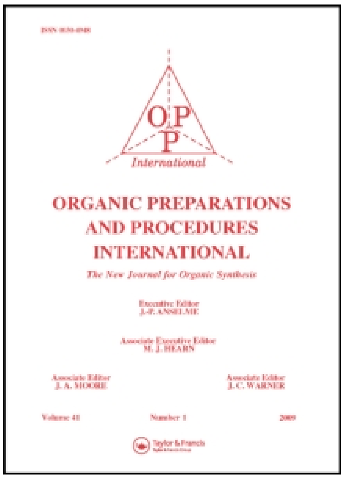

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HALOGENATION TABLES

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INTRODUCTION

Halogenation and other methods of preparation of halogen derivatives include an enormous number of reactions and reagents available for introducing halogens into organic products and intermediates. The Halogenation Tables is an attempt to correlate starting materials, products and halogenating agents to facilitate an orientation in this field of chemistry and to show what reactions are suitable for a specific purpose. Isolated and exceptional cases are omitted, but most common types of organic compounds and halogenating agents are included. A critical evaluation of the individual applications are shown in different markings: circled ⊕ means most common use, + means applicable, and (+) means of limited or rare application. The tables are based on the monographs listed at the end, on original literature references, and on the author's experiences.

Explanations of Symbols

RH	Aliphatic and alicyclic hydrocarbons and saturated hydrocarbon chains far enough from functional groups
C=C	Alkenes, cycloalkenes and their functional derivatives
C=C-CH	Allylic systems
C≡C	Acetylenes and their derivatives
C≡CH	Terminal acetylenes and their derivatives
ArH	Aromatic hydrocarbons and aromatic heterocyclics and their derivatives having at least one hydrogen in the aromatic ring

ArCH	Benzylic systems
RX	Halogen derivatives other than those of the reacting halogen
ROH	Alcohols and exceptionally phenols
RCHOR	Ethers having at least one hydrogen next to oxygen
ROR'	Ethers, aliphatic and aliphatic-aromatic
ArCHO	Aromatic aldehydes
CHO,-CO-	Aldehydes, ketones
CHCHO,CHCOR	Aldehydes and ketones having at least one α-hydrogen
$COCH_3$	Methyl ketones (in haloform reaction)
CO_2H,RCO_2H	Carboxylic acids
$CHCO_2H$	Carboxylic acids having at least one α-hydrogen
CHCZ,CHCN	Acyl halides, esters and nitriles having at least one α-hydrogen
CONH	Primary or secondary amides
CONHR	Secondary amides and their tautomers -C(OH)=N- in heterocycles
$CONR_2$	Tertiary amides
RSH,RSSR	Mercaptans, thiophenols and disulfides
RSO_2H	Sulfinic acids
$RSO_3H,ArSO_3H$	Sulfonic acids, aromatic sulfonic acids
$ROSO_2R'$	Alkyl sulfonates
SO_2NH	Primary or secondary sulfonamides
$ArNO_2$	Aromatic nitro compounds
CHN_2	Aliphatic diazo compounds, especially diazoketones
$ArN_2^{\oplus}$	Aromatic diazonium compounds
C=NOH	Oximes, especially ketoximes
RNH	Primary and secondary amines
C-C	Carbon-carbon bond cleavage (halogenolysis)
P,S,I	Tertiary phosphines, sulfides and aryl iodides (conversion to high-valency states of P,S,I)

BROMINATION

Starting Compound ↓	RH	C=C	C=C	C=C	C=C	C=C-CH	C≡C	C≡C	C≡C	C≡CH	ArH	ArH	ArCH	RX[a]	ROH	CHOR	ROR'	RCHO	CHO, -CO-	CHCHO CHCOR
Product	RBr	CBr-CBr	CH-CBr	C(OH)-CBr	CY-CBr[b]	C=C-CBr	CBr=CBr CBr_2-CBr_2	CH=CBr CH_2-CBr_2	CO-CBr_2	C≡CBr	ArH.6Br	ArBr	ArCBr	RBr	RBr	CBrOR	RBr	RCOBr	$CHBr_2$, -CBr_2-	CBrCHO CBrCOR
Br_2	⊕	⊕		⊕[c]	⊕[d]	⊕	⊕			+[e]	⊕[f]	⊕	⊕	⊕		⊕		⊕		⊕
BrF[i]					⊕															
BrCl					⊕							⊕								
BrI					⊕							(+)								
HBr			⊕					⊕						+	⊕		⊕[j]		(+)	
HOBr, NaOBr				⊕					⊕	⊕		+								+
$SOBr_2$															+					
NOBr																				
PBr_3															⊕					
$POBr_3$																				
PBr_5															⊕				⊕	
$AlBr_3$														⊕			(+)[n]			
LiBr, KBr $CaBr_2$														⊕						
CuBr, $CuBr_2$																				
ROBr												(+)								
RCONHBr				⊕[c]	⊕[o]	+[p]						(+)	+[p]							+
$(CH_2CO)_2NBr$				⊕[c]		⊕[p]						(+)	⊕[p]		+[q]					+
Ph_3PBr_2 $(RO)_3PBr_2$															⊕		+			
CBr_4												(+)								
RCOBr															(+)					

