

REARRANGEMENT IN ALKYL GROUPS DURING SUBSTITUTION REACTIONS

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Received April 12, 1965

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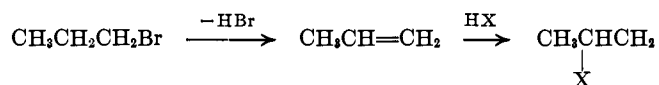
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I. INTRODUCTION

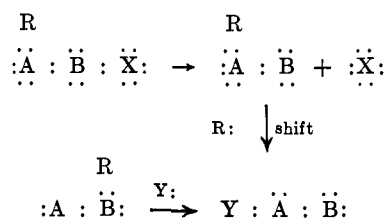
A knowledge of the rearrangements which alkyl groups may undergo in various circumstances is relevant to the isomeric purity of many organic chemical products. The widely used reactions of alkylation by Grignard reagents or other organometallics, by alkyl halides, or by alcohols, for example, all require for their understanding a detailed knowledge of the isomeric purity of the starting materials, rearrangement which may accompany the reaction, and possible rearrangement of the product after its initial formation.

The occurrence of isomeric impurities in commercially available organic chemicals has become more evident in recent years as a result of scrutiny by infrared and gas chromatographic techniques. Many commercial samples of alkyl halides are mixtures. Of five specimens of "*n*-butyl chloride" recently examined all except one contained *sec*-butyl chloride in amounts varying from 2 to 18% (72), while "2-bromooctane" contained only 54% of the named isomer, together with 3- (28%) and 4- (18%) bromooctanes (60). "2-Bromopentane" similarly contained *ca.* 30% 3-bromopentane (178).

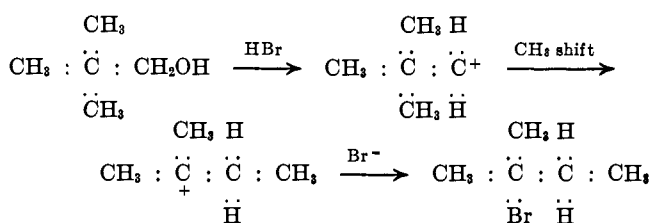
The earliest reported examples of alkyl rearrangement included the formation of isopropyl alcohol from *n*-propylamine and nitrous acid in 1867 (105), the isomerization of alkyl bromides at 250° (*n*-propyl to isopropyl, and isobutyl to *t*-butyl) (3, 4, 39), and the formation of isopropylbenzene by the Friedel-Crafts alkylation of benzene with *n*-propyl bromide (85). In general, the products obtained were those which would be expected if an olefin were formed as intermediate, and subsequently reacted in accordance with Markownikoff's rule.



Explanations of molecular rearrangement based on the electron-pair theory of valency began to develop in the 1920's (92, 110, 138, 159, 174), particularly as a result of the research of Meerwein, who introduced the idea of ionization as an essential step (113-115), and were unified by Whitmore in 1932 in a paper entitled "The Common Basis of Intramolecular Rearrangements" (179). In this it was postulated that an intermediate carbonium cation formed.

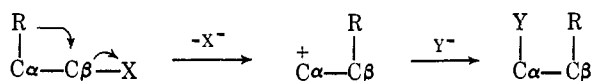


In a series of papers published between 1932 and 1938 this mechanism was illustrated (177, 179-187), and it was further shown that in those reactions where an octet of electrons appeared to be preserved, rearrangement did not occur. Thus, while neopentyl alcohol reacted with hydrogen bromide to give *t*-amyl bromide (186), the amide trimethylacetamide, $(\text{CH}_3)_3\text{CCONH}_2$



decomposed with nitrous acid to give trimethylacetic acid without rearrangement (184) and underwent Hofmann degradation to give only neopentylamine.

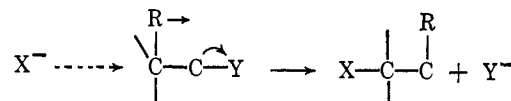
Dostrovsky, Hughes, and Ingold (38) recognized two conditions involved in an ionic mechanism: (a) a kinetic condition, requiring initial bond fission to give an incomplete octet, and (b) a thermodynamic condition that the ion so formed will rearrange only if the relevant free energy change is favorable. The concept of simultaneous ionization and rearrangement has been developed to account for increase in reaction rate when rearrangement is involved, and the terms "synartetic acceleration" or "anchimeric assistance" (93, 191) are used to describe this concept.



In general it may be said that where primary carbonium ions may be postulated as forming, they have been found to rearrange to secondary or tertiary ions, in accordance with the expected stabilizing effect of hyperconjugation. Recent molecular orbital calculations have also brought out the particular stability of *t*-carbonium ions (59). The question is, does each individual carbonium ion of necessity rearrange, or are there factors determining whether or not rearrangement will occur?

Other mechanisms of rearrangement can, however, operate, and examples are known in which rearrangement occurs in the reverse order (*e.g.*, *sec*- to *n*-butyl; *iso*- to *n*-propyl), *e.g.*, in free-radical reactions (83, 134, 166) or in cases where steric factors are important (88-90).

Finally, the possibility of a concerted bimolecular rearrangement process must be considered (70, 154).



In many reactions, insufficient evidence is available for the mechanism to be known with certainty. The purpose of this review is, however, to define the conditions under which rearrangement does occur in those cases where specific mention of the isomeric purity of products is made. It is confined to saturated, open-chain alkyl groups.

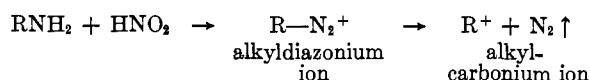
II. REACTIONS INVOLVING CARBON-NITROGEN FISSION

A. NITROUS DEAMINATIONS

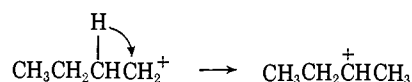
In 1867 it was reported (105, 106) that *n*-propylamine gave both *n*- and isopropyl alcohols. The forma-



tion of rearranged alcohols from primary aliphatic amines may involve an intermediate primary carbonium ion.

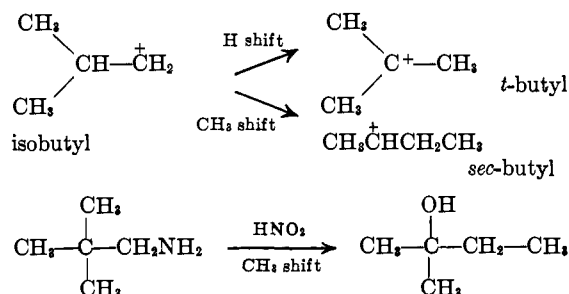


n-Butylamine afforded *n*- and *sec*-butyl alcohols (184) but, contrary to the earlier report (109), no isobutyl alcohol was formed. This isomerization is presumed to entail the migration only of hydrogen.

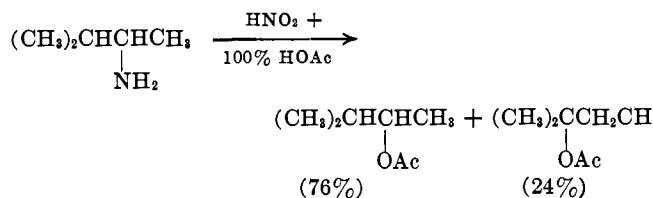


The possibility of an ethyl shift has been ruled out by tracer studies; 1-aminobutane-1,1- d_2 , $\text{CH}_3\text{CH}_2\text{CH}_2\text{-CD}_2\text{NH}_2$, yielded no $\text{CH}_3\text{CH}_2\text{CD}_2\text{CH}_2\text{OH}$ (173).

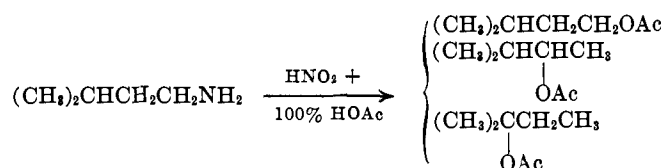
In examples in which there is chain branching at the β -carbon atom, methyl migration may be observed. Thus isobutylamine can give isobutyl alcohol in addition to *t*-butyl alcohol by hydrogen shift (107) or *sec*-butyl alcohol by methyl shift (25), and in like manner *t*-amyl alcohol was obtained from neopentylamine (55).



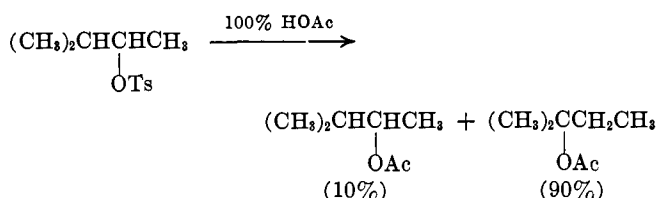
The formation of both 3-methyl-2-butyl and *t*-amyl products from 3-methyl-2-butylamine (162) could be explained on the basis of either hydrogen or methyl migration, but no experiments to elucidate this point have been reported.



From isopentylamine, isopentyl, 3-methyl-2-butyl, and *t*-pentyl products were obtained (162).



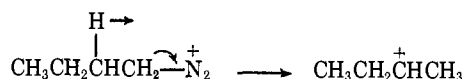
It is noteworthy that the intermediate carbonium ions in these reactions, and in the deamination of *t*-amylamine, are considered to be in some way different from "normal solvolytic ions," *i.e.*, those produced in reactions such as the solvolysis of tosyl esters, since the



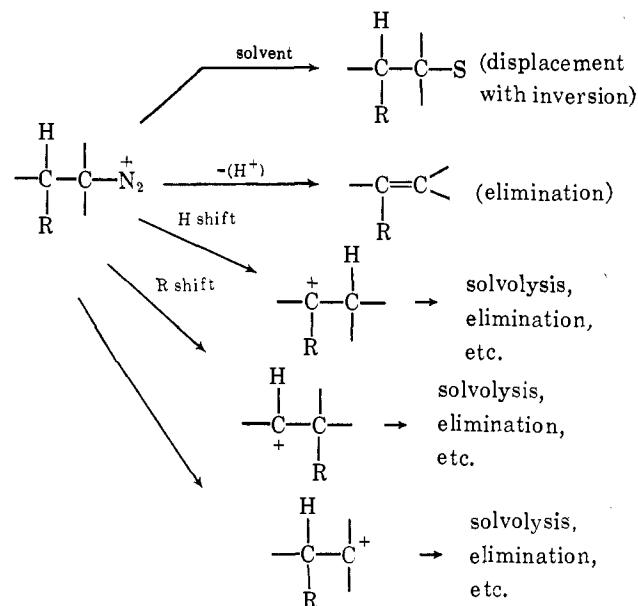
proportions of the olefinic by-products ($\text{Me}_2\text{CHCH}=\text{CH}_2$, $\text{Me}_2\text{C}=\text{CHMe}$, and $\text{CH}_2=\text{CMeCH}_2\text{Me}$), as well as of the substitution products, are different (162).

The occurrence of carbonium ions in nitrous deaminations was indicated by the formation of methyl chloride when sodium chloride was added to the reaction of methylamine with nitrous acid (41).

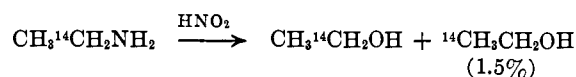
From a study of optically active 1-aminobutane-1-*d*, it was concluded that the last *common* intermediate in nitrous deaminations is not the alkyl but the alkyldiazonium ion, which can undergo a number of competing reactions including rearrangement (173).



