

Liquid Phase Halogenation with Metal Halides

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Recent studies on the liquid phase halogenation of alkanes, olefins, acetylenes, and arenes with metal or metalloidal halides are reviewed. Some characteristics in these halogenation, reactions, as compared with halogenation by molecular halogens, are mentioned.

Various kinds of halogenating agents have been employed to replace a hydrogen atom in paraffinic and aromatic hydrocarbons with a halogen atom, or to add a halogen molecule to unsaturated hydrocarbons, though certain choice of reagent depending on substrate would be necessary. Liquid phase halogenation of various hydrocarbons with metal or metalloidal halides, which are mostly used in the form of higher valency states, shows interesting features in many respects, particularly in selectivities. In this paper, several recent results on these halogenation reactions, including our data are reviewed concisely, placed an emphasis on comparisons between halogen and metal halide halogenation.

I. HALOGENATION OF OLEFINS AND ACETYLENES

Several metal and metalloidal halides (CuBr_2 , CuCl_2 , SbCl_5 , $\text{TiCl}_3 \cdot 4\text{H}_2\text{O}$, PCl_5 , AuCl_3 etc.) have been known to effect direct halogenation of olefins or acetylenes. Various examples are collected in Table 1. Some data relating to product distribution and stereochemistry are also summarized in Table 2.

Halogenation with CuX_2 ($\text{X} = \text{Br}, \text{Cl}$) is easily achieved in a homogeneous system using acetonitrile (with¹⁾ or without²⁾ LiX as solvent. Though other solvents such as alcohols^{1,3)} and acetic acid (with NaOAc)¹⁾ can be used effectively for this reaction, the formation of solvent-incorporated products is unavoidable owing to their high nucleophilicity. The reactivity of olefins toward CuX_2 suggests that this halogenation would be surely electrophilic. As for CuBr_2 , the reaction is completely stereospecific and *trans*; whereas in the case of less reactive CuCl_2 , the specificity is considerably sensitive to substrate structure and reaction medium.⁴⁾ In contrast to this, the addition of bromine or chlorine to simple olefins is known to be highly stereospecific. A predominant *trans*-1,4-adduct formation from butadiene and CuBr_2 would be interesting, since the fact is known that the halogenation with bromine molecule affords nearly equal amounts of 1,2- and *trans*-1,4-dibromides (as kinetically controlled products) in various solvents.⁵⁾

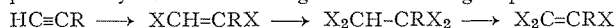
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Table 1. Halogenation of Olefins and Acetylenes with Metal and Metalloidal Halides