BROMINATION

Starting Compound ↓	$COCH_3$	CO_2H	RCO_2H	$CHCO_2H$	CHCZ CHCN	CONH	CONHR	$CONR_2$	RSH RSSR	RSO_2H	RSO_3H	$ROSO_2R'$	RSO_2NH	RNO_2	CHN_2	ArN_2^+	C=NOH	RNH	C–C
Product	CO_2H+$CHBr_3$	COBr	RBr	$CBrCO_2H$	BrCZ CBrCN	CONBr	CBr=NR	CN+2RBr	RSBr	RSO_2Br	RBr	RBr	RSO_2NBr	RBr	$CHBr_2$ CH_2Br	ArBr	CBr(NO)	RNBr	CBr+BrC
Br_2			⊕	⊕[g]	⊕	⊕			⊕	+	⊕		⊕[h]	⊕	⊕		⊕	⊕	⊕
BrF																			
BrCl																			
BrI																			
HBr															⊕	⊕			(+)
HOBr, NaOBr	⊕					⊕[k]							⊕				⊕	(+)	
$SOBr_2$		+																	
NOBr															+[l]				
PBr_3		+																	
$POBr_3$							⊕[m]												
PBr_5		⊕					⊕[m]	⊕											
$AlBr_3$																			
LiBr, KBr $CaBr_2$												⊕							
CuBr, $CuBr_2$																⊕			
ROBr																			
RCONHBr																	+		
$(CH_2CO)_2NBr$					+												+		
Ph_3PBr_2 $(RO)_3PBr_2$																			
CBr_4																			
RCOBr																			

FOOTNOTES TO BROMINATION

a) X = F, Cl, I

b) Y = F, Cl, F, OR, OCOR

c) In the presence of water

d) In the presence of methanol, Y = OMe

e) Reaction with acetylenic organometallics

f) Under ultraviolet irradiation

g) In the presence of phosphorus or phosphorus tribromide

h) In the presence of alkalies or mercuric oxide

i) Generated in situ from hydrogen fluoride and N-bromoamides, or from bromine trifluoride and bromine

j) Including cleavage of oxides to bromohydrins

k) Alkali hypobromite prepared in situ from alkalies and bromine

l) Direct replacement of primary amino group without isolation of diazo compound

m) Also in tautomers -C(OH)=N- (in heterocycles)

n) Also boron bromide cleaves the ethers to alkyl bromides

o) In the presence of alcohols (Y = OR), in the presence of acids (Y = OCOR)

p) Presence of peroxides is sometimes necessary

q) N-Bromosuccinimide + triphenylphosphine

FLUORINATION

Starting Compound ↓	RH	C-C	C=C	C=C	C≡C	C≡C	ArH	ArH	RX	CHX_2 CX_3	ROH	-CHO -CO-	$COCH_2$	CO_2H	COCl	$CONH_2$	$ROSO_2R'$	SO_2Cl	CHN_2	ArN_2^+	C-C	P S I
Product	RF	CF-CF	CH-CF	a) CX-CF	CF_2-CF_2	CH=CF CH_2-CF_2	b) ArH+6F	ArF	RF	CHXF, CHF_2 CXF_2, CF_3	RF	-CHF_2 -CF_2-	COCHF	CF_3	COF	CONHF	RF	SO_2F	CH_2F CHFX	ArF	CF+FC	c) PF_2 SF_2 IF_2
F_2 or electrolysis in HF	⊕	⊕			(+)		⊕	(+)	(+)	+						⊕					⊕	⊕
FCl[d)]				⊕																		
FBr[d)]				⊕															+			
FI[d)]				⊕																		
$FClO_3$													⊕[e]									
HF[f)]			⊕			⊕			(+)	⊕	(+)								⊕	⊕		+[g]
SF_4									(+)		+	⊕		⊕[h]								⊕
SeF_4, MoF_6												⊕										
NOF, NO_2F				⊕																		
AsF_3, SbF_3, SbF_3Cl_2									(+)	⊕												
SbF_5		(+)					(+)			⊕												
SiF_4, Na_2SiF_6										⊕										(+)		
HBF_4, $NaBF_4$																				⊕		
AgF, HgF			+[i]						⊕													
HgF_2									⊕	⊕												
AgF_2, CoF_3 (MnF_3, CeF_4, BiF_5)	⊕	⊕					⊕		(+)	⊕												
LiF, NaF, KHF_2, TlF															⊕			+				
KF(RbF, CsF)			⊕[j]	+[k]					⊕[l]	⊕					⊕		⊕	⊕				
XeF_2	⊕	⊕						⊕														
$ArIF_2$		⊕						(+)														
$ArSF_3$												⊕		⊕								
Et_2NSF_3											⊕	⊕										
Ph_3PF_2, Ph_2PF_3											⊕											
Et_2NCF_2CHClF											⊕											
$PbF_2(OAc)_2$		⊕																				
CF_3OF	⊕			⊕				⊕														
COF_2, COClF											+											

