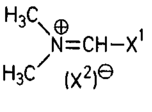
Conversion of Alcohols to Alkyl Halides using Iminium Salts

Masakuni Yoshihara, Tsunehito Eda, Keishi Sakaki, Toshihisa Maeshima

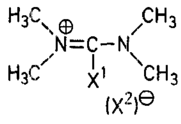
Department of Applied Chemistry, Faculty of Science and Engineering, Kinki University, Higashi-osaka, 577 Japan

Iminium salts react readily with various nucleophiles[1], and 2-halo-1-methylpyridinium salts have been found to be useful reagents for the synthesis of carboxylic esters, carboxamides, lactones, and alkyl halides[2]. We report here the synthesis of several new iminium salts and their use in the preparation of alkyl halides from alcohols.

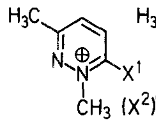
The iminium salts used in the present investigation are *N,N*-dimethylhalomethaniminium salts (**1**; derived from dimethylformamide), tetramethylurea chloride phosphorodichloridate (**2a**) or tetramethylurea dihalides (**2b,c**; derived from tetramethylurea), 6-halo-1,3-dimethylpyridazinium salts (**3**), and 6-chloro-1,3-dimethyl-4,5-dihydropyridazinium phosphorodichloridate (**4**).



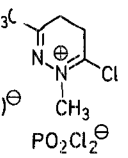
1a $X^1 = Cl$, $X^2 = PO_2Cl_2$
1b $X^1 = X^2 = Br$
1c $X^1 = X^2 = Cl$



2a $X^1 = Cl$, $X^2 = PO_2Cl_2$
2b $X^1 = X^2 = Br$
2c $X^1 = X^2 = Cl$

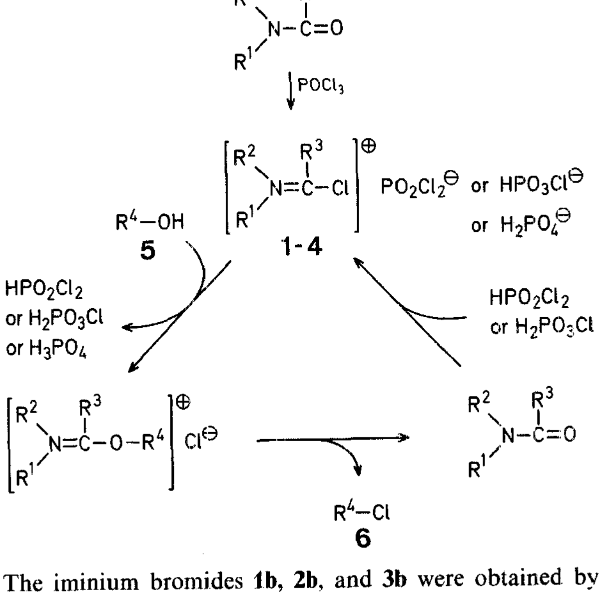


3a $X^1 = Cl$, $X^2 = PO_2Cl_2$
3b $X^1 = X^2 = Br$
3c $X^1 = X^2 = Cl$



4

These iminium salts were prepared in solution and were used (with or without isolation) for the conversions of alcohols (**5**) into alkyl halides (**6**). In the following scheme, the entire sequence of the conversion of alcohols (**5**) into alkyl chlorides (**6**, $X^1 = Cl$) is shown for the use of iminium phosphorodichloridates (**1a**, **2a**, **3a**, **4**) as chlorinating agents.



The iminium bromides **1b**, **2b**, and **3b** were obtained by passing dry hydrogen bromide through the solutions of iminium chlorides **1c**, **2c**, and **3c**, respectively, which were in turn obtained from the corresponding amines or 6-oxopyridazine derivatives and thionyl chloride in chloroform.

As shown in Table 2, the yields of alkyl halides obtained by our method are generally high. For comparison, some of the alcohols were also converted into alkyl halides using phosphoryl chloride. It was found that the use of iminium salts afforded far better yields of alkyl chlorides than the use of phosphoryl chloride.

6-Chloro-1,3-dimethylpyridazinium Phosphorodichloridate (3a):
1,3-Dimethyl-6-oxo-1,6-dihydropyridazine (1.98 g, 15 mmol) and phosphoryl chloride (2.35 g, 15 mmol) are stirred in dry chloroform (20 ml) for 1 h at 0 °C. Upon addition of a small amount of dry ether to the solution, a colorless hydroscopic precipitate is obtained which is isolated by suction; yield: 2.79 g (63%); m.p. 132–134 °C.

