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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 (CuBr₂, CuCl₂, SbCl₅, TlCl₃·4H₂O, PCl₅, AuCl₃ *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 streochemistry are also summarized in Table 2.

Halogenation with CuX_2 (X = Br, 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 CuX₂ suggests that this halogenation would be surely electrophilic. As for CuBr₂, the reaction is completely stereospecific and *trans*; whereas in the case of less reactive CuCl₂, 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 CuBr₂ 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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Olefin or Acetylene	Halide	Reaction Conditions	Product (Yield, %) ^a	Ref.
CH ₂ =CH-CH ₂ OH	CuBr ₂	in CH3OH, 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
$C_6H_5C\equiv CC_6H_5$	CuBr ₂	in CH3OH, 64°, 25 hr	$t-C_6H_5CBr=CBrC_6H_5$ (19)	3
C ₆ H ₅ C≡CH	$CuBr_2$	in CH3OH, 64°, 15 hr	$C_6H_5CBr=CBr_2$ (67) ^b	3
CH≡C-CH₂OH	$CuBr_2$	in CH ₃ OH, 64°, 0.5 hr	$Br_2C=CBrCH_2OH$ (93) ^b	3
$(CH_3)_2C=C(CH_3)_2$	CuCl ₂	in CH ₃ CN, 60-80°, 2-4 hr	$(CH_3)_2CClCCl(CH_3)_2$ (53)	2
CH ₂ =CH ₂	$CuCl_2$	in CH ₃ CN, 60-80°, 2-4 hr	$ClCH_2CH_2Cl$ (32)	2
$C_6H_5CH=CH_2$	$CuCl_2$	in AcOH+NaOAc, 90°, 5 hr	$C_6H_5CHClCH_2Cl$ (71)	1
$C_6H_5CH=CH_2$	$CuCl_2$	in CH ₃ CN+LiCl, 82° , 10 hr	$C_6H_5CHClCH_2Cl$ (74)	1
CH ₂ =CH-CN	$CuCl_2$	in CH ₃ CN+LiCl, 82° , 22 hr	ClCH ₂ CHClCN (42)	16
CH≡C-CH₂OH	$CuCl_2$	in CH ₃ OH, 64°, 22 hr	Cl ₂ C=CClCH ₂ OH (23) ^b	3
n-C ₆ H ₁₃ CH=CH ₂	$SbCl_5$	in CCl ₄ , 30–35°, 10 min	$n-C_6H_{13}CHClCH_2Cl$ (~100)	8
n-C ₆ H ₁₃ CH=CH ₂	$TlCl_3 \cdot 4H_2O$	in CCl ₄ , 77°, 2 hr	$n-C_6H_{13}CHClCH_2Cl$ (26)	11
n-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

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

a. Mostly based on metal halides charged.

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

 $HC \equiv CR \longrightarrow XCH = CRX \longrightarrow X_2CH - CRX_2 \longrightarrow X_2C = CRX$

Informations on the reaction mechanism of this type of halogenation have been obtained from recent kinetic studies. For the reaction with $CuCl_2$, a mechanism involving an electrophilic attack of $CuCl_2$ molecule (eq. 1) has been suggested, based on rather

(rate-detg. step: (a) in acetonitrile, (b) in *n*-propanol)

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 unsymmetricallybridged 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

$$2CuBr_2 \rightleftharpoons 2CuBr + Br_2$$

(2)

