

LEAD(IV) ACETATE-METAL HALIDE REAGENTS III.  
 A NEW METHOD FOR THE SYNTHESIS OF TETRAHYDROFURAN,  
 TETRAHYDROPYRAN AND LACTONE DERIVATIVES

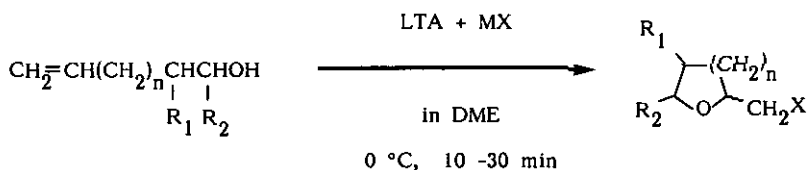
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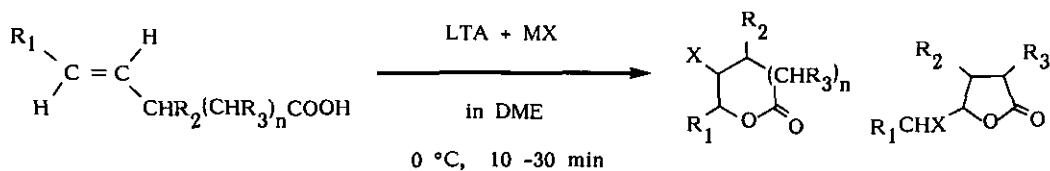
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**Abstract** - A new method for the synthesis of tetrahydrofuran, tetrahydropyran and lactone derivatives from  $\gamma\delta$ -,  $\delta\epsilon$ -unsaturated alcohols and  $\beta\gamma$ -,  $\gamma\delta$ -carboxylic acids is described.

The intramolecular cyclizations of an unsaturated carboxylic acids and unsaturated alcohols, which were assisted with formation of a cyclic three membered iodonium or bromonium ion by electrophilic attack of a positive iodine or bromine species on the double bond, are well known as halogenolactonization<sup>1</sup> and a useful method for the synthesis of tetrahydrofuran and tetrahydropyran derivatives<sup>2, 3, 4</sup>.

In the previous paper, we have reported<sup>5</sup> a new reagent, lead(IV) acetate-metal halide(LTA-MX), for the conversion of alkenes into the corresponding  $\beta$ -halo carboxylates and  $\beta$ -iodo ethers. In continuation of our research on LTA-MX reagents, we now wish to report here the application of this reagents to the intramolecular cyclization of  $\gamma\delta$ - and  $\delta\epsilon$ -unsaturated alcohols and  $\beta\gamma$ - and  $\gamma\delta$ -unsaturated carboxylic acids.





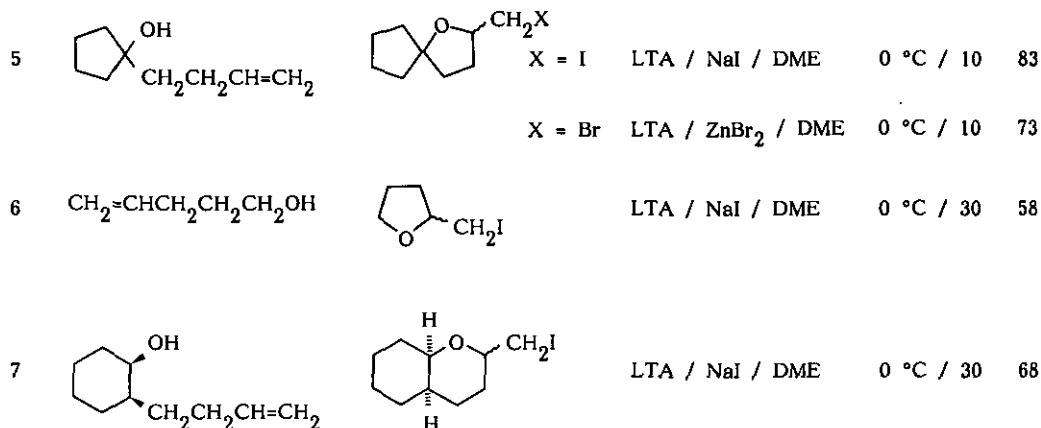
The intramolecular cyclization of  $\gamma\delta$ -unsaturated alcohols with LTA-NaI or LTA-ZnBr<sub>2</sub> gave the corresponding 2-iodomethyl or 2-bromomethyltetrahydrofuran derivatives in good yield ( Entry 1-4 in Table 1 ).