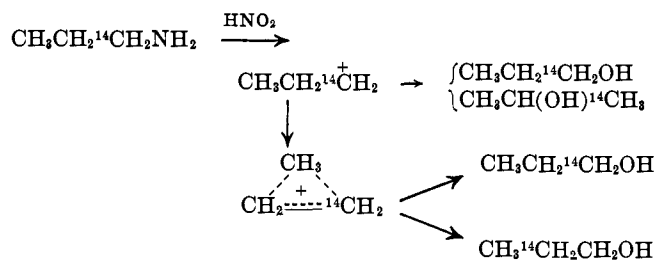
This theory has been used in the discussion of many examples according to the following general scheme (172).



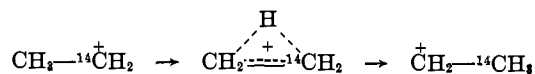
By the use of radioactive ^{14}C , hydrogen migration has been shown to occur in the deamination of ethylamine (149) while in the example of *n*-propylamine several



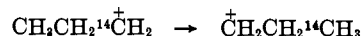
observations have been made. From 1-aminopropane-1- ^{14}C , isopropyl alcohol and *n*-propyl alcohol were obtained, showing an isotope position isomerization of 8.5% (146). On comparing this with the 1.5% rear-



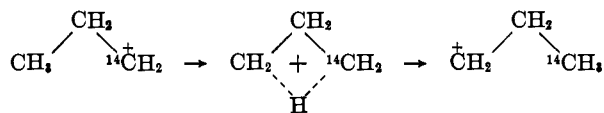
angement noted in the ethyl system, which was also formulated as proceeding by a cyclic, nonclassical, carbonium intermediate, the conclusion was drawn that methyl groups have a higher intrinsic migratory apti-



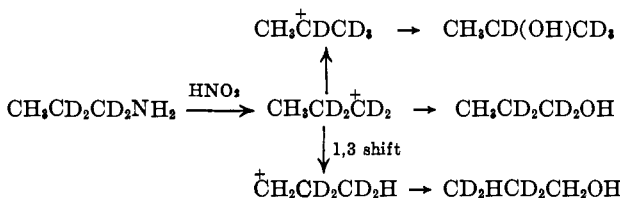
tude than hydrogen when the degree of substitution of the methylene groups of the intermediate is the same. Criticism of this work has been presented more recently (141) because ^{14}C in the 2-position of the propyl group could not be detected, but there was evidence of a 1,3 shift. Two successive 1,2 shifts of hydrogen may



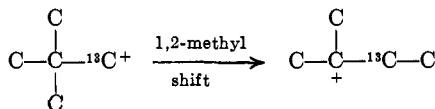
be involved, or a direct 1,3 migration involving a cyclic intermediate of the type shown (139).



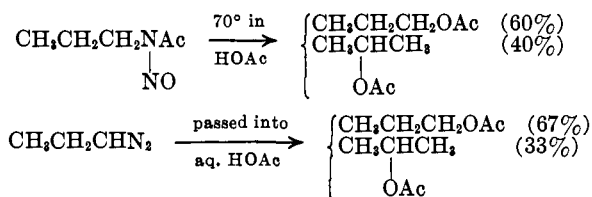
N.m.r. studies on the deamination of 1-propylamine-1,1,2,2- d_4 favor the 1,3-migration, as 11.8% of the propan-1-ol formed contained a H atom shifted from the 3- to the 1-position, and the propan-2-ol obtained had no H at the 2-position (95).



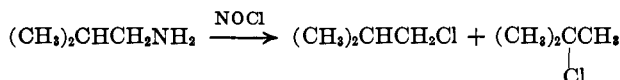
N.m.r. and mass spectroscopic analysis of the *t*-amyl alcohols, obtained from neopentyl-1- ^{13}C and neopentyl-1,1- d_2 amines, show the labeled C atom to end up exclusively as shown, excluding in this case the possibility of 1,3-hydride shifts, protonated cyclopropane, or H-bridged intermediates, and indicating the occurrence of a simple methyl migration (96).



Closely related to the amine-nitrous acid systems are the carbonium-ion decompositions of nitrosoacylamines and alkyl diazo esters, believed again to proceed *via* the intermediate formation of RN_2^+ (91). The percentage rearrangements agree closely with that observed in the corresponding deamination of *n*-propylamine in acetic acid (32%).

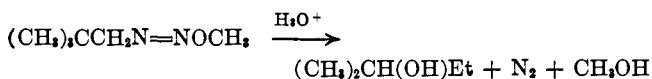


Similarly, the action of nitrosyl chloride upon primary amines can give rearranged halides, presumably *via* the intermediate alkyldiazonium ion (167).

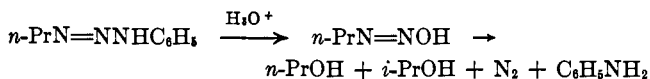


B. DECOMPOSITION OF NITRAMINES AND TRIAZENES

The fission of carbon-nitrogen bonds includes the acid-catalyzed decomposition of O-methyl-N-neopentyl-nitramine, which gives *t*-amyl alcohol (18), and the de-



composition of aliphatic-aromatic triazenes by acetic acid in aqueous-alcoholic or hydrocarbon media to give isomerized alcohols and esters (1), *e.g.*



C. PYROLYSIS OF BORON-NITROGEN COMPOUNDS

Pyrolysis of alkylammonium tetrachloro- or tetrabromoborates at 350–360° to give N-alkyl-B-halogenoborazoles has given alkyl halides as by-products (21). Whereas the alkyl chlorides were obtained without rearrangement of the alkyl group, the bromides, obtained in higher yields, underwent considerable rearrangement as shown in Table I. Whether this occurs after formation or by virtue of a different initial mechanism of formation is not known.

TABLE I

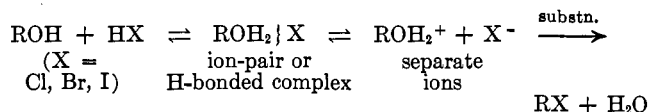
R in $\text{RNH}_3^+\text{BR}_4^-$	RBr, mole	Composition R in RBr, %			
		<i>n</i> -	<i>i</i> -	<i>sec</i> -	<i>t</i> -
<i>n</i> -Pr	0.48	72	28
<i>i</i> -Pr	0.75	13	87
<i>n</i> -Bu	0.33	76	..	24	..
<i>i</i> -Bu	0.79	1	44	..	55
<i>sec</i> -Bu	0.83	4	..	95	1
<i>t</i> -Bu	1.0	7	93

Pyrolysis of the borazole $(\text{BrBN-}i\text{-Bu})_3$ at 360° also gave alkyl bromides containing, apparently, all four isomeric bromobutanes.

III. REPLACEMENT OF HYDROXYL BY HALOGEN

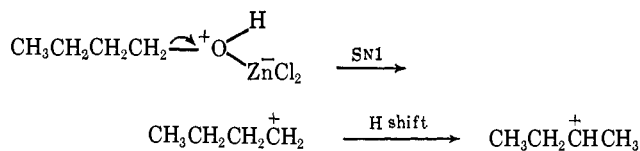
A. HYDROGEN HALIDE-ALCOHOL REACTIONS

The over-all sequence of reactions is represented in its simplest terms as follows (69, 80).

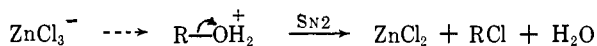


Primary *n*-alkyl groups (*n*-Pr, *n*-Bu, *n*-pentyl, *n*-octyl) do not rearrange even at temperatures up to 160°, which suggests that the replacement is by a bimolecular ($\text{S}_{\text{N}}2$) process (69, 70), but if zinc chloride is used to catalyze the formation of the alkyl chloride (84, 128) then considerable rearrangement to a *sec*-alkyl group may occur. Thus *n*-propyl alcohol gives both *n*- and isopropyl chlorides (69, 151), *n*-butyl alcohol gives *n*- and *sec*- (but no iso- or *t*-) butyl chlorides (69, 151), *n*-pentyl alcohol gives 1-, 2-, and 3-chloropentanes (69, 183), *n*-octyl alcohol gives 1-, 2-, 3-, and 4-chlorooctanes (69), and dodecyl alcohol gives at least 1- and 2-chlorododecanes (175, 176). The percentage rearrangement varies considerably with catalyst concentration and may be as high as 20%. It seems likely that ionization of the C–O bond is facilitated by co-

ordination to the zinc chloride. At concentrations below 0.2 mole, however, zinc chloride causes no rear-

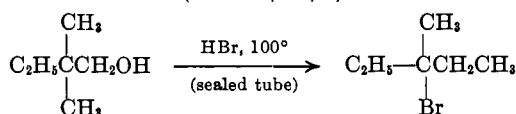
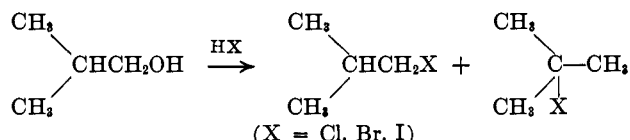


rangement although its catalytic effect is still high. It probably also functions by maintaining a high effective concentration of hydrogen chloride (as the complex ions ZnCl_3^- , ZnCl_4^{2-}) at the reaction temperature. Cer-

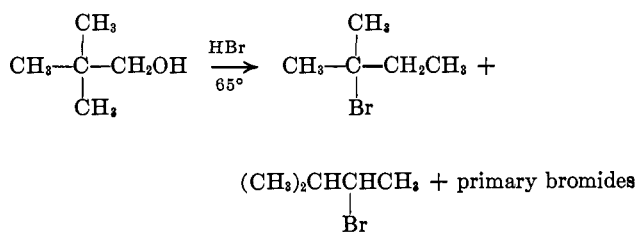


tain bases, such as pyridine and dimethylamine, which form dihydrochlorides, $[\text{R}_3\text{NH}]^+ [\text{HCl}_2]^-$, also catalyze this reaction without effecting rearrangement when heated under reflux (105–125°), but at 160° in a sealed tube 1-butanol, pyridine (1 mole), and hydrogen chloride (3 moles) gave *sec*-butyl chloride (5.5%) (68). The use of concentrated sulfuric acid in the preparation of *n*-alkyl bromides causes no significant rearrangement (70, 183).

Primary alcohols branched at the β -carbon atom react much more slowly and generally give rearranged products. Isobutyl alcohol affords both iso- and *t*-butyl halides (19, 54, 116, 118, 127), 2,2-dimethylbutan-1-ol gives the tertiary halide, 2-bromo-2-ethylbutane (43), and neopentyl alcohol reacts slowly with



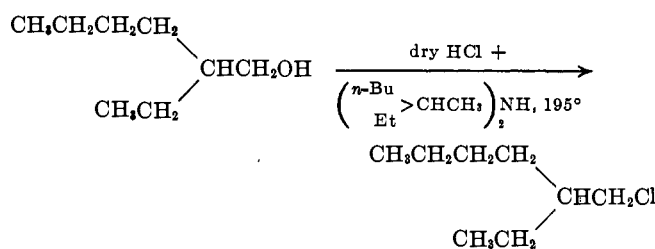
anhydrous hydrogen bromide to give *t*-amyl bromide (72%), a secondary bromide (probably *sec*-isoamyl bromide) (8%), and one or more primary bromides (20%) (186). Study of its rearrangement to *t*-amyl



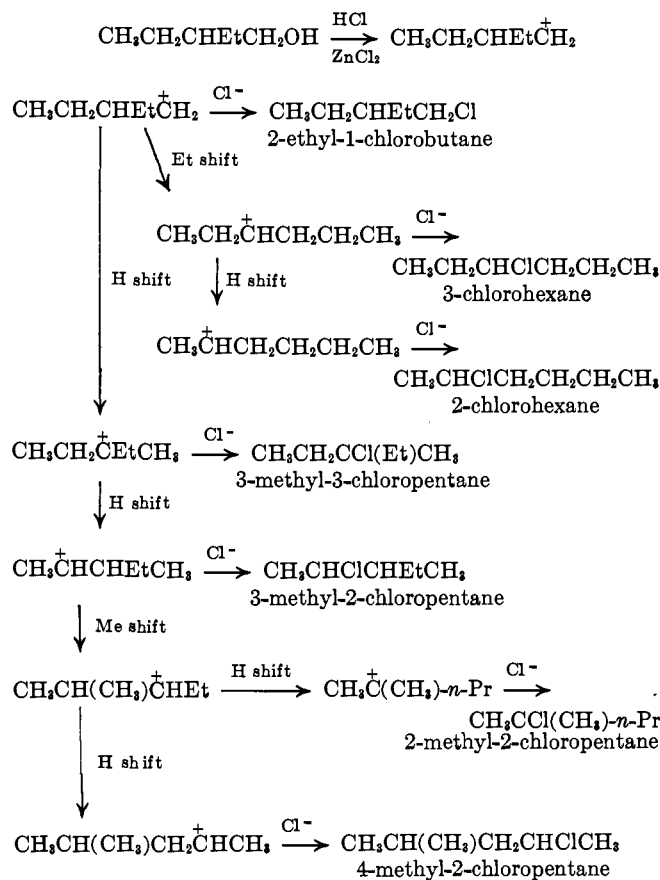
bromide by the use of ^{14}C indicates that a simple methyl shift occurs and that protonated cyclopropane intermediates are not involved (94).