Liquid Phase Halogenation with Metal Halides

Substrate	Halogen source	Reaction Conditions	Product (Yield, %)	trans Addition	Ref.
c-CH3-CH=CH-CH3	Br ₂	in CH ₃ CN, 25°	dl-CH3CHBrCHBrCH3	100	16
с-СН3-СН=СН-СН3	CuBr ₂	in CH3CN, 25°, 10 min	dl-CH ₃ CHBrCHBrCH ₃ (91)	100	2
t-CH ₃ -CH=CH-CH ₃	Cl_2	in $CF_2ClCFCl_2$, -9°	meso-CH ₃ CHClCHClCH ₃	100	17
t-CH ₃ -CH=CH-CH ₃	$CuCl_2$	in CH3OH, 140°, 3 hr	meso- & dl-CH3CHClCHClCH3 (10)	62	4
t-CH ₃ -CH=CH-CH ₃	SbCl_5	in CCl ₄ , 76°, 10 min	meso- & dl-CH3CHClCHClCH3 (96)	18	8 ,
$\langle \rangle$	Br_2	in CH3CN, 0°, 1.5 hr	$ \begin{array}{c} & & \\ & & $	100	2
$\langle $	CuBr ₂	in CH3CN, 0°, 1.5 hr	$ \begin{array}{c} & & \\ & & $	100	2
$\langle \rangle$	Cl_2	in CCl4, 0°, 10 min		100	9
$\langle \rangle$	CuCl ₂	in CH ₃ CN, 60–80°, 2–4 hr	$c- \& t- \bigvee_{\substack{Cl \\ Cl \\ Cl}} (73)$	95	2
$\langle \rangle$	CuCl ₂	in AcOH, 150°, 2 hr	c- & t- Cl Cl	88	4
$\langle \rangle$	SbCl_5	in CCl₄, 76°, 5 min	$c- \& t- \sum_{Cl Cl} (67)$	17	8
$\langle \rangle$	TlCl ₃ •4H ₂ O	in CCl ₄ , 76°, 2 hr	$c-\& t-\bigvee_{Cl}$ (17)	98	11
$\langle \rangle$	PCl ₅	neat, 80°, 10 hr	(87)	100	12
CH2=CH-CH=CH2	CuBr ₂	in CH ₃ CN, 25°, 10 min	only t-BrCH ₂ CH=CHCH ₂ Br (92)		2
CH ₂ =CH-CH=CH ₂	$CuCl_2$	in CH ₃ CN, 60°, 2–4 hr	a mixture of CH ₂ CICHCI-CH=CH ₂ , c- & /-CICH ₂ CH=CHCH ₂ Cl (43) (ratio 15:5:80)		2
CH ₂ =CH–CH=CH ₂	$SbCl_5$	in CCl ₄ , 0°, 10 min	a mixture of CH ₂ CICHCl-CH=CH ₂ , c - & t-CICH ₂ CH=CHCH ₂ Cl (50) (ratio 32:21:47)		9
	Cl_2	in CH3CN, 6–11°	c- & t-	95	18
	CuCl ₂	in CH3CN+ LiCl, 82°, 22 hr	$c- \& t- \underbrace{\begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$	70	18

Table 2. Product Distribution and Stereochemistry in Haloganation of Olefins

S. UEMURA and M. OKANO

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 $CuBr_2$ in acetonitrile, it is highly probable that the reaction proceeds through a smooth supply of Br_2 (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-dichlobutene-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, TlCl₃·4H₂O 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 occured.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.

$$2PCl_{5} \rightleftharpoons PCl_{4}^{+} + PCl_{6}^{-}$$

$$>C=C\langle + \overset{r}{P}Cl_{4} \longrightarrow >C \overset{c}{\longrightarrow} C\langle \overset{cl^{-}}{\longrightarrow} >C \overset{cl}{\longrightarrow} \overset{cl}{\rightarrow} C \overset{cl}{\longrightarrow} \overset{c}{\rightarrow} \overset$$

The chlorination with $AuCl_3$ 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:

$$2CuCl_2+I_2 \longrightarrow 2CuCl+2ICI$$
 (5)

$$2CuCl_2 + I^- \longrightarrow 2CuCl + ICI + Cl^- \tag{6}$$

If an olefin is present in this system, the formation of a mixed halide would be expective. In fact, various combinations have been known; $HgCl_2-I_2,^{13}$ CuCl_2-I_2,²) CuCl_2-MI(*e.g.*, NH₄I, KI, CuI),²) and SbCl₅-I₂¹⁴) systems are suitable for the synthesis of chloroiodoalkanes, 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