In the case of the cyclization of  $\delta\epsilon$ -unsaturated alcohols, 2-iodomethyl or 2-bromomethyltetrahydropyran derivatives were obtained in moderate yield ( Entry 5-7 in Table 1 ).

In all cases of  $\gamma\delta$ - and  $\delta\epsilon$ -unsaturated alcohols, the intramolecular cyclization occurred regioselectively in a Markovnikov sense to give the mixture of diastereomers. The regiochemistry of these compounds was determined from their NMR data.

Table 1

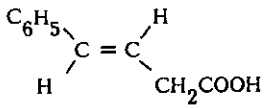
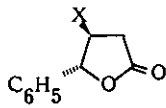
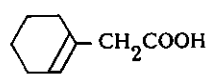
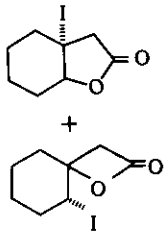
Entry	Substrate	Product	Reagent		Temp.	Yield(%)
			LTA / MX / Solvent	/ Time(min)		
1			LTA / NaI / DME	0 °C / 10	89	
2			X = I	LTA / NaI / DME	0 °C / 10	87
			X = Br	LTA / ZnBr <sub>2</sub> / DME	0 °C / 10	86
3			LTA / NaI / DME	0 °C / 10	79	
4			LTA / NaI / DME	0 °C / 30	75	