The use of pyridine as catalyst has, however, enabled isobutyl chloride of >99% purity to be prepared from isobutyl alcohol (69), while certain secondary amines

have been claimed as catalysts for the formation of 2-alkyl-1-chloroalkanes from alcohols of the type $\text{RCH}_2\text{-CH}(\text{CH}_2\text{R}')\text{CH}_2\text{OH}$ (24).



As with the straight-chain alcohols, much rearrangement occurs in the presence of zinc chloride; isobutyl alcohol gave little isobutyl chloride (111), and from 2-ethylbutan-1-ol at least seven different chlorides were obtained (181) by a series of rearrangements depicted as follows.



The transitory existence of the carbonium ion $\text{CH}_3\text{-CHMeCHEt}^+$ was assumed although the corresponding chloride was not isolated. It was demonstrated that these rearrangements occurred during and not after alkyl halide formation.

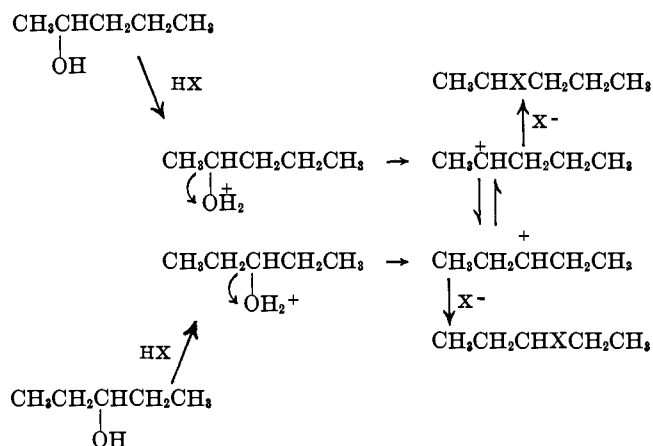
The more remotely branched isoamyl alcohol also gave rearranged halides (28%) in addition to isoamyl chloride (37%) when treated with hydrogen chloride in the presence of zinc chloride (35).

TABLE II
 REACTIONS OF SECONDARY ALCOHOLS WITH HYDROGEN HALIDES

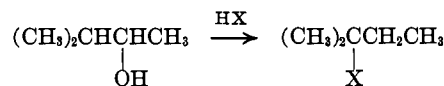
R in ROH	Reagent	Temp., °C.	% isomers in product ^a			Ref.
			2-	3-	4-	
CH ₃ (CH ₂) ₂ CHCH ₃	Anhydr. HCl	20	92-95	5-8	...	182
	Anhydr. HCl	100	80	20	...	70
	Anhydr. HBr	20	93	7	...	70
	Anhydr. HBr	80-90	86	14	...	135
	Anhydr. HBr	100	87	13	...	70
	Concd. aq. HBr	115	76	24	...	70
	Concd. aq. HBr ^b	123	72	28	...	135
	Anhydr. HI	100	76	24	...	70
	Concd. aq. HI	115	72	28	...	70
	Et ₂ CH	Anhydr. HCl	20	25	75	...
Anhydr. HCl		20	5	95	...	70
Anhydr. HCl		100	20	80	...	69
Anhydr. HBr		80-90	20	80	...	135
Concd. aq. HBr		115	23	77	...	70
Concd. aq. HBr ^b		123	40	60	...	135
Concd. aq. HI		115	32	68	...	70
CH ₃ (CH ₂) ₅ CHCH ₃	Anhydr. HCl	20	~100	Trace	0	70
	Anhydr. HCl	100	94	5.5	0.5	69
	Anhydr. HBr	20	93	7	0	70
	Anhydr. HBr	100	92	8	Trace	70
	Anhydr. HI	20	92	8	0	70
	Anhydr. HI	100	92	8	0	70

^a 2- or 3-halogenopentanes, or 2-, 3-, and 4-halogenooctanes. ^b Plus concentrated H₂SO₄.

Secondary alcohols, both straight- and branched-chain, give rearranged halides even at low temperatures (see Table II). The 2- and 3-pentyl structures are thus readily interconvertible, octan-2-ol affords the 2-, 3-, and traces of 4-octyl compounds, and in the example of optically active octan-2-ol some loss in rotatory power also occurs (69, 70, 156, 157, 182). Rearrangement to a primary alkyl group is not observed and a carbonium-ion mechanism (in part at least) will explain the results.



With branching adjacent to the secondary alcoholic carbon atom, the corresponding tertiary halides invariably result. *sec*-Isoamyl alcohol thus reacts with hydrogen iodide (193) or hydrogen chloride (180) at ordinary temperatures to give *t*-amyl halides. Some secondary, and possibly primary chlorides, may also be

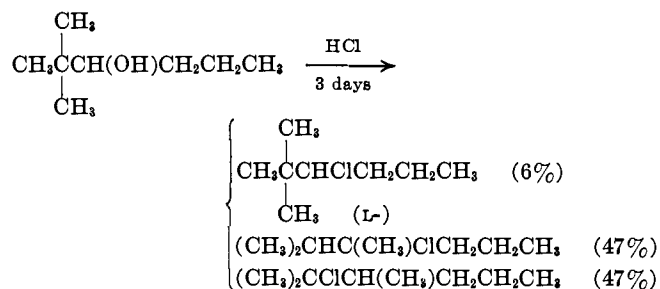


formed. Tertiary chlorides are similarly obtained by the reaction of hydrogen chloride with Me₂CHCH(OH)CH₂CH₃, Me₂CHCH(OH)CH₂CH₂CH₃, and Me₂CHCH(OH)CHMe₂, but not Me₂CHCH₂CH(OH)CH₃, Me₂CHCH₂CH₂CH(OH)CH₃, or Me₃CCH₂CH(OH)CH₃, in which branching is not adjacent to the alcoholic carbon atom (180). Correlation has also been made between the effect on rotatory power of branched alkyl groups in various carbinols and their propensity to rearrangement in reactions with hydrogen chloride. At 25° the following percentage rearrangements to tertiary halides were observed (possible rearrangement to other secondary structures not being accounted for) (171).

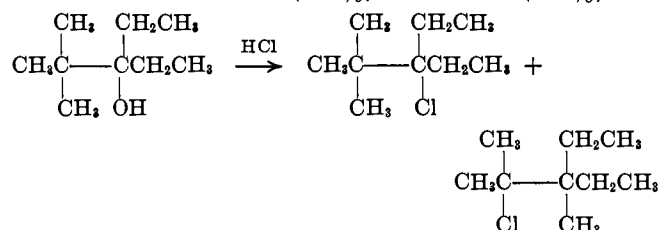
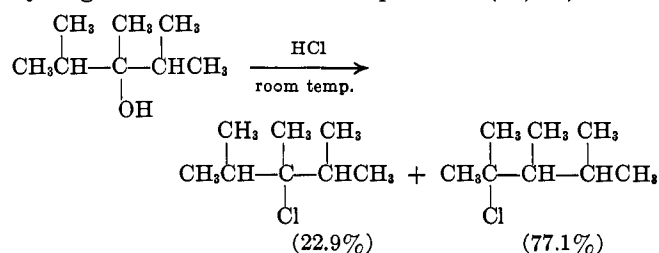
Alcohol	Per cent tertiary chloride
CH ₃ CHOH- <i>n</i> -C ₄ H ₉	1
CH ₃ CHOH- <i>i</i> -C ₄ H ₉	92-93
CH ₃ CHOH- <i>c</i> -C ₄ H ₉	80-81
CH ₃ CHOH- <i>t</i> -C ₄ H ₉	99-100
<i>n</i> -C ₅ H ₁₁ CHOH- <i>t</i> -C ₄ H ₉	94-95

Optically active *D*-2,2-dimethylhexan-3-ol gave, with hydrogen chloride, a mixture of two inactive tertiary halides and a smaller amount of the unrearranged *L*-secondary chloride (170).

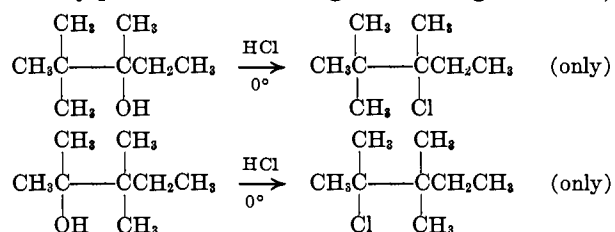
Simple tertiary alcohols react very rapidly with hydrogen halides, presumably by a carbonium-ion mechanism, but only rearrange if alternative tertiary structures are available. Their rearrangement to *sec*-



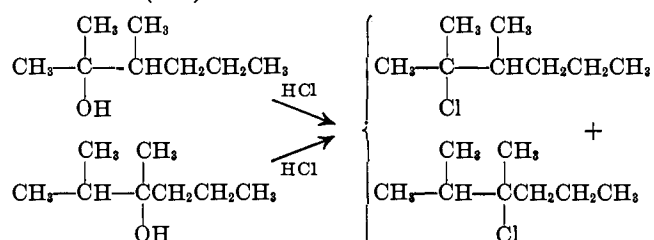
or *n*-alkyl halides has never been reported. 2,3,4-Trimethylpentan-3-ol and 2,2-dimethyl-3-ethylpentan-3-ol give mixtures of tertiary halides by reaction with hydrogen chloride at room temperature (12, 13).



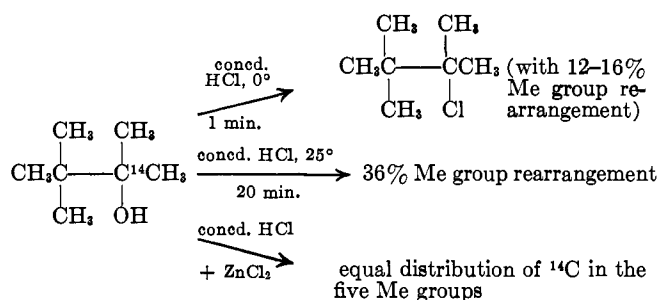
In contrast, 2,2,3-trimethylpentan-3-ol and 2,3,3-trimethylpentan-2-ol do not give rearranged halides, a



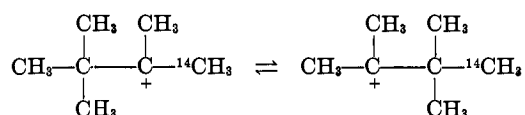
difference which has been explained on the basis of steric factors; *e.g.*, the presence of two ethyl groups on the alcoholic carbon atom of 2,2-dimethyl-3-ethylpentan-3-ol may block approach to either face of the planar carbonium ion and encourage rearrangement (14). Complete loss of rotatory power accompanies rearrangement in the reaction of L-2,3-dimethylhexan-2-ol with hydrogen chloride at room temperature, and a similar chloride mixture results from 2,3-dimethylhexan-3-ol (170).



