Hydro-dehalogenation of α-Haloketones by Halogen and Pseudo Halogen, Sulfur and Aromatic Compounds in Combination with Metal Halides

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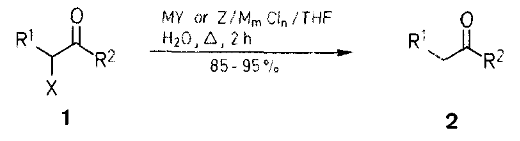
α-Haloketones **1** were successfully hydro-dehalogenated to their corresponding ketones **2** by sulfur and aromatic compounds (benzene, aniline and pyridine) in combination with metal halides in tetrahydrofuran. For comparison, α-haloketones **1** were also dehalogenated by metal halides alone in tetrahydrofuran.

The authors have previously published the dehalogenation by sodium iodide,[1] halogen and pseudo halogen compounds,[2] and sodium hydrogen sulfide,[3] in combination with metal halide in tetrahydrofuran. However, recently sulfur compounds such as sodium sulfide, sodium sulfite, sodium hydrogen sulfite and sodium thiosulfite and aromatic compounds such as benzene, aniline, and pyridine have been found to dehalogenate α-haloketones **1** satisfactorily. The effective dehalogenation by sulfur compounds and aromatic compounds is now reported.



1, 2	R^1	R^2	X
a	H	C_6H_5	Cl
b	H	C_6H_5	Br
c	H	$3\text{-}CH_3OC_6H_4$	Br
d	H	$4\text{-}CH_3C_6H_4$	Br
e	H	$4\text{-}ClC_6H_4$	Br
f	$-(CH_2)_4-$		Cl
g	H	OCH_3	Cl
h	CH_3	CH_3	Cl

As shown in Table 1, α-haloketones **1a–h** were effectively hydro-dehalogenated in good yield (87–95%) by sodium hydrogen sulfide with help of tin(II) chloride in aqueous tetrahydrofuran. In the dehalogenation of α-chloroacetophenone (**1a**), in the absence of water, acetophenone (**2a**) was afforded in poor yield (70%). The dehalogenation of **1a** in the absence of tin(II) chloride gave a poor yield (65%); in the absence of tin(II) chloride and water, the yield was worse (60%). Thus, tin(II) chloride acts as activator to promote dehalogenation. Other metal halides, such as tin(IV), iron(II), iron(III), aluminum(III) and chromium(III) chloride, also promoted the dehalogenation. In the dehalogenation, only the aprotic solvents tetrahydrofuran and acetonitrile were suitable. The dehalogenation in protic solvents, such as methanol and ethanol, afforded many products and high-boiling impurities (GLC analysis).

In Table 2 and 3, sodium sulfide and sodium hydrogen sulfite also dehalogenated α-haloketones **1a–h** (85–92%) as effectively as sodium hydrogen sulfide.[3] Sodium sulfite and sodium thiosulfite (in Table 4 and 5) were also effective. In these dehalogenation, just as above, the water added to the tetrahydrofuran was important. Metal halides (hard acid)[5,6] such as tin(II), tin (IV), iron(II), iron(III), chromium(III) and aluminum(III) chloride similarly promoted the dehalogenation. However, in the dehalo-

Table 1. Hydro-dehalogenation of α-Haloketones by NaHS and a Metal Halide[a]

