (Cl^{35}) 15.65 (Cl^{37})	37
Cl	- 60	21.5	11.5	17.4	38,40
CCl_2CH_2Cl	- 40	--	10.5	10.5	38

in the chlorine atom, which indicated a 7-8% spin delocalization to the orbitals of chlorine from the radical center [37,41]. The delocalization of the odd electron onto the chlorine orbital has been suggested to involve a hyperconjugative delocalization onto the C-Cl σ-bond[41] or a p-p homoconjugative interaction of 3p orbital of chlorine to the radical center[37].

The anomalously small β-proton hyperfine splitting constant has also been suggested to indicate that there is some distortion at the β-carbon so that the β-protons are moving towards the nodal plane. Such a distortion was





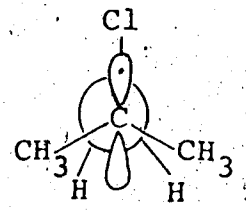
10

proposed to result from the interaction between the orbitals on chlorine and the radical center [37,40,43].

Cooper, Hudson, and Jackson [38] have also observed that the α-chloro-substitution leads to a marked decrease in the β-chlorine hyperfine splitting constant (see Table I). This behaviour has been attributed to the pyramidal character of α-chloroalkyl radicals [44]. Bending at the radical center and introduction of s-character into the odd electron orbital would be expected to reduce both hyper-

conjugation and homoconjugation.

More recently, Wood et al.[9] reported that β-chloro-tert-butyl radicals, produced by X-irradiation of isobutyl chloride in a matrix of adamantane-d_{16} at 77°K, prefer the eclipsed conformation, 11. The positive tem-

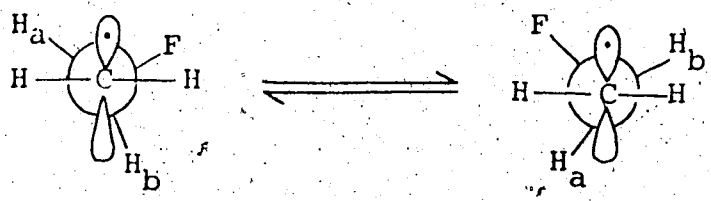


11

perature dependence of the methyl proton hyperfine splitting, like that of the tert-butyl radical[23,45], indicates a non-planar equilibrium radical site geometry, while the absence of line width alternation and the small size and equivalence of the methyl proton hyperfine splitting indicates that the chlorine prefers to be eclipsed with the orbital of the unpaired electron.

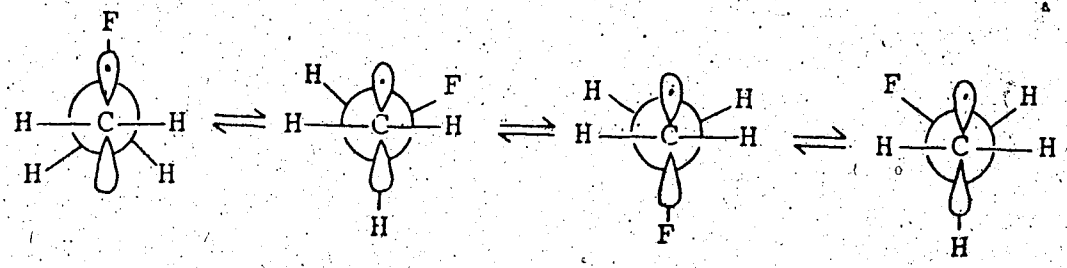
Conflicting reports have, however, appeared on the conformational effects of fluorine and bromine substituents on simple alkyl radicals. β-Fluoroethyl radicals in solution have been shown to prefer the staggered conformation[35,40], 12. The β-hyperfine splittings are similar to those of the 1-propyl radical (see Table I); these results suggested a low barrier to rotation about the C-C bond in

the β-fluoroethyl radical. At the low temperature limit, it is believed to be undergoing rapid exchange between conformation 12a and 12b [35,40].



12a 12b

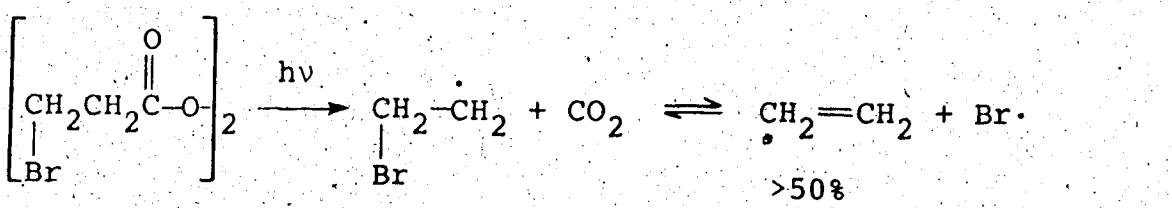
However, Wood et al. [9] have also studied the β-fluoro-tert-butyl radical and find that this radical prefers the eclipsed conformation, like the β-chloro-tert-butyl radical, 11. Kochi et al. [46] have recently suggested that the β-fluoroethyl radical has some proclivity to adopt the eclipsed conformation 13a and 13b, although in this case it represented only one of two stable rotamers.



13a 12a 13b 12b

Edge and Kochi [35,36] attempted to examine β-bromoalkyl radicals by esr spectroscopy. They were unable to observe these species in solution under a wide variety

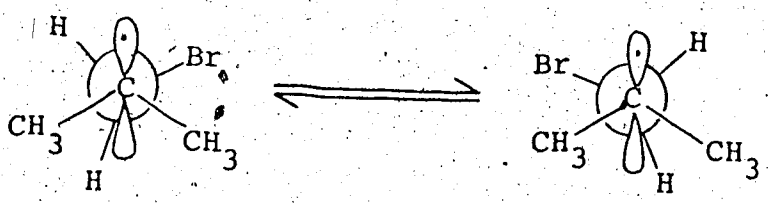
of conditions which were highly effective for the study of β-chloroalkyl radicals. The failure to observe β-bromoalkyl radicals is partly due to their extreme instability [3,47-52]; for example, photolysis of 3-bromopropionyl peroxide or perester gave a >50% yield of ethylene based on the carbon dioxide liberated. Although Edge and



Kochi [35,36] have been unsuccessful in observing this species in solution, two laboratories [9,41] claimed to have observed the β-bromoalkyl radicals independently. Lyons and Symons [41] investigated the photolysis of a frozen solution of ethylene and bromine at 77°K, and report the detection of the esr spectrum of the β-bromoethyl radical. Unfortunately, the proton hyperfine splittings were not resolved under their conditions and the radical species could not be positively identified. However, a large β-bromine splitting was indicated. The authors suggested that the radical structure is a hyperconjugatively frozen one, 14, similar to that of β-chloroethyl radical, 10 [39].

Contrary to Symons' results [41], Wood et al. [9] report a low hyperfine splitting for bromine in the β-bromo-tert-butyl radicals in an admantane-d_{16} matrix at

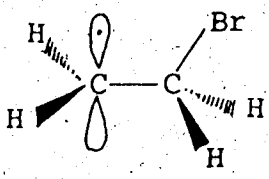
77°K. The authors strongly suggested that the esr spectrum of this radical can best be explained by the staggered conformation, 15. The expected line broadening for the two methylene protons in the region of intermediate rate of exchange between 15a and 15b were also present in the spectrum.



15a 15b

Although the esr studies showed the detection of β-bromoalkyl radicals, to date there is no consistent evidence which necessitates that a β-bromoalkyl radical prefers a bromine-bridged structure. If the β-bromoalkyl radical possesses a bridged structure, there is no chemical evidence which provides a distinction between an unsymmetrically bridged structure 14 (either stabilized by hyperconjugation or homoconjugation) or a completely symmetrically bridged structure, 16. Evidence against a symmetrically bridged species, 16, was reported by Hargis and Shevlin [8]. The CIDNP signal observed during the thermolysis (119°C) of benzoyl-β-bromopropionyl peroxide, 17, in chlorobenzene-bromotrichloromethane solution gave em-

mission at δ 4.5 due to the α-protons of the product 18 and enhanced absorption at δ 3.6 resulting from the β-protons. An unpolarized signlet at δ 3.4 corresponding to the methylene protons of 1,2-dibromoethane 19 as predicted from radical 14 was also observed. The CIDNP results established conclusively that the ground state of β-bromoethyl radical has non-equivalent methylene groups, thus excluding a symmetrically bridged structure, 16.



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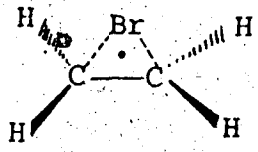

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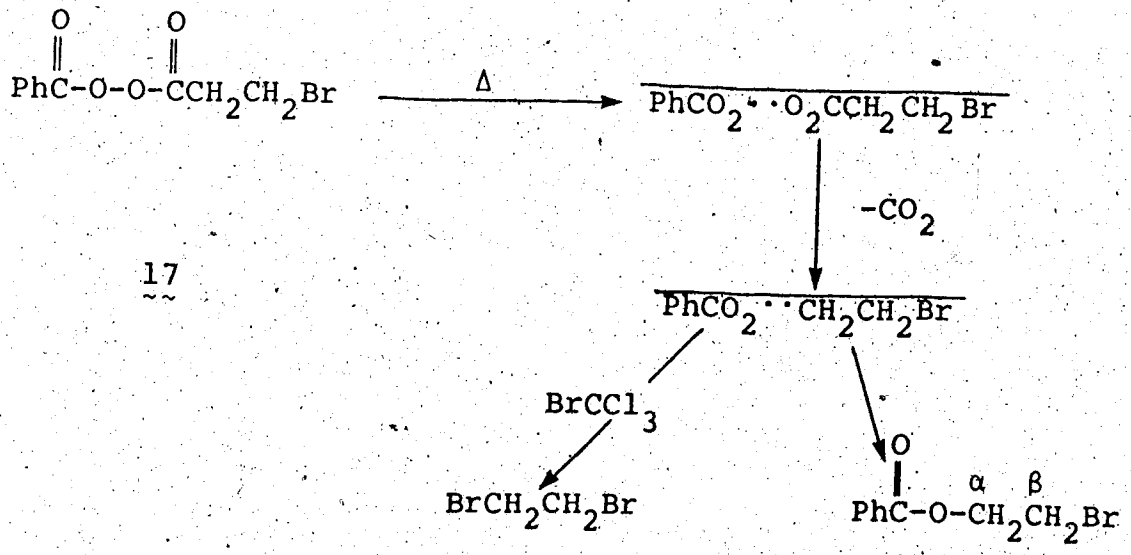

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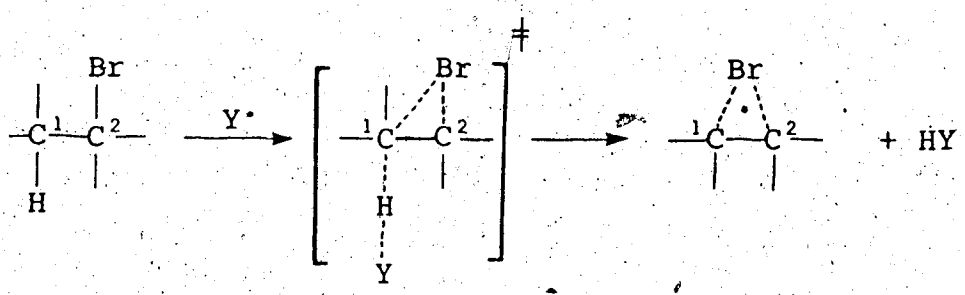
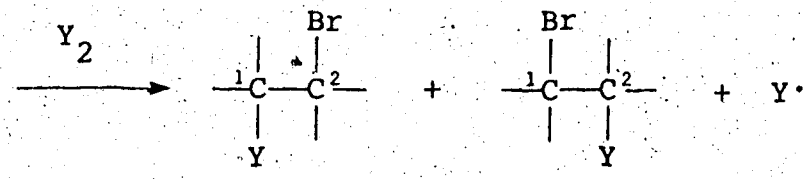
18

Although it has not been studied in great detail, the mechanism of the free radical 1,2-bromine atom migration has some bearing upon the structure of the β-bromoalkyl radical. If the bridged intermediate is formed by neighbouring bromine participation in the transition state

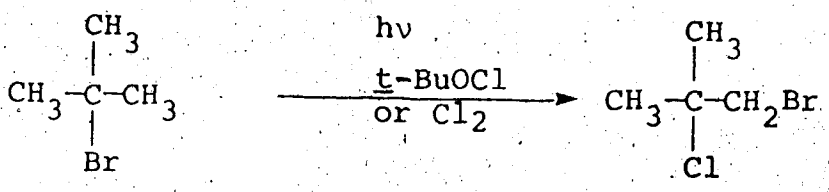




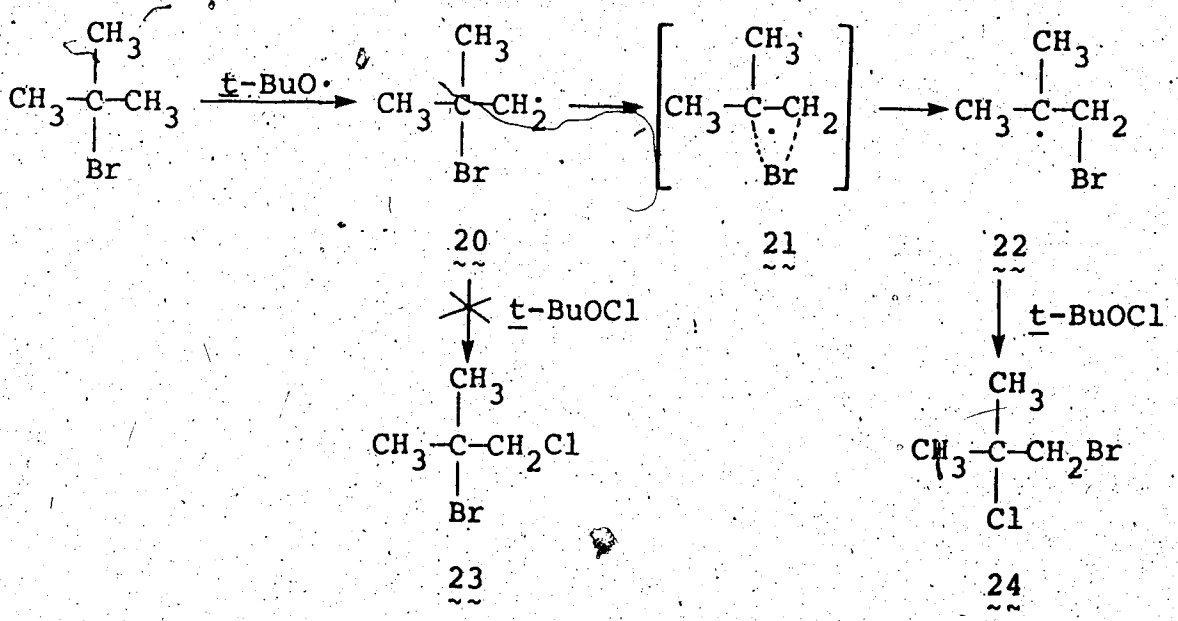
leading to hydrogen abstraction, then transfer of the intermediate with some transfer agent may lead to a 1,2-bromine atom migration. Many authors have, however, attempted to explain this bromine atom migration as resulting from the formation of a bromine-bridged radical intermediate. Arguments against it are usually based on indirect experimental evidence to show that the bromine atom from the elimination of β-bromoalkyl radicals can be trapped with an additive in the chlorination reaction.

Skell et al.[53] and Juneja and Hodnett[54] have

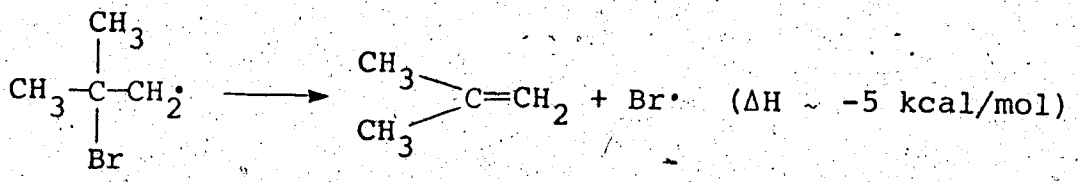
independently claimed 1,2-bromine migration in the photochlorination of tert-butyl bromide with tert-butyl hypochlorite and molecular chlorine respectively. In both cases, 1-bromo-2-chloro-2-methylpropane was claimed to be the exclusive product. Similarly, chlorination of 2-bromopropane [53] with tert-butyl hypochlorite gave 2-bromo-2-chloro-propane as well as the rearrangement product 1-bromo-2-chloropropane. These authors suggest that the production



of the rearranged product can be explained with the formation of a bromine-bridged radical intermediate, 21. The following scheme was suggested..

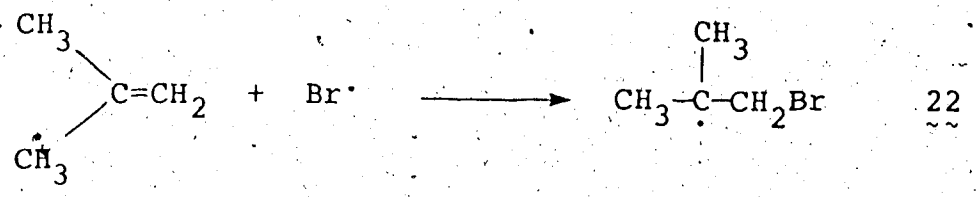


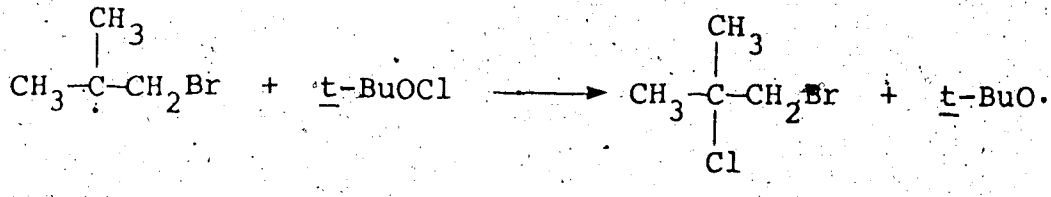
Haag and Heiba [48] have reinvestigated the chlorination of tert-butyl bromide with tert-butyl hypochlorite. The unrearranged product 23, which would be expected from the initially formed intermediate radical, 20, was not observed by previous authors [53,54]. Haag and Heiba [48] carrying out the reaction at -78° in carbon disulfide as a solvent found both the rearranged 24 and the unrearranged 23 products. Moreover, the proportion of the normal product, 23, increased with increasing tert-butyl hypochlorite concentration and reached about 30% in 2.5 M tert-butyl hypochlorite. Since radical 20 can be trapped via chlorine transfer from tert-butyl hypochlorite, these authors suggested the classical radical, 20, is a true intermediate and as the elimination of bromine atom from this intermediate radical is exothermic and should have a relatively low activation energy, it is therefore expected to be a relatively fast reaction even at -78°. Evidence was obtained which supported the elimination

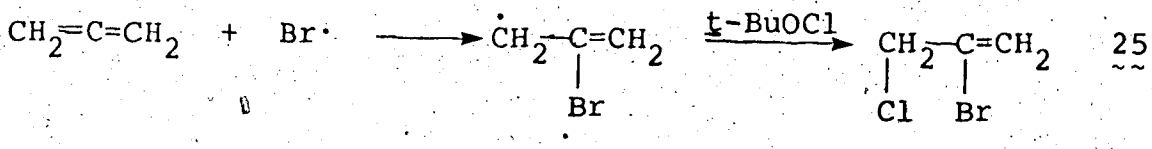


process when the chlorination was carried out in the presence of 1-4 molar allene. Upon the addition of allene, an excellent bromine atom scavenger, bromochloropropene, 25, was obtained in a 42% yield (based on the tert-butyl

hypochlorite which had reacted). The bromochloropropene was found at the expense of the rearranged product, 24. These authors suggested that the formation of the rearranged product could be explained by a facile elimination of the bromine atom from the intermediate radical, 20, to give isobutylene followed by the rapid addition of a bromine atom to this olefin to give the more stable tertiary radical 22.





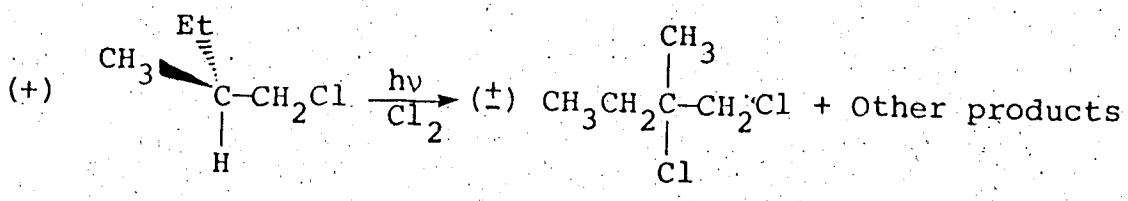


The best mechanistic probe for the structure of β-bromoalkyl radicals is obtained by the investigation of the stereochemistry of the reaction products which are derived from the photobromination of an optically active alkyl bromide. If the radical is planar, the reactions leading to or proceeding via radical intermediates should

involve complete loss of optical activity, provided that the carbon atom that becomes the intermediate radical is the one which was originally dissymmetric. Since the dissymmetric molecule goes through a symmetric intermediate, the reaction of the intermediate must lead to an enantiomeric pair of products, which are formed in equal amounts. It must be realized that, although the loss of stereochemical identity is consistent with a planar structure for the radical, it does not demand such a structure. A pyramidal radical (dissymmetric intermediate) which is interconverted, through molecular vibrations, with its enantiomer at a rate much faster than the rate at which it reacts to form products is consistent with the experimental facts.

A number of free radical reactions involving the production of free radical intermediates at the asymmetric center have been investigated [5,6,55-57]. Brown, Kharasch, and Chao [56] first investigated the stereochemistry of the making and breaking of bonds to an asymmetric carbon atom in a free radical mechanism. The authors observed that the photochlorination of optically active (+)-1-chloro-2-methylbutane, 26, produced completely racemized 1,2-dichloro-2-methylbutane, 27. This phenomenon has been attributed to either a planar structure of the radical, 28, or to a pyramidal structure, 29, which inverts at a rate greater than the rate of the transfer step to form the product. Further investigations [58-61] have led to the con-

clusion that the formation of free radicals at asymmetric centers in optically active compounds generally leads to optically inactive products.

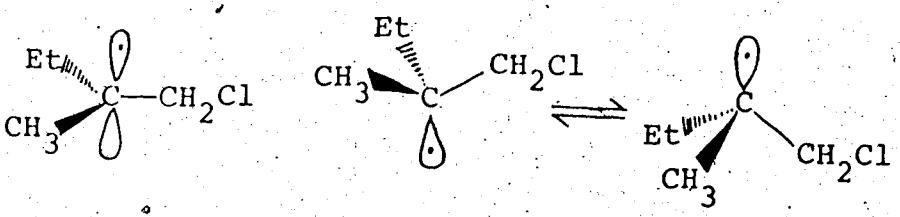


Active

26

Racemic

27



28

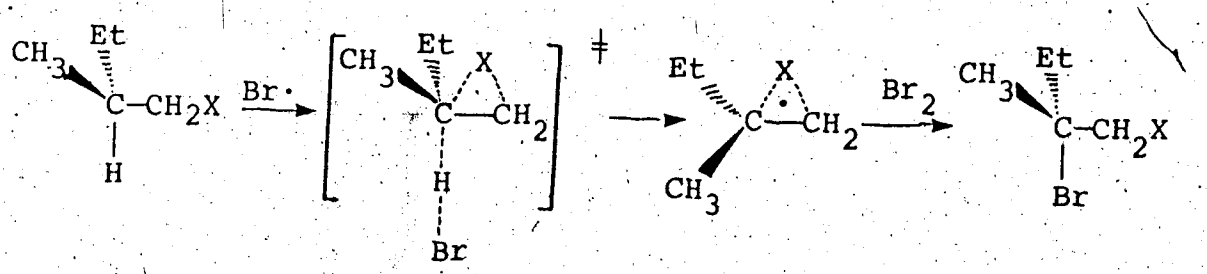
29a

29b

Exceptions to this generalization are the photobromination by a number of free radical brominating agents (viz. molecular bromine, tert-butyl hypobromite, and N-bromosuccinimide) of (+)-1-bromo-2-methylbutane, (+)-1-chloro-2-methylbutane, and (+)-1-cyano-2-methylbutane.

Skell et al.[55] have studied the bromination of optically active (+)-1-bromo-2-methylbutane, 30, and (+)-1-chloro-2-methylbutane, 26, and obtained optically active (-)-1,2-dibromo-2-methylbutane, 32a, and (-)-1-chloro-2-bromo-2-methylbutane, 32b, respectively as the only ob-

servable product. However, neither the absolute configuration of these dihalides nor their optical purities had been determined. The retention of activity in the brominated products has been attributed to the formation of an intermediate halogen bridged radical, 31. The formation of this bridged species was presumed to occur by the assisted removal of the tertiary hydrogen atom by the neighbouring halogen atom to form a halogen-bridged radical, 31, followed by transfer with molecular bromine to give the brominated product 32, with retained configuration.



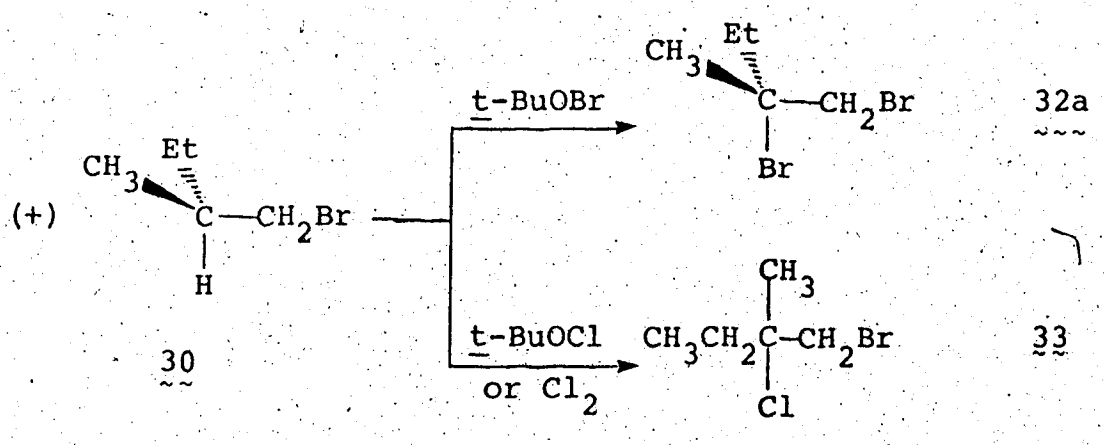
30 X=Br
26 X=Cl

31

32 a. X=Br
b. X=Cl

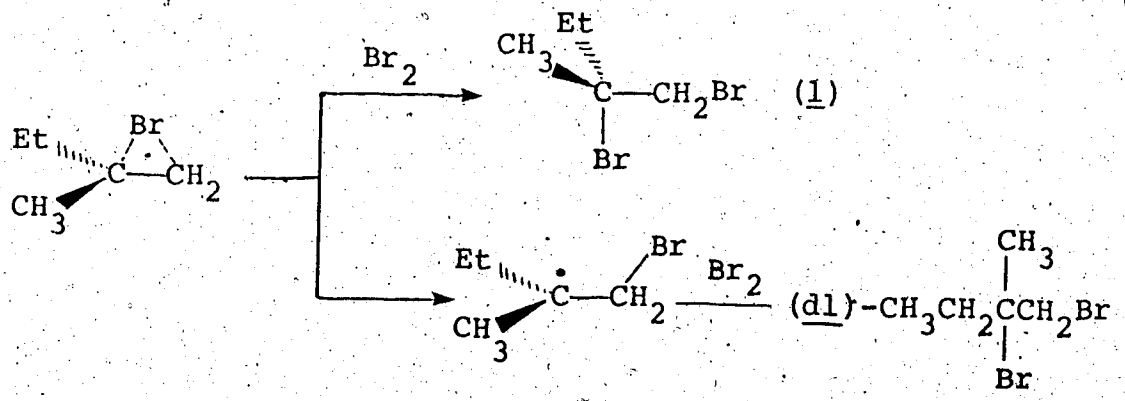
Skell et al. [55] also carried out the halogenation of optically active 30 with tert-butyl hypobromite, tert-butyl hypochlorite, and molecular chlorine. Optically active 32a was obtained using tert-butyl hypobromite as the brominating agent. In contrast, all of the chlorinating agents produced inactive 1-bromo-2-chloro-2-methylbutane, 33. These reactions showed no evidence of anchimeric

assistance by the β bromo substituent, with substitution occurring at all C-H bonds. In these instances, the authors suggested that although there was no requirement for bridging in the transition state leading to the radical, the preservation of optical activity in the bromination product of 30 with tert-butyl hypobromite bromination is consistent with a mechanism in which bromine bridging occurs after the abstraction process, but before a rotation about C_1–C_2 bond can occur. This bridged radical is trapped by tert-butyl hypobromite, but opens to allow rotation before reaction with either tert-butyl hypochlorite or molecular chlorine occurs [55,62].



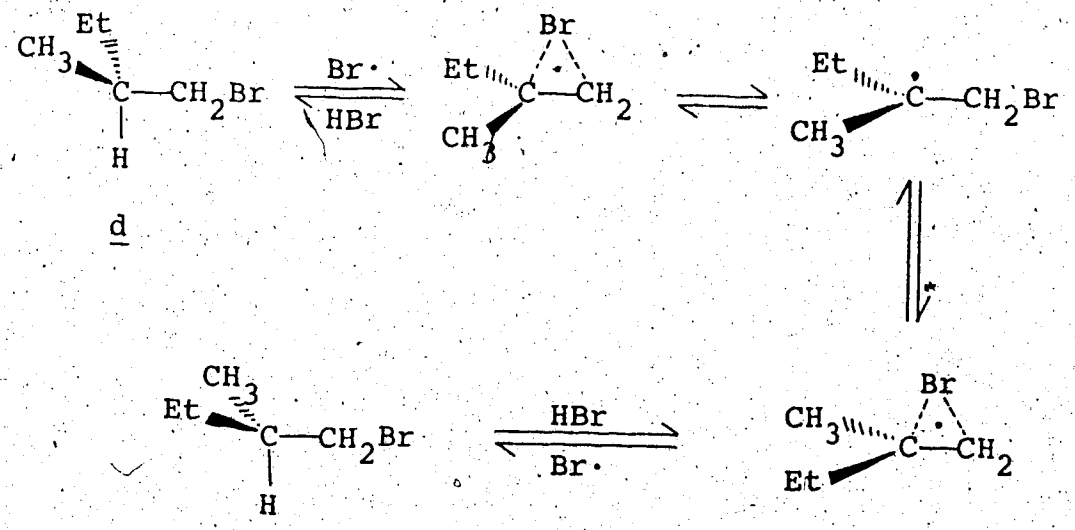
The observed rotation, α, of the product varied with bromine concentration and with temperature. Low concentrations of bromine or using N-bromosuccinimide as the brominating agent produce only a slightly optically active product [55]. The optical activity of the product was, likewise, decreased by using elevated temperature (72-80°).