Liquid Phase	Halogenation	with	Metal	Halides
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Olefin	Metal Halide & Halogen Donor (molar ratio)	Reaction Conditions	Product (Yield %)	Ref.
CH2=CH2	$CuCl_2 + I_2$ (2:1)	in C ₆ H ₁₂ , 80°, 2 hr	ICH ₂ CH ₂ Cl (85)	2
CH2=CH-OCOCH3	$CuCl_2+I_2$ (2:1)	in CH ₃ CN, 25° 2 hr	CH ₂ ICHCl(OCOCH ₃) (83)	2
CH ₃ CH=CH ₂	$CuCl_2 + I_2$ (2:1)	in CH ₃ CN, 50°, 2 hr	CH ₃ CHClCH ₂ I (64) & CH ₃ CHICH ₂ Cl (21)	2
CH ₂ =CH-Cl	$CuCl_2+I_2$ (2:1)	in CH ₃ CN, 50°, 15 hr	CH_2ICHCl_2 (57) & $CH_2CICHCII$ (24)	2
$(CH_3)_2C=CH_2$	$HgCl_2 + I_2$ (1:2)	in $(C_2H_5)_2O$, 25° , 1 hr	$(CH_3)_2CClCH_2I$ (67)	13
$C_6H_5CH=CH_2$	$CuCl_2+KI$ (2:1)	in CH ₃ CN, 80°, 1 hr	$C_6H_5CHClCH_2I$ (75)	2
$\langle \rangle$	$CuCl_2 + I_2$ (2:1)	in CH ₃ CN, 80°, 2 hr	(90)	2
$\langle \rangle$	$CuCl_2+KI$ (2:1)	in CH3CN, 80°, 2 hr	(78)	2
$\langle \rangle$	$SbCl_5 + I_2$ (1:1)	in CCl ₄ , 76°, 10 min	(94)	14
$\langle \rangle$	$CuCl_2 + Br_2$ (2:1)	in CH ₃ CN, 80°, 1 hr	$ \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\$	2
$\langle \rangle$	$CuCl_2+NH_4Br(2:1)$	in CH3CN, 80°, 1 hr	$ \begin{array}{c} $	2
$\langle \rangle$	$SbCl_5 + Br_2$ (1:1)	in CCl ₄ , 30°, 5 min	$\bigcirc (96) \& \bigcirc (\sim0)$	14
$\langle \rangle$	$SbCl_5+LiBr$ (1:1)	in CCl ₄ , 76°, 5 min	$\bigotimes_{Cl} (81), \qquad \bigotimes_{Br} (\sim 0)$	14
Coll-CH-CH	ShCla+Bra (1.1)	in CCl. 0° 10 min	& $c-$, $t-$ (trace) Cl Cl CoH-CHClCHaBr (87)	14
0110011-0112	00013 - Diz (T.T)	m 0014, 0, 10 mm	CONSCREEMENTS (07)	τ.τ

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

trans fashion with high stereospecificity, and the products are generally in accord with Markovnikov's rule. No competitive iodination is found in chloroiodination; 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); $I_2 : ICl = 1 : 10^5$, $Br_2 : BrCl = 1 : 4 \times 10^2$). 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

$$SbCl_{5}+Br_{2} \xrightarrow{} [SbCl_{5}Br]^{-}Br^{+} \xrightarrow{} SbCl_{4}Br+BrCl$$
 (7)

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.

S. UEMURA and M. OKANO

II. HALOGENATION OF ARENES

For the halogenation of rather reactive aromatics, the use of various metal or metalloidal halides (SbCl₅, FeCl₃, VCl₄, MoCl₅, PCl₅, TlCl₃·4H₂O, CuBr₂, TlBr₃·4H₂O *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