By the use of ^{14}C , pentamethylethanol has been shown to undergo varying degrees of methyl group rearrangement depending on reaction conditions (150).



Treatment of the chloride with concentrated hydrochloric acid plus zinc chloride containing radioactive chlorine gave complete equilibration, possibly *via* solvated carbonium ions.

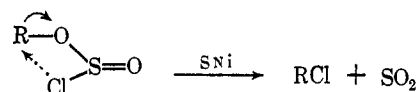


B. THIONYL HALIDE-ALCOHOL REACTIONS

Thionyl chloride affords unrearranged alkyl chlorides from straight-chain primary alcohols such as 1-butanol, both in the absence or presence of pyridine (69), and has been reported as doing so also from straight-chain secondary alcohols (pentan-2-ol, pentan-3-ol, or octan-2-ol) (26, 69, 182). The slight loss in optical purity which accompanies inversion in the example of (+)-octan-2-ol has been attributed to a small contribution from the internal (S_{Ni}) mechanism in the decomposition of the chlorosulfite (69). The main reaction is formulated as follows.



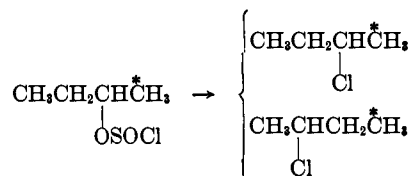
The subsidiary reaction is



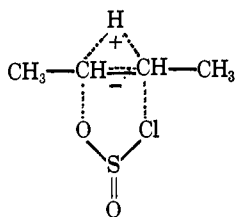
The S_{Ni} mode also apparently accounts for the preponderant retention of configuration which occurs on decomposition in dioxane (9, 104), again without rearrangement (63).

Recent work has shown, however, that small amounts ($\leq 1\%$) of 3-chlorooctane may be obtained by decomposition of the 2-octyl chlorosulfite under certain conditions, *e.g.*, in hydrocarbon media (63). Alkyl chloride is the minor product of these reactions, and large amounts of olefin are formed. It seems likely therefore that in most cases any carbonium ion produced undergoes elimination to give olefin, but it may in certain experimental conditions yield a little rearranged halide.

Varying degrees of isotope position rearrangement, resulting from a 1,2-hydride shift, have been reported in the thermal decomposition of 1-¹⁴C-2-butyl chlorosulfite in dioxane (4%), acetonitrile (6%), thionyl chloride (13–18%), formic acid (22–23%), and toluene (16–21%).



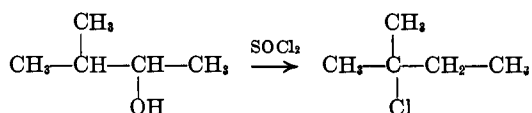
An ion-pair mechanism, involving the following intermediate, has been proposed (102). In the presence of pyridine no rearrangement occurred.



From the branched 2-ethylbutan-1-ol, thionyl chloride and pyridine at 60–90° yield pure 1-chloro-2-ethylbutane (181).

Decomposition of neopentyl chlorosulfite at 100° in the presence of quinoline hydrochloride gives both neo- and *t*-pentyl chlorides (81).

The branched secondary alcohol, 3-methylbutan-2-ol, gives the rearranged tertiary halide exclusively (103).



With thionyl bromide, rearrangement in the case of 3-pentanol, has also been observed (26), the product containing 2-bromopentane (1–3%).

C. BORON HALIDE-ALCOHOL REACTIONS

The formation of alkyl halides by the interaction of boron trichloride or boron tribromide with alcohols occurs *via* the decomposition of intermediate alkyl dihalogenoborinates (see Tables III and IV) and dialkyl halogenoborinates (76–78).

TABLE III
DECOMPOSITION OF ALKYL DICHLOROBORINATES

R in ROBCl ₂	Temp., °C.	% isomers in product				Ref.
		1-	2-	3-	4-	
<i>n</i> -Pr	125	77	23	73
<i>n</i> -Bu	150	75	25	72
CH ₃ (CH ₂) ₃ CH ₂	140	48	31	21	..	73
CH ₃ (CH ₂) ₂ CHCH ₃	20	0	63	37	..	73
Et ₂ CH	20	0	38	62	..	73
CH ₃ (CH ₂) ₆ CH ₂	195	68	25	6	1	73
CH ₃ (CH ₂) ₅ CHCH ₃	20	0	62	35	3	73
CH ₃ (CH ₂) ₄ CHEt	20	0	26	61	13	73
<i>n</i> -BuCH- <i>n</i> -Pr	20	0	2	25	73	73

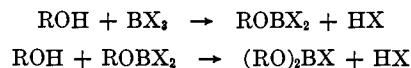
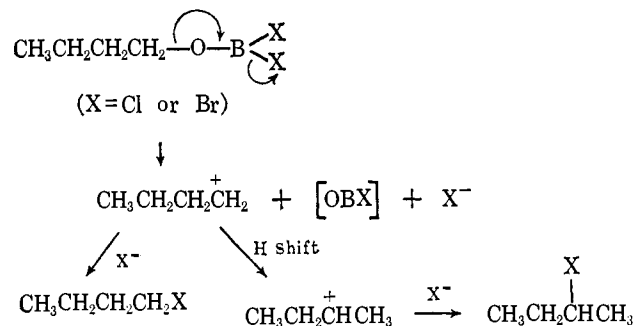


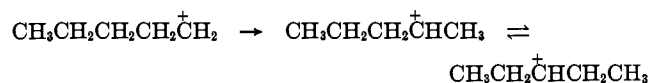
TABLE IV
DECOMPOSITION OF ALKYL DIBROMOBORINATES AT 20°

R in ROBR ₂	% isomers in product				Ref.
	1-	2-	3-	4-	
<i>n</i> -Pr	72	28	73
<i>n</i> -Bu	72	28	73
CH ₃ (CH ₂) ₃ CH ₂	72	16	12	..	73
CH ₃ (CH ₂) ₂ CHCH ₃	0	88	12	..	73
Et ₂ CH	0	43	57	..	73
CH ₃ (CH ₂) ₆ CH ₂	76	14	8	2	73
CH ₃ (CH ₂) ₅ CHCH ₃	0	45	36	19	73
CH ₃ (CH ₂) ₄ CHEt	0	36	37	27	73
<i>n</i> -BuCH- <i>n</i> -Pr	0	8	28	64	73

Carbonium-ion formation is presumably facilitated by the electrophilic character of boron in the halogeno esters and, as in the example of nitrous deamination (105, 184), *n*-alkyl groups (*n*-Pr, *n*-Bu, *n*-pentyl, *n*-octyl) rearrange to give secondary alkyl halides (72, 73).

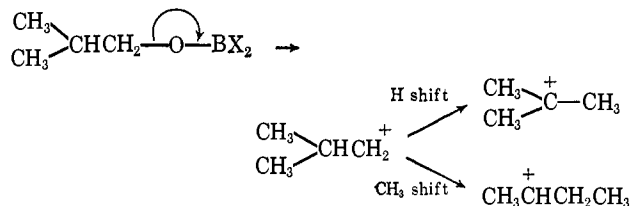


Only hydrogen migration occurs with straight-chain alkyl groups; the *sec*-alkyl systems, although readily rearranging among themselves, do not give *n*-alkyl



halides. Rearrangement among the octyl isomers is similar.

The branched isobutyl dichloroborinate decomposes with both hydrogen and methyl shift (as in the example nitrous deamination), the product containing *t*-butyl chloride (75%), *sec*-butyl chloride (>20%), and isobutyl chloride (<5%). Isobutyl dibromoborinate similarly gives *t*- (74%), *sec*- (>21%), and iso- (<5%) butyl bromides.



Dialkyl chloroboronates decompose similarly, but yield a slightly lower proportion of rearranged product (see Table V). This is to be expected, as electron donation to boron from each oxygen will be less than in the monoalkyl esters.

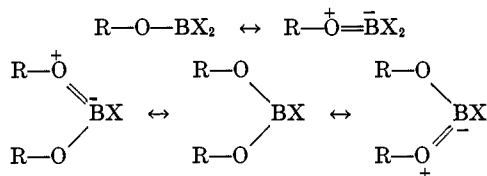
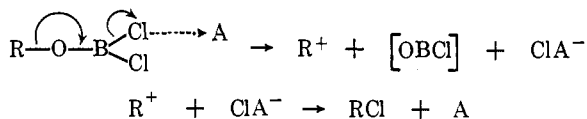


TABLE V

DECOMPOSITION OF DIALKYL CHLOROBORONATES

R in (RO) ₂ BCl	Temp., °C.	% isomers in product				Ref.
		n-	sec-	i-	t-	
n-Bu	155	85	15	0	0	73
i-Bu	200	0	7	11	82	73

All the above rearrangements were increased by the presence of acid catalysts (AlCl₃, FeCl₃, or TiCl₄) which are believed to function as follows.

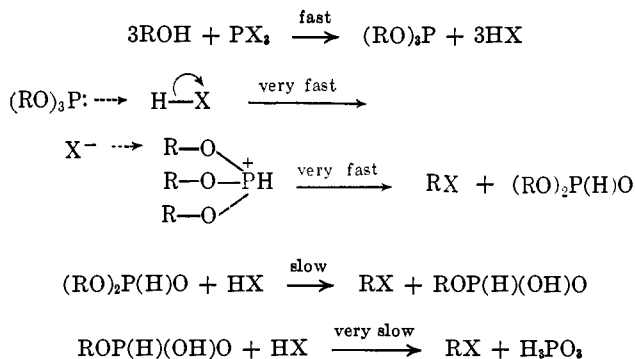


Boron trichloride however reduced the rate of reaction.

D. PHOSPHORUS SYSTEMS

1. Phosphorus Halide-Alcohol Reactions

Whereas the interaction of phosphorus trichloride or tribromide with primary normal alcohols affords isomerically pure alkyl halides (31, 32), the preparation of secondary alkyl halides by the use of these reagents has always presented difficulties although *sec*-butyl alcohol has been converted to the bromide without rearrangement as shown by isotopic labeling with ¹⁴C (160, 165). Rearrangement of 2- and 3-pentanol, however, occurs under normal preparative conditions (26, 135, 156, 157) with phosphorus tribromide or pentabromide, to afford mixtures of 2- and 3-bromopentanes (containing 5-30% rearranged isomer according to procedure), and with phosphorus pentachloride, *sec*-isoamyl alcohol gives *t*-amyl chloride (180, 193). Heated under reflux with phosphorus tribromide, neopentyl alcohol gives rearranged bromides, but if sufficient quinoline to remove free hydrogen bromide is added, then pure neopentyl bromide is said to be obtained (168, 169). It has been shown (61) that in the interaction of alcohols with phosphorus tribromide or chloride, the alkyl halide is formed in a stepwise series of dealkylations of the intermediate trialkyl phosphite by hydrogen halide, thus



More recent examination of these reactions by the use of gas chromatography has shown that the rearranged *sec*-alkyl halides arise only in the third very slow dealkylation of the monoalkyl dihydrogen phosphite, a reaction thought therefore to proceed at least in part by an ionic (S_N1) mechanism (31, 32). Isolation of the alkyl halide produced only in the first very rapid dealkylation is achieved by passing a rapid stream of carbon dioxide through the reaction mixture at -10° in order to carry away excess of hydrogen halide and/or immediate quenching in iced water. Isomerically and (apparently) optically pure *sec*-alkyl halides are thus obtained. The 2- and 3-chloro- and -bromopentanes, and 2-chloro- and -bromooctanes have been so prepared in a pure state. Although the slow second dealkylation also gives isomerically and optically pure products, overlap with the third dealkylation always gives rise to the presence of rearranged halides if the reaction is allowed to proceed too far beyond the first dealkylation stage. From octan-2-ol, some 3-bromooctane and a trace of 4-bromooctane are thus formed.

