68-15,953

STOLDT, Stephen Howard, 1938-
THE FRIEDEL-CRAFTS REACTION OF 1,1-BIS(BROMOMETHYL)CYCLOHEXANE; BROMINATION REACTIONS AT ADSORBENT SURFACES.

The City University of New York, Ph.D., 1968
Chemistry, organic

University Microfilms, Inc., Ann Arbor, Michigan

THE FRIEDEL-CRAFTS REACTION OF 1,1-BIS(BROMOMETHYL)CYCLOHEXANE

BROMINATION REACTIONS AT ADSORBENT SURFACES

by

STEPHEN HOWARD STOLDT

A dissertation submitted to
the Graduate Faculty in Chemistry
in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy, The City
University of New York.

1968

This manuscript has been read and accepted for the University Committee in Chemistry in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy

April 10, 1968 Leonard H. Schwartz
date Chairman of Examining Committee

April 10, 1968
date Executive Officer

Leonard H. Schwartz Leonard H. Schwartz
Amos Turk Amos Turk
Theodore Axenrod Theodore Axenrod
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ACKNOWLEDGEMENTS

The author wishes to express his appreciation to Professors Amos Turk and Leonard H. Schwartz for their continual guidance, encouragement, and patience throughout this research.

The author also wishes to acknowledge financial support in the forms of a National Defense Education Act (Title IV) Fellowship (1962-1964), City University of New York Research Assistantships (1964-1966), and a National Aeronautics and Space Administration Traineeship (1966-1967).

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THE FRIEDEL-CRAFTS REACTION OF 1,1-BIS(BROMOMETHYL)CYCLOHEXANE

INTRODUCTION

"The alkylation of aromatic compounds with alkyl halides has been intensively studied ever since the original work of Friedel and Crafts but to date no general agreement has yet been reached on the mechanism of the reaction. Although it is easy to produce alkylbenzenes by alkylation with alkyl halides the accompanying phenomena are diverse and abundant."[1]

These phenomena which accompany alkylation include rearrangement of the alkylating agent prior to alkylation, rearrangements within alkyl side chains attached to the aromatic nucleus, and dealkylation of products. Moreover, the mechanism of reaction may vary depending on the catalyst, structures of alkylating agent and aromatic compound, solvent, etc. This section will attempt a brief review of these phenomena insofar as they are related to the results to be presented in this thesis.

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(1) F. A. Drahowzal in "Friedel-Crafts and Related Reactions," G. A. Olah, Ed, Interscience Publishers, Inc., New York, N. Y., 1964, Vol II, p 417.

Rearrangements Prior to Alkylation

Rearrangements of the alkylating agent in Friedel-Crafts reactions are common and are related to the relative stabilities of the corresponding carbonium ions. The literature on these rearrangements is extensive, and only a few illustrative examples of each type discussed will be given in this section. Unless otherwise noted, reactions were carried out in excess benzene using less than an equimolar quantity of anhydrous aluminum chloride as catalyst.

Primary alkyl halides containing no branching on the *β*-carbon undergo rearrangement by hydrogen migration in the Friedel-Crafts reaction. An early report claimed that n-propyl chloride reacted with benzene and aluminum chloride to give propylbenzenes containing 40% isopropylbenzene at -6° and 60% isopropylbenzene at 35°.[2] Later work using better analytical techniques showed this reaction to be relatively insensitive to temperature, giving 65% isopropylbenzene at -18°, 66% at -6°, 67% at 35°, and 69% at 80°.[3] In either case, however, the extent of rearrangement increased as the temperature was raised.[2,3]

Similar results were obtained with n-butyl chloride. At 0°, 65% of the product was *sec*-butylbenzene. At 80°, 77% of the product resulted from rearrangement. This rearranged portion of the product consisted of a 4:1 mixture

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(2) V. N. Ipatieff, H. Pines, and L. Schmerling, *J. Org. Chem.*, **5**, 253 (1940).

(3) R. M. Roberts and D. Shiengthong, *J. Am. Chem. Soc.*, **82**, 732 (1960).

of *sec*- and isobutylbenzene, the latter being formed by isomerization of the former at the higher temperature (see page 20 for further discussion of this phenomenon).[3]

Primary alkyl halides with branching further than the *β*-carbon atom can undergo successive rearrangements. Konovalov in 1898 studied the Friedel-Crafts reaction of isoamyl chloride. At high or low temperatures the products were isoamylbenzene, 3-phenyl-2-methylbutane, and *tert*-amylbenzene, resulting from no, one, and two hydrogen migrations, respectively.[4]

Branching at the *β*-carbon atom apparently leads to exclusive rearrangement of the *β*-hydrogen to give *tert*-alkyl derivatives. In the reaction of isobutyl chloride with toluene, Konovalov concluded that complete isomerization of the isobutyl group had occurred to give only *meta*- and *para*-*tert*-butyltoluene.[5] However, since oxidation of the products gave some terephthalic acid, it is possible that rearrangement of the isobutyl group to the *tert*-butyl group was not complete. Later workers found that isobutyl chloride gave only *tert*-butylbenzene with aluminum chloride, even at as low a temperature as -18°.[2,3] In these and other such systems rearrangement usually involves migration of hydrogen, and carbon skeleton rearrangements are relatively rare.[2,6]

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(4) M. Konovalov and J. Egorov, *J. Russ. Phys.-Chem. Soc.*, **30**, 1031 (1898); through *Chem. Zentr.*, **70**, I, 776 (1899).

(5) M. Konovalov, *J. Russ. Phys.-Chem. Soc.*, **30**, 1036 (1898); through *Chem. Zentr.*, **70**, I, 777 (1899).

(6) L. Schmerling, *Ind. Eng. Chem.*, **45**, 1447 (1953).

An exception to the last generalization occurs when the β-carbon atom in an alkyl chain contains no hydrogen, as in neopentyl chloride. Here alkylation produced a 24% yield of 3-phenyl-2-methylbutane by migration of a methyl group.[7] The tendency of neopentyl systems to rearrange by methyl group migration is well known. However, alkylation of benzene with neopentyl alcohol and aluminum chloride gave a 9% yield of neopentylbenzene.[7]

Secondary alkyl halides ordinarily do not rearrange unless other secondary or tertiary structures are available. At 0° sec-butyl chloride produced only sec-butylbenzene, but at 80° 65% of the product was isobutylbenzene, formed by isomerization of sec-butylbenzene[3] as mentioned on page 4.

Isomerizations between secondary positions were found in the Friedel-Crafts reaction of 2- and 3-pentanol. From either alcohol, a mixture containing 65% of 2- and 25% of 3-phenylpentane was obtained, indicating rapid equilibration between the alternative secondary carbonium ions prior to alkylation.[8]

Tertiary alkyl halides usually do not rearrange prior to alkylation; tert-butylbenzene resulted from tert-butyl chloride. At 25-30° tert-pentyl chloride gave, in addition to tert-pentylbenzene, what were claimed to be some 3-phenyl-2-methylbutane and 1-phenyl-2-methylbutane[9] (Here

(7) H. Pines, L. Schmerling, and V. N. Ipatieff, *J. Am. Chem. Soc.*, **62**, 2901 (1940).

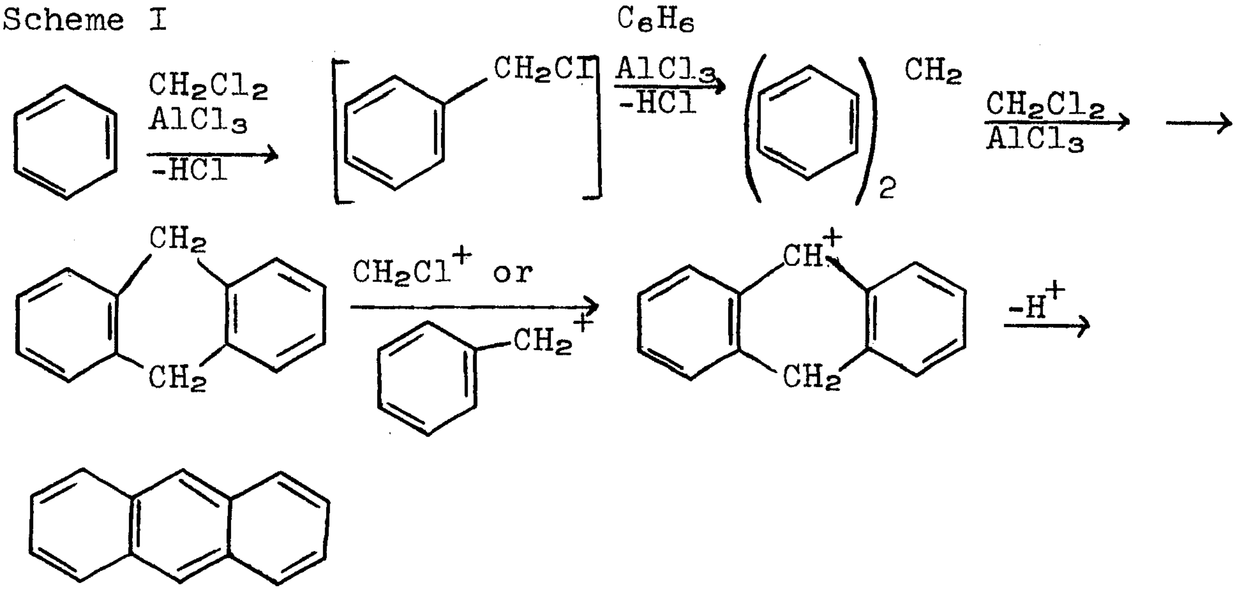
(8) A. Streitwieser, Jr., D. P. Stevenson, and W. D. Schaeffer, *J. Am. Chem. Soc.*, **81**, 1110 (1959).

(9) M. Inatome, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *J. Am. Chem. Soc.*, **74**, 292 (1952).

the isomerization was postulated to occur after the alkylation step; see page 23 for a discussion).

Dihaloalkanes have been used extensively in Friedel-Crafts reactions. Methylene chloride reacted with benzene and aluminum chloride, probably in a stepwise manner, giving first benzyl chloride and then diphenylmethane.[10,11] With excess methylene chloride, reaction proceeded further to give 9,10-dihydroanthracene and finally anthracene.[10,11] Benzyl chloride, because of its great reactivity under these conditions, could not be isolated (Scheme I).

Scheme I



1,1-Dichloroethane and 1,1-dichlorobutane each yielded the corresponding 1,1-diphenyl compound,[12] as did 1,1-dichloro-3,3-dimethylbutane.[13] In the presence of a hydride

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(10) Y. Lavaux and M. Lombard, *Bull. Soc. Chim. France*, **7**, 913 (1910); through *Chem. Abstr.*, **4**, 2448 (1910).

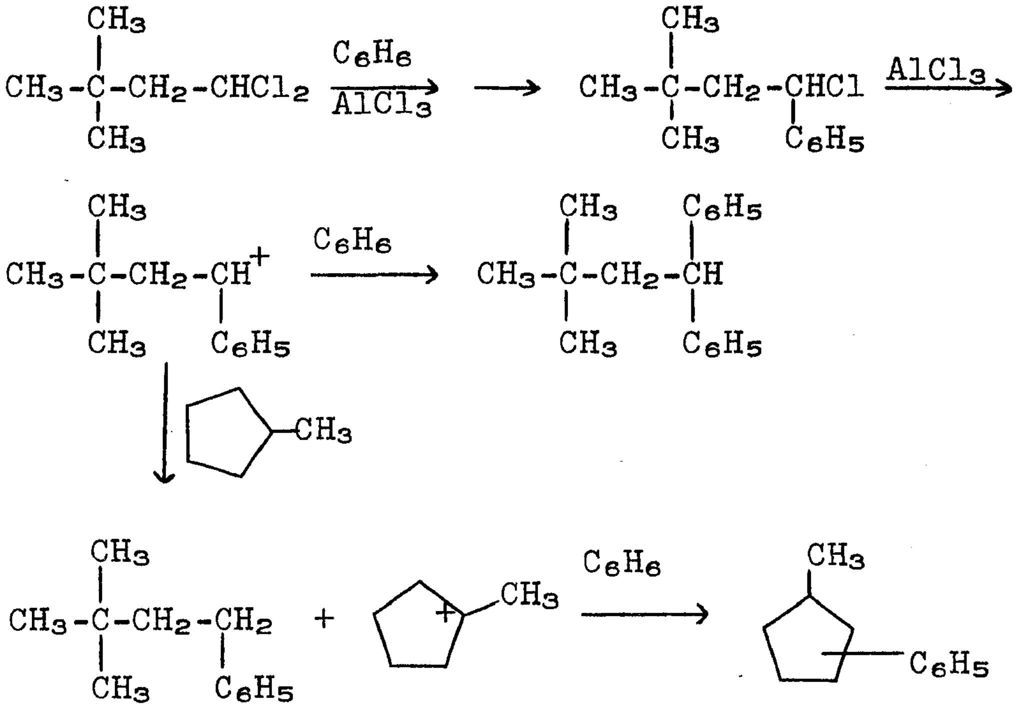
(11) C. Friedel and J. M. Crafts, *Ann. Chim. Phys.*, **11**, 263 (1887).

(12) L. Schmerling, R. W. Welch, and J. P. Luvisi, *J. Am. Chem. Soc.*, **79**, 2636 (1957).

(13) L. Schmerling, J. P. Luvisi, and R. W. Welch, *J. Am. Chem. Soc.*, **77**, 1774 (1955).

donor (methylcyclopentane or methylcyclohexane) the corresponding 1-phenylalkanes were also formed (Scheme II).[13]

Scheme II



Dihalides containing a tertiary carbon atom (1,1-dichloro-3-methylbutane and (2,2-dibromoethyl)cyclohexane) acted as their own intermolecular hydride donors to give 1-phenyl-3-methylbutane and 1-phenyl-2-cyclohexylethane, respectively.[12]

Ethylene chloride, a 1,2-dihaloalkane, yielded mainly 1,2-diphenylethane (equation 1).[14-16] The intermediate *β*-

$$C_6H_6 + ClCH_2CH_2Cl \xrightarrow[-HCl]{AlCl_3} C_6H_5CH_2CH_2Cl \underset{-HCl}{\xrightarrow[AlCl_3]{C_6H_6}} C_6H_5CH_2CH_2C_6H_5 \qquad (1)$$

phenylethyl chloride reacted further with benzene to give

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(14) R. D. Silva, *Compt. rend.*, **89**, 606 (1879).

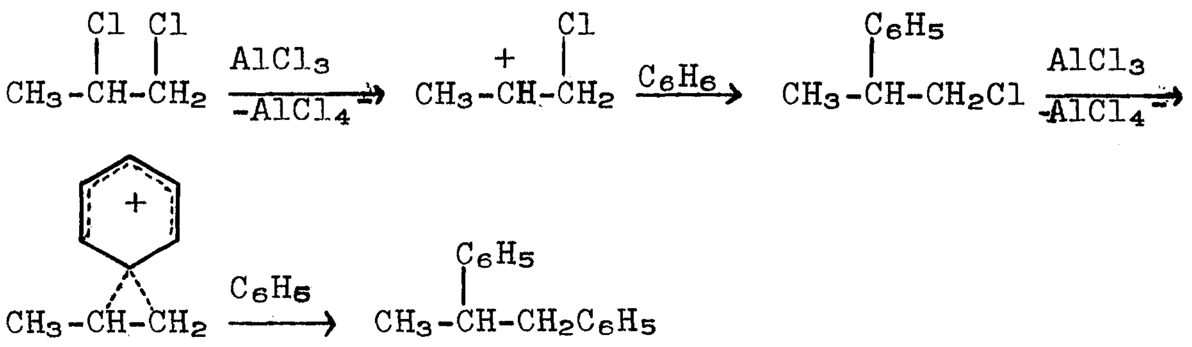
(15) R. D. Silva, *Jahresbericht uber die Fortschritte der Chemie*, 379 (1879).

(16) B. N. Dolgov and N. A. Larin, *J. Gen. Chem. U.S.S.R.*, **20**, 450 (1950); through *Chem. Abstr.*, **45**, 566 (1951).

1,2-diphenylethane. The intermediate in this reaction has been shown by C^{14} labelling to be symmetrical; a phenonium ion was postulated.[17]

Propylene dibromide or dichloride gave mainly 1,2-diphenylpropane <u>via</u> the pathway shown in Scheme III.[14,15,18]

Scheme III



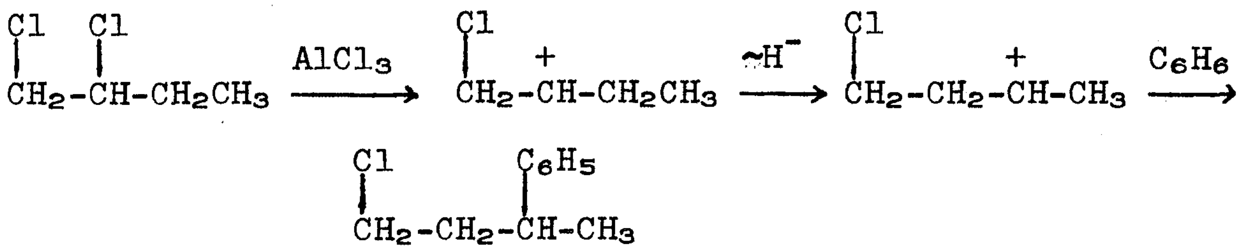
A <u>β</u>-phenylethyl type intermediate, 1-chloro-2-phenylpropane, was postulated to form and react rapidly, although none of this intermediate was isolated.[18]

1,2-Dichlorobutane reacts differently. In this case, there are two possible secondary carbonium ions, the more stable being the one in which the positive charge is farther removed from the electron-attracting chlorine atom. The initially formed secondary carbonium ion rearranged, and the major product (80%) was 1-chloro-3-phenylbutane (Scheme IV). Here the phenyl group is on the <u>γ</u>-carbon, and its participation in ionization of the primary chlorine is not as favorable. Lesser amounts of diphenylbutanes also were formed.[18]

(17) M. A. McMahon and S. C. Bunce, <u>J</u>. <u>Org</u>. <u>Chem</u>., **29**, 1515, (1964).

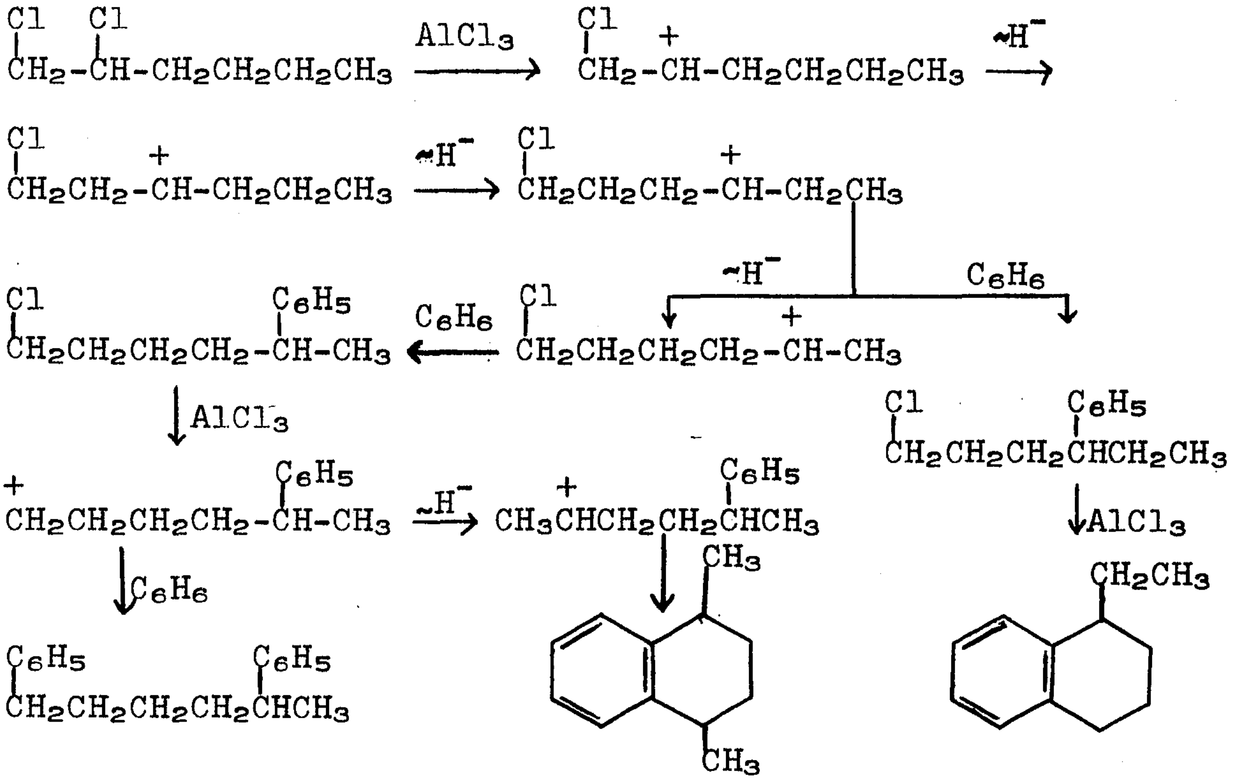
(18) D. L. Ransley, <u>J</u>. <u>Org</u>. <u>Chem</u>., **31**, 3595 (1966).

Scheme IV



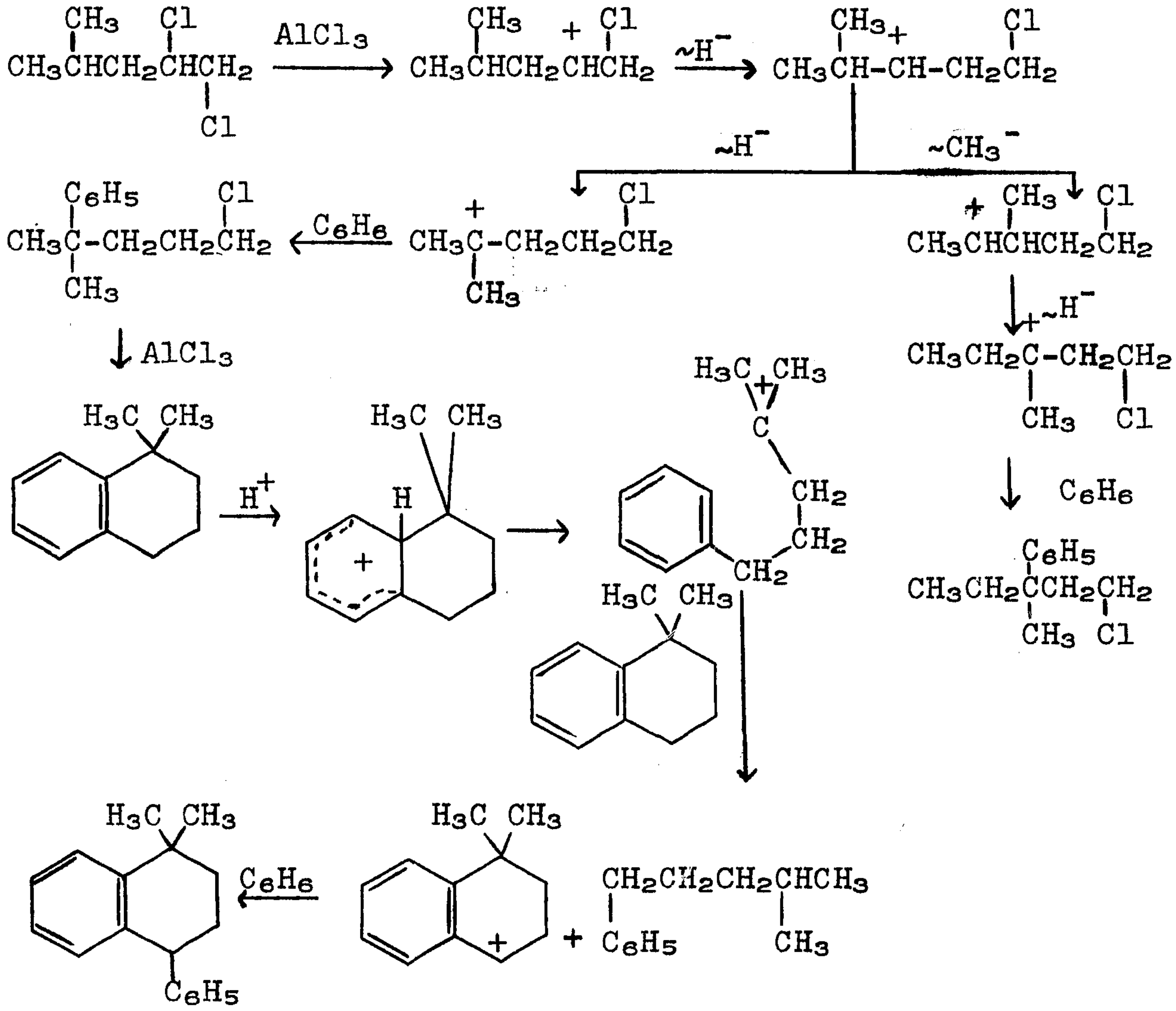
With 1,2-dichlorohexane the possibilities are even more complex. The major pathway of reaction involved three successive hydride migrations to place the charge on the penultimate carbon atom, the secondary carbon furthest from the electron-withdrawing chlorine. The 1-chloro-5-phenylhexane thus formed was initially the main product, and this then reacted further. Some alkylation of benzene occurred after only two hydride migrations to give 1-chloro-4-phenylhexane which cyclized (Scheme V).[18]

Scheme V[18]



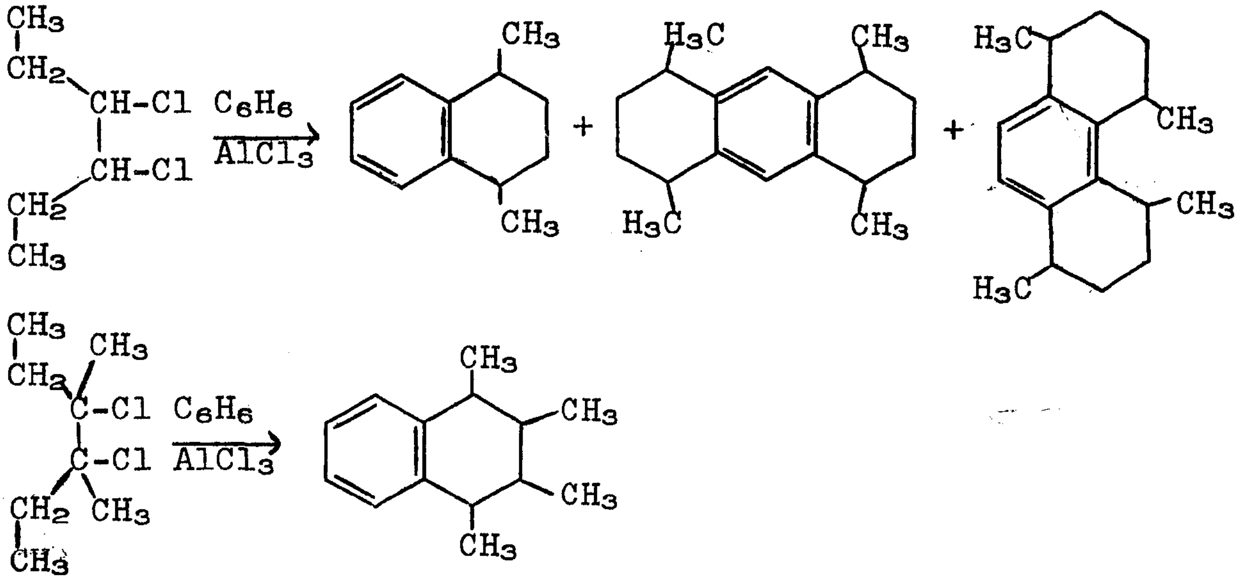
1,2-Dichloro-4-methylpentane gave initially a large yield of 1-chloro-4-phenyl-4-methylpentane *via* similar ionization and hydride migration. This compound cyclized to give 1,1-dimethyltetralin which underwent secondary reactions. A methyl group migration competed with a hydride migration to give 1-chloro-3-phenyl-3-methylpentane. The situation is summarized in Scheme VI.[18]

Scheme VI[18]



1,2-Dihalides in which the halogens are internally located in the carbon chain generally cyclialkylate aromatics with rearrangement. The formation of tetralin derivatives from 3,4-dichlorohexane[19,20] and 3,4-dichloro-3,4-dimethylhexane[21] are illustrative (Scheme VII).

Scheme VII



The literature with regard to 1,3-dihaloalkanes is somewhat contradictory. 1-Bromo-3-chloropropane gave at 6-12° 1-bromo-3-phenylpropane and at 80-85° mainly 1,3-diphenylpropane.[22] 1,3-Dihalobutanes have been reported to cyclialkylate benzene to give 3-methylindane and its 5-(3'-chlorobutyl)- derivative,[23] but other papers indicated only formation of 1-bromo (or chloro)-3-phenylbutane[18,24] or

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(19) K. Shishido and H. Nozaki, *J. Soc. Chem. Ind. Japan*, **47**, 516 (1944); through *Chem. Abstr.*, **48**, 2016 (1954).

(20) K. Sisido and H. Nozaki, *J. Am. Chem. Soc.*, **70**, 1288 (1948).

(21) K. Sisido and H. Nozaki, *J. Am. Chem. Soc.*, **69**, 961 (1947).

(22) I. P. Tsukervanik and K. Yatsimirskii, *J. Gen. Chem. U.S.S.R.*, **10**, 1075 (1940); through *Chem. Abstr.*, **35**, 3981 (1941).

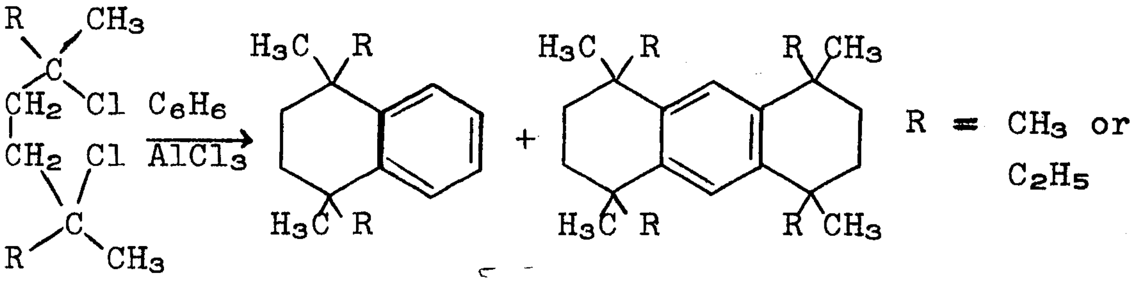
(23) W. Reppe and coworkers, *Ann.*, **596**, 1 (1955), p 97.

(24) I. P. Tsukervanik and L. U. Bugrova, *Zh. Obshchei Khim.*, **31**, 2143 (1961); through *Chem. Abstr.*, **56**, 362 (1962).

further reaction to 2,3 (and 1,3)-diphenylbutane and sec-butylbenzene.[21,24] 1,3-Dichloro-3-methylbutane alkylated benzene to yield 1-chloro-3-phenyl-3-methylbutane which reacted further to produce a diphenylated compound.[25]

1,4-Dihaloalkanes often cyclialkylate benzene. 1,4-Dichlorobutane gave tetralin and further condensation products.[19,23,26,27] The reaction involved intermediate formation of a phenylalkyl chloride which then underwent intramolecular alkylation.[28] 2,5-Dichlorohexane similarly gave 1,4-dimethyltetralin.[29] 2,5-Dichloro-2,5-dimethylhexane yielded 1,1,4,4-tetramethyltetralin and 1,1,4,4,5,5,8,8-octamethyl-1,2,3,4,5,6,7,8-octahydroanthracene (Scheme VIII),[28,30] and 3,6-dichloro-3,6-dimethyloctane yielded the

Scheme VIII



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(25) L. Schmerling, R. W. Welch, and J. P. West, J. Am. Chem. Soc., 78, 5406 (1956).

(26) K. M. Shadmanov, Doklady Akad. Nauk Uzbek. S.S.R., No. 11, 37 (1957); through Chem. Abstr., 53, 5214 (1959).

(27) S. Yura and R. Oda, J. Soc. Chem. Ind. Japan, 46, 531 (1943); through Chem. Abstr., 42, 6348 (1948).

(28) H. A. Bruson and J. W. Kroeger, J. Am. Chem. Soc., 62, 36 (1940).

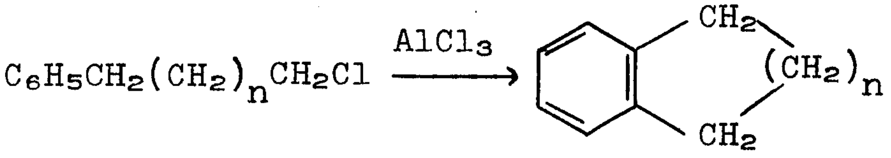
(29) G. A. Olah in "Friedel-Crafts and Related Reactions," G. A. Olah, Ed, Interscience Publishers, Inc., New York, N. Y., 1964, Vol I, p 57.

(30) L. R. C. Barclay and E. E. Betts, J. Am. Chem. Soc., 77, 5735 (1955).

corresponding tetraethyltetramethyl compound.[31]

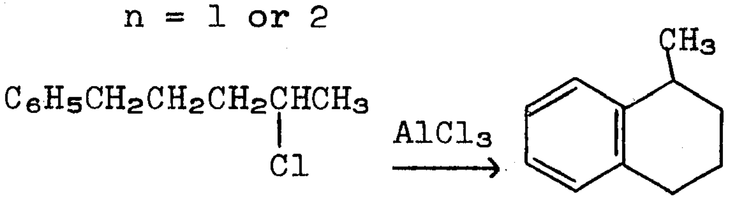
A 1,5-dichloro compound, 2,6-dichloro-2,6-dimethylheptane, was reported to cyclialkylate 1,1,4,4-tetramethyltetralin to give 1,1,4,4,5,5-hexamethyl-8-isopropyl-1,2,3,4,5,6,7,8-octahydroanthracene (60%) and the corresponding 1,2,3,4,5,6-hexahydroanthracene (12%). The reaction was shown not to produce an intermediate benzosuberane which could have rearranged further but rather to proceed by rearrangement within the alkyl chain prior to alkylation.[32]

As compared to intermolecular alkylations, intramolecular alkylations are generally faster and more free from alkyl group isomerizations. Primary, secondary, or tertiary phenylalkyl halides all undergo ring closure with little or no isomerization.[33] Some examples have been discussed already, and others are given in equations 2-5.[33]

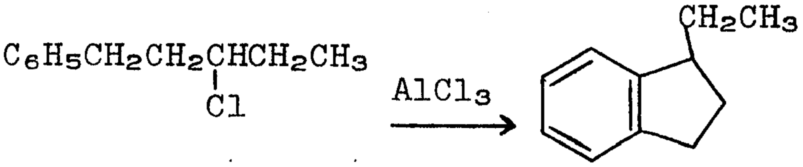


(2)

n = 1 or 2



(3)

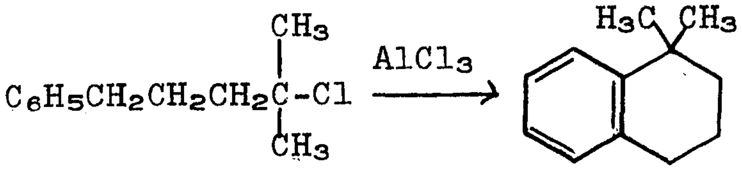


(4)

(31) L. R. C. Barclay in "Friedel-Crafts and Related Reactions," G. A. Olah, Ed, Interscience Publishers, Inc., New York, N. Y., 1964, Vol II, Table XXIVa, p 931.

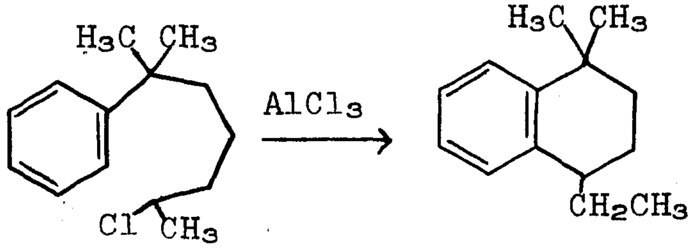
(32) L. R. C. Barclay, B. A. Ginn, and C. E. Milligan, Can. J. Chem., 42, 579 (1964).

(33) G. Baddeley and R. Williamson, J. Chem. Soc., 4647 (1956).

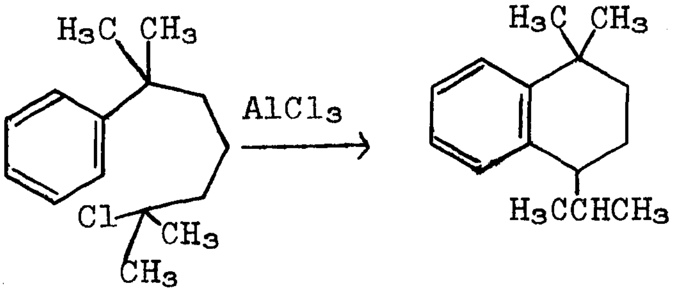


(5)

It was originally thought that 5-phenyl-1-chloropentane (equation 2, n = 3) yielded benzosuberane,[33] but later work showed that 1-methyltetralin was the product.[32] Also, 6-phenyl-6-methyl-2-chloroheptane and 6-phenyl-2,6-dimethyl-2-chloroheptane yielded 1,1-dimethyl-4-ethyltetralin and 1,1-dimethyl-4-isopropyltetralin, respectively (equations 6 and 7), rather than benzosuberanes.[32] However, 1,1,4,4-tetramethyl-6,7-benzocycloheptene was obtained together with two parts of 1-isopropyl-3,3-dimethyltetralin in the boron trifluoride etherate-catalyzed cyclization of 6-phenyl-2,5,5-trimethyl-2-hexene (equation 8). The use of aluminum chloride as catalyst yielded only the tetralin.[34]



(6)



(7)

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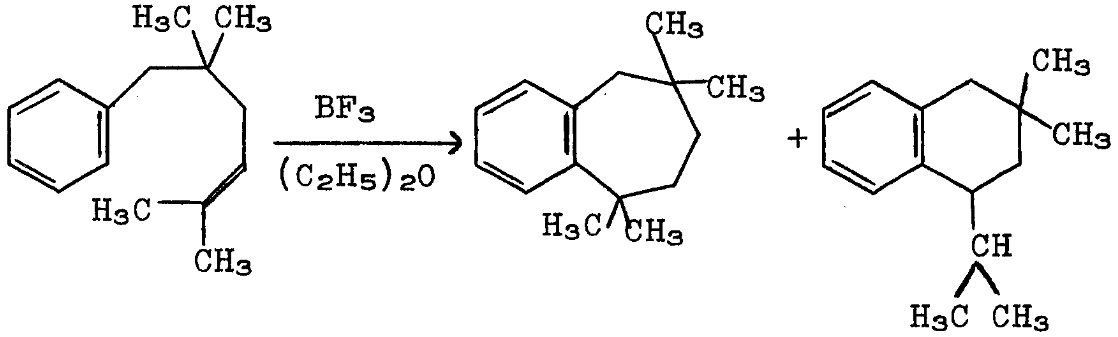
(34) H. Hart and J. L. Corbin, J. Am. Chem. Soc., 87, 3135 (1965).



(8)

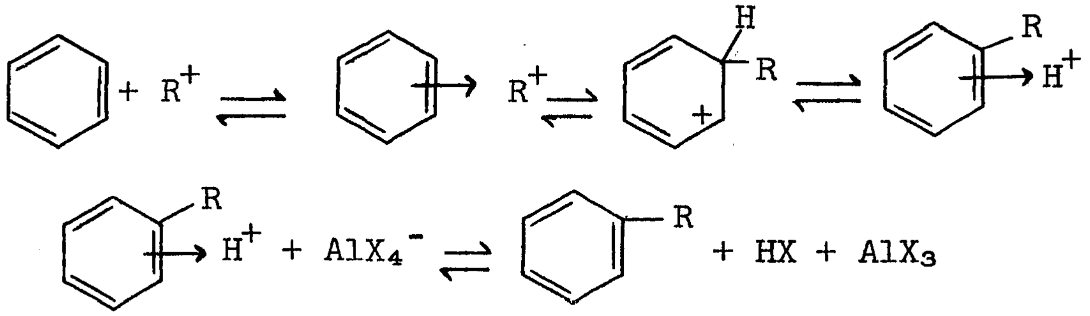
Mechanisms

Throughout the preceding discussion it has been tacitly assumed that the results presented could be explained in terms of carbonium ion intermediates. Such is actually the case in the majority of instances. The rates of reaction of alkyl halides in the Friedel-Crafts reaction increase in the series methyl, ethyl, isopropyl, tert-butyl, the same order as that generally found in S_N1 reactions. Moreover, the rearrangements are almost always in the direction primary ⟶ secondary ⟶ tertiary, the same direction as is found in reactions involving carbonium ions.

Tertiary and ordinary benzylic halides react essentially <u>via</u> the carbonium ion mechanism outlined in Scheme IX.[35] The

Scheme IX

$$RX + 1/2Al_2X_6 \rightleftharpoons R^+AlX_4^-$$



available evidence indicates that secondary compounds also form carbonium ions under Friedel-Crafts conditions. Optically active 2-butanol[36,37] and its methyl ether[38] alkylated

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(35) K. L. Nelson and H. C. Brown in "The Chemistry of Petroleum Hydrocarbons," B. T. Brooks, C. E. Boord, S. S. Kurtz, Jr., and L. Schmerling, Eds, Reinhold Publishing Corporation, New York, N. Y., 1955, Vol III, p 522.

benzene in the presence of boron trifluoride with greater than 99% racemization. Use of aluminum chloride gave complete racemization.[36] The possibility of racemization by rapid hydride transfer between the two secondary carbon atoms in the *sec*-butyl carbonium ion (see page 5 for a discussion of similar rearrangements between 2- and 3-pentyl carbonium ions) led Streitwieser[39] to study the similar reaction of optically active 2-propanol-$\underline{d}_3$. The results (more than 93% racemization with some net inversion) indicated that the isopropyl cation was a largely free intermediate and that the Friedel-Crafts reaction of secondary alkyl derivatives resembled an S_N1 solvolysis.[39]

The reactions of some primary alkyl compounds, however, lead to the conclusion that an S_N2 type of mechanism may also operate. The reactions of 3,4-dichlorobenzyl chloride and *para*-nitrobenzyl chloride with aromatic hydrocarbons and aluminum chloride in nitrobenzene solution were third order (equation 9). The rate increased slightly as more

$$-\frac{d[RCl]}{dt} = k_3[ArH][RCl][AlCl_3] \qquad (9)$$

basic aromatics were used, but in approximately the same ratios as those in which the stabilities of $\underline{\pi}$-complexes

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(36) C. C. Price and M. Lund, *J. Am. Chem. Soc.*, **62**, 3105 (1940).

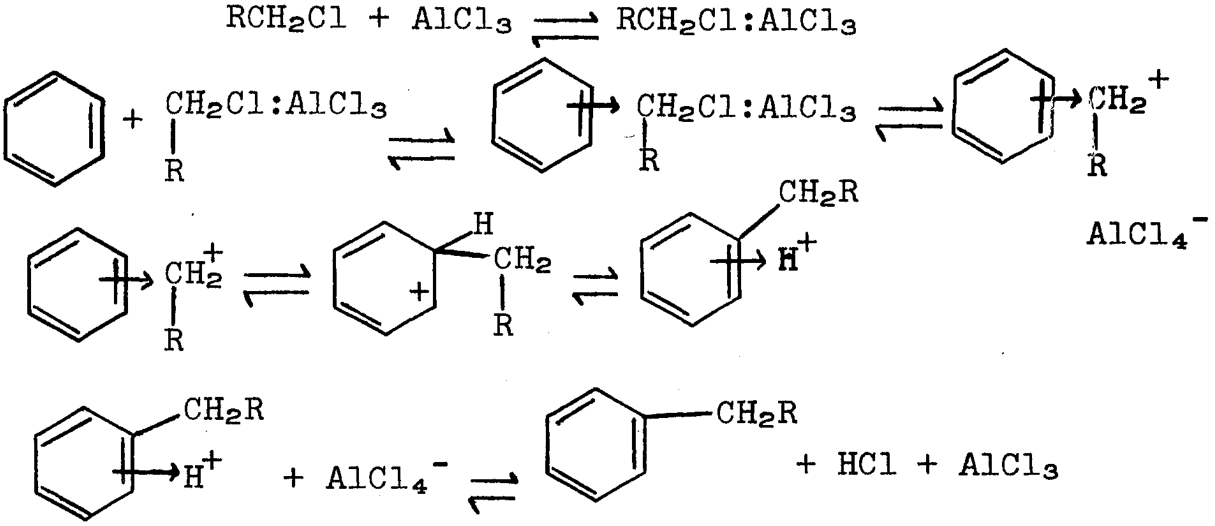
(37) R. L. Burwell, Jr. and S. Archer, *J. Am. Chem. Soc.*, **64**, 1032 (1942).

(38) R. L. Burwell, Jr., L. M. Elkin, and A. D. Shields, *J. Am. Chem. Soc.*, **74**, 4570 (1952).

(39) A. Streitwieser, Jr. and P. J. Stang, *J. Am. Chem. Soc.*, **87**, 4953 (1965).

increased and nowhere near the ratios in which the stabilities of *σ*-complexes and the rates of some other aromatic substitution reactions increased. It was concluded that the transition state was therefore closer to a *π*-complex than to a *σ*-complex[40,41] and that it probably came about by nucleophilic attack by the aromatic compound on the polarized alkyl halide-aluminum halide addition compound.[42-44] The overall mechanism in this case is shown in Scheme X.[40,41,43,44]

Scheme X



Some of the n-propylbenzene,[2,3] n-butylbenzene,[3] and isoamylbenzene[4] formed from the corresponding primary alkyl halides (pages 3-4) may also come about by a displacement

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(40) H. C. Brown and M. Grayson, *J. Am. Chem. Soc.*, **75**, 6285 (1953).

(41) Reference 33, p 525.

(42) H. C. Brown and H. Jungk, *J. Am. Chem. Soc.*, **77**, 5584 (1955).

(43) H. C. Brown and H. Jungk, *J. Am. Chem. Soc.*, **78**, 2182 (1956).