As an explanation of these results, Skell suggested that the bridged radical can open to the classical radical which could compete with the transfer of the bridged radical with bromine. The low concentration of bromine effectively increases the lifetime of the bridged radical and allows it to open to the classical radical which is racemized.



The bromination of optically active 30 with molecular bromine ($RBr:Br_2$ = 2:1) has been reinvestigated by Tanner, Yabuchi, and Blackburn [5]. They found that the rotation of the product 32a was essentially the same as that reported by Skell et al.[55]. The recovered unreacted starting bromide was found to have racemized 3-7% during the reaction. It has been suggested that the bromine bridged mechanism has several limitations [5]. If the bridged radical is the first formed intermediate, then this racemization cannot be explained by transfer of the open radical with hydrogen bromide, but, if one adheres to the principle of microscopic reversibility, the racemization of starting

material (6-14% of radicals formed) must arise from the formation of an open radical, which then undergoes rotation, closes again to a bridged radical, and then transfers with hydrogen bromide to give back starting material.

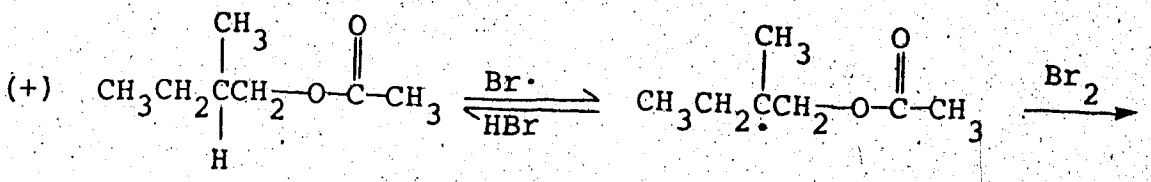


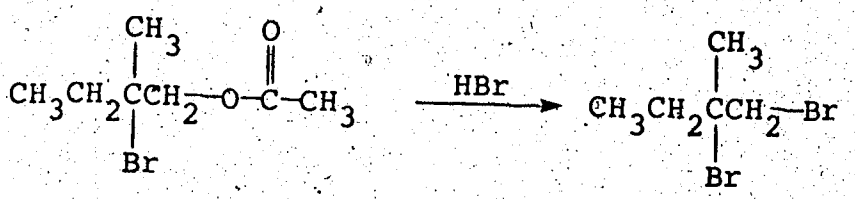
d

l

Tanner et al.[5] have also investigated the photobromination of optically active (+)-1-fluoro-2-methylbutane and (+)-2-methylbutyl acetate. In both instances, the recovered starting materials were substantially racemized, 86-88% in the case of (+)-1-fluoro-2-methylbutane and 44% for (+)-2-methylbutyl acetate. These results indicate the importance in these reactions of the reversal reaction between hydrogen bromide and the initially formed radicals. A multitude of products is formed in both reactions. How-

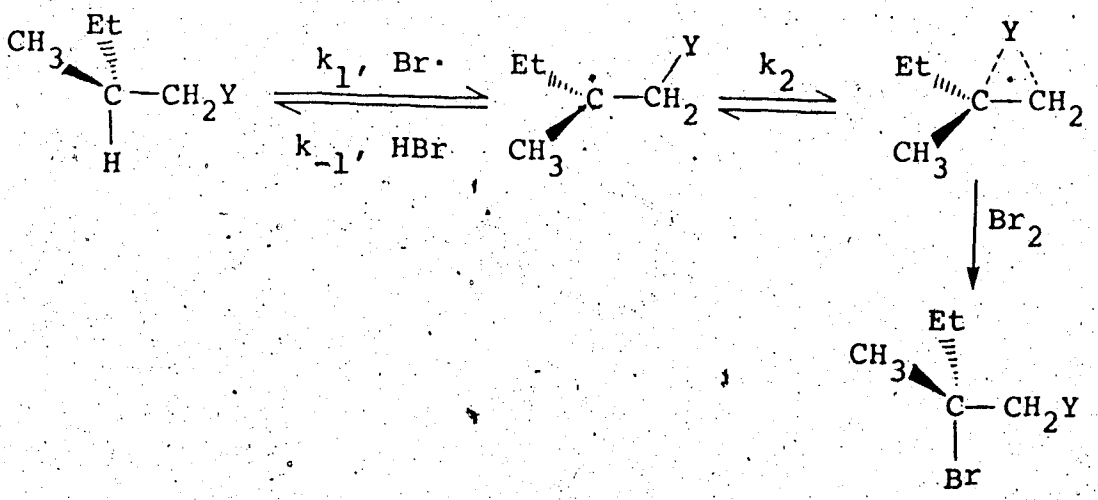
ever, the isolated 1-fluoro-2-bromo-2-methylbutane was found to be optically inactive. In the case of the bromination of (+)-2-methylbutyl acetate, no bromoacetate could be positively identified or isolated. It has been concluded that the bromoacetate when formed is rapidly destroyed by hydrogen bromide under the conditions of the reaction. The isolated 1,2-dibromo-2-methylbutane was found completely racemized.





Racemic

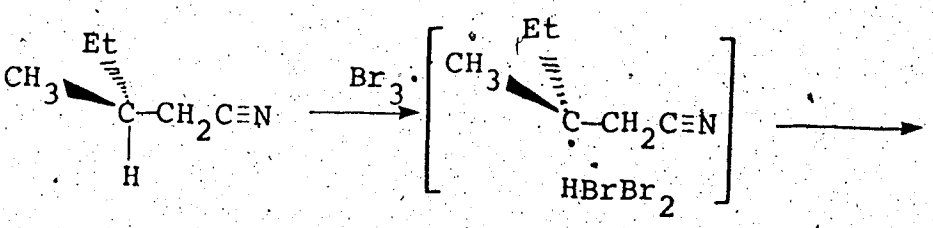
Tanner et al. [5] have suggested several explanations to rationalize the observations. One explanation cited the formation of a bridged species after the radical is formed, in order to account for the retention of activity in the bromination of (+)-1-bromo-2-methylbutane. If the bridging step, k_2, is faster than the molecular rotation of C_1–C_2 bond, then transfer of the radical with bromine would give products with retained activity, while a competing transfer of hydrogen bromide with open radical



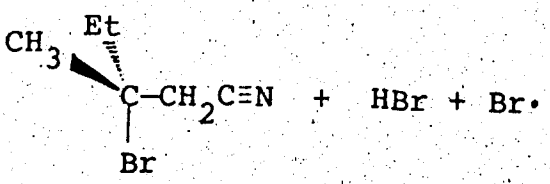
(k_{-1}) would lead to the racemization of the starting material. The inability of the fluorine atom to expand its octet could explain the racemization of both the product and starting material in the bromination of optically active fluoride. In the case of the acetate, the results would confirm the observation that a single bridged intermediate acetoxy radical is not the sole intermediate in the formation of products from a β-acetoxylalkyl radical [63]. An alternative explanation for the results obtained from the bromination of active 1-substituted 2-methylbutane would be a modification of the mechanism proposed by Haag and Heiba [57].

In 1965, Haag and Heiba [57] reported that the liquid phase photobromination of optically active (+)-1-cyano-2-methylbutane with 1 molar bromine proceeded with high selectivity at the tertiary asymmetric carbon to yield optically active (+)-1-cyano-2-bromo-2-methylbutane.

Since they believed that neighbouring group participation leading to bridged cyano radical was most unlikely, an alternate mechanism was proposed. It was suggested that, under the high concentration of bromine necessary for the observation of the retention of optical activity in the product, the abstracting species was the $Br_3^{\cdot}$ radical rather than bromine atom and that alkyl radical and the bromination species are formed as a geminate pair. Accordingly, the retention of activity was due to a rapid cage reaction



$[\alpha]_{548.1} = +7.98°$



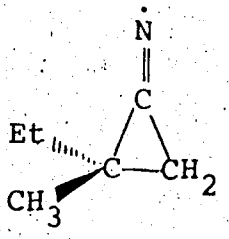
$[\alpha]_{548.1} = +1.69°$

between them before molecular rotation of the radical could occur. No evidence was presented concerning the degree of optical purity or chemical purity of the product.

It was subsequently pointed out that a bridged cyano group was not as unlikely as Haag and Heiba had first believed. Such a radical would be an imidyl radical, 34,

and there was considerable precedent for considering such an intermediate [64-66]. For example, participation of a bridged cyano group has been proposed in the rearrangement which takes place in the hypoiodite reaction of 20-hydroxy-20-cyano steroids [66], where a bridged imidyl radical, 35, was suggested as an intermediate.

In the case of the recombination of geminately caged radicals, the loss of optical activity need not occur, and some degree of retention of configuration has been ob-



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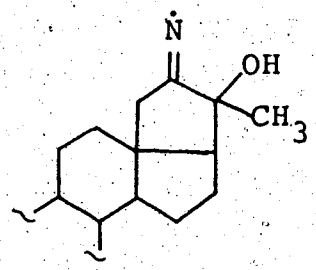


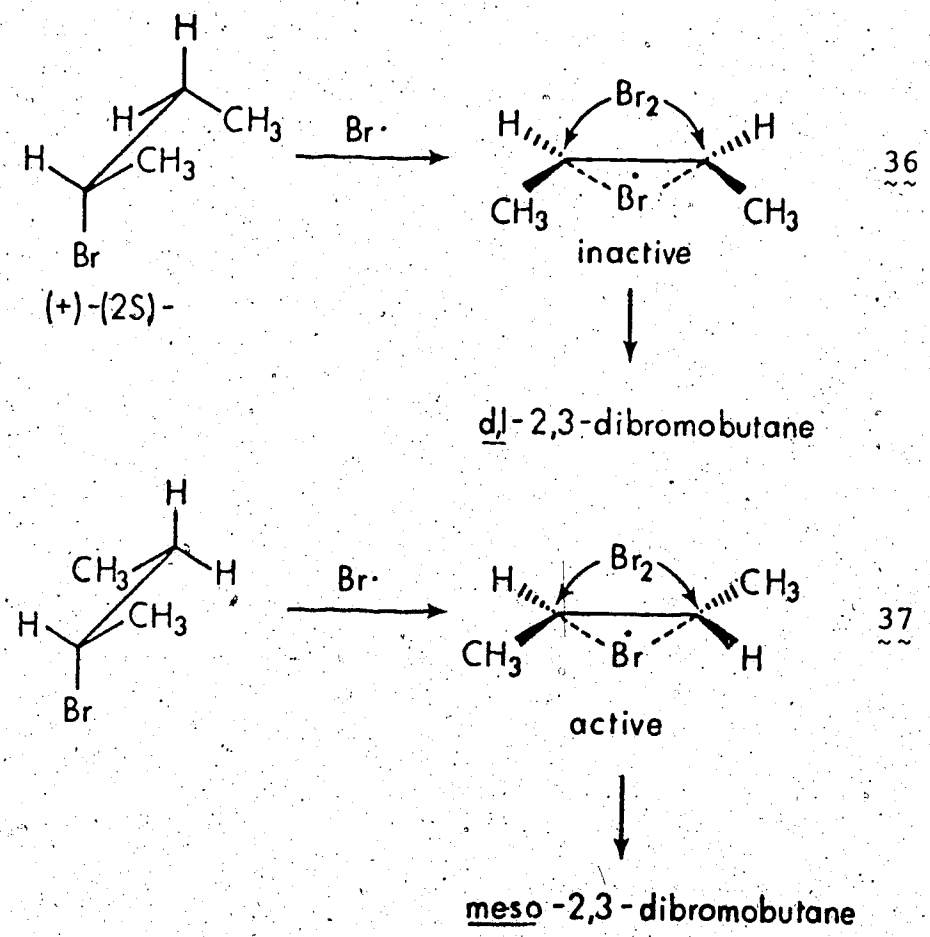
35

served for many years. Bartlett and McBride [67] have reported that the photolysis of meso- and dl-azobis-3-methyl-2-phenyl-2-butane in a methylcyclohexane glass matrix at 77°K gave 100% stereospecificity in the products meso- and dl-diphenyl-2,3,4,5-tetramethylhexane respectively. Kopecky and Gillan [68] have shown that the cage coupling products obtained from the decomposition of some optically active 1,1'-diphenyl-1-methylazomethanes were formed with a net retention of configuration. Greene [69] has investigated the decomposition of optically active

peroxide of hydratropic acid and observed that a significant amount of ester was formed with retention of optical activity.

During the course of this work, Skell and Shea[70] reported their investigation of the bromination of optically active (+)-(S)-2-bromobutane. They reported that the optically active bromide yielded on bromination meso- and dl-2,3-dibromobutanes. These authors concluded that these observations are not consistent with a classical radical intermediate. They rationalized their conclusion by involving the formation of two bridged intermediates, one inactive, 36, the other active, 37. The active bridged intermediate led to the meso product as shown in Scheme I. In a subsequent study,[7,71] Skell reported that photobromination of optically active (+)-(S)-2-bromobutane with molecular bromine and NBS in Freon 11 as solvent, produced the dl-2,3-dibromobu[illegible]had some residual activity. At 1.25 M bromine co[illegible]n, dl-2,3-dibromobutane was obtained with a ro[illegible]of $[\alpha]_{365}^{20}$ = -5.2° (95% racemic product). The optical [illegible]vity of the dl-2,3-dibromobutane did not change o[illegible]a 100-fold decrease in bromine concentration. The con[illegible]uration of the levorotatory dibromide was assigned [illegible](-)-(2S,3S)-dibromobutane by correlating it with the (-)-(2S,3S)-dibromobutane obtained from the treatment of (+)-(3S)-bromobutane-(2R)-ol with triphenylphosphine and bromine. These authors concluded that "if one ignores for the moment the small component

Scheme I



36

37

of this reaction which leads to active (-)-2,3-dibromobutane, the major reactions can be rationalized by the previous scheme", (Scheme I).

The empirically useful Brewster's Rules [72] have been utilized to predict the sign of rotation of the brominated products of (+)-1-substituted 2-methylbutanes, where the substituents are bromine [5,55], chlorine, [55] and cyano [5,6] groups. The configuration has been assumed to have been retained on bromination. The calculations predicted that the brominated products should have an

opposite sign to the starting materials. This is in fact observed in the case of the photobromination of (+)-1-bromo-[5,55] and (+)-1-chloro-2-methylbutane [55], but contrary to this prediction, the sign of the 2-brominated bromocyanide obtained from (+)-1-cyano-2-methylbutane was unchanged [57]. However, it is recognized that a molecule with two polar groups on adjacent carbon atoms may exhibit strong dipolar interactions or solvent interactions favoring or disfavoring a particular conformation and the observed rotation may be quite different from what is predicted. When the magnitude of the rotation is small, even an inversion of sign may be observed. Thus, the nature of the radicals derived from this compound required further clarification. We have therefore reinvestigated the photobromination of (+)-1-cyano-2-methylbutane. We have also studied the photobromination of (+)-2-methylbutyl acetate using Br_2-NBS mixture in order to prevent the acid catalyzed decomposition of brominated products. It has been previously shown that the acetoxy group does not form a bridged radical [63].

In order to get further insight into the nature of β-bromoalkyl radicals and the stereochemical course of their reactions, the liquid phase photobromination of optically active (-)-(R)-2-bromobutane was also investigated. Optically active (-)-(R)-2-bromobutane was chosen for this study since the stereochemistry of the

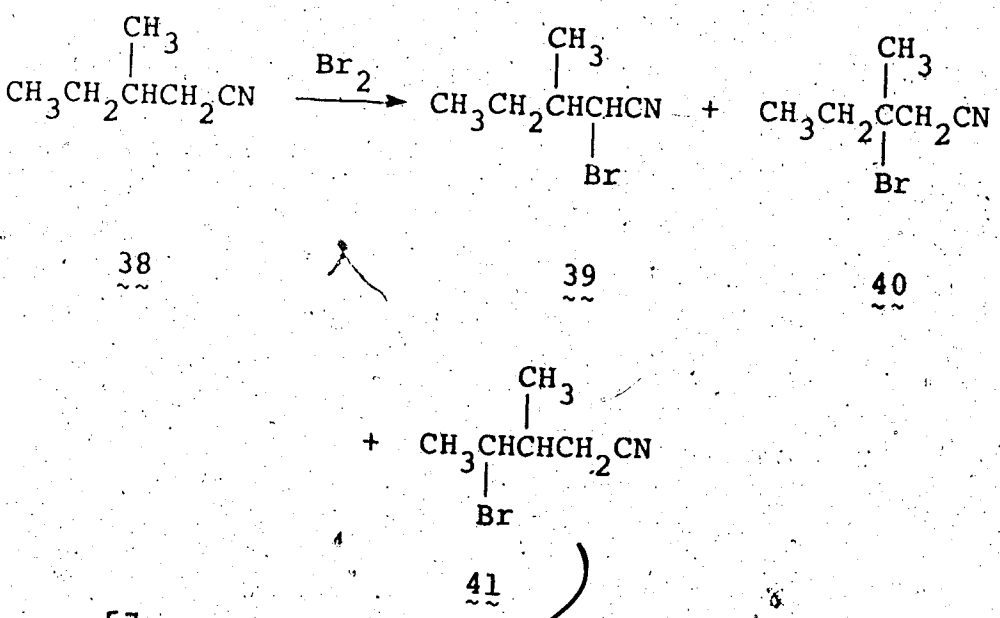
products would distinguish between the classical radical and bromine-bridged radical mechanisms, and photobromination of dl-2-bromobutane had been extensively studied previously[73-75], and the products had been well characterized.

It is well known that β-bromoalkyl radicals can also undergo elimination of bromine atom to form olefins, which would subsequently add bromine to give inactive dibromide. In order to test whether the β-bromoalkyl radicals would eliminate bromine atoms during bromination, the bromination of 2-bromobutane using isotopically enriched molecular bromine-81 (97.81% bromine-81 and 2.19% bromine-79) was investigated. It was anticipated that if olefin formation takes place, some excess enrichment of the bromine-81 in the product vicinal dibromides and of bromine-79 in the hydrogen bromide would be observed. It was expected that a combination of the optically active (-)-(R)-2-bromobutane studies and the isotopically enriched bromine-81 brominations would give a clear picture of the reaction mechanism.

RESULTS AND DISCUSSION

Photobromination of (±)-1-Cyano-2-methylbutane with Molecular Bromine and Bromine-NBS Mixture.

The photoinitiated reaction of 1-cyano-2-methylbutane, 38, with molecular bromine (see Table II) yielded three monobromination products, 1-cyano-1-bromo-2-methylbutane, 39, 1-cyano-2-bromo-2-methylbutane, 40, and 1-cyano-3-bromo-2-methylbutane, 41. Contrary to the previous



38 39 40

41

study [57], where only 40 was reported, the major isomeric monobromide obtained from the bromination was 1-cyano-1-bromo-2-methylbutane, 39, 78-95%. The minor isomers 40 and 41 were formed in a relative yield 4-17% and 1-5% respectively. The absolute yield of the three monobromides was low and ranged from 71% at 2:1 ($RCN:Br_2$) to 57% at 10:1 ($RCN:Br_2$) ratios of substrate to bromine.

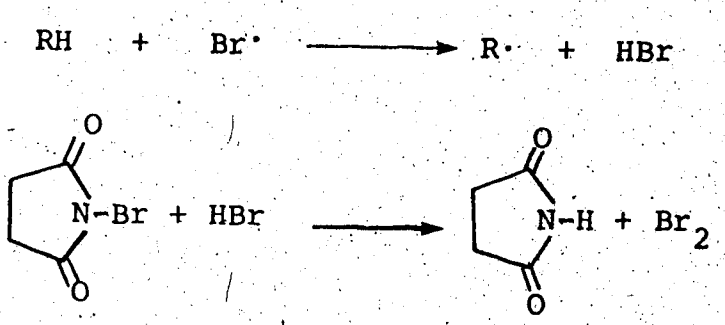
Table II

Bromination of (±)-1-Cyano-2-methylbutane, 38, with Molecular Bromine.

Reaction #	Mole Ratio RCN:Br_2	Temp. °C	Relative Yields of Monobromides		Yield %
1	2:1	24	39	95	
			40	4	
			41	1	
2	2:1	40	39	93	
			40	5	
			41	2	
3	13:1	24	39	78	
			40	17	
			41	5	
4	13:1	40	39	87	
			40	10	
			41	3	
5	2:1	25	39	93	66.3
			40	5.6	3.8
			41	1.4	0.9
6	4.5:1	25	39	90	53.1
			40	7	4.1
			41	3	1.8
7	10:1	25	39	92	52.4
			40	6.2	3.5
			41	1.8	1.1

It was apparent from the isomer distribution obtained from the bromination of 38 with molecular bromine that a radical bromination was not leading to the production of the major product 39, since the expected product of radical bromination would result from the substitution of the tertiary hydrogen. A likely explanation for the formation of 39 was an acid catalyzed α-bromination of the methylene position adjacent to the activating cyano group.

The acid catalyzed ionic bromination could be greatly minimized by the addition of solid N-bromosuccinimide (NBS) to the reaction mixture. The NBS functions as a source of molecular bromine which forms by the reaction of the hydrogen bromide produced in the reaction with the NBS. Photobromination of 38 using mixtures of solid NBS



and molecular bromine in carbon tetrachloride ($RCN:Br_2$: NBS = 6:1:5) gave a 29% yield of the three monobrominated products in the ratio of (39:40:41) 5:85:10, when the reaction was carried out so that 60% of the active bromine was consumed (see Table III, reaction 6).

The two chiral isomeric monobromides (+)-1-cyano-1-bromo-2-methylbutane, 39a, and (+)-1-cyano-3-bromo-

Table III

Bromination of (+)-1-Cyano-2-methylbutane, 38a, with NBS and Molecular Bromine in Carbon Tetrachloride.

Reaction #	Reactants in CCl_4[a] Mole x 10^2	Temp. °C	Products 39a : 40 : 41a
1 - 2	38a, 43.4	25	6 : 80 : 14
	Br_2, 5.4		14 : 68 : 18
	NBS, 10.9		
3 - 4	38a, 37.3	21	10 : 71 : 19
	Br_2, 4.5		12 : 70 : 18
	NBS, 9.3		
5	38a, 25.0	22	5 : 80 : 15
	Br_2, 3.2		
	NBS, 15.7		
6	38a, 22.3	33	5 : 85 : 10
	Br_2, 3.6		
	NBS, 16.3		

a) In 100 ml CCl_4 solution.

2-methylbutane, 41a, which are formed in minor amounts during the bromine-NBS brominations were synthesized by independent reactions and isolated by preparative glpc.

Since the mechanism of the tert-butyl hypobromite bromination of alkanes proceeds by a free radical chain, carried by the less selective (relative to bromine) tert-butoxy radical [76], it was anticipated that a more random distribution of products would be obtained from its use as the reagent for brominating (+)-1-cyano-2-methylbutane, 38a. The bromination of 38a with tert-butyl hypobromite (2:1 mole ratio) at 25° yielded upon glpc analysis five monobrominated products in the ratio of 19:32:39:4:6. The compounds corresponding to the first two peaks were (+)-1-cyano-1-bromo-2-methylbutane, 39a, and presumably the inactive 1-cyano-2-bromo-2-methylbutane, 40. The compounds corresponding to peak 3 was identified as a dextrorotatory mixture of erythro and threo isomers of 1-cyano-3-bromo-2-methylbutane, 41a, $[\alpha]_{546}^{26} = +9.40°$ (see Table IV). The nmr spectrum of 41a showed it to be an equal molar mixture of the erythro- and threo-isomers.

The chiral monobromide, (+)-1-cyano-1-bromo-2-methylbutane, 39a, was synthesized from (+)-1-cyano-2-methylbutane, 38a, ($[\alpha]_{546}^{24} = +8.97°$) with phosphorus tribromide and bromine and was found to have a rotation of $[\alpha]_{546}^{27} = +6.62°$ (See Table IV).

The photoinitiated bromination of 38a with

Table IV

Specific Rotation of (+)-1-Cyano-2-methylbutane 38a, (+)-1-Cyano-1-bromo-2-methylbutane 39a, and (+)-1-Cyano-3-bromo-2-methylbutane 41a in CCl_4

λ, mμ	$[\alpha]_\lambda^{24}$, 38a	$[\alpha]_\lambda^{27}$, 39a	$[\alpha]_\lambda^{26}$, 41a
589	+ 7.65°	+ 5.64°	+ 7.88°
578	+ 7.98°	+ 5.89°	+ 8.18°
546	+ 8.97°	+ 6.62°	+ 9.40°
436	+14.83	+10.48°	+15.85°
365	+22.40°	+15.09°	+25.21°

mixtures of molecular bromine and NBS was carried out in the same manner as the bromination of the racemic mixture of that cyanide, 38. Fractional distillation of the product mixture, after the destruction of the excess brominating agent, yielded unreacted starting material (37-40°/8 mm) and a fraction boiling at 52-53°/1 mm. Glpc analysis of this fraction showed it to be primarily 1-cyano-2-bromo-2-methylbutane, 40. The reisolated starting material was purified by preparative glpc and was found to be racemized 3-4% (see Table V). The fraction containing 1-cyano-2-bromo-2-methylbutane was redistilled using a 10" Vigreux column and a fraction boiling at 48-49°/1.2 mm was collected. Glpc analysis of this fraction showed the presence of small amounts of (+)-1-cyano-1-bromo-2-methylbutane (1.4%) and (+)-1-cyano-3-bromo-2-methylbutane (7.0%) as well as the desired 1-cyano-2-bromo-2-methylbutane (91.6%). Measurement of the optical rotation following isolation of the desired 2-bromoisomer by preparative glpc showed that it was completely racemized. Therefore, no further attempt was made to isolate the tertiary bromide from the reaction mixture by preparative glpc since previous attempts to isolate (-)-1,2-dibromo-2-methylbutane in this manner led to extensive racemization, whereas distillation allowed its isolation [5]. Furthermore, glpc treatment of 40 leads to small amounts (~3%) of products resulting from the

Table V

Optical Rotation of (+)-1-Cyano-2-methylbutane, 38a, Before and After the Br_2-NBS Bromination in CCl_4

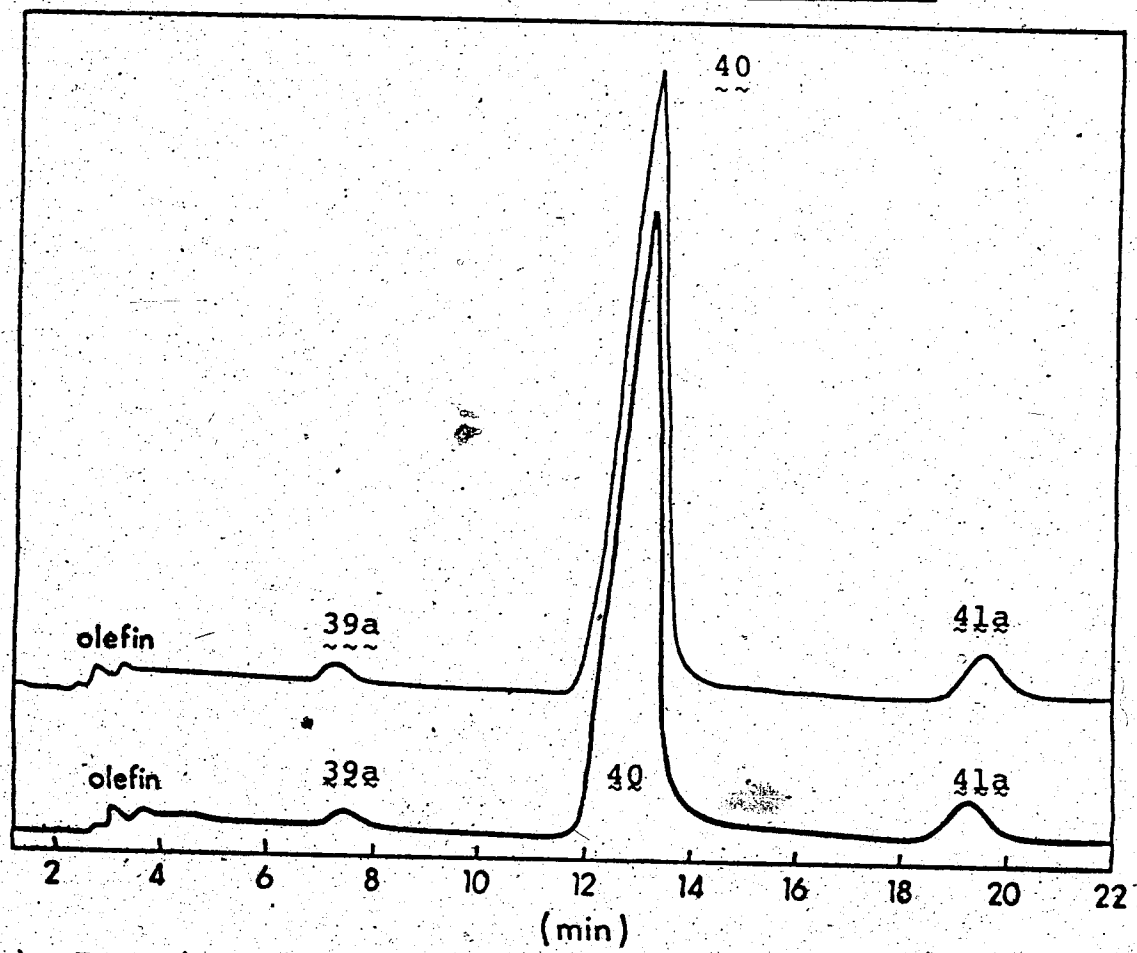
λ, mμ	$[\alpha]_\lambda^{24}$, 38a (Before Reaction)	$[\alpha]_\lambda^{24}$, 38a (After Reaction)	% Racemization
589	+ 7.65°	+ 7.40°	3
578	+ 7.98°	+ 7.63°	4
546	+ 8.97°	+ 8.61°	4
436	+14.83°	+14.45°	3
365	+22.40°	+21.70°	3

elimination of hydrogen bromide (see experimental section). The tertiary bromide, (±)-1-cyano-2-bromo-2-methylbutane, could be synthesized and obtained as a pure material from the reaction of anhydrous hydrogen bromide and a mixture of 1-cyano-2-methyl-1-butene and 1-cyano-2-methyl-2-butene. The product, 40, was found to be unstable and decomposed, giving off hydrogen bromide, upon standing for several days; however, with some care, it was possible to store the pure material.