$C_6H_8Cl_3N_2O_2P$	calc.	C 25.95	H 2.88	N 10.09
(277.5)	found	26.09	3.17	10.25

6-Chloro-1,3-dimethyl-4,5-dihydropyridazinium Phosphorodichloridate (4):

1,3-Dimethyl-6-oxo-1,4,5,6-tetrahydropyridazine (1.90 g, 15 mmol) and phosphoryl chloride (2.31 g, 15 mmol) are stirred in dry chloroform (20 ml) for 24 h at room temperature. Upon addition of a small amount of dry ether to the solution a yellow, hygroscopic precipitate is formed which is isolated by suction; yield: 2.86 g (68%); m.p. 161–163 °C.

$C_6H_{10}Cl_3N_2O_2P$	calc.	C 25.76	H 3.58	N 10.02
(279.5)	found	25.69	3.56	10.09

6-Chloro-1,3-dimethylpyridazinium Chloride (3c)[3]**:**

A mixture of 1,3-dimethyl-6-oxo-1,6-dihydropyridazine (1.98 g, 15 mmol), thionyl chloride (1.90 g, 15 mmol), and dry chloroform (20 ml) is stirred at 60 °C for 2 h and is then evaporated in vacuo to give **3c** as a yellow hygroscopic precipitate; yield: 2.34 g (82%); m.p. 133–135 °C. An analytical sample may be obtained by recrystallization from ethyl acetate; m.p. 133–134 °C.

$C_6H_8Cl_2N_2$	calc.	C 40.22	H 4.47	N 15.64
(179.1)	found	40.20	4.43	15.61

6-Bromo-1,3-dimethylpyridazinium Bromide (3b):

Dry hydrogen bromide is passed through a solution of 6-chloro-1,3-dimethylpyridazinium chloride (**3c**; 2.34 g, 13 mmol) in dry chloroform (20 ml) for 3 h at 0 °C. The mixture is then evaporated in vacuo (exclusion of moisture). The resultant yellow crystals are washed with a small amount of chloroform and sublimed at 160 °C/2 torr; yield: 2.45 g (72%); m.p. 138–139 °C.

$C_6H_8Br_2N_2$	calc.	C 16.60	H 3.23	N 6.46
(267.9)	found	16.56	3.22	6.43

Table 1. Iminium Salts **1–4**

Iminium Salt	Yield[a] [%]	m.p. [°C]	Molecular formula[b] or m.p. reported	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
1a	72	[c]	—	3.50 (s, 3H)
2a	74	[c]	—	3.37 (s, 3H)
3a	63	132–134°	$C_6H_8Cl_3N_2O_2P$ (277.5)	7.56 (d, 1H); 7.06 (d, 1H); 3.78 (s, 3H); 2.05 (s, 3H)
4	68	161–163°	$C_6H_{10}Cl_3N_2O_2P$ (279.5)	3.72 (s, 3H); 2.42 (s, 4H); 2.03 (s, 3H)
1b	62	155–157°	156–158°[3]	3.50 (s, 3H)[d]
2b	70	113–115°	$C_5H_{12}Br_2N_2$ (259.8)	3.45 (s, 3H)[d]
3b	72	138–139°	$C_6H_8Br_2N_2$ (267.8)	6.95 (d, 1H); 6.75 (d, 1H); 4.25 (s, 3H); 2.52 (s, 3H)[d]
1c	63	135.5–138°	138–142°[4]	3.48 (s, 3H)
2c	72	109–113°	110–112°[1]	3.43 (s, 3H)
3c	82	133–135°	$C_6H_8Cl_2N_2$ (179.1)	7.26 (s, 1H); 3.79 (s, 3H); 2.35 (s, 1H)

[a] Yield of isolated product.
[b] The microanalyses were in satisfactory agreement with the calculated values: C, ±0.30; H, ±0.12; N, ±0.21.
[c] Hygroscopic crystalline mass.
[d] In acetonitrile-d_3.

Table 2. Alkyl Halides from Alcohols and Various Halogenating Agents (*in situ*)

Alkyl Halide from Corresponding Alcohol	Reagent	Yield [%]		b.p./torr [°C]		^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
		Isolated Product	by G.L.C. Analysis[a]	found	reported	
n-C_3H_7—Cl	**4**	—	82			3.62–3.40 (t, 2H); 2.00–1.08 (m, 16H); 1.08–0.60 (m, 3H)
	4	—	70[b]			
n-$C_{10}H_{21}$—Cl	$POCl_3$	27	31	126–127.5°/15	137–142°/24[5]	3.62–3.43 (t, 2H); 2.00–1.10 (m, 20H); 1.06–0.70 (m, 3H)
	4	66	68			
n-$C_{12}H_{25}$—Cl	$POCl_3$	20	24	115–118°/15	243–244°[6]	
	1a	87	93			
	3a	50	57			
	4	71	73			
n-C_6H_{13}—CHCl—CH_3	**1a**	90	—	65–66°/20	54–55°/12[7]	5.20–4.90 (m, 1H); 1.90–1.10 (m, 10H); 1.10–0.65 (m, 6H)
C_6H_5—CH_2—Cl	$POCl_3$	24	28	74–76°/20	61–62°/11[6]	7.22 (s, 5H); 4.50 (s, 2H)
	1a	84	87			
	2a	71	74			
	3a	83	87			
	4	65	70			
t-C_4H_9—Cl	**2a**	—	97			
	3a	—	100			
	4	—	100			
t-C_4H_9—Br	**1b**[d]	—	32[c]			
	2b[d]	—	32[c]			
	3b[d]	—	33[c]			

