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FORMYLATION OF ORGANOMETALLIC COMPOUNDS WITH LITHIUM (OR SODIUM) FORMATE. PART I. A FACILE SYNTHESIS OF ALDEHYDES FROM GRIGNARD REAGENT

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Summary: Grignard reagent reacts with lithium (or sodium) formate in boiling THF giving the corresponding aldehydes in good yields. This reaction can be carried out at room temperature as well, but stirring of the reaction mixture for two or three days is required.

Aldehydes can be obtained by the reaction of Grignard reagent with a variety of compounds[1] and, recently, with several N-formyl amines[2-4]. Some of this formamides give the aldehydes free of secondary alcohol by-product. It has been also shown that aldehydes can be prepared in good yields by the reaction of scrupulously anhydrous formic acid with two moles of Grignard reagent, provided the reaction is carried out in THF solution[5]. The earlier described synthesis of aldehydes from formic acid [or copper(II) formate] and Grignard reagents, on account of low yields, was of no preparative value[6,7].

In this paper we have investigated the possibility of avoiding the use of formic acid (the drying of this acid is a rather tedious process) and have found that the formylation of Grignard reagent with lithium or sodium formate is very convenient, one pot procedure, and gives aldehydes without secondary alcohol as by-product ; also, in this reaction only one mole of Grignard reagent is used and the transfer of the reagent to the dropping funnel is unnecessary. These salts are commercially available or may be easily prepared in the laboratory.

Alkaline salts of formic acid are very slightly soluble in THF, but on heating, they react with Grignard reagent whereby the latter is added to the formate carbonyl group. If the reaction is carried out in ether, the yields are considerably lower, even after refluxing the reaction mixture for three days. If a mixture of ether and THF (1:2) is applied, the yields are approximately the same as those obtained in THF, but a longer heating is required ; this is significant in cases when it is more convenient to prepare Grignard reagent in ethereal than in THF solution.

Representative procedure: to 0.192 mole of Grignard reagent (prepared from 4.8 g of magnesium, 37,4 g of 2-bromoanisol and 200 ml of THF),11.5 g (0.22 mole) of lithium formate is added and the reaction mixture is heated with boiling in a nitrogen atmosphere until an almost clear solution is obtained (about 2 h); the major part of THF is removed by distillation, 100 ml of ether and about 0.1 g of hydroquinone are added to the residue, and the reaction mixture is decomposed with dilute HCl (cooled to 0°). 2-Methoxybenzaldehyde is isolated in usual way and distilled under nitrogen: bp 114°C/17 mmHg; mp 36-7°C. The yield is 23 g (85%).

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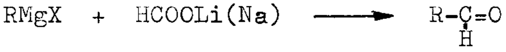
Table



$$\mathrm{RMgX} + \mathrm{HCOOLi(Na)} \longrightarrow \mathrm{R}\text{-}\underset{\mathrm{H}}{\mathrm{C}}\text{=O}$$

Entry	RMgBr(Cl)^a	R-CHO^b	Yield^c %	
			HCOOLi	HCOONa
1.	C_6H_5MgBr	C_6H_5CHO	85	79
2.	$C_6H_5MgCl^d$	C_6H_5CHO	80	72
3.	o-$CH_3OC_6H_4MgBr$	o-$CH_3OC_6H_4CHO$	85	76
4.	$(CH_3)_2CHMgCl$	$(CH_3)_2CHCHO$	80	75
5.	p-BrC_6H_4MgBr	p-BrC_6H_4CHO	83	69
6.	$C_6H_5CH_2MgCl$	$C_6H_5CH_2CHO$	79	
7.	1-Naphthyl-MgBr	1-Naphthaldehyd	78	
8.	$C_6H_5CH{=}CHMgBr$	$C_6H_5CH{=}CHCHO$	72	

[a] All reaction were perfomed on a 0.1-0.2 mol scale using a small excess of HCOOLi(Na). [b] Aldehydes are identified in the form of 2,4-dinitrophenylhydrazones. [c] Based on Grignard reagent. [d] Prepared according to H.Normant[8].

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