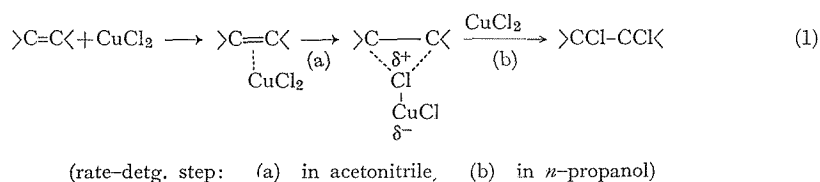
Olefin or Acetylene	Halide	Reaction Conditions	Product (Yield, %) ^a	Ref.
CH ₂ =CH-CH ₂ OH	CuBr ₂	in CH ₃ OH, 64°, 24 hr	BrCH ₂ CHBrCH ₂ OH (98)	3
(CH ₃) ₂ C=C(CH ₃) ₂	CuBr ₂	in CH ₃ CN, 25°, 5-15 min	(CH ₃) ₂ CBrCBr(CH ₃) ₂ (91)	2
C ₆ H ₅ CH=CH ₂	CuBr ₂	in CH ₃ CN, 25°, 5-15 min	C ₆ H ₅ CHBrCH ₂ Br (87)	2
CH ₂ =CH ₂	CuBr ₂	in CH ₃ CN, 25°, 5-15 min	BrCH ₂ CH ₂ Br (57)	2
CH ₂ =CH-CN	CuBr ₂	in CH ₃ CN, 60-80°, 2-4 hr	BrCH ₂ CH ₂ BrCN (32)	2
C ₆ H ₅ C≡C ₆ H ₅	CuBr ₂	in CH ₃ OH, 64°, 25 hr	<i>l</i> -C ₆ H ₅ CBr=CBrc ₆ H ₅ (19)	3
C ₆ H ₅ C≡CH	CuBr ₂	in CH ₃ OH, 64°, 15 hr	C ₆ H ₅ CBr=CBrc ₆ H ₅ (67) ^b	3
CH≡C-CH ₂ OH	CuBr ₂	in CH ₃ OH, 64°, 0.5 hr	Br ₂ C=CBrcH ₂ OH (93) ^b	3
(CH ₃) ₂ C=C(CH ₃) ₂	CuCl ₂	in CH ₃ CN, 60-80°, 2-4 hr	(CH ₃) ₂ CClCCl(CH ₃) ₂ (53)	2
CH ₂ =CH ₂	CuCl ₂	in CH ₃ CN, 60-80°, 2-4 hr	ClCH ₂ CH ₂ Cl (32)	2
C ₆ H ₅ CH=CH ₂	CuCl ₂	in AcOH+NaOAc, 90°, 5 hr	C ₆ H ₅ CHClCH ₂ Cl (71)	1
C ₆ H ₅ CH=CH ₂	CuCl ₂	in CH ₃ CN+LiCl, 82°, 10 hr	C ₆ H ₅ CHClCH ₂ Cl (74)	1
CH ₂ =CH-CN	CuCl ₂	in CH ₃ CN+LiCl, 82°, 22 hr	ClCH ₂ CHClCN (42)	16
CH≡C-CH ₂ OH	CuCl ₂	in CH ₃ OH, 64°, 22 hr	Cl ₂ C=CClCH ₂ OH (23) ^b	3
<i>n</i> -C ₆ H ₁₃ CH=CH ₂	SbCl ₅	in CCl ₄ , 30-35°, 10 min	<i>n</i> -C ₆ H ₁₃ CHClCH ₂ Cl (~100)	8
<i>n</i> -C ₆ H ₁₃ CH=CH ₂	TiCl ₃ ·4H ₂ O	in CCl ₄ , 77°, 2 hr	<i>n</i> -C ₆ H ₁₃ CHClCH ₂ Cl (26)	11
<i>n</i> -C ₆ H ₁₃ CH=CH ₂	PCl ₅	in C ₆ H ₅ Cl, 91°, 6 hr	<i>n</i> -C ₆ H ₁₃ CHClCH ₂ Cl (83)	12

a. Mostly based on metal halides charged.

b. The product may be formed through three following steps.



Informations on the reaction mechanism of this type of halogenation have been obtained from recent kinetic studies. For the reaction with CuCl₂, a mechanism involving an electrophilic attack of CuCl₂ molecule (eq. 1) has been suggested, based on rather



complex rate equations obtained in the chlorination of styrene in both acetonitrile-LiCl and *n*-propanol.¹⁾ More recently, it is shown that, in the chlorination of 1-octene in methanol, the observed rate expression almost agrees with the above mechanism, though in which the rate-determining attack of Cl⁻ rather than CuCl₂ (at step (b)) is more probable.⁶⁾ In addition, in view of the lack of stereospecificity, an unsymmetrically-bridged cationic intermediate is proposed instead of a symmetrically-bridged one.⁶⁾ In the case of CuBr₂, the bromination rate of *n*-hexene in methanol has been found to obey simple third-order kinetics (nearly second-order to CuBr₂ and first-order to the olefin), and a suggested mechanism is essentially identical to that shown in eq. 1.⁷⁾ Here no positive evidence for the generation of free bromine from CuBr₂ (eq. 2) is found. In



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Table 2. Product Distribution and Stereochemistry in Halogenation of Olefins

