Communications to the Editor

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LEAD(IV)ACETATE-METAL HALIDE REAGENTS II. A NEW METHOD FOR THE SYNTHESIS OF β-HALO CARBOXYLATES AND β-IODO ETHERS

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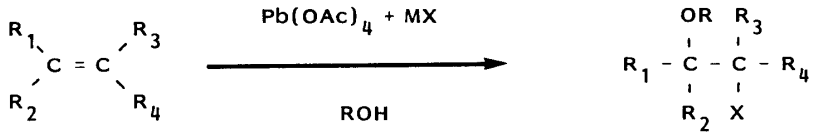
A new method for the synthesis of trans-ß-halo carboxylates and trans-ß-iodo ethers from alkenes using lead(IV)acetate-metal halide is described.

KEYWORDS——lead(IV)acetate; metal halide; alkene; trans-ß-halo carboxylate; trans-ß-iodo ether

We have reported[1] a new method for the regiospecific synthesis of α-haloketones by the application of the halogenation reaction of enol ethers or enol esters using lead(IV)acetate-metal halide. In continuation of our research on the lead(IV)acetate-metal halide reagents, we now report the reaction of various alkenes with lead(IV)acetate-metal halide(such as sodium iodide, zinc bromide or zinc chloride) and its application for the preparation of trans-ß-halo carboxylates and ß-iodo ethers.



R : CH_3CO, C_2H_5CO, CH_3, C_2H_5 X : Cl, Br, I

The reaction of alkenes with lead(IV)acetate-sodium iodide gave the corresponding ß-iodo carboxylates in high yields, while replacement of sodium iodide by zinc bromide or zinc chloride in the reaction afforded the corresponding ß-bromo carboxylates or ß-chloro carboxylates together with variable amounts of dibromide or dichloride. Treatment of 1-decene with lead(IV)acetate-metal halide reagents gave a mixture of Markovnikov and anti-Markovnikov products(Table I).

Table I

Substrate	Metal halide	Reaction conditions[a,b]	Addition product[c]	Yield % (isolated)
cyclohexene	NaI	AcOH	trans-2-iodocyclohexyl acetate	86
	$ZnBr_2$	AcOH	trans-2-bromocyclohexyl acetate	73
			trans-1,2-dibromocyclohexane	11
	$ZnCl_2$	AcOH	trans-2-chlorocyclohexyl acetate	49
			trans-1,2-dichlorocyclohexane	14
1-decene	NaI	AcOH	2-acetoxydecyl iodide	54
			2-iododecyl acetate	35
	$ZnBr_2$	AcOH	2-acetoxydecyl bromide	40
			2-bromodecyl acetate	16
			1,2-dibromodecane	30
	$ZnCl_2$	AcOH	2-acetoxydecyl chloride 2-chlorodecyl acetate	32[d]
			1,2-dichlorodecane	27
styrene	NaI	AcOH	2-iodophenethyl acetate	100
	NaI	EtCOOH	2-iodophenethyl propionate	66 e)
			2-iodophenethyl acetate	10
	$ZnBr_2$	AcOH	2-bromophenethyl acetate	72
			1,2-dibromoethyl benzene	21
	$ZnCl_2$	AcOH	2-chlorophenethyl acetate	47
			1,2-dichloroethyl benzene	40
indene	NaI	AcOH	trans-1-acetoxy-2-iodoindane	88
	$ZnBr_2$	AcOH	trans-1-acetoxy-2-bromoindane	59
			trans-1,2-dibromoindane	16
methyl 3-cyclohexene--1-carboxylate	NaI	AcOH	methyl trans-3-acetoxy-4-iodo-cyclohexane-1-carboxylate	40
			methyl trans-4-acetoxy-3-iodo-cyclohexane-1-carboxylate	32
cholesteryl acetate	NaI	CH_2Cl_2+AcOH	3β, 6β-diacetoxy-5α-iodocholestane	48
	$ZnBr_2$	CH_2Cl_2+AcOH	5α-bromo-3β, 6β-diacetoxycholestane	60[f]
			5β-bromo-3β, 6α-diacetoxycholestane	15[g]
trans-stilbene	$ZnBr_2$	AcOH	2-bromo-1,2-diphenylethyl acetate	86

a) Solvent at room temperature ; NaI : LTA : alkene = 2.2 : 1.1 : 1.0, $ZnBr_2$: LTA : alkene = 1.1 : 1.1 : 1.0, $ZnCl_2$: LTA : alkene = 2.2 : 1.1 : 1.0 .