It has not been possible to obtain isobutyl halides free of *t*-butyl isomers by the reaction of isobutyl alcohol with either phosphorus trichloride or phosphorus tribromide, although the rearrangement again occurs mainly in the third dealkylation (Cl, 28%; Br, 10%). In earlier work (158) phosphorus trichloride in the presence of zinc chloride gave both iso- and *t*-butyl chlorides together with polymerized butylenes.

Results are similar in alcohol-phosphorus triiodide reactions, but some loss in optical purity (although not rearrangement) of 2-iodooctane occurs in the first dealkylation, possibly because of the ease of racemization of the product by free hydrogen iodide. Rearrangement of the isobutyl group (<1%) is noticed only in the third dealkylation.

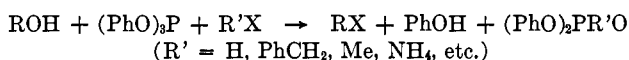
2. Triphenyl Phosphite-Alkyl (or Hydrogen) Halide-Alcohol Reactions

An extension of the phosphorus trihalide-alcohol reaction is that in which an alcohol is treated with a hydrogen halide, or certain other halides (NH₄Cl, Ph-CH₂Br, CH₃I, etc.), in the presence of triphenyl phosphite (101).

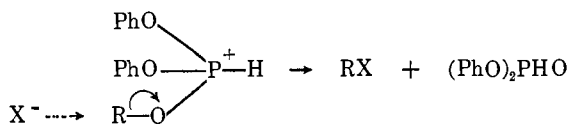
TABLE VI
DEALKYLATION OF *sec*-ALKYL PHOSPHITES BY HYDROGEN HALIDES
(32)

R in (RO) ₂ P	X in HX	Dealkylation step	-% isomers in product		
			2-	3-	4-
CH ₃ (CH ₂) ₂ CHCH ₃	Cl	1	100	0	..
		2	100	0	..
		3	78	22	..
CH ₃ (CH ₂) ₂ CHCH ₃	Br	1	100	0	..
		2	100	0	..
		3	67	33	..
CH ₃ (CH ₂) ₂ CHCH ₃	I	1	100	0	..
		2	100	0	..
		3	74	26	..
Et ₂ CH	Cl	1	0	100	..
		2	0	100	..
		3	3	97	..
Et ₂ CH	Br	1	0	100	..
		2	0	100	..
		3	35	65	..
Et ₂ CH	I	1	0	100	..
		2	0	100	..
		3	28	72	..
CH ₃ (CH ₂) ₅ CHCH ₃	Cl	1	100	0	0 ^a
		2	100	0	0 ^a
		3	93	6	1 ^b
CH ₃ (CH ₂) ₅ CHCH ₃	Br	1	100	0	0 ^a
		2	100	0	0 ^a
		3	75	23	2 ^b
CH ₃ (CH ₂) ₅ CHCH ₃	I	1	100	0	0 ^b
		2	100	0	0 ^b
		3	78	22	Trace ^b

^a Optically pure. ^b Some loss in optical purity.



Isomerically pure neopentyl iodide is stated to be obtained by this route, using triphenyl phosphite and methyl iodide, although later workers have differed in their reports on this. By infrared analysis, 6% rearrangement to *t*-amyl iodide was detected (100), although n.m.r. analysis indicated isomeric purity (96). N.m.r. analysis further indicated that triphenyl phosphite-benzyl bromide afforded pure neopentyl bromide, but that with the benzyl chloride, *ca.* 50% rearrangement to the tertiary isomer occurred (96). In the latter case the use of neopentyl-1-¹³C alcohol indicated that a simple methyl shift occurs; 1,3-shifts, protonated cyclopropanes, or hydrogen-bridged ions are not involved. A quasi-phosphonium salt may first be formed, *e.g.*, (PhO)₃PHI⁺, and exchange of one phenoxy group for alkoxy leads to a reaction system corresponding to the first-stage phosphite dealkylation described in the foregoing.

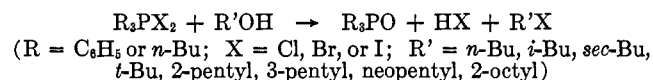


By the use of HCl, isomerically pure *n*-butyl, 2- and 3-pentyl, and 2-octyl chlorides are obtained (74), as

shown by g.l.c. analysis, the 2-octyl chloride being optically pure ($\alpha^{18D} + 30.15^\circ$ from 2-octanol $\alpha^{18D} - 7.96^\circ$) ($l = 1$) (31, 74). Neopentyl alcohol gave, however, a large proportion of *t*-amyl chloride. Hydrogen bromide or iodide afford mixtures of the 2- and 3-halogenopentanes from 2- or 3-pentanol. Isomerically pure 2-iodopentane is obtainable by the interaction of 2-pentanol with triphenyl phosphite-methiodide, although rearrangement can occur, according to reaction conditions (74).

3. Triphenylphosphine Dihalide-Alcohol Reactions

A reaction system which is also claimed to afford isomerically pure alkyl halides in high yield involves the use of triphenylphosphine dihalides (188).



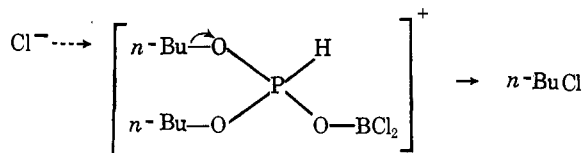
IV. INTERACTIONS OF INORGANIC ESTERS WITH COVALENT HALIDES

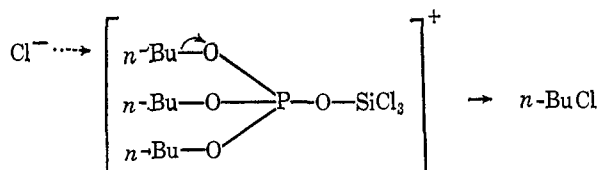
Two main types of reaction can be distinguished: (a) mutual exchange of halogen and alkoxy groups leading to the formation of halogeno esters which in certain cases may undergo further decomposition to yield alkyl halides, and (b) reactions involving more direct alkyl halide elimination and leading to the formation of mixed anhydride polymers.

A. ALKYL PHOSPHITES AND PHOSPHATES

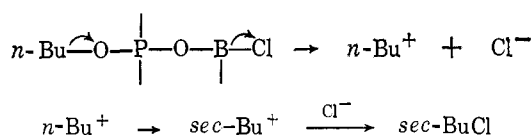
Whereas trialkyl phosphites undergo mixed mutual replacement reactions with boron trichloride (79) or silicon tetrachloride (67), no alkyl halide being formed, the dialkyl hydrogen phosphites (RO)₂PHO, trialkyl phosphates (RO)₃PO, and dialkyl phosphonates, (RO)₂PR'O, react with halides such as BCl₃, SiCl₄, TiCl₄, with subsequent elimination of alkyl halide, slowly at room temperature and then further on heating, to yield polymers containing P-O-M linkages (M = B, Si, Ti, etc.) (7, 34, 52, 53, 64, 66, 75). The alkyl halide may, or may not, be rearranged, depending on the mechanism of the reaction.

At 20°, isomerically pure *n*-alkyl halides (*n*-Pr, *n*-Bu) are obtained from the dialkyl hydrogen phosphite complexes with boron trichloride (7), silicon tetrachloride (75), and titanium tetrachloride (53), from the trialkyl phosphate complexes with boron trichloride (64, 65), boron tribromide (48), silicon tetrachloride (52, 75), and titanium tetrachloride (53), and from the reaction of di-*n*-butyl *n*-butylphosphonate with phenylboron dichloride (34). The reaction mechanisms indicated are





At higher temperatures, some rearrangement to *sec*-alkyl, and possibly *t*-alkyl groups, suggests that carbonium-ion intermediates may also be involved. Iso-



butyl esters are slow to react and give both iso- and tertiary halides. Trineopentyl phosphate reacted slowly with boron trichloride, but at 120–300° gave *t*-amyl chloride (66).

TABLE VII

R in (RO) ₂ PHO	Halide	Temp., °C.	Composition R, %	Ref.
<i>n</i> -Bu	BCl ₃	100–300	<i>n</i> -Bu 98; <i>sec</i> -Bu 2	75
<i>n</i> -Bu	TiCl ₄	100–200	<i>n</i> -Bu 50; <i>sec</i> -Bu 50	53

TABLE VIII

R in (RO) ₂ PO	Halide	Temp., °C.	Composition R, %	Ref.
<i>n</i> -Bu	BCl ₃	120–180	<i>n</i> -Bu 94; <i>sec</i> -Bu 6	65
<i>n</i> -Bu	BCl ₃	320	<i>n</i> -Bu 85; <i>sec</i> -Bu 10; <i>t</i> -Bu 5	75
<i>n</i> -Bu	SiCl ₄	200–300	<i>n</i> -Bu 98; <i>sec</i> -Bu 2	75
<i>n</i> -Bu	TiCl ₄	100–200	<i>n</i> -Bu 91; <i>sec</i> -Bu 9	53
<i>n</i> -Pr	BCl ₃	120–180	<i>n</i> -Pr 73; <i>i</i> -Pr 27	65

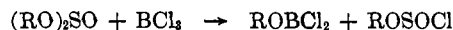
TABLE IX

	Halide	Temp., °C.	Composition R, %	Ref.
(<i>i</i> -BuO) ₂ PHO	BCl ₃	120	<i>i</i> -Bu 35; <i>t</i> -Bu 65	7
(<i>i</i> -BuO) ₂ PHO	BCl ₃	230	<i>i</i> -Bu 20; <i>t</i> -Bu 80	7
(<i>i</i> -BuO) ₂ PHO	TiCl ₄	100–200	<i>i</i> -Bu 93; <i>t</i> -Bu 7	53
(<i>i</i> -BuO) ₂ PO	BCl ₃	20–120	<i>i</i> -Bu 76; <i>t</i> -Bu 24	65
(<i>i</i> -BuO) ₂ PO	BCl ₃	120–180	<i>i</i> -Bu 47; <i>t</i> -Bu 47; <i>n</i> -Bu (?) 6	65
(<i>i</i> -BuO) ₂ PO	SiCl ₄	130	<i>i</i> -Bu 95; <i>t</i> -Bu 5	52
(<i>i</i> -BuO) ₂ PO	TiCl ₄	100–120	<i>i</i> -Bu 52; <i>t</i> -Bu 48	53

Although pure isopropyl halides are obtained from diisopropyl hydrogen phosphite and boron trichloride at 20–300° (7), and from triisopropyl phosphate and silicon tetrachloride at 85° (52), *sec*-alkyl groups having alternative secondary structures are susceptible to rearrangement. With boron trichloride at 20°, the trialkyl phosphates (R = 2- or 3-pentyl) gave mixtures of 2- and 3-chloropentanes, and the (+)-2-octyl system lost some rotatory power. With silicon tetrachloride, however, optically and isomerically pure 2-chlorooctane was obtained from the phosphate at 23°, although at 100° rearrangement to 3- and 4-chlorooctanes occurred (75).

B. ALKYL SULFITES AND SULFATES

With boron trichloride, the dialkyl sulfites undergo mixed mutual exchange reactions (27).



Dialkyl sulfates, however, afford mixed anhydride polymers and alkyl chlorides in which the alkyl group is largely rearranged (27) (see Table X).