A synthetic mixture made up of 1.36% of (+)-1-cyano-1-bromo-2-methylbutane, 39a, 6.95% of (+)-1-cyano-3-bromo-2-methylbutane, 41a, and 91.69% of (±)-1-cyano-2-bromo-2-methylbutane, 40, was analyzed by glpc. The chromatogram of the synthetic mixture was identical to that obtained from an analysis of the redistilled fraction obtained from the bromination of the active cyanide 38a (see Fig. 1). A comparison of the rotation obtained for this fraction with that of the synthetic mixture showed them to be identical; the calculated rotation expected from the synthetic mixture was, likewise, found to be identical to that which was observed (see Table VI).

The conditions used to isolate the tertiary bromocyanide 40 were the same as those used to isolate active (-)-1,2-dibromo-2-methylbutane, without racemization [5]. Since the bromination of (+)-1-cyano-2-methylbutane produced minor amounts of two other (+)-

Fig. 1. The Glpc Chromatogram of an Isolated Fraction of 40 from the Bromination (NBS-Br_2) of 38a Compared to the Chromatogram of a Synthetic Mixture of 40 and Added 39a and 41a [a]



a) Reaction Mixture (light line), Synthetic Mixture (heavy line).

Table

Optical Rotation of Product in the Br_2-NBS Bromination of (+)-1-Cyano-2-methylbutane and Synthetic Mixture of Products

λ, mμ	α^{27}_{obs} (Isolated 40)[a]	Synthetic Mixture of[b] 39a, 40, and 41a		
		Observed	α^{26}_{obs}	Calcd.
589	+0.038°	+0.036°		+0.038°
578	+0.039°	+0.039°		+0.040°
546	+0.046°	+0.048°		+0.046°
436	+0.078°	+0.077°		+0.076°
365	+0.120°	+0.122°		+0.120°

[a] The isolated material was contaminated with 1.4% of 39a and 7.0% of 41a (see Fig. 1).

[b] A synthetic mixture of 1.36% 39a, 91.69% 40, and 6.95% 41a. The calculated rotations were obtained using $[\alpha]^t_\lambda$ for 39a and 41a listed in Table IV.

chiral monobromocyanides, which could not be removed by distillation, and since the impurities which contaminated the isolated 1-cyano-2-bromo-2-methylbutane accounted for the entire observed rotation of the reaction mixture; we are forced to the conclusion that, in our hands, the bromination of (+)-1-cyano-2-methylbutane leads to inactive (±)-1-cyano-2-bromo-2-methylbutane.

The observation may not be due to the fundamental nature of the bromination of the substrate at a chiral center, but may very well be due to the instability of this particular tertiary bromide 40.

Photobromination of (+)-2-Methylbutyl Acetate With Bromine-NBS Mixture in Freon 11.

A mixture of (+)-2-methylbutyl acetate, 42, bromine, and NBS (1.3 : 1 : 1.3 mole ratio) in Freon 11 solvent was irradiated in a fashion similar to that used for the bromination of (+)-1-cyano-2-methylbutane, 38a (2 hr, 16°). Glpc analysis of the reaction mixture, after destruction of remaining brominating agent, showed six products other than the starting acetate 42. The analysis of the reaction mixture with a known amount of added o-dichlorobenzene as standard showed 11% conversion of the starting material. The products were fractionated by preparative glpc. The major product (91.0%) was identified as 2-bromo-2-methylbutyl acetate, 43. Its structure was assigned on the basis of its H^1 nmr, ir, and mass spectra. A carbon tetrachloride solution of the bromo acetate, 43, did not rotate plane polarized light (see Table VII). The recovered starting acetate 42 was found not to have racemized during the reaction as can be seen from Table VII.

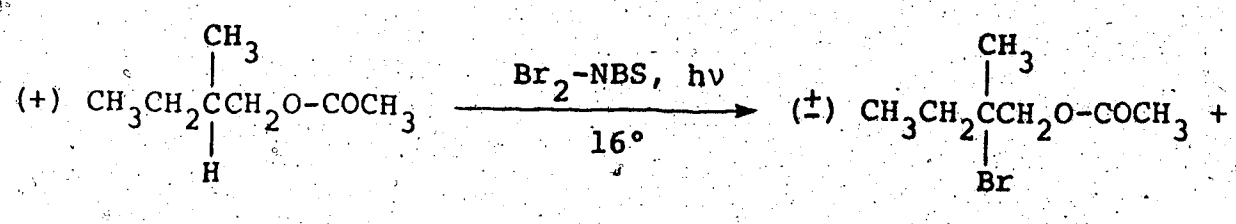
One fraction of the monobrominated product (3.4%) was identified as an equal molar mixture of erythro- and threo-3-bromo-2-methylbutyl acetate, 44a and 44b. Their structural assignments were based on H^1 nmr spectrum (see experimental section) and the mass spectrum. The mass spectrum of the mixture of compounds, 44a and 44b,

Table VII

Specific Rotation of the Product from the Photobromination of (+)-2-Methylbutyl Acetate, 42, (in CCl_4).

λ, mμ	$[\alpha]_\lambda^{25}$ Bromo Acetate 46	$[\alpha]_\lambda^{25}$ Starting Acetate 42	$[\alpha]_\lambda^{25}$ Recovered Acetate 42
589	0	+ 3.79°	+ 3.77°
578	0	+ 3.93°	+ 3.94°
546	0	+ 4.48°	+ 4.48°
436	0	+ 7.61°	+ 7.60°
365	0	+11.99°	+12.03°

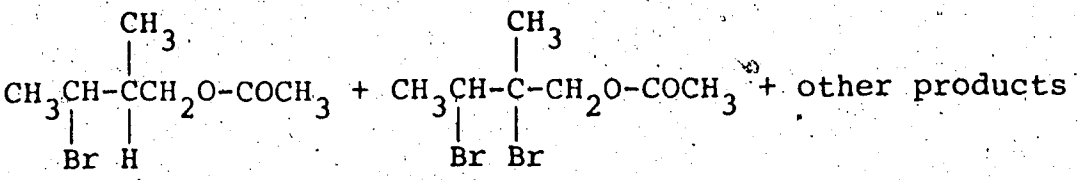
did not show a parent peak, but gave peaks at m/e 193, 195 (P-CH_3, ratio 1:1), 148, 150 (P-HOAc, ratio 1:1), 129 (P-Br), 128 (P-HBr), 70 ($C_5H_{10}^+$), 60 ($HOAc^+$), and 43 (base peak, $CH_3\overset{+}{C}=O$). Two dibrominated acetates were also isolated and their structures were assigned as erythro- and threo-2,3-dibromo-2-methylbutyl acetates, 45a and 45b (1.8%), respectively. The structural assignments were made based upon their H^1 nmr (see experimental section) and mass spectral analysis. The mass spectra of both dibrominated acetates, 45a and 45b, did not give parent peaks, but both isomers showed the same fragments corresponding to P-Br at m/e 207 and 209 (ratio 1:1) and a base peak at 43 ($CH_3\overset{+}{C}=O$). Another two products were detected but were not further characterized; presumably they were monobrominated acetates judging from their glpc retention times.



42

91.0%

43



3.4%

erythro- & threo-

44a & b

1.8%

erythro- & threo-

45a & 45b

The bromoacetate, 43, was examined for enantiomeric purity by obtaining its H^1 nmr spectrum in the presence of an optically active shift reagent, tris-(3-(heptafluoropropylhydroxymethylene)-d-camphorato)-europium (III), (Eu(Opt Shift)$_3$)[77-80]. The H^1 nmr (100 MHz) spectra of compound 43 with shift reagents, Eu(Opt Shift)$_3$ or Eu(fod)$_3$-d_{30}, (tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octadionato)europium(III)), and without shift reagent are listed in Table VIII. As can be seen from Table VIII, when the optically active shift reagent Eu(Opt Shift)$_3$ was used, each set of proton absorptions was split into two sets with equal intensity. Each set of absorptions corresponds to an enantiomer of 43. Compared with the results obtained with the optically active shift reagent, when the inactive Eu(fod)$_3$-d_{30} was added to the nmr sample and the spectrum taken showed a comparable induced downfield shift, but each set of proton

Table VIII

H^1 nmr Spectral Data (100 MHz) of 2-Bromo-2-methylbutyl Acetate, 43, with and without Shift Reagents in $CFCl_3$ Using TMS as Internal Standard at 30°

Shift Reagent	CH_3	CH_2	CH_3 / C / Br	CH_2	$O\text{-}COCH_3$
			δ, ppm		
None	1.05 (t)	1.81 (q)	1.67 (s)	4.17 (s)	2.02 (s)
$Eu(fod)_3$-d_{30} (80 mg)[a]	2.15 (t)	3.78 (m)	3.50 (s)	11.06 (s)	8.76 (s)
$Eu(Opt\ Shift)_3$ (100 mg)[a]	1.98 (t) 2.03 (t)	3.65 (m)	3.30 (s) 3.39 (s)	10.43 (bd)[b]	7.55 (bs)[c]

[a] In 0.5 ml of 0.4 M compound 43/Freon 11/TMS solution.

[b] Peak broaden and slightly split

[c] Broad singlet

absorptions remained unsplit. These results which are in agreement with the polarimetry measurement demonstrate that the bromo acetate 43 obtained from the bromination of optically active (+)-2-methylbutyl acetate was completely racemic.

The absence of racemization of the recovered starting acetate suggested that reversal of the abstraction reaction was not important under the conditions employed in this reaction. At low conversion (11%) of the starting material, the small amount of hydrogen bromide produced was scavenged by the large excess of NBS present in the reaction, thereby limiting the reversal process. In the case of molecular bromine bromination [5], it has been shown that the recovered starting acetate was extensively racemized (44%). The racemization demonstrated the importance of the reversal of the tertiary radical when it is formed in the presence of hydrogen bromide. Evidently, 2-bromo-2-methylbutyl acetate 43 was not observed in the molecular bromine bromination [5] because of the rapid decomposition of the bromoacetate, 43, by an acid catalyzed reaction. Under these reaction conditions, in the absence of hydrogen bromide, bromo acetate 43 was obtained as a major product (91%), however, at the expense of its enantiomeric integrity.

Mechanistic Prediction on Photobromination of (-)-(R)-2-Bromobutane.

An understanding of the mechanism of the photobromination of an alkyl bromide requires a knowledge of the structures of the intermediate radicals involved. At present there is no unequivocal piece of chemical or spectroscopic evidence which indicates that a β-bromoalkyl radical prefers a "bromine-bridged" structure rather than a "classical" structure. In the cases where such evidence has been claimed, alternate explanations can be proposed to rationalize the observed results. The bromination of optically active (-)-(R)-2-bromobutane was chosen for this investigation since it provides one of the best diagnostic tests for the bromination mechanism. The experiments were designed to distinguish between a "Classical Radical Mechanism" and a "Bromine-Bridged Radical Mechanism". Similarly, isotopically enriched bromine-81 bromination provides the distinction between a reaction involving direct substitution and one leading to racemization by an elimination-readdition reaction.

Classical Radical Mechanism (Scheme II). -- A mechanistic scheme which proceeds by an open radical predicts that photobromination of (-)-(R)-2-bromobutane would produce optically active (2R,3R)-dibromobutane and inactive meso-(2R,3S)-dibromobutane. The product

dibromides would be formed with an absence of excess incorporation of bromine-81.

Bromine-Bridged Radical Mechanism (Scheme III). -- This mechanism predicts the formation of both inactive dl-2,3-dibromobutane (equal amount of (2R,3R)- and (2S,3S)-dibromobutane) as well as meso-(2R,3S)-dibromobutane with no excess incorporation of bromine-81. Since the bridged radical intermediate that produced (2R,3R)- and (2S,3S)-dibromobutane has a plane of symmetry, the enantiomeric pair will be formed in equal quantities. Although the bridged radical that should lead to meso-2,3-dibromobutane is dissymmetric, the product contained a plane of symmetry and must be inactive. Thus both bridged radical intermediates should lead to optically inactive products.

Elimination-Readdition Mechanism (Scheme IV). -- This mechanism predicts that the dl-2,3-dibromobutane that is formed should be inactive; furthermore the vicinal dibromides (meso-2,3-, dl-2,3-, and 1,2-dibromobutanes) should be enriched in bromine-81 in the bromination of 2-bromobutane with isotopically enriched molecular bromine-81. The hydrogen bromide that was formed during the reaction should be enriched in bromine-79.

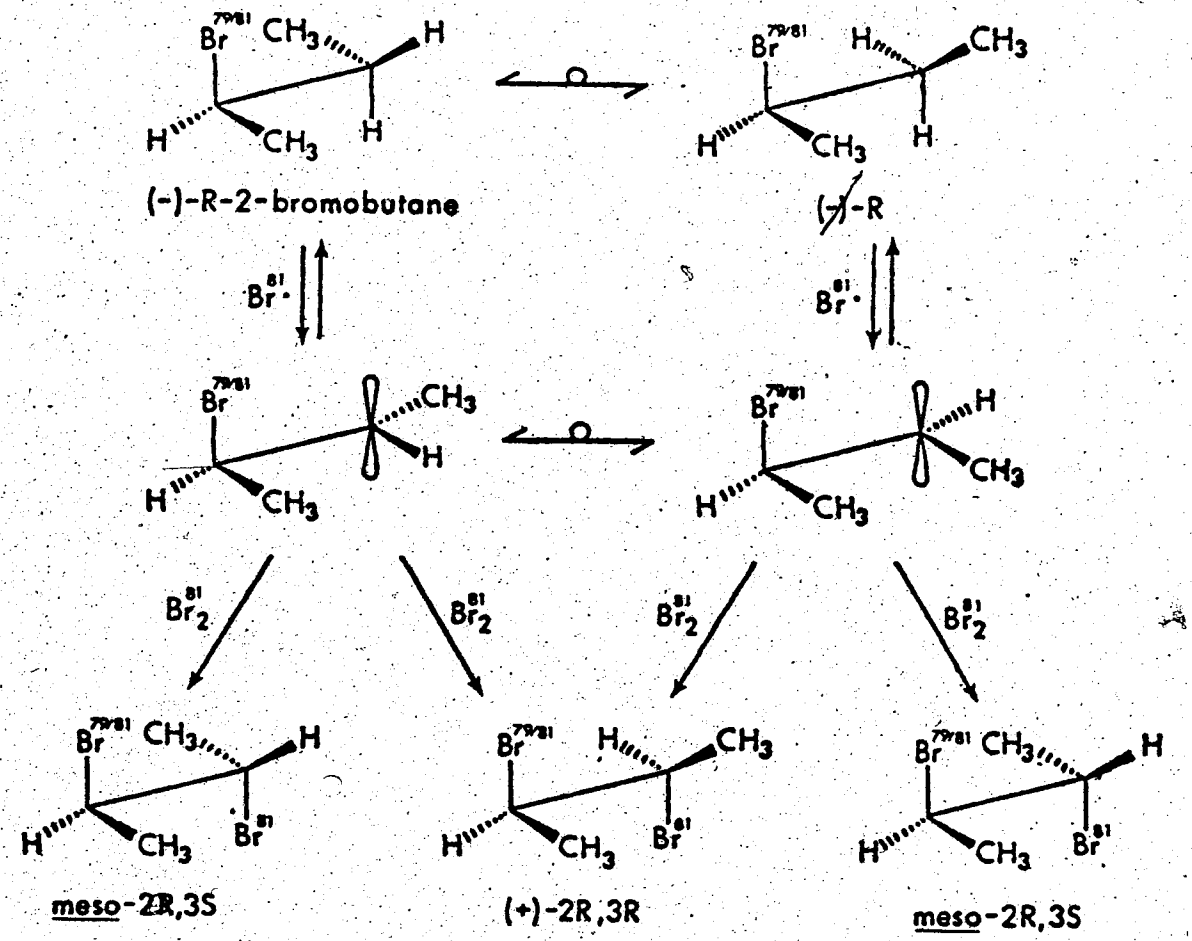
Direct substitution, i.e. of a bromine-bridged radical (Scheme III) or an open radical (Scheme II), will lead to a statistical distribution of bromine content in

the dibromides. When 2-bromobutane (50.57% bromine-79 and 49.43% bromine-81) and isotopically enriched molecular bromine-81 (2.19% bromine-79 and 97.81% bromine-81) are used in the bromination, the dibromides produced by direct substitution are calculated to contain 26.38% bromine-79 and 73.62% bromine-81 with a peak height ratio at the parent peaks: 214: 216 : 218 = 1: 45.6 : 43.7 (see Appendix).

If the dibromides, 2,2-dibromobutane (8%) and 2,3-dibromobutanes (92%), were the only products formed, and if the 2,3-dibromobutanes were formed solely from the elimination-readdition mechanism (see Scheme IV), their bromine content can be calculated by simulating the reaction stepwise. It was assumed that 92% of the attack by bromine atom was at the 3-position, and that this was constant throughout the reaction. The 3-bromo-2-butyl radicals so formed would eliminate a bromine atom which scrambles with the bromine pool prior to any other reaction (see Appendix). The bromine from the new bromine pool was then added to 2-butenes to give 2,3-dibromobutanes. The calculation predicted that the 2,3-dibromobutanes would contain 13.5% bromine-79 and 86.5 % bromine-81 with the intensities of the parent peaks in the ratio of 214 : 216 : 218 = 1 : 12.8 : 41.1 , while the 2,2-dibromobutane would contain 32.0 % bromine-79 and 68.0 % bromine-81 with a ratio of 214 : 216 : 218 = 1 : 7.39 : 6.26.

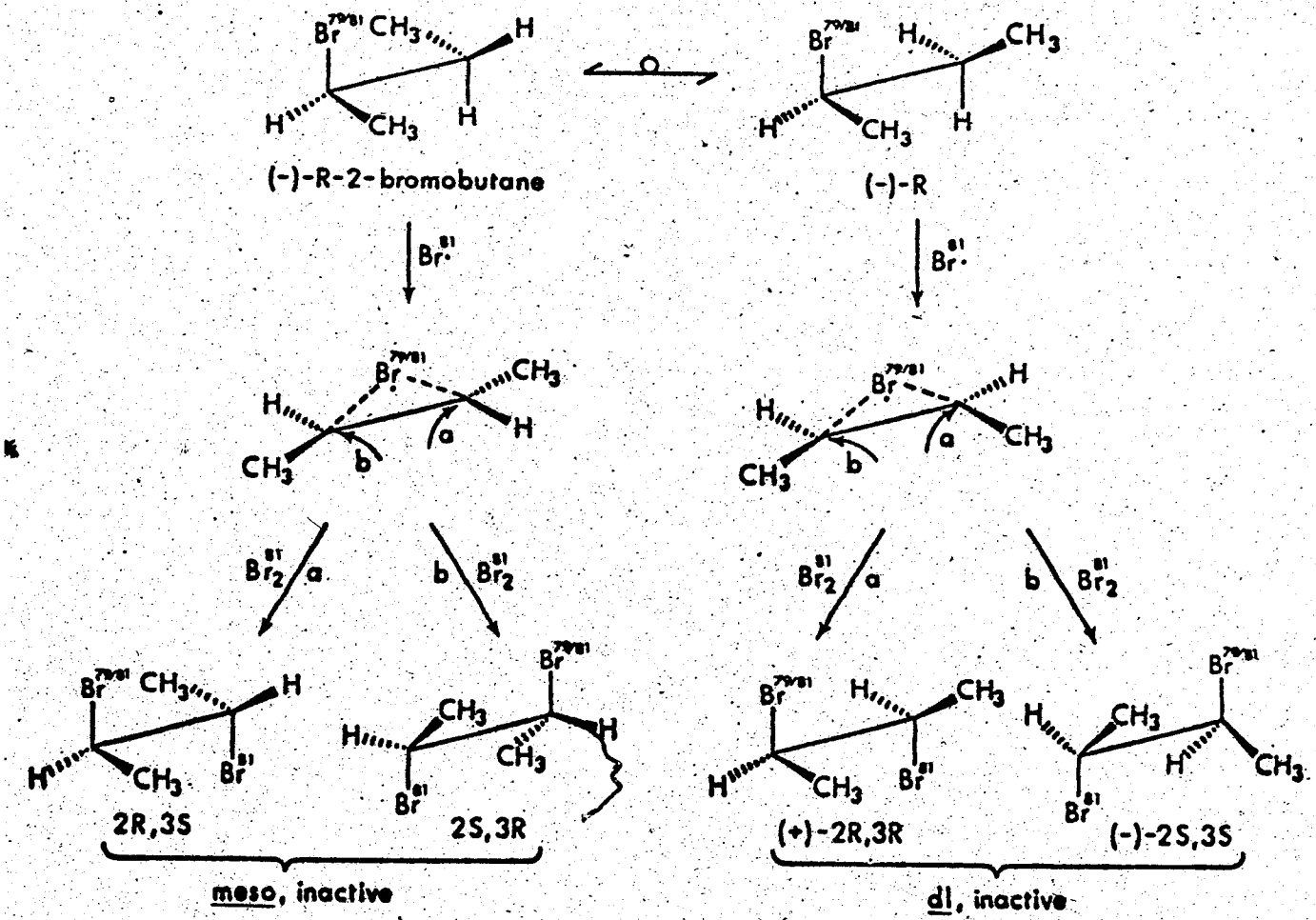
Scheme II

Classical Radical Mechanism



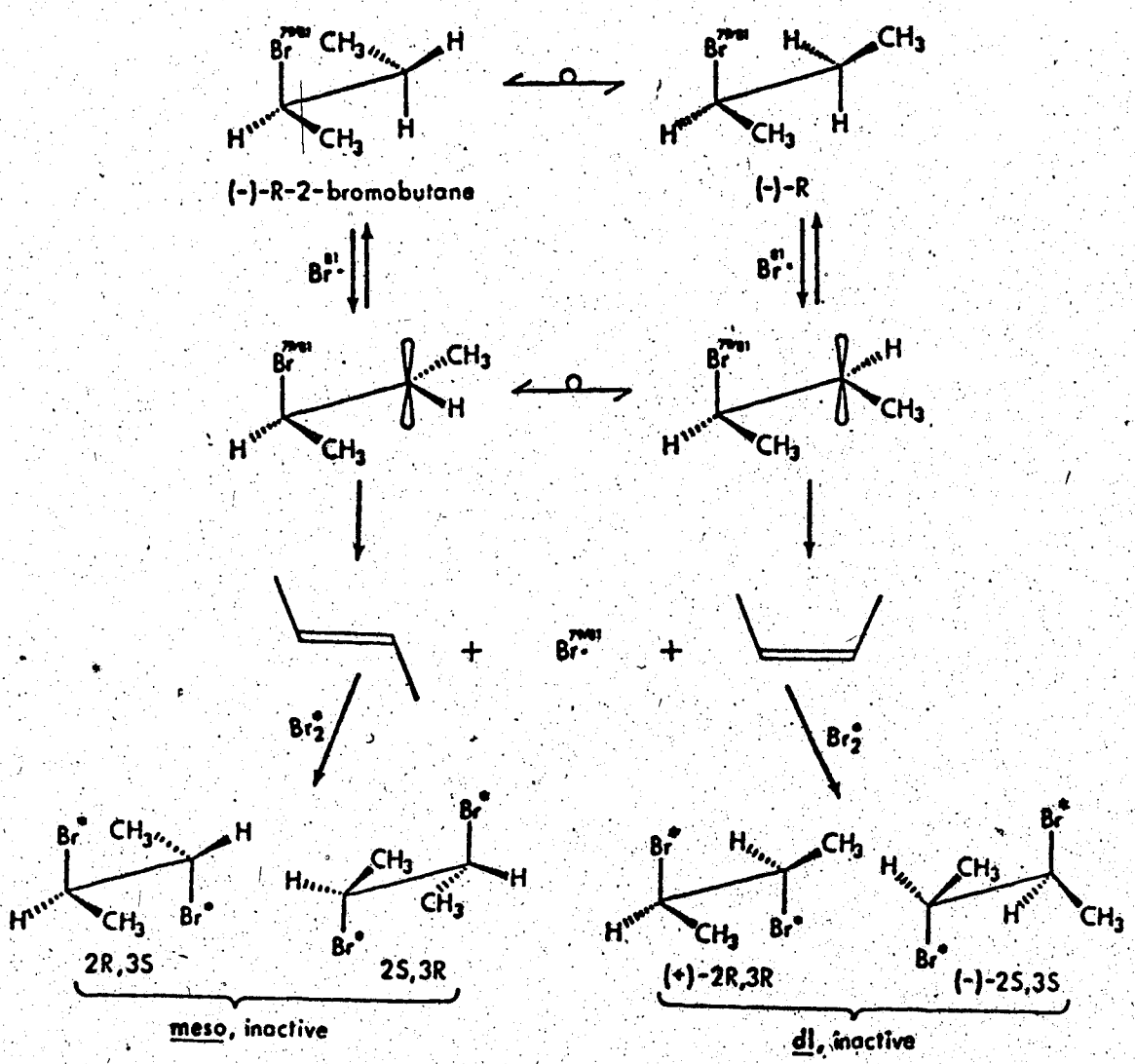
Scheme III

Bromine-Bridged Radical Mechanism



Scheme IV

Elimination-Readdition Mechanism



Br_2^*: Scrambled bromine pool.

Photobromination of (-)-(R)-2-Bromobutane with Molecular Bromine.

The photobrominations of (-)-(R)-2-bromobutane with varying concentrations of molecular bromine were carried out in degassed and sealed Pyrex reaction ampoules. In most cases, the reactions were run to completion. After the reaction, an internal standard was quantitatively added and the reaction mixture diluted with Freon 11. The mixture was then freed from excess bromine and hydrogen bromide by washing with ice-cold aqueous sodium bisulfite, water, and aqueous sodium bicarbonate. The reaction mixture was dried and then subjected to glpc analysis. The analysis showed the presence of five products as well as the unbrominated (-)-(R)-2-bromobutane. The products were isolated by preparative glpc and identified as 2,2-dibromobutane, meso-2,3-dibromobutane, dl-2,3-dibromobutane, 1,2-dibromobutane, and 2,2,3-tribromobutane by comparison of the ir, nmr, and mass spectra with those of authentic materials. The product distribution is listed in Table IX. The unbrominated 2-bromobutane, 2,3-dibromobutane (dl-fraction), and 2,2,3-tribromobutane were subjected to polarimetric measurement in order to determine their optical rotations. The results are given in Table X. In all cases, the material balance for the reactions ranged from 97-103% based on starting

Table IX

Photobromination of (-)-2-Bromobutane with Molecular Bromine[a]

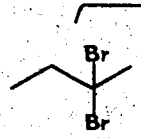
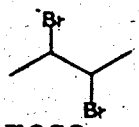
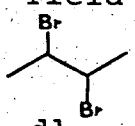
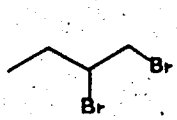
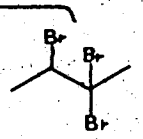
Reaction	RBr:Br_2 ($[Br_2]$)	Temp. °C	% Yield[b] 	 meso	 dl		
1	15 : 1 (0.6M)[c]	30	10.7	61.5	25.3	--	tr
2	6 : 1 (1.4M)[c]	30	10.2	60.0	26.1	--	3.4
3	4 : 1 (2.0M)[c]	30	10.7	57.6	24.7	--	7.0
4	3.9: 1 (2.0M)[c]	20	9.8±0.1	58.0±0.2	26.1±0.3	tr	6.1±1.2
5	3.6: 1 (2.2M)[c]	20	9.4±0.2	54.8±0.5	25.4±0.1	tr	10.4±0.3
6	3 : 1 (2.6M)[c]	17 (3)[d]	7.3±0.3	55.9±2.3	25.5±0.8	1.9±0.4	9.5±2.5
7	2 : 1 (3.6M)[e]	17	9.0±0.3	57.2±0.3	27.1±0.3	2.0±0.2	4.7±0.3
8	2 : 1 (3.6M)[f]	5	5.6±0.2	61.2±0.1	29.3±0.1	1.5±0.1	2.4±0.2
9	1 : 1 (5.7M)[g]	-20	3.0±0.1	57.7±0.3	24.5±0.2	2.2±0.1	12.7±0.3

Table continued on next page

Table IX continued

[a] Reactions 1-3 are taken from Ref. 81.

[b] The errors indicated are average deviations from the mean.

[c] To complete reaction of bromine.

[d] Average of three independent experiments.

[e] At 30% conversion of starting material.

[f] At 10% conversion of starting material.

[g] At 46% conversion of starting material.