(44) H. Jungk, C. R. Smoot, and H. C. Brown, *J. Am. Chem. Soc.*, **78**, 2185 (1956).

mechanism acting in competition with a mechanism involving carbonium ions and rearrangements to secondary alkyl derivatives. The formation of 9% neopentylbenzene from neopentyl alcohol, benzene, and aluminum chloride (page 5)[7] may also be the result of the operation of a displacement mechanism. Furthermore, ethyl chloride labelled with C^{14} in the *β* position alkylated benzene at high temperatures to give ethylbenzene with no rearrangement of the label, whereas the label was almost completely equilibrated by aluminum chloride in the absence of benzene in one hour at room temperature.[45] Ethyl chloride in this case also apparently reacted by the displacement mechanism. In addition, some of the cyclialkylations and intramolecular alkylations with primary halides (pages 12-13) probably proceed by the displacement mechanism.

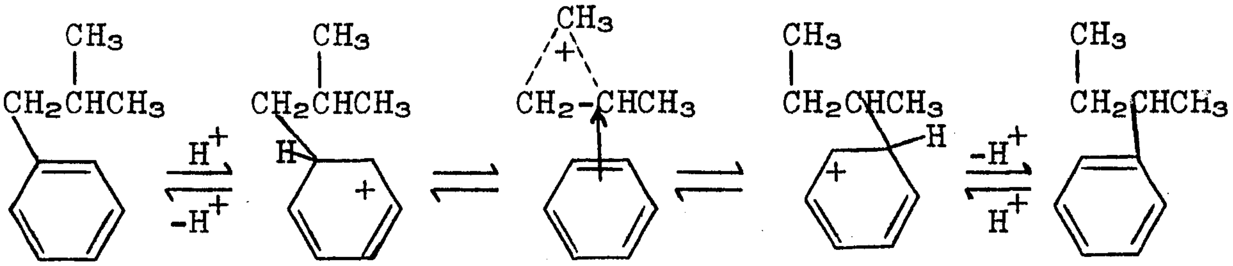
(45) R. M. Roberts, G. A. Ropp, and O. K. Neville, *J. Am. Chem. Soc.*, **77**, 1764 (1955).

Secondary Reactions of Products

The instability of alkylation products to the reaction conditions and their further reaction under these conditions are well known. Some examples have already been encountered (the rearrangement of *sec*-butylbenzene to isobutylbenzene,[3] preferred formation of secondary alkylbenzenes from some tertiary alkyl halides and carbonium ions,[7,8] and reaction of 1,1-dimethyltetralin[18] in Scheme VI, page 10).

Reaction of either *sec*-butylbenzene or isobutylbenzene with moist aluminum chloride at 100° resulted in formation of an equilibrium mixture containing one part of the former to two parts of the latter. Disproportionation and dealkylation also occurred. The results were explained on the basis of a bridged π-complex which could be formed from, and collapse to, either isomer (Scheme XI). Dissociation of the complex resulted in the observed dealkylation and disproportionation.[46]

Scheme XI



The formation of 3-phenyl-2-methylbutane from *tert*-

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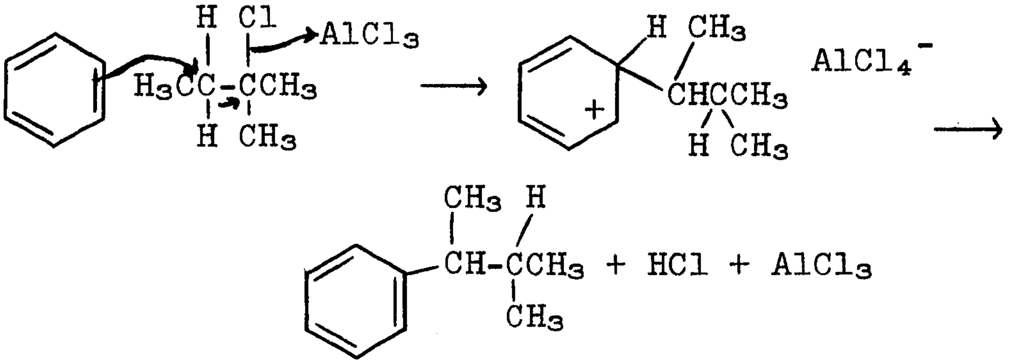
(46) R. M. Roberts, J. H. Han, C. H. Schmid, and D. A. Davis, *J. Am. Chem. Soc.*, **81**, 640 (1959).

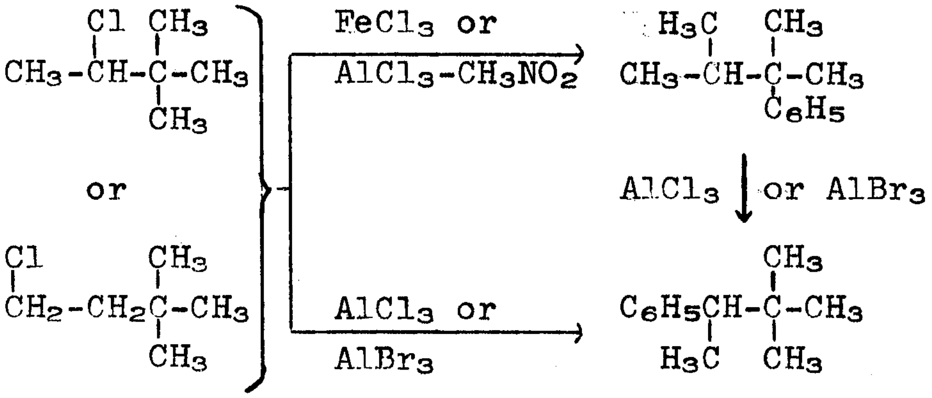
pentyl chloride[9] was first proposed to proceed through a mechanism similar to the displacement mechanism (Scheme XII).[6]

Scheme XII



Subsequent work[47] indicated that products in some Friedel-Crafts reactions depended on the activity of the catalyst. Thus, 1- or 2-chloro-3,3-dimethylbutane and benzene gave 3-phenyl-2,2-dimethylbutane with aluminum chloride or bromide, but 2-phenyl-2,3-dimethylbutane was the product with the weaker catalysts ferric chloride or aluminum chloride in nitromethane (Scheme XIII). These results led

Scheme XIII



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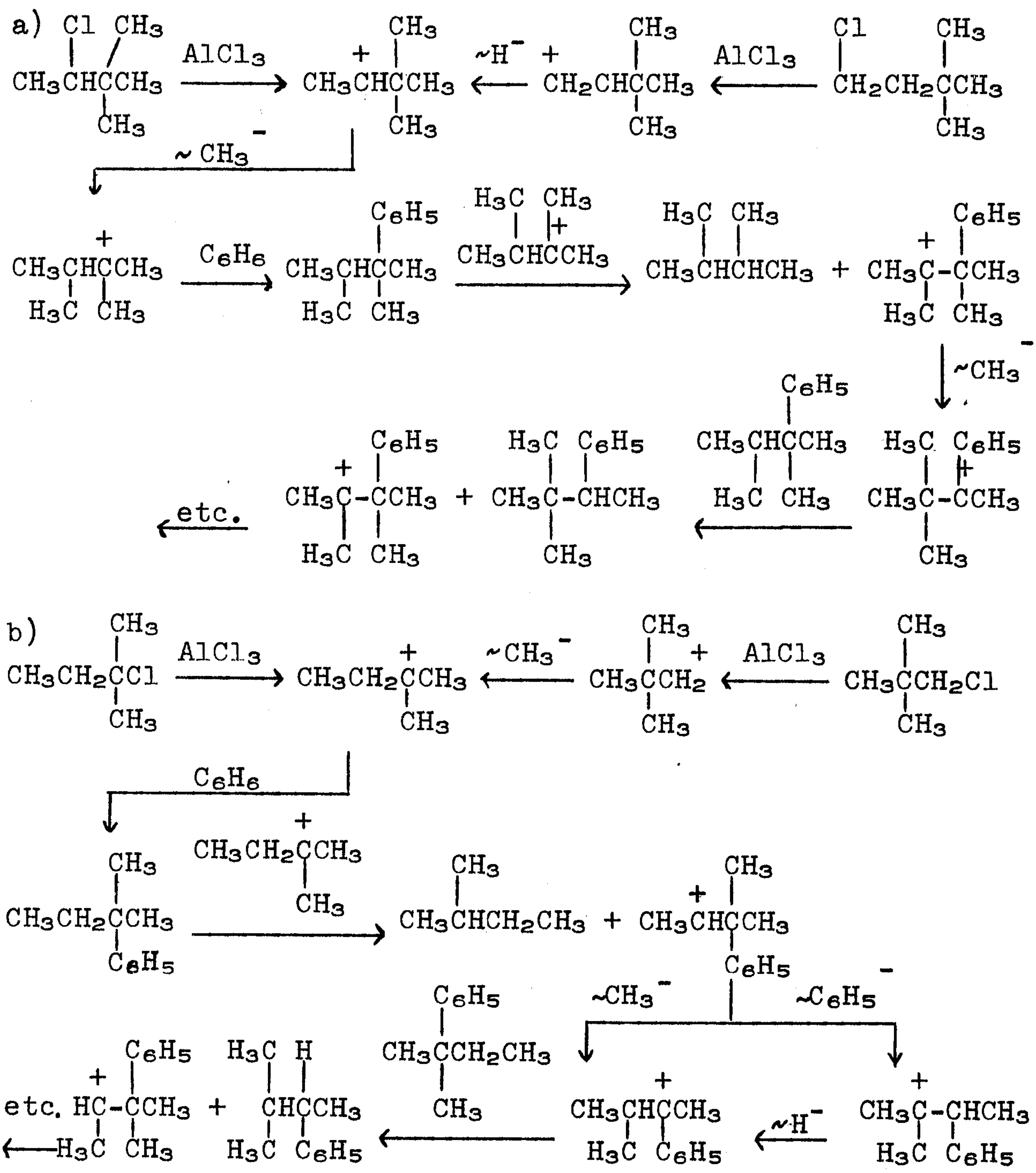
(47) L. Schmerling and J. P. West, J. Am. Chem. Soc., 76, 1917 (1954).

to the conclusions that the tertiary carbonium ion was formed and that this ion reacted with benzene to give a tertiary alkylbenzene which then rearranged further in the presence of strong catalysts but not weaker ones (Scheme XIVa).[46] A similar mechanism (Scheme XIVb) accounts

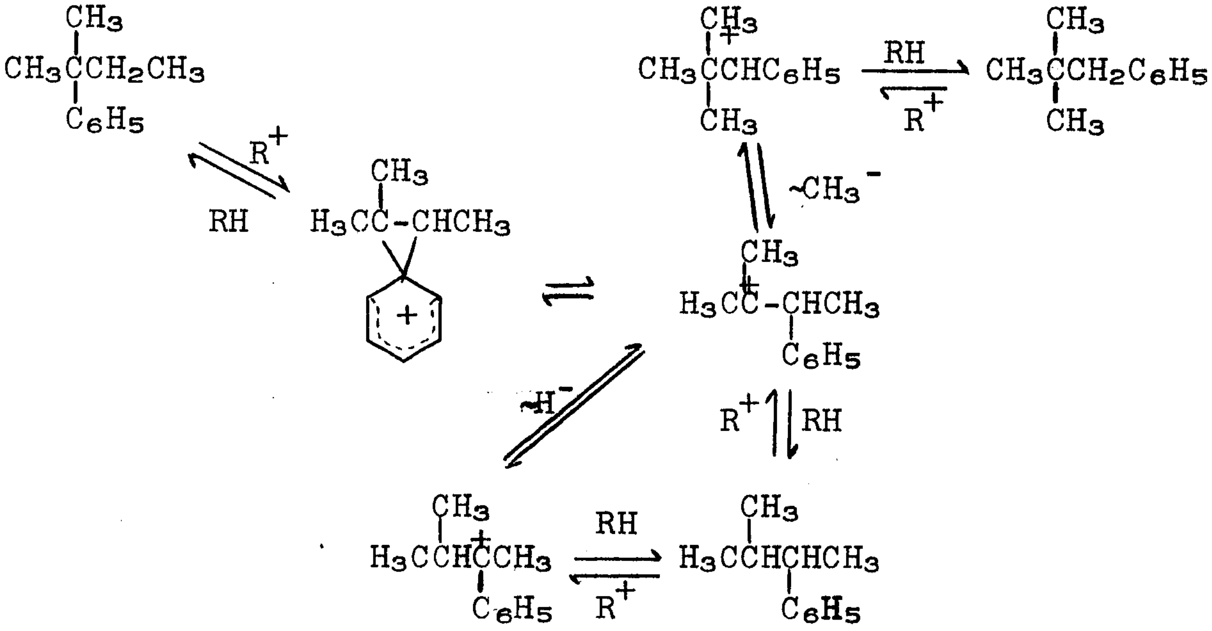
Scheme XIV



for the formation of 3-phenyl-2-methylbutane from either neopentyl chloride[7] or tert-pentyl chloride.[9] The aliphatic hydrocarbons resulting from intermolecular hydride transfer were observed, in support of the proposed mechanism.[46]

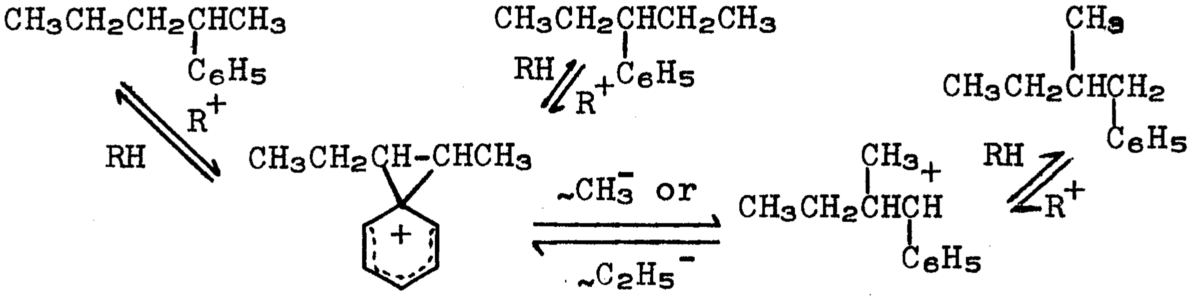
A more recent study has been conducted on the isomerization of the pentylbenzenes under the influence of moist aluminum chloride. It was found that tert-pentylbenzene rapidly isomerized to 3-phenyl-2-methylbutane which was slowly converted to neopentylbenzene (Scheme XV).

Scheme XV



2-Phenylpentane and 3-phenylpentane rapidly interconverted, and each was slowly changed to 1-phenyl-2-methylbutane (Scheme XVI). Isopentyl- and n-pentylbenzene were relatively stable under these conditions. Hydride abstraction and interconversion of carbonium ions via bridged structures were used to explain the transformations.[48] Re-

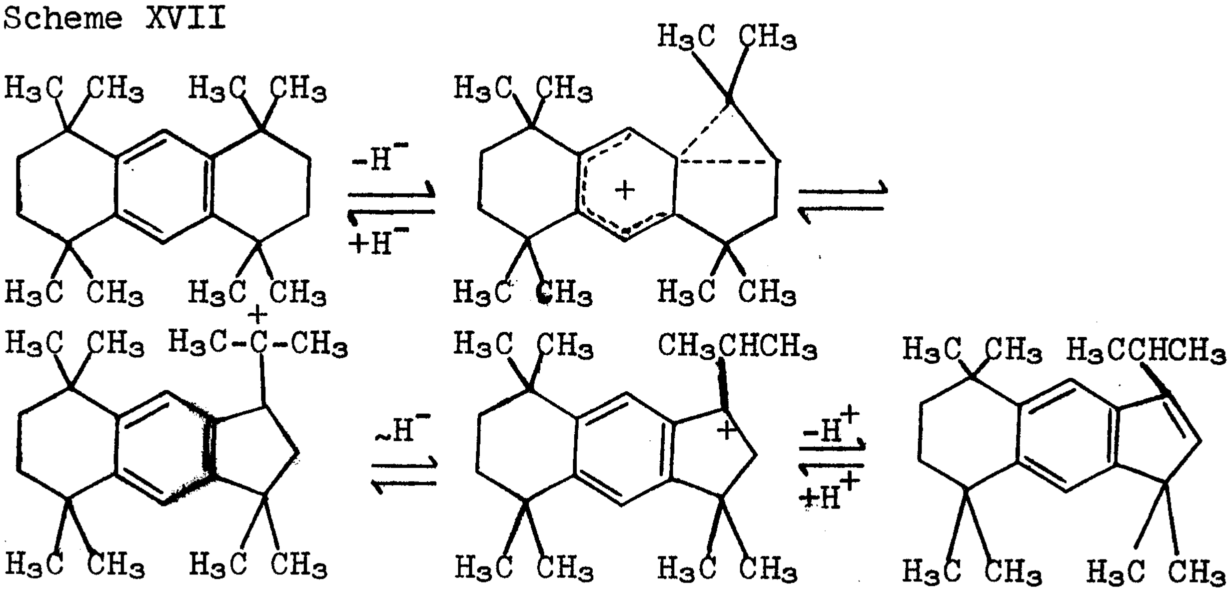
Scheme XVI



arrangement of the latter two compounds would involve relatively unstable primary carbonium ions.

Similar hydride abstractions from alkylbenzenes followed by isomerizations are known in tetralin compounds. Thus, 1,1,4,4,5,5,8,8-octamethyl-1,2,3,4,5,6,7,8-octahydroanthracene was isomerized in 80% yield to an indene derivative (Scheme XVII).[49,50]

Scheme XVII



(48) R. M. Roberts and Y. W. Han, *J. Am. Chem. Soc.*, **85**, 1168 (1963).

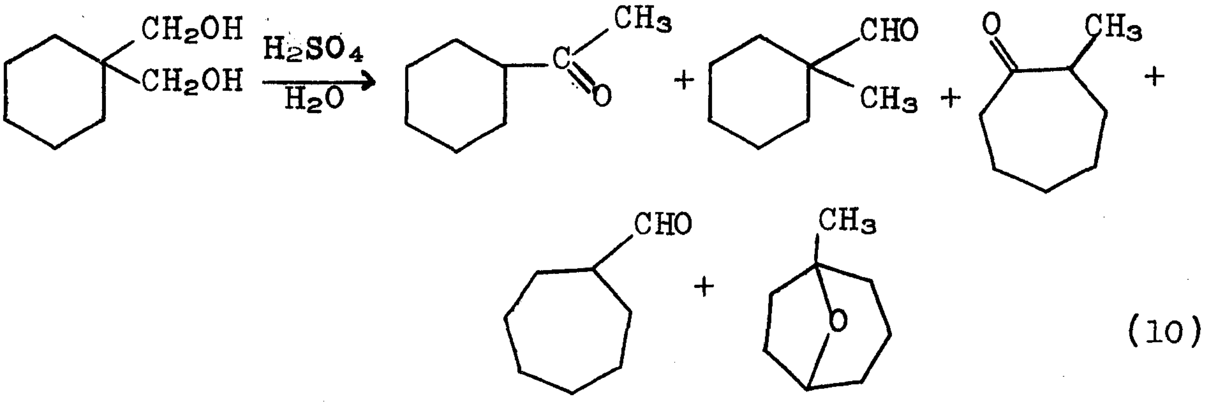
(49) L. R. C. Barclay and A. H. Gray, *Chem. and Ind.*, 1350 (1959).

(50) L. R. C. Barclay, A. H. Gray, and C. E. Milligan, *Can. J. Chem.*, **39**, 870 (1961).

Alkylbenzenes, especially tertiary ones, can also undergo protodealkylation, the reverse of alkylation. The formation and decomposition of 1,1-dimethyltetralin[18] (Scheme VI, page 10) has already been mentioned. As the Friedel-Crafts reaction proceeds the concentration of hydrogen halide increases. The hydrogen halide-aluminum halide is a very strong protonating agent. Thus, formation of tertiary alkylbenzene at the low acid concentration prevailing during the early stages of the reaction, followed by its decomposition in the later stages in which the acidity of the medium is increased, can be understood.

The Problem

Previous work in these laboratories[51] and elsewhere[52] has disclosed interesting rearrangements in the acid-catalyzed hydrolysis of 1,3-diols. Cyclohexane-1,1-dimethanol in aqueous sulfuric acid yields a mixture from which five major products have been isolated and identified (equation 10).[51] The last of these products is especially



(10)

interesting because its structure implies a possible transannular reaction.

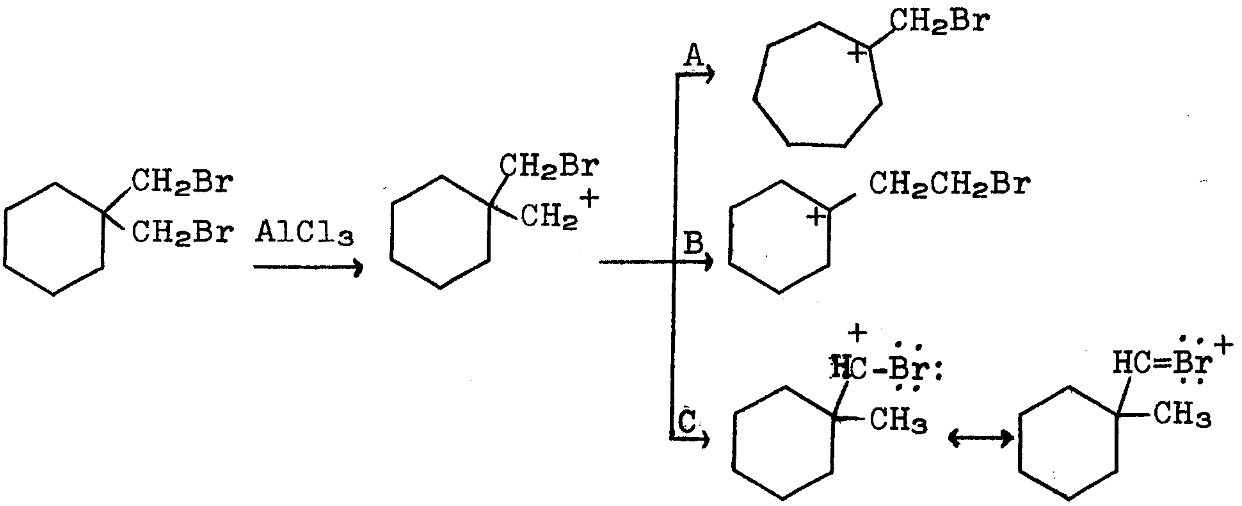
In the light of these results, and since the Friedel-Crafts reactions of 1,3-dihalo compounds have not been studied nearly as extensively as have those of either 1,2- or 1,4-dihalo compounds, it was of interest to investigate the Friedel-Crafts reaction of 1,1-bis(bromomethyl)cyclohexane. This 1,3-dihalo compound has both bromine atoms attached to primary carbon atoms, and it might therefore be

(51) L. H. Schwartz, A. J. Kascheres, C. Ovrut, and A. M. Levine, unpublished results, City College of the City University of New York.

(52) H. M. Gladstone, Ph.D. Thesis, Polytechnic Institute of Brooklyn, 1961.

expected to react by a displacement mechanism rather than through a carbonium ion intermediate. However, each bromomethyl group resembles that in neopentyl bromide, and displacement reactions in the neopentyl system are extremely slow compared to other primary systems. The rationale for this is that the three methyl groups attached to the _β_-carbon atom hinder backside attack. In the 1,1-bis(bromomethyl)-cyclohexane system, this hindrance to attack from the rear of the leaving group should be increased by the presence of the ring and the bromomethyl group attached to the _β_-carbon atom. Thus the mechanism for this primary alkyl halide could be diverted to the carbonium ion type, and the nature of the groups attached to the _β_-carbon atom makes possible the following rearrangements of the initial real or incipient carbonium ion: (A) ring enlargement, (B) migration of a bromomethyl group, and (C) 1,3-hydride transfer (Scheme XVIII).

Scheme XVIII



To determine the relative importances of these three possible rearrangements in the case of 1,1-bis(bromomethyl)-cyclohexane, the Friedel-Crafts reaction of this compound with benzene and aluminum chloride was studied.

EXPERIMENTAL[53]

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(53) Microanalyses were performed by Schwartzkopf Microanalytical Laboratory, Woodside 77, New York.

Melting points were determined on a Thomas-Hoover apparatus and are corrected; boiling points are uncorrected.

Gas-liquid chromatography was performed on a Microtek Model GC 2500R (analytical work) or on an Aerograph Model A-90-P (preparative work).

Mass spectra were determined on a Hitachi RMU-6 by Morgan-Schaffer, Montreal, Canada.

Other spectra were taken on the following instruments: ultraviolet, Cary 14; infrared, Perkin-Elmer 137 (absorption maxima are expressed in reciprocal centimeters); nuclear magnetic resonance, Varian A-60 (chemical shifts are expressed in ppm ($\underline{\delta}$) downfield from internal tetramethylsilane ($\underline{\delta}$ = 0)).

(A) Preparation of 1,1-Bis(bromomethyl)cyclohexane

(1) Preparation of 4,4-Bis(hydroxymethyl)cyclohexene[54]

In a 5-l three-necked flask, equipped with a reflux condenser, a mechanical stirrer, and a Claisen adapter containing an addition funnel and a reflux condenser, were placed 480 g (4.36 moles) of Δ^3-cyclohexenecarboxaldehyde, 1200 ml of methanol, and 1050 ml of 36.5% formalin (12.2 moles). To the stirred cloudy mixture at 40° was added one ml of a solution of 336 g (5.1 moles) of potassium hydroxide in 375 ml of water. The resulting clear yellow solution was heated to 67°, and the remainder of the potassium hydroxide solution was added dropwise over a 2-hr period. The resulting amber mixture was refluxed at 79° for 1 hr, cooled, and extracted with three portions of ether (1000, 450, 450 ml; the last extraction was colorless). Water was salted out of the combined ether solution by addition of sodium sulfate. The ether solution was dried over sodium sulfate, filtered, and concentrated (rotary evaporator). The resulting mixture of white solid and brown liquid was filtered with suction, and the solid was recrystallized from benzene-hexane (7:3) to give 402 g (65%) of white needles: mp 90.5-92.0° (lit[54] mp 90.0-93.0°); nmr ($CDCl_3$): δ1.57 (triplet, J = 6 cps, 2 H, 5-methylene), δ1.7-2.2 (complex, 4 H, 3- and 6-methylenes), δ2.90 (broad

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(54) H. E. French and D. M. Gallagher, *J. Am. Chem. Soc.*, **64**, 1497 (1942).

singlet, 2 H, disappears on treatment with D_2O, hydroxyl), δ3.62 (singlet with slight splitting at base which disappears on treatment with D_2O, 4 H, oxymethylene), δ5.67 (multiplet, 2 H, olefinic); ir (KBr): 3250 (s, OH), 3020 (m, olefin-H), 2900, 2840 (s, alkyl-H), 1650 (w, olefin), 1460, 1435 (s, methylene), 1040 (s, primary alcohol), 709 (s, cis-olefin).

(2) Preparation of 1,1-Bis(hydroxymethyl)cyclohexane[54]

4,4-Bis(hydroxymethyl)cyclohexene (page 30) was first recrystallized from water to remove an impurity which poisoned the hydrogenation catalyst. A total of 392 g (2.76 moles) was then hydrogenated using a Parr medium pressure apparatus at 50 psig initial pressure in 60 g portions, using 200 ml of ethanol and 0.6 g of 5% rhodium-on-alumina per run. After filtration from the catalyst, the solvent was removed (rotary evaporator) from the combined filtrates to give a white solid which was recrystallized from benzene-hexane (7:3) to yield 366 g (92%) of white needles: mp 97.0-98.7° (lit[54] mp 98.5°); nmr ($CDCl_3$): $\underline{\delta}$1.43 (singlet, 10 H, ring methylenes), $\underline{\delta}$2.99 (singlet, 2 H, hydroxyl), $\underline{\delta}$3.63 (singlet, 4 H, oxymethylene); ir (KBr): 3300 (s, OH), 2930, 2860 (s, alkyl-H), 1485, 1470, 1450 (s, methylene), 1040 (s, primary alcohol).

(3) Preparation of 1,1-Bis(tosyloxymethyl)cyclohexane[55]

To a 5-l three-necked flask, equipped with a reflux condenser containing a drying tube, a mechanical stirrer, and a suspended thermometer, were added 366 g (2.54 moles) of 1,1-bis(hydroxymethyl)cyclohexane (page 32) and 2700 ml of dry pyridine. The solution was cooled to -2°, and 1351 g (7.10 moles) of p-toluenesulfonyl chloride was added in portions over a 4-hour period, the temperature being kept between 0° and 5°. The mixture was stirred at 2-3° for 1/2 hr and then at room temperature for 1/2 hr. The mixture of light-colored solid and brown liquid was poured with stirring into a mixture of ice and 2850 ml of conc hydrochloric acid. The resulting brown oil slowly solidified to a tan solid. The water layer was extracted twice with chloroform. The solid was dissolved in chloroform, and the combined chloroform solution was washed once with water and dried over magnesium sulfate. After filtration and removal of solvent (rotary evaporator), the resulting tan solid was recrystallized from methanol to yield 874 g (76%) of white solid: mp 86.7-88.2° (two melting points have previously been reported for this compound: 74°[55,56] and 86-88°[56]); nmr ($CDCl_3$): δ1.32 (singlet, 10 H, ring methylenes), δ2.47 (singlet, 6 H, aromatic methyl), δ3.86 (singlet, 4 H, oxymethylene), δ7.30, 7.44, 7.70, 7.84

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(55) E. R. Buchman, D. H Deutsch, and G. I. Fujimoto, *J. Am. Chem. Soc.*, **75**, 6228 (1953).

(56) M. Henis, Honors Thesis, City College of the City University of New York, 1964.

(A½B½, 8 H, aromatic-H); ir (KBr): 3030 (w, aromatic-H), 2920, 2860 (m, alkyl-H), 1600, 1495 (m, aromatic), 1460 (m, methylene), 1350, 1180 (s, sulfonate ester), 820 (vs, *para*-disubstituted aromatic).

(4) Preparation of 1,1-Bis(bromomethyl)cyclohexane[55]

To a 3-l three-necked flask equipped with a mechanical stirrer, a reflux condenser, and a suspended thermometer, were added 309 g (0.682 mole) of 1,1-bis(tosyloxymethyl)-cyclohexane (page 33) and 1400 ml of diethylene glycol. The mixture was heated to 140° with stirring, and 178 g (1.73 moles) of sodium bromide was added over a 13-min period, during which time the solution turned orange and the temperature rose to 151°. The mixture was heated at 155-165° for 3 1/3 hr, then cooled and poured into 1500 ml of water to give a brown oil. The aqueous solution was extracted with eight 150-ml portions of carbon tetrachloride, and the combined oil and carbon tetrachloride solution was washed with 150 ml of water and dried over sodium sulfate. After filtration, the solvent was removed (rotary evaporator), and the resulting dark liquid was distilled through a 2-ft column packed with glass helices. The product was obtained as a colorless liquid: bp (0.06-0.08 mm) 55-59° (lit[55] bp 117°(6mm)), 123 g (67%); nmr (see page 70) (CCl_4): $\underline{\delta}$1.51 (broad singlet, 10 H, ring methylenes), $\underline{\delta}$3.48 (sharp singlet, 4 H, bromomethyl); ir (see page 71) (liquid film): 2940, 2870 (s, alkyl-H), 1460, 1430 (s, methylene), 1260 (s), below 670 (m, bromine).

(B) Preparation of 1-Methyl-6,7-benzobicyclo[3.2.2]non-6-ene

(1) Preparation of 4-Phenylcycloheptanone Semicarbazone[57-59]

A 1-l three-necked flask, equipped with a mechanical stirrer, a pressure-equalizing addition funnel, and a Claisen adapter containing a suspended thermometer and a drying tube, was flushed with dry nitrogen and charged with 16.0 g (0.092 mole) of 4-phenylcyclohexanone (Gallard-Schlesinger, recrystallized from cyclohexane: mp 77.0-78.7°), 0.60 g (0.0044 mole) of anhydrous potassium carbonate, and 350 ml of absolute ethanol. To this rapidly stirred suspension at -8° was added dropwise a solution of 14.26 g (0.108 mole) of N-nitroso-N-methylurethane in 325 ml of absolute ethanol. The temperature was kept between -12° and -2° throughout the addition, which required 5 3/4 hr. The mixture was stirred overnight while it warmed to room temperature. The resulting pale yellow mixture was treated with one ml of glacial acetic acid, and the solution was decanted from the white residue and concentrated (rotary evaporator) until solid began to precipitate. The slurry was redissolved in a minimum quantity of ethanol. This solution was added to a filtered solution of 10.3 g (0.092 mole) of semicarbazide hydrochloride, 25.8 g (0.19 mole) of sodium acetate trihydrate, and 105 ml of water, and the

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(57) P. Yates and C. D. Anderson, Can. J. Chem., **41**, 1033 (1963).

(58) E. D. Bergmann and S. Yaroslavsky, J. Am. Chem. Soc., **81**, 2772 (1959).

(59) W. von E. Doering and A. A. R. Sayigh, J. Org. Chem., **26**, 1365 (1961).

mixture was heated at 75° for 1/2 hr and allowed to stand overnight. Suction filtration yielded a wet white solid: 24.9 g; mp 158.5-162.0°. This solid was recrystallized from methanol to give 9.1 g (41%) of white crystals: mp 173.0-175.0° (lit[59] mp 175-177°). Successive concentrations of the mother liquor gave three additional portions of white crystals: 2.0 g, mp 166-169°; 2.0 g, mp 167.5-170.5°; and 1.3 g, mp 168.8-170.6°, respectively. The first crystals were recrystallized from ethanol to give 7.8 g of white crystals: mp 175.7-176.7°; ir (KBr): 3400 (vs, NH), 3030 (m, phenyl-H), 2900, 2850 (m, alkyl-H), 1675 (s, carbonyl), 1635 (s, primary amide), 1585 (s, phenyl), 1540 (m, secondary amide), 1485 (m, phenyl), 1450 (s, methylene), 1420 (m, primary amide), 757, 697 (s, monosubstituted phenyl).

(2) Preparation of 4-Phenylcycloheptanone[58,59]

4-Phenylcycloheptanone semicarbazone (page 36) (6.7 g, 27 mmoles) was dissolved in 52 ml of 10.5 N hydrochloric acid and 12 ml of water and extracted with ether (300 ml) in a continuous liquid-liquid extractor for 17 hr. The ether layer was washed with 60 ml of water, 50 ml of 1 N potassium carbonate, and two 50-ml portions of saturated sodium chloride. After drying over magnesium sulfate and filtration, the ether was removed to give 4.5 g of low-melting yellowish crystals.

The aqueous acid was extracted with a second portion of ether (200 ml) for 24 hr. The ether solution was treated as above to give an additional 0.3 g of solid (92% crude yield).

These two fractions were combined with 3.4 g of 4-phenylcycloheptanone (mp 49.3-55.0°) obtained from a similar experiment. Three recrystallizations from hexane gave white needles: mp 57.5-59.1° (lit[59] mp 52-53°); nmr ($CDCl_3$); $\underline{\delta}$1.4-2.2 (complex multiplet, 6 H, 3-, 5-, and 6-methylenes), $\underline{\delta}$2,3-2.8 (complex multiplet, 5 H, 2- and 7-methylenes and 4-H), $\underline{\delta}$7.12 (singlet, 5 H, phenyl); ir (KBr): 3050, 3020 (m, phenyl-H), 2910, 2850 (s, alkyl-H), 1700 (s, carbonyl; lit[59] $\underline{\nu}_{C=O}$ 1700), 1600, 1495 (m, phenyl), 1450 (s, methylene), 756, 698 (s, monosubstituted phenyl).

(3) Preparation of 4-Phenyl-1-methylcycloheptanol

To a 100-ml three-necked flask in a glove-bag filled with dry nitrogen were added 15 ml of a 1.7 M solution (25.5 mmoles) of methyllithium in ether. The flask was stoppered, removed from the bag, and quickly equipped with a mechanical stirrer, a reflux condenser containing a drying tube, and a pressure-equalizing addition funnel containing a solution of 1.27 g (6.76 mmoles) of 4-phenylcycloheptanone (page 38, mp 57.5-59.1°) in 15 ml of ether. The system was flushed with nitrogen, and the ketone was added dropwise over a 1-1/2-hr period. The cloudy mixture was stirred for an additional 2 hr and quenched by dropwise addition of water until the lithium hydroxide dissolved. The layers were separated. The aqueous layer was extracted with two 50-ml portions of ether, and the combined clear colorless ether layers were dried over sodium sulfate. Filtration and solvent removal (rotary evaporator) gave 1,35 g (98% crude yield) of a white solid, mp 80-83°. Seven recrystallizations from hexane gave a white solid: mp 103.5-104.0°; nmr (see page 70) ($CDCl_3$): $\underline{\delta}$1.25 (singlet, 3 H, 1-methyl), $\underline{\delta}$1.3-2.2 (multiplet, 10 H, ring methylenes), $\underline{\delta}$1.83 (singlet, 1 H, hydroxyl), $\underline{\delta}$2.3-2.9 (broad multiplet, 1 H, 4-H), and $\underline{\delta}$7.22 (singlet, 5 H, phenyl); ir (see page 71) (KBr): 3400 (s, OH), 3080, 3030 (m, phenyl-H), 2920, 2860 (s, alkyl-H), 1600, 1485 (m, phenyl), 1470, 1450, 1430 (m, methyl and methylene), 1365 (m, methyl), 1130 (s, tertiary alcohol), 757, 699 (s, monosubstituted phenyl).

Anal. Calcd for $C_{14}H_{20}O$: C, 82.26; H, 9.87. Found: C, 82.19; H, 9.72.

Although seven recrystallizations were necessary to achieve constant melting point of what was probably an initial mixture of *cis* and *trans* isomers, the spectra did not change appreciably after the first recrystallization. For preliminary experiments in the preparation of 1-methyl-6,7-benzobicyclo[3.2.2]non-6-ene (see page 42), material from the first through the fourth recrystallizations (mp 96.0-97.5°, 99.5-100.5°, 101.3-102.0°, and 102.5-103.2°, respectively) was used.

(4) Preparation of 1-Methyl-6,7-benzobicyclo[3.2.2]non-6-ene[60]

One ml of 85% sulfuric acid in a 5-ml flask equipped with a magnetic stirrer and a reflux condenser was cooled to 0°. 4-Phenyl-1-methylcycloheptanol (page 39, mp 103.5-104.0°) (197 mg, 0.97 mmole) was added in small portions over a 1-hr period. The mixture was warmed to room temperature, stirred for 2 hr (a second liquid layer slowly formed), and poured into 35 ml of water. The mixture was extracted with 50 ml of benzene; the benzene solution was washed with 25 ml of 10% sodium carbonate, then with 25 ml of 10% sodium sulfate, and dried over sodium sulfate. Filtration and solvent removal (rotary evaporator) gave a cloudy liquid. Gas chromatography on polar (cyclohexanedimethanol succinate) and nonpolar (Apiezon L) columns indicated, in each case, a single volatile component. Preparative gas chromatography yielded 105 mg (58%) of a clear colorless liquid: nmr (see page 72) (CCl_4): *δ*1.33 (singlet, 3 H, 1-methyl), *δ*1.2-2.1 (complex multiplet, 10 H, alkyl), *δ*2.8-3.1 (multiplet, 1 H, 5-H), *δ*6.9-7.2 (complex multiplet, 4 H, aromatic); ir (see page 73) (liquid film): 3080, 3020 (m, phenyl-H), 2920, 2860 (s, alkyl-H), 1600 (w), 1485 (s, aromatic), 1455, 1450 (m, methyl and methylene), 1375 (m, methyl), 748 (vs, *ortho*-disubstituted benzene), additional bands at 1365, 1340, 1300, 1265, 1245, 1200, 1150, 1115, 1110, 1065, 1055 (all w), 1035 (m), 1015, 985, 975, 950,

(60) Patterned after the method of D. Perlman, D. Davidson, and M. T. Bogert, *J. Org. Chem.*, **1**, 288 (1936).

937, 910, 870, 855, 837 (all w).

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 90.41; H, 9.59.

Similar results were obtained by heating 4-phenyl-1-methylcycloheptanol at 120° for 4 hr in 85% phosphoric acid,[61] but this procedure led to formation of small amounts of volatile side products, as shown by glc analysis.

In preliminary experiments, the samples of 4-phenyl-1-methylcycloheptanol which had been recrystallized from one to four times (see page 40) were used with identical results.

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(61) Based on the procedure of Ng. Ph. Buu-Hoi, H. Le Bihan, and F. Binon, *ibid.*, **16**, 185 (1951).

(C) Preparation of 1-Bromo-1-(bromomethyl)cycloheptane

(1) Preparation of Ethyl 1-(1-Hydroxycycloheptyl)-acetate[62,63,64]

To a 2-l three-necked flask equipped with a reflux condenser containing a drying tube, a mechanical stirrer, and a pressure-equalizing addition funnel were added 65.4 g (1.00 mole) of zinc dust, 150 ml of a solution prepared from dry cycloheptanone (112 g, 1.00 mole), ethyl bromoacetate (167 g, 1.00 mole), benzene (400 ml), and toluene (350 ml), and two small crystals of iodine. Heating to 105° with rapid stirring initiated the reaction. After the initial vigorous reaction, the remainder of the cycloheptanone-ethyl bromoacetate solution was added over a 55-min period, and the mixture was refluxed 3 hr. After cooling in an ice bath, sulfuric acid (10%, 465 ml) was cautiously added. The organic layer was washed with 100 ml of water and dried over magnesium sulfate. After filtration, most of the solvent was removed at room temperature and 13 mm pressure, and the residue was distilled under reduced pressure to yield 18.9 g of recovered cycloheptanone (bp

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(62) N. A. Abraham and M. Vilkas, Compt. rend., 248, 2880 (1959).

(63) M. Vilkas and N. A. Abraham, Bull. Soc. Chim. France, 1196 (1960).

(64) Based on the procedure of R. L. Shriner, "Organic Reactions," Vol. I, John Wiley and Sons, New York, New York, 1942, p 17. Also see A. I. Vogel, "Practical Organic Chemistry," 3d ed., John Wiley and Sons, Inc., New York, New York, pp 874-876.

82° at 2.3 mm) and 84.3 g (51% based on unrecovered cycloheptanone) of ethyl 1-(1-hydroxycycloheptyl)acetate: bp 94-96° (1.3-2.0 mm); nmr (CCl_4): $\underline{\delta}$1.27 (triplet, J = 7 cps, 3 H, methyl), $\underline{\delta}$1.57 (broad, 12 H, ring methylenes), $\underline{\delta}$2.40 singlet, 2 H, $\underline{\alpha}$-methylene), $\underline{\delta}$3.37 (singlet, 1 H, disappears on shaking with D_2O, hydroxyl), $\underline{\delta}$4.14 (quartet, J = 7 cps, 2 H, methylene of carboethoxy); ir (liquid film): 3500 (m, OH), 2920, 2860 (s, alkyl-H), 1720 (s, carbonyl), 1460, 1440 (m, methyl and methylene), 1370 (m, methyl), 1180 (s, tertiary alcohol).

(2) Preparation of 1-(1-Hydroxycycloheptyl)acetic Acid[62,63]

A solution of 75.0 g (0.375 mole) of ethyl 1-(1-hydroxycycloheptyl)acetate (page 43) in 375 ml of 2 M methanolic potassium hydroxide was refluxed overnight. Most of the methanol was removed (rotary evaporator) to give a white solid and an amber liquid. Water (500 ml) was added with cooling, and the mixture was extracted with 50 ml of benzene. The aqueous solution was acidified with 70 ml of 12 N hydrochloric acid, and the cloudy mixture was extracted with four 50-ml portions of ether. The combined ether solution was dried over sodium sulfate, and after filtration the ether was removed (rotary evaporator) to yield 61.9 g (96%) of the acid as a viscous orange residue: nmr ($CDCl_3$): $\underline{\delta}$1.58 and 1.77 (overlapping broad singlets, 12 H, ring methylenes), $\underline{\delta}$2.55 (singlet, 2 H, $\underline{\alpha}$-methylene), $\underline{\delta}$7.67 (singlet, 2 H, mean of the values for the rapidly exchanging $\underline{\beta}$-hydroxy and carboxylic acid protons); ir (liquid film): 3300-2700 (m, OH and COOH), 2920, 2860 (s, alkyl-H), 1715 (vs, carboxylic acid), 1460, 1440 (m, methylene), 1400 (m), 1200 (s), 920 (w, carboxylic acid), 1135 (m, tertiary alcohol).

(3) Preparation of Methylenecycloheptane[62,63]

This preparation was carried out three times according to the directions of Abraham and Vilkas,[62,63] but their claimed high purity of product (absence of 1-methylcycloheptene) could not be reproduced. The purities of the methylenecycloheptane from the three runs were 92, 78, and 84% respectively, as determined by vpc on a silver nitrate-triethylene glycol column.[65] A typical experiment follows.

A mixture of 45.8 mg of copper powder, 13.1 g (76.2 mmoles) of 1-(1-hydroxycycloheptyl)acetic acid (page 45), and 9.1 ml (10.0 g, 77.5 mmoles) of freshly distilled quinoline was heated at 200-210° with stirring for 3 hr in a flask attached to a distillation assembly, The upper layer of the distillate was removed and dried over potassium carbonate.

Pure methylenecycloheptane was obtained by preparative glc of the 92% pure material (see above) on a silver nitrate-triethylene glycol column: nmr (see page 72) ($CDCl_3$): $\underline{\delta}$1.56 (broad singlet, 8 H, 3-, 4-, 5-, and 6-methylene), $\underline{\delta}$2.30 (broad singlet, 4 H, 2- and 7-methylene), $\underline{\delta}$4.72 (multiplet, 2 H, olefin); ir (see page 73) (liquid film): 3060 (w, olefin-H), 2910, 2860 (s, alkyl-H), 1645 (m, olefin), 1450 (s, methylene), 880 (s, 1,1-disubstituted olefin).

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(65) J. Shabtai, J. Chromatog., 18, 302 (1965).

(4) Preparation of 1-Bromo-1-(bromomethyl)cycloheptane[66,67,68]

A solution of methylenecycloheptane (page 46) (0.847 g, 7.7 mmoles), methylene chloride (15 ml), and dry pyridine (0.62 ml, 0.61 g, 7.7 mmoles) was cooled to -78° under nitrogen in a 100-ml three-necked flask wrapped with aluminum foil and equipped with a mechanical stirrer, a reflux condenser containing a drying tube, and a pressure-equalizing addition funnel. A solution of 0.39 ml (1.23 g, 7.7 mmoles) of bromine in 30 ml of methylene chloride was added in a slow trickle to the rapidly stirred olefin solution over a 55-min period. The mixture was stirred an additional 15 min at -78° and warmed to room temperature. Solvent was removed (rotary evaporator) from the yellow liquid to give a mixture of colorless liquid and orange solid (probably pyridinium bromide perbromide) which was extracted with four portions of hexane. A residue of orange solid remained. The hexane was removed (rotary evaporator) to give 1.42 g (68%) of a colorless oil: nmr (see page 74) (CCl_4): $\underline{\delta}$1.68 (broad singlet, 8 H, 3-, 4-, 5-, and 6-methylene), $\underline{\delta}$2.15 (broad, 4 H, 2- and 7-methylene), $\underline{\delta}$3.89 (singlet, 2 H,

[66] J. Wolinsky and K. L. Erickson, J. Org. Chem., **30**, 2208 (1965).

