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THE OXIDATION OF ALCOHOLS TO CARBONYL COMPOUNDS VIA ALKOXYMAGNESIUM BROMIDES

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Alkoxymagnesium bromides prepared from alcohols and ethylmagnesium bromide are oxidized with N-chlorosuccinimide in the presence of lithium tert-butoxide to afford the corresponding carbonyl compounds in good yields.

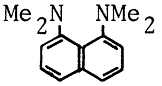
In the preceding report$^{1)}$, it was shown that triethyltin alkoxides prepared from alcohols and triethyltin methoxide are readily oxidized with bromine to afford the corresponding carbonyl compounds in good yields. In the present communication, the possibility of substituting triethyltin alkoxide in the above oxidation for other metal alkoxides was examined. After a number of experiments by using various metal alkoxides, alkoxymagnesium bromides were successfully oxidized with N-chlorosuccinimide (NCS) in the presence of lithium tert-butoxide to give the corresponding carbonyl compounds in good yields.

This process provides an efficient and new method among currently available procedures$^{2-8)}$ for the oxidation of alcohol. Especially, none of the previous methods by means of NCS gave satisfactory result for the oxidation of alcohols$^{2)}$.

Cinnamyl alcohol were used to determine the optimum experimental conditions. The oxidation of cinnamyloxymagnesium bromide, prepared from ethylmagnesium bromide and cinnamyl alcohol, to cinnamaldehyde was examined by using oxidizing agents such as tert-butyl hypochlorite, N-bromosuccinimide (NBS), N-bromoacetamide (NBA) and NCS.

$$\mathrm{PhCH{=}CHCH_2OMgBr} \xrightarrow[\text{base}]{\text{oxidizing agent}} \mathrm{PhCH{=}CHCHO}$$

Table 1. The Oxidation of Cinnamyl Alcohol to Cinnamaldehyde

Oxidizing Agent	Base	Yield (%)
t-BuOCl	——	36
NBS	——	58[a]
NBA	——	65
NCS	——	69
	NaH	49
		20
	t-BuOLi	**98**

a) 2,3-Dibromo-3-phenylpropanol was isolated as a by-product.

As shown in Table 1, it was clearly indicated that, in the case of the oxidation of cinnamyl alcohol, cinnamaldehyde was obtained in optimum yield by using NCS in the presence of lithium tert-butoxide.

The following example demonstrates the simplicity and efficiency of the present process and illustrates the typical ratio of reactants and solvent used. To a solution of C_2H_5MgBr in THF (3 ml)[9] was added dropwise a solution of cinnamyl alcohol (134 mg, 1.0 mmol) in THF (5 ml) at room temperature under an argon atmosphere. After stirring for 1 hr, a solution of t-C_4H_9OLi (2.4 mmol) in THF (4 ml) and n-hexane (1.5 ml)[10] was added, and the mixture was stirred for an additional hour at the same temperature. Then, NCS (321 mg, 2.4 mmol) was added, and the suspension was stirred for 1 hr. The resulting mixture was quenched with brine (10 ml) and $Na_2S_2O_3 \cdot 5H_2O$ (1.0 g) and was extracted with ether (30 ml). The ethereal layer was washed with 10% K_2CO_3 solution (10 ml) and with brine (10 ml). Vapor phase chromatographic analysis indicated a yield of 98% of cinnamaldehyde (naphthalene as internal standard with 10% Carbowax 20 M column). The R_f value for the tlc of the product was identical with that of authentic sample.

Similarly, octan-1-ol, octan-2-ol, benzhydrol, benzyl alcohol, p-nitrobenzyl alcohol, (E)-hex-2-en-1-ol, 3-phenylpropan-1-ol, cyclohexanol and furfuryl alcohol were oxidized to the corresponding carbonyl compounds in good yields as shown in Table 2.

Table 2. The oxidation of Alcohols by Using NCS

Alcohol	Yield (%)	
Cinnamyl alcohol	98[a)]	(69)
Octan-1-ol	92[a)]	(81)
Octan-2-ol	92[a)]	(50)
Benzhydrol	99[b)]	(73)
Benzyl alcohol	94[a)]	(80)
p-Nitrobenzyl alcohol	64[b)]	(66)
(E)-Hex-2-en-1-ol	59[a)]	(31)
3-Phenylpropan-1-ol	59[a)]	(68)
Cyclohexanol	80[a)]	(58)
Furfuryl alcohol	55[a)]	(59)

Values in parentheses indicate the yields of carbonyl compounds obtained by the oxidation in the absence of t-BuOLi.

a) Yield determined vapor phase chromatography with 2 m, 10% Carbowox 20 M column

b) Isolated yield after silica gel thin layer chromatography

It is noted that the present reaction is applicable to the oxidation of aliphatic primary alcohols to the corresponding aldehydes in good yields.

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9) A solution of C_2H_5MgBr in THF (3 ml) was prepared from Mg (29 mg, 1.2 mmol) and C_2H_5Br (144 mg, 1.3 mmol) in the presence of catalytic amount of iodine.

10) A solution of t-C_4H_9OLi was prepared by adding a solution of n-C_4H_9Li (2.4 mmol) in n-hexane (1.5 ml) to a solution of t-C_4H_9OH (178 mg, 2.4 mmol) in THF (4 ml) at room temperature.

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