Table X

Optical Rotation of Products from the Molecular Bromine Bromination of (-)-(R)-2-Bromobutane

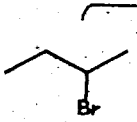
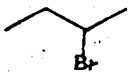
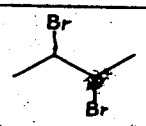
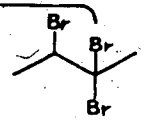
Reaction	RBr:Br_2 Mole ratio	($[Br_2]$)	$[\alpha]^{25}_{365}$  Before	(O.P.)	 After	% Rac.	 Obs.	Corr[c]	 Obs.
1	3 : 1	(2.6M)[d]	-69.16°	(53.6%)	-60.44°	12.6%	+2.83°	+5.28°	+1.65°
2	3 : 1	(2.6M)[d]	-68.91°	(53.4%)	-62.70°	9.0%	+2.83°	+5.30°	+1.91°
3	3 : 1	(2.6M)[d]	-76.00°	(58.9%)	-68.36°	10.1%	+3.49°	+5.93°	+1.79°
4	2 : 1	(3.6M)[e]	-68.91°	(53.4%)	-67.92°	1.5%	+2.74°	+5.13°	+1.15°
5	2 : 1	(3.6M)[f]	-76.00°	(58.9%)	-73.71°	3.0%	+2.96°	+5.02°	--
6	1 : 1	(5.6M)[g]	-76.00°	(58.9%)	-62.31°	18.0%	+1.75°	+2.97°	--
7	3 : 1	(2.6M)[h]	-76.00°	(58.9%)	-76.01°	0	--	--	--
8	3 : 1	(2.6M)[i]	-76.00°	(58.9%)	-75.73°	0.4%	--	--	--

Table continued on next page

Table X continued

[a] All the rotations are measured in CCl_4 solvent except for starting material (measured as neat liquid).

[b] Optical purity (O.P.) based on maximum reported value $[\alpha]_D = 39.4°$ (Ref. 82).

[c] Corrected for optical purity of starting material.

[d] To complete reaction of bromine.

[e] At 30% conversion of starting material.

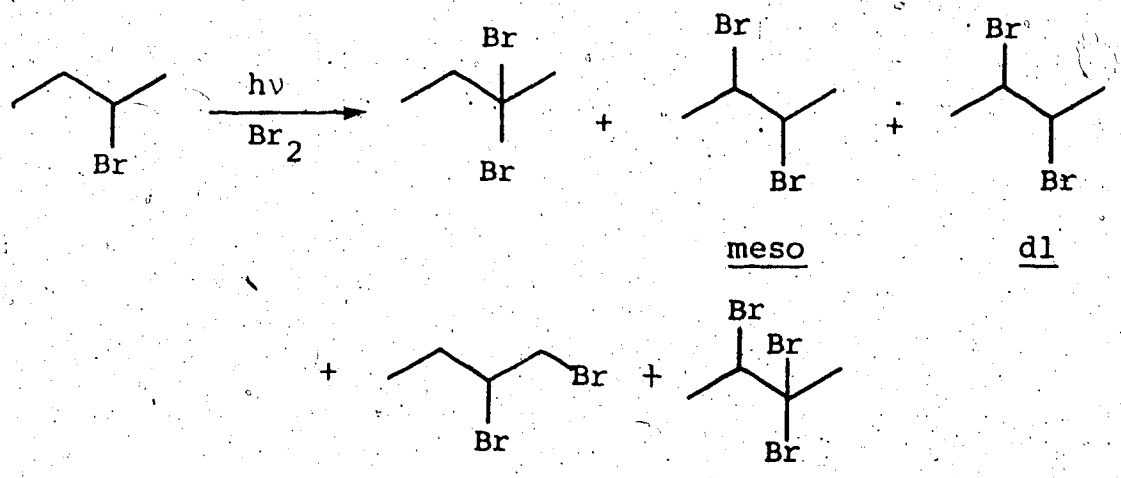
[f] At 10% conversion of starting material.

[g] At 46% conversion of starting material and at -20°.

[h] Dark reaction under photoinitiated reaction conditions.

[i] Dark reaction with added hydrogen bromide ($RBr:Br_2:HBr$ = 3 : 1 : 1) under photoinitiated reaction conditions.

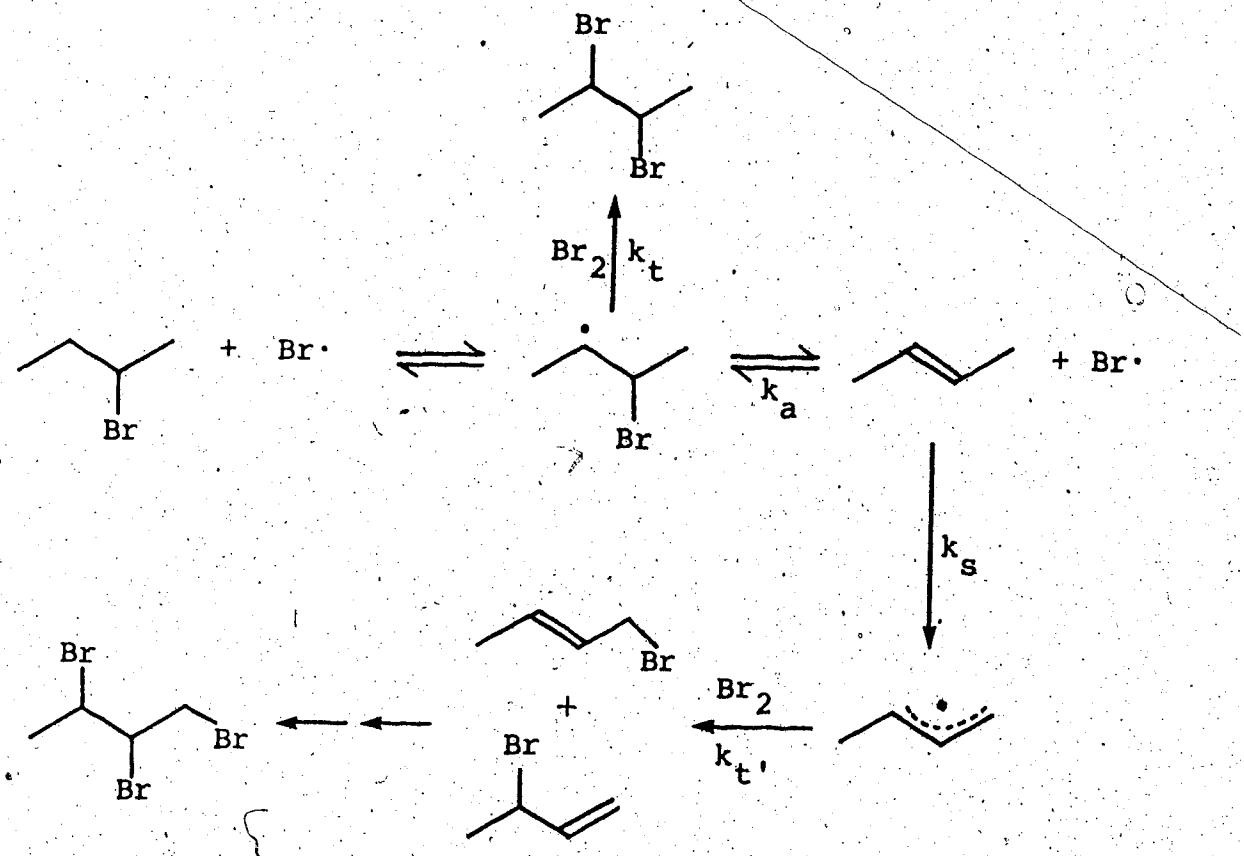
material and on bromine consumed.



The product distributions listed in Table IX are similar to those previously reported for liquid phase [73] and the vapor phase [74] brominations of 2-bromobutane. Thaler [73] investigated the liquid phase bromination (60°) and found only three products: 2,2-dibromobutane (16.3%), meso-2,3-dibromobutane (58.3%), and dl-2,3-dibromobutane (25.4%). Tedder et al. [75] reported that almost a 100% yield of 2,2-dibromobutane was found in the gas phase reaction at 146° (fast flow system). Kharasch et al. [74] observed five products in their vapor phase bromination at 100°. The isolated products were shown to be 2,2-dibromobutane (19%), meso-2,3-dibromobutane (22%), dl-2,3-dibromobutane (10%), tribromobutane (34%, very rich in 1,2,3-tribromobutane), and 1,2,3,4-tetrabromobutane (6%).

In this work, 2,2,3-tribromobutane was always observed, even at low conversion (10%) of starting material (see Table IX, reaction 8). Compared with the vapor phase bromination reported by Kharasch et al.[74], the tribromide formed in liquid phase bromination is 2,2,3-tribromobutane not 1,2,3-tribromobutane. A possible route to 1,2,3-tribromobutane as a major tribromide of the 2-bromobutane vapor phase bromination could be via allylic bromination of 2-butene, formed by elimination of a bromine atom from the 3-bromo-2-butyl radical as shown in Scheme V.

Scheme V



In this scheme, the 3-bromo-2-butyl radicals are either trapped by molecular bromine or hydrogen bromide or eliminate bromine atom to give 2-butenes. The alkenes may add bromine to give meso- and dl-2,3-dibromobutanes or be allylically brominated to give a mixture of 1-bromo-2-butene and 3-bromo-1-butene. 1,2,3-Tribromobutane is then formed by addition of bromine to these allylic bromides.

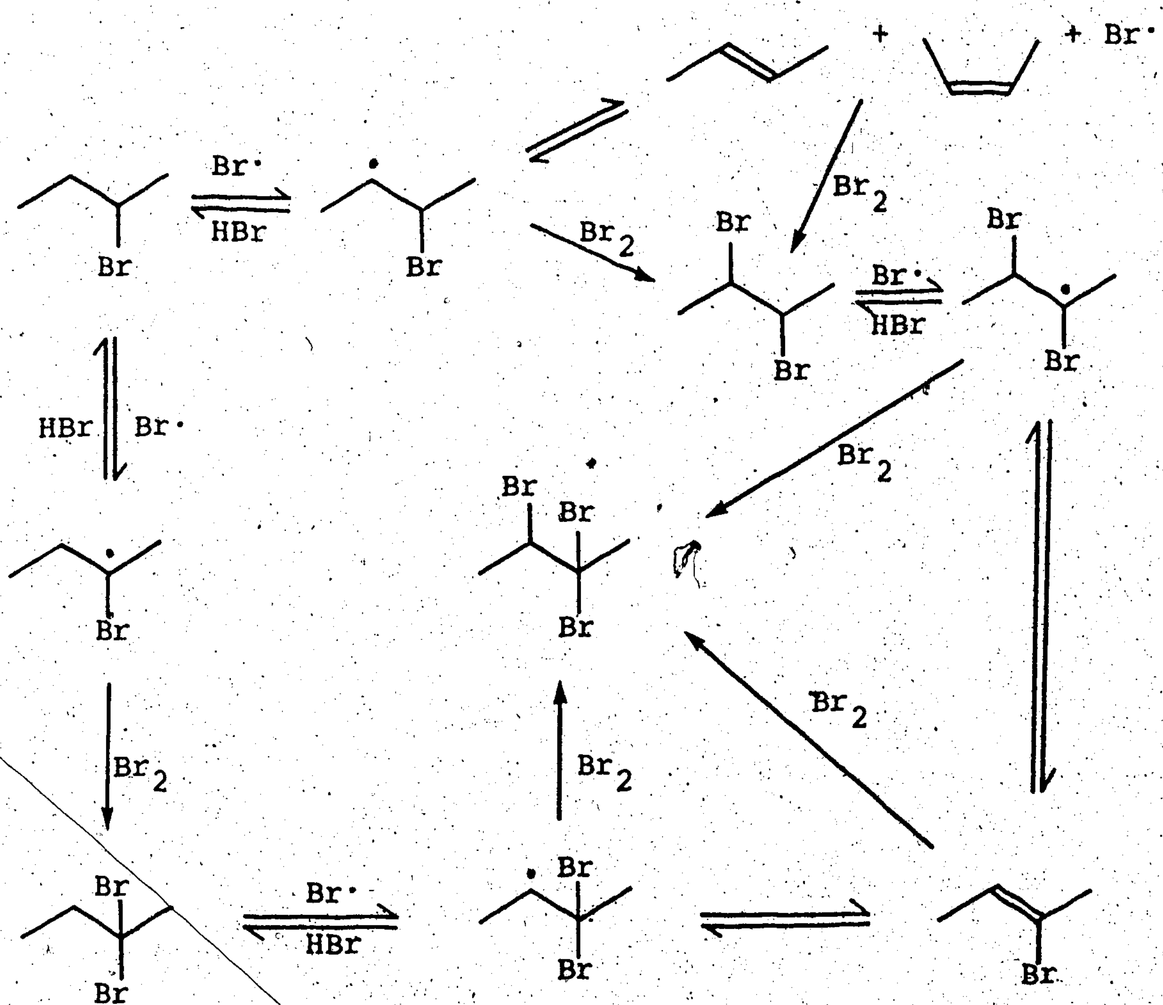
There are numerous precedents for elimination from β-bromoalkyl radicals [3,47-52,73]. This elimination process is also responsible for the rapid isomerization of trans- and cis-alkenes by bromine [1,3,83-86]. Also, it is well known that allylic bromides are formed in high yields in the bromination of alkenes when the bromine concentration is kept low; this is, after all, the reason for allylic bromination of alkene by N-bromosuccinimide, where the NBS serves as a source of a low, steady state concentration of bromine [83]. It was also shown by Sixma and Riem [87] and McGrath and Tedder [84] independently that in the liquid phase photobromination of cyclohexene, 3-bromocyclohexene was formed in 80% yield when the gaseous bromine was slowly introduced into the refluxing carbon tetrachloride solution in a stream of nitrogen.

The preferential allylic bromination of alkene is, of course, dependent on the rate constant for bromine atom attack at the allylic position (k_s) compared to the

rate constant for addition to the alkene (k_a). However, under the reaction conditions of high temperature and low bromine concentration, allylic substitution will be favored at the expense of addition, since addition is highly reversible [3,83-85]. The formation of the allylic radical is not appreciably reversible [3], however, and thus the allylic radical survives to react with molecular bromine, even if the latter is present in low concentrations, and allylic bromide is formed rather than dibromide. Since 1,2,3-tribromobutane was produced in the vapor phase bromination of 2-bromobutane, presumably the allylic bromide ionically added bromine in the condensed phase to produce the tribromide [74].

The production of 2,2,3-tribromobutane in the liquid phase bromination is the result of the bromination of several of the product dibromides (see Scheme VI). The polar addition of bromine to simple olefins is a rapid process in liquid phase, and will be an important competitor to the radical process. Furthermore, the usual bromine concentrations in solution phase reactions are much higher than for the vapor phase reactions; therefore, it is expected that any olefin produced will add bromine rapidly to give the addition product. Several pieces of evidence showed that this is true. At a high ratio of $[RBr]/[Br_2]$ (15:1), very little 2,2,3-tribromobutane was found, even though at this low bromine concentration,

Scheme VI



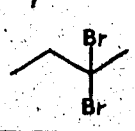
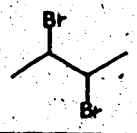
the elimination process is favored, the polar addition of bromine is preferred. Furthermore, elimination-re-addition process must give inactive product whereas the 2,2,3-tribromobutane formed is optically active (see Table X). Therefore it appears that the bromination process is not proceeding exclusively by an elimination-

readdition mechanism.

The liquid phase bromination of 2-bromobutane at high temperatures gives progressively increasing yield of 2,2-dibromobutane with increasing temperature (see Table XI). This result can be accommodated by a reaction scheme where there are two competing reactions for the formation of 2,2-dibromobutane (k_{22}) and for 2,3-dibromobutane (k_{23}) with different activation energies ($E_{22}>E_{23}$) and at lower temperature with $k_{23}>k_{22}$. As the temperature is raised, k_{22} increases faster than k_{23}, thereby increasing the concentration of 2-bromo-2-butyl radical available for the 2,2-dibromobutane formation of subsequent reaction with molecular bromine. Over the range of temperature from 0° to 100°, when a plot is made of the absolute yield of 2,2-dibromobutane as a function of temperature ($Y = mT + c$), a straight line was obtained with a correlation coefficient of 0.994 ($m = 0.1747$ and $c = 4.826$) (see Fig. 2). If the rate of formation of 2,2-dibromobutane in the liquid phase reaction is assumed to be the same as in the vapor phase reaction, then the plot (extrapolated to 146°) shows that only a 30% yield of 2,2-dibromobutane would be obtained in both of the liquid phase and the vapor phase reactions at this temperature. However, this is contrary to the results as the formation of almost 100% of 2,2-dibromobutane has been reported[75]. A preliminary investigation of the vapor phase reaction

Table XI

Photobromination of 2-Bromobutane with Molecular Bromine with Varying Temperature (liquid phase reaction)

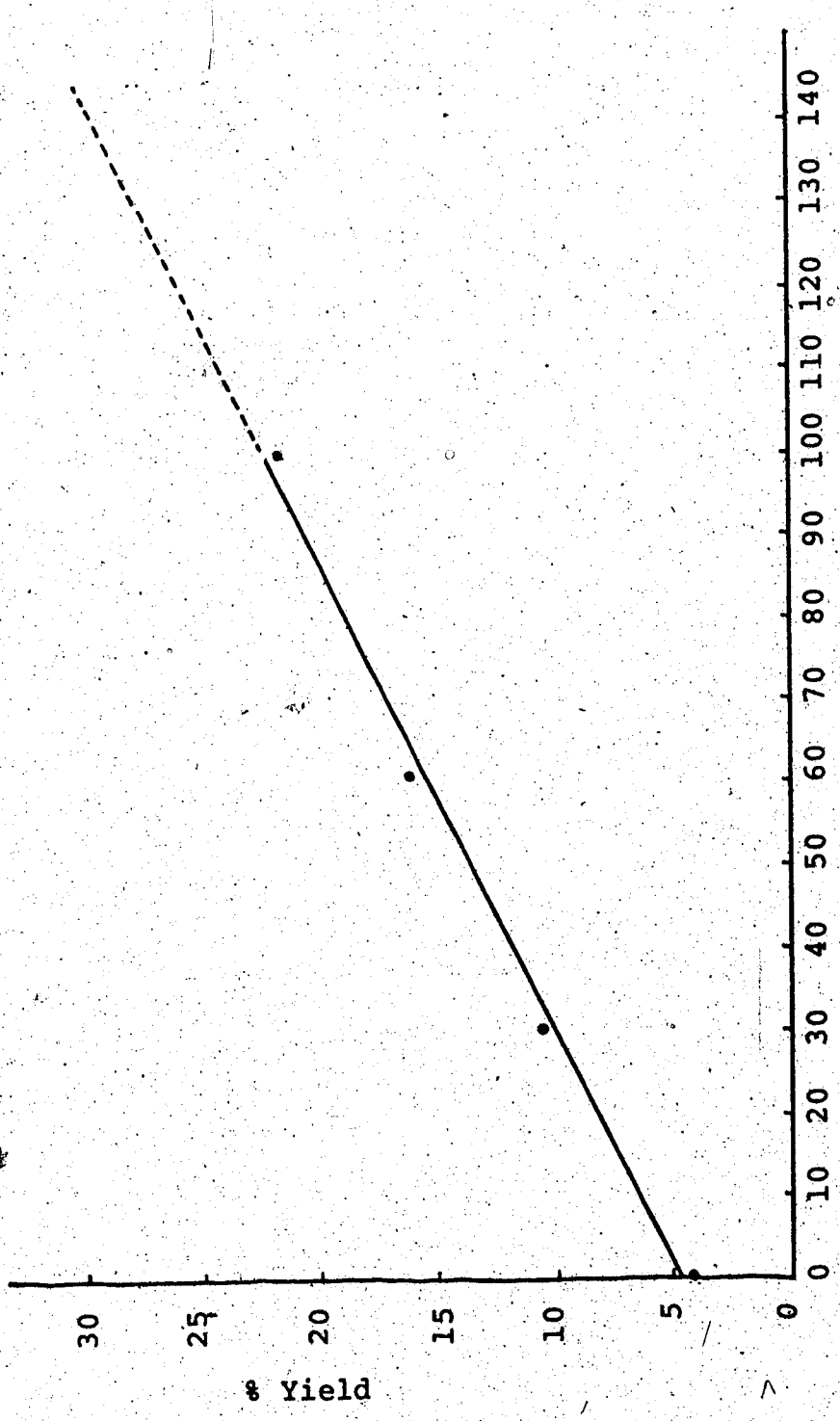
Reaction	Temp., °C	% Yield[a] 	meso 	dl
1	0	4.4±0.1	57.5±0.1	26.2±0.1
2	17	7.3±0.3	55.9±2.3	25.5±0.8
3	30[b]	10.7	57.6	24.7
4	60[c]	16.3	58.3	25.4
5	100	21.6±0.1	45.5±0.2	25.4±0.2

[a] Absolute yield (mole %) based on bromine consumed. The errors indicated are the average deviations from the mean.

[b] Taken from Ref. 81.

[c] Taken from Ref. 73.

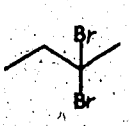
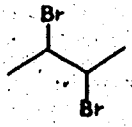
Fig. 2. Absolute yield curve of 2,2-dibromobutane as a function of temperature in liquid phase photobromination.



showed that a multitude of products is formed with a poor material balance of the dibromides formed (at elevated temperature, see Table XII) [86]. A likely explanation for this observation is attributed to the considerable instability of the β-bromoalkyl radicals under reaction conditions. Dissociation of β-bromoalkyl radical intermediates to an olefin and bromine atom are followed by subsequent preferential bromination of the olefin allylically, and then by subsequent addition of bromine to give polybromides. This process became extremely important in the vapor phase reaction. As can be seen from the results listed in Table XII, the material balance of the observed dibromides (2,2-, meso- and dl-2,3-dibromobutanes) decreases with increasing reaction temperature (from 93% at 20° to 27% at 146°). It appears that the yield of 2,2-dibromobutane was not significantly affected by increasing the reaction temperature in the vapor phase reaction. In opposition to the observation, the yields of the 2,3-dibromobutanes were substantially depressed by increasing the temperature (from 71% at 20° to 5% at 146°). Furthermore, glpc analysis of the vapor phase reaction mixture showed presence of 1-bromo-2-butene and 1,4-dibromo-2-butene (allylic bromination products) by the comparison of the glpc retention times with those of the authentic materials. One polybrominated product, with a glpc retention time similar to that of 1,2,3-tribromo-

Table XII

Vapor Phase Bromination of 2-Bromobutane[a]

Reactions #	Temp. °C	% Yield[b,c]  meso	 dl	% Yield of Dibromides
1	20	21.6±0.2	52.7±1.0	18.5±0.3	92.8±1.4
2	60	25.6±0.5	30.1±0.5	10.7±0.2	66.4±1.0
3	100	21.5±0.4	10.9±1.0	4.3±0.5	36.7±1.5
4	146	22.0±0.4	3.5±0.4	1.5±0.3	27.0±0.8

[a] 2-Bromobutane (19.93×10^{-5} mole) : Br_2 (6.44×10^{-5} mole).

[b] Absolute yield (mole %) based on bromine consumed.

[c] The errors indicated are deviations from duplicate run.

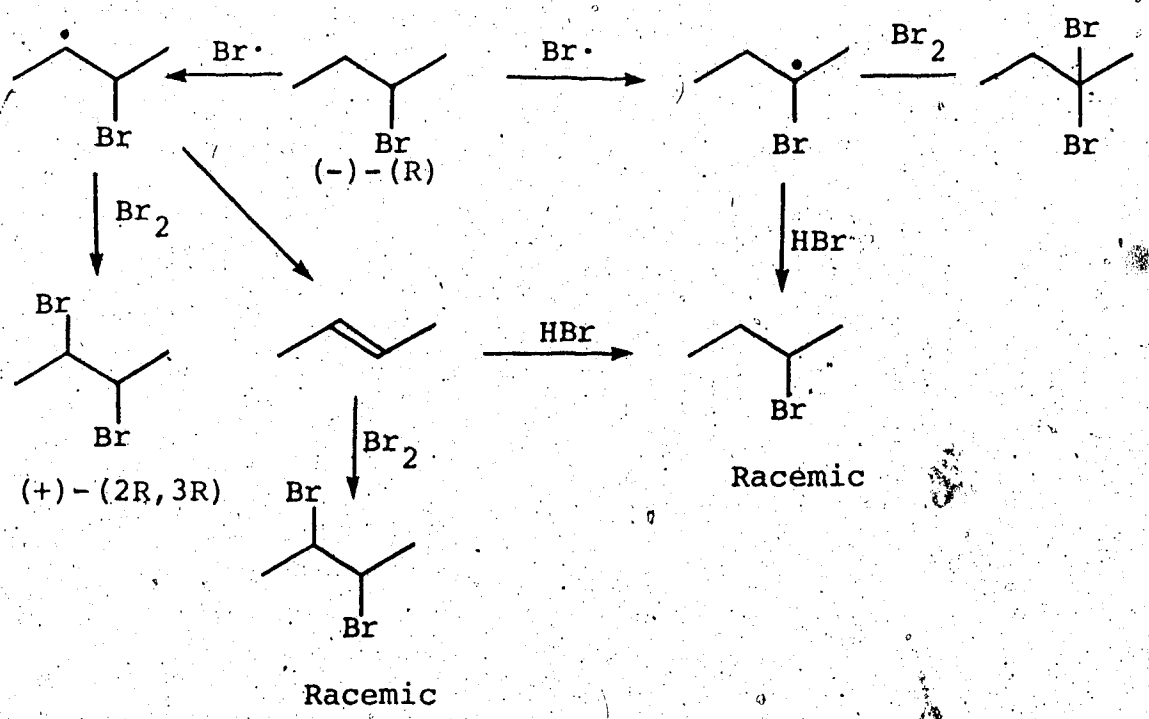
butane, was also detected. These observations strongly suggest that the previously observed 100% yield of 2,2-dibromobutane in the vapor phase bromination at 146° may very well be due to the loss of the polybrominated products under the reported reaction conditions [75].

The unbrominated starting (-)-(R)-2-bromobutane that was recovered was found to have racemized about 10% (see Table X, reaction 1-3). The racemization can not be related to an ionic reaction. The validity of this observation was verified by subjecting the starting (-)-(R)-2-bromobutane to the reaction conditions in the presence of molecular bromine or of molecular bromine and hydrogen bromide, and isolation procedures in the absence of photoinitiation, thereby confirming that the racemization takes place during the reaction (see Table X, reaction 7-8).

The observed racemization of the starting material can be rationalized by involving a transfer reaction between 2-bromo-2-butyl radicals and hydrogen bromide or by the elimination-readdition reaction shown in Scheme VII. Both of these processes lead to racemic 2-bromobutane. Since it is apparent that the reversible abstraction reaction with hydrogen bromide [3,88] is competitive with the transfer reactions with molecular bromine, this hydrogen transfer reaction should be minimized by carrying out the reaction in an NBS-Br_2

mixture or in a high concentration of molecular bromine. As can be seen from the results listed in Table XV (reaction 1-4, see page 82), when the brominations were run in the presence of an NBS-Br_2 mixture, the racemization

Scheme VII

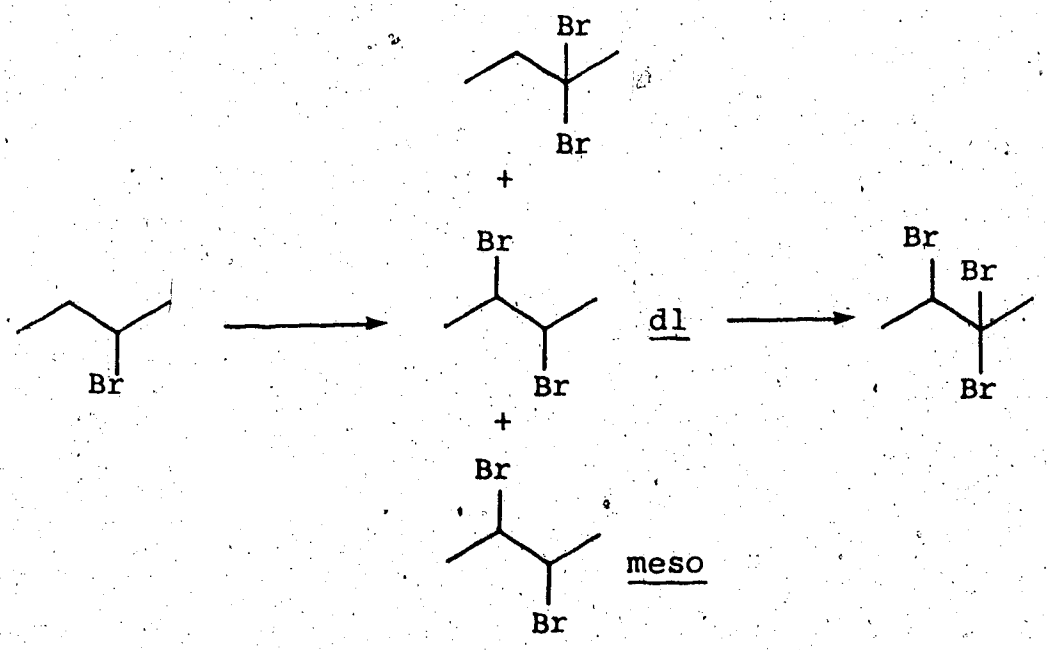


of starting material was reduced from 10% to 1-2%. It is known that, as the reaction proceeded, hydrogen bromide was produced which on reaction with the large excess of NBS present in the reaction yielded succinimide and molecular bromine. This procedure minimized the presence of hydrogen bromide in the reaction mixture. When the

reaction was run using 2:1 ($RBr:Br_2$) ratio and stopped at about 30% conversion of the starting material (this is essentially the same as using 3:1 ratio to complete reaction of bromine), the results indicated that only 1.5% racemization of starting bromide was observed (see Table X, reaction 4). These two results indicate that hydrogen bromide is involved in the racemization of 2-bromobutane during the reaction. This may be due to the reversal of the 2-bromo-2-butyl radicals with hydrogen bromide or due to the addition of hydrogen bromide to 2-butenes formed by elimination of a bromine atom from the 3-bromo-2-butyl radical (see Scheme VII). The results give no indication of the relative importance of these two pathways, however, when 2-bromobutane was brominated with isotopically enriched molecular bromine-81, the recovered starting material had incorporated a substantial amount of bromine-81 (see page 84). This indicates that the elimination-readdition mechanism must be taking place to a significant extent producing racemized 2-bromobutane.