Substrate	Halogen source	Reaction Conditions	Product (Yield, %)	trans Addition	Ref.
$c\text{-CH}_3\text{-CH=CH-CH}_3$	Br_2	in CH_3CN , 25°	$dl\text{-CH}_3\text{CHBrCHBrCH}_3$	100	16
$c\text{-CH}_3\text{-CH=CH-CH}_3$	CuBr_2	in CH_3CN , 25° , 10 min	$dl\text{-CH}_3\text{CHBrCHBrCH}_3$ (91)	100	2
$t\text{-CH}_3\text{-CH=CH-CH}_3$	Cl_2	in $\text{CF}_2\text{ClCFCl}_2$, -9°	$meso\text{-CH}_3\text{CHClCHClCH}_3$	100	17
$t\text{-CH}_3\text{-CH=CH-CH}_3$	CuCl_2	in CH_3OH , 140° , 3 hr	$meso\text{-}$ & $dl\text{-CH}_3\text{CHClCHClCH}_3$ (10)	62	4
$t\text{-CH}_3\text{-CH=CH-CH}_3$	SbCl_5	in CCl_4 , 76° , 10 min	$meso\text{-}$ & $dl\text{-CH}_3\text{CHClCHClCH}_3$ (96)	18	8
	Br_2	in CH_3CN , 0° , 1.5 hr	 (63) &  (27)	100	2
	CuBr_2	in CH_3CN , 0° , 1.5 hr	 (93) &  (1)	100	2
	Cl_2	in CCl_4 , 0° , 10 min		100	9
	CuCl_2	in CH_3CN , $60\text{--}80^\circ$, 2-4 hr	$c\text{-}$ & $t\text{-}$  (73)	95	2
	CuCl_2	in AcOH , 150° , 2 hr	$c\text{-}$ & $t\text{-}$ 	88	4
	SbCl_5	in CCl_4 , 76° , 5 min	$c\text{-}$ & $t\text{-}$  (67)	17	8
	$\text{TiCl}_3 \cdot 4\text{H}_2\text{O}$	in CCl_4 , 76° , 2 hr	$c\text{-}$ & $t\text{-}$  (17)	98	11
	PCl_5	neat, 80° , 10 hr	 (87)	100	12
$\text{CH}_2=\text{CH-CH=CH}_2$	CuBr_2	in CH_3CN , 25° , 10 min	only $t\text{-BrCH}_2\text{CH=CHCH}_2\text{Br}$ (92)	—	2
$\text{CH}_2=\text{CH-CH=CH}_2$	CuCl_2	in CH_3CN , 60° , 2-4 hr	a mixture of $\text{CH}_2\text{ClCHCl-CH=CH}_2$, $c\text{-}$ & $t\text{-ClCH}_2\text{CH=CHCH}_2\text{Cl}$ (43) (ratio 15 : 5 : 80)	—	2
$\text{CH}_2=\text{CH-CH=CH}_2$	SbCl_5	in CCl_4 , 0° , 10 min	a mixture of $\text{CH}_2\text{ClCHCl-CH=CH}_2$, $c\text{-}$ & $t\text{-ClCH}_2\text{CH=CHCH}_2\text{Cl}$ (50) (ratio 32 : 21 : 47)	—	9
	Cl_2	in CH_3CN , $6\text{--}11^\circ$	$c\text{-}$ & $t\text{-}$  (trace amounts)	95	18
	CuCl_2	in $\text{CH}_3\text{CN} + \text{LiCl}$, 82° , 22 hr	$c\text{-}$ & $t\text{-}$  (58)	70	18

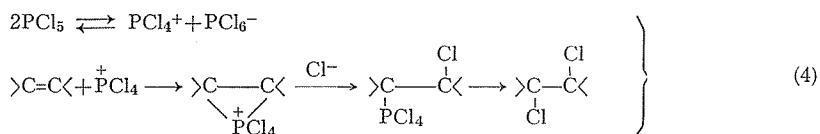
CuBr₂-acetonitrile system, however, a somewhat different situation has been known, *i.e.*, a spectrophotometric evidence is present for the dissociation of CuBr₂ according to eq. 3, and the bromination of olefins in acetonitrile is extremely rapid compared to the reaction



in other solvents. Thus, as for the bromination with CuBr₂ in acetonitrile, it is highly probable that the reaction proceeds through a smooth supply of Br₂ (by eq. 3 including a round path) followed by its attack on an olefin.²⁾

Chlorination of olefins can also be easily accomplished by SbCl₅ in chlorocarbon solvents.⁸⁾ Although the reaction is not so general as halogenation with CuX₂ (*e.g.*, styrene gives only tarry product and acrylonitrile does not give any product), a favourable *cis*-adduct formation is quite characteristic. The ratio of *cis*- and *trans*-additions changes with solvent and reaction temperature.⁹⁾ For example, the ratios (*cis*/*trans*) for the chlorination of cyclohexene in boiling dichloroethane ($\epsilon = 10.37$) (at 83°) and in carbon tetrachloride ($\epsilon = 2.23$) (at 30°) are 8.5 and 1.5, respectively. Further, in the chlorination products from butadiene considerable amounts of *cis*-1,4-dichlorobutene-2 are found,⁹⁾ though it has never been obtained in the chlorination with chlorine.¹⁰⁾ Such characteristic results may be explained by assuming a near-concerted attack of dimeric SbCl₅ species to an unsaturated component.