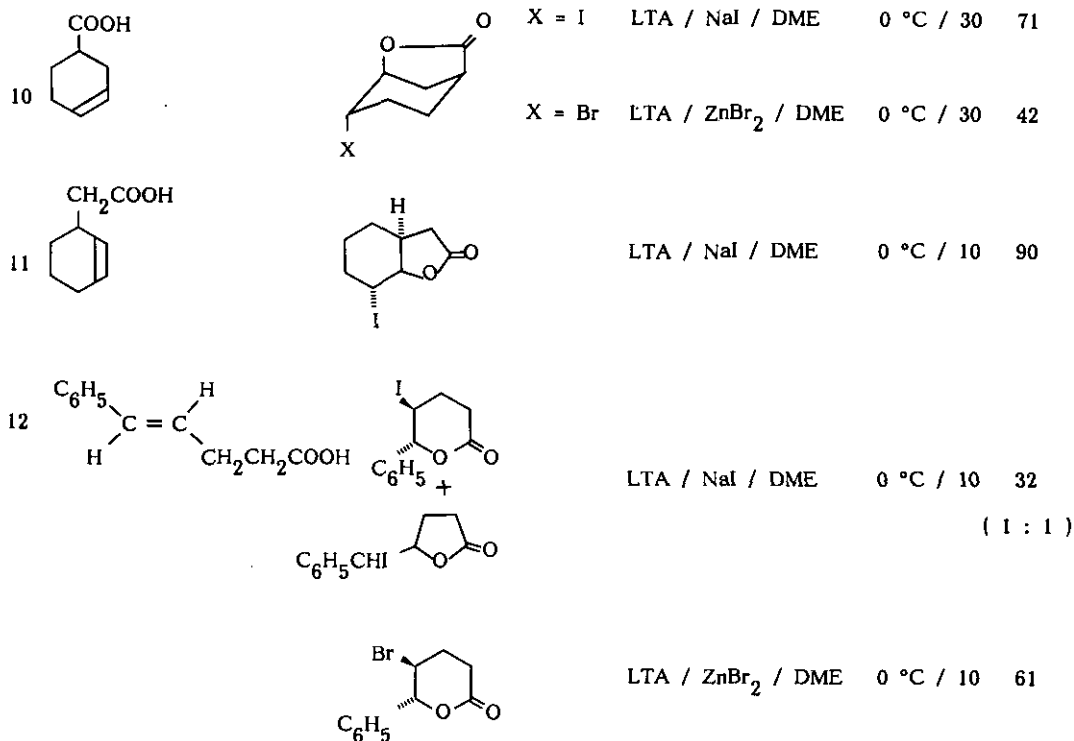


The intramolecular cyclization of  $\beta\gamma$ -unsaturated carboxylic acids with LTA-NaI or LTA-ZnBr<sub>2</sub> gave the corresponding  $\beta$ -iodo or  $\beta$ -bromo- $\gamma$ -lactones and  $\gamma$ -iodo- $\beta$ -lactone in moderate yield ( Entry 8, 9 in Table 2 ).

When 3-cyclohexenecarboxylic acid and 2-cyclohexeneacetic acid were treated under the same reaction conditions, the  $\delta$ -iodo or  $\delta$ -bromo- $\gamma$ -lactone was obtained ( Entry 10, 11 in Table 2 ) in accord with the work of van Tamelen<sup>6</sup> and House<sup>7</sup>. However, the reaction of 5-phenyl-4-pentenoic acid with LTA-NaI gave the mixture of  $\delta$ -iodo- $\gamma$ -lactone and  $\gamma$ -iodo- $\delta$ -lactone, and with LTA-ZnBr<sub>2</sub> gave the only  $\gamma$ -bromo- $\delta$ -lactone ( Entry 12 in Table 2 ).

Table 2

Entry	Substrate	Product	Reagent	Temp.	Yield(%)	
			LTA / MX / Solvent	/ Time(min)		
8			X = I    LTA / NaI / DME X = Br    LTA / ZnBr <sub>2</sub> / DME	0 °C / 10	75 55	
9			LTA / NaI / DME	0 °C / 10	61 ( 1 : 1 )	



The results summarised in Table 1 and 2 indicated that the present reactions are useful as a convenient method for the synthesis of tetrahydrofuran, tetrahydropyran and lactone derivatives from  $\gamma\delta$ - and  $\delta\epsilon$ -unsaturated alcohols and  $\beta\gamma$ - and  $\gamma\delta$ -unsaturated carboxylic acids.

The lead(IV) acetate and metal halide reagents supplement the established intramolecular cyclization reagents such as iodine<sup>1, 4, 7, 8</sup>, N-bromosuccinimide<sup>2</sup>, bromine<sup>3</sup> and thallium(I) carboxylate-iodine<sup>9</sup> for  $\gamma\delta$ - and  $\delta\epsilon$ -unsaturated alcohols and  $\beta\gamma$ - and  $\gamma\delta$ -unsaturated carboxylic acids to haloethers and halolactones.

#### GENERAL PROCEDURE

To a stirred solution of 90% lead(IV) acetate (1.1 or 2.2mM) in 1,2-dimethoxyethane (4ml), the unsaturated alcohol or carboxylic acid (1.0mM) in 1,2-dimethoxyethane (2ml) is added at 0°C. Then metal halide (2.2mM) in 1,2-dimethoxyethane (4ml) is added and stirring is continued for 10-30 min at 0°C.

The reaction mixture is poured into a solution of ice-cold water (30ml) and 10% hydrochloric acid (10ml), and extracted with ether (50mlx3). The combined

ether extract is washed successively with saturated sodium hydrogen carbonate solution (20ml), 10% sodium thiosulfate solution (5ml), and brine (10ml), and dried over sodium sulfate. Evaporation of the solvent gave the crude tetrahydrofuran, tetrahydropyran or lactone derivatives, which are separated and purified by column chromatography, by high pressure liquid chromatography, by recrystallization, or distillation under reduced pressure.

## REFERENCES

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