Aromatic compound	Halogenating agent	Reaction Conditions	Product (Yield, %; <i>o p</i> ratio)	Ref.
C ₆ H ₅ Cl	SbCl ₅	neat, 41–59°, 2 hr	C ₆ H ₄ Cl ₂ (82; 0.2)	20
C ₆ H ₅ Cl	FeCl ₃	neat, 125–140°, 3 hr	$C_6H_4Cl_2$ (86; 0.1)	19
C ₆ H ₅ Cl	VCl ₄	neat, 118–121°, 2.5 hr	C ₆ H ₄ Cl ₂ (70; 0.2)	21
C_6H_5Cl	MoCl ₅	neat, 105–110°, 2.5 hr	$C_6H_4Cl_2$ (31; 0.1)	21
$C_6H_5CH_3$	$SbCl_5$	neat, 18–31°, 2.5 hr	CH ₃ C ₆ H ₄ Cl (87; 0.9)	20
$C_6H_5CH_3$	$TlBr_3 \cdot 4H_2O$	in CCl ₄ , 78°, 1 hr	$CH_{3}C_{6}H_{4}Br$ (20; 1.6)	24
$C_6H_5CH_3$	$TlCl_3 \cdot 4H_2O$	in CCl ₄ , 78°, 2 hr	$CH_{3}C_{6}H_{4}Cl (28; 1.0) \& CH_{3}C_{6}H_{4}COOH(10; 0.7)$	22
Anthracene	CuCl ₂	in CCl ₄ , 78°, 7 hr	9-Chloroanthracene (98)	27
C ₆ H ₅ OH	$CuCl_2$	in DMF+LiCl, 150°, 5 min	ClC ₆ H ₄ OH (60; 0.1–0.2)	25
β -C ₁₀ H ₇ OH	$CuBr_2$	in aq. CH3OH+KBr, 25°, 15 hr	α -Bromo- β -naphthol (50)	26
C_6H_6	AlI_3+CuCl_2	neat, 80°, 5 hr	$C_{6}H_{5}I$ (65)	28
$C_6H_5CH_3$	${}^{\mathrm{FeI}_{2} \cdot 4\mathrm{H}_{2}\mathrm{O}}_{\mathrm{+CuCl}_{2}}$	neat, 110°, 3 hr	$CH_{3}C_{6}H_{4}I$ (81;1.1)	28
C_6H_5OH	$I_2 + CuCl_2$	in C ₆ H ₅ Cl, 130°, 29 hr	<i>p</i> -IC ₆ H ₄ OH (69)	28
$\mathrm{C_6H_5N(CH_3)_2}$	$I_2 + CuCl_2$	in C_6H_6 , 60°, 0.5 hr	$p - IC_6 H_4 N(CH_3)_2$ (47)	28

Table 4. Aromatic Halogenation with Metal Halides

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

		Halotoluene				
Halogen source	Reaction Conditions	Is	somer Rat	Rel. Rate	Ref.	
		0	т	Þ	$k_{\rm T}/k_{\rm B}$	
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 (TlCl ₃ ·4H ₂ O cat)	in CCl ₄ , 78°	64	0	36	43	23
$TlCl_3 \cdot 4H_2O$	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; SbCl₅> FeCl₃, VCl₄>MoCl₅, CuCl₂, and this correlates well with their oxidizing ability.^{19~21}) Though the activity of TlCl₃·4H₂O 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 Cl₂ and Cl⁺. When SbCl₅ or TlCl₃·4H₂O 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 SbCl₄⁺ and TlCl₂⁺, may function (see eq. 8).^{20,23)} In cases of FeCl₃, VCl₄,

$$2SbCl_{5} \rightleftharpoons [Cl_{4}^{\overset{\circ}{5}+}Cl \rightarrow \overset{\circ}{5}bCl_{5}] \rightleftharpoons SbCl_{4}^{+}+SbCl_{6}^{-}$$

$$(8)$$

$$(8)$$

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})

$$\bigotimes + \stackrel{\delta^{+}}{\underset{l}{\text{cl}}} + \stackrel{\delta^{-}}{\underset{l}{\text{cl}}} + \stackrel{\delta^{-}}{\underset{l}{\text{FeCl}_{3}}} \longrightarrow \bigotimes -\text{Cl} + 2\text{FeCl}_{2} + \text{H}^{+} + \text{Cl}^{-}$$
(9)

On the other hand, the selectivity data in the bromination with $TlBr_3 \cdot 4H_2O$ indicate that the reaction is essentially the same as that with bromine in the presence of $TlBr_3$ catalyst.²⁴⁾

Though CuX₂ 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 CuCl₂-iodine donor combinations (*cf.* eq. 5 and 6) has recently been developed.²⁸⁾ Some examples are included in Table 4. FeI₂ and AlI₃ 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 metalloidal halides (*e.g.*, PCl_5 , SbCl₅, FeCl₃ *etc.*) can be used in place of halogen elements. Some examples are given in Table 6.