In all the reactions, the isolated dl-2,3-dibromobutane fraction was optically active and was dextrorotatory. The measured rotations were found to be $[\alpha]^{25}_{365}$ = +5° to +6° in carbon tetrachloride solution (see Table X, reaction 1-5). Furthermore, the tribromide, 2,2,3-tribromobutane, which can be produced from the subsequent bromination of either 2,2-dibromobutane, meso-,

or dl-2,3-dibromobutane, was found also optically active (see Table X, reaction 1-4). In the present case, only one of the precursors of the tribromide, dl-2,3-dibromobutane, does not have a plane of symmetry, therefore, the optical activity of (+)-2,2,3-tribromobutane must come from the bromination of optically active (+)-2,3-dibromobutane. The optical rotation of the (+)-2,2,3-tribromobutane, therefore, must be greater than the observed value listed



in Table X. The retained activity in the 2,3-dibromobutane (dl-fraction) and 2,2,3-tribromobutane strongly demonstrated that the radical intermediate initially formed in the reaction is the classical 3-bromo-2-butyl radical, since it can be trapped as a classical unsymmetrical

structure to give optically active dibromide. The formation of the optically active (+)-2,3-dibromobutane can therefore be rationalized by Scheme II (classical radical mechanism). The configuration of this dibromide may, therefore, be unequivocally assigned as (2R,3R)-configuration according to this mechanism, since the assymetric center of (-)-(R)-2-bromobutane remains untouched in the bromination process. Similarly, (+)-2,2,3-tribromobutane, derived from (+)-(2R,3R)-dibromobutane, should ~~have~~ the (R)-configuration. The optical purity of these two products were not known, since the preparations of these two compounds (optically pure) have not been reported. However, Skell et al. [7] recently reported that the optically pure (+)-2,3-dibromobutane has a rotation of $[\alpha]_{365} = +100°$. Their estimation of the rotation was obtained by differential scanning calorimetric measurement of the enantiomeric purity of the partially resolved (+)-2,3-dibromobutane. Its configuration has been assigned as (2R,3R), since (-)-2,3-dibromobutane has been synthesized from the reaction of (+)-(3S)-bromobutane-(2R)-ol with triphenylphosphine and bromine and was on this basis assigned the configuration of (-)-(2S,3S) [7].

From a calculation based on Brewster's method, but using the known nmr data for the population of the three

rotamers [89] of dl-2,3-dibromobutane*, Berti and Marsili [90] were able to calculate the sign of the rotation of (2R,3R)-dibromobutane. This prediction also showed that the (2R,3R)-enantiomer should be dextrorotatory with a molar rotation in the order of $[M]_D = +110°$, in agreement with the configuration predicted by the classical radical mechanism (Scheme II) and the experimentally observed positive rotation. Furthermore, in support of the (2R,3R)-configuration for (+)-2,3-dibromobutane, (2R,3R)-dichlorobutane is known to be dextrorotatory [91].

The optical purity of (+)-(2R,3R)-dibromobutane (5-6%), obtained from molecular bromine bromination, is not high, if Skell's value ($[\alpha]_{365} = +100°$) [7] is accepted**. Since direct substitution of (-)-(R)-2-bromobutane via an open radical predicts 100% optical purity of the (+)-(2R,3R)-dibromobutane formed, there must be other pathways which have led to the racemic 2,3-dibromobutane.

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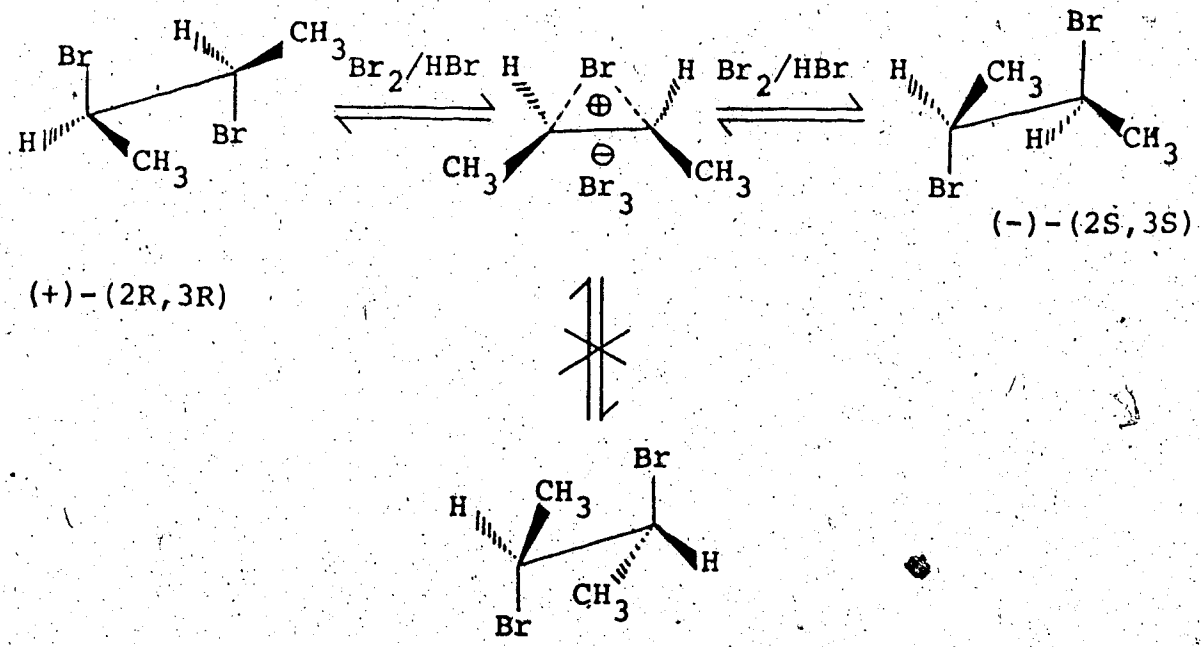
* According to Brewster's selection rules, only one of the three rotamers, a minor one, can be considered and therefore the calculation is not meaningful.

** The minimum experimentally observed rotation for the optical pure (-)-2,3-dibromobutane calculated from the resolution process showed that it can be at least as high as $[\alpha]^{25}_{365} = -84.9°$ (see page 137).

It is especially important to show that the active product formed is stable under the reaction conditions. Optically active (-)-2,3-dibromobutane was obtained from the selective destruction of dl-2,3-dibromobutane with brucine (see experimental section). The partially resolved (-)-2,3-dibromobutane was found to be unstable in the dark under the reaction conditions. It was racemized to about 12% in the presence of molecular bromine and hydrogen bromide ($RBr:Br_2:HBr = 1.2 : 0.9 : 1$) in the dark for the same period of time as in the photo-initiation reactions (22 hr., at 17°). The mechanism of this ionic racemization process undoubtly involves a bromonium ion intermediate as shown in Scheme VIII. This type of reaction is similar to that of the displacement and solvolysis reactions of vicinal dibromides which have been studied by other workers [92-94]. It has been shown that the reaction of optically active threo-3-bromo-2-butanol with hydrogen bromide leads to the completely racemized product, dl-2,3-dibromobutane [92]. The reaction of silver nitrate with dl-2,3-dibromobutane leads similarly to the immediate formation of threo-3-bromo-2-butanol nitrate in acetonitrile solvent [93]. A cis-bromonium ion intermediate was proposed for both reactions. The reaction was completely stereospecific, since no indication of isomerization of the dibromide to meso-2,3-dibromobutane was observed. It is clear that this process

Scheme VIII



(+)-(2R,3R)

(-)-(2S,3S)

meso

provides an important contribution to the racemization of the active product formed in the bromination.

Since all the reaction products were isolated by preparative glpc using 10% Carbowax 20M TPA on Chromosorb PAW, the optically active dibromide was subjected to these isolation conditions. It was found that the optically active (+)- or (-)-2,3-dibromobutane, collected by preparative glpc, racemized to substantial amounts, 15-16% on a 10' x 1/4" glass column and 5-6% on a 6' x 1/4" glass column (see Table XIII). This

Table XIII

Racemization of Optically Active

2,3-Dibromobutane on glpc Isolation [a]

Column	Before $[\alpha]_{365}^{25}$ [b]	After	% Rac.
10' x 1/4"	-28.81° [c]	-24.17° [c]	16.1%
	-26.83° [c]	-22.52° [c]	16.1%
	+ 3.49°	+ 2.98°	14.6%
6' x 1/4"	-15.96°	-14.86°	6.5%
	+ 3.97°	+ 3.77°	5.1%
	+ 4.72°	+ 4.49°	4.9%

[a] Glpc conditions: Using 10% Carbowax 20M TPA on 60-80 mesh Chromosorb PAW (glass column); Column temp: 75-110°; Detector and Injector temp: 110°.

[b] The rotations were measured in CCl_4 solution.

[c] Observed rotation, α, measured with neat liquid.

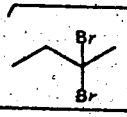
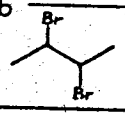
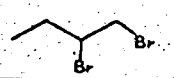
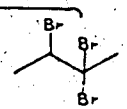
racemization process is presumably similar to those of the thermal isomerization of 5α,6β-dibromocholesteroids which have been studied [94-96].

Photobromination of (-)-(R)-2-Bromobutane With NBS-Br_2-Mixture in Freon 11.

On photobromination of (-)-(R)-2-bromobutane with molecular bromine, we have found that the unbrominated starting bromide may be racemized (see Table X) and that the optically active products formed in the reaction were not stable under the reaction conditions. These observations are attributed to the presence of hydrogen bromide (and molecular bromine) in the reaction mixture. We have therefore investigated the bromination of (-)-(R)-2-bromobutane with a mixture of NBS-Br_2 in order to minimize the amount of hydrogen bromide and to minimize the effect of reversible hydrogen abstraction of the intermediate radicals, as well as to limit the ionic racemization of the product, (+)-(2R,3R)-dibromobutane, formed during the reaction. Using essentially the same reaction conditions as were used in the molecular bromine brominations, a stirred mixture of (-)-(R)-2-bromobutane, NBS, molecular bromine, and solvent Freon 11, in a sealed degassed Pyrex reaction flask, was irradiated with light from an incandescent lamp. The reaction mixture was isolated and analyzed by the procedure used for the molecular bromine brominations. The products formed were found to be identical to those found in the molecular bromine bromination (see Table XIV). In all

Table XIV

Photobromination of (-)-2-Bromobutane with Br_2-NBS in Freon 11

RBr : NBS : Br_2 Mole ratio	([Br_2])	% Conversion[a]	°C Temp.	% Yield[b] 	meso		dl		
3 : 2 : 1.5	(3.3M)	15	2	8.3±0.3	63.8±0.2	27.8±0.1	tr		tr
3 : 2 : 1	(2.1M)	28	17	11.7±0.1	55.5±0.1	23.8±0.1	tr		8.9±0.1
3 : 2 : 1	(2.1M)	30	17	11.5±0.2	56.5±0.5	23.9±0.2	tr		7.7±0.8
4 : 2 : 1	(2.0M)	36	20	12.0±0.1	56.0±0.3	24.7±0.2	tr		7.3±0.8
3 : 2 : 3	(5.2M)	36	17	8.2±0.2	58.3±0.8	25.5±0.2	0.4±0.1		7.6±0.9
3.3 : 3.3 : 1	(0.17M)	46	17	15.9±0.4	51.6±0.5	19.0±0.2	tr		13.5±0.8
38 : 38 : 1	(0.015M)	62	17	15.7±0.3	47.1±0.6	14.8±0.2	tr		22.3±0.8
3.7 : 3.6 : 1	(0.15M)	71	17	15.3±0.2	42.1±0.2	12.6±0.2	tr		30.0±0.2
1 : 1 : 1	(1.2M)	72	20	13.3±0.2	42.3±0.2	12.7±0.2	tr		31.7±0.5

[a] Percentage conversion of starting material.

[b] In all cases, material balance was >97% based on starting material consumed.

cases, the desired products, (+)-2,3-dibromobutane and (+)-2,2,3-tribromobutane as well as the unbrominated starting bromide were collected by preparative glpc using a 6' x 1/4", 10% Carbowax 20M TPA glass column and the optical rotations were measured (see Table XV).

There are two noteworthy features that can be recognized in these reactions. Firstly, the unbrominated starting material was found to be racemized only 1-2% at 15-36% conversion, and 6% at 72% conversion. This amount of racemization, as expected, was smaller than in the corresponding molecular bromine bromination (see Table X and XV). The observation strongly supported the suggestion that reversible hydrogen abstraction served as an important route to this racemization process in the molecular bromine bromination.

Secondly, the degree of the retention of optical activity in the product, (+)-2,3-dibromobutane, was greater than in the bromination carried out in the absence of NBS (see Table X and XV). The observed rotation, $[\alpha]_{365}^{25} = +8°$ to $+9.4°$, was not affected appreciably by changing the bromine concentrations from 0.15 to 2M. However, at higher or lower bromine concentrations, a bromine concentration dependence was observed. At a 5 M concentration, the rotation was decreased to +5.98°. The observation may be attributed to the instability of the (+)-2,3-dibromobutane under high concentration of

Table XV

Optical Rotation of Products from the Br_2-NBS Bromination of (-)-2-Bromobutane

Reaction	RBr:NBS:Br_2 Mol ratio	($[Br_2]$)	% conversion	$[\alpha]^{25}_{365}$ Recovered	(% Rac.)[a]	Obs.	Corr.[b]	Obs.
1	3 : 2 : 3	(5.2M)	36	-74.37°	(2.2%)	+3.52°	+5.98°	+2.36°
2	3 ; 2 :1.5	(3.3M)	15	-74.93°	(1.4%)	+3.97°	+6.74°	--
3	3 : 2 : 1	(2.1M)	30	-74.43°	(2.1%)	+4.90°	+8.32°	+3.22°
4	3 : 2 : 1	(2.1M)	28	-75.21°	(1.0%)	+4.72°	+8.01°	--
5	1 : 1 : 1	(1.2M)	72	-71.28°	(6.2%)	+4.68°	+7.95°	+3.02°
6	3.3:3.3: 1	(0.17M)	46	-73.95°	(2.7%)	+5.45°	+9.25°	+3.19°
7	3.7:3.6: 1	(0.15M)	71	--	--	+5.54°	+9.41°	+2.94°
8	38:38 : 1	(0.015M)	62	-72.06°	(5.2%)	+2.10°	+3.57°	+0.40°

[a] Starting material before reaction has a rotation of $[\alpha]^{25}_{365}$ = -76.00° (58.9% optical purity).

[b] Corrected for optical purity of starting material.

molecular bromine. This ionic reaction was postulated to occur by a mechanism in which a bromine molecule brings about the ionization of the (+)-2,3-dibromobutane to give a symmetrical cis-bromonium ion which in turn leads to racemization (see Scheme VIII). Similar ionization reactions are known to occur with tertiary alkyl bromides [97]. At 0.015 M bromine concentration, the observed activity sharply dropped to +3.57°. The decrease in observed rotation can be attributed to an effectively increased life time of the intermediate radical to be trapped with molecular bromine which increases the possibility of the elimination of β-bromoalkyl radicals to 2-butenes. Addition of molecular bromine to 2-butenes must give racemic 2,3-dibromobutane. This elimination process is well known [3,48-52,73] for the bromination reaction. The optical activity observed in the product, (+)-2,3-dibromobutane, seems quite inconsistent with a bromine-bridged radical mechanism suggested by Skell et al.[7], since such a mechanism should produce only inactive 2,3-dibromobutane (see Scheme III).

The Photobromination of 2-Bromobutane (50.57% Bromine-79 and 49.43% Bromine-81) with Isotopically Enriched Bromine-81 (2.19% Bromine-79 and 97.81% Bromine-81)

In order to determine the importance of the contribution of the elimination-readdition mechanism (Scheme IV) in the bromination of the optically active (-)-(R)-2-bromobutane, the photobromination of 2-bromobutane with isotopically enriched bromine-81 was studied.

2-Bromobutane (215.5 mg, 15.73 μmol) and bromine-81 (86.0 mg, 5.31 μmol) were degassed and sealed in a breakseal reaction ampoule. The reaction mixture was then irradiated at 16° until the bromine color was discharged. The hydrogen bromide produced during the reaction was introduced into a vacuum line and distilled into cyclohexene (200 ul) by trap to trap distillation. The cyclohexene and hydrogen bromide were shaken for 12 hours at room temperature and the cyclohexyl bromide formed was collected by preparative glpc. The reaction mixture was allowed to warm to room temperature and a small amount of sodium bicarbonate powder was carefully added to remove any remaining undistilled hydrogen bromide. The products from this reaction were isolated by glpc and were analyzed by an AEI high resolution MS-9 mass spectrometer to determine the bromine-79 and bromine-81 content (see Table XVI).

Table XVI

Photobromination of 2-Bromobutane with Bromine-81

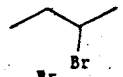
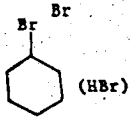
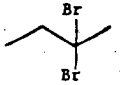
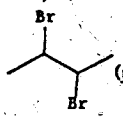
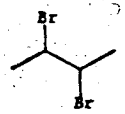
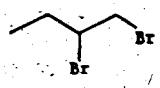
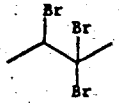
Compound	m/e	Peak Ratio	Total Bromine Content[a] Br-79/Br-81	Average Isotopic Abundance[a] (%) Br atom #1 Br-79/Br-81	Br atom #2 Br-79/Br-81
	P[b]	0.970 : 1	49.23±0.26/50.77±0.26	--	--
	P-29[c]				
 (HBr)	P[d]	0.207 : 1	17.15±0.10/82.85±0.10	--	--
	P-29[e]	1 : 10.29 : 9.57	29.49±0.15/70.51±0.15	49.17/50.83	9.75/90.25
	P-Br[f]	0.419 : 1			
 (meso)	P[g]	1 : 11.46 : 17.87	22.28±0.20/77.72±0.20	34.94/65.06	9.44/90.56
	P-Br[f]	0.288 : 1			
 (dl)	P[g]	1 : 10.90 : 18.05	21.61±0.09/78.39±0.09	32.93/67.07	10.14/89.86
	P-Br[f]	0.277 : 1			
	P[g]	1 : 13.4 : 47.8[h]	12.4±0.1/87.6±0.1	--	--
		(1 : 14.7 : 52.4)[i]	(12.3/87.7)	(14.1/85.9)	(10.4/89.6)
	P[j]	0.5 : 12.6 : 82.9 : 122.7	16.7±0.1/83.3±0.1	k	k
		±0.2 ± 0.3 ±0.4 ±0.4			

Table continued on next page

Table continued

[a] Calculated from the observed peak ratio (see Appendix). The errors indicated are the average deviations from the mean.

[b] P. 136, 138

[c] P-29, 107, 109

[d] P, 162, 164

[e] P-29, 185, 187, 189

[f] P-Br, 135, 137

[g] P, 214, 216, 218

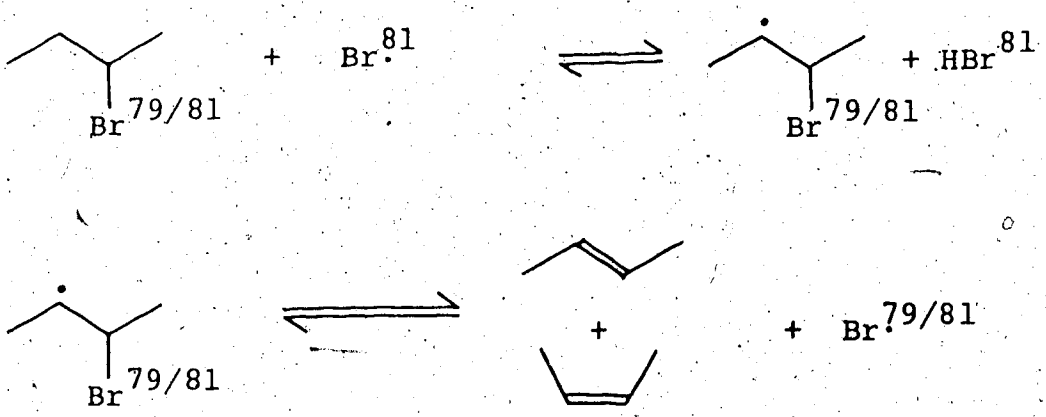
[h] Measured peak intensities are 2.3±0.2 : 30.8±0.3 : 110.0±0.4 (in mm).

[i] Calculated using the peak intensities of 2.1 : 30.8 : 110.0.

[j] P, 292, 294, 296, 298. Reported as actual peak intensities (in mm).

[k] The average isotopic abundances of each of the three bromine atoms in this tribromide are 32.4/67.6, 11.7/88.3, and 6.0/94.0 respectively.

Analysis of the parent peaks of cyclohexyl bromide (m/e 162 and 164 corresponding to $C_6H_{11}Br^{79}$ and $C_6H_{11}Br^{81}$) showed that it contained 17.15 ± 0.10% bromine-79 and 82.85 ± 0.10% bromine-81; this value represented the bromine content of the hydrogen bromide formed during the bromination. For a direct substitution mechanism, the bromine content of the hydrogen bromide and the second bromine introduced in the dibromides should be the same as that of the initial molecular bromine, i.e. 2.19% bromine-79 and 97.81% bromine-81. The result showed that the hydrogen bromide was greatly enriched in bromine-79.



$$Br_2^{81} + Br\cdot^{79/81} \rightleftharpoons Br^{81}Br^{79/81} + Br\cdot^{81}$$

$$HBr^{81} + Br^{81}Br^{79/81} \rightleftharpoons HBr_3^{79/81} \rightleftharpoons HBr^{79/81} + Br_2^{81}$$

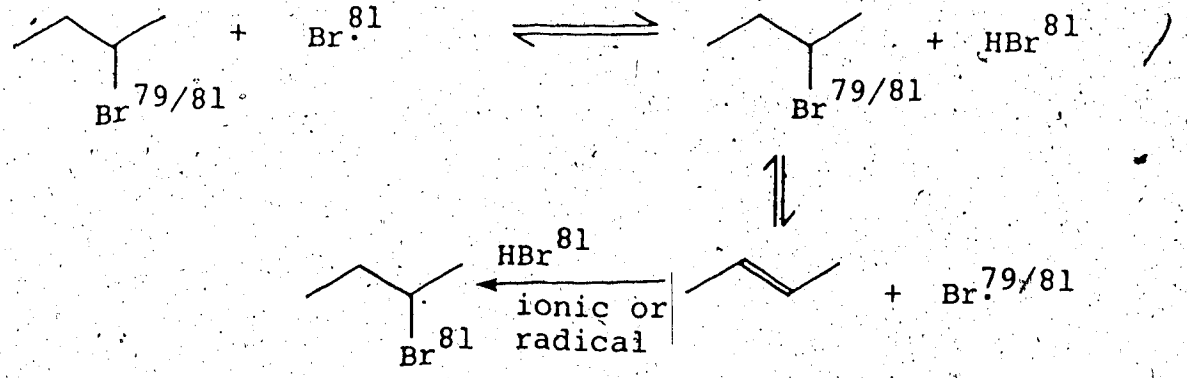
This enrichment must have been due to the bromine atom coming off the starting 2-bromobutane, since there was no other source for the bromine-79. The most reasonable mechanism for scrambling of the isotope of bromine-79 is elimination of the bromine atom from 3-bromo-2-butyl radicals. This eliminated bromine atom was then rapidly scrambled with the bromine pool and hydrogen bromide [98,99].

The unbrominated 2-bromobutane was found slightly enriched in bromine-81 (49.23 ± 0.26% bromine-79 and 50.77 ± 0.26% bromine-81). This gain in bromine-81 indicated that exchange between the starting 2-bromobutane (50.57% bromine-79 and 49.43% bromine-81) and the molecular bromine-81 pool occurred during the reaction. There are four possible pathways that lead to bromine-81 incorporation into the starting 2-bromobutane (Scheme IX).

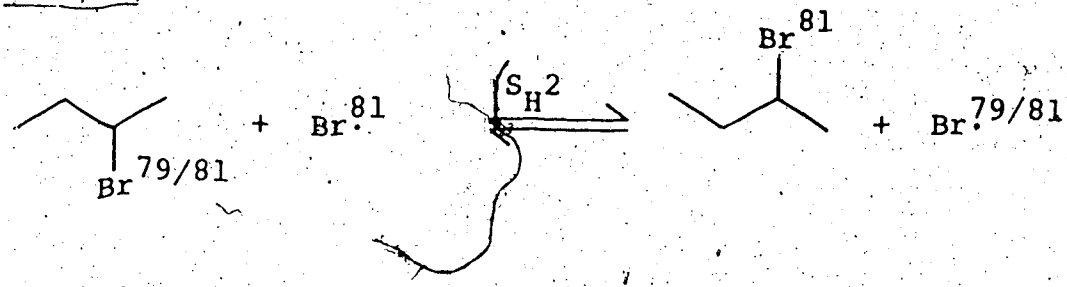
In all cases, if optically active (-)-(R)-2-bromobutane were used in the bromination, the reaction would lead to net racemization of (-)-(R)-2-bromobutane with incorporation of bromine-81 (e.g. S_H2 gives the inverted configuration). Control reactions were therefore carried out either in the presence of molecular bromine or of molecular bromine and hydrogen bromide in the dark using identical conditions to those employed for the photo-initiated bromination. The results showed that the recovered (-)-(R)-2-bromobutane was not more than 0.4% racemized (see Table X, reaction 7-8): The ionic mech-

Scheme IX

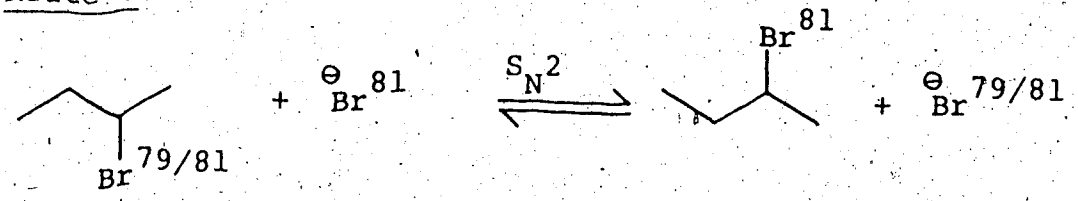
Route 1.



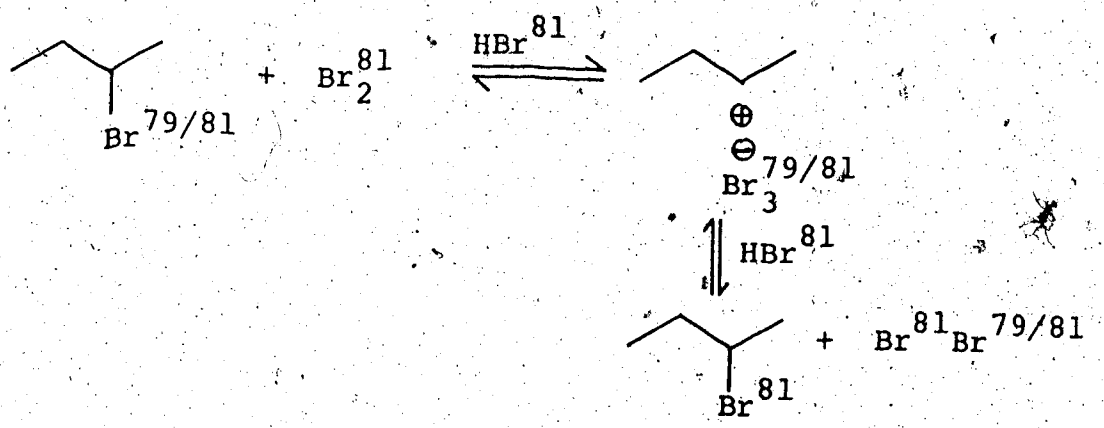
Route 2.



Route 3.

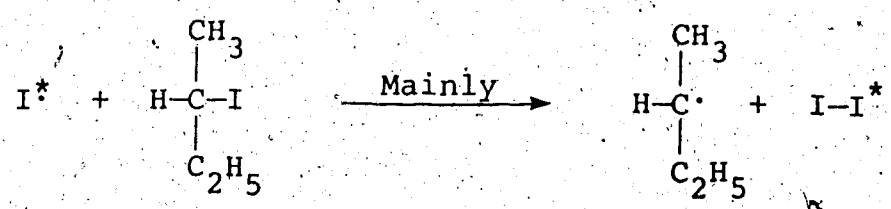


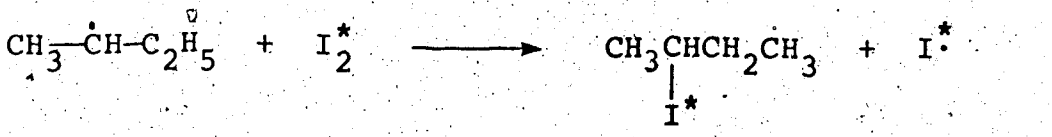
Route 4.



anisms (Route 3 and 4) can therefore only be of minor importance in the incorporation of bromine-81 (<0.4% of total incorporation) into 2-bromobutane.

The mechanism of Route 2 involves attack either on bromine or on carbon by a bromine-81 atom; this is reminiscent of the reaction of optically active 2-iodobutane containing radioactive iodine [100]. Benson [100] showed that this reaction proceeds mainly by attack on the iodo substituent by radioactive iodine atoms as shown in the following scheme.

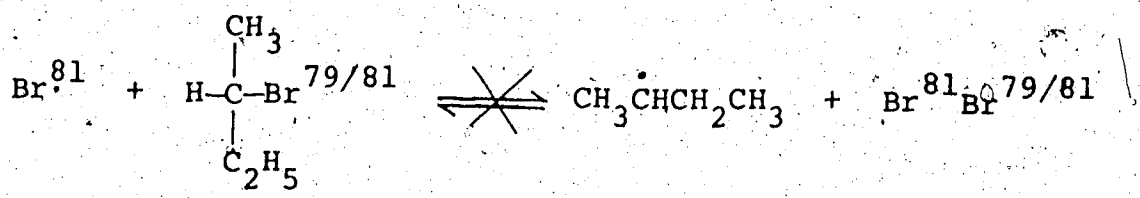




racemized product containing radioactive iodide

The direct S_H2 displacement on the carbon, which would also produce racemization and exchange, occurs very little if at all [100,101]. The analogous reaction for bromine attack on the bromo substituent of 2-bromobutane,

however, appears unreasonable, since this process should be endothermic by at least 22 kcal, while the attack by bromine atom on saturated carbon by an S_H2 process is unprecedented, with the possible exception of the unique reaction of bromine with cyclopropane [102,103].