[67] J. Wolinsky, R. Novak, and K. L. Erickson, Abstracts of Papers Presented at the 152nd National Meeting of the American Chemical Society, New York, New York, Sept. 12-16, 1966, page S2.

[68] Private communication from Prof. J. Wolinsky to Prof. L. H. Schwartz, Feb. 7, 1967. We are indebted to Professor Wolinsky for communicating details of his procedure to us prior to publication.

bromomethyl).

Bromination under similar conditions of methylenecycloheptane containing 8% 1-methylcycloheptene (page 46) yielded a mixture as indicated by nmr (page 74) which showed a singlet at $\underline{\delta}2.00$, attributable to a methyl group attached to a carbon bearing a bromine atom. This absorption was absent in the product of bromination of pure methylenecycloheptane.

(D) Preparation of 1-Phenylcycloheptylmethyl Tosylate

(1) Preparation of Cycloheptyl Phenyl Ketone[69]

Magnesium shavings (18.4 g, 0.767 mole) and a solution of 14 ml of dry bromobenzene in 120 ml of anhydrous ether were added to a 3-l three-necked flask equipped with a mechanical stirrer, a reflux condenser containing a drying tube, and an addition funnel. The mixture was warmed gently until refluxing began and cloudiness was observed, then stirring was begun (vigorous reaction) and a solution of 66 ml of bromobenzene in 580 ml of ether was added over a 90-min period at a rate which maintained gentle reflux. The mixture was stirred for 30 min, cooled to -10°, and a solution of 75.0 g (0.61 mole) of cycloheptyl cyanide in 100 ml of ether was added dropwise. The mixture was stirred at room temperature overnight, then cooled to 0°. A slurry of ice and water (1000 ml) followed by an ice-cold solution of 75 ml of concentrated sulfuric acid in 150 ml of water were added. The aqueous layer was extracted twice with ether, and the combined ether solution was washed with 5% sodium carbonate and water and dried over sodium sulfate. Distillation yielded 108.4 g (88%) of light yellow liquid: bp 137-138° (1.9-2.4 mm) (lit bp 185° (35 mm),[69] 115-117° (0.1 mm)[70]); nmr (CCl_4): *δ*1.63 (broad singlet with a shoulder on the low-field side, 12 H, cycloalkyl), *δ*3.1-3.6 (broad

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(69) J. W. Wilt, J. F. Zawadzki, and D. G. Schultenover, S.J., *J. Org. Chem.*, *31*, 876 (1966).

(70) C. H. Tilford and M. G. Van Campen, Jr., *J. Am. Chem. Soc.*, *76*, 2431 (1954).

multiplet, 1 H, hydrogen adjacent to benzoyl), δ7.1-7.6 and 7.7-8.1 (complex multiplets, 5 H, aromatic; this absorption resembles that of the benzoyl group published by Castellano and Bothner-By[71]); ir (liquid film): 3060, 3020 (w, aromatic-H), 2910, 2850 (s, alkyl-H), 1680 (vs, aromatic ketone), 1600, 1580 (m, conjugated phenyl), 1480 (w), 1456, 1443 (s, phenyl and methylenes), 776, 692 (s, monosubstituted phenyl). The 2,4-dinitrophenylhydrazone, after recrystallization from methanol, melted at 167-169° (lit mp 168-169°,[69] 170-171°[70]).

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(71) S. Castellano and A. A. Bothner-By, *J. Chem. Phys.*, **41**, 3863 (1964).

(2) Preparation of 1-Chlorocycloheptyl Phenyl Ketone[69]

Sulfuryl chloride (100 ml, 167 g, 1.24 moles) was cooled in a 250-ml three-necked flask equipped with a mechanical stirrer, a reflux condenser containing a drying tube, and a pressure-equalizing addition funnel. Cycloheptyl phenyl ketone (page 49) (20.3 g, 0.10 mole) was added over a 20-min period. The mixture was warmed to room temperature (gas evolution). When spontaneous gas evolution ceased, the mixture was heated under reflux for 2 hr, then stirred at room temperature overnight.

The mixture was poured onto excess ice, and a yellow oil settled out. The aqueous layer was extracted twice with carbon tetrachloride, and the combined organic solution was washed with saturated aqueous sodium bicarbonate and saturated aqueous sodium chloride. Removal of the carbon tetrachloride (rotary evaporator) gave a yellow oil which, because of its instability,[69] was used directly without further purification in the preparation of 1-phenylcycloheptanecarboxylic acid (page 52).

(3) Preparation of 1-Phenylcycloheptanecarboxylic Acid[69]

To a stirred solution of unpurified 1-chlorocycloheptyl phenyl ketone (total crude yield from the preparation on page 51) in 180 ml of dioxane (freshly distilled from sodium hydroxide) in a 500-ml flask equipped with a reflux condenser was added a solution of 34 g (0.20 mole) of silver nitrate in 20 ml of distilled water. The mixture was heated in a bath at 70-75° for 5 hr with stirring, cooled, and filtered with suction to give 14.2 g (99%) of silver chloride. The yellow filtrate was diluted with 500 ml of water and extracted with four 60-ml portions of ether. The combined ether solution was extracted with four 20-ml portions of 10% sodium carbonate. The combined basic aqueous solution was boiled briefly, cooled, and carefully acidified by dropwise addition of conc hydrochloric acid to pH 1. The mixture was filtered with suction to give 5.5 g (23%, based on the conversion of cycloheptyl phenyl ketone to the acid) of a light tan solid. Recrystallization from heptane gave white prisms: mp 130.7-131.4° (lit[69] mp 127.5-128.5°); nmr ($CDCl_3$): $\underline{\delta}$1.61 (broad singlet, 8 H, 3-, 4-, 5-, and 6-methylenes), $\underline{\delta}$2.0-2.6 (complex multiplet, 4 H, 2- and 7-methylenes), $\underline{\delta}$7.38 (singlet with splitting at the base, 5 H, phenyl), $\underline{\delta}$11.50 (broad, 1 H, carboxylic acid) (lit[69] nmr (no solvent given): $\underline{\delta}$1.42-2.50, $\underline{\delta}$7.07-7.50, and $\underline{\delta}$12.13); ir (KBr): 3600-2400 (m, broad, carboxylic acid), 3030 (m, phenyl-H), 2900, 2840 (s, alkyl-H), 1695 (vs, carboxylic acid), 1600, 1580, 1493 (m, phenyl), 1462, 1440 (m, methylenes), 1398 (m), 1266 (s), 931 (m, carboxylic acid), 758 (m), 695 (s, monosubstituted phenyl) (lit[69] ir (KBr): 1695 (carboxylic acid)).

(4) Preparation of 1-Phenylcycloheptylcarbinol[69]

Lithium aluminum hydride (1.04 g, 27 mmoles) and anhydrous ether (55 ml) were stirred in a 250-ml three-necked flask equipped with a mechanical stirrer, a reflux condenser containing a drying tube, and a pressure-equalizing addition funnel. A solution of 3.55 g (16 mmoles) of 1-phenylcycloheptanecarboxylic acid (page 52) in 120 ml of ether was added dropwise over a 40-min period, and the reaction mixture was refluxed gently overnight. The reaction was quenched by dropwise addition of 25 ml of water followed by enough 10% sulfuric acid (54 ml) to dissolve the aluminum salts. The aqueous layer was extracted with 25 ml of ether, and the combined ether solution was washed with two 25-ml portions of 10% sodium carbonate and dried over magnesium sulfate. Filtration and solvent removal gave a quantitative yield of a cloudy, pale yellow oil: nmr ($CDCl_3$): $\underline{\delta}1.52$ (broad singlet, 8 H, 3-, 4-, 5-, and 6-methylenes), $\underline{\delta}1.65$ (singlet, 1 H, hydroxyl), $\underline{\delta}1.8$-2.4 (complex multiplet, 4 H, 2- and 7-methylenes), $\underline{\delta}3.37$ (singlet, 2 H, oxymethylene), $\underline{\delta}7.30$ (singlet with splitting at the base, 5 H, phenyl) (lit[69] nmr (no solvent given): $\underline{\delta}1.2$-2.33, $\underline{\delta}2.43$, $\underline{\delta}3.22$, and $\underline{\delta}7.27$); ir (liquid film): 3330 (m, broad, hydroxyl), 3020 (w, phenyl-H), 2890, 2830 (s, alkyl-H), 1598 (w), 1492 (m, aromatic), 1462, 1437 (m, methylenes), 1055 (s, primary alcohol), 753, 696 (s, monosubstituted phenyl) (lit[69] ir (neat liquid): 3355 (hydroxyl) and 1064 (primary alcohol)).

(5) Preparation of 1-Phenylcycloheptylmethyl Tosylate[69]

To a 100-ml flask equipped with a magnetic stirrer and a reflux condenser containing a drying tube were added 3.21 g (15.7 mmoles) of 1-phenylcycloheptylcarbinol (page 54), 15 ml of dry pyridine, and a solution of 5.10 g (26.8 mmoles) of para-toluenesulfonyl chloride in 10 ml of dry pyridine. The mixture was stirred at room temperature for 17 hr and poured into a mixture of ice and conc hydrochloric acid. The resulting cloudy mixture was extracted twice with chloroform, and the combined chloroform solution was washed with water and dried over magnesium sulfate. After filtration and solvent removal (rotary evaporator), the resulting yellow solid was recrystallized from benzene-hexane to yield 3.23 g of white needles: mp 83.0-83.5° (lit[69] mp 79.5-80.5°). Concentration of the mother liquors yielded another 1.93 g of white needles: mp 82.4-83.4° (total yield 92%). The spectra of each crop were identical: nmr ($CDCl_3$): δ1.49 (broad singlet, 8 H, 3-, 4-, 5-, and 6-methylenes), δ1.7-2.1 (complex multiplet, 4 H, 2- and 7-methylenes), δ2.39 (singlet, 3 H, aromatic methyl), δ3.90 (singlet, 2 H, oxymethylene), δ7.15, 7.28, 7.50, 7.63 (A½B½, 4 H, aromatic hydrogens of the para-toluenesulfonyl group), δ7.24 (singlet, 5 H, aromatic hydrogens of the 1-phenyl group) (lit[69] nmr (no solvent given): δ1.33-2.33 (multiplet, ring methylenes), δ2.4 (singlet, aromatic methyl), δ3.83 (singlet, oxymethylene), and δ7.4 (multiplet, aromatic hydrogens)); ir (KBr): 3060, 3000 (w, aromatic-H), 2890, 2830 (m, alkyl-H), 1595, 1485 (m, aromatic), 1455, 1442, 1432 (m, methyl and methylene), 1352, 1172 (s, sulfonate ester), 810 (m, *para*-disubstituted aromatic), 753 (m), 693 (s, monosubstituted phenyl) (lit[69] ir (KBr): 1350 and 1178 (sulfonate ester)).

(E) Preparation of 4-Phenyl-1-methylcycloheptyl Bromide

Hydrobromic acid (48%, 2 ml, 17.8 mmoles) was cooled to 0° in a 5-ml flask. 4-Phenyl-1-methylcycloheptanol (page 39) (48.4 mg, 0.237 mmole) was added, a reflux condenser was attached, and the mixture was stirred at room temperature for 1/2 hr, during which time a yellow oil separated out. The mixture was poured into 20 ml of water and extracted with 20 ml of benzene. The benzene solution was washed with 3.5 ml of saturated sodium bicarbonate followed by 3 ml of saturated sodium bromide and dried over sodium sulfate. Filtration and solvent removal (rotary evaporator) gave 70.6 mg of an oil which contained some benzene: nmr (C_6H_6; values were calculated assuming the C_6H_6 peak to be at δ7.27): δ1.75 (singlet, 3 H, 1-methyl), δ1.27-2.04 (broad complex multiplet, 6 H, 3-, 5-, and 6-methylenes), δ2.07-2.88 (broad complex multiplet, 5 H, 2- and 7-methylenes and 4-H); the phenyl protons were hidden by the large benzene absorption; no olefinic protons were observed. This material was used directly in a Friedel-Crafts reaction (page 65).

(F) Friedel-Crafts Reactions

(1) Friedel-Crafts Reaction of 1,1-Bis(bromomethyl)cyclohexane

(a) Kinetic Studies

A typical kinetic run was carried out as follows. A 2-l three-necked flask equipped with a mechanical stirrer, a reflux condenser containing a drying tube, and a gas inlet tube was flushed with dry nitrogen for 3 hr while being heated at 80°. A stirred mixture of 900 ml of benzene (Reagent Grade dried over silica gel, distilled, and the center cut boiling at 79.9° stored over Dri-Na) and 0.35 g (2.6 mmoles) of powdered anhydrous aluminum chloride was thermostated in the flask at 40.0 ± 0.1°, and a mixture of 2.516 g (9.32 mmoles) of 1,1-bis(bromomethyl)cyclohexane (page 35) in 100 ml of benzene was added at zero time. Aliquots (50 ml) were removed at intervals of approximately 250 sec and quenched by adding each one to 50 ml of 3N hydrochloric acid. Each organic layer was washed with 25 ml saturated aqueous sodium bicarbonate, dried over sodium sulfate, filtered, and concentrated (rotary evaporator). The residues were analyzed by glc (diethylene glycol succinate, 20% on 60/80 mesh Chromosorb P, 60 cc of helium per min, 195°). A plot of log [100(area of the 1,1-bis(bromomethyl)cyclohexane peak) / (sum of areas of all the peaks)] vs time (see page 75) gave a straight line initially, intercepting the y-axis at 2.00. From the slope of the straight line portion of the curve, the pseudo-first-order rate constant was calculated to be 1.6 x 10^{-3} $\sec^{-1}$ to t = 1019 sec. (This method assumes that each product molecule contains only one organic moiety from 1,1-bis(bromomethyl)cyclohexane, or that the total concentration of organic solutes is constant, and that each compound has the same thermal conductivity.) The pseudo-first-order rate constants obtained from the equation

$$k_1 = \frac{2.303}{t} \log \frac{1}{\text{mole fraction of 1,1-bis(bromomethyl)cyclohexane}}$$

decreased with time; $10^3 k$ = 1.6 $\sec^{-1}$ up to 1019 sec, 1.1 $\sec^{-1}$ at 2262 sec, 0.97 $\sec^{-1}$ at 3003 sec, 0.80 $\sec^{-1}$ at 3788 sec, and 0.47 $\sec^{-1}$ at 7290 sec (Table 3, page 83). See pages 83-84 for a discussion of this phenomenon.

(b) Product Studies

Six runs were performed, each using approximately 1900 ml of benzene, 0.7 g (5.2 mmoles) of aluminum chloride, and 5.1 g (19 mmoles) of 1,1-bis(bromomethyl)cyclohexane in 100 ml of benzene. The procedure was similar to that of the kinetic studies (page 58), except that each reaction was quenched after 15 min and worked up as above. The combined residues after removal of benzene were distilled under vacuum through a spinning-band column. The collected fractions are indicated in Table 1.

Table 1: Distillation Fractions from Friedel-Crafts Reaction of 1,1-Bis(bromomethyl)cyclohexane.

Fraction no.	bp (mm)	Volume
1	81-87° (1.7)	0.4 ml
2	88-96° (1.7-1.8)	6.1
3	96-97° (1.8)	2.7
4	95° (1.75)	0.4
5	94-95° (1.7-1.8)	7.2
6	97° (2.0)	0.7
7	101-102° (2.0)	0.4
8	103° (1.95)	0.6

Fraction 3 was shown by glc to contain the highest proportion of "primary product." Preparative gas chromatography of this fraction (cyclohexanedimethanol succinate, 25% on 70/80 mesh Gaschrom R, 65-75 cc of helium per min, 200°) yielded 1-methyl-6,7-benzobicyclo[3.2.2]non-6-ene ("primary product") as a clear colorless liquid: uv (see page 76)(95% ethanol): 270 (log ϵ = 2.63), 262.5 (log ϵ = 2.66), 259 (s, log ϵ = 2.54), 256 (s, log ϵ = 2.50), 250 (s, log ϵ = 2.31), and 2.09 mμ (log ϵ = 3.94); nmr (see page 77)(CCl_4): δ1.33 (singlet, 3 H, 1-methyl), δ1.2-2.1 (complex multiplet, 10 H, alkyl), δ2.8-3.1 (multiplet, 1 H, 5-hydrogen), δ6.9-7.2 (complex multiplet, 4 H, aromatic); the mass spectrum is described in Table 2, page 62 and reproduced on page 78.

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 90.31; H, 9.85.

Table 2: Relative Intensities of Peaks in the Mass Spectra of 1-Methyl-6,7-benzobicyclo[3.2.2]non-6-ene ("Primary Product") Derived from Different Starting Materials.

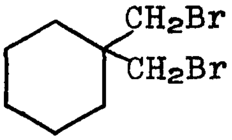
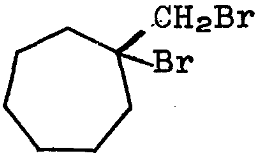
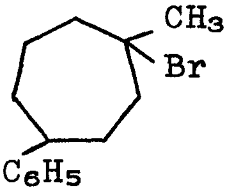
	Starting Material		
m/e			
188	0.78	1.0	0.91
187	5.54	5.32	6.32
186	36.1	36.2	40.4
185	2.08	2.0	2.28
172	1.98	2.0	2.15
171	13.72	14.2	14.2
165	0.46	0.50	0.56
159	0.70	0.69	0.75
158	5.66	5.43	5.68
157	9.73	9.29	8.35
156	1.05	1.2	1.1
155	1.22	1.3	1.3
154	0.57	0.77	0.66
153	1.25	1.5	1.4
152	1.32	1.5	1.5
151	0.33	0.54	0.52
146	1.09	1.0	1.2
145	13.77	13.5	14.5
144	68.75	67.0	76.78
143	100.00	100.00	100.00
142	12.16	12.1	11.8
141	12.17	12.5	12.0
140	0.95	0.77	0.81
139	1.77	1.7	1.7
132	0.67	0.77	0.77
131	3.99	4.39	4.39
130	10.25	11.1	10.2
129	41.70	41.2	37.9
128	40.78	42.2	37.0
127	10.78	11.1	9.32
126	1.28	1.3	1.3
118	1.64	2.0	2.63
117	5.02	5.78	6.09
116	4.42	4.35	4.39
115	20.21	20.0	19.2
114	0.82	0.66	0.66
113	0.62	0.54	0.62
108	1.09	0.39	0.79
105	1.48	1.9	2.38

Table 2 (continued)

104	1.75	2.5	8.00
103	2.17	2.6	2.65
102	2.50	2.6	2.36
101	0.80	0.62	0.81
97	0.22	0.54	0.25
95	0.42	0.62	1.5
93	1.36	1.1	2.13
92	0.93	1.2	1.3
91	8.76	9.56	10.1
89	2.33	2.3	2.46
87	0.63	0.62	0.64
83	0.26	0.50	0.50
82	0.34	0.62	1.1
81	0.46	0.85	0.99
79	1.58	1.8	2.30
78	2.44	2.9	2.73
77	6.49	6.24	6.61
76	2.01	1.7	1.8
75	1.59	1.4	1.2
74	0.70	0.54	0.62
71	2.00	1.8	2.24
70.5	0.90	0.74	1.2
70	0.75	0.81	0.99
69	0.96	0.92	1.1
67	1.16	1.1	2.24
66	0.40	0.54	0.66
65	3.90	3.6	4.08
64	1.79	1.7	1.7
63	3.98	3.8	3.67
62	0.72	0.58	0.72
58	0.49	0.58	0.58
57.5	0.92	0.77	0.95
57	0.56	0.89	0.64
56	0.30	0.54	0.46
55	4.29	3.4	3.25
53	2.30	2.2	2.55
52	1.48	1.3	1.3
51	5.54	4.78	4.62
50	1.48	1.3	1.4
44	0.43	2.4	1.5
43	2.50	2.4	2.13
42	1.98	1.2	1.2
41	7.12	6.05	6.17
40	1.18	1.0	0.93
39	8.47	7.28	6.90
38	0.43	0.54	0.50

(2) Friedel-Crafts Reaction of 1-Bromo-1-(bromomethyl)-cycloheptane

This reaction was conducted similarly to the product studies in the reaction of 1,1-bis(bromomethyl)cyclohexane (page 60). 1-Bromo-1-bromomethylcycloheptane (page 47) (1.22 g, 4.54 mmoles) in 40 ml of benzene was added to a mixture of 310 ml of benzene and 0.16 g (1.18 mmoles) of aluminum chloride. After 15 min the reaction was quenched and worked up by the already-stated procedure to yield 0.93 g of a cloudy yellow liquid. Gas chromatography (cyclohexanedimethanol succinate, 25% on 70/80 mesh Gaschrom R, 61 cc of helium per min, 190°) indicated a mixture similar in composition to that obtained from 1,1-bis(bromomethyl)cyclohexane (see page 60). The peak corresponding to 1-methyl-6,7-benzobicyclo[3.2.2]non-6-ene was of greater relative intensity in this mixture. Preparative glc gave a clear colorless liquid: ir (see page 79)(liquid film): 3040, 3000 (m, phenyl-H), 2905, 2840 (s, alkyl-H), 1602 (w), 1478 (s, aromatic), 1454, 1445 (s, methyl and methylene), 1368 (m, methyl), 748 (vs, *ortho*-disubstituted benzene), additional bands at 1350, 1338, 1297, 1259, 1242, 1197, 1146, 1113, 1107, 1065, 1049 (all w), 1035 (m), 1011, 982, 974, 948, 935, 908, 869, 853, 836 (all w); the mass spectrum is described in Table 2, page 62.

(3) Friedel-Crafts Reaction of 4-Phenyl-1-methylcycloheptyl Bromide

Addition of 63.3 mg (0.237 mmole) of 4-phenyl-1-methylcycloheptyl bromide (page 57) in 10 ml of benzene to a mixture of 50 ml of benzene and 14.1 mg (0.105 mmole) of aluminum chloride at 40° for 15 min gave, after treatment as already described, 61.0 mg of a yellow oil. Gas chromatography (see page 64 for conditions) indicated two major components, the first-eluted of which had the same retention time as 1-methyl-6,7-benzobicyclo[3.2.2]non-6-ene, and many minor peaks with the same retention times as the major by-products in the Friedel-Crafts reaction of 1,1-bis(bromomethyl)cyclohexane. The two major components were isolated as clear colorless liquids by preparative glc. The first-eluted of these components was 1-methyl-6,7-benzobicyclo[3.2.2]non-6-ene: ir (see page 79) (liquid film): 3040, 3000 (m, phenyl-H), 2905, 2840 (s, alkyl-H), 1602 (w), 1480 (s, aromatic), 1455, 1445 (s, methyl and methylene), 1370 (m, methyl), 748 (vs, ortho-disubstituted benzene), additional bands at 1350, 1340, 1299, 1260, 1242, 1198, 1147, 1115, 1108, 1065, 1051 (all w), 1037 (m), 1011, 984, 976, 950, 937, 909, 872, 853, 837 (all w); the mass spectrum is described in Table 2, page 62.

(4) Friedel-Crafts Reaction of 1-Phenylcycloheptylcarbinol

(a) In the Absence of Benzene[60]

One ml of 85% sulfuric acid in a 5-ml flask equipped with a magnetic stirrer and a reflux condenser was cooled to 0°. 1-Phenylcycloheptylcarbinol (page 54) (105 mg, 0.51 mmole) was added dropwise with vigorous stirring. The mixture was stirred for three hours at room temperature and poured into 30 ml of water. The mixture was extracted with two 10-ml portions of benzene, and the combined benzene solution was washed with 10 ml of 10% sodium carbonate, then with 10 ml of 10% sodium sulfate, and dried over sodium sulfate. Filtration and solvent removal (rotary evaporator) gave a cloudy yellow liquid which gas chromatography indicated to contain nine components. One of these compounds had a retention time 2% greater than that of 1-methyl-6,7-benzobicyclo[3.2.2]non-6-ene, but its area was no more than 6% of the total areas of all the peaks.

(b) In the Presence of Benzene[72]

This reaction was conducted similarly to the Friedel-Crafts reactions previously mentioned (pages 58-65). Aluminum chloride (182 mg, 1.36 mmoles) was added to a stirred solution of 1-phenylcycloheptylcarbinol (page 54) (226 mg, 1.11 mmoles) in 100 ml of benzene at 40°. After 1-1/2 hr the reaction was quenched and treated by the previously stated procedure to give a cloudy yellow oil. Gas chromatography (see page 58 for conditions) showed eight major and ten minor monophenyl products plus two products of longer retention time which are probably diphenyl compounds. One of the major products had a retention time 2% greater than that of 1-methyl-6,7-benzobicyclo[3.2.2]non-6-ene, but its area was no more than 4% of the total areas of the monophenyl compounds and no more than 3% of the total areas of all the products.

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(72) A. Schriesheim in "Friedel-Crafts and Related Reactions," G. A. Olah, Ed, Interscience Publishers, Inc., New York, N. Y., 1964, Vol II, pp 486-508.

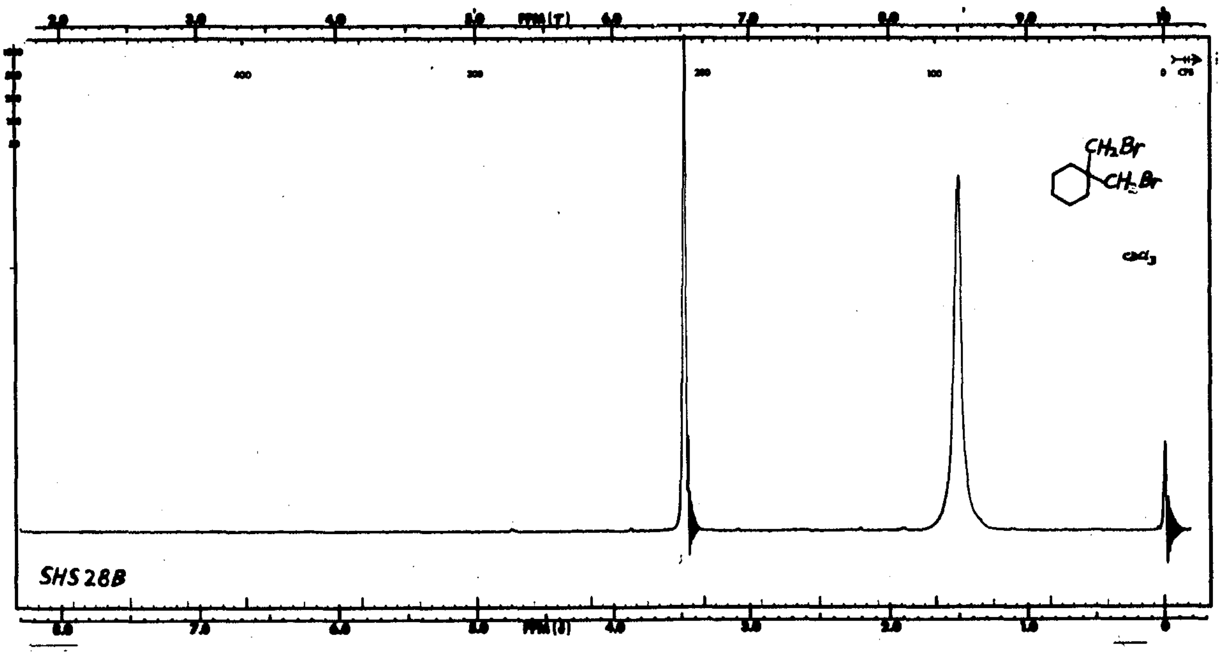
(5) Friedel-Crafts Reaction of 1-Phenylcycloheptylmethyl Tosylate[73]

Addition of aluminum chloride (189 mg, 1.50 mmoles) to a solution of 1-phenylcycloheptylmethyl tosylate (page 55) (400 mg, 1.12 mmoles) in 100 ml of benzene at 40° gave, after 1-1/2 hr reaction time and the usual treatment, a cloudy white liquid. Gas chromatography (see page 58 for conditions) showed five major and nine minor monophenyl compounds plus four products of longer retention time which are probably diphenyl compounds. The peak area of the major product with a retention time 2% greater than that of 1-methyl-6,7-benzobicyclo[3.2.2]non-6-ene again constituted no more than 4% of the total areas of the monophenyl compounds and no more than 3% of the total areas of all the products.

---

(73) F. A. Drahowzal in "Friedel-Crafts and Related Reactions," G. A. Olah, Ed, Interscience Publishers, Inc., New York, N. Y., 1964, Vol II, pp 648-653.

SPECTRA
AND
GRAPHS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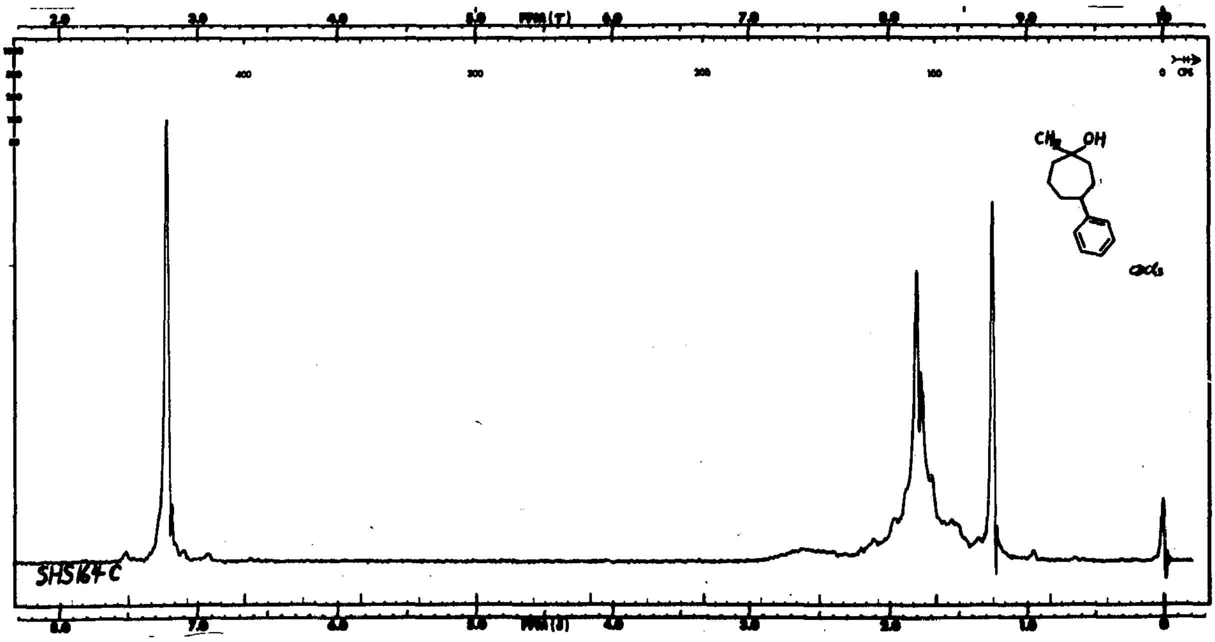
3.0
4.0
5.0
PPM(τ)
6.0
7.0
8.0
9.0
10
400
300
200
100
0 CPS
CH_2Br
CH_2Br
$CDCl_3$
SHS 28B
8.0
7.0
6.0
5.0
PPM(δ)
4.0
3.0
2.0
1.0
0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5.0
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100
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CH_3 OH
$CDCl_3$
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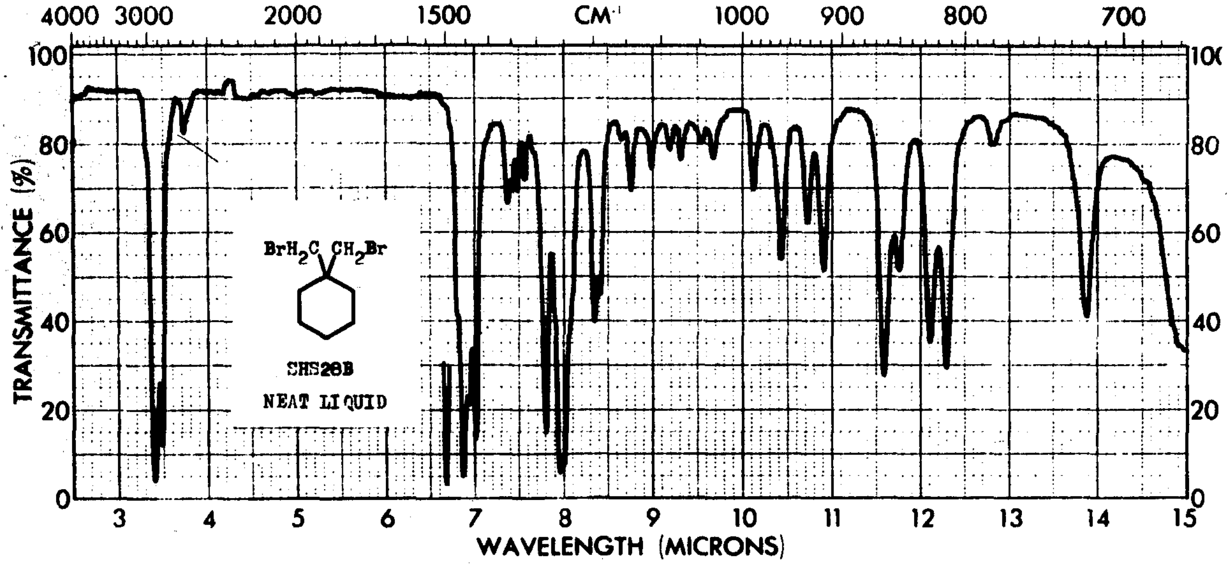
2.0
1.0
0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80
60
40
20
0
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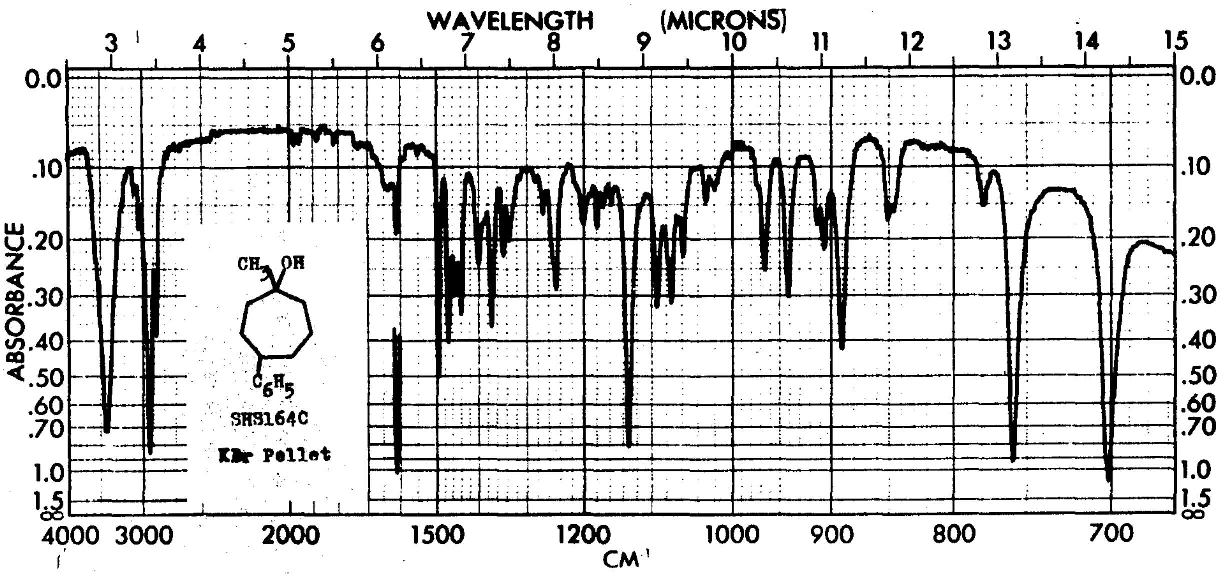
WAVELENGTH (MICRONS)
BrH_2C CH_2Br
SHS28B
NEAT LIQUID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ABSORBANCE
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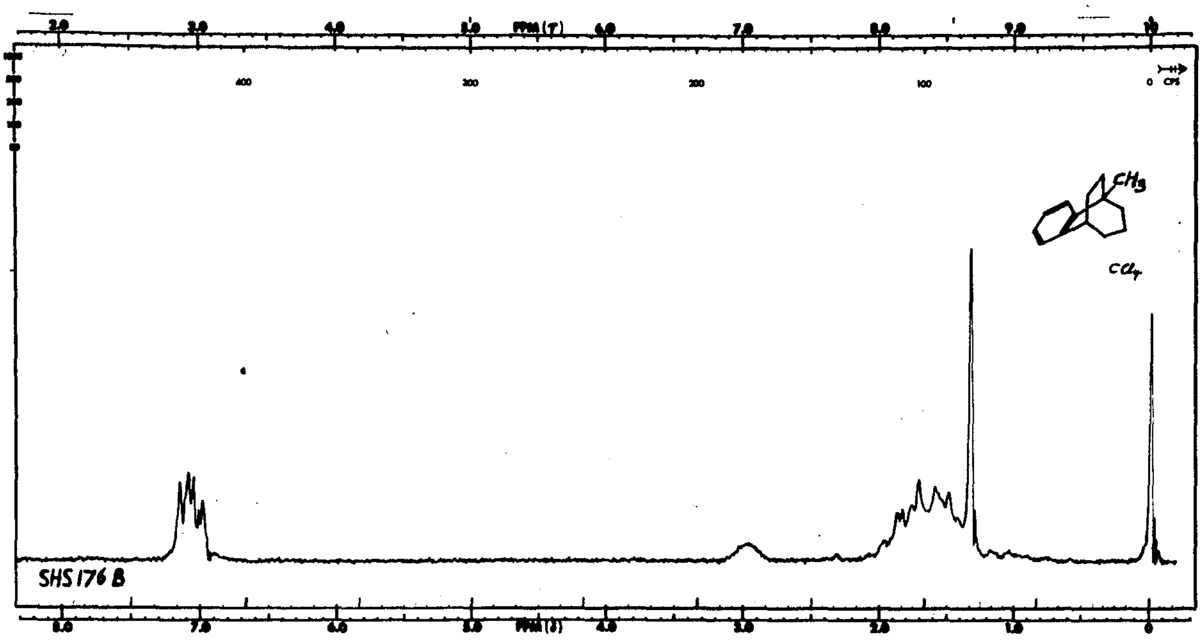
.10
.20
.30
.40
.50
.60
.70
1.0
1.5
∞
CH_3 OH
C_6H_5
SHS164C
KBr Pellet
4000 3000 2000 1500 1200 1000 900 800 700
CM⁻¹


PPM (τ)
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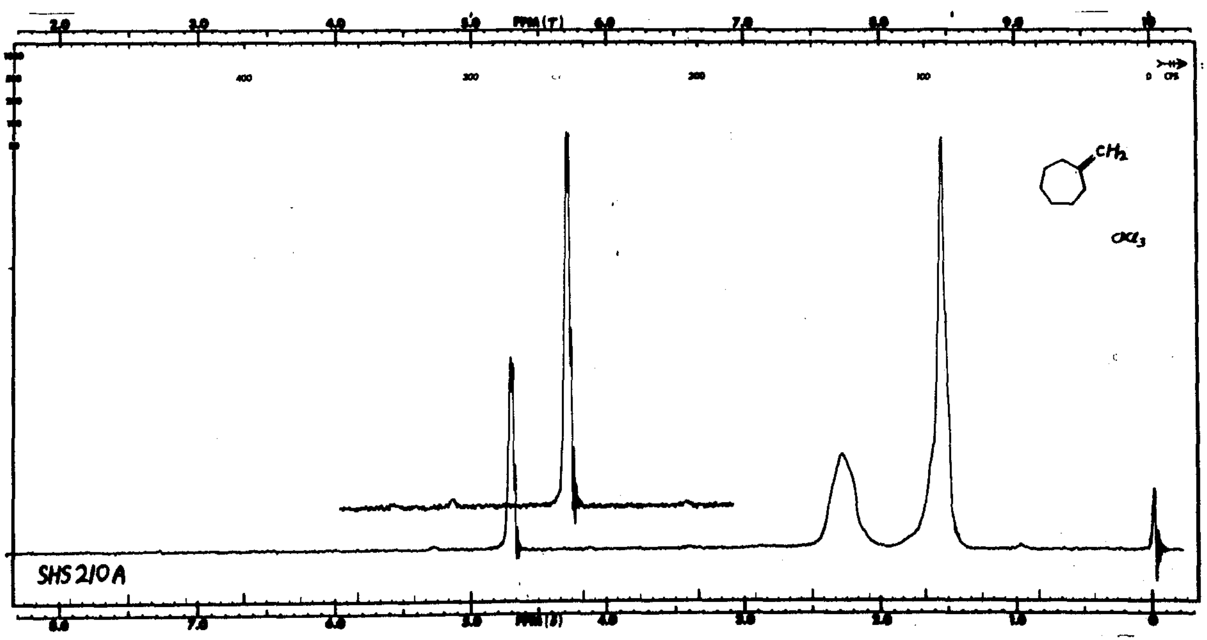
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10
400
300
200
100
0 CPS
CH3
CCl4
SHS 176 B
PPM (δ)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0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3.0
4.0
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6.0
7.0
8.0
9.0
10
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300
200
100
0 CPS
CH2
CCl3
SHS 210 A
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6.0
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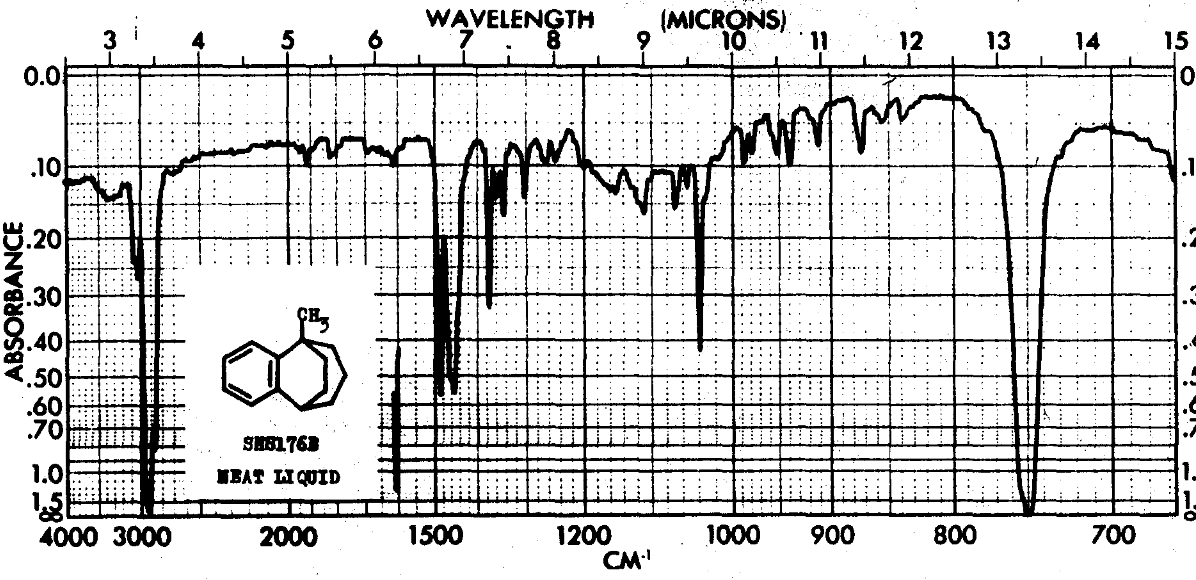
4.0
3.0
2.0
1.0
0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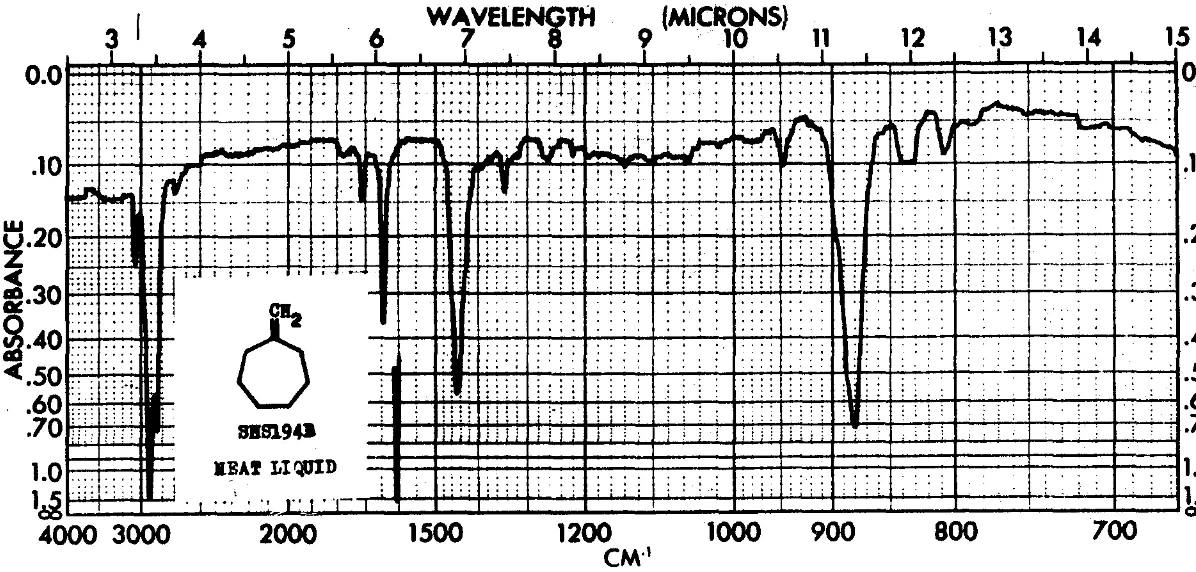
CM⁻¹
CH3
SHS176B
NEAT LIQUID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ABSORBANCE
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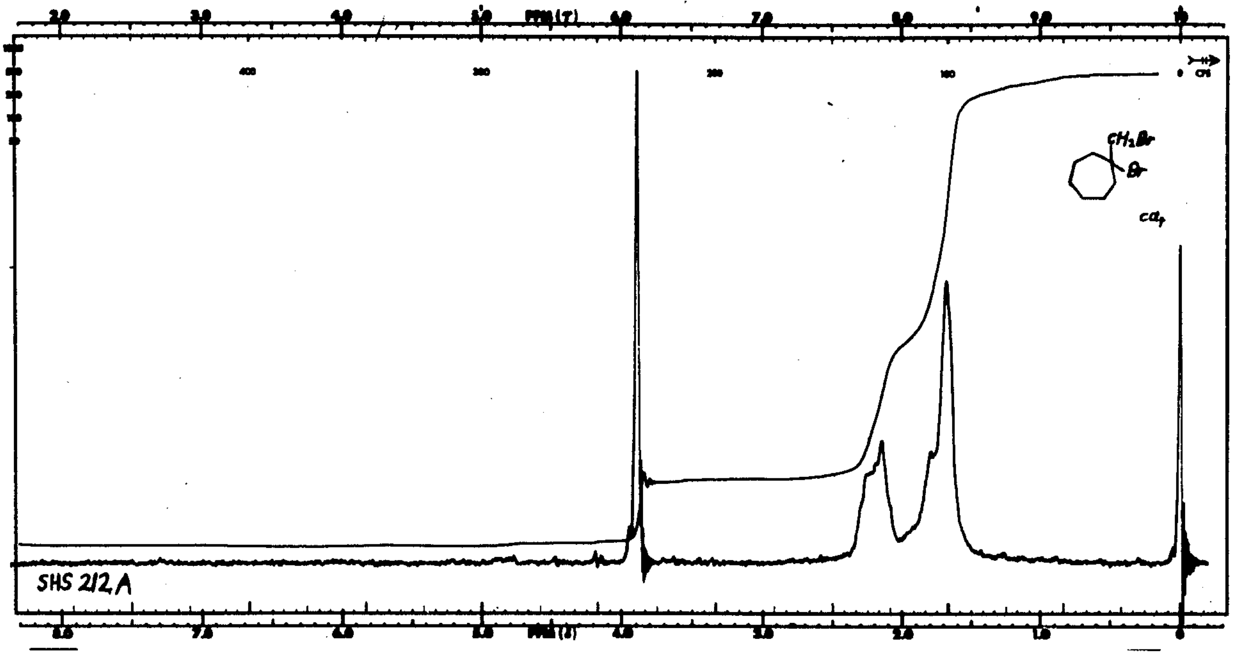
CM⁻¹
CH2
SHS194B
NEAT LIQUID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3.0
4.0
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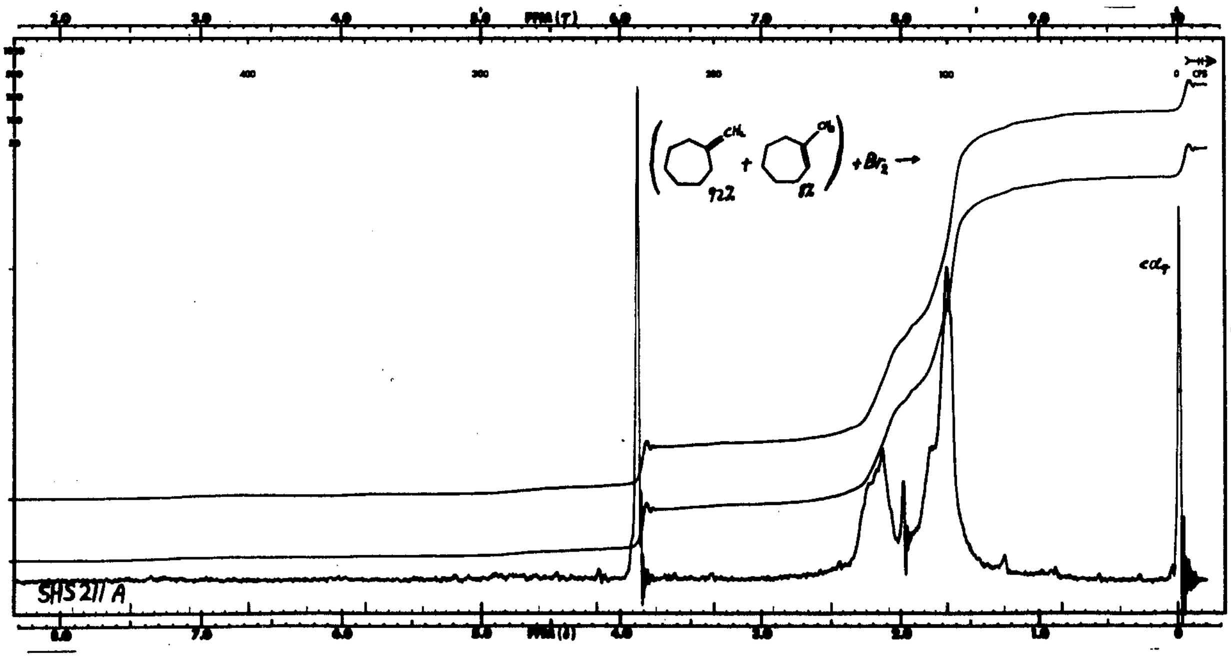
6.0
7.0
8.0
9.0
10
400
300
200
100
0 CPS
CH₂Br
Br
ccl₄
SHS 212 A
8.0
7.0
6.0
5.0
PPM (δ)
4.0
3.0
2.0
1.0
0