Substrate (mmol)	Product	Metal Halide (mmol)	Yield (%)
1a (3.3)	**2a**	$SnCl_2$ (10.6)	92
1b (2.5)	**2a**	$SnCl_2$ (10.6)	95
1c (2.2)	**2c**	$SnCl_2$ (10.6)	90
1d (2.3)	**2d**	$SnCl_2$ (10.6)	90
1e (2.2)	**2e**	$SnCl_2$ (10.6)	87
1f (3.7)	**2f**	$SnCl_2$ (10.6)	90
1g (4.0)	**2g**	$SnCl_2$ (10.6)	95
1h (4.7)	**2h**	$SnCl_2$ (10.6)	92
1a (3.3)	**2a**	$SnCl_4$ (7.6)	75
1a (3.3)	**2a**	$FeCl_2$ (15.7)	90
1a (3.3)	**2a**	$FeCl_3$ (12.3)	70
1a (3.3)	**2a**	$AlCl_3$ (14.9)	80
1a (3.3)	**2a**	$CrCl_3$ (13.0)	85
1a (3.3)	**2a**	$SnCl_2$ (10.6)	70[b]
1a (3.3)	**2a**	–	65
1a (3.3)	**2a**	–	60[b]
1a (3.3)	**2a**	$SnCl_2$ (10.6)	87[c]
1a (3.3)	**2a**	$FeCl_2$ (15.7)	89[c]

[a] A mixture of substrate, NaHS (53.5 mmol) and metal halide in H_2O/THF (30 mL, 1 : 5) is heated under reflux for 2 h.

[b] In this run, the reaction was performed in the absence of water.

[c] In this run, the solvent was CH_3CN.

Table 2. Hydro-dehalogenation of α-Haloketones by Na_2S und $SnCl_2$[a]

Substrate (mmol)	Product	Yield (%)	b.p. (°C)/Torr	
			found	reported
1a (3.3)	**2a**	85	120/60	119.8/60[7]
1b (2.5)	**2a**	87	120/60	119.8/60[7]
1c (2.2)	**2c**	90	124/12	125/12[8]
1d (2.3)	**2d**	87	118/20	115–20/20[9]
1e (2.2)	**2e**	88	125/24	124–6/24[10]
1f (3.7)	**2f**	36	91/100	90.4/100[7]
1g (4.0)	**2g**	92	23.5/200	24.0/200[7]
1h (4.7)	**2h**	91	78.5	79.6[7]

[a] A mixture of substrate, Na_2S (42.9 mmol) and $SnCl_2$ (10.6 mmol) in H_2O/THF (27 mL, 1 : 12.5) is heated under reflux for 2 h.

Table 3. Hydro-dehalogenation of α-Haloketones by $NaHSO_3$ and a Metal Halide[a]

Substrate (mmol)	Product	Metal Halide (mmol)	Yield (%)
1a (3.3)	**2a**	$SnCl_2$ (10.6)	88
1b (2.5)	**2a**	$SnCl_2$ (10.6)	90
1c (2.2)	**2c**	$SnCl_2$ (10.6)	87
1d (2.3)	**2d**	$SnCl_2$ (10.6)	86
1e (2.2)	**2e**	$SnCl_2$ (10.6)	90
1f (3.7)	**2f**	$SnCl_2$ (10.6)	90
1g (4.0)	**2g**	$SnCl_2$ (10.6)	91
1h (4.7)	**2h**	$SnCl_2$ (10.6)	92
1a (3.3)	**2a**	$SnCl_2$ (10.6)	70[b]
1a (3.3)	**2a**	–	40[c]
1a (3.3)	**2a**	$SnCl_4$ (7.6)	90
1a (3.3)	**2a**	$SnCl_4$ (7.6)	65[b]

[a] A mixture of substrate, $NaHSO_3$ (28.8 mmol) and $SnCl_2$ (10.6 mmol) in H_2O/THF (27 mL, 1 : 12.5) is heated under reflux for 2 h.

[b] In this run, the reaction was performed in the absence of water.

[c] In this run, the reaction was performed in the absence of water and metal halide.