If the S_H2 displacement on carbon, however, were considered, then every molecule displaced with bromine-81 would produce a two fold racemization of starting (-)-(R)-2-bromobutane, since every act of exchange (bromine-81 for bromine-79 or bromine-81 for bromine-81) replaces one molecule of the (-)-enantiomer with the (+)-enantiomer. The mass spectral analysis showed that the recovered 2-bromobutane contained 49.23 ± 0.26% bromine-79 and 50.77 ± 0.26% bromine-81, i.e. a 1.3% enrichment in bromine-81. Since the starting 2-bromobutane contained 50.57% bromine-79 and 49.43% bromine-81, there is nearly equal opportunity for displacing bromine-79 or bromine-81. The excess enrichment in bromine-81 (1.3%) indicates that there are at least 2.6% of the molecules whose configuration is inverted; one would then expect 5.2% racemization of (-)-(R)-2-bromobutane if S_H2 displacement on carbon is

taking place. As can be seen in Table XV (reaction 1-4), when the brominations were carried out using bromine and NBS mixture, only 1-2% racemization of recovered (-)-(R)-2-bromobutane was observed. This process, therefore, can at most be only a minor contribution to the excess incorporation of bromine-81 into 2-bromobutane, if it occurs at all.

The mechanism (Route 1) involving bromine atom elimination-readdition process is, however, not precluded. β-Bromoalkyl radicals are unstable, and dissociations to olefin and bromine atom are well documented in chemical literature [3,48-52,73]. Rapid elimination of bromine atom from β-bromoalkyl radicals is responsible for the well known bromine induced isomerization of olefins [3,83-86].

Thaler [73] studied the liquid phase photochlorination of 1-bromobutane; in addition to normal chlorination products, 1,2-dichlorobutane (5% of total products) was also obtained, which accounted for 22% of total 1,2-dihalobutanes (1-bromo-2-chlorobutane and 1,2-dichlorobutane) observed. Tedder [49] has reported that 1,2-dichlorobutane was also produced in the vapor phase chlorination of 1-bromobutane at 35° in place of the expected 1-bromo-2-chlorobutane. Similarly, chlorination of bromocyclopentane produced significant quantities of dichloride which could be minimized only to 2% of the dihalo

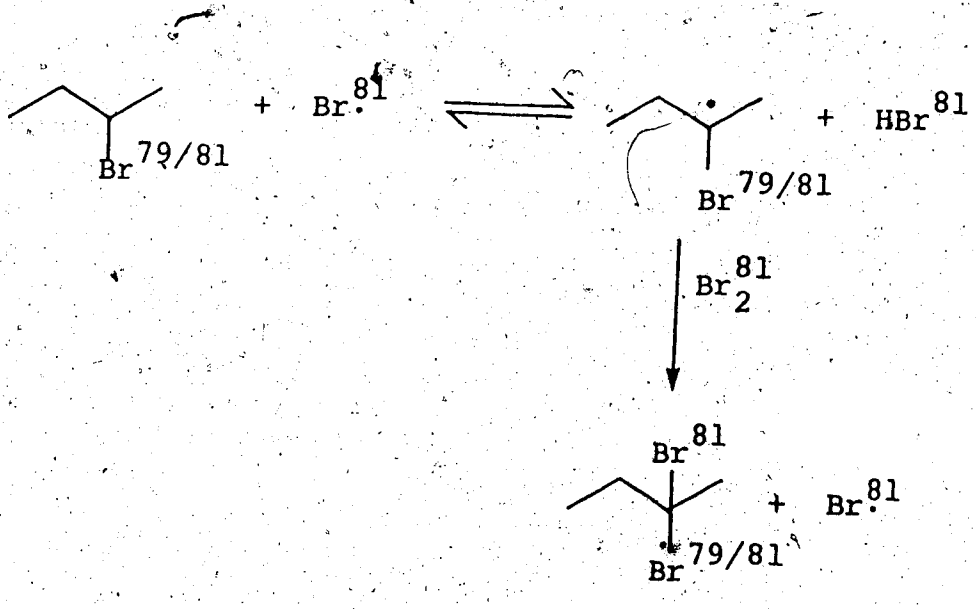
products by performing the reaction at -30° [51,52]. These literature examples strongly suggest that the elimination-readdition mechanism (Route 1) may be an important route leading to excess incorporation of bromine-81 in 2-bromobutane as well as a route to the production of the vicinal dibromides.

If the mechanism for the formation of 2,3-dibromobutanes involves a bridged intermediate or proceeds by a direct substitution reaction, the dibromides formed must contain 26.38% bromine-79 and 73.62% bromine-81 with a peak height ratio of the parent peaks 214 : 216 : 218 = 1 : 45.6 : 43.7. The predicted peak height ratios were calculated using the binomial expansion (see Appendix) for a molecule of dibromide containing two different bromine atoms, with different bromine isotope content, by taking one of the bromine atoms as the original one present in 2-bromobutane (50.57% bromine-79 and 49.43% bromine-81) and the other one having the isotopic composition of the molecular bromine-81 used (2.19% bromine-79 and 97.81% bromine-81). The two mechanisms (bromine-bridged and direct substitution), by themselves cannot explain the incorporation of bromine-79 into hydrogen bromide and bromine-81 into 2-bromobutane or the deviation of the isotopic ratios in the product 2,3-dibromobutanes from that predicted.

The product, 2,2-dibromobutane, presumably can

only be derived from direct substitution, it should have the bromine content predicted for this mechanism. The experimental results showed that it contained 29.49 ± 0.15% bromine-79 and 70.51 ± 0.15% bromine-81 (see Table XVI). A calculation was made for the prediction of the isotopic distribution for the formation of 2,2-dibromobutane by direct substitution. The average bromine content of the starting 2-bromobutane (before and after reaction), i.e. 49.90% bromine-79 and 50.10% bromine-81, reacting by this mechanism with the average bromine content in the bromine pool (at the beginning and at the end of the reaction), i.e. 9.67% bromine-79 and 90.33% bromine-81, predicted that the 2,2-dibromobutane would contain 29.79% bromine-79 and 70.21% bromine-81. The coincidence of the predicted and observed isotopic distributions substantiates the mechanism assigned for the formation of 2,2-dibromobutane. Furthermore, the average isotope content of each bromine atom in this dibromide may be calculated from the observed peak height ratio of its parent peaks (see Appendix). The calculations show that one of the bromine atoms, containing 49.17% bromine-79 and 50.83% bromine-81, was very similar to that of the average bromine content of 2-bromobutane (before and after reaction), and the other bromine atom, containing 9.75% bromine-79 and 90.25% bromine-81, was also identical (within experimental error) with that of the average bromine content in the bromine

pool. These results are in excellent agreement with the direct substitution mechanism to yield 2,2-dibromobutane. Since the bromine-81 pool was expected to be diluted with bromine-79 atoms which came from the elimination of β-bromoalkyl radicals, it was predicted that this compound will be enriched in bromine-79. The reversal reaction of 2-bromo-2-butyl radicals and hydrogen bromide would lead to racemization of (-)-(R)-2-bromobutane with no incorporation of bromine-81.



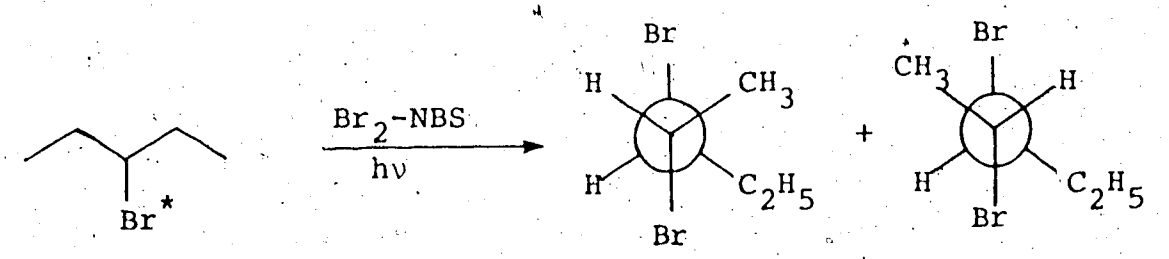
The dibromides, meso- and dl-2,3-dibromobutane, were found to be highly enriched in bromine-81 (see Table XVI). Contrary to the expected value for the direct substitution reaction, the experimental results showed 22.28 ± 0.20% bromine-79 and 77.72 ± 0.20% bromine-81 (peak height ratio 214 : 216 : 218 = 1 : 11.5 : 17.9) in

the meso-isomer and 21.61 ± 0.09% bromine-79 and 78.39 ± 0.09% bromine-81 (peak height ratio 214 : 216 : 218 = 1 : 10.9 : 18.1) in the dl-isomer. It can be seen clearly from the observed peak height ratio that the last peak, with two bromine-81 atoms, is the largest. If these dibromides were produced by the direct substitution mechanism, they would be expected to contain a bromine atom originating from 2-bromobutane and a bromine atom from the bromine-81 pool. The mass spectral peak ratio of the parent peaks would show the center peak, with one bromine-79 and one bromine-81 combination, to be the highest. The calculation from the observed mass spectral peak intensities (see Appendix) showed that both bromine atoms in these dibromides have different relative isotopic abundance (see Table XVI), and neither one contained the original bromine atom from 2-bromobutane (50.57% bromine-79 and 49.43% bromine-81) or from the bromine-81 pool (2.19% bromine-79 and 97.81% bromine-81). It is apparent that in 2,3-dibromobutane, the original bromine of 2-bromobutane had been substantially lost. These dibromides therefore cannot be produced exclusively by a direct substitution mechanism. These results strongly support the idea of facile elimination of bromine atom from 3-bromo-2-butyl radicals to give 2-butenes, followed by subsequent rapid addition of molecular bromine to give vicinal dibromides (see Scheme IV). However, the pure elimination-

readdition mechanism (Scheme IV) would predict both bromine atoms in the addition product dibromides would have the same bromine content. The observed difference in the isotopic content of the two bromine atoms in 2,3-dibromobutane can be attributed to simultaneous reaction pathways involving a direct substitution mechanism (bridging or classical, Scheme III and II) and an elimination-readdition mechanism (Scheme IV). The contribution from these two processes of the elimination-readdition scheme to the formation of vicinal dibromides may be calculated from the results listed in Table XVI (see Appendix). These are found to be 37% and 40 % for meso- and dl-2,3-dibromobutane respectively.

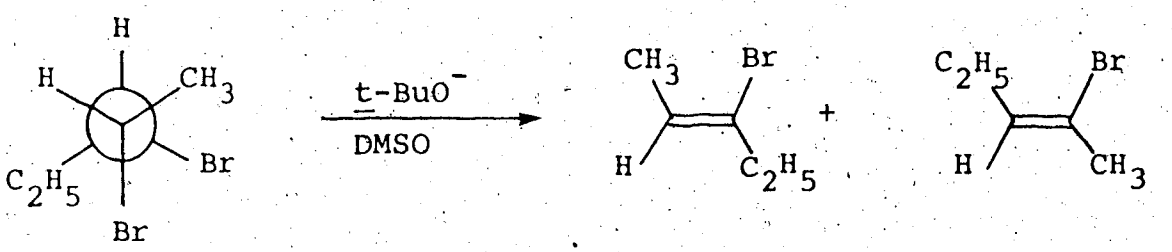
Skell et al. [7] reported that the photobromination of radioactive labelled 3-bromopentane-Br^{82} with ordinary molecular bromine and NBS mixture led to a mixture of erythro- and threo-2,3-dibromopentanes. The dehydrobromination of threo-2,3-dibromopentane showed that the original radioactive bromine atom was completely scrambled between the carbon-2 and carbon-3 in the product. Skell et al. [7] concluded that the bromination of 3-bromopentane-Br^{82} proceeded through either a completely symmetrical bromine-bridged radical or an intermediate where 1,2-bromine atom migration occurs faster than trapping by molecular bromine.

However, Skell's observation is inconsistent



threo RMA = 0.94 erythro RMA = 1.00

RMA = 1.02



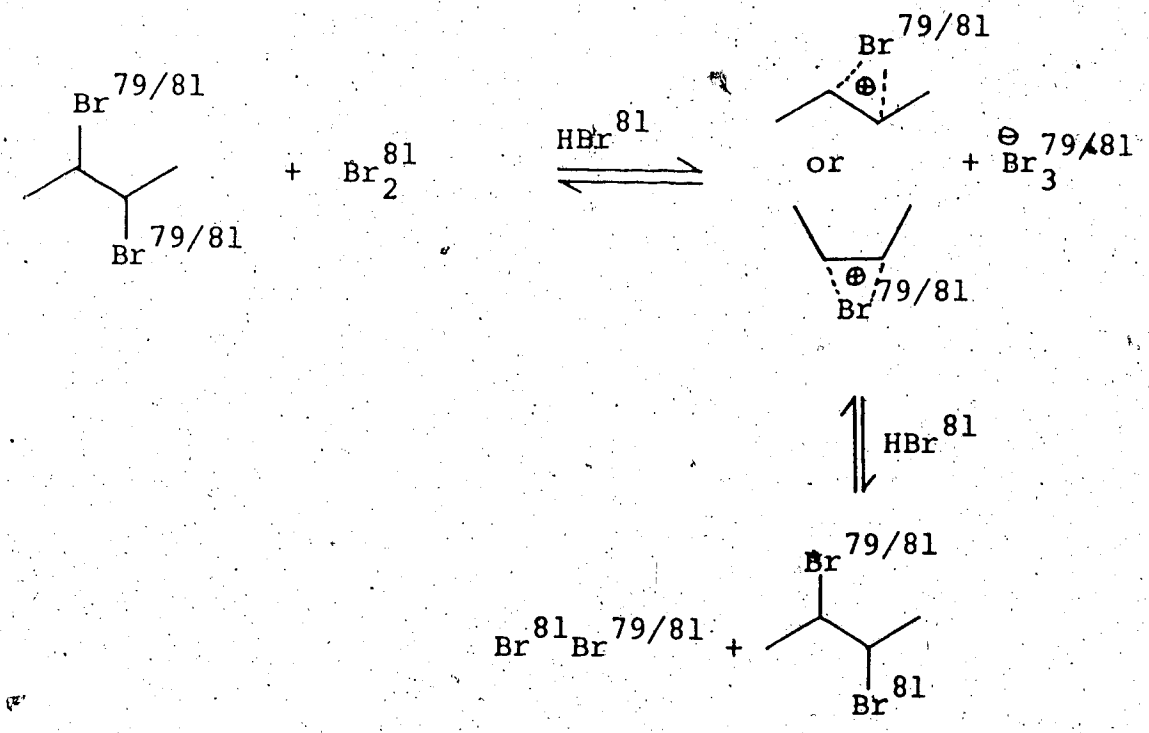
threo RMA = 1.02 RMA = 0.98

(RMA = Relative molar radioactivity)

with the results obtained from this work. We have found that two bromine atoms in the vicinal dibromides were different, and neither one is from the original bromine-81 pool or from 2-bromobutane. Furthermore, the bromination of optically active (-)-(R)-2-bromobutane yields optically active (+)-2,3-dibromobutane, which could not arise from a symmetrical bromine-bridged intermediate. From our experience, it was found that the optically active (-)-1,2-dibromo-2-methylbutane [5] and (+)-2,3-dibromobutane were extensively racemized during glpc isolation. It seems possible that Skell's obser-

vation of scrambling of the radioactive bromine in the product might be due to the scrambling in their glpc isolation (16 ft column). At the present time, it is otherwise difficult to explain this discrepancy.

Unfortunately, the bromine-81 incorporations in meso- and dl-2,3-dibromobutane are complicated by the partial contribution from the ionic reaction as shown in the following scheme. When partially resolved (-)-2,3-dibromobutane (α^{25}_{365} = -29.61°, neat) and molecular bromine



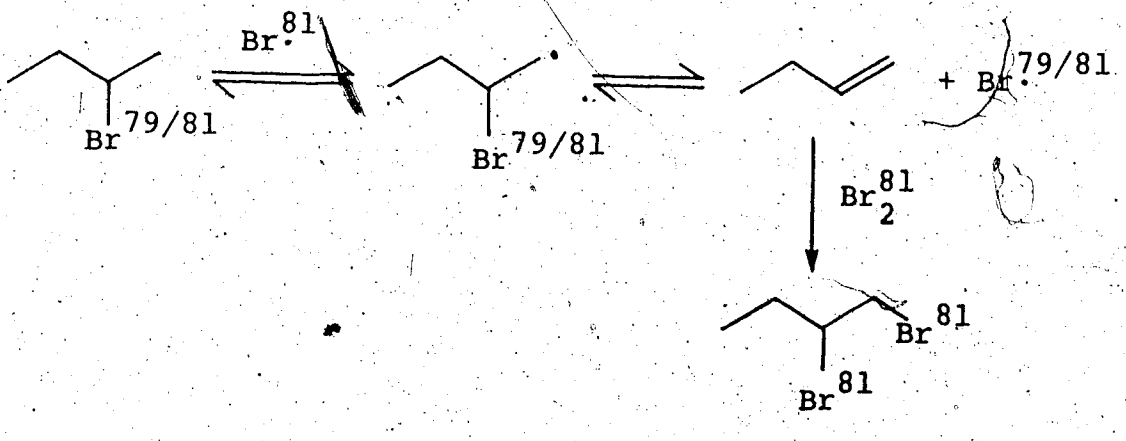
in a ratio of 3 : 1 were subjected to the reaction conditions in the dark, the recovered (-)-2,3-dibromobutane (α^{25}_{365} = -28.81°, neat) was found to be 2.7% racemized.

More extensive racemization was observed in the presence of molecular bromine and hydrogen bromide; when a 1.2 : 0.9 : 1 ratio (RBr : Br_2 : HBr) was used, 12% racemization was detected. The photochemical reaction is expected to give less racemization, since the ratio of RBr : Br_2 : HBr at 50% and 100% conversion of molecular bromine are approximately 2.5 : 0.5 : 0.5 and 2 : 0 : 1, respectively. Although, racemization of (-)-2,3-dibromobutane was detected in this dark reaction, no indication of isomerization of this compound to the more stable meso-2,3-dibromobutane was observed. If one assumes that the excess bromine-81 incorporation in the products was only realized by this ionic process, and that the dibromides initially formed came from direct substitution without excess incorporation, then from the experimentally observed total bromine content in dl-2,3-dibromobutane (21.61% bromine-79 and 78.39% bromine-81) it would be expected that a minimum of 19% of the dl-2,3-dibromobutane must have undergone observable exchange (i.e. bromine-79 replaced with bromine-81). Since in every act of exchange there is only a 26% chance of the bromine-79 being replaced by bromine-81 and since this exchange always leads to racemization, a minimum of 73% racemization would have to occur concomitant with this exchange reaction. Since only 12% racemization was observed in the control experiment, a maximum of 16% of the total exchange found

can come from this process. This is therefore not sufficient to explain the observed bromine-81 excess incorporation, and therefore the racemization must have arisen from other pathways.

1,2-Dibromobutane and 2,2,3-tribromobutane were also found to have contained an excess of bromine-81 (see Table XVI). In the case of 1,2-dibromobutane (12.4 ± 0.1% bromine-79 and 87.6 ± 0.1% bromine-81), its bromine-81 content was found much higher than those of meso- and dl-2,3-dibromobutane. It is apparently not produced by the direct substitution reaction as it would be the same as that of 2,2-dibromobutane. A likely explanation for its observed isotopic distribution is that the precursor radical intermediate, the 2-bromo-1-butyl radical, may possibly eliminate a bromine atom at a faster rate than the corresponding 3-bromo-2-butyl radical. The calculation for the average bromine isotopic ratio from its spectral peak height ratio at the parent peaks did not give a real solution. Nonreal solutions are due to the measuring error of its mass spectral peak height, since the first peak (m/e 214), corresponding to two bromine-79 combinations, is so small (2.3 ± 0.2 mm). The measuring error on this peak (m/e 214) gives a large error in the peak height ratio, but shows little effect in the total bromine content (see Table XVI). If 2.1 mm peak height (within experimental error) at m/e 214 was taken for the

calculation (i.e. m/e 214 : 216 : 218 = 1 : 14.7 : 52.4), then a set of real solutions was obtained (see Table XVI) from the calculations (see Appendix). The calculated results also showed that both bromine atoms in 1,2-dibromobutane are neither from the original bromine-81 pool nor from the original bromine in 2-bromobutane. The calculated average isotopic ratio of the two bromine atoms of 1,2-dibromobutane showed them to be extensively scrambled. This was further substantiated by the calculation of the fraction of the 1,2-dibromobutane derived from the elimination-readdition mechanism (86%), see Appendix.



In the case of the 2,2,3-tribromobutane, if one assumes that it was derived from the bromination of 2,2-, meso- and dl-2,3-dibromobutanes in their observed isotopic ratios, by a direct substitution mechanism, it may be calculated that the bromine content of 2,2,3-tribromobutane should be 18.4% bromine-79 and 81.6%

bromine-81. The bromine content was obtained by using the final bromine content of the dibromides, and assumed that the third bromine atom had the same bromine isotopic ratio as the average bromine pool; and further assumed that the three different dibromides had been brominated at equal rates. The experimental result showed that 2,2,3-tribromobutane contained more bromine-81 than the calculated value. Therefore, it may also be produced by the elimination-readdition mechanism (see Scheme VI). The average isotopic abundances for each of the bromine atoms in the 2,2,3-tribromobutane may also be calculated from the observed mass spectral peak intensities of the parent peaks (see Appendix). This calculation showed that the three bromine atoms in the tribromide have different relative isotopic ratios (32.4/67.6, 11.7/88.3, and 6.0/94.0 respectively, see Table XVI), and that none had originated exclusively from the initial bromine-81 nor from the original bromine in 2-bromobutane.

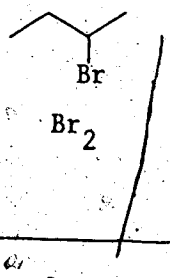
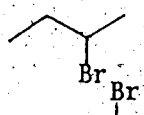
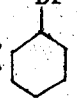
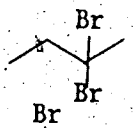
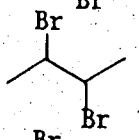
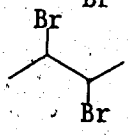
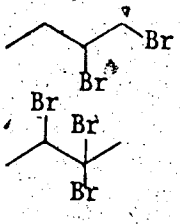
Due to the complication of the ionic pathway, at the present time, we are unable to determine exactly the relative importance of the contributions of the elimination-readdition and ionic mechanism in the incorporation of bromine-81 into the products. However, the results of the bromination of 2-bromobutane with bromine-81 strongly indicated that a pathway which exchanges the bromine substituent with the bromine pool is important

in the reaction. We feel that the elimination-readdition mechanism is a major contributor to this exchange, although both mechanisms -- ionic or radical elimination -- lead to incorporation and racemic products.

The material balance for bromine-79 and bromine-81 in the products after reaction was found to be in good agreement with the isotopes in the starting 2-bromobutane and the isotopically enriched bromine-81 used (see Table XVII).

Table XVII

Material Balance on Bromine-79 and Bromine-81 of 2-Bromobutane Bromination with Isotopically Enriched Bromine-81

Reactants	Br^{79} (mol)	(atom %)	Br^{81} (atoms/molecule)	(10^4)
	795.5		777.5	
Br_2	23.3		1038.7	
	818.8		1816.2	
Products				
	535.6		552.4	
HBr ()	91.1		439.9	
	20.9		49.9	
 (meso)	120.8		421.4	
 (dl)	53.5		193.9	
	2.3		16.1	
	23.1		115.2	
	847.3	(103.5%)	1788.8	(98.5%)

Mechanistic Conclusion of the Photobromination of 2-Bromobutane.

An objective examination of the characteristics of the photobromination of the optically active (-)-(R)-2-bromobutane with molecular bromine and Br_2-NBS mixtures supported the conclusion that the reaction must proceed through the formation of a "classical radical" as an initially formed intermediate, and the reversal reaction of hydrogen bromide and the intermediate radicals is important in the molecular bromine bromination.

The data from the bromine-81 brominations (Table XVI) reveals the importance of bromine exchange processes. The bromine substituent originally in 2-bromobutane was extensively exchanged with the bromine-81 pool. These exchange processes can be attributed to the elimination of a bromine atom from the β-bromoalkyl radical to yield olefin, which by subsequent addition of molecular bromine gives bromine-81 enriched vicinal dibromides (see Scheme IV), and to the contribution of an ionic racemization process. Both processes not only led to the incorporation of bromine-81, but also led to the formation of racemic product. These phenomena explained well the low optical purity obtained in the product, (+)-(2R,3R)-dibromobutane.

On the other hand, the results must also be

accommodated by a mechanism involving a classical radical intermediate (see Scheme II) which is captured by transfer with molecular bromine before β-scission or before passing through a symmetric intermediate, and which gives optically active product.

Consider the possibility that the radical intermediate leading to the formation of 2,3-dibromobutane possessed a bromine-bridged structure. Then the bromination of (-)-(R)-2-bromobutane would be expected to produce, through a symmetrical bromine-bridged radical intermediate (see Scheme III), 2,3-dibromobutane with complete loss of the optical activity. However, recent esr [9] and CIDNP [8] results showed that β-bromo-tert-butyl [9] and β-bromoethyl [8] radicals are not bridged. Furthermore, the 2,3-dibromobutane (dl-fraction) and the 2,2,3-tribromobutane produced from the -(-)-(R)-2-bromobutane brominations were found to be optically active. Clearly these reactions have all of the characteristics of simple classical radical processes, since the radical intermediate, 3-bromo-2-butyl radicals, can be trapped by molecular bromine to give optically active (+)-(2R,3R)-dibromobutane (see Table X and XV). Its stereochemistry is also consistent with the classical radical mechanism (see Scheme II).

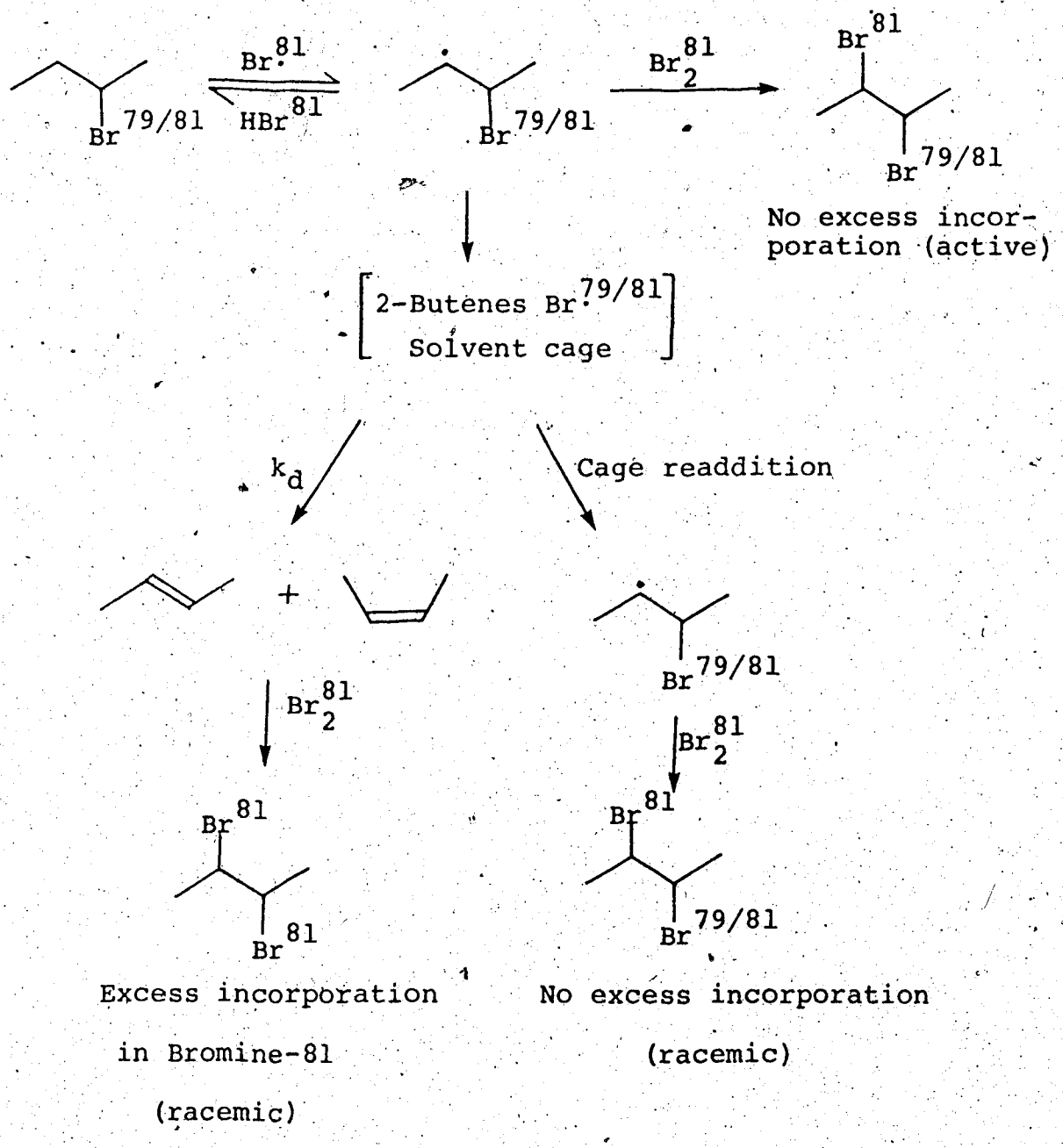
The overall experimentally observed racemization processes (elimination-readdition, ionic exchange, glpc

isolation, and the racemization of the starting 2-bromobutane) were found insufficient to account for the observed activity in the (+)-(2R,3R)-dibromobutane. Other pathways leading to racemization are therefore considered.

Several processes can be envisaged to rationalize the observation that racemization can occur without excess incorporation of bromine-81. The first, the formation of a symmetrically bridged species after abstraction, or as a transition state leading to a 1,2-bromine migration can not be ruled out. A second proposal can be suggested which involves the previously established facile elimination reaction leading to a caged olefin-bromine atom pair, followed by readdition of the radical to the achiral substrate. Since incorporation will only occur upon reaction subsequent to diffusion the possibility exists, although unsubstantiated, that the addition process will be competitive with diffusion (Scheme X). It has recently been demonstrated that the cage reversal between the alkyl radical-hydrogen bromide pair is competitive with diffusion [104-106]. Since in the vapor phase bromination of 1-butene [106], it has been demonstrated that addition is competitive with transfer of the β-bromoalkyl radical (a near diffusion controlled process), it is not unlikely that cage addition can occur in competition with diffusion. This process may therefore mask the contribution of elimination-re-

addition in the product vicinal dibromides in the isotopically enriched bromine-81 bromination.