[a] 2 m Column, SE-30 20M, 180 °C.
[b] In dichloromethane as solvent.
[c] In tetrahydrofuran as solvent.
[d] Reaction carried out with isolated reagent.

Benzyl Chloride from Benzyl Alcohol; Typical Procedure:
A solution of benzyl alcohol (32.4 g, 0.3 mol) in dry chloroform (50 ml) is added to a stirred solution of dimethylformamide (7.3 g, 0.1 mol) and phosphoryl chloride (15.3 g, 0.1 mol) in dry chloroform (50 ml) and stirring is continued for 24 h at room temperature. The solvent is evaporated and the residue stirred with cold water (50 ml) and ether (100 ml). The ethereal solution is dried with calcium chloride and evaporated. The residual product is distilled in vacuo; yield: 32.0 g (84%); b.p. 74–76 °C/20 torr (Ref.[6], b.p. 61–62 °C/11 torr).

***t*-Butyl Bromide from *t*-Butanol; Small-Scale Procedure:**
6-Bromo-1,3-dimethylpyridazinium bromide (**3b**; 0.85 g, 3.9 mmol) and *t*-butanol (0.87 g, 11.7 mmol) are stirred in dry tetrahydrofuran (10 ml) for 24 h at room temperature. The yield of *t*-butanol is then determined by G.L.C. analysis of the mixture (internal standard method).

2-Chlorooctane from 2-Octanol; Typical Procedure:
A solution of 2-octanol (13.0 g, 0.1 mol) in dry chloroform (50 ml) is added to a stirred solution of dimethylformamide (7.3 g, 0.1 mol) and phosphoryl chloride (15.3 g, 0.1 mol) in dry chloroform (50 ml) and stirring is continued for 24 h at room temperature. Cold water (20 ml) is then added to the stirred mixture, the chloroform layer is separated, evaporated, and the residue distilled in vacuo; yield: 13 g (90%); b.p. 65–66 °C (Ref.[7], b.p. 54–55 °C/12 torr).

1-Chlorododecane from 1-Dodecanol; Typical Procedure:
A solution of 1-dodecanol (55.8 g, 0.3 mol) in dry chloroform (100 ml) is added to a stirred solution of 1,3-dimethyl-6-oxo-1,6-dihydropyridazine (13.2 g, 0.1 mol) and phosphoryl chloride (15.3 g, 0.1 mol) in dry chloroform (100 ml) and stirring is continued for 24 h at room temperature. Cold water (50 ml) is then added to the stirred mixture. The chloroform layer is dried with calcium chloride and evaporated. The residual product is distilled in vacuo; yield: 30.7 g (50%); b.p. 115–118 °C/15 torr (Ref. [6], b.p. 243–244 °C).

Received: July 31, 1979
(Revised form: February 8, 1980)

---

[1] H. Eilingsfeld, M. Seefelder, H. Weidinger, *Angew. Chem.* **836**, 22 (1960).

[2] T. Mukaiyama, M. Usui, E. Shimada, K. Saigo, *Chem. Lett.* **1975**, 1045.
E. Bald, K. Saigo, T. Mukaiyama, *Chem. Lett. 1975*, 1163.
K. Narasaka, T. Masui, T. Mukaiyama, *Chem. Lett.* **1976**, 373.

[3] Z. Arnold, A. Holy, *Collect. Czech. Chem. Commun.* **26**, 3059 (1961).

[4] H. H. Bosshard, R. Mory, M. Schmid, H. Zollinger, *Helv. Chim. Acta* **42**, 1653 (1959).

[5] S. S. Rossander, C. S. Marvel, *J. Am. Chem. Soc.* **50**, 1491 (1928).

[6] J. B. Conant, R. E. Hussey, *J. Am. Chem. Soc.* **47**, 476 (1925).

[7] A. Mckenzie, T. M. A. Tudhope, *J. Biol. Chem.* **62**, 551 (1924).

0039-7881/80/0932-0748 $ 03.00