Lead(IV) Acetate/Metal Halide Reagents; I. Synthesis of α-Haloketones

Shigeyasu MOTOHASHI*, Masakichi SATOMI

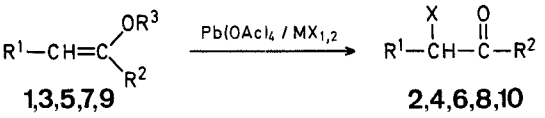
Department of Pharmacy, College of Science and Technology, Nihon University, 1-8 Kandasurugadai, Chiyoda-Ku, Tokyo 101, Japan

Yasuo FUJIMOTO*, Takashi TATSUNO

The Institute of Physical and Chemical Research, 2-1 Hirosawa, Wako-Shi, Saitama 351, Japan

In a previous paper[1], we have reported a novel lead(IV) acetate-promoted Favorskii-type rearrangement of a ketone or an enol ether to give ring contraction products. In continuation of our research we have found that treatment of enol ethers or enol esters with lead(IV) acetate in the presence of metal halides gives the corresponding α-haloketones, while the reaction of enol ethers with lead(IV) acetate/boron trifluoride etherate mainly affords ring contraction products.

In this communication, we describe a new method for the regiospecific synthesis of α-haloketones by application of the halogenation reaction of enol ethers or enol esters using the lead(IV) acetate/metal halide reagent. The results summarized in Table 1 indicate that (1) α-haloketones are produced regiospecifically in good yields under mild reaction conditions, (2) the halogen atom to be introduced can be selected freely by exchange of the metal halide, (3) the applicable metal halides are not restricted to sodium and potassium halides, but calcium and zinc halides are also suitable as halogen sources.

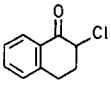
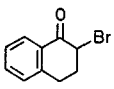
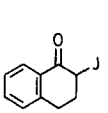
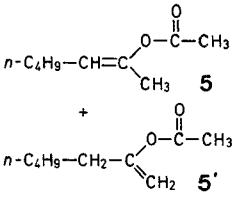
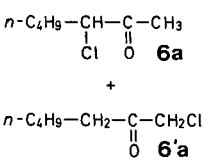
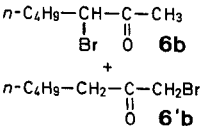
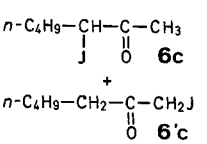


The lead(IV) acetate/metal halide reagents supplement the established halogenation methods such as bromine[2,3], *N*-halosuccinimides[4,5,6], silver acetate/iodine[7], and thalium(I) acetate/iodine[8] for the conversion of enol ethers and esters to α-haloketones.

α-Haloketones; General Procedure:

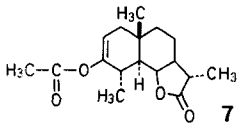
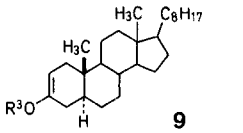
To a stirred suspension of the metal halide (2.2 equiv) in methanol (10 ml), 90% lead(IV) acetate (3.3 equiv) and the enolate (2.2 mmol) in methanol (3 ml) are added successively at 0–25 °C, and stirring is contin-

Table 1. Reactions of Enol Ethers and Acetates with Lead(IV) Acetate/Metal Halides