Scheme X



EXPERIMENTAL

Materials

Bromine (McArthur Chemical Co., Ltd.) was washed with concentrated sulfuric acid and distilled from phosphorus pentoxide prior to use. Isotopically enriched bromine-81 (2.19 ± 0.5% bromine-79 and 97.81 ± 0.5% bromine-81) was purchased from Isotope Development Center, Oak Ridge National Laboratory and was distilled twice prior to use.

(-)-2-Methylbutanol (Aldrich Chemical Co., Ltd.), $[\alpha]_{589}^{27} = -5.76°$ (lit. [107] $[\alpha]_{D}^{20} = -5.90°$), and (+)-2-butanol (Norse Laboratories, Inc.), $[\alpha]_{589}^{25} = +12.57°$ (lit. [108] $[\alpha]_{D}^{20} = +13.9°$), were used as purchased.

Carbon tetrachloride (spectroanalyzed reagent), tert-butanol, and chlorobenzene were purchased from Fisher Scientific Company and used without further purifications. Freon 11 (fluorotrichloromethane) and Freon 113 (1,1,2-trifluorotrichloroethane) (Matheson of Canada Ltd.) as well as cis- and trans-2-butenes (Research grade, >99.8 mole %, Phillips Petroleum Company) were used as supplied.

1-Bromo-2-butene was obtained from the preparative glpc collection (50°, 6' x 1/4" 10% Carbowax 20M TPA glass column) of commercial available crotyl bromide (Aldrich Chemical Company, Ltd.). A freshly collected

sample had n_D^{25} = 1.4804 (lit.[109] n_D^{20} = 1.4822). The sample isomerized to a mixture of 1-bromo-2-butene and 3-bromo-1-butene on standing[110].

1,2,3-Tribromobutane (City Chemical Corp.), 1,4-dibromo-2-butene (Aldrich Chemical Co., Ltd.), and 1,2-dibromobutane (Eastman Kodak Co.) were used as supplied.

Nmr shift reagents, Tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octadionato)europium (III), $Eu(fod)_3$-d_{30} (Norell Chemical Co., Inc.), and Tris-(3-(heptafluoropropylhydroxymethylene)-d-camphorato)europium (III), $Eu(Opt\ Shift)_3$ (Willow Brook Laboratories, Inc.), were used as purchased.

Hydrogen bromide (Matheson of Canada Ltd.) was passed over molecular sieve 4A, degassed, and distilled twice prior to use.

Brucine (Fisher Scientific Co.) was dried by pumping in a high vacuum line for more than two days, and was stored in a vacuum desiccator in the presence of phosphorus pentoxide, m.p. 177.5° (lit.[111] m.p. 178°).

dl-2-Bromobutane (J.T. Baker Chemical Co.) was purified by washing with concentrated sulfuric acid, water, saturated sodium bicarbonate, and drying over anhydrous sodium sulfate followed by subsequent fractional distillation. The middle cut fraction was collected, b.p. 88°/700 mm, n_D^{25} = 1.4346 (lit.[112] b.p. 91.2°/760 mm,

n_D^{20} = 1.4366).

2-Bromo-2-butene (trans- and cis-mixture) (J.T. Baker Chemical Co.) was purified by fractional distillation prior to use, b.p. 83-5°/693 mm, n_D^{25} = 1.4576 (lit.[113] b.p. 84.5-85.0°/740 mm, n_D^{25} = 1.4565 for trans-isomer).

meso- and dl-2,3-Dibromobutane were prepared in about 90% yields by the addition of a bromine/Freon 113 solution to trans- and cis-2-butene respectively [114] and were isolated by distillation under reduced pressure. meso-2,3-Dibromobutane had b.p. 66°/38 mm, n_D^{20} = 1.5115 (lit.[113] b.p. 73.5-74°/50 mm, n_D^{25} = 1.5093). dl-2,3-Dibromobutane had b.p. 74°/45 mm, n_D^{20} = 1.5150 (lit.[113] b.p. 75.5-76.5°/50 mm, n_D^{25} = 1.5126).

2,2,3-Tribromobutane was prepared in a method similar to that of the meso- and dl-2,3-dibromobutanes from 2-bromo-2-butene (trans- and cis- mixture). The colorless liquid had b.p. 50-1°/2.1 mm (lit.[115] b.p. 83-4°/11.5 mm) and n_D^{25} = 1.5610 (lit.[116] n_D^{20} = 1.5602). Nmr $\tau(CCl_4)$ 7.89 (3H; d; 3-CH_3), 7.23 (3H; s; 1-H), and 5.43 (1H; q; 3-H). The mass spectrum of this tribromide gave parent peaks at m/e 292, 294, 296, and 298 (1 : 3 : 3 : 1 ratio).

tert-Butyl hypobromite was prepared by the method of Walling and Padwa [76] and was assayed for purity by thiosulfate titration of the iodine liberated from KI in the presence of acetic acid [117]. Results indicated

94% purity, b.p. 40°/63 mm (lit.[76] b.p. 44-5°/85 mm). It was stored in a brown bottle protected from light at a temperature less than 0° and removed only prior to use in an experiment. Mass spectral analysis (70 eV) was consistent with that anticipated for tert-butyl hypobromite: m/e 152 and 154 (parent peaks, 1 : 1 ratio), 57 (base peak, $(CH_3)_3C^+$), and additionally showed contamination by tert-butanol, m/e 59 ($(CH_3)_2\overset{+}{C}$-OH). Nmr $\tau(CCl_4)$ 8.74 (singlet).

(+)-1-Cyano-2-methylbutane, 38a, was prepared by the treatment of the p-toluene sulphonate ester of (-)-2-methylbutanol with potassium cyanide[5]. The tosylate (60 g, 0.25 mol) and a solution of potassium cyanide (86 g, 1.32 mol) in diethylene glycol (80 g) were heated until the reaction commenced. The mixture was maintained at reflux for three hours and the crude product was distilled from the reaction mixture under reduced pressure. Fractional distillation of the crude product yielded 18 g (72%) of pure (+)-1-cyano-2-methylbutane, b.p. 152-154°/699 mm (lit.[118] 151.4-152.6°/743 mm), $n_D^{23} = 1.4075$ (lit.[118] $n_D^{25} = 1.4070$). The specific rotation of the active cyanide (in CCl_4) is listed in Table IV (lit.[57] $[\alpha]_{548.1} \leq +7.98°$). The optical rotation of the active cyanide after reisolation by preparative glpc gave the same rotation. Nmr $\tau(CCl_4)$ 7.77 (2H; d; 1-H), 8.0-8.8 (3H; m; 2- and 3-H), 8.93 (3H; d; 2-CH_3), and

9.06 (3H; t; 4-H). I.R. (liq. film) 2970(s), 2940(s), 2880(s), 2860(s), 2240(m), 1460(s), 1425(m), 1380(m), 1350(w), 1345(w), 1155(w), and 970(w) cm^{-1}.

Anal. Calcd. for $C_6H_{11}N$: C, 74.17; H, 11.41. Found: C, 74.08; H, 11.21.

1-Cyano-2-methyl-1-butene and 1-Cyano-2-methyl-2-butene. -- The method of Whyte and Cope [119] was used to synthesize a mixture of these olefins. A benzene solution (150 ml) of methyl ethyl ketone (225 g, 3.1 mol), cyanoacetic acid (245 g, 2.9 mol), glacial acetic acid (90 g, 1.5 mol), and ammonium acetate (46.6 g, 0.6 mol) was heated under a Dean-Stark trap until all of the water had separated. The benzene solvent was removed by distillation and the crude mixture was heated at 145° for 5 hours. The reaction products were then distilled at 80 mm. The distillate was washed with water and then dried over anhydrous sodium sulfate. Redistillation gave 149 g (54%) of a mixture of 1-cyano-2-methyl-1-butene and 1-cyano-2-methyl-2-butene, b.p. 82-84°/50 mm, n_D^{23} = 1.4396. I.R. (liq. film) 2243 ($—CH_2CN$), 2220 ($—\overset{|}{C}=CHCN$), and 1627 ($>C=C<$) cm^{-1}.

Anal. Calcd. for C_6H_9N: C, 75.74; H, 9.54. Found: C, 75.79; H, 9.64.

(±)-1-Cyano-2-bromo-2-methylbutane, 40 -- Anhydrous hydrogen bromide was bubbled through a stirred solution of 31 g (0.33 mole) of a mixture of 1-cyano-2-

methyl-1-butene and 1-cyano-2-methyl-2-butene in 220 ml of ether at 0° for 6 hours. The reaction mixture was washed with water, 5% sodium bicarbonate, water, and dried over anhydrous sodium sulfate. Distillation under reduced pressure gave 35.3 g (61%) of (±)-1-cyano-2-bromo-2-methylbutane, b.p. 70.5-71°/5 mm (lit.[120], b.p. 85-86°/13 mm), n_D^{23} 1.4745 (lit.[120], n_D^{22} 1.4772). I.R. (liq. film) 2980(s), 2940(s), 2920(sh), 2880(s), 2840(sh), 2240(m), 1455(s), 1500(sh), 1430(m), 1415(s), 1385(s), 1345(w), 1315(w), 1300(w), 1285(w), 1240(w), 1150(w), 1115(s), 1110(sh), 1088(m), 1015(w) cm^{-1}. N.m.r. τ (CCl_4) 7.07 (2H; s; 1-H), 8.05 (2H; q; 3-H), 8.15 (3H; s; 2-CH_3), and 8.89 (3H; t; 3-CH_3).

The pure material could be stored for days in the dark at 0°. If left to stand on the bench top for several days it fumed and gave off hydrogen bromide.

Anal. Calcd. for $C_6H_{10}BrN$: C, 40.93; H, 5.72; Br, 45.39; N, 7.96. Found: C, 40.90; H, 5.83; Br, 45.50; N, 7.94.

(+)-1-Cyano-1-bromo-2-methylbutane, 39a. -- A mixture of (+)-1-cyano-2-methylbutane (13.6 g, 0.14 mol), bromine (24.6 g, 0.15 mol) and 2 ml of phosphorus tribromide was heated at 80° for 4 hours. The reaction mixture was allowed to cool to room temperature and then was distilled under reduced pressure (water pump). The distillate was washed with water, 5% sodium bicarbonate,

and water again, and dried over anhydrous magnesium sulfate. Redistillation gave 16.3 g. (66%) of (+)-1-cyano-1-bromo-2-methylbutane, b.p. 94°/25.5 mm, n_D^{25} 1.4644. The specific rotation is given in Table IV. N.m.r. τ (CCl_4) 5.74 (1H; d; 1-H), 8.70-7.90 (3H; m; 2- and 3-H), 8.82 and 8.79 (3H; d and d; 2-CH_3)*, 8.98 and 9.01 (3H; t and t; 3-CH_3)*. I.R. (liq. film) 2960(s), 2935(s), 2880(s), 2860(sh), 2238(m), 1460(s), 1385(s), 1350(w), 1330(w), 1295(w), 1270(w), 1250(w), 1175(s), 1120(w), 970(m), 935(w), 890(m), 880(sh), 800(w), 770(s), 765(sh), 690(s), and 670(s) cm^{-1}.

Anal. Calcd. for $C_6H_{10}BrN$: Calcd. C, 40.93; H, 5.72; Br, 45.39; N, 7.96. Found: C, 40.61; H, 5.84; Br, 45.53; N, 7.91.

(+)-2-Methylbutyl acetate, 42 -- Acetyl chloride (36.5 g, 0.47 mol) was added to a stirred solution of (-)-2-methylbutanol (39.9 g, 0.45 mol), pyridine (43.0 g, 0.54 mol), and 100 ml of Freon 113 over 60 minutes at 0°C. The solution was allowed to stir for another 50 minutes at room temperature and 170 g of an ice-water mixture was added. The organic layer was separated and washed with water, dilute hydrochloric acid, water, aqueous sodium bicarbonate, and water, and dried over anhydrous sodium

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* Chemical shifts and couplings that are reported are for the equal mixture of erythro- and threo-isomers.

sulfate. Distillation gave 52.3 g (88%) of (+)-2-Methylbutyl acetate, b.p. 61.5°/42 mm, n_D^{20} = 1.4020 (lit.[121] b.p. 141-2°, n_D^{20} = 1.4012). The specific rotation of this active acetate was listed in Table VII (lit.[121] $[\alpha]_D^{20}$ = +3.30°). N.m.r. (HA-100) $\tau(CCl_4)$ 9.10 (3H; t; 3-CH_3), 9.10 (3H; d; 2-CH_3), 8.75 (2H; m; 3-H), 8.37 (1H; m; 2-H), 8.05 (3H; s; $COCH_3$), and 6.18 (2H; octaplet; 1-H).

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.57; H, 10.92.

(-)-(R)-2-Bromobutane. -- This compound was prepared by the displacement reaction of (+)-2-butanol with anhydrous hydrogen bromide. A three neck, 200 ml round-bottom flask was fitted with a magnetic stirring bar, a condenser with a gas outlet tube, a thermometer, and a gas inlet bubbler. (+)-2-Butanol (86.0 g, 1.16 mol) was placed in the flask and saturated with anhydrous hydrogen bromide for an hour at -10°, the solution was stirred for an additional hour at room temperature (20°), and was finally heated at 60° for four hours. The organic layer was separated, washed with cold concentrated sulfuric acid, an ice-water mixture, a saturated sodium bicarbonate solution, and dried over anhydrous sodium sulfate. Fractional distillation yielded 134.0 g (84%) of (-)-(R)-2-bromobutane, b.p. 88°/700 mm, n_D^{20} = 1.4370 (lit.[112] b.p. 90-1°/760 mm, $n_D^{19.5}$ = 1.4359). Glpc analysis (10' x 1/8" 10% Carbowax 20M TPA glass column) showed only a single

peak. The nmr, ir, and mass spectra are identical with those of the authentic sample. The specific rotation of the active bromide is listed in Table XVIII (lit.[82] $[\alpha]_D = +39.4°$, $[\alpha]^{20}_{589} = +34.5°$[122,123] for (+)-(S)-2-bromobutane). The active (-)-(R)-2-bromobutane after reisolation by preparative glpc using a 10' x 1/4" glass column packed with 10% Carbowax 20M TPA gave the same rotation.

Instruments

Infrared (IR) spectra were recorded on either a Perkin-Elmer model 421 or a Perkin-Elmer Model 337 recording spectrophotometer. The nuclear magnetic resonance (NMR) spectra are proton spectra. The spectra were obtained on either a Varian Associates A-60, A-56/60, or HA-100 high resolution nmr spectrometer. The rotations were recorded on a Perkin-Elmer model 141 automatic polarimeter. Mass spectra were recorded on a Metropolitan Vickers MS2, an AEI MS12 instrument with an on-line connection to a glpc instrument, or an AEI MS9 high resolution mass spectrometer. Refractive indexes were measured on a Bausch and Lomb refractometer.

Gas Liquid Partition Chromatograph (glpc) Analysis

Throughout the course of this work, two types of glpc columns were used for both analytical and prepa-

Table XVIII

The Specific Rotation of (-)-(R)-2-Bromobutane

λ, mμ	α^{25}_{obs}, 1 dm[a]	$[\alpha]^{25}_{\lambda}$[b]	Opt. Purity[c]
589	-29.08°	-23.20°	
578	-30.38°	-24.23°	
546	-34.59°	-47.58°	58.9%
436	-59.55°	-47.50°	
365	-95.27°	-76.00°	

[a] The rotations measured with neat liquid.

[b] Calculated by using $d^{25} = 1.2536$.

[c] Based on maximum available value, $[\alpha]_D = +39.4°$ (ref. 82).

rative purposes. They were either a 10% Carbowax 20M TPA on Chromosorb PAW or a 10% DEGS on Chromosorb PAW. Only glass columns were used, since some of the products decomposed when metal columns were used. The length and size of the column used are specified in the individual experiments. Analyses were carried out in triplicate. Peak areas were calculated by multiplying the peak height by the peak width at one-half the peak height or by means of a disc integrator or a Hewlett Packard 3380A digital integrator. All the methods used were consistent with each other. The precision was always better than 2%. Glpc response calibration factors ($f_{x/s}$) of the products relative to the standard were obtained by dividing the mole ratio (M_x/M_s) of the product to the added standard by the area ratio (A_x/A_s), which were obtained from a standard product mixture of known composition which was similar to that of the reaction mixture [124]. Under the same glpc conditions, these factors can be used to calculate the number of moles of product formed according to the following equation:

$$f_{x/s} = (M_x/M_s)/(A_x/A_s)$$

Therefore, $$M_x = (f_{x/s})(M_s)(A_x/A_s)$$

Relative mole % of product formed =

$$(M_x/\Sigma M_x)(100\%)$$

General Procedures for Reactions

Reaction ampoules were made of Pyrex tubes joined to 10/30 joints. The ampoules were cleaned with chromic acid solution, water, concentrated ammonium hydroxide, and distilled water, then oven-dried at 120°. In subdued light, the reactants were placed in the ampoules and then degassed by three freeze-thaw cycles at <2μ. After degassing, the ampoules were sealed under vacuum, allowed to thaw and then equilibrated at the desired temperature. The ampoules were irradiated with incandescent lamps for the appropriate reaction time. After irradiation, the reaction mixtures were frozen in liquid nitrogen and subjected to the various isolation and analytical procedures.

Photobromination of (+)-1-cyano-2-methylbutane with tert-butyl hypobromite

A mixture (2 : 1 mole ratio) of (+)-1-cyano-2-methylbutane and tert-butyl hypobromite was sealed in a degassed Pyrex ampoule. The ampoule was thermostatted at 25° and irradiated with a 100 watt incandescent lamp until colorless (4 hours). Glpc analysis of the reaction mixture using an Aerograph 202 gas chromatograph equipped with a 10' x 1/4" 10% Carbowax 20M TPA column (135° isothermal) indicated five monobromo-1-cyano-2-methylbutanes and a small amount (~5%) of a high boiling component, in

addition to tert-butanol and unreacted starting material. GC-Mass spectral analysis of the reaction mixture showed the first five products to be monobrominated cyanides. They were present in the following ratio: 19 : 32 : 39 : 4 : 6. The compounds corresponding to peaks 1, 2, and 3 were isolated by preparative glpc using a 10' x 1/4" 10% DEGS column. Peaks 1 and 2 were identified respectively as 1-cyano-1-bromo-2-methylbutane, 39a, and 1-cyano-2-bromo-2-methylbutane, 40, by a comparison of their glpc retention times, and their ^{1}H nmr and ir spectra with those of authentic samples. Nmr analysis showed the compound corresponding to peak 3 to be 1-cyano-3-bromo-2-methylbutane, 41a. Its specific rotation is listed in Table IV. Nmr*τ(CCl_4) 8.86 and 8.79 (3H; d and d; 2-CH_3), 8.29 and 8.26 (3H; d and d; 3-CH_3), 8.20-7.70 (1H; m; $-\overset{|}{C}H-$), 7.62 and 7.53 (2H; q and q; $-CH_2-$), 5.92 and 5.81 (1H; quintet and octet; $-CHBr-$). IR (in CCl_4) 2245 ($-C\equiv N$).

Anal. Calcd. for $C_6H_{10}BrN$: C, 40.93; H, 5.72; Br, 45.39; N, 7.96. Found: C, 40.99; H, 5.86; Br, 45.36; N, 8.20.

Peaks 4 and 5 presumably corresponded to 1-cyano--2-(bromomethyl)butane and 1-cyano-4-bromo-2-methylbutane respectively. Both of these compounds had parent ions at

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* See footnote page 116.

m/e 175 and 177 ($C_6H_{10}BrN$), peaks at 93 and 95 (CH_2Br) and a base peak at 55 (C_4H_7).

Photobromination of (±)-1-Cyano-2-methylbutane with Molecular Bromine.

The brominations were carried out under a helium atmosphere and were isolated from the air by a dioctylphthalate bubbler [5]. Mixtures of (±)-1-cyano-2-methylbutane and molecular bromine (under a helium atmosphere) were placed in a thermostated Pyrex water bath; and were irradiated using incandescent light. The solution, which was continually stirred, was irradiated until the bromine color had been discharged. A copious evolution of hydrogen bromide was observed to bubble out through the dioctylphthalate. The reaction mixture was washed with ice cold aqueous [redacted]osulfate solution, 5% sodium bicarbonate and drie[redacted]ydrous sodium sulfate. The reaction mixtures [redacted]bjected to glpc analysis, using the 10% DEGS colum[redacted]he major product (>90%) was 1-cyano-1-bromo-2-methylbut[redacted] which was isolated and identified by comparison of [redacted] glpc retention time, and nmr and ir spectra with those [redacted] an authentic sample. The minor products, 1-cyano-2-bromo-2-methylbutane and 1-cyano-3-bromo-2-methylbutane were identified by comparison of their glpc retention times with those of authentic samples on two columns (DEGS and Carbowax 20M TPA). The conditions used and the

relative yields of products are listed in Table II (reactions 1-4).

The brominations were repeated in degassed, sealed Pyrex ampoules. The solutions were irradiated until the bromine color was discharged, the tubes were opened, and a known amount of chlorobenzene and o-dichlorobenzene was added. The reaction mixture was washed with ice cold aqueous thiosulfate solution, saturated sodium bicarbonate, and dried over anhydrous sodium sulfate. The mixture was then subjected to glpc analysis using a 10% Carbowax 20M TPA on 60-80 mesh Chromosorb PAW, 10 x 1/8" glass column (135° isothermal). The absolute yield of the products was obtained, Table II (reactions 5-7), by using standard calibration factors for the response of the products and starting material vs chlorobenzene and o-dichlorobenzene.

Photobromination of (+)-1-Cyano-2-methylbutane with NBS and Molecular Bromine in Carbon Tetrachloride.

The reactions were carried out in degassed, sealed Pyrex ampoules with constant shaking (see Table III, reaction 1-2) or with continual stirring (see Table III, reaction 3-6). The thermostatted reaction mixtures were irradiated through the side of the Pyrex water bath with 2 x 140 watt Hanovia Utility lamps for 68-365 hours. At the end of the reaction, solid NBS remained in the bottom of the reaction vessel. The reaction mixtures were

washed with ice cold aqueous sodium thiosulfate solution, water, saturated sodium bicarbonate, water again, and dried over anhydrous sodium sulfate, and then analyzed by glpc using the 10' x 1/8" glass column packed with 10% Carbowax 20M TPA. The results and reaction conditions are given in Table III.

Reaction mixtures (Table III, reaction 3-6) were distilled under reduced pressure (60 mm) to remove the carbon tetrachloride solvent and the unbrominated starting material (37-40°/8 mm); and finally the fraction boiling at 52-53°/1 mm was collected and was found by glpc analysis to be primarily 1-cyano-2-bromo-2-methylbutane, 40. This fraction was redistilled and collected at 48-49°/1.2 mm. Glpc analysis of the redistilled fraction showed the presence of small amounts of (+)-1-cyano-1-bromo-2-methylbutane (1.4%), 39a, and (+)-1-cyano-3-bromo-2-methylbutane (7.0%), 41a, see Fig. 1. The rotation of this mixture is listed in Table VI. A synthetic mixture of 1.36% of 39a, 6.95% of 41a, and 91.69% of 40 was made and its observed rotation was compared with that of the material collected by distillation from the reactions, see Table VI. The glpc analysis of the synthetic mixture was also compared to these isolated fractions, see Fig. 1.

The reisolated unreacted starting material was purified by preparative glpc on 10' x 1/4" glass column packed with 10% Carbowax 20M TPA and its specific rotation

was compared to the starting material, 38a, see Table V.

Small, variable, amounts of olefins (~3%) were formed during the analysis and were shown to be formed from the decomposition of 40, since the glpc isolated material when reanalyzed still showed these small amounts of olefins. The olefins had retention times identical with those of a synthetic mixture of 1-cyano-2-methyl-1-butene and 1-cyano-2-methyl-2-butene. Compound 40, isolated by glpc, was shown to be racemic.

The absolute yield was determined for the reaction (Table III, reaciton 6) by the analysis of the mixture, after the addition of known amounts of chlorobenzene and o-dichlorobenzene. The extent of reaction was determined by iodometric titration. The reaction mixture was washed with water, sodium bicarbonate solution, again with water, and dried over anhydrous sodium sulfate. The reaction mixture was then analyzed by glpc (10% Carbowax 20M TPA, 10' x 1/8" column). The absolute yield of the three monobromides (Table III, reaction 6) was found to be 29% based on the active bromine consumed (60%).

Photobromination of (+)-2-Methylbutyl Acetate with NBS and Molecular Bromine in Freon 11.

(+)-2-Methylbutyl acetate (6.50 g, 0.05 mol), NBS (9.00 g, 0.05 mol), and bromine (6.30 g, 0.04 mol), and solvent, Freon 11 (24 g), were placed in a Pyrex

reaction flask containing a teflon magnetic stirring bar, the solution was degassed and the flask sealed. The reaction mixture was then equilibrated in a 16° thermostated water bath and irradiated through the water bath with a GE sunlamp (275 watt) for 2 hours. The reaction was worked up by washing with ice-cold aqueous sodium bisulfite solution to remove any unreacted bromine and NBS and extracted with Freon 11. The Freon solution was washed with water, aqueous sodium bicarbonate, and dried over anhydrous sodium sulfate. Glpc analysis of the products after adding o-dichlorobenzene as standard showed that the major components were 2-bromo-2-methylbutyl acetate, 43, (91% yield based on starting material consumed (11% conversion)), erythro- and threo-3-bromo-2-methylbutyl acetate (3.4%), 44a and 44b, as well as erythro- and threo-2,3-dibromo-2-methylbutyl acetate (1.8%), 45a and 45b. Two other products were not identified; presumably they were monobrominated acetates judging from their glpc retention times. The reaction mixture was fractionated through a 6" Vigreux column to remove solvent and unbrominated starting acetate (49.5°/22 mm). Finally the remaining residue was subjected to preparative glpc to isolate the products using a 6' x 1/4" 10% Carbowax 20M TPA column. The reisolated (+)-2-methylbutyl acetate was shown not to have racemized during the reaction (see Table VII). The isolated major

product was identified as 2-bromo-2-methylbutyl acetate, 43, and was racemic (see Table VII): Nmr $\tau(CFCl_3)$ 8.95 (3H; t; 3-CH_3), 8.33 (3H; s; 2-CH_3), 8.19 (2H; q; 3-H), 7.98 (3H; s; $COCH_3$), and 5.83 (2H; s; 1-H). I.R. (CCl_4) 2970(s), 2930(s), 2878(s), 1740(s), 1455(s), 1380(s), 1220(s), 1125(w), 1105(m), 1040(s), 910(w), 890(w), 635(w), and 600(w) cm^{-1}. The mass spectrum of 43 did not give a parent peak, but gave fragment ions corresponding to this compound at m/e 181, 179 (P-Et, 1 : 1 ratio), 151, 149 (P-OAc, 1 : 1 ratio), 137, 135 ($C_4H_8Br^+$, 1 : 1 ratio), 129 (P-Br), 128 (P-HBr), 86 ($C_5H_{10}O^+$), 69 ($C_5H_9^+$), 60 ($CH_3\overset{+}{C}(OH)_2$), 55 ($C_4H_7^+$), and 43 (CH_3CO^+, base peak). A fraction of monobrominated product (3.4%) was identified as an equal molar mixture of erythro- and threo-3-bromo-2-methylbutyl acetate, 44a and 44b, based on nmr and mass spectral data (see Results and Discussion). The nmr spectrum recorded using CCl_4 solvent had spectral data as follows: $\tau(CCl_4)$ 9.00 (3H; t; 2-CH_3), 8.32 (3H; d; 3-CH_3), 7.97 (3H; s; $COCH_3$), 8.2-7.9 (1H; m; 2-H), and 6.4-5.6 (3H; m; 1-H and 3-H). A complete split spectrum of these erythro- and threo-diasteromers was obtained by replacing the solvent with perdeuterated benzene (C_6D_6). Its spectral data is as follows: $\tau(C_6D_6)$ 9.14 and 9.11 (3H; d and d; 2-CH_3), 8.53 and 8.51 (3H; d and d; 3-CH_3), 8.21 and 8.20 (3H; s and s; $COCH_3$), 8.4-7.7 (1H; m; 2-H), 6.4-5.8 (3H; m; 1-H and 3-H).

The two isolated dibromides were identified as erythro-2,3-dibromo-2-methylbutyl acetate, 45a, and threo-2,3-dibromo-2-methylbutyl acetate, 45b, based on nmr spectral data. One of the isomers 45a or 45b had nmr data as follows: τ ($CDCl_3$) 8.19 (3H; s; 2-CH_3), 8.09 (3H; d; 3-CH_3), 7.86 (3H; s; $COCH_3$), 5.58 (2H; s; 1-H), and 5.42 (1H; q; 3-H). Another isomer, 45b or 45a, had nmr spectral data as follows: τ ($CDCl_3$) 8.11 (3H; s; 2-CH_3), 8.10 (3H; d; 3-CH_3), 7.88 (3H; s; $COCH_3$), 5.64 (1H; q; 3-H), and 5.53 (2H; s; 1-H).

The optical purity of 2-bromo-2-methylbutyl acetate, 43, was determined by nmr spectroscopy, using a Freon 11 solution of the compound 43 isolated from reaction mixture (0.5 ml of 0.4 M compound 43/Freon 11/TMS) and the optically active shift reagent, tris-(3-(heptafluoropropylhydroxymethylene)-d-camphorato)europium (III) (100 mg). The result showed that the compound 43 contained equal amounts of d- and l-enantiomer (racemic) in agreement with the polarimetry result (see Table VII). An nmr spectrum was also recorded using inactive shift reagent, Eu(fod)$_3$-d_{30} (tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octadionato)europium (III), see Table VIII.

Photobromination of (-)-(R)-2-bromobutane with Molecular Bromine.