Table 4. Hydro-dehalogenation of α-Haloketones by Na_2SO_3 and a Metal Halide[a]

Substrate (mmol)	Product	Metal Halide (mmol)	Yield (%)
1a (3.3)	**2a**	$SnCl_2$ (10.6)	86
1b (2.5)	**2a**	$SnCl_2$ (10.6)	87
1c (2.2)	**2c**	$SnCl_2$ (10.6)	88
1d (2.3)	**2d**	$SnCl_2$ (10.6)	87
1e (2.2)	**2e**	$SnCl_2$ (10.6)	90
1f (3.7)	**2f**	$SnCl_2$ (10.6)	40
1g (4.0)	**2g**	$SnCl_2$ (10.6)	93
1h (4.7)	**2h**	$SnCl_2$ (10.6)	92
1a (3.3)	**2a**	$SnCl_4$ (7.6)	81
1a (3.3)	**2a**	$FeCl_2$ (15.7)	80
1a (3.3)	**2a**	$FeCl_3$ (12.3)	78
1a (3.3)	**2a**	$CrCl_3$ (13.0)	35
1a (3.3)	**2a**	$AlCl_3$ (14.9)	40

[a] A mixture of substrate, Na_2SO_3 (23.8 mmol) and metal halide in H_2O/THF (26 mL, 1 : 25) is heated under reflux for 2 h.

Table 5. Hydro-dehalogenation of α-Haloketones by $Na_2S_2O_3$ and a Metal Halide[a]

Substrate (mmol)	Product	Metal Halide (mmol)	Yield (%)
1a (3.3)	**2a**	$SnCl_2$ (10.6)	90
1b (2.5)	**2a**	$SnCl_2$ (10.6)	90
1c (2.2)	**2c**	$SnCl_2$ (10.6)	89
1d (2.3)	**2d**	$SnCl_2$ (10.6)	88
1e (2.2)	**2e**	$SnCl_2$ (10.6)	91
1f (3.7)	**2f**	$SnCl_2$ (10.6)	60
1g (4.0)	**2g**	$SnCl_2$ (10.6)	90
1h (4.7)	**2h**	$SnCl_2$ (10.6)	92
1d (2.3)	**2d**	$SnCl_4$ (7.6)	85
1f (3.7)	**2f**	$SnCl_4$ (7.6)	40
1g (4.0)	**2g**	$SnCl_4$ (7.6)	90
1a (3.3)	**2a**	$SnCl_4$ (7.6)	89
1a (3.3)	**2a**	$FeCl_2$ (15.7)	90
1a (3.3)	**2a**	$FeCl_3$ (12.3)	88

[a] A mixture of substrate, $Na_2S_2O_3$ (18.9 mmol) and metal halide in H_2O/THF (30 mL, 1 : 5) is heated under reflux for 2 h.

genation by sodium sulfite (Table 4), the dehalogenation in combination with chromium(III) and aluminum(III) chloride gave poor results.

In the hydro-dehalogenation of 2-chlorocyclohexanone (**1f**) by sulfur compounds, sodium hydrogen sulfide and sodium hydrogen sulfite (with active hydrogen) gave better yield (90%) than the other sulfur compounds (36–60%). Aliphatic and alicyclic haloketones are generally more poorly dehalogenated[4] than aromatic haloketones. In this study, aromatic haloketones as well as 2-chlorocyclohexanone (**1f**) were effectively dehalogenated.

Aromatic compounds such as benzene, aniline and pyridine (soft base)[5,6] also effectively dehalogenated α-haloketones **1a–h** to their corresponding ketones **2**. As shown in Table 6, **1a–h** were effectively dehalogenated by aniline with the help of tin(II) chloride in the aqueous tetrahydrofuran. In the absence of water, α-chloroacetophenone (**1a**) was dehalogenated in 75% yield. The system of aniline/iron(II) chloride in the absence of water dehalogenated **1a** in only 70% yield.