Substrate	Product[a]	R^3	Metal Halide/ Solvent	Temperature [°C]/ Time [min]	Yield [%]
 1	 2a	C_2H_5	$CaCl_2/CH_3OH$	r.t./10	99
		CO—CH_3	NaCl/CH_3OH	0°/10	77
	 2b	C_2H_5	NaBr/CH_3OH	0°/10	90
		CO—CH_3	NaBr/CH_3OH	0°/10	82
		$Si(CH_3)_3$	NaBr/CH_3OH	0°/10	47
	 2c	C_2H_5	NaJ/CH_3OH	r.t./10	85
		CO—CH_3	NaJ/CH_3OH	r.t./10	85
		$Si(CH_3)_3$	NaJ/CH_3OH	r.t./10	87
 3	 4a	CH_3	$CaCl_2/CH_3OH$	0°/15	76
		CH_3	NaCl/CH_3OH	r.t./10	74
		CO—CH_3	NaCl/CH_3OH	0°/120	91
		$Si(CH_3)_3$	NaCl/CH_3OH	r.t./10	58
		$Si(CH_3)_3$	KCl/CH_3OH	r.t./10	88
	 4b	CH_3	NaBr/CH_3OH	0°/10	93
		CO—CH_3	NaBr/CH_3OH	0°/120	95
		$Si(CH_3)_3$	NaBr/CH_3OH	0°/10	96
	 4c	CH_3	ZnJ_2/CH_3OH	r.t./10	67
		CH_3	NaJ/CH_3OH	r.t./10	79
		CO—CH_3	NaJ/CH_3OH	r.t./10	75
		$Si(CH_3)_3$	NaJ/CH_3OH	r.t./10	68
 5 + 5'	 6a + 6'a		$CaCl_2/CH_3OH$	r.t./10	93[b,c]
	 6b + 6'b		NaBr/CH_3OH	0°/10	82[b,c]
	 6c + 6'c		NaJ/CH_3OH	r.t./10	92[b,c]

0039-7881/82/1232-1021 $ 03.00

Table 1. (Continued)

Substrate	Product[a]	R^3	Metal Halide/ Solvent	Temperature [°C]/ Time [min]	Yield [%]
 **7**	 **8a**		$CaCl_2/CH_3OH$	0°/60	73[d]
	 **8b**		$NaBr/CH_3OH$	0°/10	66[d]
	 **8c**		NaJ/AcOH	r.t./30	59[d]
 **9**	 **10b**	$CO—CH_3$	$ZnBr_2$/ether	0°/10	73[e]
	 **10c**	CH_3	ZnJ_2/ether	r.t./10	55[f]
		$CO—CH_3$	NaJ/AcOH	r.t./10	58[e]

[a] Products **2a–c** are >98% pure by G.L.C. (silicone XE-60, 2%, 3 mm × 2 m).
Products **4a, b,** and **10b** are purified by column chromatography on silica gel eluting with chloroform or 1 : 1 hexane/chloroform.

[b] Substrate is a 38 : 62 mixture, see Ref.[8].

[c] Product is a 4 : 6 mixture as determined by G.L.C. and ^{1}H-N.M.R.

[d] Substrate is prepared from 3-oxo-5α(H),4,6,11β(H)-eudesman-6,13-olide and isopropenyl acetate according to general method of Ref.[4]; see also Ref.[9].

$C_{17}H_{24}O_4$	calc.	C 69.82	H 8.29
(292.4)	found	69.66	8.01

[e] See Ref.[8] for substrate.

[f] See Ref.[10] for substrate.