FOOTNOTES TO FLUORINATION

a) $X = Cl, Br, I$. In reaction with NOF and NO_2F, $X = NO$ or NO_2. In reaction with CF_3OF, $X = OCF_3$

b) Addition of six fluorines to aromatics and halogenated aromatics with partial and/or total replacement of hydrogens or halogens by fluorine

c) High-valency fluorides of phosphorus, sulfur and iodine

d) Prepared in situ from hydrogen fluoride and N-chloro-, bromo- and iodo amides, resp.; from fluorine tribromide and bromine, or iodine pentafluoride and iodine, resp.

e) Replacement of hydrogens in enol ethers, enamines, and in β-dicarbonyl and β-dicarboxyl compounds only

f) Frequently in the presence of catalysts: antimony chlorides in liquid phase, and ferric or chromic salts in vapor phase reactions

g) Preparation of $ArIF_2$ from ArIO

h) Intermediate RCOF can be isolated if limited amount of sulfur tetrafluoride is used

i) Silver fluoride in the presence of hydrogen fluoride

j) In the presence of proton donors such as formamide

k) In the presence of iodine, $X = I$

l) KF replaces also aromatic halogens activated for nucleophilic displacement and halogen atoms in aromatic polyhalogen compounds

IODINATION

Starting Compound ↓	C=C	C=C	C=C	C=C	C≡C	C≡C	C≡CH	ArH	RY[a]	ROH	ROR'	CHO, -CO-	CHCHO CHCOR	$COCH_3$	CO_2H	RCO_2H	$CHCO_2H$	CONH	$ROSO_2R'$	CHN_2	ArN_2^+
Product	CI–CI	CH–CI	C(OH)–CI	CX–CI[b]	CI=CI CI_2–CI_2	CH=CI CH_2–CI_2	C≡CI	ArI	RI	RI	RI	CHI_2, $-CI_2-$	CICHO CICOR	CO_2H+CHI_3	COI	RI	$CICO_2H$	CONI	RI	CH_2I CHI_2	ArI
I_2	⊕		+[c]	⊕[d]	⊕		⊕[e]	⊕[f]				+[g]	⊕[f]	⊕[h]		⊕	+[f]	⊕		⊕	
IF				⊕[i]																	
ICl				⊕				⊕									+				
IBr				⊕													+				
HI		⊕				⊕			+[j]	⊕	⊕									⊕	+
NaOI,KOI							⊕	+						⊕							
S_2I_2								(+)													
PI_3										⊕					+						
AlI_3										+											
NaI,KI									⊕										⊕		⊕
RCO_2I				+[k]			(+)	+													
$(CH_2CO)_2NI$													+								
$(PhO)_3PI_2$ $(PhO)_3PMeI$										⊕											

Footnotes to Iodination

a) Y = Cl, Br
b) X = F, Cl, Br
c) In the presence of water and mercuric oxide (hypoiodous acid in situ)
d) In the presence of mercuric oxide and alcohol (X = OR)
e) From acetylenic organometallics
f) Presence of oxidizing agents such as HIO_3, H_2O_2, etc. is necessary
g) From hydrazones of aldehydes and ketones
h) In the presence of alkali
i) From hydrogen fluoride and N-iodosuccinimide
j) Only with very reactive halogen derivatives such as acyl chlorides, α-chloroethers, etc.
k) Acyl hypoiodite, generated in situ from silver carboxylate and iodine; X = OCOR