In carbon tetrachloride, TiCl₃·4H₂O reacts slowly with olefins to afford dichlorides, but the yields are rather poor.¹¹⁾ In the case of PCl₅, olefins react with it in the cold to give compounds in which the elements of Cl-PCl₄ have been added, whereas at elevated temperatures (*ca.* 100°) to give dichlorides in which *trans* addition has occurred.¹²⁾ Though the following pathway has been proposed, the possibility of chlorine chlorination cannot be excluded, because a slight (a few %) dissociation of PCl₅ near 100° has been known.



The chlorination with AuCl₃ is also known, but the reaction appears to be non-stereospecific.³⁶⁾

The addition of a halogen or halide anion to a suitable metal halide yields a mixed halogen by a redox reaction as follows. For example:



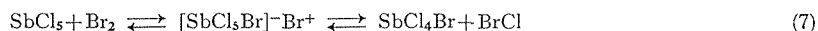
If an olefin is present in this system, the formation of a mixed halide would be expective. In fact, various combinations have been known; HgCl₂-I₂,¹³⁾ CuCl₂-I₂,²⁾ CuCl₂-MI (*e.g.*, NH₄I, KI, CuI),²⁾ and SbCl₅-I₂¹⁴⁾ systems are suitable for the synthesis of chloriodoalkanes, and SbCl₅-Br₂¹⁴⁾ and SbCl₅-LiBr¹⁴⁾ systems are excellent for the synthesis of bromochloroalkanes. Some examples are shown in Table 3. The addition proceeds in

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Table 3. Mixed Halogenation of Olefins with Mixtures of Metal Halides and Halogen Donors

Olefin	Metal Halide & Halogen Donor (molar ratio)	Reaction Conditions	Product (Yield %)	Ref.
$\text{CH}_2=\text{CH}_2$	$\text{CuCl}_2 + \text{I}_2$ (2:1)	in C_6H_{12} , 80°, 2 hr	$\text{ICH}_2\text{CH}_2\text{Cl}$ (85)	2
$\text{CH}_2=\text{CH}-\text{OCOCH}_3$	$\text{CuCl}_2 + \text{I}_2$ (2:1)	in CH_3CN , 25°, 2 hr	$\text{CH}_2\text{ICHCl}(\text{OCOCH}_3)$ (83)	2
$\text{CH}_3\text{CH}=\text{CH}_2$	$\text{CuCl}_2 + \text{I}_2$ (2:1)	in CH_3CN , 50°, 2 hr	$\text{CH}_3\text{CHClCH}_2\text{I}$ (64) & $\text{CH}_3\text{CHICH}_2\text{Cl}$ (21)	2
$\text{CH}_2=\text{CH}-\text{Cl}$	$\text{CuCl}_2 + \text{I}_2$ (2:1)	in CH_3CN , 50°, 15 hr	$\text{CH}_2\text{ICHCl}_2$ (57) & $\text{CH}_2\text{ClCHClI}$ (24)	2
$(\text{CH}_3)_2\text{C}=\text{CH}_2$	$\text{HgCl}_2 + \text{I}_2$ (1:2)	in $(\text{C}_2\text{H}_5)_2\text{O}$, 25°, 1 hr	$(\text{CH}_3)_2\text{CClCH}_2\text{I}$ (67)	13
$\text{C}_6\text{H}_5\text{CH}=\text{CH}_2$	$\text{CuCl}_2 + \text{KI}$ (2:1)	in CH_3CN , 80°, 1 hr	$\text{C}_6\text{H}_5\text{CHClCH}_2\text{I}$ (75)	2
	$\text{CuCl}_2 + \text{I}_2$ (2:1)	in CH_3CN , 80°, 2 hr	 (90)	2
	$\text{CuCl}_2 + \text{KI}$ (2:1)	in CH_3CN , 80°, 2 hr	 (78)	2
	$\text{SbCl}_5 + \text{I}_2$ (1:1)	in CCl_4 , 76°, 10 min	 (94)	14
	$\text{CuCl}_2 + \text{Br}_2$ (2:1)	in CH_3CN , 80°, 1 hr	 (54) &  (23)	2
	$\text{CuCl}_2 + \text{NH}_4\text{Br}$ (2:1)	in CH_3CN , 80°, 1 hr	 (47) &  (3)	2
	$\text{SbCl}_5 + \text{Br}_2$ (1:1)	in CCl_4 , 30°, 5 min	 (96) &  (~0)	14
	$\text{SbCl}_5 + \text{LiBr}$ (1:1)	in CCl_4 , 76°, 5 min	 (81),  (~0) & <i>c</i> -, <i>t</i> -  (trace)	14
$\text{C}_6\text{H}_5\text{CH}=\text{CH}_2$	$\text{SbCl}_3 + \text{Br}_2$ (1:1)	in CCl_4 , 0°, 10 min	$\text{C}_6\text{H}_5\text{CHClCH}_2\text{Br}$ (87)	14