PPM (τ)
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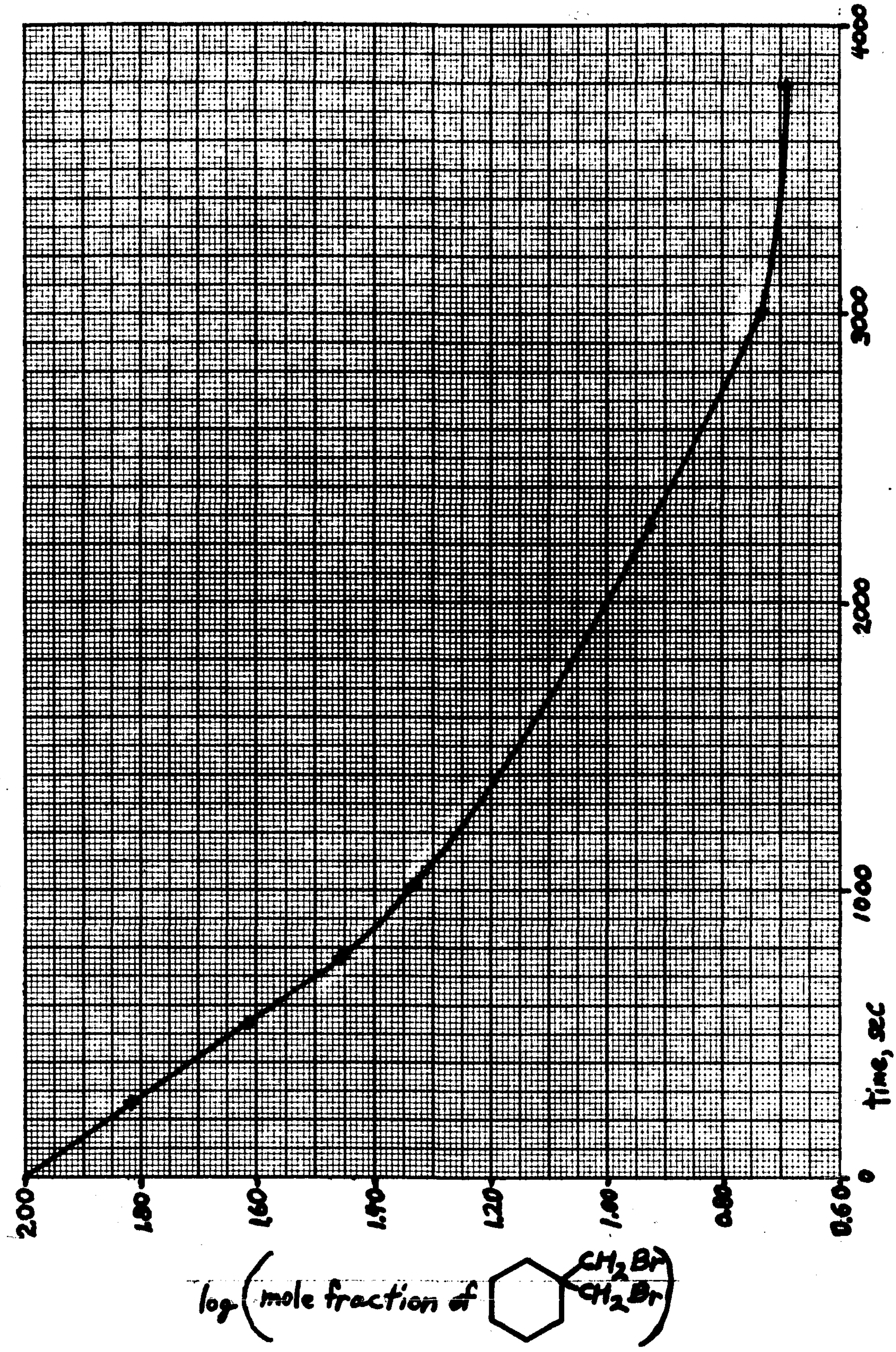
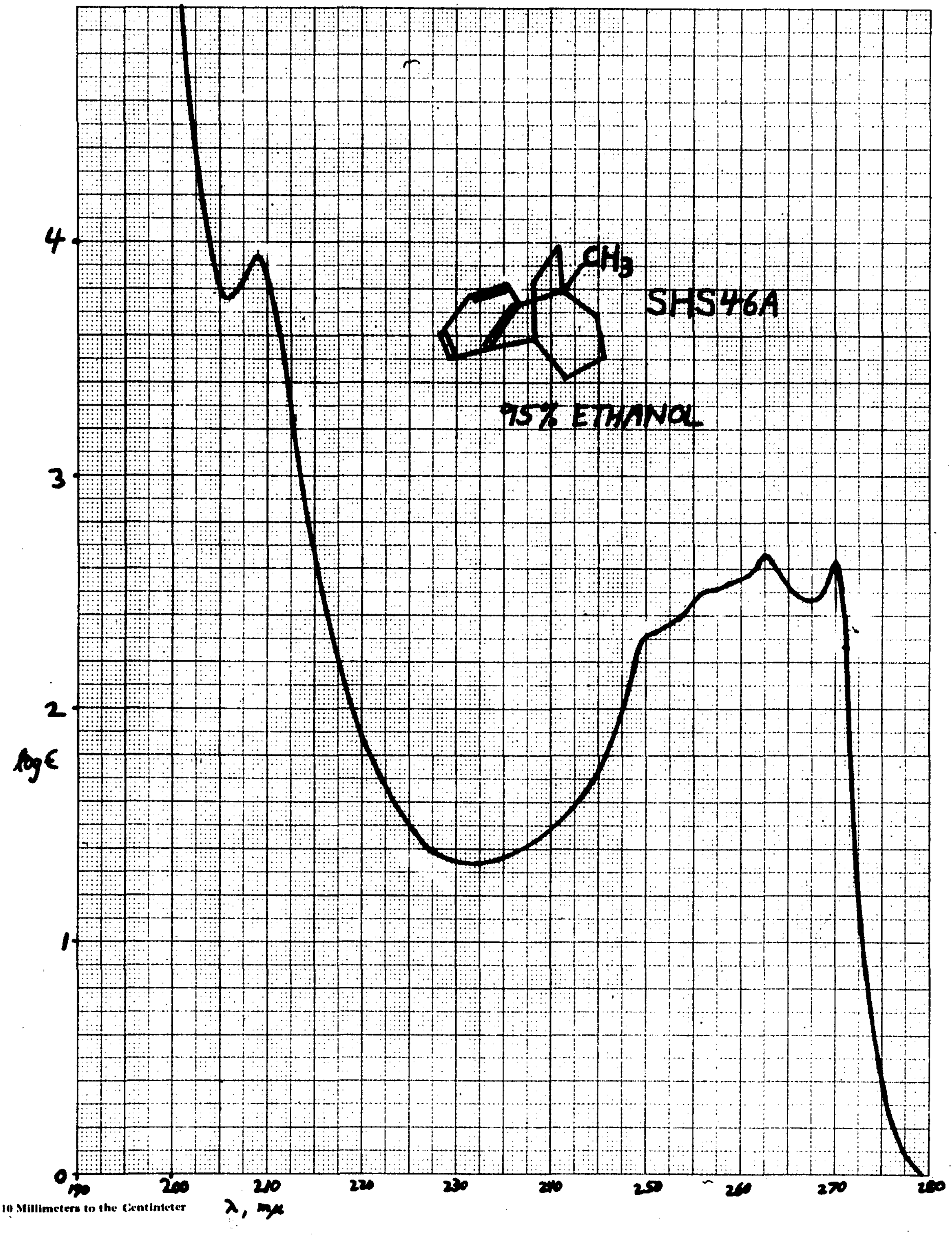
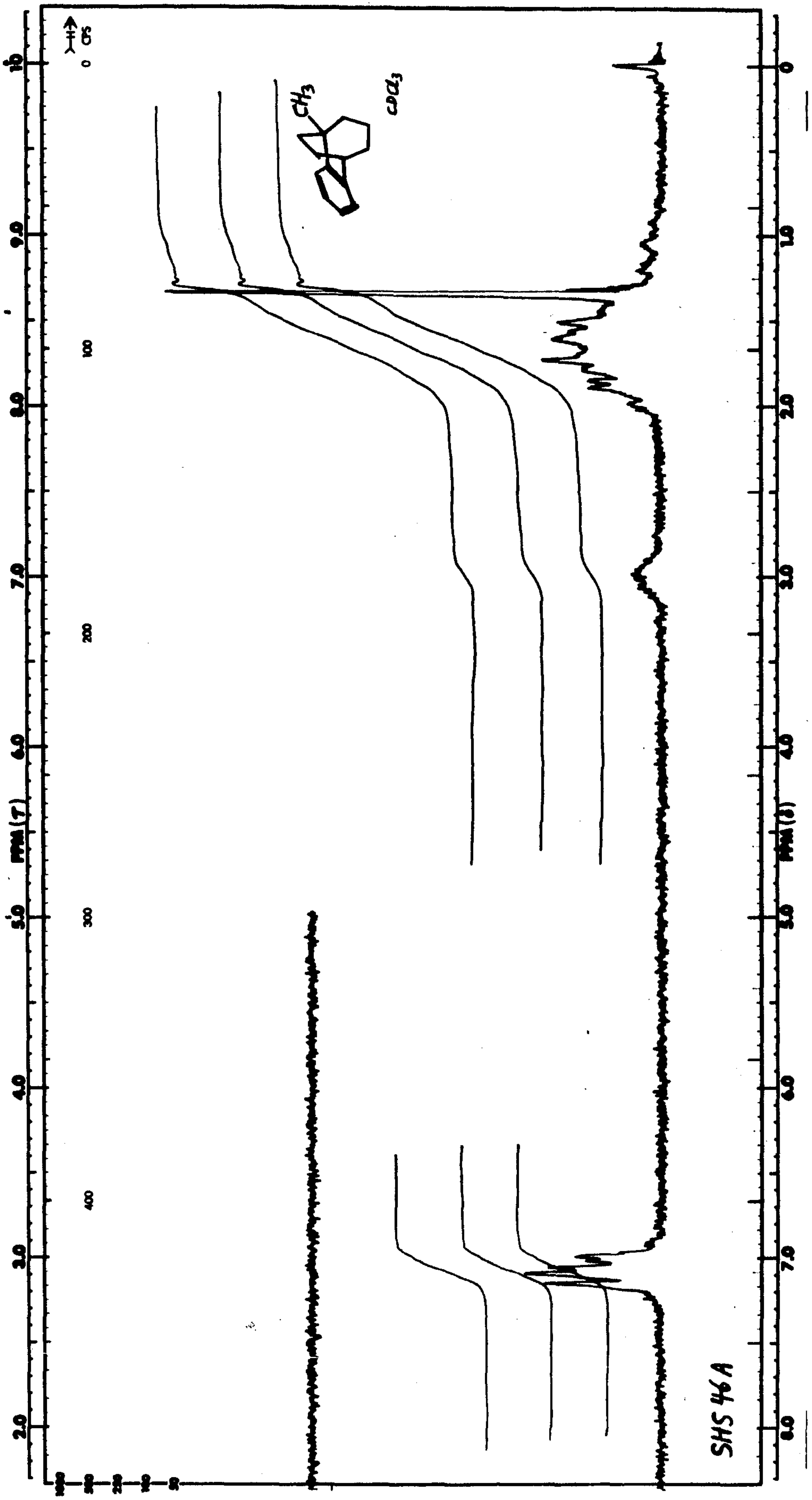
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10
400
300
200
100
0 CPS
CH₂
CH₃
+
92%
8%
+Br₂ →
ccl₄
SHS 211 A
8.0
7.0
6.0
5.0
PPM (δ)
4.0
3.0
2.0
1.0
0

Kinetics of the Friedel-Crafts Reaction of 1,1-Bis(bromomethyl)cyclohexane with Benzene and Aluminum Chloride.




4
3
2
1
0
log ε
190
200
210
220
230
240
250
260
270
280
λ, mμ
10 Millimeters to the Centimeter
CH3
SHS46A
95% ETHANOL


SHS 46A
CDCl3
CH3
PPM (τ)
PPM (δ)
CPS
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100
200
300
400
10
9.0
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6.0
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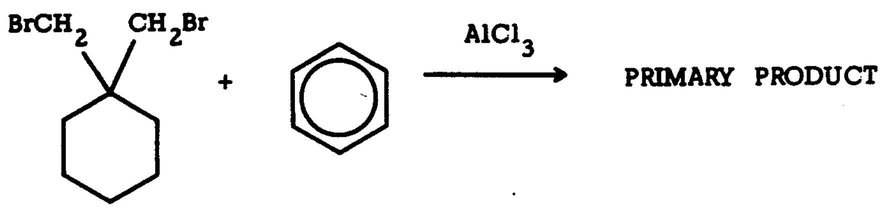
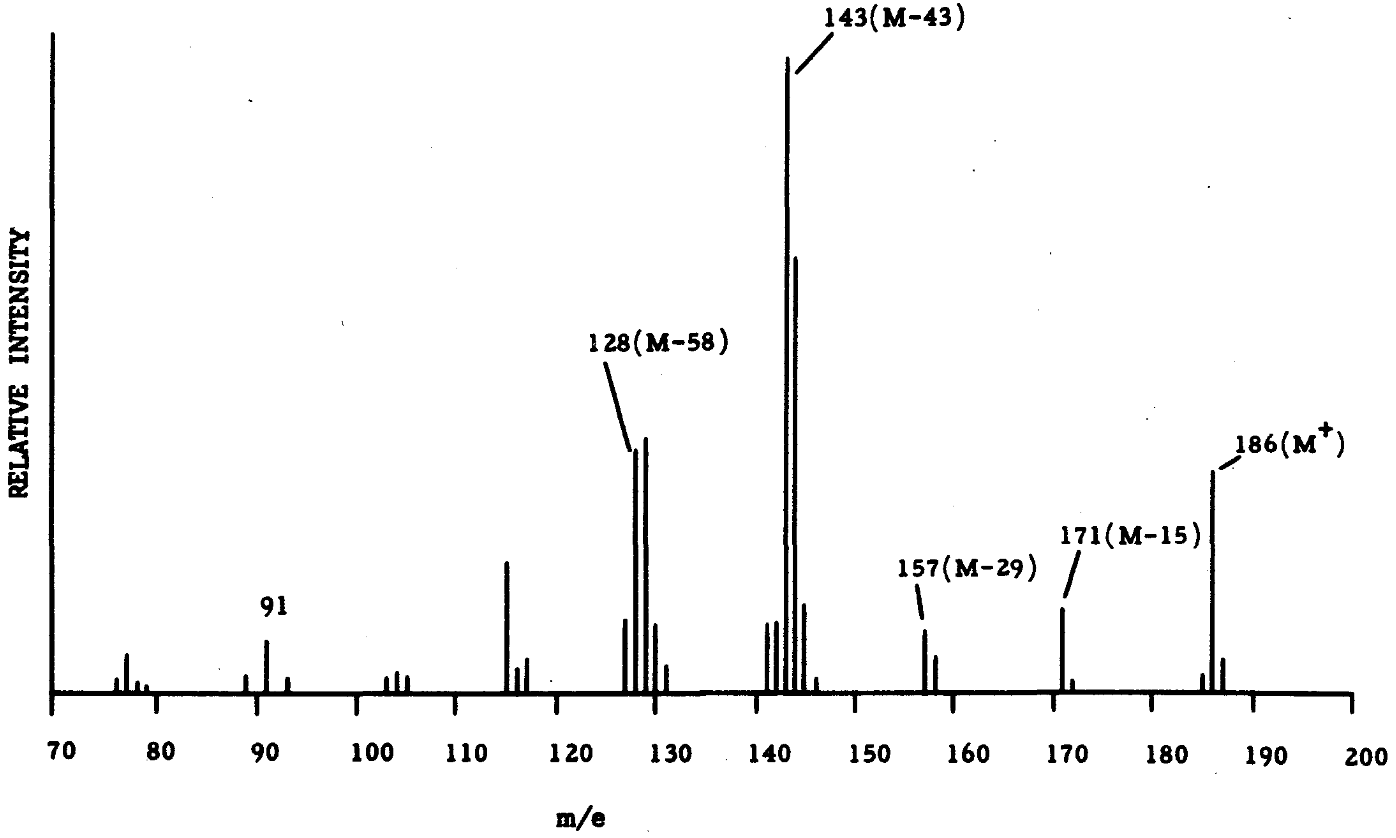
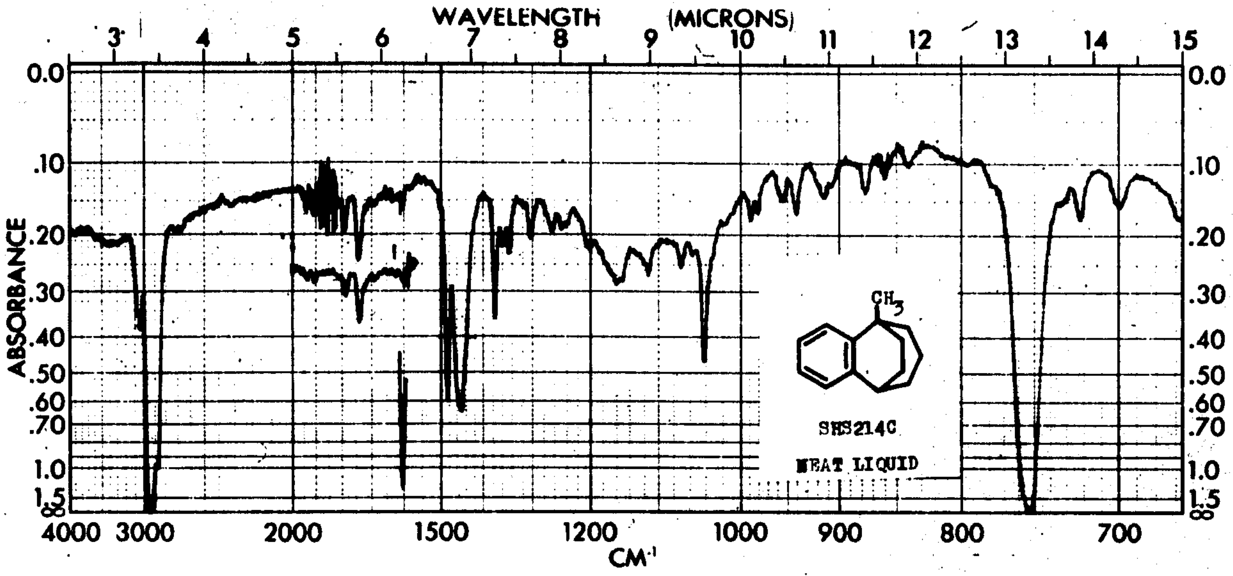
5.0
6.0
7.0
8.0


BrCH$_2$
CH$_2$Br
+
AlCl$_3$
PRIMARY PRODUCT


RELATIVE INTENSITY
143(M-43)
128(M-58)
186(M$^+$)
171(M-15)
157(M-29)
91
70
80
90
100
110
120
130
140
150
160
170
180
190
200
m/e


WAVELENGTH (MICRONS)
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ABSORBANCE
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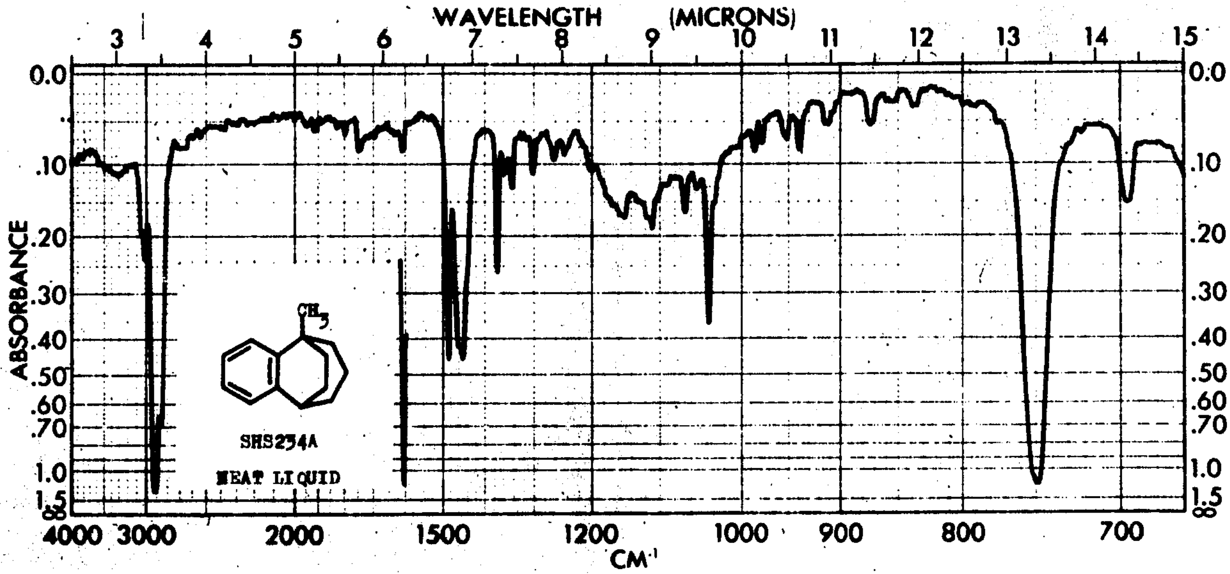
CM⁻¹
CH3
SHS214C
NEAT LIQUID


WAVELENGTH (MICRONS)
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ABSORBANCE
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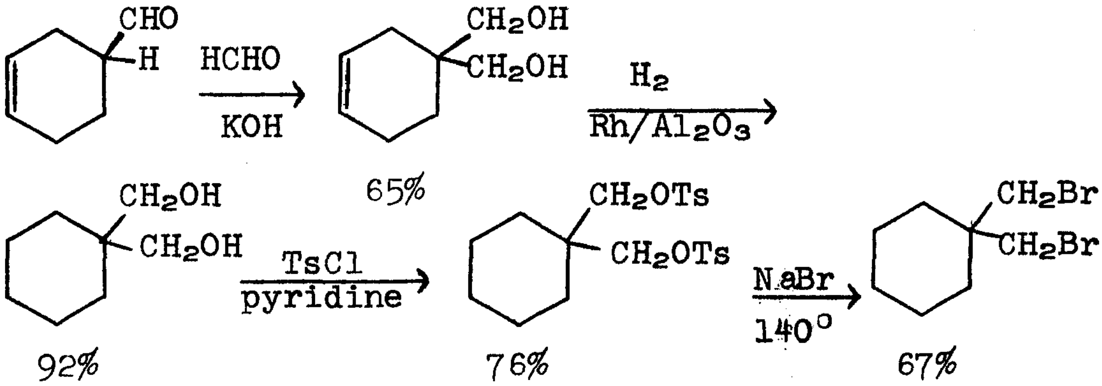
4000 3000 2000 1500 1200 1000 900 800 700
CM⁻¹
CH3
SHS234A
NEAT LIQUID

RESULTS
AND
DISCUSSION

Preparation of 1,1-Bis(bromomethyl)cyclohexane

1,1-Bis(bromomethyl)cyclohexane was prepared in 31% overall yield as follows. Reaction of Δ^3-cyclohexenecarboxaldehyde with excess formaldehyde and base yielded an unsaturated diol,[54] which was hydrogenated in high yield to 1,1-bis(hydroxymethyl)cyclohexane.[54] The diol was converted to the ditosylate[55] which, on treatment with sodium bromide at 140°, gave the desired dibromide.[55] The synthesis is summarized in Scheme XIX.

Scheme XIX



Friedel-Crafts Reaction of 1,1-Bis(bromomethyl)cyclohexane

After 1/2 hour at 40°, the reaction of 1,1-bis(bromomethyl)cyclohexane with aluminum chloride and a large excess of benzene yielded a complex mixture of more than twenty products, as determined by gas chromatography. A kinetic study of this reaction was carried out, with 50-ml aliquots being withdrawn from the reaction mixture at intervals of approximately 250 seconds and analyzed by glc.

In a reaction in which the initial mole ratio of dibromide to aluminum chloride was 1:1, the dibromide reacted completely within 1000 seconds. One product (hereafter called the "primary product") was at its highest concentration in the first aliquot, of which it was the main constituent, and then it progressively decreased in concentration in subsequent aliquots. All other products increased in concentration throughout the reaction. Even after all the starting dibromide had reacted, the "primary product" continued to decrease in concentration relative to the other products.

When the initial concentration of the catalyst was 1/4 that of the 1,1-bis(bromomethyl)cyclohexane, both the disappearance of the latter and the formation and decay of the "primary product" could be readily followed. At its maximum the "primary product" constituted 46% of the total solute concentration and more than 50% of the total product concentration.

If the reasonable assumption is made that each product molecule contains only one organic moiety from the dibromide (i.e., that the sum of the concentrations of the organic solutes remains constant), then the mole fraction of the dibromide in the solutes is directly proportional to its concentration in the solution. The method of analysis which was used (solvent removal and gas chromatography; see Experimental section, page 58) made the former quantity more convenient to calculate than the latter. A plot of log(mole fraction of 1,1-bis(bromomethyl)cyclohexane) against time gave a good straight line to beyond 80% reaction, intercepting the y-axis at mole fraction of 1,1-bis(bromomethyl)cyclohexane = 1.00. From this plot a pseudo-first-order rate constant of 1.6×10^{-3} sec^{-1} was calculated ($t_{1/2}$ = 433 sec). During the later stages of reaction, the rate constant decreased markedly. The calculated pseudo-first-order rate constants at various times in the reaction are shown in Table 3.

Table 3: Pseudo-first-order Rate Constants at Various Times for the Reaction of 1,1-Bis(bromomethyl)cyclohexane.

10^3k (sec^{-1})	time (sec)
1.6	0 to 1019
1.1	2262
0.97	3003
0.80	3788
0.47	7290

This phenomenon of decreasing pseudo-first-order rate constants was previously observed by McMahon and Bunce[17] in the Friedel-Crafts reaction of β-phenylethyl chloride with toluene and was attributed by them to the formation of a loose σ-complex (equation 11).[40] Such a phenomenon

$$C_6H_5CH_3 + HCl + Al_2Cl_6 \rightleftharpoons C_6H_6CH_3^+ \; Al_2Cl_7^- \qquad (11)$$

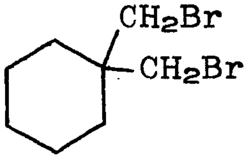
should also operate in the system under study, since mono- and dialkylbenzenes, formed concurrently with hydrogen chloride (and/or bromide), would be expected to complex with the hydrogen halide and aluminum chloride. As this removal of aluminum chloride from the system progresses, the assumption that the reaction is following pseudo-first-order kinetics (in the sense that aluminum chloride concentration is constant) would break down, and the apparent rate "constant" would decrease. The fact that this rate decrease does not become obvious until two half-lives have passed may indicate that the chief complex-forming agents are some of the secondary products and not the "primary product."

In order to isolate sufficient material for analysis, the products of six fifteen-minute reactions were combined to give a mixture which gas chromatographic analysis showed to be rich in "primary product." The mixture was distilled at reduced pressure through a spinning-band column to yield a distillation fraction enriched in "primary product." Pure "primary product" was then obtained from this fraction using preparative gas chromatography.

Structure of the "Primary Product"

The structure assignment of the "primary product" is based on the following evidence.

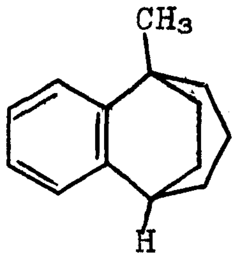
Elemental analysis and molecular weight determination showed the material isolated by preparative gas chromatography to have the formula $C_{14}H_{18}$. The parent-plus-one peak in the mass spectrum is 15.5% that of the parent peak (calculated, 15.42%), in good agreement with this formula. Thus, both bromine atoms in the 1,1-bis(bromomethyl)cyclohexane have reacted, but only one phenyl group has been added. The stoichiometry of the reaction is as shown in equation 12.



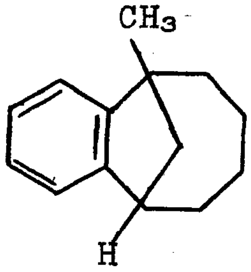
$$+ C_6H_6 \xrightarrow{AlCl_3} C_{14}H_{18} + 2HBr \qquad (12)$$

The nmr spectrum (see page 77) shows complex multiplets at δ6.9-7.3 (4 H, aromatic), δ2.9-3.1 (1 H, benzylic), and δ1.25-2.1 (10 H, alkyl) surmounted by a sharp singlet at δ1.33 (3 H, methyl on a benzylic carbon). For comparison, the methine and methyl hydrogens in isopropylbenzene appear at δ2.87 and δ1.23, respectively (all spectra in carbon tetrachloride solution). The ir spectrum shows bands at 1375 cm^{-1} and 748 cm^{-1} attributable to methyl and *ortho*-disubstituted benzene, respectively. In addition the usual aromatic and aliphatic carbon-carbon and carbon-hydrogen bands are present, but olefinic bands are absent.

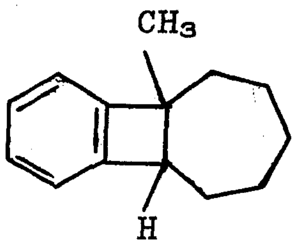
The "primary product" failed to decolorize potassium permanganate solution at an appreciable rate. This further indicates the absence of olefin. Therefore the two units of unsaturation as yet unaccounted for appear to be two rings. Only three possible structures can be written for the "primary product:" I, II, and III.



I



II



III

The ultraviolet spectrum (see page 76) shows bands at 250-270 mµ but is of little use for distinguishing between structures I, II, and III, since benzocyclobutene, indane, and tetralin all show similar spectra. These spectra are compared in Table 4, from which it can be seen that the

Table 4: Ultraviolet Spectra of "Primary Product" and Reference Compounds.

Compound	Solvent	λ_{max} (log ϵ)	Ref.
"Primary product"	95% ethanol	250 (s, 2.31), 256 (s, 2.50), 259 (s, 2.54), 262.5 (2.66), 270 (2.63)	this work
Tetralin	95% ethanol	259 (2.69), 266 (2.84), 274 (2.90), 286 (2.28)	(74)
Indane	hexane	254 (s, 2.75), 260 (3.00), 267 (3.16), 273.6 (3.25)	(75)
Benzocyclobutene	95% ethanol	260 (3.09), 265.5 (3.28), 271.5 (3.27)	(76)

extinction coefficients of the "primary product" are closest to those of tetralin, possibly favoring I as the structure of the "primary product."

Other spectral data also favor structure I over II and III. In the infrared, tetralin shows a single absorption at 742 cm^{-1}.[76,77a] Indane shows a slight splitting of this band into a doublet at 738 and 752 cm^{-1},[76,77b] and benzocyclobutene shows a more widely spaced doublet at 714 and 781 cm^{-1}.[76] (All spectra are of neat liquids.) As indicated above (page 85), the "primary product" shows a single absorption at 748 cm^{-1}.

The complexity of the δ2.9-3.1 nmr absorption for the benzylic hydrogen of the "primary product" can be rationalized for structures I or II, in which this hydrogen atom has four neighboring nonequivalent hydrogen atoms, but not for structure III, with only two nonequivalent neighbors, without the invocation of long-range coupling.

Finally, an examination of the cracking pattern and of the metastable ions in the mass spectrum (see pages 62 and 78) reveals the fragmentation pathways shown in Scheme XX. The major routes of decay of the molecular ion involve loss of two-carbon ($C_2H_5^{\bullet}$) and three-carbon (C_3H_6 and $C_3H_7^{\bullet}$)

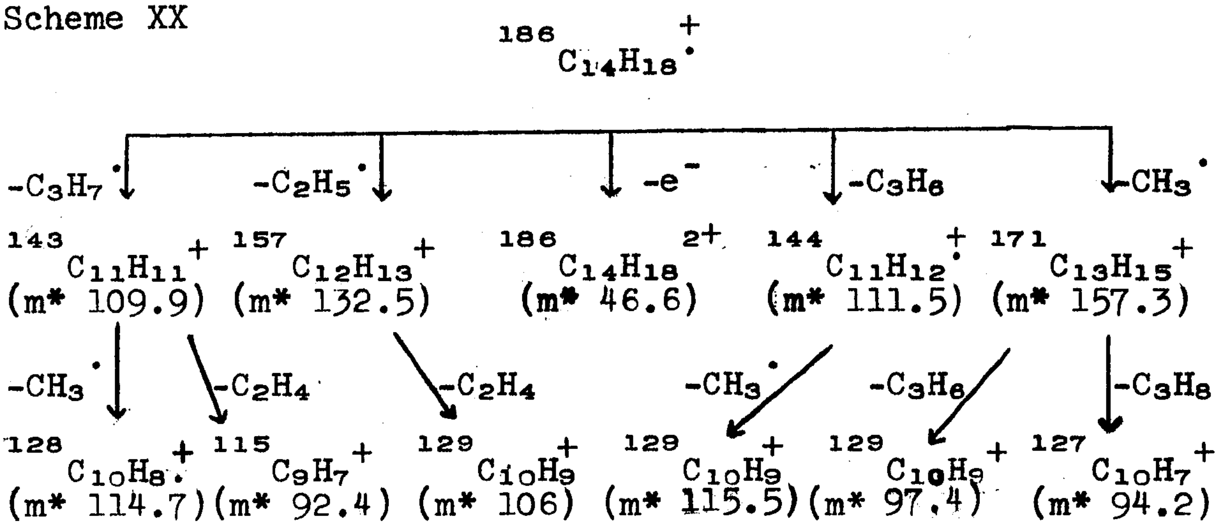
(74) Z. J. Vejdelek and B. Kakac, *Collection Czech. Chem. Commun.*, **20**, 571 (1955).

(75) R. A. Morton and A. J. A. Gouveia, *J. Chem. Soc.*, 911 (1934).

(76) M. P. Cava and D. R. Napier, *J. Am. Chem. Soc.*, **80**, 2255 (1958).

(77) Catalog of Infrared Spectral Data, American Petroleum Institute Research Project 44, National Bureau of Standards, Washington, D. C. (a) Numbers 463, 1422. (b) Number 1147.

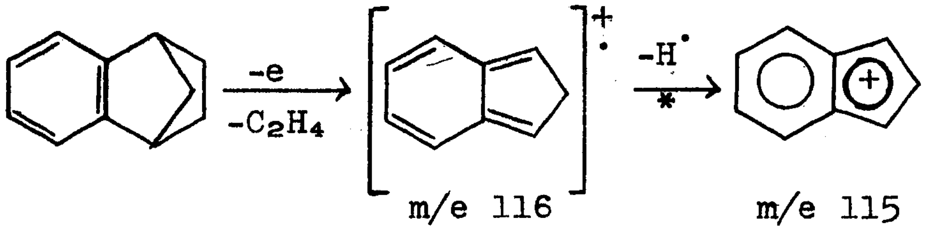
Scheme XX



* Denotes a metastable transition.

fragments.

Recent work on the mass spectroscopy of benzobicyclic compounds[78] indicates a number of preferred modes of decomposition of those compounds containing a two-carbon bridge. Thus, benzobicyclo[2.2.1]heptene undergoes a retro-Diels-Alder cleavage to lose ethylene and give the isoindene ion (m/e 116), which was detected by a peak at m/e 115 and a metastable transition from m/e 116 to m/e 115 (equation 13).

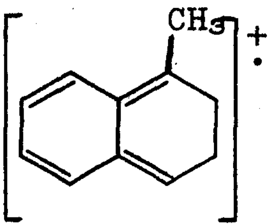


(13)

Loss of the three-carbon bridge from I (M-42, m/e 144) could proceed similarly to give the 1-methyl-2,3-dihydronaphthalene ion (IV).

Benzobicyclo[2.2.2]octene, although also undergoing a

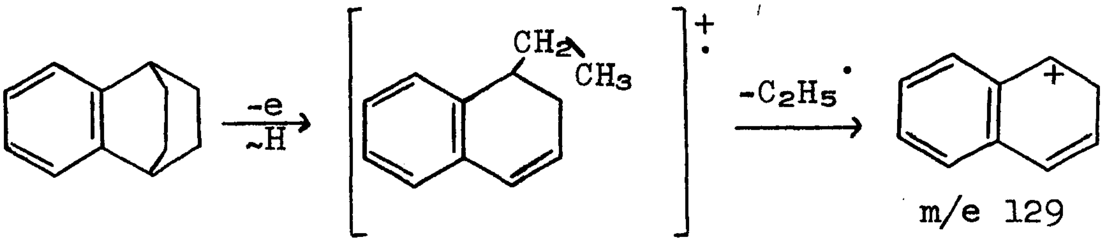
(78) T. Goto, A. Tatematsu, Y. Hata, R. Muneyuki, H. Tanida, and K. Tori, Tetrahedron, 22, 2213 (1966).



m/e 144

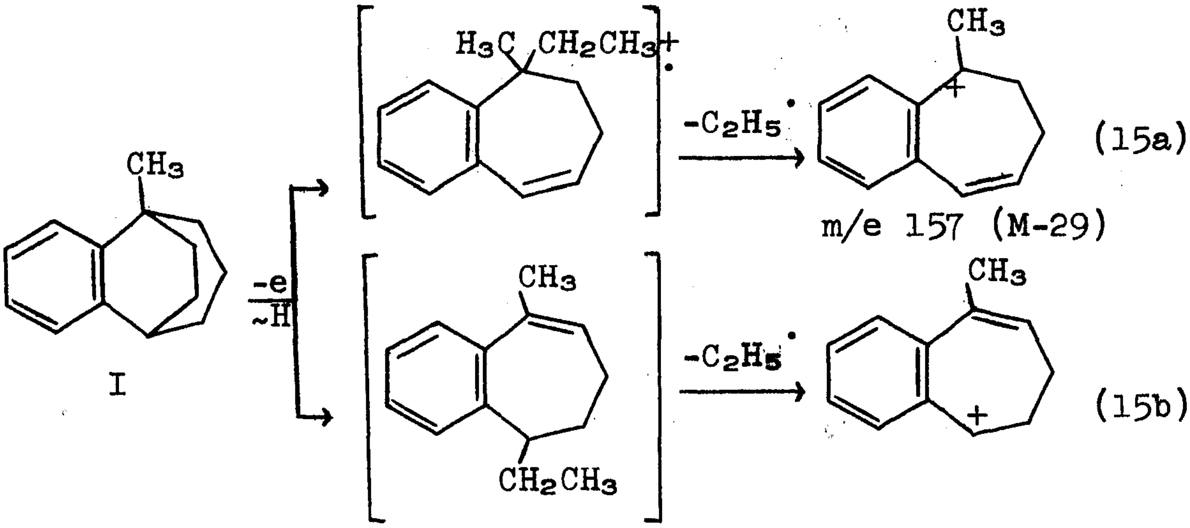
IV

retro-Diels-Alder cleavage to lose ethylene, has as its major fragmentation pathway the "rupture of a bond with hydrogen transfer, followed by elimination of a two-carbon fragment (C_2 + H) as a radical,"[78] the base peak thus being at M - (C_2H_4 + H), or M-29 (equation 14). It is this latter

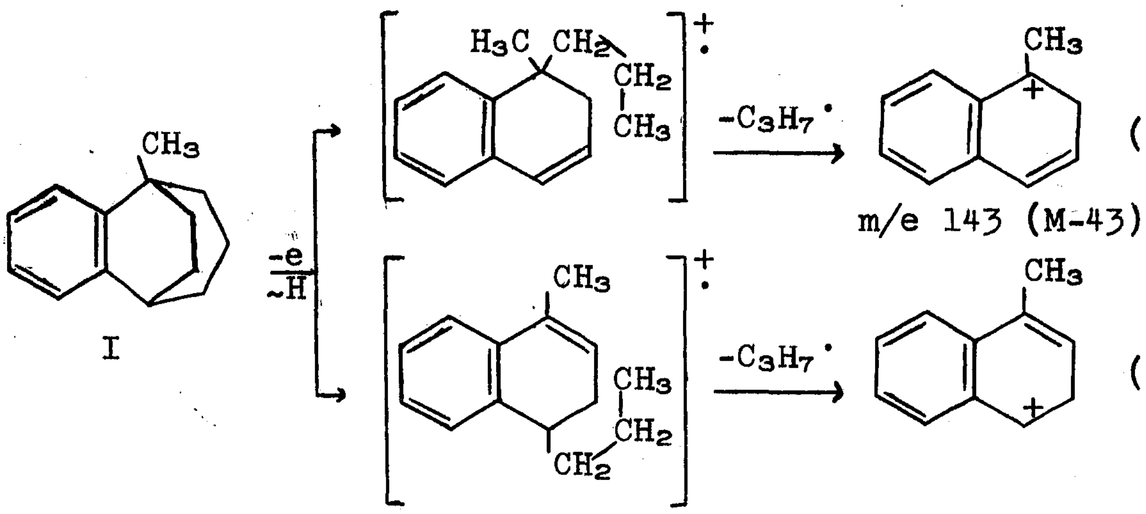


(14)

pathway which can account for the prominent m/e 157 (M-29) peak in the mass spectrum of the "primary product," assuming this compound to have structure I (equation 15).



A similar pathway involving loss of the three-carbon bridge will account for the m/e 143 (M-43) (base) peak (equation 16).