b) Reaction time : ten minutes.

c) All known products have been identified by comparison (IR, ^{1}H-NMR, MS, GC, mp, bp) with authentic samples. All new compounds described in this paper gave satisfactory spectral (IR, ^{1}H-NMR and MS) and analytical data. The stereochemistry of the addition product from the action of LTA and metal halide on cyclohexene was confirmed by a detailed examination of its ^{1}H-NMR spectrum(ref. 6).

d) Product is a 4 : 1 mixture as determined by ^{1}H-NMR.

e) Product is a mixture as determined by ^{1}H-NMR.

f) Treatment of the ß-bromo acetate with methanolic potassium hydroxide gave 3ß-hydroxy-5ß, 6ß -epoxycholestane.

g) Treatment of the ß-bromo acetate with methanolic potassium hydroxide gave 3ß-hydroxy-5α, 6α -epoxycholestane.

When the reaction was carried out in methanol or ethanol, the corresponding ß-iodo ether was formed in fair to good yield(Table II). In all cases, formation of ß-iodo ether from unsymmetrical alkenes was found to be a regiospecific addition occurring in a Markovnikov sense.

Table II

Substrate	Metal halide	Reaction condition[a,b]	Addition product[c]	Yield % (isolated)
cyclohexene	NaI	MeOH	trans-2-iodocyclohexyl methyl ether	63
styrene	NaI	MeOH	2-methoxy-2-phenylethyl iodide	78
	NaI	EtOH	2-ethoxy-2-phenylethyl iodide	75
indene	NaI	MeOH	trans-1-methoxy-2-iodoindane	60
1-decene	NaI	MeOH	2-methoxydecyl iodide	73
	NaI	EtOH	2-ethoxydecyl iodide	58

a) Solvent at room temperature ; NaI : LTA : alkene = 2.2 : 1.6 : 1.0 .

b) Reaction time : ten minutes.

c) All known products have been identified by comparison (IR, ^{1}H-NMR, MS, GC, mp, bp.) with authentic samples.

The results summarised in Tables I and II indicated that the present reactions are useful as a convenient method for the synthesis of ß-halo carboxylates and ß-iodo ethers, and that the species of halogen atom and acyl or alkoxy group to be introduced can be selected freely by choice of metal halide and solvent.

It is particularly noteworthy that lead(IV)acetate and metal halide are readily available and easier to handle than the other ß-halo carboxylate or ß-halo ether-producing reagents such as halogen-silver carboxylate,[2] N-halosuccinimide,[3,4,5] thallium(I)acetate-iodine,[6] alkyl hypohalite,[7,8,9] iodine trichloride-silver acetate.[10]

GENERAL PROCEDURES

To a stirred solution of 90% lead(IV)acetate (1.1 mmol) in acetic acid or methanol (4 ml), the alkene (1.0 mmol) and the metal halide in acetic acid or methanol (3 ml) are added successively at room temperature, and stirring is continued for 10 min. The reaction mixture is poured into a solution of ice-cold water (30 ml) and 10% hydrochloric acid (10 ml), and extracted with ether (50 ml x 3). The combined ether extract is washed successively with saturated sodium hydrogen carbonate solution (20 ml), 10% sodium thiosulfate solution (5 ml), and brine (10 ml), and dried with sodium sulfate. Evaporation of the solvent leaves crude β-halo carboxylates or β-iodo ethers which are separated and purified by column chromatography, by high pressure liquid chromatography, by recrystallization, or by distillation under reduced pressure.

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