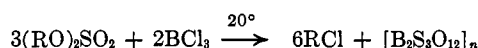


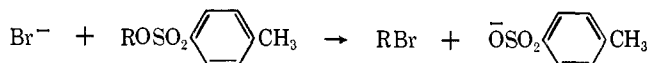
TABLE X

R in (RO) ₂ SO ₂	Composition R in RCl, %
<i>n</i> -Pr	<i>n</i> -Pr 3; <i>i</i> -Pr 97
<i>n</i> -Bu	<i>n</i> -Bu 4; <i>sec</i> -Bu 96
<i>n</i> -Bu ^a	<i>n</i> -Bu 15; <i>sec</i> -Bu 85
<i>n</i> -Octyl ^a	<i>sec</i> -Octyl present

^a In *n*-pentane solution.

C. ALKYL SULFONATES AND SULFINATES

The method of alkyl halide preparation by displacement of a *p*-toluenesulfonyl group by halide ion has been shown to afford rearranged *sec*-alkyl bromides unless strictly anhydrous conditions are adhered to (26).



Pure anhydrous dimethylformamide or dimethyl sulfoxide are recommended as reaction media for the preparation of pure isomers. In "technical" dimethyl sulfoxide, 3-amyl tosylate gave a product containing 2-bromopentane (10%), and the addition of water to purified dimethyl sulfoxide also caused formation of 8% of the 2-isomer.

Neopentyl *p*-toluenesulfonate is reported to yield only neopentyl iodide by treatment with sodium iodide (10).

Interactions of boron trichloride with alkyl alkane- and arenesulfonates (28) or sulfinates (48, 49) afford rearranged halides (see Table XI).

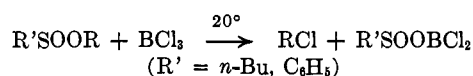
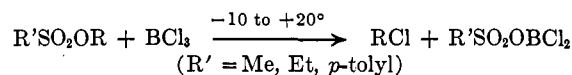


TABLE XI

Ester	Composition of R in RCl, %	Ref.
<i>p</i> -CH ₃ C ₆ H ₄ SO ₂ O- <i>n</i> -Pr	<i>n</i> -Pr 16; <i>i</i> -Pr 84	28
CH ₃ SO ₂ O- <i>n</i> -Bu	<i>n</i> -Bu 11; <i>sec</i> -Bu 89	28
C ₂ H ₅ SO ₂ O- <i>n</i> -Bu	<i>n</i> -Bu 15; <i>sec</i> -Bu 85	28
C ₆ H ₅ SO ₂ O- <i>n</i> -Bu	<i>n</i> -Bu 14; <i>sec</i> -Bu 86	28
<i>p</i> -CH ₃ C ₆ H ₄ SO ₂ O- <i>n</i> -Bu	<i>n</i> -Bu 15; <i>sec</i> -Bu 85	28
CH ₃ SO ₂ O- <i>sec</i> -Bu	<i>sec</i> -Bu 100	28
CH ₃ SO ₂ O- <i>i</i> -Bu	<i>t</i> -Bu 86; <i>i</i> -Bu + <i>sec</i> -Bu 14	28
CH ₃ SO ₂ O-2-Oct	2-Oct 36; 3-Oct 36; 4-Oct 28	28
<i>n</i> -Bu SOO- <i>n</i> -Bu	<i>n</i> -Bu 65; <i>sec</i> -Bu 35	48
<i>n</i> -Bu SOO- <i>i</i> -Bu	<i>t</i> -Bu 62; <i>i</i> -Bu + <i>sec</i> -Bu 22; <i>n</i> -Bu (?) 16	48
C ₆ H ₅ SOO- <i>n</i> -Bu	<i>n</i> -Bu 50; <i>sec</i> -Bu 50	49

Similarly at 20°, the reaction with *n*-butyl dichloroborate, $p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{O-}n\text{-Bu} + n\text{-BuOBCl}_2 \rightarrow 2\text{BuCl} + (p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{OBO})_2$, gives butyl chlorides containing 88% of the secondary isomer (28).

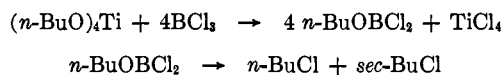
Alkyl chlorosulfates, ROSO_2Cl , react readily with titanium tetrachloride at 20°, to give alkyl halide in which the alkyl group is largely rearranged, indicative of a carbonium in mechanism (Table XII). A polymeric residue is obtained (50).

TABLE XII

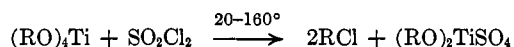
R in ROSO_2Cl	Composition R in RCl , %
<i>n</i> -Pr	<i>n</i> -Pr 13; <i>i</i> -Pr 87
<i>n</i> -Bu	<i>n</i> -Bu 7; <i>sec</i> -Bu 93

D. ALKYL TITANATES

The reaction of tetra-*n*-butoxy titanate with boron trichloride gives both *n*- (25%) and *sec*- (75%) butyl chlorides (62). It is probable that a mixed mutual exchange reaction first yields *n*-butyl dichloroborate, which is catalytically decomposed by titanium tetrachloride.



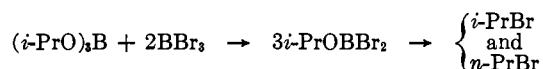
With sulfuryl chloride, alkyl halide is formed as follows (51).



Rearrangement of the *n*-butyl group to *sec*-butyl is only ca. 1% in this case, while almost pure *n*-propyl chloride is obtained from the *n*-propyl titanate. With two molecular proportions of sulfuryl chloride, however, 3 moles of butyl chloride are obtainable, and ca. 10% rearrangement occurs.

E. ALKYL BORATES

Reaction of tri-*n*-butyl borate with hydrogen chloride or hydrogen bromide at 100–120° yields 0.8–0.9 mole of isomerically pure *n*-butyl halide. With boron halides, the borates form halogeno esters (78), which generally decompose as described earlier under the boron halide-alcohol section, to give similar amounts of rearranged isomers (73). An exceptional rearrangement is observed in the interaction of triisopropyl borate with boron tribromide, in that *n*-propyl bromide (8%) is obtained (73). Surprisingly, the direct interaction of iso-



propyl alcohol with boron tribromide gives only isopropyl bromide, and boron trichloride affords only isopropyl chloride with either isopropyl borate or isopropyl alcohol (73).

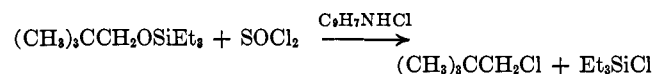
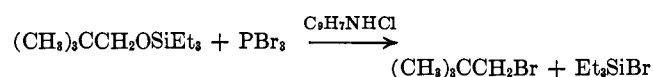
TABLE XIII

REACTIONS OF ALKYL BORATES WITH BORON HALIDES

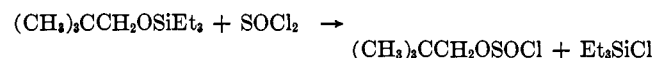
R in $(\text{RO})_3\text{B}$	X in BX_3	-% isomers in product—				Ref.
		1-	2-	3-	4-	
<i>i</i> -Pr	Cl	0	100	73
<i>i</i> -Pr	Br	8	92	73
$\text{CH}_3(\text{CH}_2)_5\text{CHCH}_3$	Cl	0	58	37	5	73
$\text{CH}_3(\text{CH}_2)_5\text{CHCH}_3$	Br	0	63	30	7	73

F. SILICON ESTERS

Neopentyl bromide and chloride are reported to be prepared without rearrangement from triethylneopentoxysilane, by heating under reflux with phosphorus tribromide or thionyl chloride, respectively, in the presence of quinoline hydrochloride (168, 169). It has been



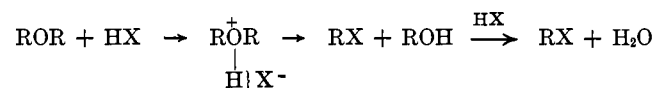
shown, however, that the silane and thionyl chloride alone give neopentyl chlorosulfite (81, see also ref. 44)



and that the latter undergoes decomposition at 100° in the presence of quinoline hydrochloride to give both neo- and *t*-pentyl chloride (81). The latter is removed by prolonged washing with 2 *N* nitric acid.

V. ETHER FISSION

Ether fission by hydrogen or boron halides results in the formation of alkyl halides, the first step in the process probably being coordination of the ether oxygen. Rearrangement of a 2-pentyl ether in reaction with hydrogen bromide to yield 2- and 3-bromopentanes has

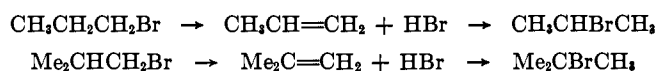


been reported (20), although it is not clear whether the isomerization occurs during the fission, or after formation of the bromide. Rearrangement of a *n*-alkyl group (*n*-Bu) has also been demonstrated recently (22) in the fission of di-*n*-butyl ether with boron trichloride. Rearrangement will clearly occur as a result of the final dihalogenoborate decomposition, although there is strong evidence that the initial fission occurs with some rearrangement too.

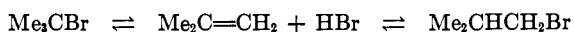
VI. ISOMERIZATION OF ALKYL HALIDES

Aronstein, who observed the rearrangement of *n*-propyl to isopropyl bromide in a sealed tube at 280° (3, 4), thought that both this and the previously re-

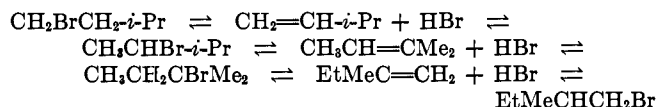
ported rearrangement of iso- to *t*-butyl bromide under similar conditions (39) proceeded by the intermediate formation of olefin and hydrogen bromide, which then recombined according to Markownikoff's rule. Subsequently Favorskii showed the reverse processes to be



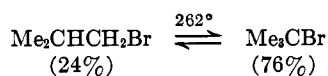
possible, implying the occurrence of some anti-Markownikoff addition (42). Prolonged heating of isopropyl bromide at 250° gave partial conversion into *n*-propyl bromide, and the following equilibria involving iso- and *t*-butyl bromides were postulated to exist at 210–220°. Similarly, the isomerization of isoamyl bromide re-



ported (39) to afford *t*-amyl bromide at 256–260° was shown to give other isomers. At 220° the following equilibria, which in part contravene both Markownikoff's and Saytzeff's rules, were necessary to account for all the halides isolable if olefin intermediates were involved. A number of dibromo derivatives behaved similarly (42).



More detailed investigation of the above isomerizations (116–119) showed that direct intramolecular rearrangement, rather than dissociation, appeared more likely. Isobutyl chloride showed little sign of rear-



angement in 3 hr. at 262°, but slowly increasing rearrangement was observed at 306° (117).

In the gas phase isomerization of isobutyl bromide, side reactions may give isobutene and hydrogen bromide, which through recombination afford either predominantly *t*-butyl bromide or an equilibrium mixture, depending on the presence or absence of traces of unidentified catalytic materials (8, 19).

More recent investigations of the propyl isomerization also show that the equilibrium mixture of *n*- and isopropyl bromides can be reached from either side by heating the chosen isomer in a sealed tube. Refractive index measurements indicated the following equilibrium compositions (11)

	<i>n</i> -Propyl, %	Isopropyl, %
250°; 100 hr.	30	70
275°; 36 hr.	33	67

while infrared analysis showed $52 \pm 0.1\%$ *n*-propyl bromide to be present at equilibrium in the gas phase at 250°, from which various physico-chemical constants were calculated (2). *n*-Propyl chloride did not, however,

isomerize in 96 hr. at 200–210°, or 250° (11). The secondary and tertiary halides (*e.g.*, propyl and butyl) are reported to isomerize to the corresponding primary halides at 350°F. or higher under 200 p.s.i. (131).