trans fashion with high stereospecificity, and the products are generally in accord with Markovnikov's rule. No competitive iodination is found in chloriodination; whereas considerable competition with bromine is observed in chlorobromination, depending on the redox combination. This is largely due to differences in reactivities between halogens and mixed halogens (relative reactivities¹⁵); $\text{I}_2 : \text{ICl} = 1 : 10^5$, $\text{Br}_2 : \text{BrCl} = 1 : 4 \times 10^2$. In addition, if the formation of a mixed halogen proceeds through an ionic adduct (*e.g.*, eq. 7), the Lewis acidity of an original metal halide would become an important factor



for the concentration of a mixed halogen. In fact, it has been found¹⁴) that the product selectivity in chlorobromination decreases as the Lewis acidity of metal chlorides decreases.

II. HALOGENATION OF ARENES

For the halogenation of rather reactive aromatics, the use of various metal or metalloid halides (SbCl_5 , FeCl_3 , VCl_4 , MoCl_5 , PCl_5 , $\text{TiCl}_3 \cdot 4\text{H}_2\text{O}$, CuBr_2 , $\text{TlBr}_3 \cdot 4\text{H}_2\text{O}$ etc.) as halogenating agents has been reported. Representative examples are summarized in Table 4. Isomer distribution and relative rate data in the halogenation of toluene using various halogenating agents are collected in Table 5.

Based on the reactivity toward aromatics and the favorable *ortho-para* orientation, the halogenation with Lewis acid halides is considered to proceed by an electrophilic

Table 4. Aromatic Halogenation with Metal Halides

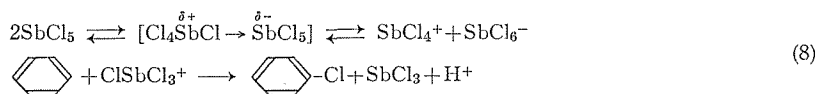
Aromatic compound	Halogenating agent	Reaction Conditions	Product (Yield, %; <i>o/p</i> ratio)	Ref.
$\text{C}_6\text{H}_5\text{Cl}$	SbCl_5	neat, 41–59°, 2 hr	$\text{C}_6\text{H}_4\text{Cl}_2$ (82 ; 0.2)	20
$\text{C}_6\text{H}_5\text{Cl}$	FeCl_3	neat, 125–140°, 3 hr	$\text{C}_6\text{H}_4\text{Cl}_2$ (86 ; 0.1)	19
$\text{C}_6\text{H}_5\text{Cl}$	VCl_4	neat, 118–121°, 2.5 hr	$\text{C}_6\text{H}_4\text{Cl}_2$ (70 ; 0.2)	21
$\text{C}_6\text{H}_5\text{Cl}$	MoCl_5	neat, 105–110°, 2.5 hr	$\text{C}_6\text{H}_4\text{Cl}_2$ (31 ; 0.1)	21
$\text{C}_6\text{H}_5\text{CH}_3$	SbCl_5	neat, 18–31°, 2.5 hr	$\text{CH}_3\text{C}_6\text{H}_4\text{Cl}$ (87 ; 0.9)	20
$\text{C}_6\text{H}_5\text{CH}_3$	$\text{TlBr}_3 \cdot 4\text{H}_2\text{O}$	in CCl_4 , 78°, 1 hr	$\text{CH}_3\text{C}_6\text{H}_4\text{Br}$ (20 ; 1.6)	24
$\text{C}_6\text{H}_5\text{CH}_3$	$\text{TiCl}_3 \cdot 4\text{H}_2\text{O}$	in CCl_4 , 78°, 2 hr	$\text{CH}_3\text{C}_6\text{H}_4\text{Cl}$ (28 ; 1.0) & $\text{CH}_3\text{C}_6\text{H}_4\text{COOH}$ (10; 0.7)	22
Anthracene	CuCl_2	in CCl_4 , 78°, 7 hr	9-Chloroanthracene (98)	27
$\text{C}_6\text{H}_5\text{OH}$	CuCl_2	in DMF+LiCl, 150°, 5 min	$\text{ClC}_6\text{H}_4\text{OH}$ (60 ; 0.1–0.2)	25
$\beta\text{-C}_{10}\text{H}_7\text{OH}$	CuBr_2	in aq. CH_3OH +KBr, 25°, 15 hr	α -Bromo- β -naphthol (50)	26
C_6H_6	$\text{AlI}_3 + \text{CuCl}_2$	neat, 80°, 5 hr	$\text{C}_6\text{H}_5\text{I}$ (65)	28
$\text{C}_6\text{H}_5\text{CH}_3$	$\text{FeI}_3 \cdot 4\text{H}_2\text{O} + \text{CuCl}_2$	neat, 110°, 3 hr	$\text{CH}_3\text{C}_6\text{H}_4\text{I}$ (81 ; 1.1)	28
$\text{C}_6\text{H}_5\text{OH}$	$\text{I}_2 + \text{CuCl}_2$	in $\text{C}_6\text{H}_5\text{Cl}$, 130°, 29 hr	$p\text{-IC}_6\text{H}_4\text{OH}$ (69)	28
$\text{C}_6\text{H}_5\text{N}(\text{CH}_3)_2$	$\text{I}_2 + \text{CuCl}_2$	in C_6H_6 , 60°, 0.5 hr	$p\text{-IC}_6\text{H}_4\text{N}(\text{CH}_3)_2$ (47)	28