Table 6. Hydro-dehalogenation of α-Haloketones by Aniline and a Metal Halide[a]

Substrate (mmol)	Product	Metal Halide (mmol)	Yield (%)
1a (3.3)	**2a**	$SnCl_2$ (10.5)	90
1b (2.5)	**2a**	$SnCl_2$ (10.5)	95
1c (2.2)	**2c**	$SnCl_2$ (10.5)	91
1d (2.3)	**2d**	$SnCl_2$ (10.5)	92
1e (2.2)	**2e**	$SnCl_2$ (10.5)	91
1f (3.7)	**2f**	$SnCl_2$ (10.5)	40
1g (4.0)	**2g**	$SnCl_2$ (10.5)	93
1h (4.7)	**2h**	$SnCl_2$ (10.5)	92
1a (3.3)	**2a**	$SnCl_4$ (7.6)	90
1a (3.3)	**2a**	$SnCl_2$ (10.5)	75[b]
1a (3.3)	**2a**	$FeCl_2$ (10.0)	85
1a (3.3)	**2a**	$FeCl_2$ (10.0)	70[b]
1a (3.3)	**2a**	$FeCl_3$ (12.3)	83

[a] A mixture of substrate, aniline (21.4 mmol) and metal halide in H_2O/THF (27 mL, 1 : 12.5) is heated under reflux for 2 h.

[b] In this run, the reaction was performed in the absence of water.

As represented in Table 7 and 8, pyridine and benzene, showed satisfactory dehalogenation of aromatic and aliphatic α-haloketone (90–93%), as was also the case for sodium nitrite (soft base, border line base) (90–96%) (Table 9). The presence of water was again an important factor. In this system, chromium(III) chloride and aluminum(III) chloride gave poor yields (50%).

IN Tables 6–9 the dehalogenation of 2-chlorocyclohexanone (**1f**) by the system of aniline, pyridine, benzene, or sodium nitrite, in combination with metal halides, gave poor yields (40–65%). In this study, aliphatic α-haloketones as satisfactorily dehalogenated as aromatic ones.[4]

Table 7. Hydro-dehalogenation of α-Haloketones by Pyridine and $SnCl_2$[a]

Substrate (mmol)	Product	Yield (%)
1a (3.3)	**2a**	90
1b (2.5)	**2a**	91
1c (2.2)	**2c**	92
1d (2.3)	**2d**	93
1e (2.2)	**2e**	90
1f (3.7)	**2f**	65
1g (4.0)	**2g**	92
1h (4.7)	**2h**	93

[a] A mixture of substrate, pyridine (25.3 mmol) and $SnCl_2$ (10.5 mmol) in H_2O/THF (27 mL, 1 : 12.5) is heated under reflux for 2 h.

Table 8. Hydro-dehalogenation of α-Haloketones by Benzene and $SnCl_2$[a]

Substrate (mmol)	Product	Yield (%)
1a (3.3)	**2a**	91
1b (2.5)	**2a**	93
1c (2.2)	**2c**	90
1d (2.3)	**2d**	90
1e (2.2)	**2e**	92
1f (3.7)	**2f**	40
1g (4.0)	**2g**	93
1h (4.7)	**2h**	92

[a] A mixture of substrate, benzene (23.0 mmol) and $SnCl_2$ (10.5 mmol) in H_2O/THF (27 mL, 1 : 12.5) is heated under reflux for 2 h.

Table 9. Hydro-dehalogenation of α-Haloketones by Sodium Nitrite and a Metal Halide[a]

Substrate (mmol)	Product	Metal Halide (mmol)	Yield
1a (3.3)	**2a**	$SnCl_2$ (10.5)	90
1b (2.5)	**2a**	$SnCl_2$ (10.5)	92
1c (2.2)	**2c**	$SnCl_2$ (10.5	93
1d (2.3)	**2d**	$SnCl_2$ (10.5)	92
1e (2.2)	**2e**	$SnCl_2$ (10.5)	91
1f (3.7)	**2f**	$SnCl_2$ (10.5)	50
1g (4.0)	**2g**	$SnCl_2$ (10.5)	95
1h (4.7)	**2h**	$SnCl_2$ (10.5)	96
1a (3.3)	**2a**	$SnCl_4$ (7.6)	78
1a (3.3)	**2a**	$FeCl_2$ (10.0)	85
1a (3.3)	**2a**	$FeCl_3$ (12.3)	70
1a (3.3)	**2a**	$SnCl_2$ (10.5)	50[b]
1a (3.3)	**2a**	$FeCl_2$ (10.0)	45[b]
1a (3.3)	**2a**	$CrCl_3$ (12.6)	50
1a (3.3)	**2a**	$AlCl_3$ (15.0)	50

[a] A mixture of substrate, $NaNO_2$ (43.0 mmol) and metal halide in H_2O/THF (27 mL, 1 : 12.5) is heated under reflux for 2 h.