(16a)

(16b)

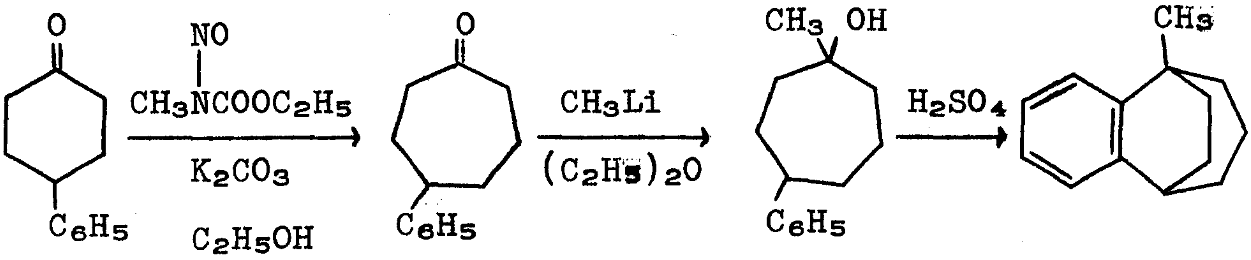
These data can be accounted for only with difficulty by structures II and III.

Thus, all the spectral evidence indicated that I, 1-methyl-6,7-benzobicyclo[3.2.2]non-6-ene, was the most probable structure of the "primary product."

Synthesis of the "Primary Product"

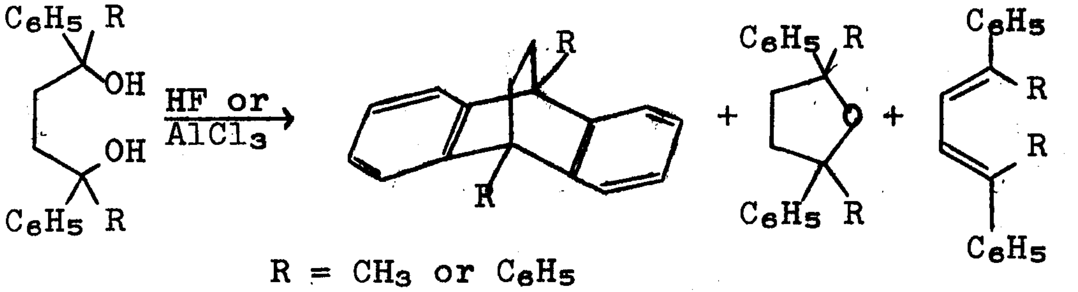
In order to achieve a final confirmation of the structure of the "primary product," the synthesis of structure I was undertaken as outlined in Scheme XXI.

Scheme XXI



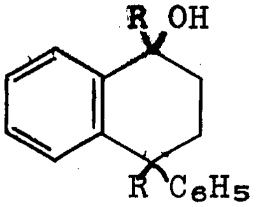
Commercially available 4-phenylcyclohexanone was subjected to diazomethane ring expansion using N-methyl-N-nitrosourethane and potassium carbonate in absolute ethanol[57] to yield the known[58,59] 4-phenylcycloheptanone. Treatment with methyllithium gave in high yield a mixture of isomers of 4-phenyl-1-methylcycloheptanol (for analysis and properties see pages 39-40). This compound was cyclized with either sulfuric acid[60] or phosphoric acid[61] to yield a single product (single peak on polar and nonpolar gas chromatographic columns) which was identical in all respects (retention times on polar and nonpolar gas chromatographic columns, nmr (see page 72) and ir (see page 73) spectra) with the "primary product." The above assignment of the structure of the "primary product" as I (page 90) is thus confirmed.

In addition, this last reaction shows some promise in the synthesis of benzobicyclo[n.2.2](n+6)-enes, where n [illegible] 2. Recent work indicates a similar formation of a bicyclic structure *via* the Friedel-Crafts reaction[79] (equation 17).



$R = CH_3$ or C_6H_5 (17)

It is reasonable to assume stepwise cyclialkylations, in which case a likely intermediate would be V, similar in



V

structure to 4-phenyl-1-methylcycloheptanol.

(79) L. R. C. Barclay and R. A. Chapman, *Can. J. Chem.*, **43**, 1754 (1965).

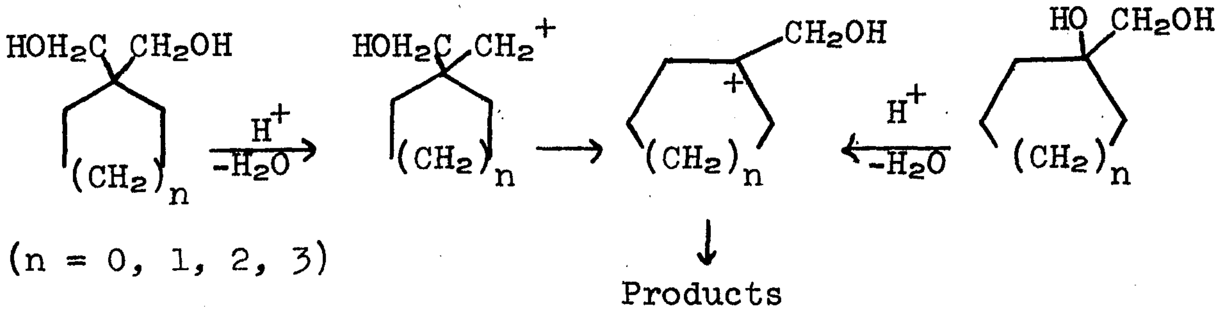
Mechanistic Considerations

The unequivocal assignment of the structure of the major product in the Friedel-Crafts reaction of 1,1-bis-(bromomethyl)cyclohexane was followed by a study of the mechanism of its formation. The general approach to the elucidation of this mechanism was to subject postulated intermediates or their precursors to the reaction conditions (benzene and aluminum chloride at 40°) and to compare the respective product mixtures with that obtained in the reaction of 1,1-bis(bromomethyl)cyclohexane.

A simple comparison of the structures of the starting dibromide and of the "primary product" I shows that a deep-seated rearrangement of the former has occurred. The structure of I alone requires, at the very least, the occurrence of a ring expansion (as in path A, Scheme XVIII, page 27) and a transannular interaction.

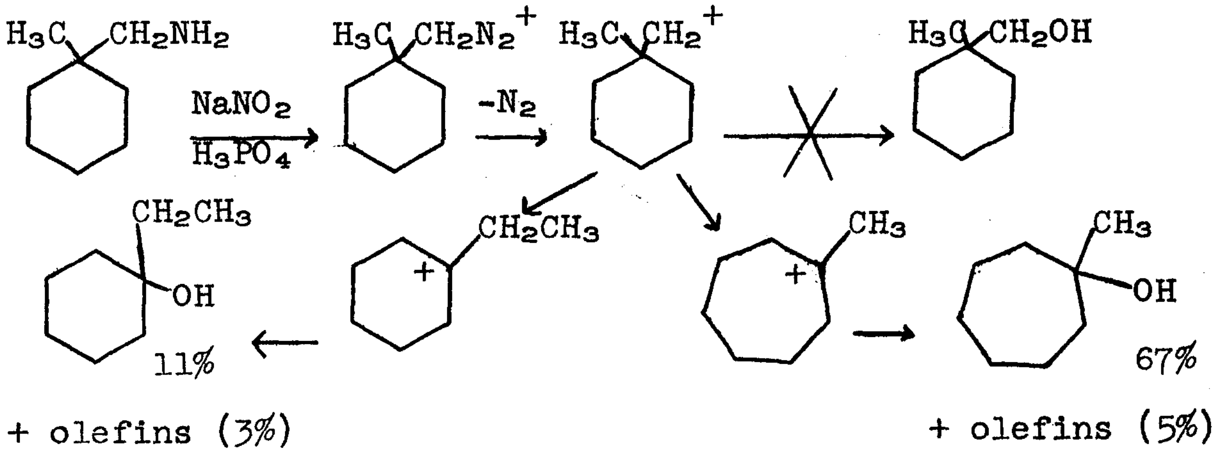
Ring expansion of a cycloalkylcarbinyl system is not unexpected. Formation of at least three of the products in the acid hydrolysis of 1,1-bis(hydroxymethyl)cyclohexane[51] (equation 10, page 26) requires such a ring expansion. Other 1,1-bis(hydroxymethyl)cycloalkanes have also been shown to rearrange primarily through ring expansion in aqueous sulfuric acid. The reaction pathway was indicated by the similarity of the products in the acid hydrolyses of the 1,1-bis(hydroxymethyl)cycloalkanes and of the respective 1-hydroxymethylcycloalkanols with one more ring carbon atom. The intermediate tertiary cations from the latter would be the same as those formed from the former by ionization and ring expansion (Scheme XXII).[52]

Scheme XXII



Furthermore, the 1-methylcyclohexylcarbinyl cation (from diazotization of the corresponding amine in dilute aqueous phosphoric acid - the Demjanov rearrangement) gives predominantly those products formed <u>via</u> a ring expansion, with none of the product of direct displacement and only minor quantities of the products of a methyl migration (Scheme XXIII).[80] In contrast the cyclohexylcarbinyl cation

Scheme XXIII

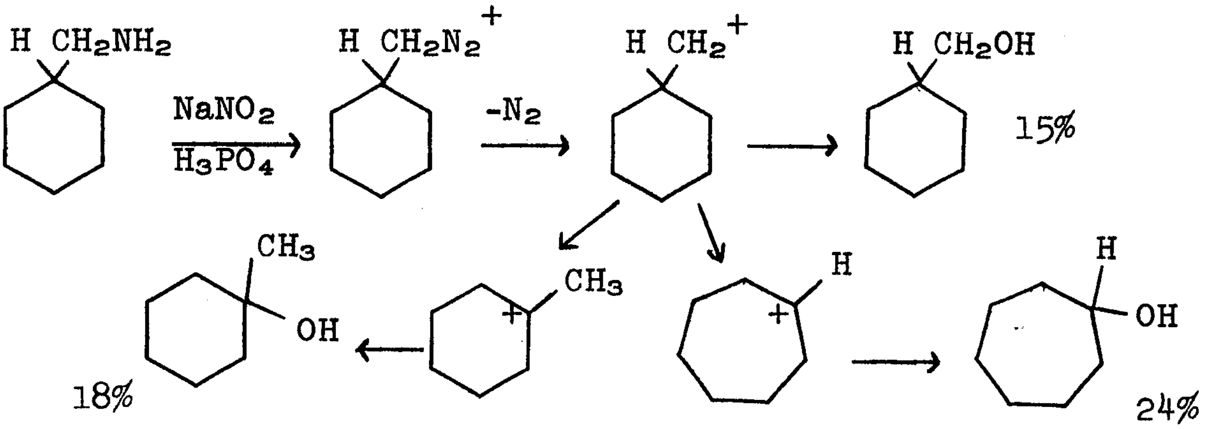


yields only 24% of the alcohol produced by ring expansion and a large amount (15%) of the alcohol produced by direct

(80) R. Kotani, J. Org. Chem., 30, 350 (1965).

displacement. (Scheme XXIV).[81-83]

Scheme XXIV



Ring expansion in the 1-methyl compound is favored relative to that in the unsubstituted compound because a tertiary ion may be formed, whereas only a secondary ion can be formed by ring enlargement in the unsubstituted case.[80]

Substitution of a hydroxyl group at the 1-position increases still further the percentage of ring expansion (the Tiffeneau-Demjanov rearrangement). No hydrogen atom is present to migrate in competition with a ring carbon atom, and the charge in the ion formed by ring expansion is stabilized by conjugation with the hydroxyl group.[82] Deamination of 1-aminomethylcyclohexanol is used as a preparative route to cycloheptanone (equation 18).[84]

It should be stressed that no direct analogies are

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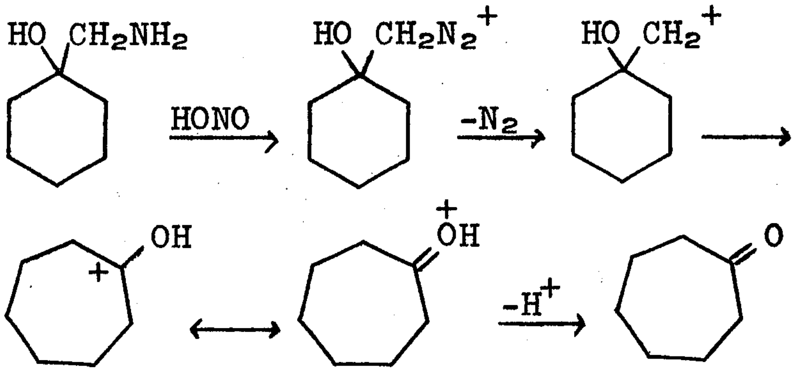
(81) P. A. S. Smith and D. R. Baer, J. Am. Chem. Soc., 74, 6135 (1952).

(82) P. A. S. Smith and D. R. Baer, in "Organic Reactions," Vol 11, R. Adams, ed, John Wiley and Sons, Inc., New York, N.Y., 1960, pp 157-188.

(83) R. Kotani, J. Chem. Eng. Data, 11, 248 (1966).

(84) H. G. Dauben, Jr., H. J. Ringold, R. H. Wade, D. L. Pearson, and A. G. Anderson, Jr., "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, ed, John Wiley and Sons, Inc., New York, N.Y., 1963, p 221.

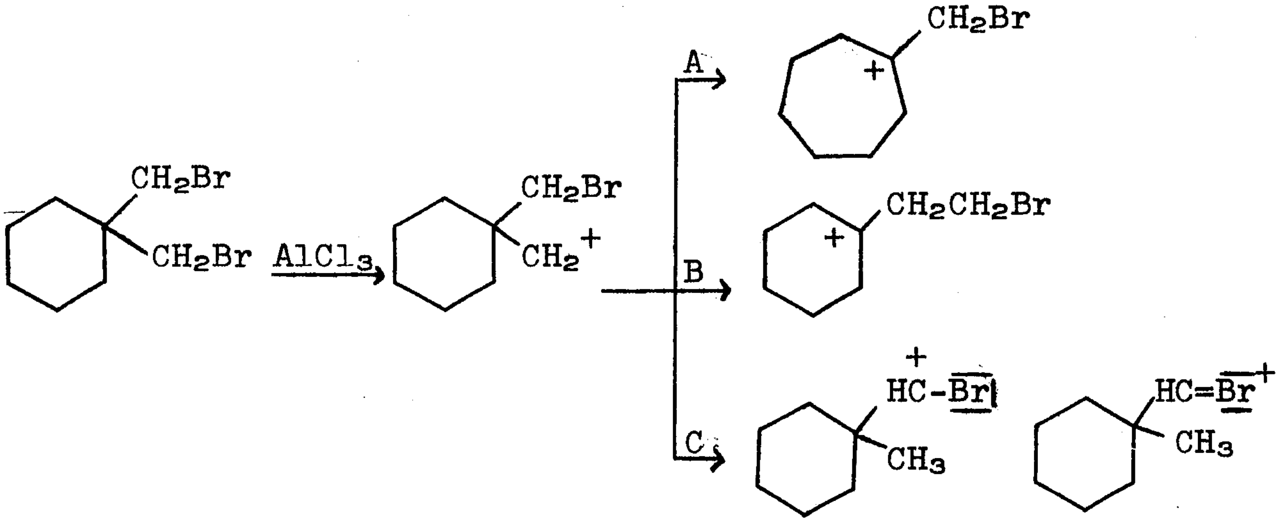


(18)

being drawn between these reactions and the one under study. Differences in solvation, reaction conditions, solvent systems, reversibility of ion formation, etc., make any such analogies extremely tenuous and risky. The above data have been presented only to demonstrate that ring expansions from the cyclohexylcarbinyl system to the cycloheptyl system are known.

The possible rearrangements of the initial real or incipient carbonium ion formed from 1,1-bis(bromomethyl)-cyclohexane are: (A) ring enlargement, (B) migration of a bromomethyl group, and (C) 1,3-hydride transfer (Scheme XVIII).

Scheme XVIII



It has been shown that, although a few per cent of the 1-propanol from deamination of n-propylamine occurs by 1,3-hydride migration via a protonated cyclopropane,[85] none of this rearrangement occurs in deamination of neopentylamine. The 1,3-shift can compete with 1,2-shifts in the former system but not in the latter for two reasons. In the latter system methyl group migration yields a tertiary carbonium ion, whereas hydride migration in the former system gives only a secondary ion. Also, conversion of the neopentyl cation to the tert-amyl cation gives a greater release of nonbonded interactions than does conversion of the 1-propyl cation to the 2-propyl ion.[86] For similar reasons, 1,3-hydride migration in the neopentyl-like system under study (path C, Scheme XVIII) might not be expected to compete with 1,2-migrations (paths A and B).

On the other hand, 1,3-hydride migration might be expected on the basis of the relative stabilities of the initially formed real or incipient primary carbonium ion and the α-bromo-carbonium ion which would be formed by such a rearrangement. In the latter ion the positive charge could be stabilized by donation of a pair of nonbonding electrons from the bromine atom (see path C, Scheme XVIII). In this case the 1,3-hydride migration would be energetically favorable. Thus, the possibility of a 1,3-hydride migration cannot be discounted.

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(85) A. A. Aboderin and R. L. Baird, J. Am. Chem. Soc., 86, 2300 (1964).

(86) G. J Karabatsos, C. E. Orzech, Jr., and S. Meyerson, J. Am. Chem. Soc., 86, 1994 (1964).

The migratory aptitude of a bromomethyl group in carbonium ion rearrangements should be less than that of a methyl group because of the electron-withdrawing inductive effect of the bromine atom. Since the 1-methylcyclohexylcarbinyl carbonium ion rearranges mainly via ring expansion, rather than methyl group migration,[79] it seemed likely that rearrangement of the 1-bromomethylcyclohexylcarbinyl cation should proceed to an even greater extent by way of a ring expansion (path A, Scheme XVIII). In addition, as mentioned above (page 93), the structure of the "primary product" requires a ring expansion. Therefore, by analogy with the general approach of Gladstone[52] mentioned above (page 93), the heretofore unknown 1-bromo-1-(bromomethyl)cycloheptane was synthesized and its behavior in the Friedel-Crafts reaction was studied.

Synthesis of 1-bromo-1-(bromomethyl)cycloheptane poses an interesting problem in itself. The most obvious route, that via bromine addition to methylenecycloheptane, is complicated by two pitfalls. The thermodynamic instability of exocyclic olefins relative to the isomeric endocyclic olefins is reflected by the ready tendency of the former to isomerize to the latter either in acid[87] or in base.[88] Preparation and isolation of pure exocyclic olefins is complicated by this rearrangement. In addition, bromination

(87) A. C. Cope, D. Ambros, E. Ciganek, C. F. Howell, and Z. Jacura, J. Am. Chem. Soc., 81, 3153 (1959); 82, 1750 (1960).

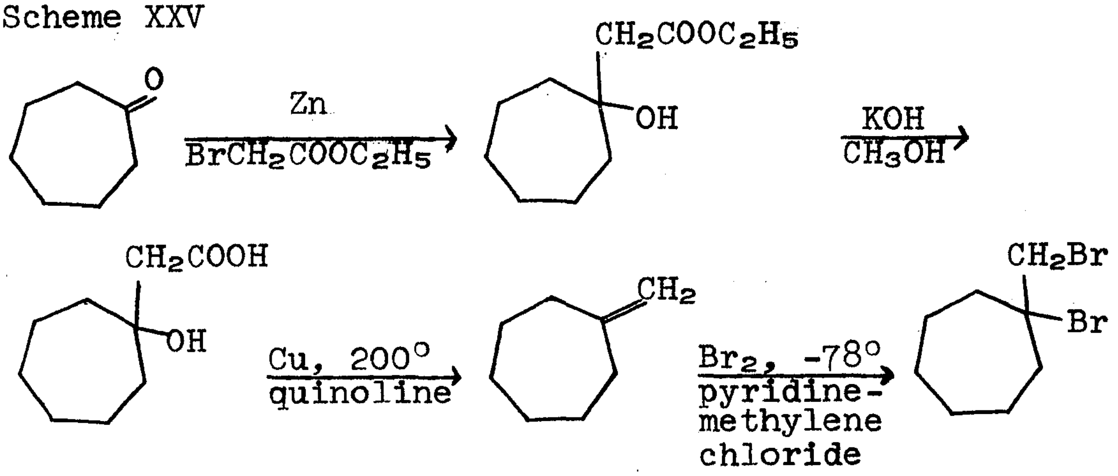
(88) A. Schriesheim, R. J. Muller, and C. A. Rowe, Jr., J. Am. Chem. Soc., 84, 3164 (1962).

of exocyclic olefins produces large quantities of isomeric 1,2-dibromo-1-methylcycloalkanes.[66,67] Allylic bromination competes with normal bromine addition and produces small quantities of hydrogen bromide as a by-product. This hydrogen bromide isomerizes exocyclic to endocyclic olefins which are brominated to give rearranged dibromides. It has been claimed, however, that the presence of a soluble base such as pyridine will minimize this formation of isomeric dibromides by neutralizing the hydrogen bromide before it can isomerize the olefin.[66,67] It thus appeared that bromination of methylenecycloheptane could be controlled to give the desired 1-bromo-1-(bromomethyl)cycloheptane. Accordingly the synthesis of methylenecycloheptane was undertaken.

The method chosen for preparation of methylenecycloheptane was that of Abraham and Vilkas,[62,63] who claimed to have prepared the compound in 99% isomeric purity. Reformatsky reaction of cycloheptanone with ethyl bromoacetate followed by alkaline saponification of the resulting _β_-hydroxyester produced 1-hydroxycycloheptylacetic acid. Decarboxylation-dehydration of this acid by the published method (copper powder and quinoline at 200°),[62,63] however, produced methylenecycloheptane in isomeric purities ranging from only 78% to 92%. Preparative gas chromatography, using a silver nitrate-triethylene glycol column,[65] was necessary to obtain pure methylenecycloheptane.

Bromine addition to methylenecycloheptane in pyridine-methylene chloride at -78°[66-68] did indeed give only unrearranged dibromide. When methylenecycloheptane containing 8% 1-methylcycloheptene was brominated under the same conditions the nmr spectrum had a singlet at δ2.00, which was attributable to the methyl group in 1,2-dibromo-1-methylcycloheptane. The product of bromination of pure methylenecycloheptane did not have this peak (or any other peaks which could not be assigned to 1-bromo-1-(bromomethyl)cycloheptane). The synthesis is summarized in Scheme XXV.

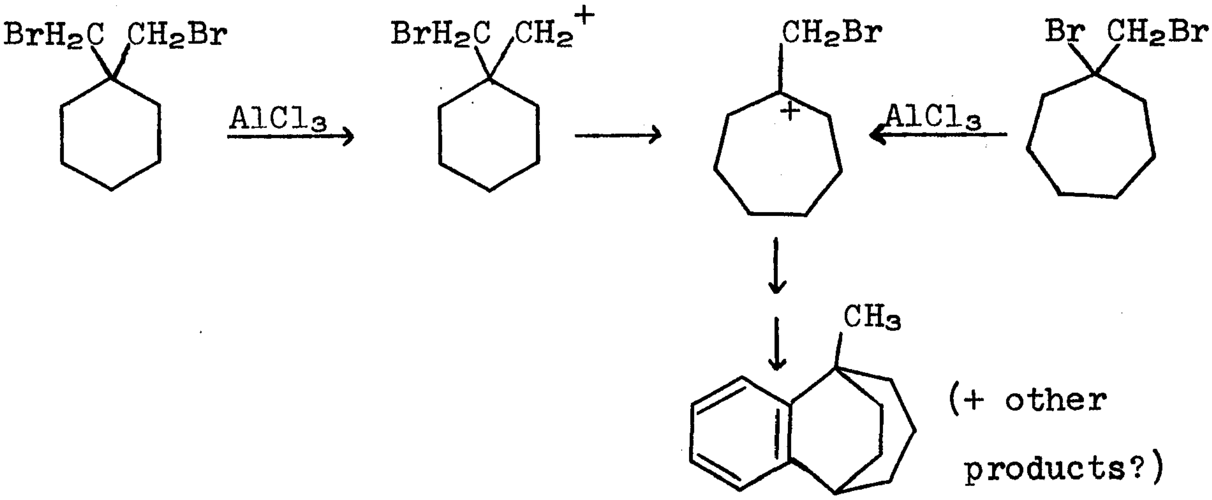
Scheme XXV



Friedel-Crafts reaction of 1-bromo-1-(bromomethyl)cycloheptane was carried out under conditions identical with those for the reaction of 1,1-bis(bromomethyl)cyclohexane. Gas chromatographic analysis of the product mixture showed that it was indeed similar to that from 1,1-bis(bromomethyl)cyclohexane, both in retention times of all products and in relative proportions of minor products. The "primary product" constituted an even greater fraction of the products from 1-bromo-1-(bromomethyl)cycloheptane than it did of the products from 1,1-bis(bromomethyl)cyclohexane. The material was isolated by preparative gas chromatography and was shown to be "primary product" by the identity of their respective infrared and mass spectra.

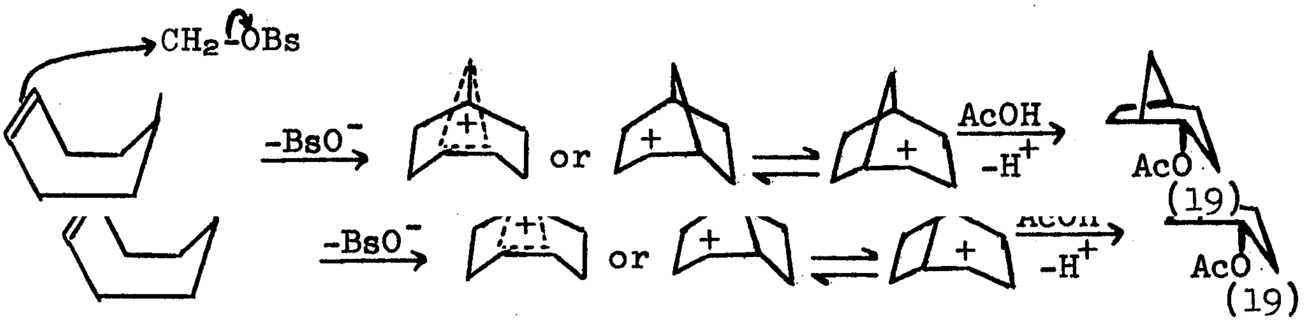
These results suggest that the first step in the Friedel-Crafts reaction of 1,1-bis(bromomethyl)cyclohexane is ring expansion to the 1-bromomethylcycloheptyl cation (Scheme XXVI).

Scheme XXVI



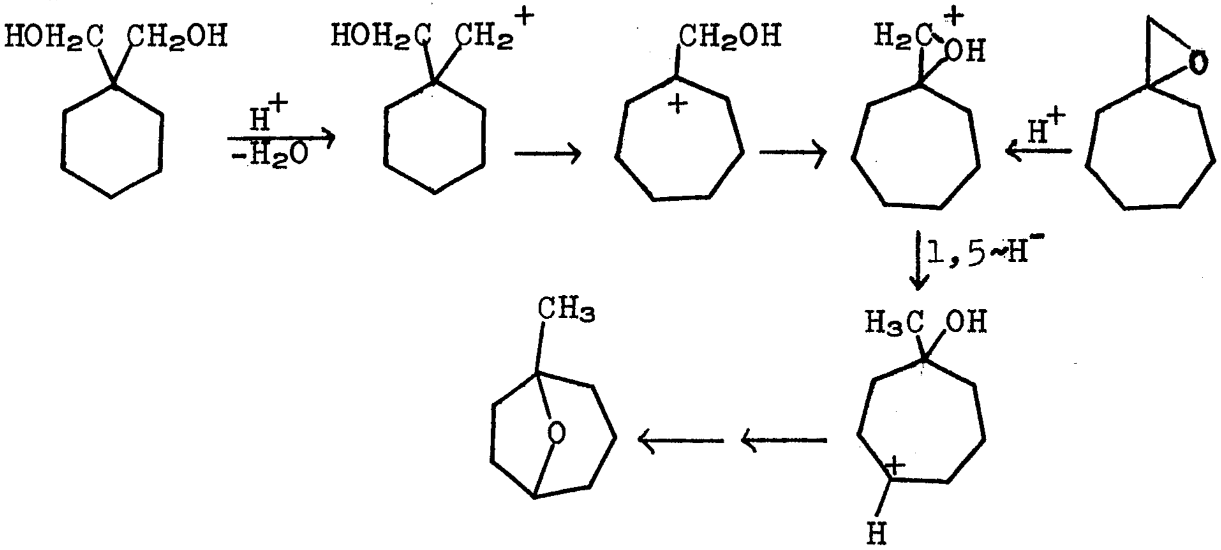
As with the ring expansion step, precedent also exists for transannular interaction in a cycloheptylcarbinyl system. The major product of acetolysis of cyclohept-4-enylmethyl brosylate is *endo*-2-bicyclo[3.2.1]octyl acetate, with minor amounts of the *exo*-isomer and of 2-bicyclo[2.2.2]octyl acetate. The major intermediate cation is formed by participation of the double bond in the ionization step as shown in equation 19.[89,90]

(89) G. LeNy, *Compt. rend.*, *251*, 1526 (1960).
(90) H. Felkin, G. LeNy, C. Lion, W. D. K. Macrosson, J. Martin, and W. Parker, *Tetrahedron Letters*, 157 (1966).



A transannular 1,5-hydride migration has been postulated to explain the formation of 1-methyl-8-oxabicyclo[3.2.1]octane in the acid-catalyzed hydrolysis of 1,1-bis(hydroxymethyl)cyclohexane[51] (Scheme XXVII). Production of 1-methyl-8-oxabicyclo[3.2.1]octane from methylenecycloheptane epoxide (1-oxaspiro[2.6]nonane) under these conditions has also been proposed to involve a transannular 1,5-hydride migration (Scheme XXVII).[91]

Scheme XXVII



Scheme XXVIII depicts two possible pathways for the formation of "primary product" from 1,1-bis(bromomethyl)-cyclohexane, both proceeding through the 1-bromomethylcycloheptyl cation. These pathways differ in whether the transannular shift in the cycloheptylcarbinyl system precedes or

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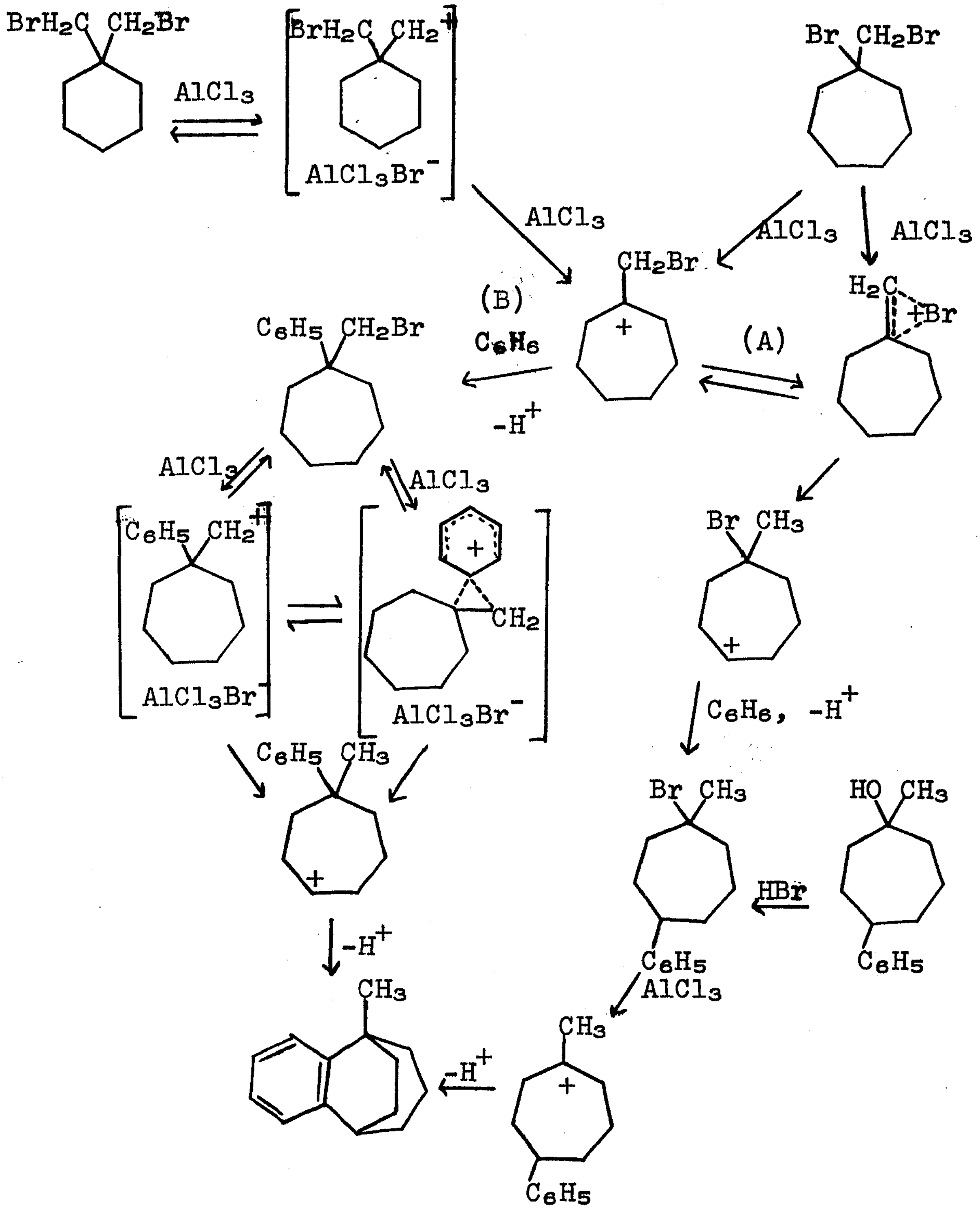
(91) L. H. Schwartz, M. Feil, A. J. Kascheres, K. Kaufmann, and A. M. Levine, Tetrahedron Letters, 3785 (1967).

follows the first alkylation step. Each pathway requires the intermediacy of a neutral species containing a bromine atom and a phenyl group.

Scheme XXVIII[92]



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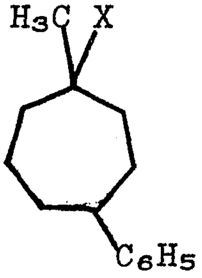
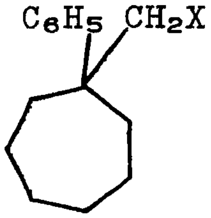
(92) Reaction steps involving structures in brackets may be synchronous.

Before proceeding further, it might be instructive to review what little is known of the reactions of these two systems, 4-phenyl-1-methylcycloheptyl- (VI) and 1-phenylcycloheptylcarbinyl- (VII).



VI



VII

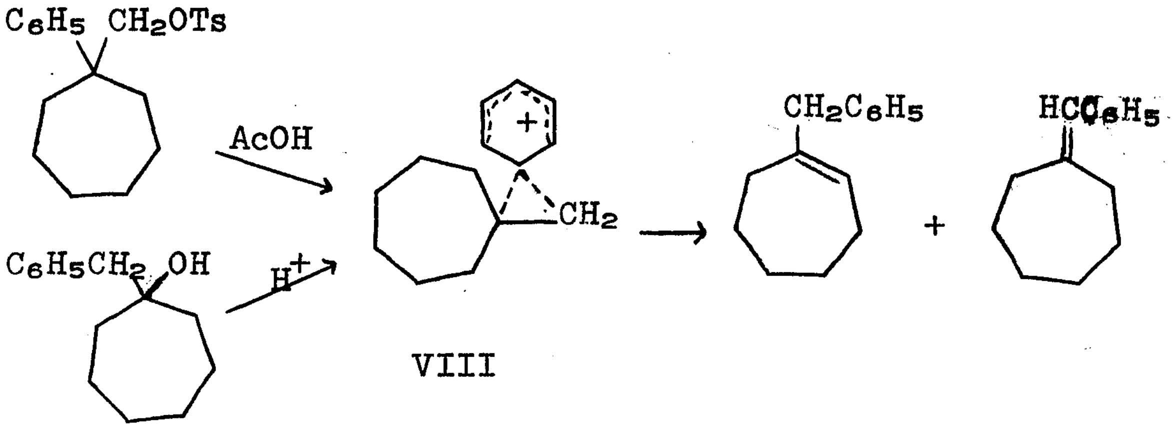
The former system (VI) was unknown prior to this work. It has already been seen (page 91) that treatment of the alcohol (VI, X = OH) with 85% sulfuric acid at 0° produced only "primary product." This was to be expected, since cyclialkylations readily proceed without rearrangement where formation of a six-membered ring is possible,[28] as in this case. It would therefore be expected that the corresponding bromo compound (VI, X = Br) on treatment with aluminum chloride in benzene would also give "primary product."

The only published information on the 1-phenylcycloheptylcarbinyl system is that of Wilt and coworkers,[69,93] who studied cationic, free radical, and carbenoid rearrangements in the 1-phenylcycloalkylcarbinyl series. Acetolysis of 1-phenylcycloheptylcarbinyl tosylate (VII, X = OTs) at 25° to 47° proceeded with exclusive migration of the phenyl

(93) J. W. Wilt and D. D. Roberts, J. Org. Chem., **27**, 3434 (1962).

group to the exocyclic carbon to produce a quantitative yield of the olefins 1-benzylcycloheptene (71%) and benzylidenecycloheptane (29%). Almost identical results were obtained in the dehydration of 1-benzylcycloheptanol, and migration of the phenyl group to the exocyclic carbon via the bridged phenonium ion (VIII) was suggested as the sole course of the acetolysis reaction (Scheme XXIX).[69,93]

Scheme XXIX



This information suggests that 1-phenylcycloheptylcarbinyl bromide (VII, X = Br).would not be as likely an intermediate in formation of "primary product" in the reaction under study as would be 4-phenyl-1-methylcycloheptyl bromide (VI, X = Br). However, its possible intermediacy in formation of other products cannot be excluded.

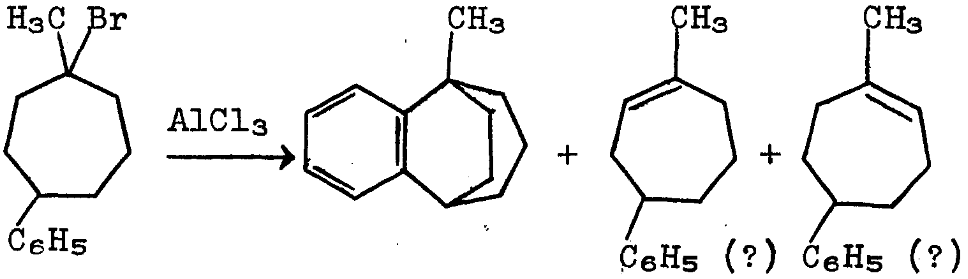
From these data it appears that path A in Scheme XXVIII (intermediacy of 4-phenyl-1-methylcycloheptyl bromide) is more likely than path B.

4-Phenyl-1-methylcycloheptyl bromide (the intermediate in path A, Scheme XXVIII) was prepared from the already discussed corresponding alcohol (page 91) by reaction with

48% hydrobromic acid.

4-Phenyl-1-methylcycloheptyl bromide with aluminum chloride in benzene gave a mixture similar to those obtained from 1,1-bis(bromomethyl)cyclohexane and from 1-bromo-1-(bromomethyl)cycloheptane containing two major products. The "primary product" (isolated by gas chromatography and identified by infrared and mass spectra) constituted an even greater fraction of the total product than it did with either of the two dibromo compounds.

The second major component of this mixture was isolated by preparative gas chromatography. Mass spectrometry indicated it probably to be 4- or 5-phenyl-1-methylcycloheptene or a mixture of the two isomers (equation 20).



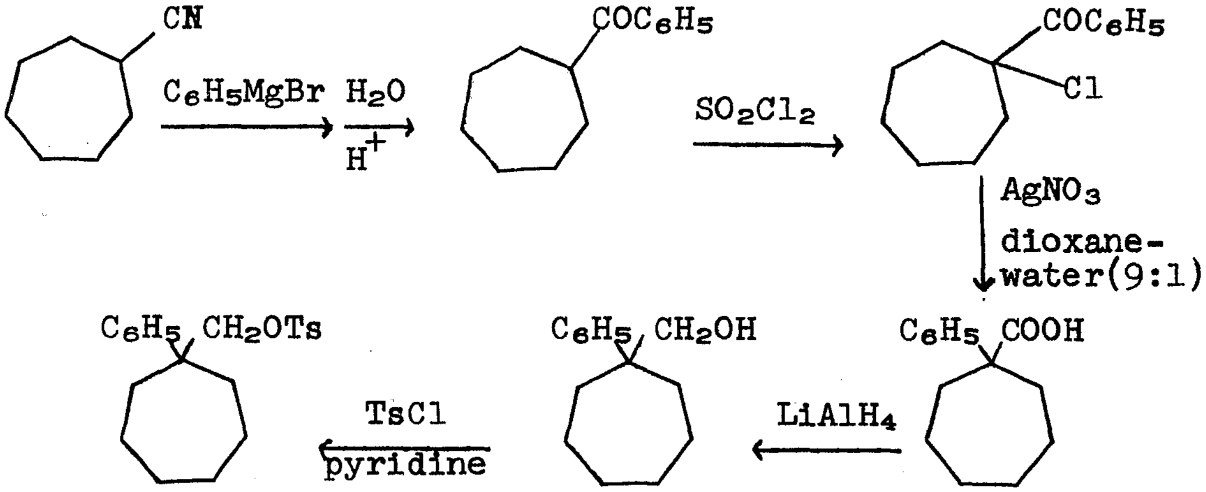
(20)

The formation of "primary product" from 4-phenyl-1-methylcycloheptyl bromide was, as mentioned above (page 104), expected. This information does not, however, prove the intermediacy of this compound in the reaction under study, for its formation from the first major intermediate, the 1-bromomethylcycloheptyl cation, is still unproven.

Synthesis of 1-phenylcycloheptylcarbinyl bromide (the intermediate in path B, Scheme XXVIII) could not be accomplished. The corresponding alcohol and tosylate (VII, X = OH and OTs) were prepared by the procedure of Wilt[69] with little difficulty and in some cases with improvement of yields and purities (see Experimental section, pages 49-56).

Reaction of phenylmagnesium bromide with cycloheptyl cyanide gave after hydrolysis cycloheptyl phenyl ketone, which was converted to the α-chloroketone with sulfuryl chloride. Favorsky-type rearrangement, promoted by silver nitrate, produced 1-phenylcycloheptanecarboxylic acid. Lithium aluminum hydride reduction gave a quantitative yield of the alcohol which was converted in 92% yield to the tosylate (Scheme XXX).

Scheme XXX



Treatment of the tosylate with either sodium bromide in diethylene glycol at 140°[94] (procedure similar to preparation of 1,1-bis(bromomethyl)cyclohexane, pages 35 and 81) or lithium bromide in dimethyl sulfoxide at 85°[95] produced

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(94) H. L. Herzog, in "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, ed, John Wiley and Sons, Inc., New York, N.Y., 1963, p 753.

(95) S. W. Staley, J. Am. Chem. Soc., **89**, 1532 (1967).

mixtures which contained olefinic bonds (infrared spectroscopy). The product mixture from the latter procedure also showed carbonyl and conjugated aromatic bands in the infrared.

Reaction of the alcohol with phosphorus tribromide[96] also gave mixtures of products containing unsaturation. Conversion of the alcohol to the trimethylsilyl ether with trimethylsilyl chloride and quinoline was complete within one hour at room temperature. Treatment of this ether for 24 hours with phosphorus tribromide likewise gave a mixture, which after hydrolysis was found to be mainly the starting alcohol, indicating that the trimethylsilyl ether had not reacted with the phosphorus tribromide.

It therefore became necessary to attempt to obtain indirect evidence as to whether 1-phenylcycloheptylcarbinyl bromide was an intermediate in the formation of "primary product."

Treatment of the alcohol (VII, X = OH) with 85% sulfuric acid at 0°[60] (similar to the reaction of 4-phenyl-1-methylcycloheptanol, pages 41 and 91) gave a mixture of nine products, as indicated by gas chromatography. One of these compounds, which constituted no more than 6% of the product mixture, had a gas chromatographic retention time 2% greater than that of "primary product." It can thus be concluded that no more than 6% of the "primary product" was present.

Since alcohols[72] and tosylates[73] undergo Friedel-Crafts

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(96) L. H. Sommer, H. D. Blankman, and P. C. Miller, J. Am. Chem. Soc., 76, 803 (1954).

reactions in the presence of Lewis acid catalysts, each of these compounds (VII, X = OH and OTs) was treated with aluminum chloride in benzene at 40°. The 1-phenylcycloheptylcarbinol completely reacted within 1-1/2 hours and produced a mixture very similar to that obtained from its acid-catalyzed dehydration (previous paragraph), containing eight major and eleven minor monophenylated products and two products of longer retention time which are probably diphenyl compounds. Once again one of the compounds in this mixture had a gas chromatographic retention time 2% greater than that of "primary product," but it constituted no more than 3% of the total mixture and no more than 4% of that portion of the mixture consisting of monophenyl compounds.

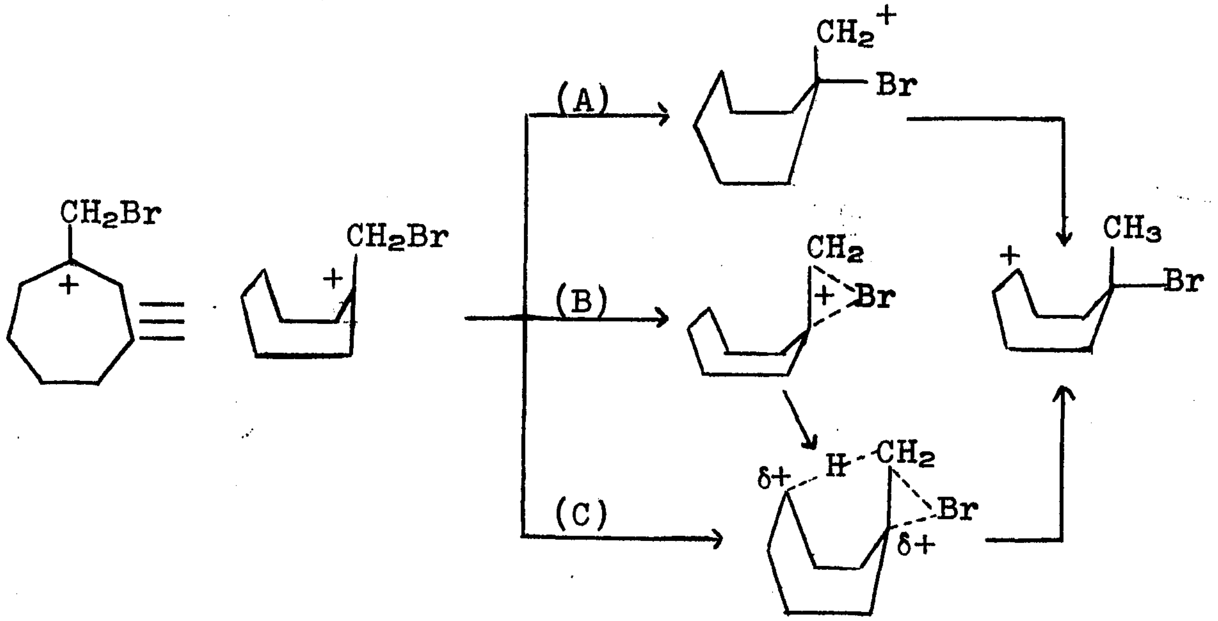
The corresponding tosylate reacted similarly under these conditions to produce a very similar mixture of five major and nine minor monophenyl products in addition to four diphenyl compounds.