Table 5. Isomer Distribution and Relative Rate in Halogenation of Toluene

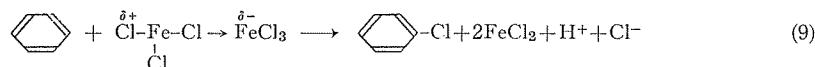
Halogen source	Reaction Conditions	Halotoluene			Rel. Rate $k_{\text{T}}/k_{\text{B}}$	Ref.
		Isomer Ratio				
		<i>o</i>	<i>m</i>	<i>p</i>		
Cl ₂	in aq. CH ₃ COOH, 25°	60	0.5	39.5	345	29
Cl ₂ (SbCl ₅ cat)	neat, 25–30°	72	2	26	—	20
SbCl ₅	neat, 18–31°	47	2	51	—	20
Cl ₂ (TiCl ₃ ·4H ₂ O cat)	in CCl ₄ , 78°	64	0	36	43	23
TiCl ₃ ·4H ₂ O	in CCl ₄ , 78°	52	0	48	26	23
FeCl ₃	neat, 50–60°	12	<1	88	—	19
VCl ₄	neat, 7–25°	15	1	84	—	21
Br ₂	in aq. CH ₃ COOH, 25°	33	0	67	605	29
Br ₂ (TlBr ₃ ·4H ₂ O cat)	in CCl ₄ , 78°	58	0	42	7	24
TlBr ₃ ·4H ₂ O	in CCl ₄ , 78°	62	0	38	15	24

substitution. The rough chlorinating ability is given in the following order; $\text{SbCl}_5 > \text{FeCl}_3, \text{VCl}_4 > \text{MoCl}_5, \text{CuCl}_2$, and this correlates well with their oxidizing ability.¹⁹⁻²¹⁾ Though the activity of $\text{TiCl}_3 \cdot 4\text{H}_2\text{O}$ appears to be rather low, the reaction with this chloride in carbon tetrachloride shows somewhat different behavior, *i.e.*, conversion of benzene into chlorobenzene and benzoic acid occurs concurrently.²²⁾

Isomer distributions in metal chloride chlorination of toluene are clearly different from those in chlorination using chlorine molecule without or with metal chloride catalysts. This implies that metal chloride can effect substitution without prior degradation to free chlorine and the electrophiles here would be species other than Cl_2 and Cl^+ . When SbCl_5 or $\text{TiCl}_3 \cdot 4\text{H}_2\text{O}$ is the reagent, somewhat lower *o/p* ratios and considerably low k_T/k_B value are obtained, and this suggests that a reactive and somewhat bulky attacking species, such as SbCl_4^+ and TiCl_2^+ , may function (see eq. 8).^{20,23)} In cases of $\text{FeCl}_3, \text{VCl}_4$,



and MoCl_5 , the attack of a polarized dimer complex, which is more bulky, has been postulated on the basis of quite less *ortho*-substitution (see eq. 9).^{19,21)}