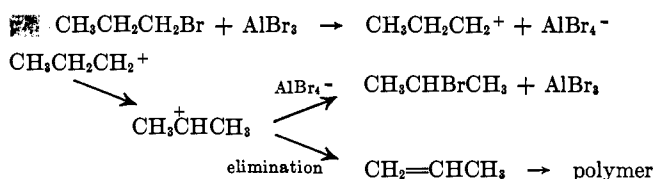
In the aforementioned systems the operation temperatures are much higher than those prevailing in the systems discussed in the previous sections.

Lewis acids isomerize many alkyl halides and give rise to olefins and polymeric by-products. *n*-Propyl bromide was first converted into isopropyl bromide by the action of aluminum bromide, either on boiling (97) or at room temperature (86), while both this and *n*-propyl chloride are isomerized to the isopropyl halides in the vapor phase over aluminum chloride-silica gel mixtures (125). The degree of isomerization of *n*- to isopropyl chloride (33), or of *n*- to *sec*-butyl chloride (72) by aluminum chloride in the liquid phase, depends upon the proportions of reactants used, as deactivation of the catalyst is apparently caused by the polymeric by-products. With a 0.5 molar concentration of aluminum chloride, formation of hydrocarbon by-products is high and from *n*-butyl chloride some tertiary halide is obtained in addition to the main product, *sec*-butyl chloride (72).

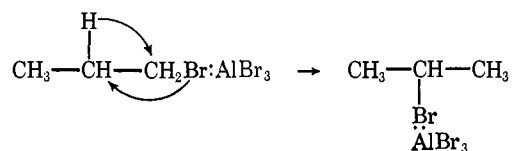
Isomerization of chloroalkanes (*e.g.*, *n*-propyl chloride to give isopropyl chloride, and isobutyl chloride to give *t*-butyl chloride) by both aluminum and boron halides, and of primary, secondary or tertiary alkyl halides by fluorine-containing catalysts, has been the subject of various patent claims (29, 130). Isobutyl chloride has also been isomerized to *t*-butyl chloride by catalytic dehydrochlorination, followed by recombination of the isobutene and hydrogen chloride in contact with alumina below 150° (129).

Boron trichloride does not affect *n*-butyl chloride under reflux or in a sealed tube at 100° (3 hr.), but at 225° (5 hr.) gives *sec*-butyl (2.5%) and *t*-butyl (1%) chlorides (75).

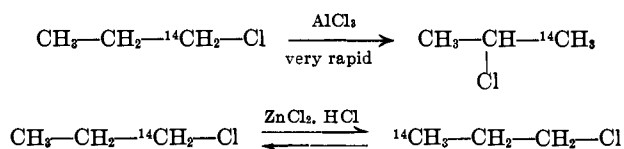
Rearrangement can be explained on the basis of a carbonium-ion mechanism.



An intramolecular mechanism is, however, equally feasible, the carbon-bromine bond being weakened, though not completely ionized, by the aluminum bromide (17).

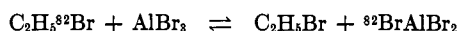


Different degrees of freedom of the carbonium intermediates possible are indicated by the rapid isomerization of *n*-propyl-1-¹⁴C chloride to isopropyl chloride, by aluminum trichloride, whereas zinc chloride and hydrogen chloride cause only isotope position isomerization by a 1,3-hydrogen shift (*cf.* nitrous deamination) (144).

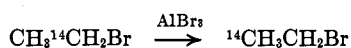


Zinc chloride alone does not isomerize *n*-butyl chloride under reflux (72), although secondary halides such as 2- and 3-chloropentanes readily equilibrate on shaking with ZnCl₂ + HCl at room temperature (182).

Bromine exchange between ethyl and aluminum bromides in nitrobenzene, diethyl ether, or acetonitrile is extremely slow because of complex formation, and in carbon disulfide the kinetics (third order: rate ∝ [Et-Br][AlBr₃]²) are interpreted as indicating that there is no carbonium-ion formation (164).

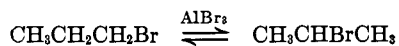


A study of the rearrangement of ethyl bromide-1-¹⁴C by aluminum bromide, in the presence of deuterium bromide, further shows that elimination to give hydrogen bromide and ethylene, followed by re-addition, is not involved (163).



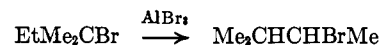
The isomerization of *n*-propyl to isopropyl chloride by aluminum chloride (practically complete in 1 hr. at 0°; 60–75% in 5 min.) is also shown to occur without appreciable elimination and recombination of hydrogen chloride. Thus, in the presence of deuterium chloride, the isopropyl chloride formed contains no deuterium, although propylene and deuterium chloride combine under similar conditions (124).

Rearrangement generally proceeds from normal to secondary, or secondary to tertiary structures, although there are some exceptions. Equilibrium mixtures of *n*- and isopropyl bromides result on heating either isomer under reflux with aluminum bromide (0.02 mole). By infrared measurement, 1.3% of the *n*-propyl



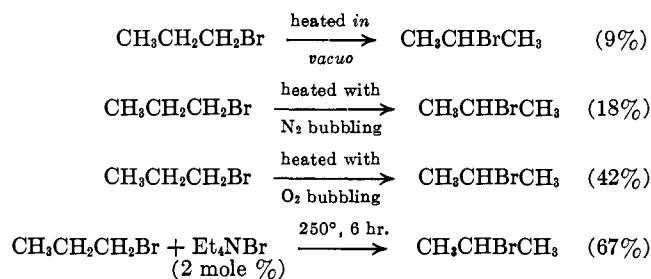
isomer was shown to be present after 6 hr. (2), while by gas-liquid chromatography 2% was detected (73). Isopropyl bromide also gave *n*-propyl bromide (3%) after 24 hr. at 20° in contact with aluminum bromide (0.1 mole) (73). Although *n*-propyl chloride, *n*-butyl chloride, and *n*-butyl bromide all yield the secondary isomers on heating with the corresponding aluminum halides, rearrangement is not found to be reversible in

these examples (73). *t*-Amyl bromide is isomerized to *sec*-isoamyl bromide by aluminum bromide (6).



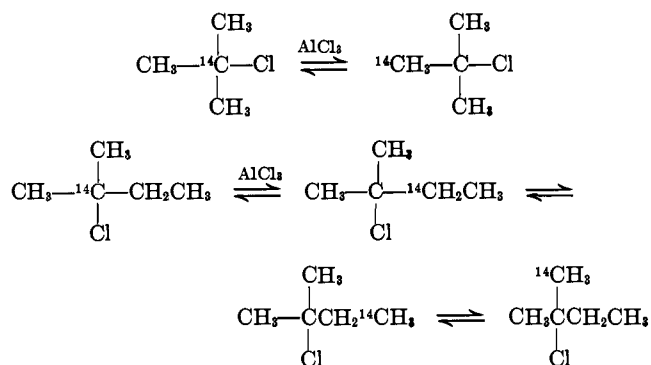
The presence of oxygen is apparently important in the isomerization of propyl bromides and was studied alongside the effect of certain bromides (112). Rearrangement by loss and subsequent re-addition of hydrogen bromide was thought to occur in these systems by two mechanisms: (i) nonchain, accelerated by bromide salts and retarded by removal of hydrogen bromide, and (ii) atom-chain, accelerated by oxygen and inhibited by antioxidants.

Thus *n*-propyl bromide gave 9–30% isopropyl bromide when heated for 6 hr. at 250° in the absence of air, but in its presence 11–25% more rearrangement occurred.

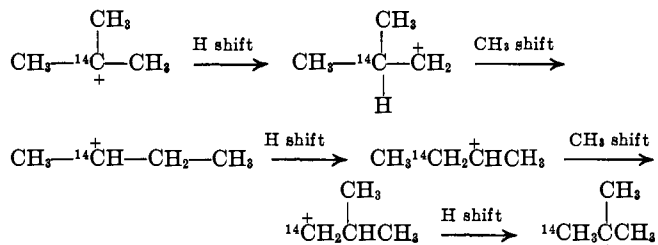


Mercuric bromide and di-*n*-butylamine were only slightly less effective than tetraethylammonium bromide; lithium bromide had no effect. The equilibrium composition (67% isopropyl bromide, at 250°) was reached after 139 hr. in the absence of catalysts, after 36 hr. in air, and after 12 hr. in the presence of tetraethylammonium bromide. Iso- and *t*-butyl chlorides did not rearrange in 6 hr. at 250°, but underwent 10% rearrangement in 7 hr. at 300°, and 26% in 15 hr. Tetraethylammonium chloride (3 mole %) increased this to 78% in 7 hr. at 300°.

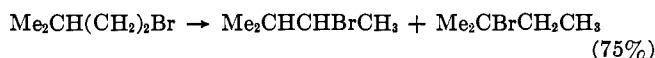
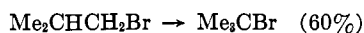
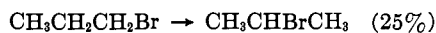
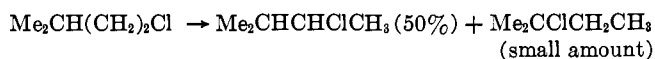
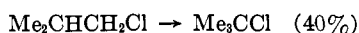
Rearrangement of an isotopically labeled carbon atom within the *t*-butyl and *t*-amyl groupings appears to proceed as follows (147, 148).



The changes are interpreted as involving a series of hydride and methyl shifts in carbonium intermediates (not necessarily completely free ions), *e.g.*

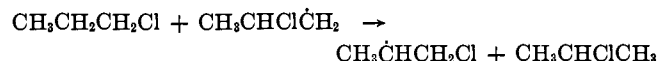
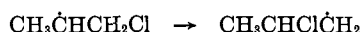


Other inorganic halides which affect the isomerization of alkyl groups are of the type MCl_2 ($\text{M} = \text{Ba}, \text{Ni}, \text{Co}, \text{Fe}, \text{Cd}, \text{Pb}$) but not the type MCl ($\text{M} = \text{Ag}, \text{Na}, \text{K}$). At 300° , decomposition of alkyl chlorides ($\text{Et}, \text{Pr}, i\text{-Bu}, i\text{-Am}$) to hydrogen chloride and olefins may be followed by recombination; *e.g.*, isobutyl chloride gives *t*-butyl chloride. Alkyl bromides behave similarly with salts MCl_2 or MBr_2 , and iodides with MI_2 . Chromic chloride has no effect on alkyl chlorides at 300° (152). At 250° in sealed tubes, anhydrous barium or thallium chloride isomerize primary alkyl chlorides and bromides to the secondary or tertiary isomers (153).

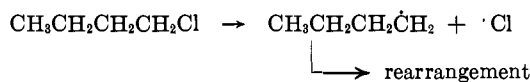


Isomerization of isobutyl iodide to the tertiary halide under the influence of ultraviolet light was reported (40). *n*-Propyl iodide likewise gave isopropyl iodide by photolysis (2537-Å. Hg line), a reaction which has been explained in terms of either a "hot-radical" intermediate or the intermediacy of propylene and hydrogen iodide (120, 121).