The available evidence indicates that reaction of 1,1-bis(bromomethyl)cyclohexane to yield "primary product" follows path A in Scheme XXVIII, page 103.

The conversion of the 1-bromomethylcycloheptyl cation to the 1-bromo-1-methyl-4-cycloheptyl cation obviously involves displacement of bromine from the primary exocyclic carbon to the tertiary ring carbon. It is possible to envisage this as a stepwise procedure involving two consecutive migrations (Scheme XXXI, path A), but such a rearrangement would involve conversion of a tertiary carbonium ion to a primary one, a highly unlikely transformation. This path may therefore be rejected.

Two alternate pathways are possible which do not involve

Scheme XXXI



a free primary carbonium ion. One (path B) involves the possibility that the 1-bromomethylcycloheptyl cation may form a bridged species. In formation of this bridged ion from 1,1-bis(bromomethyl)cyclohexane, the bromine could form a bridge to the charged tertiary carbon atom after ring expansion, whereas the bridged bromonium ion could form directly in the reaction of 1-bromo-1-bromomethylcycloheptane. The transannular hydride migration would then displace the bromine from the exocyclic carbon while the bromine was already partially bonded to the tertiary ring carbon.

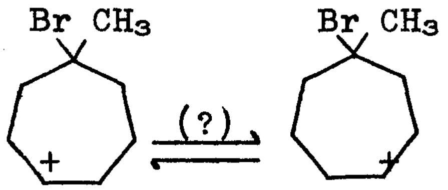
In the other possible case (path C) the reaction can be concerted. As the hydrogen begins to migrate it can start to displace bromine from the exocyclic carbon of the classical

1-bromomethylcycloheptyl cation. As the bond between the migrating hydrogen and the carbon to which it is originally attached becomes weaker, the hydrogen begins to bond to the exocyclic carbon. This incipient bond formation would start to displace the bromine from this position, and the bromine would then start to bond to the ring carbon.

These two possibilities cannot be distinguished in this work. However, it should be noted that the geometry at the exocyclic carbon atom is favorable for either of them, for the hydrogen will approach the carbon from the side opposite that to which the bromine is attached. In either case the reaction makes use of the ability of the bromine atom to bridge between two carbons, at least transiently.

The gas chromatograms in the kinetic studies of the reaction of 1,1-bis(bromomethyl)cyclohexane showed no evidence for the formation and decay of an intermediate prior to formation and decay of "primary product." This is understandable in light of what must be the high reactivity of the 4-phenyl-1-methylcycloheptyl bromide formed in situ. Brown showed that reaction of tert-butyl bromide with benzene and a molar quantity of aluminum bromide at 25° was complete within 0.005 seconds.[43] In this work, the concentration of 4-phenyl-1-methylcycloheptyl bromide at any instant must be very low, and the aluminum chloride concentration is therefore great compared to it. Furthermore, this halide undergoes intramolecular cyclialkylation, which generally proceeds more rapidly than intermolecular alkylation.[33] For these reasons intramolecular cyclialkylation of this tertiary halide would be extremely rapid, and its concentration could be expected never to reach a detectable level.

Given the transannular hydride migration to form the 1-bromo-1-methyl-4-cycloheptyl cation, it might be argued that this ion could undergo rearrangements among the various possible secondary carbonium ions via facile 1,2-hydride migrations and that these rearrangements could make possible formation of II or even III (page 86) as the "primary product" from this ion. This argument can be dismissed for two reasons. First, the fact that 4-phenyl-1-methylcycloheptyl alcohol and bromide (VI, X = OH and Br) each produce "primary product" in reactions involving carbonium ions indicates that phenylation of the 1-bromo-1-methyl-4-cycloheptyl cation takes place at the 4-position. The interconversion of the two equivalent ions (IX and IX') after the transannular hydride migration cannot be ruled out, however, without recourse to deuterium labelling.



IX IX'

Second, the Friedel-Crafts reaction of 1,2-dichlorohexane, in which there are four possible secondary carbon atoms on which a positive charge could reside, shows that hydride migrations will occur to place the positive charge on the secondary carbon furthest from the elctron-withdrawing chlorine.[18] In this work the 1-bromo-1-methyl-4-cycloheptyl cation is already formed with the charge on one of the two secondary carbon atoms furthest from the electron-attracting halogen. Hydride migration to move the charge nearer to the bromine would therefore be unlikely, although once again interconversion of the chemically and energetically equivalent cations IX and IX' is possible.

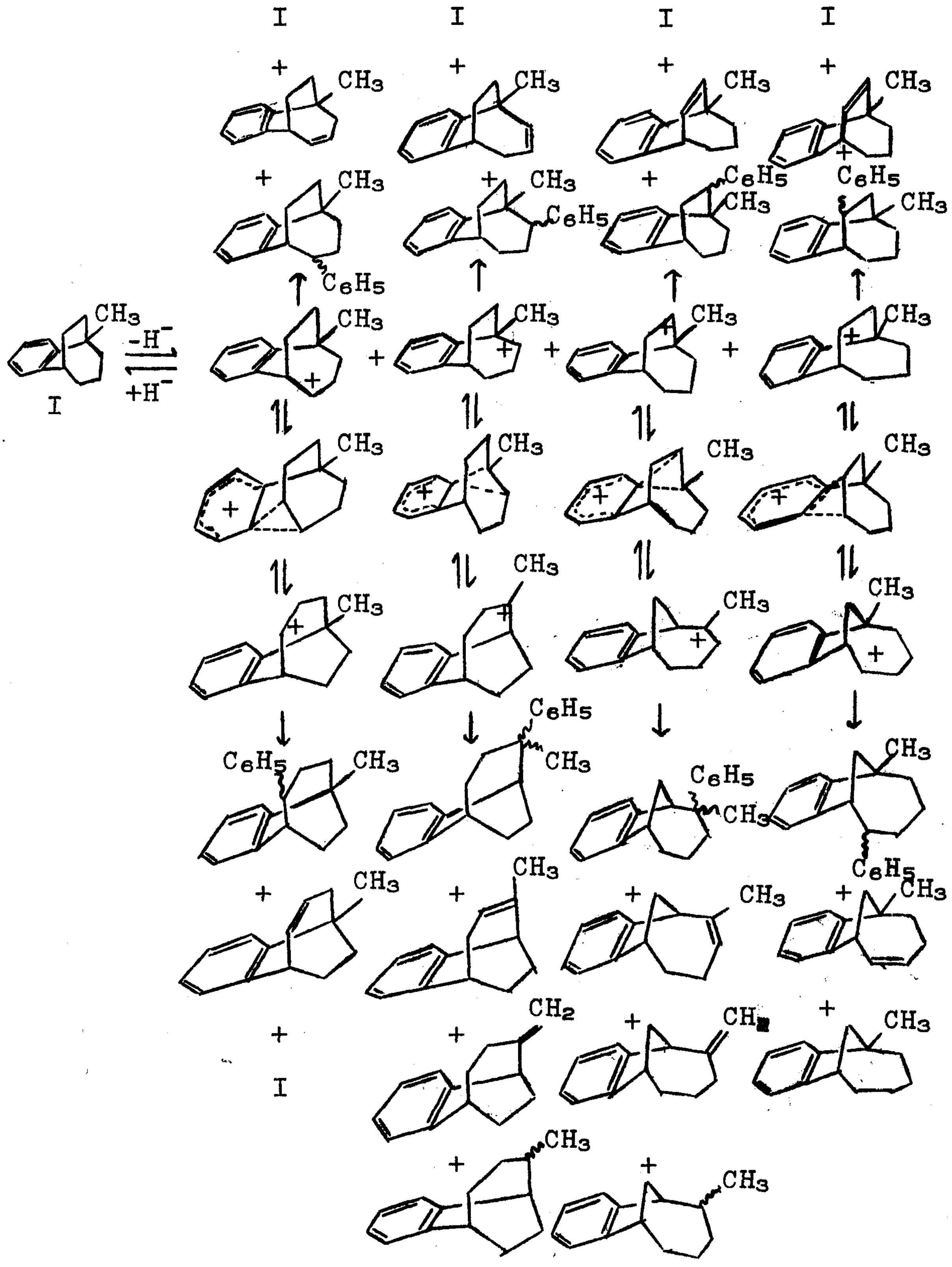
Rearrangement of "Primary Product"

A sample of synthetic "primary product" was treated with benzene and aluminum chloride at 40°. Gas chromatographic analysis of the product mixture showed formation of at least ten compounds, five of which were probably diphenylated species on the basis of their long retention times. The quantities of materials available and the incomplete gas chromatographic resolutions made in inconvenient to attempt isolation and identification of these materials, but it is possible to speculate on their identities in the light of the products formed in reactions of similar compounds.

Hydride abstraction from a β-carbon atom can follow any or all of four nonequivalent paths (Scheme XXXII, page 115; compare with Scheme XVII,[49] page 24). Three of these β-phenylethyl cations can rearrange *via* a phenonium ion to another carbonium ion, the fourth would give the same ion on rearrangement. Each of the seven possible cations can then: (1) alkylate benzene to form a diphenylated derivative, (2) eliminate a proton to give an olefin which may be reprotonated to form a carbonium ion which can react further, or (3) abstract a hydride ion from "primary product" to form a saturated hydrocarbon and to cause further reaction of "primary product." In this case, four of the ions would reform "primary product" and three would yield isomeric hydrocarbons. Secondary rearrangements of the various intermediate carbonium ions would lead to additional products which are not considered here.

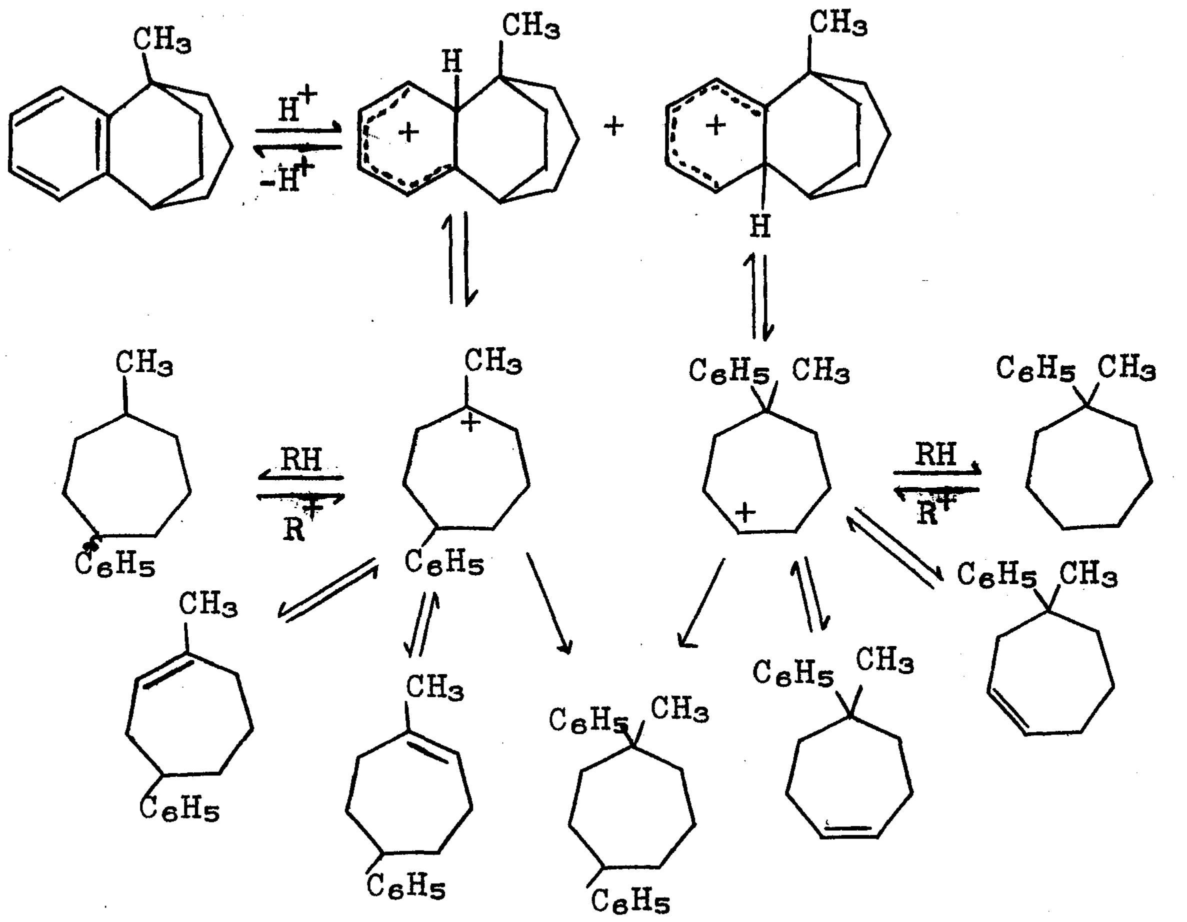
Alternatively, the "primary product" could undergo protodealkylation at either of two sites (Scheme XXXIII;

Scheme XXXII



compare with Scheme VI,[18] page 10). In addition to reforming

Scheme XXXIII



"primary product," the resulting carbonium ions could each form two olefins by proton loss or a phenylcycloalkane by hydride abstraction, and each could alkylate benzene to give the same diphenylated species. In these discussions geometrical isomerism and preferred directions for approach of benzene in alkylations have not been considered.

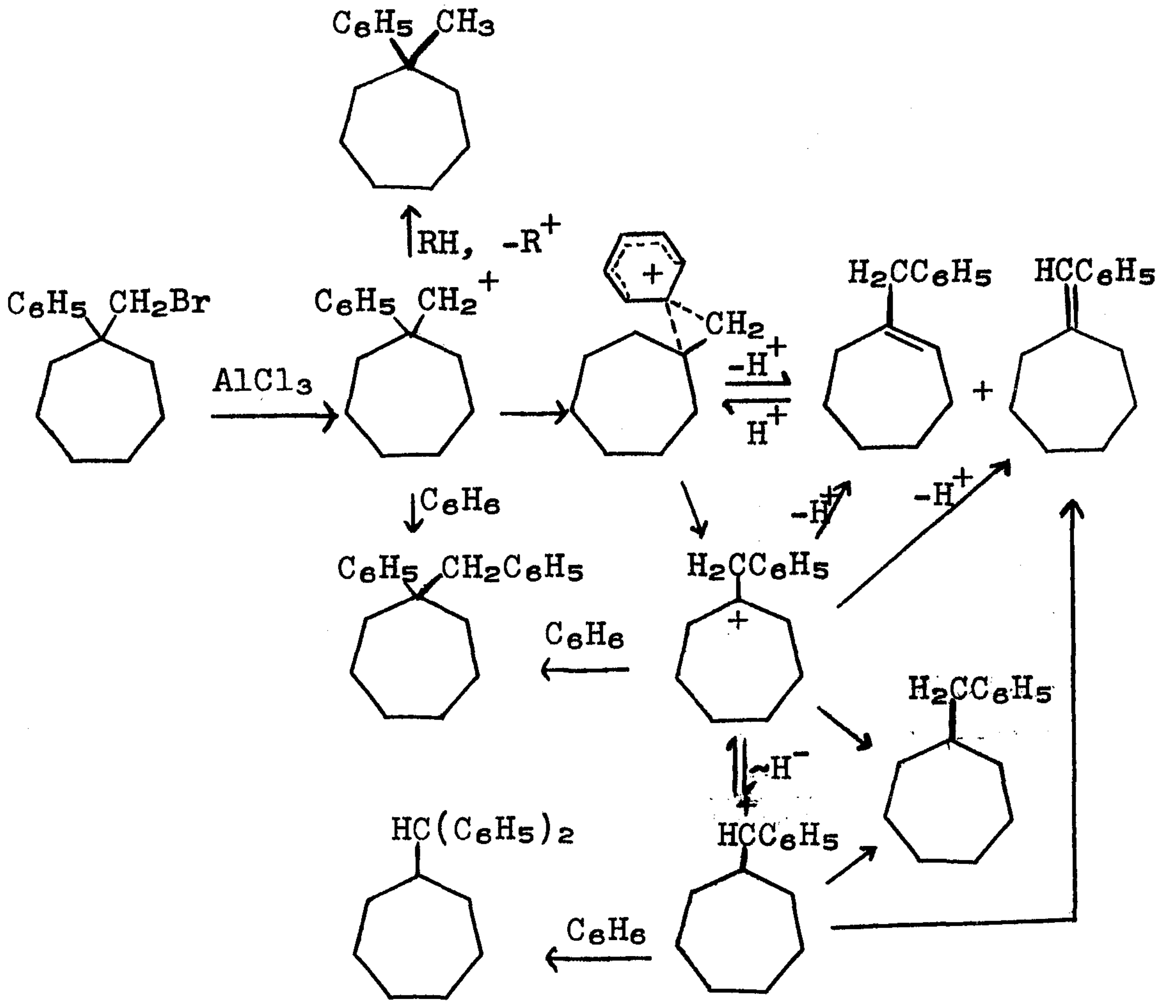
In view of the relatively large number of diphenylated species formed from further reaction of "primary product," it is likely that Scheme XXXII, or a combination of Schemes XXXII and XXXIII, represents the actual situation more accurately than does Scheme XXXIII alone. The carbonium ions in Scheme XXXIII are possibly present in the reaction mixture and could be the hydride acceptors which would initiate Scheme XXXII. One of these ions in Scheme XXXIII is the most likely precursor to "primary product," and its conversion to "primary product" early in the reaction and to other products, especially diphenylated compounds, in a later stage of the reaction may indicate kinetic control in the early stages of the reaction and thermodynamic control later in the reaction.

Other Possible Products in the Friedel-Crafts Reaction of 1,1-Bis(bromomethyl)cyclohexane

In addition to those compounds formed by secondary reaction(s) of "primary product," some of the materials detected by gas chromatography may also be first-formed products. As mentioned above (page 114), poor gas chromatographic resolution and small quantities relative to "primary product" made isolation and identification of any of these other compounds too difficult to attempt. However, it is interesting to speculate on their identities in the light of the proposed mechanism.

Intermediacy of the 1-bromomethylcycloheptyl cation in formation of "primary product" seems well proven; path A in Scheme XXVIII, page 103, accounts for formation of all of the "primary product." If the intermediate in path B of Scheme XXVIII, 1-phenylcycloheptylcarbinyl bromide, is also formed it can react as shown by Wilt[69,93] (pages 104-105) to give two olefins and/or, in this case, products of further alkylations of the corresponding carbonium ions. In addition its rearrangement product, the 1-benzylcycloheptyl cation, can undergo hydride migration to give a benzylic cation which can form another diphenylated compound. Any of these ions can also abstract a hydride ion from a neutral molecule, perhaps from "primary product." Some of these possibilities are shown in Scheme XXXIV, page 119.

Scheme XXXIV



BROMINATION REACTIONS
AT ADSORBENT SURFACES

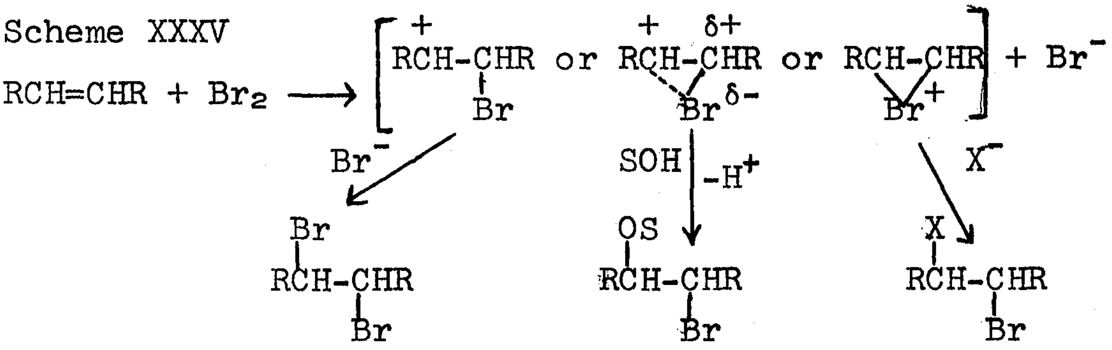
INTRODUCTION

Reaction of Bromine with Olefins

The products, kinetics, and stereochemistry of the reaction of bromine with olefins have been extensively studied. Inasmuch as a comprehensive review[97] has recently been published, only a brief survey of those aspects related to the present work will be given.

The two-step nature of liquid phase 1,2-addition of bromine to a double bond is well known. The first step involves formation of a cationic intermediate (see Scheme XXXV; the question of bridged ions will be discussed later) which reacts with bromide to give the usual product. In this second step protic solvent (SOH) or the anion from an added salt (X^-) can compete with bromide as the nucleophile.[97]

Scheme XXXV

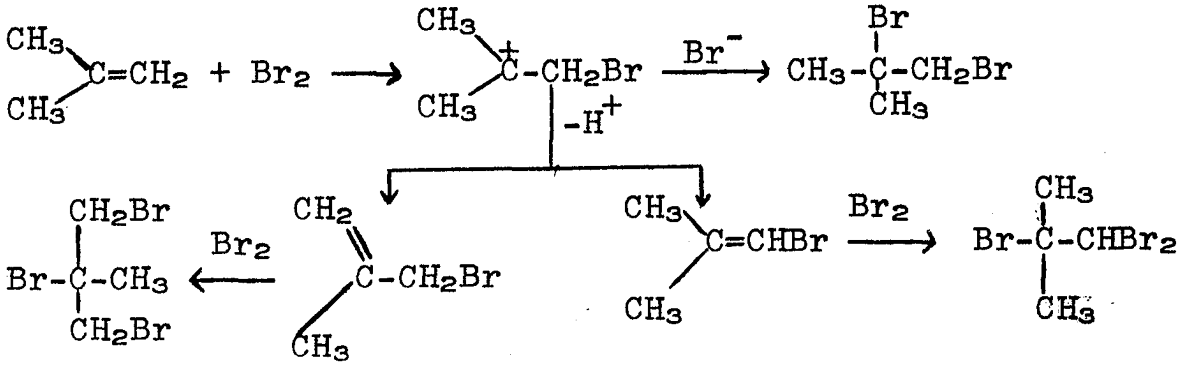


A further side reaction involves competing loss of a proton from the cationic intermediate, especially when one carbon of the double bond is highly substituted, to yield an unsaturated bromide (Scheme XXXVI) which can react further with bromine to give a tribromide. This reaction accounts for an appreciable fraction of the product from 1,1-

(97) P. B. D. de la Mare and R. Bolton, "Electrophilic Additions to Unsaturated Systems," American Elsevier Publishing Co., New York, N. Y., 1966, ch 7.

disubstituted ethylenes such as isobutene[98-100] (Scheme XXXVI) and 3-ethyl-1-hexene[67] and from medium ring methylenecycloalkanes.[66,67] At 300°, in the vapor phase, unsaturated bromides (50% methallyl bromide and 20% 1-bromo-2-methylpropene) are the major products of bromination of isobutene.[101]

Scheme XXXVI



Bromine addition to olefins exhibits complex kinetics involving high order terms in bromine, as in equation 21.[102]

$$-\frac{d[Br_2]}{dt} = k_2[\text{olefin}][Br_2] + k_3[\text{olefin}][Br_2]^2 + k_4[\text{olefin}][Br_2]^3 \qquad (21)$$

In dilute solutions of bromine in acetic acid or in aqueous and alcoholic solvents, the second order term (first order

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(98) S. V. Lebedev and Ya. M. Slobodin, J. Gen. Chem. (U.S.S.R.), 4, 23 (1934); through Chem. Abstr., 28, 5399 (1934).

(99) C. D. Hurd and L. U. Spence, J. Am. Chem. Soc., 51, 3561 (1929).

(100) B. K. Mereshkowsky, Ann., 431, 113 (1923).

(101) A. Streigler, Chem. Tech. (Berlin), 9, 523 (1957).

(102) B. E. Swedlund and P. W. Robertson, J. Chem. Soc., 630 (1947).

in bromine) predominates,[103-109] and the mechanism is essentially that shown in Scheme XXXV.

At higher concentrations of bromine in acetic acid (0.025 M), the third order term predominates.[104,110] The second molecule of bromine apparently aids in breaking the bromine-bromine bond of a bromine molecule already complexed with the olefin.[109] Scheme XXXV would then require elaboration to include the olefin-bromine complex and the second molecule of bromine, as in Scheme XXXVIIa.

Addition of water causes the reaction to revert to the second order mechanism[111] by increasing the ion-stabilizing ability of the medium and making unnecessary the ionic stabilization due to the second molecule of bromine. Also, chlorination of olefins shows no third or higher order terms, presumably because the trichloride ion is not as easily formed as is the tribromide ion.

In aprotic solvents such as chloroform and chloro-

(103) A. Berthoud and M. Mosset, *J. Chim. Phys.*, **33**, 272 (1936); through *Chem. Abstr.*, **30**, 5130 (1936).

(104) P. W. Robertson, N. T. Clare, K. J. McNaught, and G. W. Paul, *J. Chem. Soc.*, 335 (1937).

(105) P. D. Bartlett and D. S. Tarbell, *J. Am. Chem. Soc.*, **58**, 466 (1936).

(106) J. R. Atkinson and R. P. Bell, *J. Chem. Soc.*, 3260 (1963).

(107) J. E. Dubois and G. Mouvier, *Tetrahedron Letters*, 1325 (1963).

(108) W. Walisch and J. E. Dubois, *Chem. Ber.*, **92**, 1028 (1959).

(109) P. W. Robertson, J. K. Heyes, and B. E. Swedlund, *J. Chem. Soc.*, 1014 (1952).

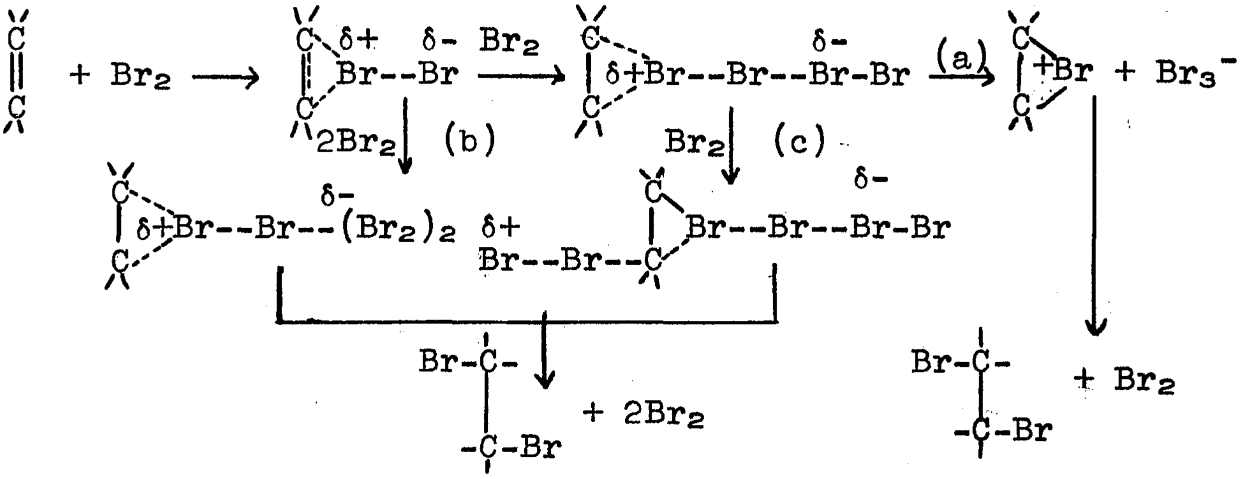
(110) I. Ting and P. W. Robertson, *J. Chem. Soc.*, 628 (1947).

(111) P. W. Robertson, P. B. D. de la Mare, and W. T. E. Johnston, *J. Chem. Soc.*, 276 (1943).

benzene, bromine addition is also mainly third order.[109,112] In carbon tetrachloride a low order heterogeneous reaction at the wall of the vessel competes with a high order homogeneous reaction.[112]

In the range of bromine concentration 0.1 to 0.2 M in acetic acid and with unreactive olefins such as *β*-bromostyrene, the fourth order term predominates.[102] Here both extra bromine molecules may aid in scission of the bromine-bromine bond (Scheme XXXVIIb) or one may act as a nucleophile (Scheme XXXVIIc). The authors proposed the mechanism shown in Scheme XXXVIII.[102]

Scheme XXXVII



Scheme XXXVIII

$$Br_2 + Br_2 \rightleftharpoons Br_4$$

$$\text{Olefin} + Br_4 \longrightarrow \text{Olefin}\cdot Br_2 + Br_2$$

$$\text{Olefin}\cdot Br_2 + Br_2 \longrightarrow \text{OlefinBrBr} + Br_2$$

The rate of reaction in the gas phase, as in carbon

(112) P. B. D. de la Mare, R. A. Scott, and P. W. Robertson, *J. Chem. Soc.*, 509 (1945).

tetrachloride,[112] is extremely sensitive to the presence of polar substances. Bromine and ethylene react rapidly in a container coated with stearic acid or cetyl alcohol, but in a container coated with paraffin wax the rate of reaction is almost zero.[113]

Normally, olefins undergo *trans*-addition of bromine. This rule holds whether the double bond is in an acyclic[114-119] or cyclic[120-126] system, and has been explained on the basis of the bridged "bromonium ion"[127] intermediate in Scheme XXXVIIa. Thus, *cis*-2-butene yields *d,l*-2,3-dibromobutane and *trans*-2-butene gives the *meso*-isomer in the liquid phase at -20°.[119] Cyclohexene[125,126] and various steroids (cholest-2-, -3-,[122] and -5-ene[123] and cholesterol[123,124]) yield *trans*-vicinal dibromides (equations 22-24).

(113) R. G. Norrish, *J. Chem. Soc.*, **123**, 3006 (1923).

(114) P. F. Frankland, *J. Chem. Soc.*, **101**, 654 (1912).

(115) A. Jovtscheff, *Chem. Ber.*, **93**, 2048 (1960).

(116) A. Jovtscheff, *Chem. Ber.*, **95**, 2629 (1962).

(117) R. E. Buckles, J. M. Badar, and R. J. Thurmaier, *J. Org. Chem.*, **27**, 4523 (1962).

(118) K. Nozaki and R. A. Ogg, *J. Am. Chem. Soc.*, **64**, 697 (1942).

(119) F. G. Bordwell and P. S. Landis, *J. Am. Chem. Soc.*, **79**, 1593 (1957).

(120) H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.*, 4136 (1959).

(121) J. Valls and E. Toromanoff, *Bull. Soc. Chim. France*, 758 (1961).

(122) G. H. Alt and D. H. R. Barton, *J. Chem. Soc.*, 4284 (1954).

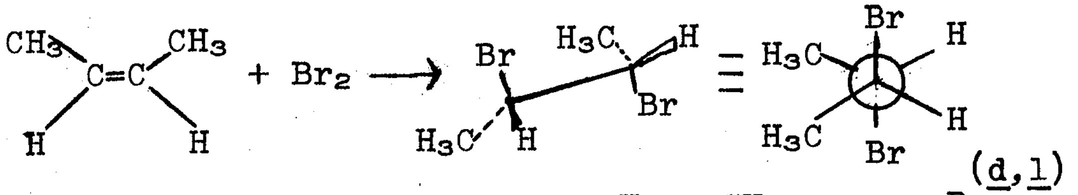
(123) D. H. R. Barton and E. Miller, *J. Am. Chem. Soc.*, **72**, 1066 (1950).

(124) D. H. R. Barton, E. Miller, and H. T. Young, *J. Chem. Soc.*, 2598 (1951).

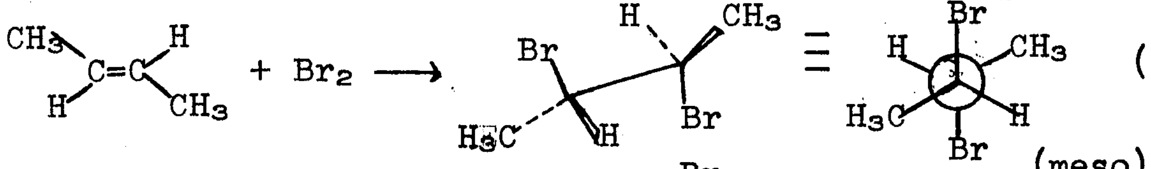
(125) H. L. Goering, P. I. Abell, and B. F. Aycock, *J. Am. Chem. Soc.*, **74**, 3588 (1952).

(126) S. Winstein, *J. Am. Chem. Soc.*, **64**, 2792 (1942).

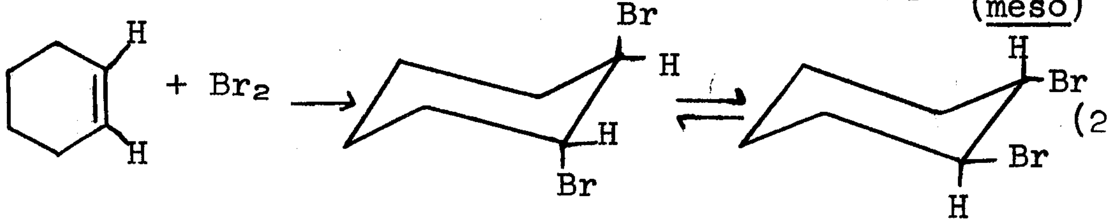
(127) I. Roberts and G. E. Kimball, *J. Am. Chem. Soc.*, **59**, 947 (1937).



(22)



(23)



(24)

Regarding chlorinations, de la Mare has stated, "Theoretically, cis-addition to an olefin might be expected to occur if the halogen molecule could present itself broadside-on to the olefinic double bond, giving a four-centre (sic) transition state."[128] Several recent examples of cis-chlorination of a double bond are known, but all of them involve intermediates capable of existing as stable classical carbonium ions.[129-135] Moreover, the ability of chlorine to bridge two adjacent carbon atoms is markedly

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(128) P. B. D. de la Mare and R. Bolton, "Electrophilic Additions to Unsaturated Systems," American Elsevier Publishing Co., New York, N. Y., 1966, ch 6, p 92.

(129) S. J. Cristol, F. R. Stermitz, and P. S. Ramey, J. Am. Chem. Soc., 78, 4939 (1956).

(130) R. K. Summerbell and H. E. Lunk, J. Am. Chem. Soc., 79, 4802 (1957).

(131) V. Georgian, L. Georgian, and A. V. Robertson, Tetrahedron, 19, 1219 (1963).

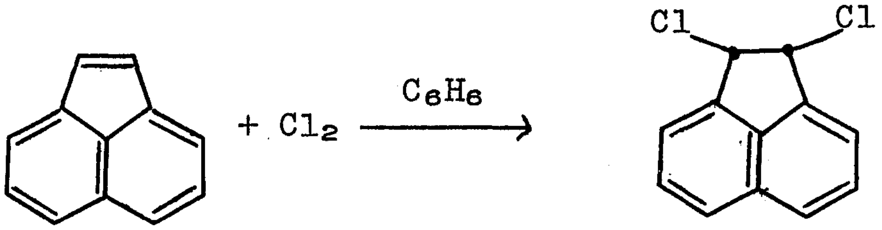
(132) R. E. Buckles and D. F. Knaak, J. Org. Chem., 25, 20 (1960).

(133) P. B. D. de la Mare, N. V. Klassen, and R. Koenigsberger, J. Chem. Soc., 5285 (1961).

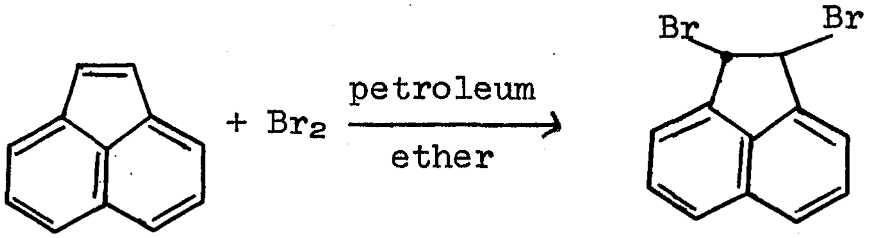
(134) P. B. D. de la Mare, N. V. Klassen, and R. Koenigsberger, J. Chem. Soc., 5327 (1964).

(135) R. C. Fahey and C. Schubert, J. Am. Chem. Soc., 87, 5172 (1965).

less than that of bromine, so that a chloronium ion intermediate and its stereochemical consequences ought to be less important in chlorination than the bromonium ion in bromination. This may be shown by the fact that chlorine gives *cis*-9,10-dichloroacenaphthene from acenaphthylene (equation 25) but bromine gives the *trans*-9,10-dibromo compound (equation 26).[129]



(25)



(26)

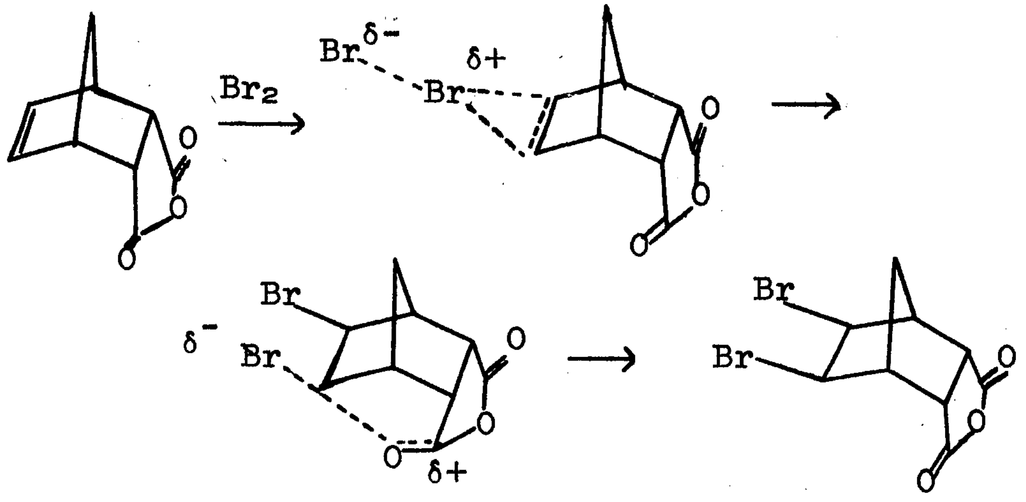
Thus the *cis*-addition of chlorine probably proceeds through classical carbonium ions and not through broadside approach of the chlorine molecule to the double bond.

Bromine adds to norbornene-*endo*-5,6-dicarboxylic anhydride to give the *exo*-2-*exo*-3-dibromo derivative (*cis*-addition), but the results were explained in terms of *trans*-participation by the carbonyl oxygen of the anhydride function (Scheme XXXIX).[136,137]

(136) J. A. Berson and R. Swidler, *J. Am. Chem. Soc.*, **76**, 4060 (1954).

(137) H. Kwart and L. Kaplan, *J. Am. Chem. Soc.*, **76**, 4078 (1954).

Scheme XXXIX



It was desired to study the stereochemical course of addition of bromine to olefins when the reactants were adsorbed on a surface. The possibility of the bromine molecule presenting itself broadside to the olefin to give cis-addition seemed enhanced under these circumstances, by analogy with the cis-addition of hydrogen to a double bond at a catalyst surface.

The olefins studied were cis- and trans-2-butene and cyclohexene, because different stereochemical modes of addition to each of these olefins will give different products. The reactions were carried out at the surfaces of both silica gel and activated carbon.

Reaction of Bromine with Aromatic Hydrocarbons

As with bromine addition to olefins, reaction of bromine with aromatic hydrocarbons has also been extensively studied. Variations in the kinetic order of reaction are as complex in the latter case as in the former, and equation 27 (similar to equation 21) shows the general possibilities which have been observed for bromination by molecular bromine without Lewis acid catalysts.

$$-\frac{d\,[Br_2]}{dt} = k_2[ArH][Br_2] + k_3[ArH][Br_2]^2 + k_4[ArH][Br_2]^3 \quad (27)$$

With the reactive aromatics anisole, mesitylene, and acetanilide, in acetic acid, reaction is second order when $[Br_2] = 10^{-3}$ M but third order when $[Br_2] = 0.01$ to 0.025 M.[111] With the less reactive aromatics toluene, naphthalene, and <u>meta</u>-xylene at $[Br_2] = 0.1$ to 0.2 M the fourth order term predominates.[111] As with bromine addition, the extra bromine in the higher order reactions probably aids in breaking the bromine-bromine bond of a complex between aromatic substrate and the first molecule of bromine to give the tribromide anion (Scheme XXXX).[138] Chlorine, which cannot so easily form the trichloride ion, reacts with aromatics with second order kinetics.

In aprotic solvents of moderate polarity such as nitromethane the order with respect to bromine is usually greater

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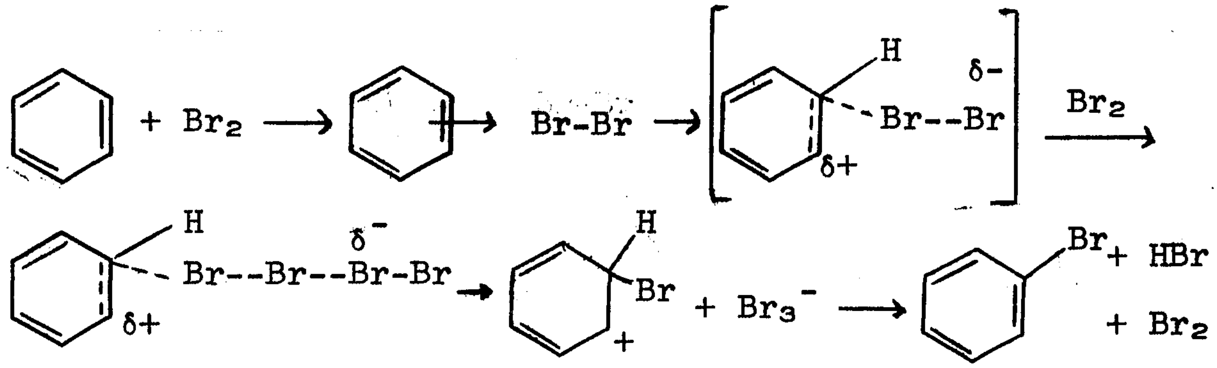
(138) R. M. Keefer, A. Ottenberg, and L. J. Andrews, *J. Am. Chem. Soc.*, **78**, 255 (1956)

than one. One report indicated the reaction to be of order

Scheme XXXX



1.5 with respect to bromine at 30° in the concentration region 0.01 to 0.04 M.[139] A later paper claimed a fifth order reaction, with solvent concentration being involved (equation 28).[140]

$$-\frac{d[Br_2]}{dt} = k_5[ArH][Br_2]^3[RNO_2] \qquad (28)$$

The presence of Lewis acid catalysts removes the need for bromine molecules to assist in heterolyzing the bromine-bromine bond (see Scheme XXXX) and reduces the kinetic order with respect to bromine. With zinc chloride in acetic acid, for example, the reaction is first order in bromine.[141]

As can be seen from Table 5, the reaction of bromine with alkylbenzenes uncatalyzed by Lewis acids shows a high

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(139) G. Illuminati and G. Marino, Gazz. chim. ital., 84, 1127 (1954); through Chem. Abstr., 52, 3705 (1958).

(140) A. H. Neyens and J. C. Jungers, Bull. Soc. Chim. France, 1481 (1958); through Chem. Abstr., 54, 14898 (1960).

(141) L. J. Andrews and R. M. Keefer, J. Am. Chem. Soc., 78, 4549 (1956).

inter- and intramolecular selectivity. In all cases shown, the rate of reaction of alkylbenzene relative to benzene is high, and *ortho-para* substitution is observed almost exclusively. Where different relative rates are shown for a particular alkylbenzene they may be attributed to different methods of measurement (direct[142] or competitive[143,145] kinetic studies). Differences in product distributions may be due to different methods of analysis (the method in reference 144 - oxidation to carboxylic acids - probably

Table 5: Bromination of Benzene and Monoalkylbenzenes with Molecular Bromine in 85% Acetic Acid Solution at 25°.

Aromatic (ArH)	$k_{ArH}:k_B$	%*o*-	%*m*-	%*p*-	Method of Analysis[a]	Ref.
Benzene (B)	1.0					
Toluene	340	31	-	69	ID	(142)
	605	32.9	0.3	66.8	IR	(143)
b	-	41.5	-	58.5	Oxid.	(144)
Ethylbenzene	290	-	-	-		(142)
b	-	18	-	82	Oxid.	(144)
Cumene	180	-	-	-		(142)
b	-	11	-	89	Oxid.	(144)
tert-Butylbenzene	110	8	-	92	ID	(142)
	138	1.20	1.47	97.3	IR	(145)

a: ID = isotope dilution, IR = infrared analysis, Oxid. = oxidation to carboxylic acids. b: 45°, excess neat aromatic.

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(142) P. W. Robertson, P. B. D. de la Mare, and B. E. Swedlund, *J. Chem. Soc.*, 782 (1953).

(143) H. C. Brown and L. M. Stock, *J. Am. Chem. Soc.*, **79**, 1421 (1957).

(144) I. N. Nazarov and A. V. Semenovskii, *Izvest. Akad. Nauk S.S.S.R., Otdel Khim. Nauk*, 840 (1957).

(145) L. M. Stock and H. C. Brown, *J. Am. Chem. Soc.*, **81**, 5615 (1959).

gives less accurate results) and/or different reaction conditions (see footnote b, Table 5). In all cases the attacking reagent is most likely molecular bromine and not an ionic species.

Use of a positively charged brominating species (protonated hypobromous acid) gives a somewhat less selective reaction, as shown in Table 6. The kinetic expression (equation 29) indicates a positive brominating agent.[146,147]

$$-\frac{d\,[BrOH]}{dt} = k_3[Arh][BrOH][H^+] \qquad (29)$$

It is likely that in aqueous acetic acid or aqueous dioxane the attacking species is $BrOH_2^+$ and not Br^+ (Scheme XXXXI), and so the reagent is only moderately electrophilic and therefore still fairly selective.[148] However, the intermolecular selectivity is somewhat reduced relative to that of molecular bromine. The increased ortho-substitution with protonated hypobromous acid may be due to this reagent

Table 6: Bromination of Benzene and Alkylbenzenes with Protonated Hypobromous Acid in 50% Aqueous Dioxane at 25°.