Table 2. Characterization of α-Haloketones

Product	m.p. [°C] or b.p. [°C]/torr	Molecular Formula or Lit. Data	I.R. (KBr or neat) $\nu_{C=O}$ [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]	M.S. *m/e*
2a	59–61°/3	81–83°/9[11]	1725	4.4 (m, 1 H)	134, 132 (M^+), 55 (100%)
2b	70–72°/3	82–85°/9[11]	1720	4.5 (m, 1 H)	178, 176 (M^+), 55 (100%)
2c	55–56°/1	54°/1[8]	1710	4.7 (m, 1 H)	224 (M^+, 100%)
4a	103–105°/1	—[12]	1685	4.6 (dd, *J* = 5 Hz, 7 Hz, 1 H)	182, 180 (M^+), 118 (100%)
4b	113–115°/1	—[12]	1685	4.7 (t, *J* = 4 Hz, 1 H)	226, 224 (M^+), 118 (100%)
4c	76–78° (hexane)	75–78°[8]	1675	5.1 (t, *J* = 4 Hz, 1 H)	272 (M^+), 145 (100%)
6a + 6′a	60–72°/18	—[13]	1720	4.1 (s, 2 H); 4.2 (t, *J* = 6 Hz, 1 H)	—
6b + 6′b	71–82°/13	—[14]	1720	3.9 (s, 2 H); 4.3 (t, *J* = 8 Hz, 1 H)	—
6c + 6′c	—	—[8]	1710	3.8 (s, 2 H); 4.5 (t, *J* = 7 Hz, 1 H)	—
8a	180° (dec) (ethanol)	178–179°[9]	1765, 1730	4.7 (dd, *J* = 6 Hz, 13 Hz, 1 H)	286, 284 (M^+), 187 (100%)
8b	150° (dec) (ethanol)	145–147°[9]	1765, 1725	4.9 (dd, *J* = 8 Hz, 13 Hz, 1 H)	330, 328 (M^+), 233 (100%)
8c	120° (dec) (ethanol)	$C_{15}H_{21}JO_3$[a] (376.3)	1765, 1720	5.1 (dd, *J* = 8 Hz, 13 Hz, 1 H)	376 (M^+, 100%)
10b	165–168° (ethanol)	170°[5]	1720	4.8 (dd, *J* = 7 Hz, 14 Hz, 1 H)	466, 464 (M^+), 311 (100%)
10c	125–128° (ethanol)	126–130°[12]	1715	5.0 (dd, *J* = 7 Hz, 14 Hz, 1 H)	512 (M^+, 100%)

[a] Calc. C 47.88 H 5.64
found 47.76 5.50

ued for 10–120 min (Table 1). The reaction mixture is poured into a solution of ice-cold water (50 ml) and 10% hydrochloric acid (10 ml), and extracted with ether (3 × 50 ml). The combined ether extract is washed successively with saturated sodium hydrogen carbonate solution (20 ml), sodium thiosulfate solution (5 ml), brine (10 ml), and dried with sodium sulfate. Evaporation of the solvent leaves crude α-haloketones which are purified by column chromatography on silica gel, by recrystallization, or by distillation under reduced pressure (Tables 1 and 2).

Received: January 26, 1982
(Revised form: April 13, 1982)

[1] H. Miura, Y. Fujimoto, T. Tatsuno, *Synthesis* **1979**, 898.
[2] M. Gaudry, A. Marquet, *Bull. Soc. Chim. Fr.* **1969**, 4169.
[3] R. H. Reuss, A. Hassner, *J. Org. Chem.* **39**, 1785 (1974).
[4] C. Djerassi, C. T. Lenk, *J. Am. Chem. Soc.* **75**, 3493 (1953).
[5] M. Rubin, B. H. Armbrecht, *J. Am. Chem. Soc.* **75**, 3513 (1953).
[6] L. Blanco, P. Amice, J. M. Conia, *Synthesis* **1976**, 194.
[7] G. M. Rubottom, R. C. Mott, *J. Org. Chem.* **44**, 1731 (1979).
[8] R. C. Cambie et al., *J. Chem. Soc. Perkin Trans. 1* **1978**, 126.
[9] W. Cocker, T. B. H. McMurry, *J. Chem. Soc.* **1956**, 4549.
[10] J. Levisalles, G. Teutsch, I. Tkatchenko, *Bull. Soc. Chim. Fr.* **1969**, 3194.

[11] S. Torii et al., *J. Org. Chem.* **45,** 2731 (1980).
[12] K. G. Rutherford, C. L. Stevens, *J. Am. Chem. Soc.* **77,** 3278 (1955).
[13] Ng. Ph. Buu-Hoi, *J. Org. Chem.* **18,** 649 (1953).
[14] H. M. E. Cardwell, *J. Chem. Soc.* **1951,** 2430.

0039-7881/82/1232-1023 $ 03.00