PCl₅ can react smoothly with alkanes in an inert solvents such as o-dichlorobenzene

S.	Uemura	and	Μ.	Okano

Substrate	Halide	Reaction Conditions	Product (Yield, %)	Ref.
n-C7H16	PCl ₅	in o-C ₆ H ₄ Cl ₂ , BPO cat, 90°, 8 hr	Mixed chloroheptanes (73)	12
$\langle \overline{H} \rangle$	PCl_5	in o-C ₆ H ₄ Cl ₂ , BPO cat, 88°, 7 hr	$\langle \overline{H} \rangle$ -Cl (70)	12
Adamantane	${\rm SbCl}_5$	in CH ₂ Cl ₂ , 40°, 3 hr	1- & 2-Chloroadamantane (69)	31
$C_6H_5CH_2CH_3$	PCl_5	neat, 105°, 16 hr	$C_6H_5CHClCH_3$ (60)	12
$(C_6H_5)_3CH$	PCl_5	neat, 140–150°, 18 hr	$(C_6H_5)_3CC1$ (93)	35
CH ₃ CH ₂ CH ₂ CHO	CuBr_2	in CH3OH, 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
$\rm CH_3COC_2H_5$	CuCl_2	in DMF+LiCl, 80-90°, 0.75 hr	CH ₃ COCHClCH ₃ (ca. 60)	25
$C_6H_5COC_2H_5$	CuCl_2	in DMF+LiCl, 80-90°, 1 hr	C ₆ H ₅ COCHClCH ₃ (72)	25

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

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. 10^{12} On the other hand, in the peroxide-catalyzed

$$PCl_5 \longrightarrow PCl_3 + Cl_2, \quad Cl_2 \longrightarrow 2Cl.$$
 (10)

Table 7. Isomer Distribution in Chlorination of n-Heptane and Adamantane

(a) Chlorination of *n*-Heptane (Ref. 30)

ττ	x-Ch	x-Chloro-n-heptane			
rialogene sour	$\frac{1}{1-2}$	-	3-	4–	
Cl_2	BPO cat., 98° 15.1 34	1.6	33.8	16.5	
PCl_5	BPO cat., 98° 2.5 36	3.4	41.5	19.5	
$PCl_3 + Cl_2$	BPO cat., 98° traces 24	1.0	52.0	24.0	
	(b) Chlorination of Adamantane (Ref. 31)			<u> </u>	
Halogene source	Reaction Conditions	C	Chloroada 1/2 r	mantane atio	
Cl_2	in SnCl ₄ (ϵ =2.87), 100°, 5 min		0.6		
Cl_2	in CH ₂ Cl ₂ (ϵ =9.08), 40°, 3 hr		0.5		
$\rm FeCl_3$	in SnCl ₄ , 110°, 3 hr		9–1	0	
FeCl ₃	in CH ₂ Cl ₂ , 40°, 7 hr		20		
$SbCl_5$	in SnCl ₄ , 110°, 15 min		9–1	0	
$SbCl_5$	in CCl ₂ FCClF ₂ (ϵ =2.24), AlCl ₃ added, 40°, 20-30 min	n	>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 $\cdot PCl_4$ (partly $\cdot Cl$) (eq. 11) would be reasonable.

 $\begin{array}{ccc} R \cdot + PCl_{5} \longrightarrow RCl + \cdot PCl_{4} \\ RH + \cdot PCl_{4} \longrightarrow R \cdot + HCl + PCl_{3} \\ \cdot PCl_{4} \longleftarrow PCl_{3} + Cl \cdot \\ RH + \cdot Cl \longrightarrow R \cdot + HCl \end{array}$ (11)

A similar reaction of FeCl₃ or SbCl₅ 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 Cl₂, FeCl₃, SbCl₅, and SbCl₅+AlCl₃ (see Table 7). SbCl₅ reacts generally at a more rapid rate than FeCl₃. Further, photolytic conditions enhance the rate of the SbCl₅ process, but does not promote the reaction with FeCl₃. This implies that SbCl₅ may be involved in a radical chain process, whereas the FeCl₃ 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.

 $[\mathrm{Ad}:\mathrm{H}\cdots\mathrm{Cl}:\mathrm{FeCl}_2]\longleftrightarrow [\mathrm{Ad}\cdot \ \mathrm{H}:\mathrm{Cl}\ \mathrm{FeCl}_2]\longleftrightarrow [\mathrm{Ad}^+\ \mathrm{H}\cdot \ \mathrm{Cl}^-\ \mathrm{FeCl}_2]$

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 dimethyl-formamide 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

$$\begin{array}{ccc} OH & O-CuCl & O & Cl \\ R-C = CHR' & \xrightarrow{l} R-C = CHR' & \longrightarrow & R-C - CHR' + Cu^{\circ} \end{array}$$
(14)

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 FeCl₃ in acetic acid has also been reported.³⁴⁾

S. UEMURA and M. OKANO

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