Aromatic (ArH)	$k_{ArH}:k_B$	%o-	%m-	%p-	Ref.
Benzene (B)	1.00				
Toluene	36.2	70.3	2.3	27.4	(146)
tert-Butylbenzene	12.0	37.7	7.2	53.2	(147)

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(146) P. B. D. de la Mare and J. T. Harvey, J. Chem. Soc., 36 (1956).

(147) P. B. D. de la Mare and J. T. Harvey, J. Chem. Soc., 131 (1957).

(148) G. A. Olah, S. J. Kuhn, S. H. Flood, and B. A. Hardie, J. Am. Chem. Soc., 86, 1039 (1964).

Scheme XXXXI

$$\begin{aligned} HOBr + H^+ &\rightleftharpoons BrOH_2^+ \\ BrOH_2^+ + ArH &\rightleftharpoons ArHBr^+ + H_2O \\ ArHBr^+ &\rightleftharpoons ArBr + H^+ \end{aligned}$$

having lesser steric requirements than does molecular bromine.

Bromination of aromatics catalyzed by Lewis acids is an extensively used preparative method, but only a few studies have been made of this reaction. Brown[149] reported that bromination of toluene at 30° with an equimolar quantity of aluminum bromide as catalyst yielded 20% *ortho*-, 30% *meta*-, and 50% *para*-bromotoluene. However, Olah and Meyer[150] have shown rapid equilibration of isomeric bromotoluenes under these conditions, the equilibrium composition of 38% *ortho*-, 44% *meta*-, and 18% *para*-isomers was reached in less than fifteen minutes. Their data indicate that *para*-bromotoluene would give Brown's[149] proportions of isomers in approximately two minutes, and it is likely that less time would be required to reach these proportions if a mixture of isomers was present initially. Crump and Gornowicz[151] also found that each bromotoluene isomer could be converted to an equilibrium mixture (37% *ortho*-, 46% *meta*-, and 17% *para*-isomer) without solvent, in the presence of excess toluene, or in dilute carbon disulfide solution. Brown's results are there-

(149) H. C. Brown and C. W. McGary, Jr., *J. Am. Chem. Soc.*, **77**, 2306 (1955).

(150) G. A. Olah and M. W. Meyer, *J. Org. Chem.*, **27**, 3464 (1962).

(151) J. W. Crump and G. A. Gornowicz, *J. Org. Chem.*, **28**, 949 (1963).

fore suspect since his conditions were favorable for rapid isomerization. Isomerization of products under the reaction conditions must be carefully guarded against in aromatic substitution reactions.[148]

Results of studies conducted under nonisomerizing conditions are shown in Table 7. Zinc chloride in acetic acid gives high intermolecular selectivity as a bromination catalyst, but isomer distribution was not reported.[141] Ferric chloride in nitromethane gives bromination with a low substrate but high positional selectivity.[148] Olah concluded that the substrate-determining step (and therefore the step that determines the relative rates) involves a transition state similar to a *π*-complex (relative reactivities of the aromatics studied were of the same order as are *π*-complex stabilities) but the product-determining step involves *σ*-complex type transition states with corresponding high *ortho-para* selectivity. The higher proportions of *ortho*-substitution than those found for molecular brominations[142-144] were explained as the result of an attacking group with small steric requirements compared to molecular

Table 7: Lewis Acid Catalyzed Bromination of Toluene.

Solvent	Catalyst and Concentration	Br_2	$k_T:k_B$[a]	%*o*-	%*m*-	%*p*-	Ref.
CH_3COOH	$ZnCl_2$, 0.1 M	0.0019 M	148				(141)
CH_3NO_2	$FeCl_3$, 3.0 M	1.5 M	3.6	68.7	1.8	29.5	(148)
CH_3NO_2	$FeCl_3$, 0.1 M	0.05 M	32	58.4	~1	40.6	(148)

a: T = toluene, B = benzene.

bromine, the incipient bromonium ion.[148]

The increase in substrate selectivity and decrease in the *ortho:para* ratio with increasing dilution indicate that increasing solvation makes the electrophile weaker and bulkier.[148] Similar solvent effects have been noted for chlorination reactions. Thus, the rate of uncatalyzed chlorination of toluene at 25° increased as the solvent was changed from ethylene dichloride to either acetic anhydride, acetic acid, or acetonitrile to nitromethane.[152] Furthermore, isomer ratios of the products are also dependent on solvent. Hydroxylic solvents give ~60% *ortho*- and 40% *para*-chlorination of toluene, while nonhydroxylic solvents invert this ratio. Mixed solvents give intermediate isomer distributions. The extreme cases were trifluoroacetic acid with 69% *ortho*- and 31% *para*-chlorination and nitromethane with 34% *ortho*- and 66% *para*-chlorination. The authors concluded that the attacking reagent was a complex between molecular chlorine and the solvent. The results could be explained by assuming that the more selective chlorination reagents (those with a greater degree of complexing with solvent) were more sensitive to the steric requirements of substituents already present on the aromatic ring.[153]

Interaction between solvent and aromatic hydrocarbon also can affect the course of aromatic substitution. When

(152) L. J. Andrews and R. M. Keefer, *J. Am. Chem. Soc.*, *81*, 1063 (1959).

(153) L. M. Stock and A. Himoe, *Tetrahedron Letters*, 9 (1960).

ortho-cresol was chlorinated in various solvents at 50°, the ratio of 4- to 6-chlorination varied from 0.9 in chloroform or carbon tetrachloride to 5.3 in nitrobenzene and 6.4 in nitromethane. Complexing of ortho-cresol with the solvents was used to explain the decreased substitution ortho- to the hydroxyl group in the more polar solvents.[154]

Finally, bromination of toluene in the vapor phase produces only benzyl bromide, whether the reaction is induced thermally or photolytically.[155]

Complexing of either the aromatic hydrocarbon[154] or the attacking halogen[148,153] with solvent decreases the ortho:para ratio. Adsorption of the halogen on the surface should increase its effective bulk and therefore also decrease the ortho:para ratio. Adsorption of the aromatic hydrocarbon, on the other hand, can either increase or decrease this ratio depending on the relative geometry between the hydrocarbon and the surface (see page 161).

It was desired to study the reaction of bromine with alkylbenzenes when the molecules were adsorbed on a surface, with the idea of examining the effects of various adsorbents on the isomer distributions obtained and of evaluating these effects in terms of steric and/or electronic factors. Toluene, cumene, and tert-butylbenzene were studied since the isomer distributions could be readily compared with

(154) A. Campbell and D. J. Shields, Tetrahedron, **21** 211 (1965).

(155) H. R. Anderson, Jr., H. A. Scheraga, and E. R. van Artsdalen, J. Chem. Phys., **21**, 1258 (1953).

those obtained for these compounds in solution. The reactions were carried out at the surfaces of alumina, silica gel, and activated carbon.

EXPERIMENTAL

Bromination Procedures

Brominations were carried out in the high-vacuum system shown in Figure 1 (page 141).[156]

The following procedure is typical of all the brominations of aromatic compounds. Carbon (refer to Table 11, page 159; 55 g) was heated (cleaned) in vacuo at 460-480° to remove any materials adsorbed from the air. Toluene (ca 5 ml) was placed in the adjacent trap, the trap was evacuated until 4.0 ml (3.5 g, 38 mmoles) of toluene remained, and the toluene vapors were allowed to diffuse onto the carbon. The oven containing the carbon was sealed off and heated at 176° for 2 hr to distribute the toluene evenly over the surface, then cooled slowly.

Bromine (0.560 ml, 1.75 g, 10.9 mmoles; stored over anhydrous potassium carbonate before use) was transferred under dry nitrogen to the reserve trap. The bromine was degassed by cooling (-78°), evacuating, warming, cooling, and evacuating. As the bromine then warmed, it was distilled through the system to the trap (cooled to -78°) adjacent to the reaction vessel. This trap was then warmed to and held at -12°, and the bromine was allowed to diffuse slowly into the reaction vessel which had been wrapped with aluminum foil to prevent light-induced reactions. Addition of bromine required three hours.

After eight days the vacuum system was flushed three

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(156) A. Turk, J. I. Morrow, and B. E. Kaplan, Anal. Chem., 34, 561 (1962).

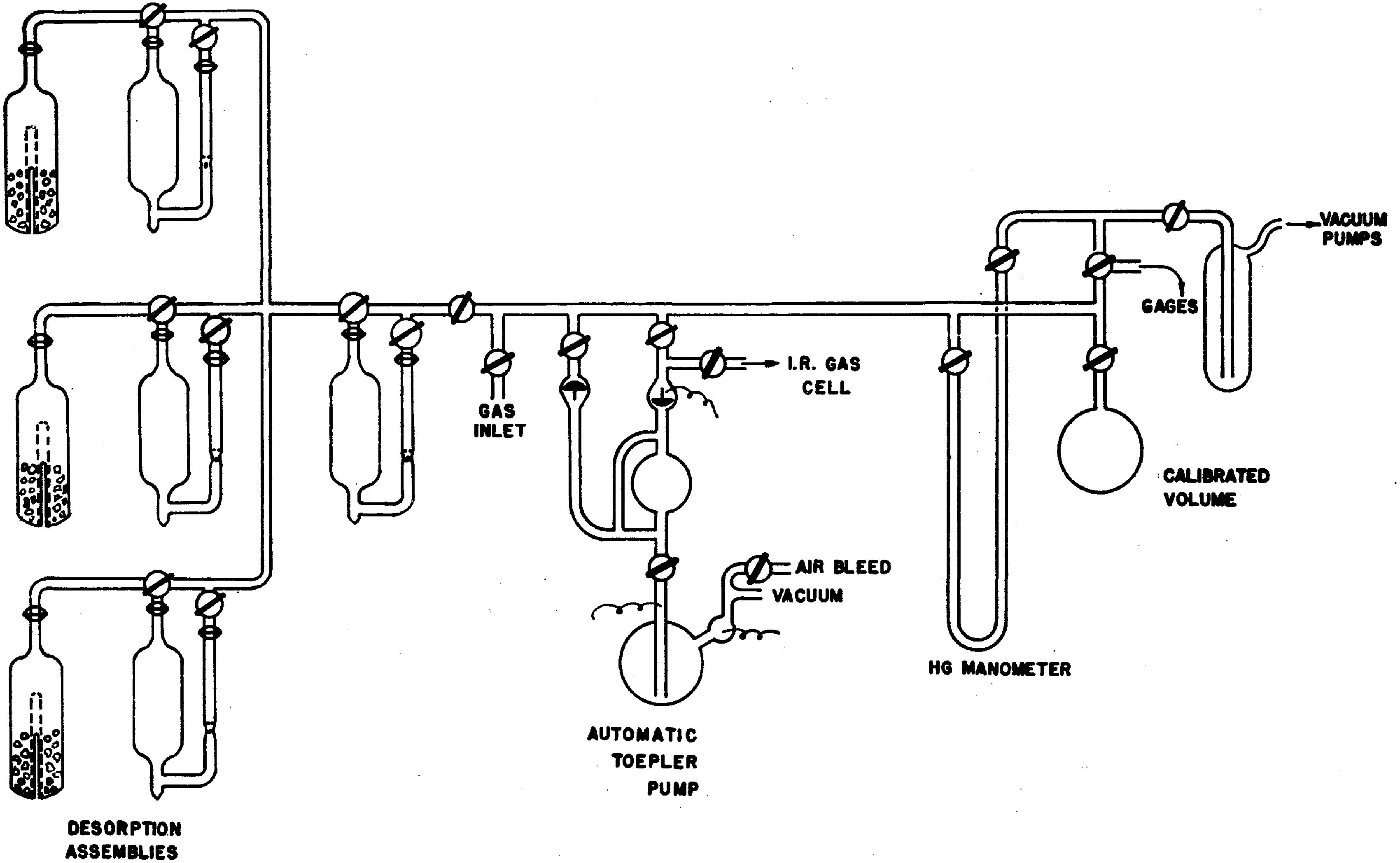


Figure 1. Vacuum desorption system

times with ethylene, with intermittent evacuations, and then filled with ethylene which was added in small portions to the reaction vessel. The cycle of filling the system with ethylene and passing the ethylene into the reaction vessel was repeated until the pressure of ethylene within the system approximated atmospheric pressure. The reaction vessel was allowed to stand two days to ensure complete reaction of the ethylene with any bromine which had not reacted with the toluene.

A glass wool plug covered with a 1-1/4-in column of Ascarite was placed in the exit arm of the trap adjacent to the reaction vessel. The trap was evacuated, cooled in liquid nitrogen, and opened to the oven to remove much of the ethylene. Then the material in the oven was desorbed at room temperature into the trap with pumping until the coolant stopped boiling vigorously. The oven was closed off, the liquid nitrogen was replaced with dry ice-acetone, and the collected ethylene was thus distilled off through the system. The liquid nitrogen bath was replaced, and the material in the oven was desorbed at successively increasing temperatures over various periods of time, as indicated for a typical experiment in Table 8. Correspondingly higher

Table 8: Desorption Conditions after Bromination of Toluene.

Minutes Desorbed	Temperature
15	Ambient
60	77°
60	168°
75	239°
60	279°
80	385°

temperatures were used when the alkylbenzene was of higher molecular weight.

The liquid nitrogen was replaced with dry ice-acetone, and the ethylene was again distilled off. After the trap was warmed to room temperature its contents were removed by pipet and washed twice with aqueous sodium bromide, once with 2 M sodium hydroxide, and twice with aqueous sodium bromide.

The organic layer was analyzed by glc. The bromotoluene isomers were partially separated on a 12 ft x 1/2 in neopentyl glycol succinate column (25% on 60/80 mesh Chromosorb P) at 112°, using 240 cc of helium per min. Under these conditions the _ortho_-bromotoluene was cleanly separated from the _meta_- and _para_-isomers, which emerged together. Analyses of standard mixtures showed that the responses of the isomers were identical within experimental error, and therefore the relative areas were used as direct measures of isomer distribution. Infrared analysis of the product mixtures and of standard mixtures showed that in all reactions the _meta_-isomer was present to the extent of less than 1%. The results are summarized in Table 10, page 156.

Reactions of bromine with olefins were conducted similarly. The olefin, if a gas, was added by the procedure described earlier for ethylene. If the olefin was a liquid, it was added as were the aromatic hydrocarbons. When it was necessary to know the exact molar quantity of gaseous olefin used, a bulb of known volume sealed onto the vacuum system was employed. Addition of bromine as described above (page 140) required 4-1/2 hr.

The instability of vicinal dibromoalkanes compared with aryl bromides necessitated milder methods of recovery and analysis. Thus, after two days reaction time the carbon was transferred to a Soxhlet extractor and extracted for 7-1/2 hr with carbon tetrachloride. The solution was concentrated (rotary evaporator), and the residue was analyzed by ir and/or nmr spectroscopy. In each case only the product of trans-addition of bromine was observed.

Preparation of 2-(ortho-Bromophenyl)-2-propanol

A solution of 14 ml (31.9 g, 0.226 mole) of methyl iodide in 32 ml of anhydrous ether was added dropwise to a stirred mixture of 5.51 g (0.226 mole) of magnesium shavings and 100 ml of anhydrous ether in a 500-ml three-necked flask equipped with a mechanical stirrer, a reflux condenser containing a drying tube, and a pressure-equalizing addition funnel. The mixture was stirred for 3/4 hr, then a solution of 15.05 g (0.070 mole) of methyl ortho-bromobenzoate in 25 ml of ether was added dropwise. The mixture was stirred overnight and poured into a mixture of 58.5 g of ammonium chloride, 160 g of ice, and 100 ml of water. The aqueous layer was extracted with two 100-ml portions of ether, and the combined ether solution was dried over magnesium sulfate. Distillation under reduced pressure yielded a slightly yellow liquid: bp 68-73° (0.37 mm). This crude alcohol was used directly in the preparation of ortho-bromocumene (see page 146).

Preparation of ortho-Bromocumene

Crude 2-(ortho-bromophenyl)-2-propanol (entire crude yield, page 145) was dissolved in 55 ml of glacial acetic acid. Perchloric acid (70%, 0.76 ml) and 0.6 g of 5% palladium-on-carbon catalyst were added, and the mixture was hydrogenated at 50 psig. After filtration, the acetic acid was removed under reduced pressure until an oil separated out. Water was added, and the mixture was saturated with sodium bicarbonate and steam distilled to give 9.5 g (68% overall yield) of a clear colorless oil which glc analysis showed to be a single compound. Distillation under reduced pressure yielded a clear colorless liquid: ir (liquid film): 3050 (w, aromatic-H), 2960, 2900, 2840 (m, alkyl-H), 1590, 1560 (w, aromatic), 1470 (m, methyl), 1420 (m, methine), 1370, 1350 (w, isopropyl), 756 (s, ortho-disubstituted benzene); nmr (CCl_4): δ1.23 (doublet, J = 7 cps, 6 H, methyl), δ2.73 (septuplet, J = 7 cps, 1 H, methine proton), δ6.9-7.3 (complex, 4 H, aromatic).

Preparation of *meta*-Bromocumene[157]

meta-Bromocumene was prepared similarly to the *ortho*-isomer. The organic layer from the steam distillate was shown by glc to be a single compound. Distillation of the organic layer under reduced pressure yielded a clear colorless liquid: ir (liquid film): 3030 (w, aromatic-H), 2940 (s), 2910, 2850 (m, alkyl-H), 1595, 1570 (m, aromatic), 1475, 1455 (m, methyl), 1418 (m, methine), 1377, 1357 (w, isopropyl), 778, 691 (s, *meta*-disubstituted benzene); nmr (CCl_4): δ1.21 (doublet, J = 7 cps, 6 H, methyl), δ2.82 (septuplet, J = 7 cps, 1 H, methine proton), δ6.98-7.40 (complex, 4 H, aromatic).

(157) M. Stiles and A. J. Sisti, *J. Org. Chem.*, **25**, 1691 (1960).

RESULTS
AND
DISCUSSION

Proof of Reaction at the Surface

In the bromination of alkenes at adsorbent surfaces, it was first necessary to establish that reaction did occur at the surface and not during the recovery procedure, which consisted of extraction with carbon tetrachloride. To this end, the following experiments were performed.

A sample of brominated carbon was treated with a slight excess of an olefin (A) (in the case of ethylene a large excess was used). After twenty-four hours an equivalent quantity of a second olefin (B) was added, and the charcoal was extracted with carbon tetrachloride, as described on page 144. For each pair of olefins used, a second reaction was carried out in which the order of addition of the olefins was reversed. In this way any differences in the composition of any products formed during extraction which would be caused by differences in olefin reactivities could have been assessed. The composition of the carbon tetrachloride solution was determined by gas chromatography and/or infrared spectroscopy. The results are summarized in Table 9.

If the bromination reaction is a surface reaction, the product should, in each case, be mainly or exclusively the bromination product of olefin A (A dibromide in Table 9). If reaction occurs in solution during extraction, however, the olefins will compete, and the products in each case will be determined by the relative reactivities of the two olefins toward bromine or, if the reaction is diffusion-

Table 9: Results of Sequential Addition of Olefins to Brominated Carbon.

Starting Olefins		Products	
A	B	A dibromide	B dibromide
Ethylene	*cis*-2-Butene	99%	1%
cis-2-Butene	Ethylene	99	1
cis-2-Butene	Cyclohexene	99	1
Cyclohexene	*cis*-2-Butene	99	1

controlled, by the relative availabilities of the olefins. In either of these latter cases the order of addition of olefins should have no effect on product ratios. On the other hand, if the bromination reaction occurs in the vapor phase above the adsorbent surface, the respective allylic bromination products of olefin A should also be observed.[101]

The data in Table 9 clearly indicate that reaction does occur at the surface, since the first-added olefin (A) in every case gives the predominant product and since no side products resulting from allylic substitution reactions could be detected (see page 151).

Furthermore, in the case of bromination of aromatic compounds, work done on the vapor phase thermal and photochemical brominations of toluene shows mainly formation of benzyl bromide.[155] Therefore, in the present study in which nuclear bromination is observed, the reaction is a surface, not a vapor phase reaction. The possibility of the occurrence of a competing vapor phase reaction to give benzyl bromide is not excluded, but such reaction will not interfere with the nuclear bromination at the surface.

Bromination of Olefins

As indicated in the Experimental Section (page 144), bromination of olefins led exclusively to the products formed by *trans*-addition of bromine. Analysis by nuclear magnetic resonance spectroscopy, utilizing the chemical shifts of the methine protons and the splitting patterns of the methyl protons,[158] showed that *cis*-2-butene gave exclusively *d,l*-2,3-dibromobutane and that *trans*-2-butene gave only the *meso*-isomer. Comparison of the infrared spectra of the 1,2-dibromocyclohexanes obtained in these reactions with the spectra of *cis*- and *trans*-1,2-dibromocyclohexanes published by Goering[125] showed that only the *trans*-isomer was produced. These results are independent of the order of addition of reactants. Variation of the bromine concentration on the charcoal between 1% and 10% by weight had no effects on the products nor, in the case of cyclohexene, did the use of silica gel in place of carbon. It is worth mentioning that this reaction on an adsorbent gave no detectable quantities of side products, in contrast to brominations in solution in which allylic substitution reactions compete with addition.

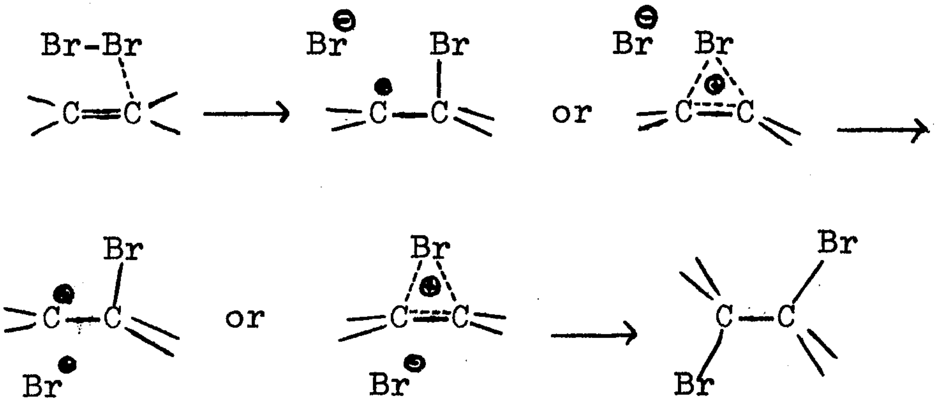
The exact cause(s) of these results is obscure. It is well established that bromination in solution proceeds by *trans*-addition, but it has already been shown (page 149) that in this study reaction occurs on the adsorbent surface

(158) F. A. L. Anet, *Proc. Chem. Soc.*, 327 (1959).

and not in solution during extraction. However, although in every experiment attempts were made to add less than a theoretical monolayer of reactants, it could not be definitely established that capillary condensation was not occurring. Such condensation would provide the opportunity for liquid-phase reaction in an ultramicro "flask," and the results would be expected to be similar to those in solution.

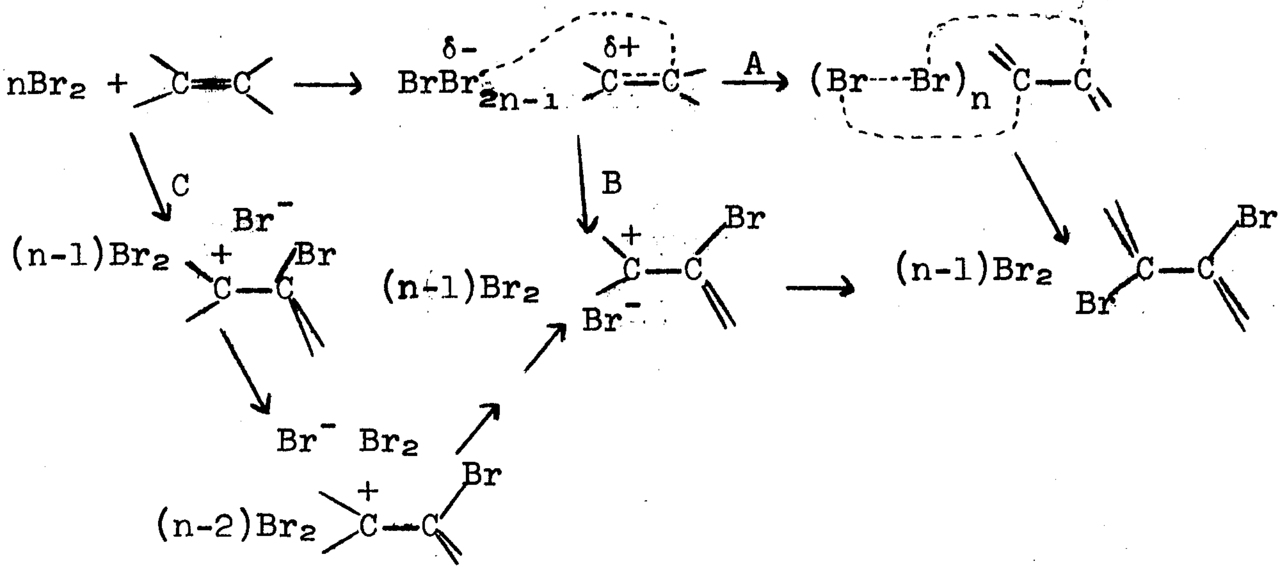
On the other hand, assuming adsorption of olefin and bromine in a monolayer without appreciable capillary condensation, a mechanism similar to that in solution (Scheme XXXXII) may apply. A molecule of olefin may be brominated in two steps, with formation of a bromonium (or β-bromocarbonium) ion and a bromide (or possibly tribromide) anion. This mechanism would require mobility of at least one of the ions on the surface to give backside attack and overall trans-addition.

Scheme XXXXII



An alternate mechanism, also assuming monolayer adsorption, may be that depicted in Scheme XXXXIII. As one bromine atom in a molecule becomes attracted to one end of

Scheme XXXXIII.



the double bond (or to the π-cloud of the double bond), its bond to the other bromine atom becomes weaker. A series of dipole-induced dipole interactions, resulting in weakening of bromine-bromine bonds within molecules and attraction between bromine atoms in different molecules, may extend around the olefin to a bromine molecule situated trans to the site of original interaction between bromine and olefin. The entire structure may collapse concertedly (path A) to give the trans-dibromide and to regenerate bromine molecules. Alternatively the structure may collapse to an ion pair (path B), with the bromide anion trans to the bromine which has already added, which would then also form the trans-dibromide. Finally path C, in which the bromide anion is transmitted around the olefin by reactions of the type shown in equations 30 and 31 may be considered.

$$\mathrm{Br{-}Br} + \mathrm{Br^-} \rightleftharpoons \mathrm{Br{-}Br{-}Br^-} \rightleftharpoons \mathrm{Br^-} + \mathrm{Br{-}Br} \qquad (30)$$

$$\mathrm{Br{-}Br} + \mathrm{Br{-}Br{-}Br^-} \rightleftharpoons \mathrm{Br{-}Br{-}Br^-} + \mathrm{Br{-}Br} \qquad (31)$$

Electrostatic attraction would keep the bromide ion from diffusing away from the cation.

The mechanism in path C differs from that in Scheme XXXXII (page 152) in the method of transport of the bromide anion to give backside attack and in the number of bromine molecules required for the bromination of each olefin molecule.

The intermediate cations in paths B and C may be bridged instead of open as shown. The alternate possibilities for transporting the bromide anion to a <u>trans</u> position will not be seriously affected. However, the cation would be more conformationally stable, and the time allowed for transporting the bromide ion to a <u>trans</u> position would increase correspondingly.

The large number of bromine molecules involved in Scheme XXXXIII may at first glance make the mechanism seem improbable. However, bromination of unreactive olefins in acetic acid has been shown to be third order in bromine in the region of bromine concentrations of 0.1 to 0.2 M.[102] The effective concentration of bromine molecules at the adsorbent surface may be considerably greater than this value. Moreover, the mobility of the adsorbed molecules is reduced relative to the mobility of these molecules in solution. For these reasons the involvement of a large number of bromine molecules in bromination of an olefin at an adsorbent surface is not at all unlikely.

Any mechanism involving free radicals may be dismissed as highly unlikely since, as mentioned above (page 151), no products which could be associated with such a mechanism could be detected.

Bromination of Aromatic Hydrocarbons

The results of the bromination of aromatic compounds at adsorbent surfaces are summarized in Table 10.

Table 10: Results of Bromination of Aromatic Hydrocarbons at Adsorbent Surfaces.

Entry	Adsorbent[a]	Hydrocarbon	Bromine Added before or after Hydrocarbon	Scavenger	% *ortho*
1	C, JD-1[b]	Toluene	before	none	64.5
2	C, JD-1	Toluene	after	Ethylene	48.8
3	C, JD-1	Toluene and Benzene[c]	after	Ethylene	d
4	C, JD-1[e]	Toluene[f]	after	Ethylene	52.2
5	C, K-3030[b]	Toluene	after	Ethylene	52.3
6	C, K-3031[b]	Toluene	after	Ethylene	52.1
7	C, K-3032[b]	Toluene	after	Ethylene	51.8
8	S	Toluene	before	Ethylene	36.2
9	S	Toluene	after	Ethylene	37.9
10	A	Toluene	after	Ethylene	27
11	C, JD-1	Cumene	after	Ethylene	28.2
12	C, JD-1	*tert*-Butylbenzene	after	Ethylene	0

a: C = activated carbon, S = silica gel, A = alumina. b: Designation of manufacturer, Barnebey-Cheney Company, Columbus 19, Ohio. See Table 11, page 159, for properties. c: Competition experiment. d: Not determined. e: The carbon was acid-washed prior to the experiment. f: Toluene "from Sulfonic Acid" (Eastman-Kodak).

A comparison of entries 1 and 2 shows that bromination of toluene at the carbon surface is not complete after eight days. When ethylene was added (entry 2) and the products were vacuum desorbed at high temperatures, significant quantities of ethylene bromide were formed, and the bromotoluenes consisted of 49% ortho-isomer. When the carbon was vacuum desorbed after reaction without ethylene being added, the bromotoluenes consisted of 64.5% ortho-isomer, and much benzyl bromide was formed. These data indicate that, if no ethylene is used, reaction occurs both on the surface and in the vapor phase at the high temperatures required for the vacuum desorption. The reaction in the vapor phase will, as has been mentioned (page 150), lead to benzyl bromide.[155] The higher temperature reaction at the surface will of course be much more rapid and less selective, and the ortho:para ratio should be closer to statistical than at ambient temperatures, as is observed.

The low proportion of meta-bromination (less than 1%) in these and in all other brominations of alkylbenzenes studied indicates high selectivity, kinetic control, and no subsequent equilibration of products.

A sample of para-bromotoluene was adsorbed on activated carbon, left eight days, and desorbed using the same procedure as was employed for the products of the bromination reactions. No alteration of the sample occurred. Olah showed that para-bromotoluene isomerizes faster under the influence of aluminum chloride than either the ortho- or meta-isomer.[150] Therefore the products obtained from the surface reactions are determined by kinetic control of the reaction and not by any secondary transformations of products.

This high selectivity is intermolecular also. A competition between equimolar quantities of benzene and toluene for a limited quantity of bromine (entry 3) gave no detectable bromobenzene by gas chromatography, indicating a substrate selectivity of toluene over benzene by a factor of at least 100 since 1% of bromobenzene in the products could easily have been detected.

When a sample of carbon which has been "cleaned" in vacuo at high temperatures is mixed with water, the pH of the water rapidly rises to 10, indicating the presence of nonvolatile basic impurities on the carbon. To determine their possible effect on the course of bromination, a sample of carbon was extracted with aqueous hydrochloric acid, washed with water, dried, and cleaned in vacuo as usual. Use of this carbon (entry 4) produced no change in the isomer distribution in the bromination of toluene. It may therefore be concluded that the presence of these nonvolatile basic impurities does not affect the reaction.

Entries 5-7 show that different pore structures and surface areas have no effect on isomer distributions. The properties of these carbons are shown in Table 11.

In all these cases it can be seen that the ortho:para ratio is larger than for the uncatalyzed reaction of toluene and bromine in 85% acetic acid[143] and that it is insensitive

Table 11: Properties of Carbons (Source: coconut shell)[159]

Manufacturer's[a] Designation of Carbon	Total Surface Area,[b] m^2/g	Most[c] Common Pore Size, Å	Pore[c] Volume, cm^3/g
JD-1	1000-1100		
K-3030	1000-1100	10-20	0.433
K-3031	500-600	10-15	0.335
K-3032	1600-1700	15-25	0.513

a: Barnebey-Cheney Company, Columbus 19, Ohio.
b: B. E. T. method.
c: By mercury porosimeter.

to several variable properties of the charcoal surface.

When neutral silica gel was used as adsorbent (entries 8 and 9), the bromination of toluene appeared to resemble more closely the same reaction in solution. Hence, Brown and Stock found 33% ortho- and 67% para-bromination of toluene in 85% acetic acid.[143] Bromination on silica gel gave 37% ortho- and 63% para-substitution. These results could be caused by the more polar adsorbent (silica gel) being better able to stabilize ionic intermediates and/or by the toluene being less strongly adsorbed on the silica gel than on carbon and thus in a condition sterically resembling more closely its condition in solution. These results also indicate the isomer composition of the bromotoluenes to be independent of the order of addition of the reactants.

Finally, bromination of toluene on neutral alumina (entry 10) decreased still further the ortho:para ratio

(159) A. Turk, J. I. Morrow, S. H. Stoldt, and W. Baecht, Journal of the Air Pollution Control Association, 16, 383 (1966).

(27% *ortho*), probably for one or both of the reasons mentioned above for silica gel.

Cumene (entry 11) gave 28.2% *ortho*-bromination, also with less than 1% *meta*-isomer. In this case side-chain bromination was actually the major process, even in the dark, and large quantities of 2-bromo-2-phenylpropane and its dehydrobromination product, 2-phenylpropene, were formed. This is of course due to the *α*-hydrogen in cumene being much more easily abstracted than those in toluene in the free radical side-chain bromination. (This observation indicates that allylic substitution, probably via a free radical mechanism, also is capable of occurring on the adsorbent surface.) With cumene, as with toluene, the *ortho*:*para* ratio is higher than for the same reaction in solution, in which 11% *ortho*- and 89% *para*-bromination are observed.[144]

tert-Butylbenzene (entry 12) gave completely *para*-substitution. It appears that in this case the effect of the carbon surface, which is to increase *ortho*-substitution in toluene and cumene, is insufficient to cause appreciable *ortho*-substitution in *tert*-butylbenzene (see page 163 for further discussion).

The results may be interpreted in the light of the diagrams in Figure 2 and the calculated values in Table 12.

Figure 2. Possible Geometries of Adsorbed Aromatic Hydro-Carbons.

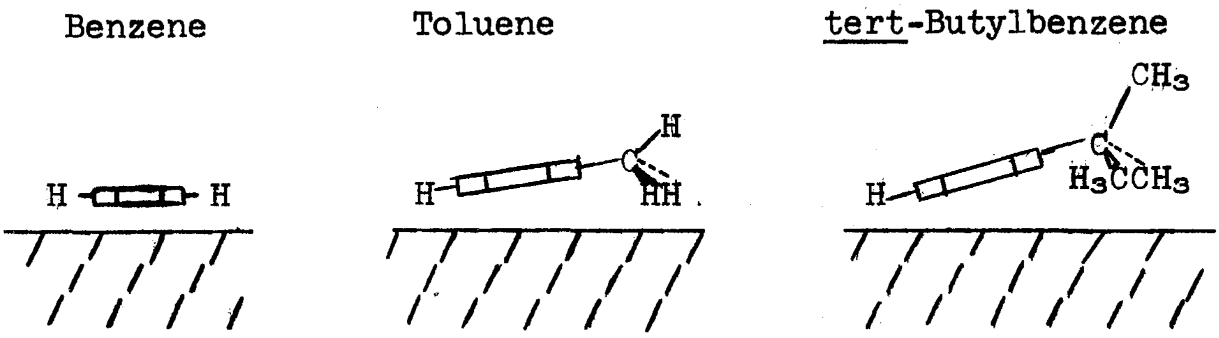


Table 12: Derived values from Table 5 (page 132) and from Table 10 (page 156).

Aromatic	o/p (Brown)	o/p (Ref. 144)	o/p (this work)
Toluene	0.49^{143}	0.71	1.1
Ethylbenzene		0.22	
Cumene		0.12	0.40
tert-Butylbenzene	0.012^{145}		~0

Whereas the corner-to-corner C_2 axis of the aromatic ring of benzene can be completely parallel to the axis of the pore in which it is adsorbed (the pore is assumed to be approximately cylindrical), the methyl substituent in toluene can prevent the C_2 axis of this aromatic ring from attaining parallelism with the axis of the pore by preventing that end of the molecule to which it is attached from approaching the surface as closely as can the other end of the molecule (Figure 2). The position para to the methyl group in toluene can therefore approach the surface more closely than can the positions ortho to the methyl group. The hindrance resulting from the presence of the surface will be correspondingly greater in the para than in the ortho position. Such a situation would lead to the expectation that the ortho:para ratio for bromination of toluene at a surface might be greater than that in solution (neglecting solvent effects). This has been shown in the present work to be true (Table 12).

As the alkyl substituent becomes more bulky the departure of the C_2 axis of the adsorbed aromatic ring from strict parallelism with the axis of the pore should increase. The hindrance caused by the surface at the para position relative to that at the ortho position should also increase as the C_2 axis of the aromatic compound is forced further from a geometry parallel to the axis of the pore.

Lack of a complete set of isomer distribution data for the series toluene, ethylbenzene, cumene, tert-butylbenzene under a uniform set of conditions makes a strict comparison of results tenuous. However, the data for toluene and cumene may be compared with the results of Nazarov and Semenovskii[144] (45°, excess aromatic hydrocarbon).

Division of the ortho:para ratio for bromination at the surface of activated carbon, 1.1, by the ortho:para ratio for liquid phase bromination at 45°,[144] 0.71, shows an increase in this ratio by a factor of 1.5. As predicted earlier, the relative increase in the ortho:para ratio for an alkylbenzene with a bulkier substituent than a methyl group should exceed that for toluene. For cumene, the <u>ortho</u>:<u>para</u> ratio at 45°[144] is 0.12. Dividing this value into the <u>ortho</u>:<u>para</u> ratio at activated carbon, 0.40, gives an enhancement of the <u>ortho</u>:<u>para</u> ratio by a factor of 3.3, more than twice the enhancement found for toluene. These results indicate the qualitative validity of the foregoing assumptions.

The data obtained for <u>tert</u>-butylbenzene indicate the fraction of <u>ortho</u>-substitution to be too low to make possible a similar comparison between Brown's results for toluene[143] and <u>tert</u>-butylbenzene[145] and those found in the present work. Thus, <u>tert</u>-butylbenzene does not follow the trend from toluene to cumene shown above. It may be that the <u>tert</u>-butyl group is too bulky to allow <u>tert</u>-butylbenzene to be adsorbed similarly to benzene, toluene, and cumene but with a geometry in which the C_2 axis is still further from being parallel with the axis of the pore.

Activated carbon is known to adsorb relatively nonpolar organic molecules more strongly than do the inorganic adsorbents silica gel and alumina. Activated carbon preferentially removes benzene from a mixture of benzene and water, while silica gel and alumina adsorb the water preferentially. Brunauer has stated, "In general, the heats of adsorption of non-polar gases on charcoal are slightly higher than on silica gel and most other adsorbents."[160]

(160) S. Brunauer, "The Adsorption of Gases and Vapors," Princeton University Press, Princeton, 1945, p 244.

If an aromatic compound is less strongly adsorbed on silica gel or alumina than on activated carbon, the departure from parallel arrangements shown in Figure 2 should be lessened. Therefore the difference between the isomer distributions in bromination of toluene in solution and in the adsorbed state should also be lessened since the surfaces of silica gel and alumina will not preferentially hinder the para position relative to the ortho position as greatly as will the activated carbon surface. The ortho:para ratio for bromination of toluene at silica gel or alumina should therefore decrease from that for bromination at activated carbon and approach the value for the toluene molecule in solution unhindered by an adsorbent.

In addition, the presence of polar silicon-oxygen and aluminum-oxygen linkages in the inorganic adsorbents makes possible a greater stabilization of charges in adsorbed species than is found with activated carbon. Thus bromination at the surfaces of silica gel and alumina should more closely resemble reaction in acetic acid solution, in which solvent has been shown to have a stabilizing effect on the ions, than will bromination at activated carbon.

Thus, two independent considerations predict that reaction on the inorganic adsorbents will more closely resemble that in solution than will reaction on activated carbon. Such has been shown to be the case; Table 10 shows that the ortho:para ratios for bromination of toluene at the surfaces of activated carbon, silica gel, and alumina are 1.1, 0.59, and 0.37, respectively, compared to 0.49 in 85%

acetic acid[143] and 0.71 in excess toluene.[144] Bromination at the surface of alumina actually gives a lower ortho:para ratio than does bromination in 85% acetic acid.

The effect of interaction between bromine and the surface on isomer distributions must also be considered.

In chlorination of toluene in various solvents the ortho:para ratios varied from 2.2 in trifluoroacetic acid to 0.52 in nitromethane. The ortho:para ratio decreased as the complexing of chlorine with solvent increased.[153]

The differential heat of adsorption of bromine is 7719 cal/mole on silica gel and 11,430 cal/mole on activated carbon; the former value is only a few hundred calories above the heat of condensation of bromine.[161] If being held more tightly on the surface would increase the selectivity of bromine for the para position of toluene over the ortho positions, then the lowest ortho:para ratios should be obtained on activated carbon. Since the opposite was observed, the combination of steric and electronic effects of the surface on the aromatic hydrocarbon is probably more important in determining the course of attack than are the effects of the surface on the bromine.

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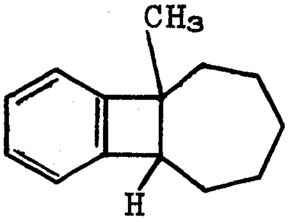
(161) L. H. Reyerson and A. E. Cameron, J. Phys. Chem., 39, 181 (1935).

APPENDIX

FRIEDEL-CRAFTS REACTION OF BENZOCYCLOBUTENE

INTRODUCTION

Early in our study of the Friedel-Crafts reaction of 1,1-bis(bromomethyl)cyclohexane, mechanistic considerations led us to believe that III was the structure of the "primary product." Since the "primary product" decomposed in benzene-aluminum chloride, the behavior under these conditions of the parent compound of III, benzocyclobutene, was investigated.



III

The reactions of benzocyclobutene and its derivatives with electrophilic reagents generally follow two competing pathways. Aromatic substitution may occur, mainly at the 4-position with minor amounts of substitution at the 3-position. In addition, electrophilic attack may occur at the bridgehead carbon to displace the alkyl side chain and give *ortho*-substituted *β*-phenylethyl derivatives. Some illustrative examples are nitration (equations 32 and 33),[162-165] acetylation (equation 34),[163,164] halogenation

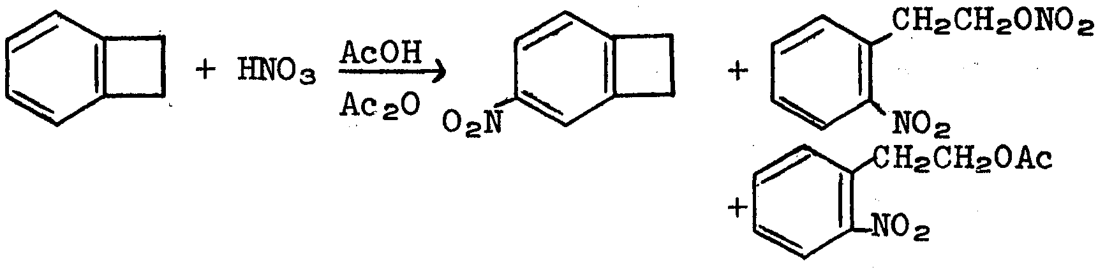
(162) L. Horner, H.-G. Schmelzer, and B. Thompson, *Chem. Ber.*, **93**, 1774 (1960).

(163) J. B. F. Lloyd and P. A. Ongley, *Tetrahedron*, **20**, 2185 (1964).

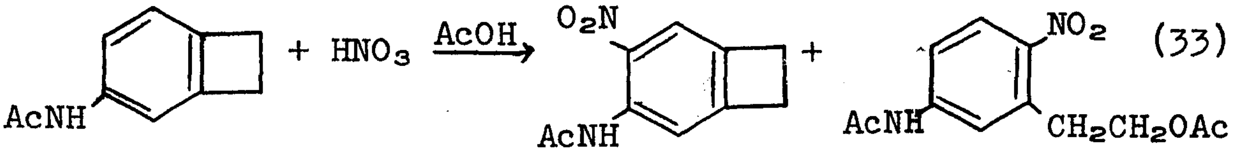
(164) L. Horner, P. V. Subramanian, and K. Eiben, *Tetrahedron Letters*, 247 (1965).

(165) J. B. F. Lloyd and P. A. Ongley, *Tetrahedron*, **21**, 2281 (1965).