The reaction mixtures, a desired mole ratio

of (-)-(R)-2-bromobutane to molecular bromine, were degassed by the freeze-thaw method and sealed in 10 ml Pyrex reaction ampoules, and the ampoules were thermostatted in the absence of light at 17° (or the desired temperature). The vapor space in the ampoule was covered with aluminum foil, and the liquid phase was irradiated with a 200 watt incandescent lamp. The ampoules were removed after complete reaction or prior to completion and cooled in liquid nitrogen. The reaction mixtures were subjected to work up procedures (carried out at 0°) by diluting with Freon 11 and washing successively with ice-cold sodium bisulfite, water, saturated sodium bicarbonate, water again, and then dried over anhydrous sodium sulfate. The product composition was determined by glpc analysis (10' x 1/8" 10% Carbowax 20M TPA) of the reaction mixture with an added known amount of standard, chlorobenzene. The results are listed in Table IX. The products were isolated by preparative glpc (6' x 1/4" 10% Carbowax 20M TPA) of the concentrated reaction mixture. They were identified by the comparison of their glpc retention times, nmr, ir, and mass spectra with those of the authentic materials. 2,2-Dibromobutane was characterized by comparing its refractive index, $n_D^{20} = 1.5017$ (lit.[125] $n_D^{20} = 1.5015$), with that of the previously reported material and by its spectral data. Nmr $\tau(CCl_4)$ 8.76 (3H; t; 3-CH_3), 7.60 (2H; q; 3-H), 7.43

(3H; s; 1-H). It had mass spectral data as follows: m/e (70 eV) 214, 216, 218 (parent peaks, 1 : 2 : 1 ratio), 185. 187, 189 (P-Et, 1 : 2 : 1 ratio), 135, 137 (P-Br, 1 : 1 ratio). The optical rotation of the glpc isolated (-)-(R)-2-bromobutane, (+)-2,3-dibromobutane, and (+)-2,2,3-tribromobutane were measured (see Table X).

Control Reaction of (-)-(R)-2-Bromobutane with Molecular Bromine in the Absence of Light.

(-)-(R)-2-Bromobutane (7.88 g, 57.5 mmol), $[\alpha]_{365}^{25}$ = -76.00° (neat), and molecular bromine (3.08 g, 19.2 mmol) were placed in a reaction ampoule. The ampoule was degassed, sealed under the vacuum, and protected from light with foil. The ampoule was then subjected to the photoinitiated conditions (at 17° for 24 hours). Analysis of the reaction mixture after work up showed no product was formed. The starting bromide was isolated by preparative glpc using 6' x 1/4" 10% Carbowax 20M TPA column. The recovered (-)-(R)-2-bromobutane had $[\alpha]_{365}^{25}$ = -76.01° (neat).

Control Reaction of (-)-(R)-2-Bromobutane with Molecular Bromine and Hydrogen Bromide in the Absence of Light.

(-)-(R)-2-Bromobutane (3.62 g, 26.4 mmol), $[\alpha]_{365}^{25}$ = -76.00° (neat), and molecular bromine (1.32 g, 8.3 mmol) were placed in a reaction ampoule and degassed.

Hydrogen bromide (8.3 mmol), triply distilled, was then introduced into the reaction ampoule. The ampoule was degassed, sealed, and subjected to the reaction conditions (17°, 22.1 hr) in the absence of light. The (-)-(R)-2-bromobutane, $[\alpha]_{365}^{25}$ = -75.73° (neat), recovered by preparative glpc (6' x 1/4" 10% Carbowax 20M TPA glass column), showed only 0.4 % racemization under these reaction conditions.

Control Reaction of (-)-2,3-Dibromobutane with Molecular Bromine in the Absence of Light.

Partially resolved (-)-2,3-dibromobutane (6.42 g, 29.7 mmol), α_{365}^{25} = -29.61° (neat), n_D^{20} = 1.5150, and molecular bromine (1.58 g, 9.88 mmol) were placed in a 10 ml Pyrex reaction ampoule, degassed and sealed. The ampoule, protected from light with foil, was placed in a 17° thermostated water bath for 22 hours. The reaction products were then isolated in the usual manner. Glpc analysis of the reaction mixture showed only traces of a compound having the same retention time as 2,2,3-tribromobutane. Fractional distillation of this reaction mixture under reduced pressure yielded (-)-2,3-dibromobutane, α_{365}^{25} = -28.81° (2.7% Race., neat) and n_D^{20} = 1.5150.

Control Reaction of (-)-2,3-Dibromobutane with Molecular Bromine and Hydrogen Bromide in the Absence of Light.

Partially resolved (-)-2,3-dibromobutane (6.15 g, 28.5 mmol), α_{365}^{25} = -29.03° (neat), n_D^{20} = 1.5150, and molecular bromine (3.33 g 20.8 mmol) were placed in a 10 ml Pyrex reaction ampoule, degassed, and hydrogen bromide (24.6 mmol) was distilled into the ampoule from a vacuum line. The reaction tube was degassed and sealed under vacuum. The ampoule, protected from light, was subjected to the photoinitiation conditions (at 17° for 22 hours). After isolation, glpc analysis of the reaction mixture showed only traces of 2,2,3-tribromobutane formed. No meso-2,3-dibromobutane was detected. The recovered (-)-2,3-dibromobutane (by fractional distillation) had a rotaion α_{365}^{25} = -25.46 (12.3% Rac., neat) and n_D^{20} = 1.5151.

Photobromination of (-)-(R)-2-Bromobutane with Br_2-NBS Mixture in Freon 11 as Solvent.

All reactions were carried out in heterogeneous Freon 11 solution with continuing stirring. Reaction mixtures, consisting of a desired mole ratio of substrate and brominating agents as well as Freon 11 solvent, were degassed and sealed under vacuum in Pyrex reaction flasks. Photolysis was conducted at the desired temperature by irradiation with a 200 watt incandescent lamp for a time sufficient to give about 30% conversion of the starting

bromide. After reaction, the reaction mixtures were isolated as described for the molecular bromine brominations, and analyzed by glpc on a 10' x 1/8" 10% Carbowax 20M TPA glass column. The results and conditions are listed in Table XIV. The unreacted starting material, 2,3-dibromobutane (dl-fraction), and 2,2,3-tribromobutane were isolated by preparative glpc using a 6' x 1/4" 10% Carbowax 20M TPA glass column. Their rotations were measured, and the results are listed in Table XV.

Vapor Phase Bromination of 2-Bromobutane with Molecular Bromine.

By means of a syringe, solutions of 2-bromobutane (19.9×10^{-5} mol) and molecular bromine (6.4×10^{-5} mol) were introduced into 50 ml reaction ampoules (this transfer technique was found to be accurate to <3% error, by weight). The reaction tubes were degassed and sealed. They were covered with foil and the reactants were allowed to vaporize and equilibrate to room temperature. The reaction tubes were then thermostated at the desired temperature (20°-146°) for 10 minutes and photolized with a 200 watt incandescent lamp. At 60°-146° reaction temperature, the bromine color was rapidly discharged (45 sec. at 60°, 30 sec. at 100°, and 20 sec. at 146°). After 3 minutes irradiation, they were cooled in liquid nitrogen. In the case of the reaction carried out at 20°, the bromine

color was discharged after 18 minutes irradiation time and a portion of the reactants were not in the vapor phase. After the reaction, aliquots of a chlorobenzene/Freon 113 solution (2 ml, 2.27 x 10^{-5} mol), Freon 113 solvent (2 ml), and saturated aqueous sodium bicarbonate (2 ml) were each added to the frozen mixture. The resulting solutions were allowed to warm to room temperature and mixed by shaking. The organic layers were separated and dried over anhydrous sodium sulfate. The reaction mixtures were then analyzed by glpc using a 10' x 1/4" 10% Carbowax 20M TPA glass column. The percentage yield of the dibromides (2,2-, meso- and dl-2,3-dibromobutanes) formed (based on bromine consumed) are listed in Table XII. The glpc chromatograms showed a multitude of products. By a comparison of their glpc retention times with those of the authentic materials, they showed the presence of 1-bromo-2-butene, 1,4-dibromo-2-butene, as well as an unidentified polybromide (its retention time is similar to that of the 1,2,3-tribromobutane). Only traces of 2,2,3-tribromobutane were detected. Several other products were not further characterized.

Photobromination of 2-Bromobutane (50.57% bromine-79 and 49.43% bromine-81) with Isotopically Enriched Molecular Bromine-81 (2.19% Bromine-79 and 97.81% bromine-81).

A degassed break-seal containing isotopically

enriched bromine-81 (86.0 mg, 5.31 μmol) was attached to a break-seal Pyrex reaction ampoule containing 2-bromobutane (215.5 mg, 15.73 μmol). The reaction ampoule was degassed and the break-seal containing the bromine-81 was broken, and the bromine was allowed to distill into the reaction ampoule containing frozen 2-bromobutane. The empty bromine-81 side arm was sealed off and the system was again degassed, and then sealed off from the vacuum line. The vapor phase in the ampoule was shielded with foil, and the liquid phase was photolyzed with a 200 watt incandescent lamp at 16°. After 24 hours the bromine color had been discharged. To the break-seal of the reaction ampoule was attached a trap to trap distillation apparatus. The hydrogen bromide produced during the reaction was distilled on a vacuum line into a tube containing cyclohexene (200 μl). When the transfer of hydrogen bromide was complete, the tube containing cyclohexene was sealed off from the reaction ampoule. The cyclohexene and hydrogen bromide were allowed to react at room temperature with constant shaking for 12 hours, and the cyclohexyl bromide formed was collected by preparative glpc on a 10% Carbowax 20M TPA, 10' x 1/4" glass column. The ampoule containing the reaction mixture was frozen in liquid nitrogen and opened. The reaction mixture was allowed to warm up slowly to room temperature and a small amount of powdered sodium bicarbonate was carefully added

to remove any undistilled hydrogen bromide. The reaction mixture was then subjected to preparative glpc on a 10' x 1/4" glass co[illegible]cked with 10% Carbowax 20M TPA. The isolated 2-[illegible]ne, 2,2-, meso-2,3-, dl-2,3-, 1,2-dibromobuta[illegible] 2,2,3-tribromobutane were analyzed by mass s[illegible]rom[illegible] (AEI MS-9 mass spectrometer) for their brom[illegible] co[illegible]nts. The mass spectra were taken by scanning at [illegible]he [illegible]propriate peak region (see Table XVI) for at least [illegible] times at slow scanning speed (70 eV). The results a[illegible] listed in Table XVI.

In [illegible] case of 2,2,3-tribromobutane (parent peaks at m/e 2[illegible] 294, 296, and 298), it was impossible to measure the [illegible]ak intensity at m/e 292, since it was so small (<1 mm). Therefore, it was calculated from the relative peak hei[illegible]t ratio (at m/e 294/292) which could be obtained at m[illegible]um amplification its peak intensity was still only [illegible]m in height (see Table XVI).

In the case of 1,2-dibromobutane (parent peaks at m/e 214, 216, and 218), the peak at m/e 214 (<3 mm) was small. Its peak height was measured using the x10 scaling factor produced by the recorder (see Table XVI).

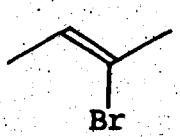
Resolution of dl-2,3-Dibromobutane with Brucine.

Preliminary experiments on the resolution of dl-2,3-dibromobutane with brucine using pentane or dioxane as solvents were only partially successful [126].

In all cases, only a small rotation was observed.

A method, similar to that reported by Skell [7], a one cycle resolution, was used and yielded (-)-2,3-dibromobutane of high optical purity. dl-2,3-Dibromobutane was mixed with brucine in approximately a 2 : 1 mol ratio. The resulting thick paste solidified and was allowed to stand for several days at room temperature. The solid was then broken up and subjected to vacuum distillation at room temperature. Two fractions were collected after 48 hours and 76 hours standing. Analysis of the distillate showed that it contained only the dehydrobromination product, trans-2-bromo-2-butene, and 2,3-dibromobutane. The dibromide was found to be optically active with high levorotatory enrichment. Furthermore, the results showed that the optical rotation increased with increasing contact time between brucine and the dibromide (i.e. with increasing formation of the dehydrobromination product). After distillation, the remaining solid was dissolved in 2 N sulfuric acid and extracted with Freon 11. The dibromide isolated from this Freon 11

$$(\pm)\text{-}CH_3\underset{\underset{Br}{|}}{CH}\text{-}\underset{\underset{Br}{|}}{CH}\text{-}CH_3 + \text{Brucine} \xrightarrow[\text{Temp.}]{\text{Room}} (-)\text{-}CH_3\underset{\underset{Br}{|}}{CH}\text{-}\underset{\underset{Br}{|}}{CHCH_3}$$

$$+ \quad \underset{Br}{\text{  }} \quad + \text{Brucine}\cdot\text{HBr}$$

solution was shown to be also levorotatory with a larger rotation than that of the distillate (see Table XIX). It had been claimed that the dextrorotatory enantiomer could be isolated from the solid brucine where it was trapped as an inclusion complex[7]. The dextrorotatory compound was reported and no olefin formation was claimed[7]. In our hands no dextrorotatory enantiomer could be obtained from the remaining solid brucine.

When dl-2,3-dibromobutane and brucine (2 : 1) were stirred in pentane solvent at room temperature for 48 hours, glpc analysis of the reaction mixture showed <1% of the dehydrobromination product. The recovered dibromide gave only a slightly negative rotation. On the other hand, if the resolution was carried out with no solvent for the same period, and pentane added to extract the products, glpc analysis showed that the pentane solution contained about 10% of the dehydrobromination product. A reaction was left to stand for 70 hours, and the resulting solid was broken up and 150 ml of pentane was added and stirred for another two hours. Analysis of this pentane solution showed that it contained 24.3% trans-2-bromo-2-butene. The observed rotation of recovered 2,3-dibromobutane is listed in Table XX. If the assumption was made that the resolution was accomplished by specific destruction of the d-enantiomer (24.3%), then the optically pure l-enantiomer should have

Table XIX

The Observed Rotation of (-)-2,3-Dibromobutane Obtained from Partial Resolution of dl-2,3-Dibromobutane with Brucine[a]

λ, mμ	α_D^{25}[b] Fraction I (48 hr.)[c]	Fraction II (76 hr.)[c]	Recovered from remaining solid (112 hr.)[c]
589	-11.35°	-13.15°	-17:01°
578	-11.84°	-13.68°	-17.74°
546	-13.42°	-15.50°	-20.11°
436	-22.48°	-25.96°	-33.70°
365	-35.04°	-40.45°	-52.60°

[a] Using 2 : 1 ratio (RBr : brucine)

[b] Observed rotations measured in neat liquid (1dm).

[c] Standing time after mixing.

Table XX

Observed Rotation of (-)-2,3-Dibromobutane After 24.3% Destruction Product Formed (70 hr. standing)

λ, mμ	α^{25}_{365} [a]
589	-11.84°
578	-12.36°
546	-14.05°
436	-23.60°
365	-37.05°

[a] Observed rotation measured in neat liquid (ldm).

a minimum observed rotation of $\alpha_{365}^{25} = -152°$ or a specific rotation of $[\alpha]_{365}^{25} = -84.9°$ (calcd, using d = 1.79).

The structural assignment of the destruction product was based upon the comparison of its refractive index and nmr spectrum of those of the authentic material. It was characterized as trans-2-bromo-2-butene (collected by preparative glpc, 6' x 1/4" 10% Carbowax 20M TPA glass column), $n_D^{25} = 1.4568$ (lit.[113] $n_D^{25} = 1.4565$), nmr[127] (CCl_4) 8.31 (3H; q of d; 3-CH_3), 7.74 (3H; quintet; 1-H), and 4.35 (1H; q of q; 3-H).

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APPENDIX

Determination of the Bromine Content and the Isotopic Abundances of the Two Bromine Atoms of the Dibromides in the Bromination of 2-Bromobutane with Isotopically Enriched Bromine-81.

Consider a dibromide consisting of two bromine atoms with the isotopic abundances of (a,b) and (a',b'), where a and a' are the relative abundances of bromine-79, b and b' are those of bromine-81, and a + b = a' + b' = 1. Then the mass spectrum for an ion containing two bromine atoms gives three peaks, the intensities of which may be calculated by the product of (a + b)(a' + b'). They are expressed as follows (e.g., at the parent peaks of the dibromobutanes):

m/e	214 ($C_4H_8Br_2^{79}$)	216 ($C_4H_8Br^{79}Br^{81}$)	218 ($C_4H_8Br_2^{81}$)
Peak Intensity	aa'	ab' + a'b	bb'
Symbolized as	r	q	p

From the expression, if a dibromide produced by a direct substitution of 2-bromobutane (50.57% bromine-79 and

49.43% bromine-81) with isotopically enriched bromine-81 (2.19% bromine-79 and 97.81% bromine-81), the dibromide would have a peak height ratio at the parent peaks 214 : 216 : 218 = 1 : 45.6 : 43.7 with a bromine content of 26.38% bromine-79 and 73.62% bromine-81.

The bromine content of the dibromides may be easily determined from the observed mass spectral peak intensities, it is expressed by equation 1.

$$\text{Since, Bromine-79 fraction} = 0.5\left(\frac{a}{a+b} + \frac{a'}{a'+b'}\right)$$

$$= \frac{0.5\,[a(a'+b') + a'(a+b)]}{(a+b)(a'+b')}$$

$$= \frac{0.5[2aa' + (ab' + a'b)]}{aa' + (ab' + a'b) + bb'}$$

$$= \frac{aa' + 0.5\,(ab' + a'b)}{aa' + (ab' + a'b) + bb'}$$

$$= \frac{r + 0.5\,q}{r + q + p}$$

Therefore,

$$\left.\begin{aligned} \text{bromine-79\%} &= \frac{r + 0.5\,q}{r + q + p} \times 100\% \\ \text{bromine-81\%} &= 100\% - \text{bromine-79\%} \end{aligned}\right\} \quad \ldots\ldots 1$$

The isotopic abundances of each of the two bromine atoms of the dibromides may also be determined. The intensities of the peaks at m/e 214 and 216 relative to 218 are given by equations 2 and 3 respectively.

$$m = \frac{r}{p} = \frac{aa'}{bb'} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots 2$$

$$n = \frac{q}{p} = \frac{ab' + a'b}{bb'} = \frac{a}{b} + \frac{a'}{b'} \quad \ldots\ldots\ldots\ldots\ldots\ldots 3$$

Multiplying equation 3 by $(\frac{a}{b})$ and substituting for $(\frac{aa'}{bb'})$ from equation 2 and rearranging gives the quadratic equation 4 or 4a. Multiplying equation 3 by $(\frac{a'}{b'})$ instead

$$(\frac{a}{b})^2 - \frac{q}{p}(\frac{a}{b}) + \frac{r}{p} = 0 \quad \ldots\ldots\ldots\ldots\ldots\ldots 4$$

or

$$(\frac{a}{b})^2 - n(\frac{a}{b}) + m = 0 \quad \ldots\ldots\ldots\ldots\ldots\ldots 4a$$

of by $(\frac{a}{b})$ gives the same expression as 4 and 4a with $(\frac{a'}{b'})$ instead of $(\frac{a}{b})$. The bromine-79/bromine-81 ratio of the two bromine atoms is therefore given by the two roots (equation 5) of this quadratic equation. The calculated results for the dibromides are listed in Table XVI.

$$(\frac{a}{b}) = \frac{n \pm \sqrt{n^2 - 4m}}{2} \quad \ldots\ldots\ldots\ldots\ldots\ldots 5$$

To determine the amount of the vicinal dibromides (1,2-, meso- and dl-2,3-dibromobutanes) that were formed by the elimination-readdition process, it was assumed that the rate of the formation of the vicinal dibromides is constant relative to that of the 2,2-dibromobutane*. Consequently, the vicinal dibromides that was formed by direct

---

* The assumption that the relative rates of product formation are constant must only be taken as an approximation and the value for E must be treated as such.

substitution had the same bromine content as 2,2-dibromobutane (i.e. 29.49% bromine-79 and 70.51% bromine-81, see Table XVI), while the vicinal dibromides formed from the addition of bromine to olefin had the same isotopic abundance as the second bromine atom introduced in 2,2-dibromobutane (i.e., 9.75% bromine-79 and 90.25% bromine-81, see Table XVI). If the fraction of vicinal dibromide produced from olefin was "E", then the experimentally observed total bromine-79 content of the vicinal dibromides (see Table XVI) may be given by equation 6. For example, in the case of dl-2,3-dibromobutane, the total bromine-79

$$29.49\ (1 - E) + 9.75\ E = \text{Total bromine-79 content of the vicinal dibromide} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ 6$$

content is 21.61%, then

$$29.49\ (1 - E) + 9.75\ E = 21.61 \qquad \text{whence } E = 0.40$$

Determination of the Bromine Content and the Isotopic Abundances of the Three Bromine Atoms of the 2,2,3-Tribromobutane.

Similar to the analysis of the dibromides, if the three bromine atoms of 2,2,3-tribromobutane had the relative isotopic abundances of (a,b), (c,d), and (e,f) respectively, where a, c, and e are the relative abun-

dances of bromine-79 and b, d, and f are those of bromine-81, and a + b = c + d = e + f = 1. Then the mass spectral peak intensities at the parent peaks of 2,2,3-tribromobutane may be expressed as follows:

m/e	292 $C_4H_7Br_3^{79}$	294 $C_4H_7Br_2^{79}Br^{81}$	296 $C_4H_7Br^{79}Br_2^{81}$	298 $C_4H_7Br_3^{81}$
peak Intensity	ace	bce+ade+acf	bde+bcf+adf	bdf
Symbolyzed as	s	r	q	p

The bromine content of the tribromide may be, therefore, expressed by equation 7.

Since Bromine-81 fraction

$$= \frac{1}{3}\left(\frac{b}{a+b} + \frac{d}{c+d} + \frac{f}{e+f}\right)$$

$$= \frac{(bdf) + \frac{2}{3}(bde + bcf + adf) + \frac{1}{3}(bce + ade + acf)}{(ace) + (bce + ade + acf) + (bde + bcf + adf) + (bdf)}$$

$$= \frac{p + \frac{2}{3}q + \frac{1}{3}r}{p + q + r + s}$$

$$\text{Therefore, bromine-81\%} = \frac{p + \frac{2}{3}q + \frac{1}{3}r}{p + q + r + s} \times 100\%$$

$$\text{bromine-79\%} = 100\% - \text{bromine-81\%} \qquad \ldots 7$$

The cubic equation for solving the bromine isotopic abundances of the 2,2,3-tribromobutane may be derived as follows.

Since, $$\frac{q}{p} = \frac{bde + bcf + adf}{bdf} = \frac{a}{b} + \frac{c}{d} + \frac{e}{f} \quad \ldots\ldots\ldots\ldots 8$$

$$\frac{r}{p} = \frac{bce + ade + acf}{bdf} = \frac{ce}{df} + \frac{ae}{bf} + \frac{ac}{bd} \quad \ldots\ldots\ldots 9$$

rearrangement of eq. 9 gives

$$\left(\frac{ae}{bf} + \frac{ac}{bd}\right) = \frac{r}{p} - \frac{ce}{df} \quad \ldots\ldots\ldots\ldots\ldots\ldots 9a$$

Multiplying eq. 8 by $\left(\frac{a}{b}\right)$ gives

$$\left(\frac{a}{b}\right)^2 + \left(\frac{ac}{bd} + \frac{ae}{bf}\right) = \frac{q}{p}\left(\frac{a}{b}\right) \quad \ldots\ldots\ldots\ldots\ldots 10$$

and substituting eq. 9a into eq. 10 gives

$$\left(\frac{a}{b}\right)^2 - \frac{q}{p}\left(\frac{a}{b}\right) + \frac{r}{p} - \frac{ce}{df} = 0 \quad \ldots\ldots\ldots\ldots\ldots 11$$

Multiplying eq. 11 by $\left(\frac{a}{b}\right)$ gives

$$\left(\frac{a}{b}\right)^3 - \frac{q}{p}\left(\frac{a}{b}\right)^2 + \frac{r}{p}\left(\frac{a}{b}\right) - \frac{ace}{bdf} = 0$$

Therefore

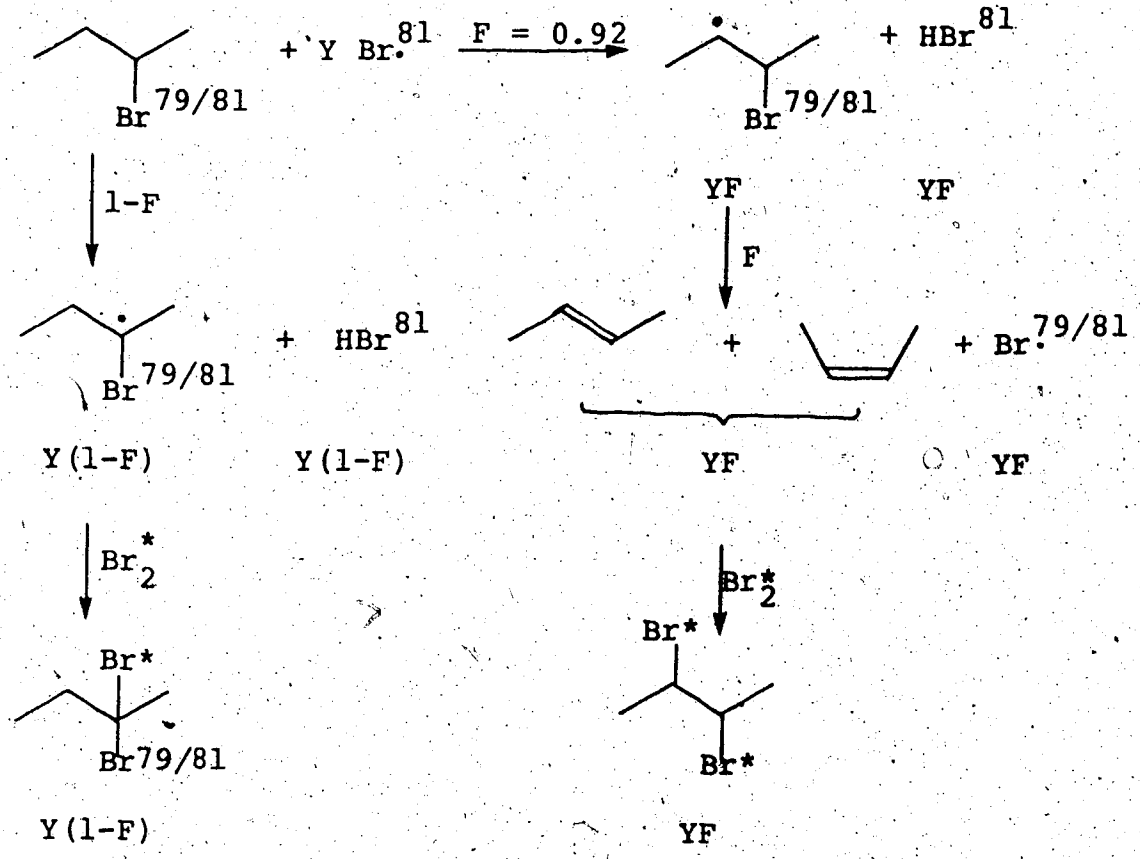
$$\left(\frac{a}{b}\right)^3 - \frac{q}{p}\left(\frac{a}{b}\right)^2 + \frac{r}{p}\left(\frac{a}{b}\right) - \frac{s}{p} = 0 \quad \ldots\ldots\ldots\ldots 12$$

By substituting the mass spectral peak intensities at the parent peaks into the cubic equation 12, three roots of this equation may be obtained, which correspond to the isotopic ratio (bromine-79/bromine-81) of each of the three atoms of 2,2,3-tribromobutane.

Simulation of the Bromination of 2-Bromobutane with Isotopically Enriched Molecular Bromine-81 for the Elimination-Readdition Mechanism.

The reaction of 2-bromobutane (50.57% bromine-79 and 49.43% bromine-81) with isotopically enriched bromine-81 (2.19% bromine-79 and 97.81% bromine-81) was simulated as shown in Scheme XI. Only the formation of 2,2-dibromo-

Scheme XI



butane, 2,3-dibromobutanes, and hydrogen bromide was considered. In each step, Y moles of Br· attack the molecule (2-bromobutane), and of these a fraction F abstracts the

hydrogens at 3-position and 1-F abstracts the hydrogen at 2-position. The 3-bromo-2-butyl radical so formed eliminates a bromine atom to give the two 2-butenes (100% elimination). The butenes then add bromine (from the scrambled bromine pool) to form the two 2,3-dibromobutanes. The amount of each product formed in each step is given in the scheme.

The program assumes that the value of F is constant with percentage reaction. The value for F was calculated as 0.92 from the data in Table IX (reaction 6). The reaction was simulated in 1000 steps, i.e. the value of Y was set at 0.001.

In each step, the $Br^{79/81}$ (YF moles) that was eliminated was scrambled with the bromine pool, P, prior to any further reaction, and the new bromine-79 content, "B", of the new bromine pool was determined (equation 13).

$$"B" = \frac{B \times P + 0.5057 \times Y \times F}{P + Y \times F} \quad \ldots\ldots\ldots\ldots 13$$

The bromine content in each of the products formed in this step was then calculated and the results accumulated. If the bromine-79 content of the 2,3-dibromobutanes was V , then the new bromine-79 content will be "V" = V + B, while for the 2,2-dibromobutane, if the bromine-79 content had been EN, then the new bromine-79 content will be as follows.

"EN" = EN + (0.5057 + B)/2

The program is listed below.

```
      IMPLICIT REAL*8(A-H,O-Z)
      B=0.0219
      V=0.0
      EN=0.0
      Y=0.001
      F=0.92
      P=2.0
      DO 1 L=1,1000
      B=(B*P+Y*F*0.5057)/(P+Y*F)
      V=V+B
      EN=EN+(0.5057+B)/2.0
    1 P=P-Y
      V81=1000.0-V
      EN81=1000.0-EN
      V7979=V*V
      V7981=2.0*V*V81/V7979
      V8181=V81*V81/V7979
      EN2=EN/10.0
      EN3=EN81/10.0
      EN2=(2.0*EN2)-50.57
      EN3=(2.0*EN3)-49.43
      EN7979=50.57*EN2
      EN7981=(EN2*49.43+EN3*50.57)/EN7979
      EN8181=49.43*EN3/EN7979
      V7=1.0
      EN7=1.0
      WRITE(6,900)V,V81,V7,V7981,V8181
  900 FORMAT(6F10.5)
      WRITE(6,900)EN,EN81,EN7,EN7981,EN8181
      STOP
      END
```