

# NEW METHOD FOR KETONE SYNTHESIS

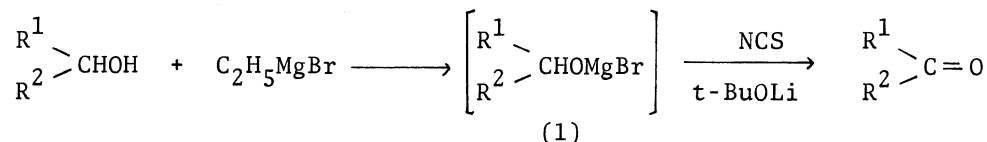
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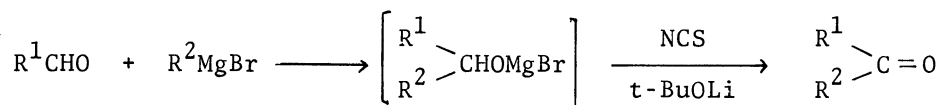
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Various ketones, including unsymmetrical ones, were prepared in good yields starting from aldehydes and Grignard reagents by utilizing the method for the oxidation of alkoxy magnesium bromide with N-chlorosuccinimide.

The previous paper<sup>1)</sup> presented that alkoxy magnesium bromide, prepared in situ from alcohol and ethylmagnesium bromide, was successfully oxidized with N-chlorosuccinimide (NCS) in the presence of lithium t-butoxide to give the corresponding carbonyl compound in a good yield. It is well known that alkoxy magnesium bromide (1), the key intermediate in the above oxidation of alcohol, is easily synthesized by the reaction of aldehyde and Grignard reagent, namely the Grignard reaction.



In this paper, we wish to report a new and convenient method for the synthesis of ketones, including unsymmetrical ones, starting from aldehydes and Grignard reagents by utilizing the above mentioned oxidation.



The following example demonstrates the simplicity and efficiency of the present process and illustrates the typical procedure: To a suspension of magnesium metal (34 mg, 1.4 mmol) in THF (0.5 ml) was added a solution of n-butyl bromide (233 mg, 1.7 mmol) in THF (4.5 ml) over a period of 20 min with vigorous stirring under an argon atmosphere. After disappearance of magnesium metal, a solution of 3-phenylpropionaldehyde (134 mg, 1.0 mmol) in THF (2 ml) was added dropwise to the solution of n-butyilmagnesium bromide, followed by addition of lithium t-butoxide, previously prepared from n-butyllithium (2.4 mmol) in hexane (1.54 ml) and t-butyl alcohol (216 mg, 2.9 mmol) in THF (4 ml). To the mixture was added NCS (322 mg, 2.4 mmol) at once. Then white precipitates appeared in a few minutes and the color of the solution changed to yellow. After stirring for 15 min, brine (10 ml) and powdered Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (1.0 g) were added into the reaction mixture. Insoluble compounds were filtered off, and the filtrate was extracted with ether (40 ml). The ethereal layer was washed

with 15% aq.  $K_2CO_3$  solution (20 ml) and brine (20 ml), and dried over anhydrous  $Na_2SO_4$ . After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel and elution with benzene gave 1-phenyl-3-heptanone (158 mg, 84%).

Similarly, various ketones were obtained by the oxidation of alkoxy magnesium bromides, prepared from aldehydes, such as benzaldehyde, 3-phenylpropionaldehyde, heptanal, cinnamaldehyde and (E)-2-hexenal, with several Grignard reagents. The results are summarized in the Table.

Table. Preparation of Ketones Starting from Aldehydes and Grignard Reagents

$R^1CHO$	$R^2MgBr^{2)}$	$R^1COR^2$ Yield (%), based on $R^1CHO$
$C_6H_5CHO$	$C_6H_5MgBr$	90
	$C_4H_9MgBr$	82
	$C_6H_5CH_2CH_2MgBr$	81
$C_6H_5CH_2CH_2CHO$	$C_6H_5MgBr$	78
	$C_4H_9MgBr$	84
	$C_6H_5CH_2CH_2MgBr$	77
$CH_3(CH_2)_5CHO$	$C_6H_5MgBr$	78
	$C_4H_9MgBr$	78
$C_6H_5CH=CHCHO$	$C_6H_5MgBr$	83
	$C_4H_9MgBr$	67
$CH_3(CH_2)_2CH=CHCHO$	$C_6H_5MgBr$	59
	$C_4H_9MgBr$	55

It is noted that the present method provides a convenient synthetic tool in the preparation of various ketones, including unsymmetrical ones.

#### Reference and Note

- 1) T. Mukaiyama, M. Tsunoda, and K. Saigo, Chem. Lett., 691 (1975).
- 2) Grignard reagents were prepared from magnesium metal and alkyl bromides. The molar ratio was as follows.

aldehyde : magnesium : alkyl halide

$C_6H_5MgBr$ :	1.0	:	1.2	:	1.4
$C_4H_9MgBr$ :	1.0	:	1.4	:	1.7
$C_6H_5CH_2CH_2MgBr$ :	1.0	:	1.5	:	1.8

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