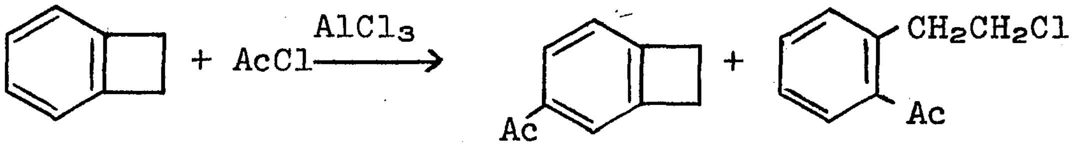
(equation 35),[164,166] and sulfonation (equation 36).[166] In addition to these reactions, protodealkylation occurs with



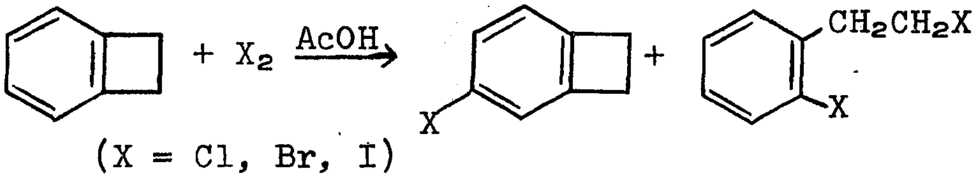
(32)



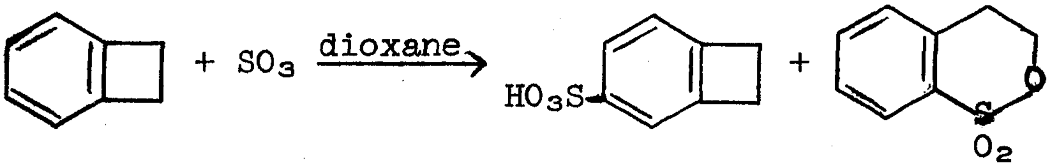
(33)



(34)



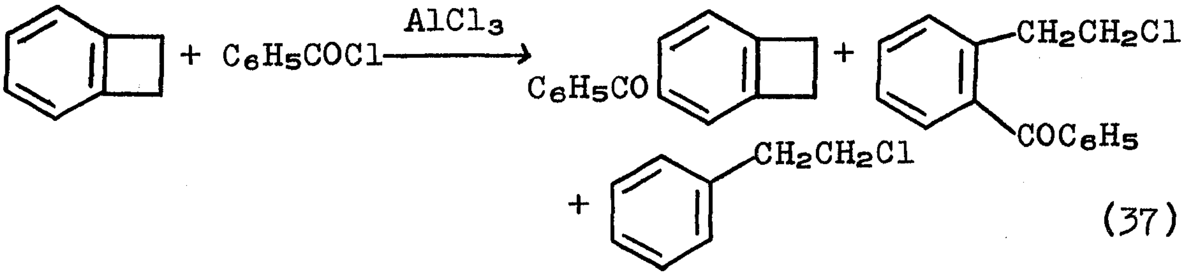
(35)



(36)

benzoyl chloride and aluminum chloride (equation 37).[166] With hydrogen bromide, protodealkylation is the main reaction (equation 38).[163] Concentrated sulfuric acid or liquid hydrogen fluoride converts benzocyclobutene to a viscous polymer,[76] apparently also by opening of the four-membered ring followed by self-alkylation.

(166) J. B. F. Lloyd and P. A. Ongley, Tetrahedron, 21, 245 (1965).



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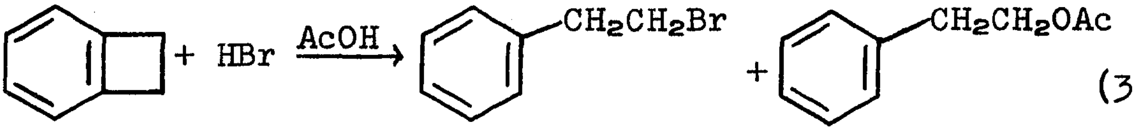

(38)

Lloyd and Ongley have suggested that ring opening of benzocyclobutene by electrophilic reagents does not proceed through benzeneonium or β-phenylethyl ion intermediates. They argued that formation of a benzeneonium intermediate, and the related transition state, would probably be precluded by strain effects, and that the ortho-substituted β-phenylethyl carbonium ions generated therefrom would be energetically improbable. Multicenter transition states were postulated.[166] It does seem possible, however, that protodealkylation can proceed by way of a β-phenylethyl or phenonium ion intermediate, and that in the presence of an aromatic hydrocarbon this intermediate can act as an alkylating agent.

To investigate this possibility, the Friedel-Crafts reactions of benzocyclobutene with benzene and toluene were studied.

EXPERIMENTAL

(A) Preparation of Benzocyclobutene

(1) Preparation of 2-Thiaindane[167,168]

Freshly cut sodium (9.6 g, 0.42 mole) was dissolved in 200 ml of absolute ethanol in a 1-l three-necked flask equipped with a mechanical stirrer, a fritted glass gas bubbler, and a Soxhlet extractor. The flask was cooled in an ice-water bath, and hydrogen sulfide was bubbled in slowly for 5 hr. A second solution of 9.6 g (0.42 mole) of sodium in 200 ml of absolute ethanol was added slowly with stirring and cooling. $\underline{\alpha}$,$\underline{\alpha}$'-Dibromo-ortho-xylene (95.5 g, 0.362 mole) was placed in the extractor cup, and the reaction mixture was heated under reflux. After extraction was complete, the mixture was refluxed overnight.

The extractor was replaced by a distillation head, and the ethanol was distilled off. Water was added to the reaction flask (a dark oil separated out), and the mixture was steam-distilled. Each of three fractions which were collected was extracted with two 50-ml portions of methylene chloride. The combined methylene chloride solution was dried over magnesium sulfate in a brown bottle (the product turns dark blue on exposure to light or on contact with ground glass joints). Filtration and solvent removal (rotary

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(167) M. P. Cava and A. A. Deana, J. Am. Chem. Soc., 81, 4266 (1959).

(168) J. A. Oliver and P. A. Ongley, Chem. and Ind., 1024 (1965).

evaporator) gave 40 g (81% crude yield) of a dark oil which crystallized on cooling to 0° but remelted at room temperature. The crude sulfide was used without further purification for preparation of the sulfone (page 172).

(2) Preparation of 2-Thiaindane-2,2-dioxide[167,168]

A cooled solution of 40 g (0.29 mole) of crude 2-thiaindane (page 170) in 25 ml of glacial acetic acid was added in small portions with swirling to a solution of 105 g of 30% hydrogen peroxide (0.94 mole) in 56 ml of glacial acetic acid cooled in an ice-water bath. Enough acetic anhydride was added to make the mixture homogeneous. After standing with occasional swirling for six days, during which time white needles began to precipitate, the mixture was concentrated (rotary evaporator) to 50 ml and diluted with 100 ml of water. The mixture was filtered with suction to yield, after washing with water, aqueous sodium bisulfite, and water, 32.6 g (67%) of white needles: mp 149.5-151.5° (lit[167,168] mp 150-151°); nmr ($CDCl_3$): $\underline{\delta}$4.37 (singlet, 4 H, benzylic), $\underline{\delta}$7.36 (singlet, 4 H, aromatic); ir (KBr): 3030 (w, aromatic-H), 2960, 2920 (m, alkyl-H), 1590 (w), 1480 (m, aromatic), 1460 (m, methylene), 1300, 1135 (s, sulfone), 756 (s, *ortho*-disubstituted phenyl).

(3) Preparation ~~of~~ Benzocyclobutene[167,168]

2-Thiaindane-2,2-dioxide (page 172) was pyrolyzed in the apparatus shown in Figure 3 on page 174. The heating element was made from 17 ft of B and S No. 26 Nichrome wire wound into a 0.5 cm diameter coil.[169] The ends of the coil were connected by stainless steel adapters shown in Figure 3, page 174[169] to tungsten rods sealed into the Pyrex glass head. A 0.5 cm diameter Pyrex rod inserted near the bottom of the tube kept the two halves of the coil apart. The approximate temperature of the heated coil was estimated from its color.[170]

A 250-ml two-necked flask equipped with a gas inlet tube reaching to the bottom of the flask was charged with 32.6 g (0.194 mole) of 2-thiaindane-2,2-dioxide (page 172) and attached to the bottom of the column. The apparatus was evacuated to 0.10 mm pressure, the cooling baths were filled (dry ice-acetone), and nitrogen was passed through the system until the pressure remained between 9.6 and 10.2 mm. The Nichrome coil was heated to ca 650° (140 volts, 2.66 amps), and the flask was heated by an oil bath at 200-205°. The products were collected in the dry ice-acetone traps. After all the sulfone had vaporized, the heaters and pump were turned off and nitrogen was bled slowly into the system.

(169) The able assistance of Mr. Joseph B. Scrandis in designing and constructing these portions of the apparatus is gratefully acknowledged.

(170) Handbook of Chemistry and Physics, 43rd Edition, Chemical Rubber Publishing Company, Cleveland, Ohio, 1961, p 2321.

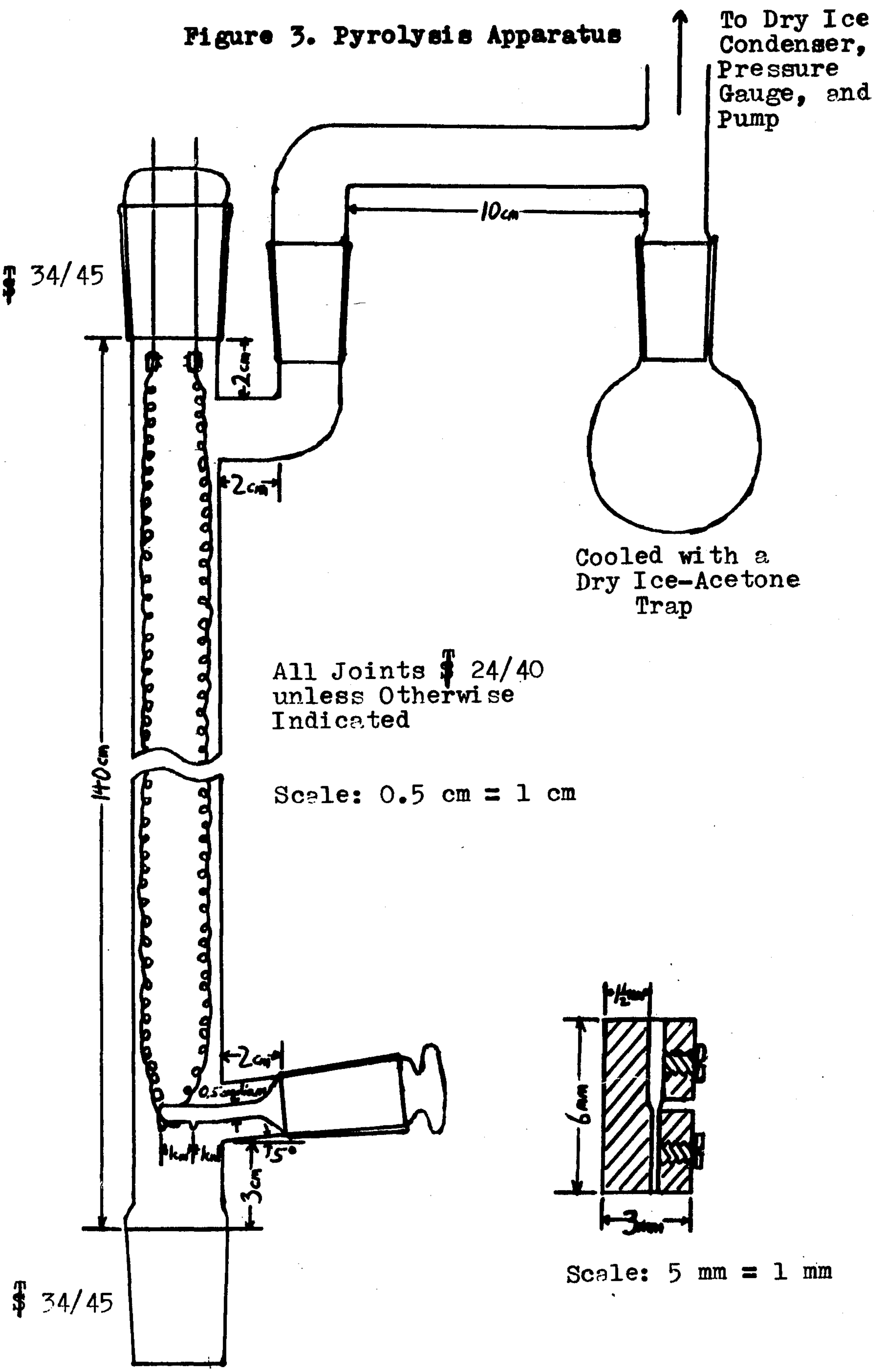

Figure 3. Pyrolysis Apparatus

The collectors were warmed to room temperature to give about 25 ml of a cloudy, slightly yellow liquid which was taken up in 25 ml of ether. The ether solution was poured into 125 ml of water. The ether layer was washed with water (10 ml), 10% sodium hydroxide (5 ml), 3% potassium permanganate (2 ml), and water (30 ml). The original aqueous layer was made basic with 10% sodium hydroxide and extracted with 20 ml of ether. This ether solution was washed with 3% potassium permanganate (1 ml) and water (20 ml), and the combined ether solution was dried over sodium sulfate. Filtration and solvent removal (rotary evaporator using an ice-water bath) gave a yellow liquid which was distilled to yield 15.3 g (76%) of a colorless liquid: bp 150° (lit bp 149-150°,[167] 148-149° (752 mm)[168]); nmr (CCl_4): $\underline{\delta}3.07$ (singlet, 4 H, benzylic methylenes), $\underline{\delta}6.93$ ($A'_2B'_2$ pattern, 4 H, aromatic) (lit nmr (CCl_4): $\underline{\delta}3.14$ (s), $\underline{\delta}7.0$ (A_2B_2 pattern);[171] (no solvent given): $\underline{\delta}3.11$ and $\underline{\delta}6.97$[172]). Analysis by glc on a diethylene glycol succinate column indicated the absence of ortho-xylene and styrene, the two reported[167] volatile by-products in this reaction.

(171) G. Fraenkel, Y. Asashi, M. J. Mitchell, and M. P. Cava, Tetrahedron, 20, 1179 (1964).

(172) E. Vogel, W. Grimme, and S. Korte, Tetrahedron Letters, 3625 (1965).

(B) Preparation of the Isomeric 1-Phenyl-2-tolylethanes

(1) Preparation of Phenyl Methylbenzyl Ketones[173]

(a) Phenyl 2-Methylbenzyl Ketone

A mixture of 25.0 g (0.167 mole) of ortho-tolylacetic acid and 11.5 g (0.0836 mole) of phosphorus trichloride, in a 500-ml flask equipped with a reflux condenser containing a drying tube, was heated with swirling in a boiling water bath for 1 hr. Anhydrous benzene (135 ml, 119 g, 1.52 moles) was added, and the resulting solution was decanted in small portions into a 500-ml flask containing anhydrous aluminum chloride (25.9 g, 0.195 mole). Cooling in an ice-water bath was necessary to control the initial vigorous reaction. A condenser was attached, and the mixture was refluxed for 1 hr, cooled, and poured with stirring into a mixture of 165 g of ice and 65 ml of concentrated hydrochloric acid. The aqueous layer was extracted with 80 ml of a 1:1 mixture of benzene and ether, and the combined organic solution was washed with 40 ml of water and dried over calcium chloride. Filtration and solvent removal (rotary evaporator) gave a yellow oil (exhibiting green fluorescence) which solidified on standing. Distillation under reduced pressure yielded 27.0 g (77%) of an almost colorless liquid which completely crystallized to a white solid: bp 143-151° (1.3-2.2 mm); mp 67-68° after recrystallization from methanol; nmr ($CDCl_3$): δ2.22 (singlet, 3 H, aromatic methyl), δ4.23 (singlet, 2 H,

(173) Patterned after C. F. H. Allen and W. E. Barker, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, New York, N. Y., 1943, p 156.

methylene), *δ*7.12 (broad singlet with splitting at the base, 4 H, aromatic), *δ*7.2-7.6, 7.8-8.1 (complex multiplets, 5 H, aromatic; these bands resemble closely those published for the benzoyl group by Castellano and Bothner-By[71]); ir (KBr): 3030 (m, aromatic-H), 2900 (m, alkyl-H), 1685 (s, carbonyl), 1595, 1580, 1490 (m, aromatic), 1455, 1440 (m, methyl and methylene), 1370 (m, methyl), 1205 (s, aromatic ketone), 750, 687 (s, mono- and *ortho*-disubstituted phenyl).

Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.68: H, 6.80.

(b) Phenyl 3-Methylbenzyl Ketone

Phenyl 3-methylbenzyl ketone was similarly prepared from *meta*-tolylacetic acid in 76% yield: bp 140-147° (1.5-1.7 mm); nmr ($CDCl_3$): *δ*2.20 (singlet, 3 H, aromatic methyl), *δ*4.09 (singlet, 2 H, methylene), *δ*7.02 (broad singlet with splitting at the base, 4 H, aromatic), *δ*7.2-7.5, 7.8-8.1 (complex multiplets, 5 H, aromatic); ir (neat liquid): 3067, 3030 (m, aromatic-H), 2924 (m, alkyl-H), 1678 (s, carbonyl), 1608, 1597, 1582, 1490 (m, aromatic), 1447 (m, methyl and methylene), 1374 (w, methyl), 1208 (s, aromatic ketone), 767, 739 (m), 689 (s, mono- and *meta*-disubstituted phenyl).

Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.69; H, 6.83.

(c) Phenyl 4-Methylbenzyl Ketone

Phenyl 4-methylbenzyl ketone was likewise prepared from *para*-tolylacetic acid in 64% yield: bp 150-160° (2.1-2.2 mm); mp 95-96° after recrystallization from methanol; nmr ($CDCl_3$): *δ*2.27 (singlet, 3 H, aromatic methyl), *δ*4.18 (singlet, 2 H, methylene), *δ*7.10 (singlet with broadening at the base, 4 H, aromatic), *δ*7.2-7.5, 7.8-8.1 (complex multiplets, 5 H, aromatic); ir (KBr): 3067, 3030 (w, aromatic-H), 2899 (w, alkyl-H), 1692 (s, carbonyl), 1597, 1582, 1515 (m, aromatic), 1449 (m, methyl and methylene), 1379 (w, methyl), 1222 (m, aromatic ketone), 780 (s, *para*-disubstituted phenyl), 758, 693 (s, monosubstituted phenyl).

Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.48; H, 6.68.

(2) Preparation of 1-Phenyl-2-tolylethanes[174]

(a) 1-Phenyl-2-(2-tolyl)ethane

To a solution of 25.4 g (0.386 mole) of potassium hydroxide in 100 ml of diethylene glycol in a 500-ml flask equipped with a partial-takeoff total-reflux distilling head fitted with a reflux condenser containing a drying tube were added a solution of phenyl 2-methylbenzyl ketone (page 176) (27.0 g, 0.128 mole) in 55 ml of diethylene glycol, followed by 21.9 ml (22.5 g, 0.450 mole) of 99-100% hydrazine hydrate. The mixture was refluxed 1-1/4 hr, then distilled until the temperature of the flask contents reached 198°. The mixture was then refluxed 3-1/4 hr, cooled, and poured into 150 ml of water. The mixture was extracted with three 50-ml portions of pentane, and the combined pentane solution was washed with 40 ml of water and dried over sodium sulfate. Filtration and solvent removal (rotary evaporator) gave a yellow liquid which was distilled under reduced pressure to yield 21.7 g (86%) of colorless liquid: bp 119-120° (2.0-2.2 mm); nmr (CCl_4): $\underline{\delta}$2.14 (singlet, 3 H, methyl), $\underline{\delta}$2.75 (singlet, 4 H, methylenes), $\underline{\delta}$6.95 (singlet, 4 H, aromatic-H, ortho-disubstituted ring), $\underline{\delta}$7.04 (singlet, 5 H, aromatic-H).

Anal. Calcd for $C_{15}H_{16}$: C, 91.78; H, 8.22. Found: C, 91.71; H, 8.48.

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(174) Patterned after L. J. Durham, D. J. McLeod, and J. Cason, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p 510.

(b) 1-Phenyl-2-(3-tolyl)ethane

Similarly, 1-phenyl-2-(3-tolyl)ethane was prepared from phenyl 3-methylbenzyl ketone (page 177) in 85% yield: bp 118° (2.0 mm); nmr (CCl_4): *δ*2.20 (singlet, 3 H, methyl), *δ*2.70 (singlet, 4 H, methylenes), *δ*6.65-6.95 (complex, 4 H, aromatic-H, *meta*-disubstituted ring), *δ*7.02 (singlet, 5 H, aromatic-H).

Anal. Calcd for $C_{15}H_{16}$: C, 91.78; H, 8.22. Found: C, 91.73; H, 8.27.

(c) 1-Phenyl-2-(4-tolyl)ethane

Likewise, 1-phenyl-2-(4-tolyl)ethane was prepared in 92% yield from phenyl 4-methylbenzyl ketone (page 177): bp 115-119° (1.8-1.95 mm); nmr (CCl_4): *δ*2.18 (singlet, 3 H, methyl), *δ*2.75 (singlet, 4 H, methylenes), *δ*6.87 (singlet, 4 H, aromatic-H, *para*-disubstituted ring), *δ*7.01 (singlet, 5 H, aromatic-H); ir (liquid film): 3030 (m, aromatic-H), 2930, 2870 (m, alkyl-H), 1610 (w), 1520, 1500 (m, aromatic), 1455 (m, methyl and methylene), 1375 (w, methyl), 806 (s, *para*-disubstituted phenyl), 734 (w), 697 (s, monosubstituted phenyl).

Anal. Calcd for $C_{15}H_{16}$: C, 91.78; H, 8.22. Found: C, 92.03; H, 8.11.

(C) Preparation of 2-(*para*-Tolyl)ethyl Bromide

(1) Preparation of 2-(*para*-Tolyl)ethanol[175]

A solution of 16.92 g (0.113 mole) of *para*-tolylacetic acid in 125 ml of anhydrous ether was added over a 1-hr period to a gently refluxing slurry of 6.086 g (0.160 mole) of lithium aluminum hydride in 200 ml of anhydrous ether in a 1-l three-necked flask equipped with a mechanical stirrer, a pressure-equalizing addition funnel, and a reflux condenser containing a drying tube. The mixture was stirred for 1 hr with gentle heating. Dilute sulfuric acid was cautiously added until the precipitated aluminum salts redissolved. The aqueous layer was extracted twice with ether, and the combined ether solution was extracted twice with sodium hydroxide. (Acidification of this aqueous solution precipitated 2.104 g of *para*-tolylacetic acid.) The ether solution was washed with water and dried over sodium sulfate. Filtration and solvent removal (rotary evaporator) yielded a light yellow oil which was distilled under reduced pressure to give 8.93 g (67% based on unrecovered starting material) of 2-(*para*-tolyl)ethanol: bp 79.7-81.0° (1.1-1.2 mm) (lit[176] bp 85° (1.2 mm)); nmr ($CDCl_3$): *δ*2.30 (singlet, 3 H, methyl), *δ*2.50 (singlet, 1 H, hydroxyl), *δ*2.77 (triplet, J = 7 cps, 2 H, benzylic methylene), *δ*3.76 (triplet, J = 7 cps, 2 H, methylene *α* to the hydroxyl), *δ*7.11 (singlet, 4 H,

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[175] Patterned after R. F. Nystrom and W. G. Brown, *J. Am. Chem. Soc.*, 69, 2548 (1947).

[176] H. Pines and J. Shabtai, *J. Org. Chem.*, **26**, 4220 (1961).

aromatic-H); ir (liquid film): 3350 (s, broad, OH), 3030 (m, aromatic-H), 2940, 2880 (s, alkyl-H), 1590 (w), 1520 (s, aromatic), 1452, 1438 (m, methyl and methylene), 1380 (m, methyl), 1045 (s, primary alcohol), 807 (s, *para*-disubstituted phenyl).

(2) Preparation of 2-(*para*-Tolyl)ethyl Bromide[177]

To 3.3 ml (9.41 g, 0.0348 mole) of phosphorus tribromide in a 50-ml three-necked flask, equipped with a mechanical stirrer, a pressure-equalizing addition funnel, and a reflux condenser containing a drying tube, was added dropwise with cooling a solution of 8.93 g (0.0656 mole) of 2-(*para*-tolyl)-ethanol (page 181) in 10 ml of methylene chloride over a 1-hr period. The mixture was stirred overnight and poured into ice-water. The aqueous layer was extracted with methylene chloride, and the combined methylene chloride solution was washed with aqueous sodium carbonate and dried over magnesium sulfate. Filtration, solvent removal (rotary evaporator), and distillation at reduced pressure gave 6.25 g (48%) of clear colorless liquid: bp 87-88° (3 mm) (lit bp 96.5° (5 mm),[176] 103.5-105° (11 mm),[178] 116° (16 mm)[179]); nmr ($CDCl_3$): $\underline{\delta}$2.33 (singlet, 3 H, methyl), $\underline{\delta}$2.9-3.7 (A_2B_2 multiplet, 4 H, methylenes), $\underline{\delta}$7.14 (singlet, 4 H, aromatic-H).

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(177) Patterned after C. R. Noller and R. Dinsmore, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, New York, N. Y., 1943, p 358.

(178) J. B. Shoesmith and R. J. Connor, *J. Chem. Soc.*, 1768 (1927).

(179) L. Ruzicka and L. Ehmann, *Helv. Chim. Acta*, **15**, 140 (1932).

(D) Friedel-Crafts Reactions

(1) Benzocyclobutene with Benzene

The Friedel-Crafts reaction of benzocyclobutene was conducted as already described for 1,1-bis(bromomethyl)-cyclohexane (page 60). Benzocyclobutene (0.595 g, 0.00572 mole) was added to a stirred mixture of 500 ml (439 g, 5.63 moles) of benzene and 0.183 g (0.00137 mole) of powdered anhydrous aluminum chloride at 40°. After 1/2 hr (see comment in part (6) below), the mixture was quenched with 3N hydrochloric acid and treated as already described (page 60) to give a quantitative yield of bibenzyl, identical in all respects (glc retention time on an Apiezon L column, nmr and ir spectra) with an authentic sample: nmr (CCl_4): $\underline{\delta}$2.81 (singlet, 4 H, methylenes), $\underline{\delta}$7.00 (singlet with slight splitting at base, 10 H, aromatic-H); ir (KBr): 3030 (m, aromatic-H), 2920, 2860 (m, alkyl-H), 1605, 1490 (m, aromatic), 1445 (m, methylene), 748, 694 (s, monosubstituted phenyl).

(2) $\underline{\beta}$-Phenylethyl Chloride with Benzene

The reaction of 1.57 g (0.0112 mole) of $\underline{\beta}$-phenylethyl chloride with 1000 ml (879 g, 11.25 moles) of benzene and 0.345 g (0.0026 mole) of aluminum chloride, carried out as described above for benzocyclobutene, also gave a quantitative yield of bibenzyl.

(3) Benzocyclobutene with Toluene

Benzocyclobutene (0.473 g, 0.00454 mole) was stirred with 500 ml (433 g, 4.71 moles) of toluene and 0.138 g (0.0010 mole) of aluminum chloride at 40° for 1/2 hr. After the usual workup, except that the toluene was distilled off at atmospheric pressure, the residue was subjected to glc analyses. An apiezon L column (14% on 60/80 mesh Chromosorb P, 16 ft, 218°, 57 cc of helium per min) separated 1-phenyl-2-(*meta*-tolyl)ethane from the *ortho*- and *para*-isomers, which were not separated. A QF 1-0065 column (20% on 60/80 mesh Chromosorb P, 12 ft, 189°, 64 cc of helium per min) separated the *ortho*- from the *meta*- and *para*-isomers. Analyses of standard mixtures showed that relative areas were proportional to concentrations. Therefore, relative proportions of the alkylation products were calculated directly from the areas. The product distribution for the alkylation of toluene with benzocyclobutene (average of two reactions) was 47.8 ± 0.8% *ortho*-, 18.2 ± 1.0% *meta*-, and 34.0 ± 0.2% *para*- (by difference). In addition, the gas chromatograms showed trace peaks with retention times corresponding, in order of elution, to ethylbenzene, styrene, benzocyclobutene, and *β*-phenylethyl chloride.

(4) *β*-Phenylethyl Chloride with Toluene

β-Phenylethyl chloride (0.690 g, 0.00491 mole) was stirred with 500 ml (433 g, 4.71 moles) of toluene and 0.141 g (0.00106 mole) of aluminum chloride for 1/2 hr at 40°.

After treatment as for benzocyclobutene (page 185), glc analyses of the residue gave the following isomer distributions (average of two reactions): 46.1 ± 0.3% _ortho_-, 18.8 ± 0.8% _meta_-, and 35.1 ± 1.1% _para_-. These results are significantly different from those of McMahon and Bunce,[17] who found mainly _para_-substitution. In addition, minor peaks with retention times corresponding to ethylbenzene, styrene, and _β_-phenylethyl chloride were also observed.

(5) Stabilities of Products

Each of two standard mixtures of the 1-phenyl-2-tolylethanes (30.9% _ortho_-, 20.1% _meta_-, 49.0% _para_-; and 9.8% _ortho_-, 69.7% _meta_-, 20.5% _para_-) was subjected to the reaction conditions and subsequent treatment described above. Recovery of material was essentially quantitative. Analyses by glc showed no alterations in the isomer distributions. Therefore the products are stable to the reaction conditions, and the isomer distributions in the alkylations are the result of kinetic control and not of thermodynamic equilibration.

(6) Comparative Rate Study of Benzocyclobutene and _β_-Phenylethyl Chloride

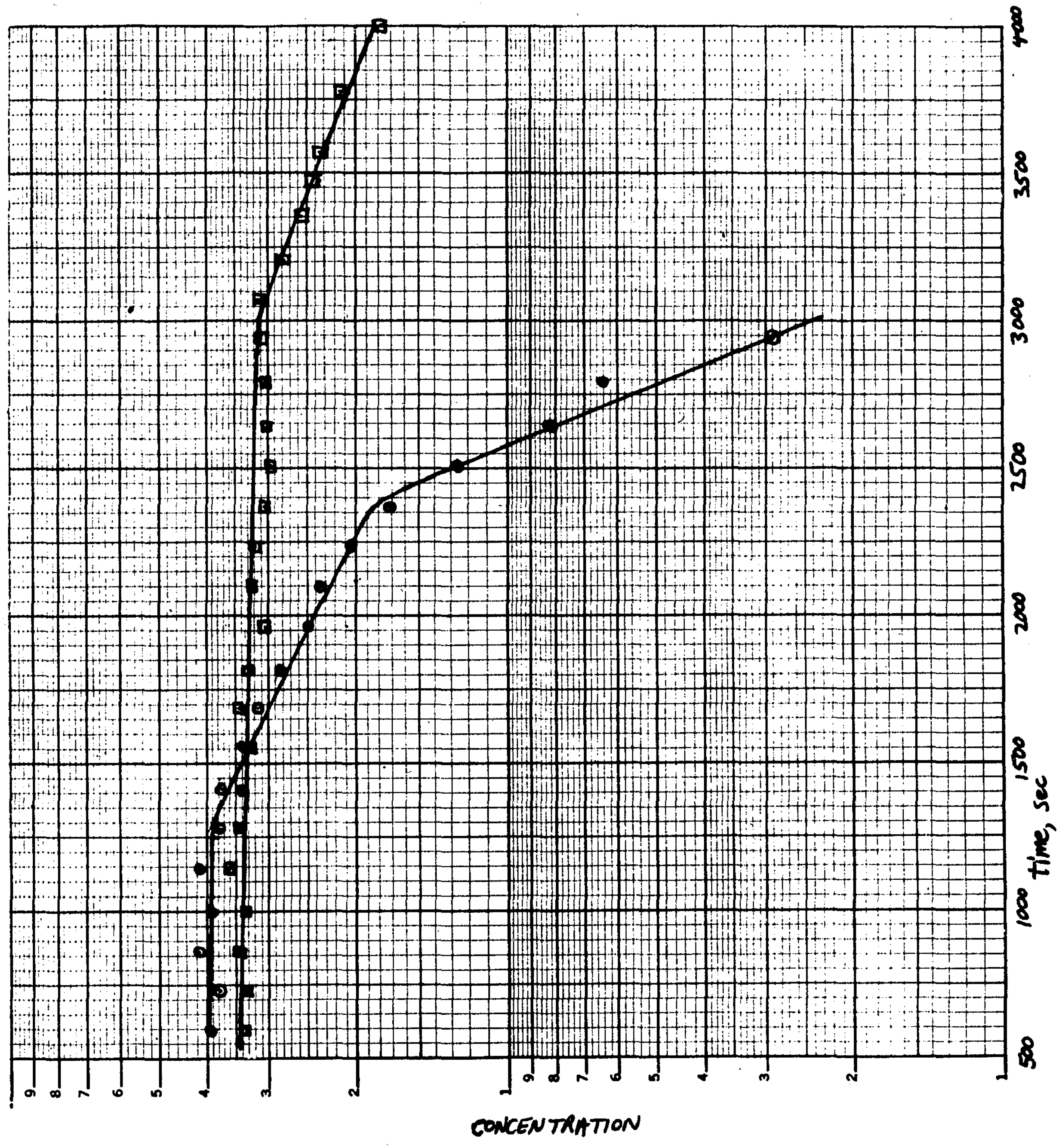
This study, in which equimolar quantities of benzocyclobutene and _β_-phenylethyl chloride were added to toluene and aluminum chloride, was initially carried out at 40°, 0.050M in each alkylating agent and 0.015M in aluminum chloride. Both alkylating agents completely reacted within 160 seconds. This is in line with previous results for β-phenylethyl chloride, which showed that the reaction of this halide (1.0M in toluene) and aluminum chloride (0.015M in toluene) has a half-life of less than ten minutes at 0°.[17] These results also indicate that the half-hour reaction times used above for Friedel-Crafts reactions (parts (1)-(4), pages 184-186) are probably unnecessarily long.

A mixture of 1.4053 g (13.5 mmoles) of benzocyclobutene and 1.9238 g (13.7 mmoles) of β-phenylethyl chloride in 20 ml of toluene was added to a rapidly stirred mixture of 250 ml of toluene and 0.1603 g (1.02 mmoles) of aluminum chloride at 0°. Aliquots were removed at convenient intervals, quenched and treated as above, and analyzed by glc (DC 550 column, 20% on 60/80 mesh Chromosorb P, 8 ft, 187°, 61 cc of helium per min). The log of the height of each peak, relative to the peak due to a small amount of benzene which was present in the toluene and which served as an internal standard, was plotted against time (see graph, page 189). Straight lines were obtained. The slope of the line for benzocyclobutene was 6.1 times that for β-phenylethyl chloride, and the derived pseudo-first-order rate constants were: benzocyclobutene: 3.3×10^{-3} sec^{-1}; β-phenylethyl chloride: 5.4×10^{-4} sec^{-1}.

(7) 2-(*para*-Tolyl)ethyl Bromide with Benzene

2-(*para*-Tolyl)ethyl bromide (page 183) (0.768 g, 3.86 mmoles) was stirred with 250 ml of benzene and 0.1346 g (1.01 mmoles) of aluminum chloride for one hour at 40°. The usual treatment yielded a cloudy yellow liquid. Analysis by nmr and glc (Apiezon L column, 20% on 60/80 mesh Chromosorb P, 10 ft, 218°, 63 cc of helium per min; and QF 1-0065 column, 20% on 60/80 mesh Chromosorb P, 10 ft, 157°, 61 cc of helium per min) showed that 1-phenyl-2-(*para*-tolyl)ethane was the only alkylation product and that no detectable amounts of the *ortho*- or *meta*-isomers were formed.

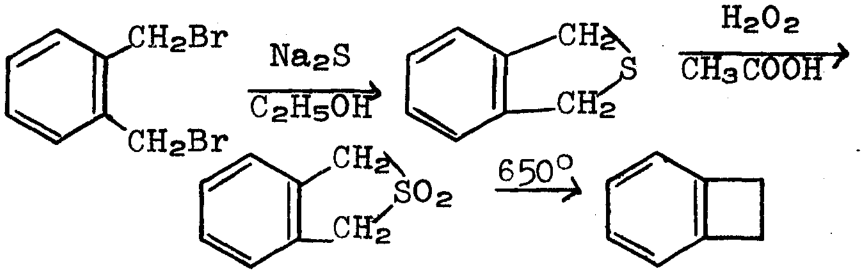
Comparative Rate Study of the Friedel-Crafts Reaction of Benzocyclobutene and β-Phenylethyl Chloride with Toluene and Aluminum Chloride.



RESULTS AND DISCUSSION

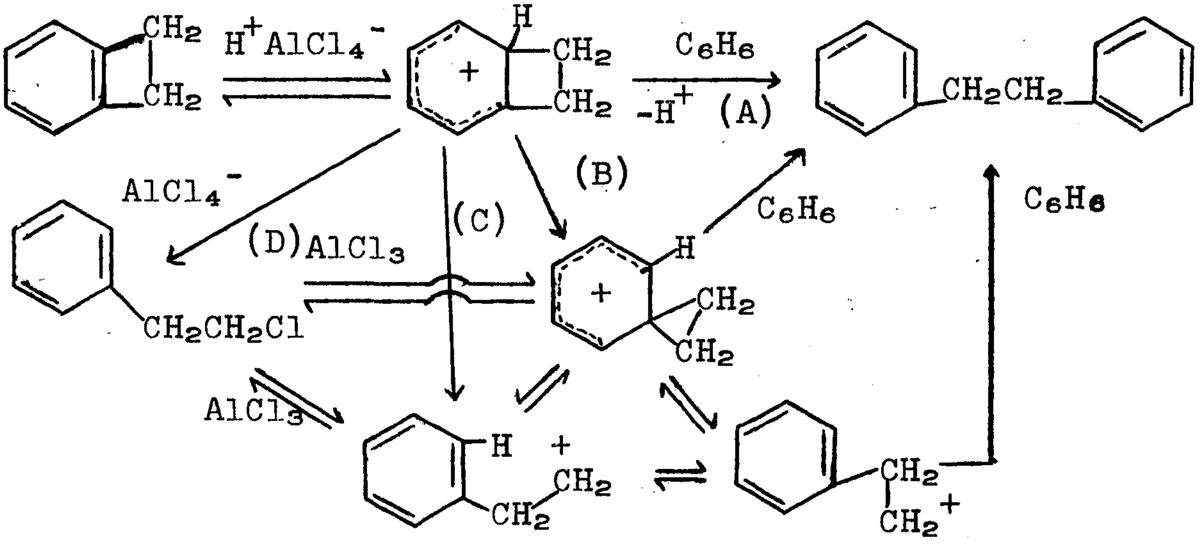
Benzocyclobutene was prepared by the procedure shown in Scheme XXXXIV.[167,168]

Scheme XXXXIV



According to our expectations, benzocyclobutene did indeed react with benzene in the presence of aluminum chloride and gave a quantitative yield of bibenzyl. Several possible pathways may be considered for this reaction (Scheme XXXXV). Protonation of benzocyclobutene at the bridgehead gives an ion which may undergo any of four possible reactions. Most simple of these is direct attack by benzene at the side chain to displace the protonated aromatic ring (path A). Alternatively, the ion could

Scheme XXXXV



collapse to either the bridged ion (path B) or the equilibrating classical *β*-phenylethyl cation (path C). These two may or may not be in equilibrium, and either would give bibenzyl on attack by benzene. These paths cannot be distinguished by the present work. Finally, attack by tetrachloroaluminate anion (path D) could convert this ion to *β*-phenylethyl chloride which could ionize to either a classical or a nonclassical ion, either of which would, as mentioned above, give bibenzyl. Indeed, *β*-phenylethyl chloride also produced bibenzyl quantitatively under these conditions. As implied in Scheme XXXXV, any opening of the four-membered ring would be essentially irreversible.

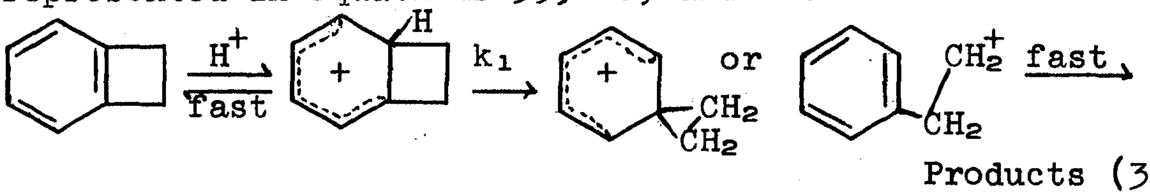
In an attempt to distinguish among these possibilities, the Friedel-Crafts reactions of benzocyclobutene and *β*-phenylethyl chloride with toluene were studied. Each alkylating agent gave essentially the same isomer distribution of 1-phenyl-2-tolylethanes: 47.8% *ortho*-, 18.2% *meta*-, and 34.0% *para*- from benzocyclobutene and 46.1% *ortho*-, 18.8% *meta*-, and 35.1% *para*- from *β*-phenylethyl chloride. Each set of figures is the mean of two runs. In contrast, McMahon and Bunce found mainly *para*-alkylation of toluene with *β*-phenylethyl chloride at 0°.[17] Apparently, this reaction becomes much less selective when the temperature is raised to 40°, although in the present work reaction at 0° still gave appreciable *meta*-substitution.[180]

(180) Preliminary results on a QF 1-0065 column, 20% on 60/80 mesh Chromosorb P, 60 cc of helium per min, 178°, 12 ft.

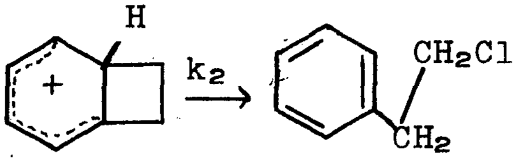
Appropriate control experiments showed that the products were stable to the reaction conditions and that no loss or alteration of product material occurred during reaction or subsequent treatment. The product mixtures from the two compounds consist therefore of first-formed products, and the essential identity of these mixtures indicates that the alkylating agents probably pass through a common intermediate on the way to forming 1,2-diarylethanes.

When β-(para-tolyl)ethyl bromide was treated with benzene and aluminum chloride at 40°, only 1-phenyl-2-(para-tolyl)ethane was formed. It is likely that if the 2-(para-tolyl)ethyl cations equilibrate they do so through a phenonium ion structure, in which the methyl group would remain in the para-position, rather than through a protonated benzocyclobutene structure, in which the methyl group could rearrange to the meta position. Therefore, since closure of β-phenylethyl chloride (or the ion) to protonated benzocyclobutene is highly unlikely, and since the alkylating agents probably pass through a common intermediate, path A (Scheme XXXXV) may be eliminated from further consideration.

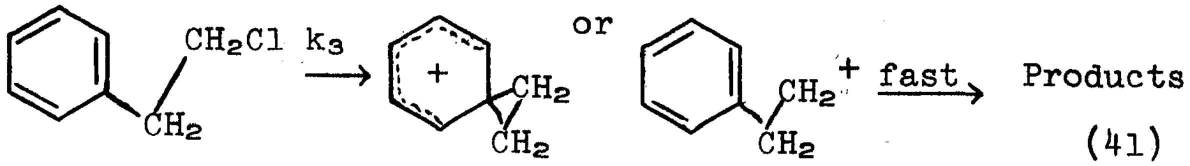
It must yet be shown whether protonated benzocyclobutene collapses to the same cation as is formed from β-phenylethyl chloride (paths B and/or C; as previously stated, no distinction can be made in the present work between the nonclassical and equilibrating classical representations of this ion) or to β-phenylethyl chloride itself (path D) which then reionizes to the cation. These possibilities are represented in equations 39, 40, and 41.



(39)



(40)



(41)

As mentioned above, equations 39 and 40 are essentially irreversible. McMahon and Bunce showed that 1-C^{14}-2-phenylethyl chloride reacts with a large excess of toluene to give, aside from a small isotope effect, complete equilibration of the methylene groups in the product. However, recovered β-phenylethyl chloride was not scrambled. This showed that the ion, once formed, reacted more rapidly with toluene than with $AlCl_4^-$.[17] Therefore equation 41 (step 1) is also irreversible.

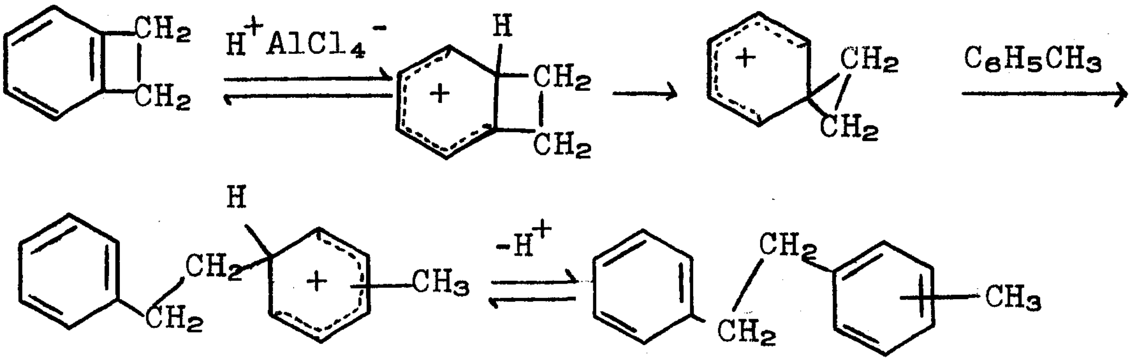
In an attempt to distinguish between the two possible pathways, a study of the relative rates at which benzocyclobutene and β-phenylethyl chloride react with aluminum chloride in toluene was undertaken. An equimolar mixture of benzocyclobutene and β-phenylethyl chloride was added to a mixture of toluene and aluminum chloride, and the rate of disappearance of each component was followed by gas chromatographic analysis of aliquots. Difficulties were encountered in the form of long and unreproducible induction periods, followed by rather rapid reaction of benzocyclobutene even at as low a temperature as 0°. The best set of data from a total of eight runs was plotted (log of concentration vs time for each component). Straight lines were obtained (see graph, page 189), showing that reaction of each compound followed pseudo-first-order kinetics. Benzocyclobutene reacted 6.3 times as rapidly as β-phenylethyl chloride.

The slope of the line for benzocyclobutene is proportional to $k_1 + k_2$. The slope of the line for β-phenylethyl chloride after all the benzocyclobutene has reacted is proportional to k_3. If k_2 were greater than k_3, the concentration of β-phenylethyl chloride in the early stages of the reaction would rise above its initial value. If k_2 were equal to k_3, the concentration of β-phenylethyl chloride would remain constant initially and then drop. If k_2 were less than k_3, β-phenylethyl chloride would decrease in concentration from the beginning of the reaction. The data rule out the first case but are not sufficiently accurate to permit a clear-cut choice between the latter two.

In any case, k_3 may be set as the upper limit for k_2. Since the reaction of benzocyclobutene ($k_1 + k_2$) proceeds at 6.1 times the rate of that of β-phenylethyl chloride (k_3), k_1/k_2 is equal to or greater than 5.1, and therefore at least 84% (5.1/6.1) of the protonated benzocyclobutene is converted directly to the cation (equation 39) without intermediate formation of β-phenylethyl chloride.

The most likely mechanism for the major pathway in the Friedel-Crafts reaction of benzocyclobutene with toluene may then be expressed as in Scheme XXXXVI.

Scheme XXXXVI



AUTOBIOGRAPHICAL STATEMENT

The author was born December 17, 1938, in New York City. He graduated from Brooklyn Technical High School in 1956 and received the Bachelor of Science degree in Chemistry from Queens College in 1960. In June 1962 he received the Master of Arts degree in Chemistry from the City College of New York; his thesis topic was "The Reductive Cleavage of Organic Sulfur Compounds with Sodium and Methanol."

In 1962 and the summers of 1963, 1964, and 1965 the author was employed in research in the field of air pollution under grants from the United States Public Health Service. While in graduate school he held teaching assistantships (1962-1963), a National Defense Education Act (Title IV) Fellowship (1962-1964), City University of New York Research Assistantships (1964-1966), and a National Aeronautics and Space Administration Traineeship (1966-1967).