The isomerization of *n*-propyl chloride by γ -radiolysis (^{60}Co source) is thought to involve the following free-radical mechanisms (189, 190), and similarly the forma-



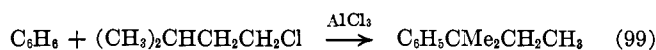
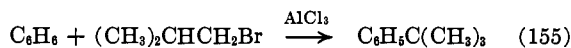
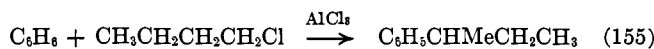
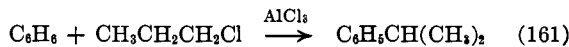
tion of *sec*- and isobutyl chlorides from *n*-butyl chloride by the action of γ -rays probably occurs with free-radical intermediates (36). Under the influence of n, γ ac-



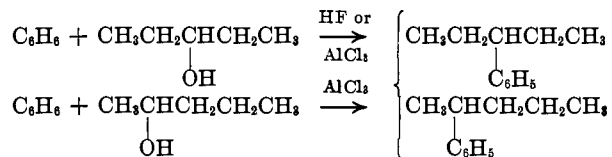
tivation *n*-, *sec*-, *iso*-, and *t*-butyl bromides all undergo isomerization by bromine shift in addition to other side reactions (124), while both *n*- and isopropyl bromides isomerize under neutron radiation. The rearrangement *iso*- to *n*-propyl bromide occurs with high probability in epithermal reactions (47).

VII. FRIEDEL-CRAFTS ALKYLATION

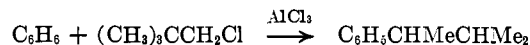
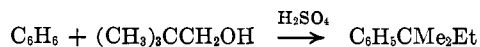
Shortly after the discovery of the alkylation of aromatic compounds by alkyl halides in the presence of aluminium halides (56-58), Gustavson found that *n*-propyl bromide afforded isopropylbenzene when added to benzene in the presence of aluminum tribromide (85). At low temperatures (-2°), *n*-propylbenzene could also be obtained (87). Before the turn of the century many similar rearrangements had been reported (see, *e.g.*, ref. 99, 155, 161). In the vast number of



alkylations studied subsequently (132), in which alkyl halides, alcohols, and ethers, etc., are used, in the presence of a large variety of Lewis acid catalysts ($\text{AlCl}_3, \text{AlBr}_3, \text{BF}_3, \text{TiCl}_4, \text{ZnCl}_2, \text{FeCl}_3, \text{HF}, \text{H}_2\text{SO}_4$), it has been seen that the rearranged product is invariably that which would be expected if olefin intermediates were involved. Thus, in general, primary alkyl groups give primary or secondary alkylbenzenes, secondary give only secondary, *iso*- give tertiary, and tertiary may give either tertiary or secondary alkylbenzenes depending upon the nature of the particular alkyl group and reaction conditions (82, 132). Secondary groups such as 2- or 3-pentyl rearrange to the alternative secondary structure (133).



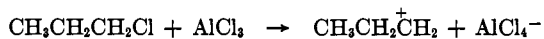
The neopentyl group rearranges to *t*-amyl or *sec*-isoamyl, although if aluminium chloride is used with



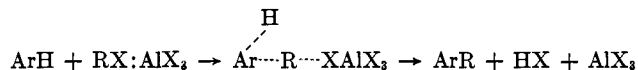
neopentanol, a 9% yield of neopentylbenzene is said to be obtained (136).

It should be stressed that in most cases, mixtures of varying proportions of rearranged and unrearranged products are obtained, depending upon reaction conditions (15).

There has been considerable controversy as to the mechanism of Friedel-Crafts reactions. Although olefins do alkylate benzene, it is not generally accepted that they are necessary intermediates in the rearrangement process. A carbonium-ion mechanism will also explain the results, although there is considerable evidence which points to the operation of a con-



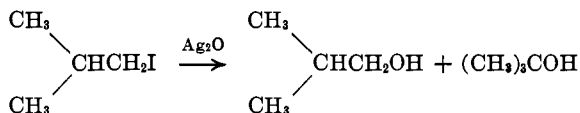
certed bimolecular process (154). Brown considers the alkylation to be bimolecular for primary halides and to involve reaction of benzene with the undissociated alkyl halide-aluminum halide complex (15).



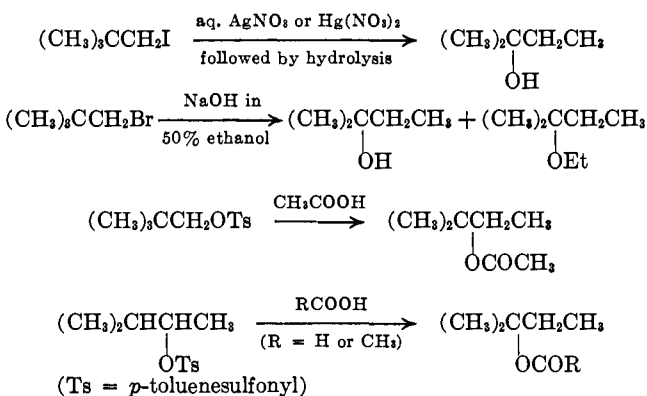
Rearranged product arises by prior rearrangement of the alkyl halide (see section VI), secondary halides then reacting by both S_N1 and S_N2 reactions, and tertiary halides by ionic reactions only. The reaction and its rearrangement products are considered in detail elsewhere (132).

VIII. SOLVOLYTIC REARRANGEMENTS

The hydrolysis of isobutyl iodide with moist silver oxide has long been known to afford both iso- and *t*-butyl alcohols (23, 108). Neopentyl halides may similarly give *t*-amyl products, the reaction being con-

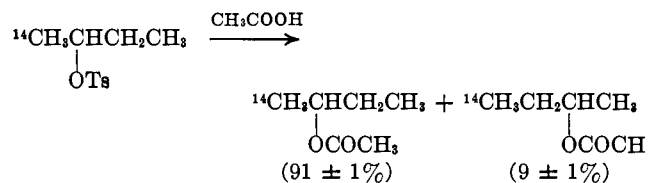


sidered to proceed *via* an intermediate carbonium ion (37). Similar rearrangements have been observed in the solvolysis of neopentyl *p*-toluenesulfonate with acetic acid (192), and of *sec*-isoamyl *p*-toluenesulfonate with either formic (46) or acetic acid (45).

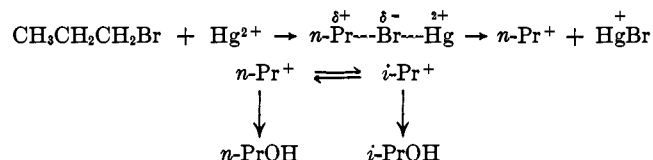


N.m.r. and mass spectral studies of neopentyl-1-¹³C and neopentyl-1,1-*d*₂ tosylates (96) indicate that simple methyl migration occurs (*cf.* nitrous deamination and phosphorus ester systems).

Reports of alkyl rearrangements involved in the solvolysis of a straight-chain alkyl compound are few in number, although the use of ¹⁴C has shown *ca.* 9% rearrangement of the *sec*-butyl group in the following reaction (145).



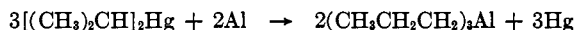
Rearrangement of the *n*-propyl group has also been noted in the mercury-catalyzed reaction of *n*-propyl bromide in aqueous formic acid, the following mechanisms being proposed (30).



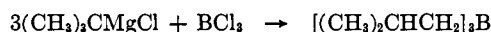
The solvolysis of (+)-2-bromooctane in 60% aqueous ethanol under conditions which cause considerable racemization has been considered (93) to proceed entirely by the S_N1 (the carbonium ion) mechanism; yet, surprisingly there are virtually no rearranged products (71).

IX. REACTIONS OF ORGANOMETALLIC OR ORGANOMETALLOID COMPOUNDS

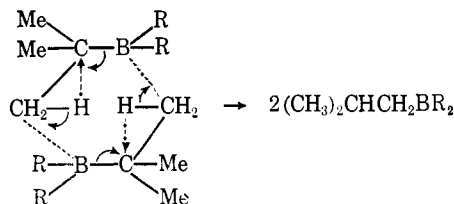
Alkyl rearrangement which accompanies the reaction of an organometallic or -metalloid compound is frequently in the opposite direction to that which occurs in a carbonium-ion system. Rearrangement from a secondary to primary, or tertiary to iso- structure, is observed. The reaction of diisopropylmercury with aluminum, for example, gives not only the isopropyl, but also the *n*-propyl derivative (137, 194).



Tri-*t*-butylboron is reported to be unobtainable (88-90, 122). From boron trichloride and *t*-butylmagnesium chloride only triisobutylboron was isolated, whereas with boron trifluoride, diisobutyl-*t*-

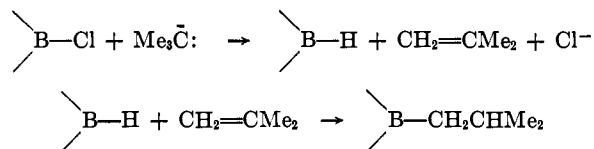


butylboron was the product. Distillation of the latter at atmospheric pressure (190°) causes isomerization to the triisobutyl compound, a rearrangement which may be depicted as a concerted bimolecular process. That only one *t*-butyl group may be attached to boron is



shown by the formation of diisobutyl-*t*-butylboron from the reaction of *t*-butyl magnesium chloride with BF₃, (MeO)₃B, *t*-BuBCl₂, or (*i*-Bu)₂BF. A carbanion mech-

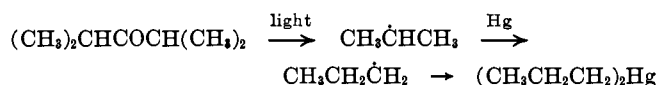
anism has also been postulated to account for the rearrangement (90), the second step being a process of



hydroboration (16). Steric factors may also be important. Tri-*sec*-butylboron can be prepared from *sec*-butylmagnesium bromide and boron trifluoride, but undergoes isomerization to tri-*n*-butylboron when heated under reflux (88). Similar isomerizations occur by the action of heat upon triisopropylboron (123), triisopropylaluminum (194), and tri-*sec*-butylaluminum (194), the corresponding normal isomers being formed.

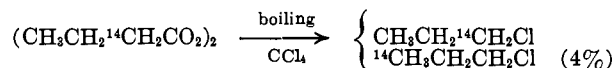
X. FREE-RADICAL REARRANGEMENTS

Rearrangement of the isopropyl radical during photolysis of diisopropyl ketone in the presence of mercury, affords di-*n*-propylmercury as follows (83). It is said that since the carbon free radical is less negative in the

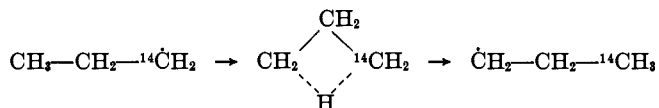


n-alkyl group than the iso group (5), tautomerism to the *n*-alkyl group is more likely in combination with a metal (electropositive) than with a halogen (electronegative).

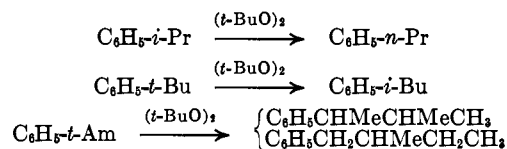
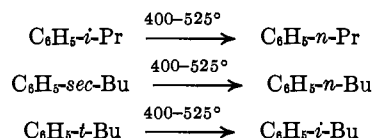
Although the free-radical decompositions of both the *n*- and isobutyryl peroxides in carbon tetrachloride under reflux yield unrearranged propyl chlorides (98), the use of carbon-14 demonstrates isotope position rearrangement in the case of the *n*-propyl compound (140, 142, 143).



A cyclic transition state may be involved in a 1,3-hydrogen shift as follows (139) and can be compared with the similar isotope position rearrangement observed in the *n*-propyl cation (141).



Isomerization of alkylbenzenes in an autoclave at 400–525° (166), or by distillation with 5% (*t*-BuO)₂ (134), probably occurs by a free-radical mechanism, the rearrangements being in the reverse order to those observed in carbonium-ion processes.



Certain other free-radical rearrangements are mentioned in section VI.

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