On the other hand, the selectivity data in the bromination with $\text{TiBr}_3 \cdot 4\text{H}_2\text{O}$ indicate that the reaction is essentially the same as that with bromine in the presence of TiBr_3 catalyst.²⁴⁾

Though CuX_2 can also act as aromatic halogenating agents, this halogenation seems to be applicable to highly reactive aromatic components, such as phenols,^{25,26)} aromatic amines,²⁶⁾ and polynuclear hydrocarbons.²⁷⁾ An interesting use of this halogenation would be the preparation of *p*-halogenated compounds of phenols and anilines. In this reaction *para*-substitution predominates, whereas usual halogenation affords a mixture of *o*- and *p*-halogenated, and/or polyhalogenated compounds.

Aromatic iodination with CuCl_2 -iodine donor combinations (*cf.* eq. 5 and 6) has recently been developed.²⁸⁾ Some examples are included in Table 4. FeI_2 and AlI_3 exhibit higher reactivity than iodine itself. The reaction would be essentially electrophilic, and is not applicable to strongly deactivated aromatics (*e.g.*, benzoic ester). Aromatics possessing functional groups that coordinate with copper salt (*e.g.*, aniline, thiophene) are often not iodinated.

III. HALOGENATION OF ALKANES

The halogenation of aliphatic hydrocarbons with chlorine or bromine molecule is usually performed in the presence of light. A few metal or metalloid halides (*e.g.*, $\text{PCl}_5, \text{SbCl}_5, \text{FeCl}_3$ *etc.*) can be used in place of halogen elements. Some examples are given in Table 6.

PCl_5 can react smoothly with alkanes in an inert solvents such as *o*-dichlorobenzene

Table 6. Halogenation of Some Aliphatic Compounds with Metal and Metalloidal Halides

Substrate	Halide	Reaction Conditions	Product (Yield, %)	Ref.
<i>n</i> -C ₇ H ₁₆	PCl ₅	in o-C ₆ H ₄ Cl ₂ , BPO cat, 90°, 8 hr	Mixed chloroheptanes (73)	12
	PCl ₅	in o-C ₆ H ₄ Cl ₂ , BPO cat, 88°, 7 hr	 -Cl (70)	12
Adamantane	SbCl ₅	in CH ₂ Cl ₂ , 40°, 3 hr	1- & 2-Chloroadamantane (69)	31
C ₆ H ₅ CH ₂ CH ₃	PCl ₅	neat, 105°, 16 hr	C ₆ H ₅ CHClCH ₃ (60)	12
(C ₆ H ₅) ₃ CH	PCl ₅	neat, 140–150°, 18 hr	(C ₆ H ₅) ₃ CCl (93)	35
CH ₃ CH ₂ CH ₂ CHO	CuBr ₂	in CH ₃ OH, 64°, 9 hr	CH ₃ CH ₂ CHBrCH(OCH ₃) ₂ (40)	3
CH ₃ CH ₂ CH ₂ CHO	CuCl ₂	in DMF, 85°, 2 hr	CH ₃ CH ₂ CHClCHO (60)	3
CH ₃ COC ₂ H ₅	CuCl ₂	in DMF+LiCl, 80–90°, 0.75 hr	CH ₃ COCHClCH ₃ (<i>ca.</i> 60)	25
C ₆ H ₅ COC ₂ H ₅	CuCl ₂	in DMF+LiCl, 80–90°, 1 hr	C ₆ H ₅ COCHClCH ₃ (72)	25

to yield alkyl chlorides, in the absence or presence of an initiator (*e.g.*, benzoyl peroxide).¹²⁾ Owing to a radical nature of the reaction, the product generally consists of a mixture of isomeric chlorides except for some cases such as the chlorination of unsubstituted cycloalkanes and monoalkylated aromatics. Interestingly, the reaction with olefins affords only dichlorides (*cf.* section I), and does not cause any attack on allyl position in olefins even in the presence of peroxide. Through competitive experiments between toluene and cyclohexane, it has been found that the thermal PCl₅ reaction has almost the same selectivity as photochlorination (relative reactivities: toluene/cyclohexane (both per C-H), PCl₅ reaction 3.0, photoreaction 2.8). Thus the attacking entity is probably a chlorine atom formed through eq. 10¹²⁾ On the other hand, in the peroxide-catalyzed