[b] *In this run, the reaction was performed in the absence of water.*

Since metal halides, such as tin(II) chloride and iron(II) chloride are reducing agents, dehalogenation by tin(II), tin(IV), iron(II) and copper(I) chloride alone was examined. As shown in Table 10, tin(II) chloride afforded appreciable dehalogenation, except for 2-chlorocyclohexanone (**1f**) (10%). The other metal halides, iron(II), tin(IV) and copper(I) chloride, dehalogenated in poor yield (10–30%). Here the presence of water also promoted the dehalogenation. Why only tin(II) chloride appreciably dehalogenated is not clear. The ratio of water/tetrahydrofuran was not constant; the optimal ratio was determined for each system, based on the dehalogenation of α-chloroacetophenone.

Table 10. Hydro-dehalogenation of α-Haloketones by a Metal Halide[a]

Substrate (mmol)	Product	Metal Halide (mmol)	Yield (%)
1a (3.3)	**2a**	$SnCl_2$ (10.5)	75
1b (2.5)	**2a**	$SnCl_2$ (10.5)	75
1c (2.2)	**2c**	$SnCl_2$ (10.5)	80
1d (2.3)	**2d**	$SnCl_2$ (10.5)	74
1e (2.2)	**2e**	$SnCl_2$ (10.5)	75
1f (3.7)	**2f**	$SnCl_2$ (10.5)	10
1g (4.0)	**2g**	$SnCl_2$ (10.5)	80
1h (4.7)	**2h**	$SnCl_2$ (10.5)	75
1a (3.3)	**2a**	$SnCl_4$ (7.6)	20
1a (3.3)	**2a**	$SnCl_2$ (10.5)	40[b]
1a (3.3)	**2a**	$FeCl_2$ (10.0)	10
1a (3.3)	**2a**	$FeCl_2$ (10.0)	0[b]
1a (3.3)	**2a**	CuCl (20.0)	30
1a (3.3)	**2a**	CuCl (20.0)	0[b]

[a] A mixture of substrate and metal halide in H_2O/THF (27 mL, 1 : 12.5), is heated under reflux for 2 h.

[b] In this run, the reaction was performed in the absence of water.

Dehalogenation of α-bromo-*p*-methylacetophenone (1d) with NaHS; Typical Procedure for Tables 1–5:

A mixture of α-bromo-*p*-methylacetophenone (**1d**; 0.5 g, 2.3 mmol), NaHS (3 g, 53.5 mmol) and $SnCl_2$ (2 g, 10.6 mmol) in H_2O/THF (30 mL, 1 : 5) is heated under reflux for 2 h. The reaction mixture is cooled, filtered and washed with acetone (3 × 5 mL). The filtrate is distilled under reduced pressure to give crude *p-methylacetophenone* (**2d**), which is analyzed by GLC, NMR and IR; yield: 0.24 g (90%).

Dehalogenation of α-bromoacetophenone (1b) with Aniline; Typical Procedure for Tables 6–10:

A mixture of α-bromoacetophenone **(1b)** (0.5 g, 2.5 mmol), aniline (2 g, 21.4 mmol), tin(II) chloride (2 g, 10.5 mmol) in H_2O/THF (27 mL, 1:12.5) is heated under reflux for 2 h. The reaction mixture is cooled, filtered and washed with acetone (3 × 5 mL). The filtrate is distilled under reduced pressure to obtain crude *acetophenone* **(2a)**, which is analyzed by GLC, IR, and NMR; yield: 0.27 g (95%).

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