CHLORINATION

Starting Compound ↓	RH	C=C	C=C	C=C	C=C	C=C-CH	C≡C	C≡C	C≡C	C≡CH	ArH	ArH	ArCH	RX[a]	ROH	RCHOR	ROR'	ArCHO	CHO,-CO-	CHCHO CHCOR
Product	RCl	CCl-CCl	CH-CCl	C(OH)-CCl	CY-CCl[b]	C=C-CCl	CCl=CCl CCl_2-CCl_2	CH=CCl CH_2-CCl_2	CO-CCl_2	C≡CCl	ArH.6Cl	ArCl	ArCCl	RCl	RCl	RCClOR	RCl[c]	ArCOCl	$CHCl_2$-,CCl_2-	CClCHO CClCOR
Cl_2	⊕	⊕		⊕[d]	⊕[e]	⊕	⊕			+[f]	⊕[g]	⊕	⊕	(+)		⊕		⊕		⊕
ClF[h]					⊕															
ClBr					⊕															
ClI					⊕															
HCl			⊕					⊕						(+)	⊕[i]		+			
HOCl,NaOCl				⊕		(+)			⊕	⊕		+								
S_2Cl_2,SCl_2	(+)				+										(+)					
$SOCl_2$												(+)	(+)		⊕		+			
SO_2Cl_2	+[g]	+										+	+[g]					(+)		+
NOCl		+			⊕															
PCl_3					+										⊕					
$POCl_3$															⊕					
PCl_5		(+)										⊕	(+)		⊕[k]	+			⊕	
$AlCl_3$														⊕						
LiCl																				
CuCl,$CuCl_2$												(+)		+						⊕
ROCl[l]				⊕	⊕	+[g]						+						+		+
RNHCl	(+)									(+)										
RCONHCl[m]				(+)[d]		+						(+)								
$(CH_2CO)_2NCl$	+[g]	(+)			+[e]	(+)						(+)	⊕[g]							
RSO_2NNaCl												(+)								
Ph_3PCl_2[n] $(RO)_3PCl_2$															⊕				⊕	
$ArICl_2$		+										(+)				(+)				
$CHCl_2OCH_3$ $PhCCl_3$															+		+		+	
RCOCl $COCl_2$,$(COCl)_2$																	(+)		+	

CHLORINATION

Starting Compound ↓	$COCH_3$	CO_2H	RCO_2H	$CHCO_2H$	CHCZ CHCN	CONH	CONHR	$CONR_2$	RSH RSSR	SO_3H	$ArSO_3H$	$ROSO_2R'$	SO_2NH	$ArNO_2$	CHN_2	ArN_2^+	C=NOH	RNH	C–C	>P,–I
Product	$CO_2H+CHCl_3$	COCl	RCl	$CClCO_2H$	CClCZ CClCN	CONCl	CCl=NR	CN+2RCl	RSCl	SO_2Cl	ArCl	RCl	SO_2NCl	ArCl	$CHCl_2$ CH_2Cl	ArCl	CCl(NO)	RNCl	CCl+ClC	$>P-Cl_2$, $-ICl_2$
Cl_2	+[d]		⊕	⊕	+	⊕			⊕		+		⊕	+	⊕		⊕		⊕	⊕
ClF																				
ClBr																				
ClI																				
HCl														(+)	⊕	⊕				
HOCl, NaOCl	⊕					⊕			+				⊕				⊕	⊕		
S_2Cl_2, SCl_2																				
$SOCl_2$		⊕					⊕	⊕		⊕	(+)			(+)						
SO_2Cl_2				+													⊕		+	
NOCl																	⊕			
PCl_3		⊕																		
$POCl_3$		⊕[j]					+													
PCl_5		⊕			+		⊕	⊕		⊕	(+)			(+)						
$AlCl_3$																				
LiCl												⊕								
CuCl, $CuCl_2$											(+)					⊕				
ROCl[i]						+												+		
RNHCl																				
RCONHCl																	⊕			
$(CH_2CO)_2NCl$				+[g]	+															
RSO_2NNaCl																	(+)			
Ph_3PCl_2 $(RO)_3PCl_2$							⊕													
$ArICl_2$																				
$CHCl_2OCH_3$ $PhCCl_3$		(+)																		
RCOCl $COCl_2$, $(COCl)_2$		⊕																		

FOOTNOTES TO CHLORINATION

a) X = F,Br,I

b) Y = F,Br,I,-OR,-S,-N,-P

c) Including chlorohydrins by cleavage of oxides

d) In the presence of water and/or alkalies

e) In the presence of alcohols or acids, Y = OR or OCOR, resp.

f) By reaction of alkali acetylides or acetylenic organometallics

g) In the presence of peroxides or under ultraviolet irradiation

h) Generated in situ from anhydrous hydrogen fluoride and alkyl hypochlorite, N-chloroamides or N-chlorosuccinimide

i) Especially in the presence of anhydrous $ZnCl_2$ (Lucas reagent)

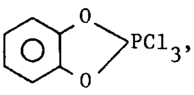
j) Only from salts

k) Also phenolic hydroxyl can be replaced

l) Also prepared in situ from chlorine and alcohols

m) N-chloroacetamide, N,2,4-trichloroacetanilide, N-chlorourea, N,N-dichloro-5,5-dimethylhydantoin, N-chlorosaccharin, etc.

n) Also



, $(PhO)_3\overset{\oplus}{P}MeCl^-$, $(PhO)_3\overset{\oplus}{P}(CH_2Ph)Cl^-$,

$Ph_3P{\cdot}CCl_4$, $(Me_2N)_3P{\cdot}CCl_4$

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