Table 7. Isomer Distribution in Chlorination of *n*-Heptane and Adamantane(a) Chlorination of *n*-Heptane (Ref. 30)

Halogene source	Reaction Conditions	<i>n</i> -Chloro- <i>n</i> -heptane			
		1-	2-	3-	4-
Cl ₂	BPO cat., 98°	15.1	34.6	33.8	16.5
PCl ₅	BPO cat., 98°	2.5	36.4	41.5	19.5
PCl ₃ +Cl ₂	BPO cat., 98°	traces	24.0	52.0	24.0

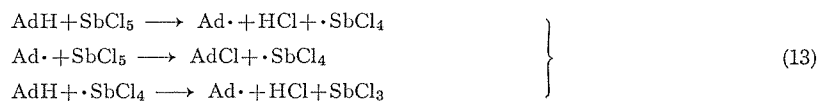
(b) Chlorination of Adamantane (Ref. 31)

Halogene source	Reaction Conditions	Chloroadamantane 1/2 ratio
Cl ₂	in SnCl ₄ ($\epsilon=2.87$), 100°, 5 min	0.6
Cl ₂	in CH ₂ Cl ₂ ($\epsilon=9.08$), 40°, 3 hr	0.5
FeCl ₃	in SnCl ₄ , 110°, 3 hr	9–10
FeCl ₃	in CH ₂ Cl ₂ , 40°, 7 hr	20
SbCl ₅	in SnCl ₄ , 110°, 15 min	9–10
SbCl ₅	in CCl ₂ FCClF ₂ ($\epsilon=2.24$), AlCl ₃ added, 40°, 20–30 min	>90

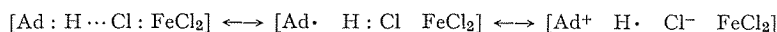
chlorination of *n*-heptane with PCl_5 and with Cl_2 , somewhat different isomer distributions have been observed (see Table 7).³⁰⁾ A suggested scheme¹²⁾ involving the attack of $\cdot\text{PCl}_4$ (partly $\cdot\text{Cl}$) (eq. 11) would be reasonable.



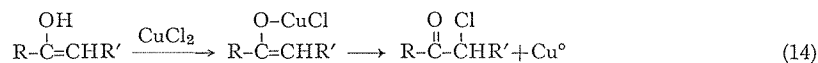
A similar reaction of FeCl_3 or SbCl_5 with C-H linkages has also been known.³¹⁾ A radical nature of the reaction has been revealed by comparison of isomer distributions in chlorination of adamantane using various reagents such as Cl_2 , FeCl_3 , SbCl_5 , and $\text{SbCl}_5 + \text{AlCl}_3$ (see Table 7). SbCl_5 reacts generally at a more rapid rate than FeCl_3 . Further, photolytic conditions enhance the rate of the SbCl_5 process, but does not promote the reaction with FeCl_3 . This implies that SbCl_5 may be involved in a radical chain process, whereas the FeCl_3 reaction is probably a nonchain process. Based on these results the following radical pathway has been proposed for each chlorination.³¹⁾



Since a slight favorable effect on the rate is observed in a more polar solvent, the contribution of somewhat polar forms in the transition state may be considered. A similar situation has been known for hydrogen abstraction reactions involving chlorine atom.



In the halogenation of enolizable aldehydes or ketones, the use of CuX_2 instead of halogen elements has been reported.²⁵⁾ The reaction proceeds smoothly in dimethylformamide solution. Some examples are included in Table 6. This reaction is essentially the same as the halogenation of phenols with CuX_2 (*cf.* section II). As a probable pathway, the following scheme involving two-electron reduction of Cu(II) within a metal chloride-enolate complex has been suggested.²⁵⁾ The observed rates of the chlorination of



acetone in water³²⁾ and methanol,³³⁾ which are approximately expressed as a sum of second- and third-order terms, seem to agree with this mechanism. Here, the contribution of the third-order term appears to imply that an external attack of Cl^- (or CuCl_2) on the complex may occur concurrently. A similar halogenation with FeCl_3 in acetic acid has also been reported.³⁴⁾

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