Tetrahedron Letters No. 8, pp 761 - 762, 1978. Pergamon Press. Printed in Great Britain.

AN ALTERNATIVE SYNTHESIS OF KETONES FROM GRIGNARD REAGENTS

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(Received in Japan 16 November 1977; received in UK for publication 6 January 1978)

Although there have been many reports on the synthesis of ketones by use of Grignard reagents, these are restricted to the reaction of the reagents with carboxylic acid derivatives.[1,2] In this letter, we wish to report an alternative and useful synthetic method for ketones from Grignard reagents using pentacarbonyliron and alkyl iodides.

Typical procedure was as follows. To the tetrahydrofuran(THF) solution (40 ml) of phenylmagnesium bromide (22 mmol), pentacarbonyliron (3 ml, 22 mmol) was injected by syringe and the mixture was stirred for 1 hr at room temperature under nitrogen atmosphere. Then, slightly excess ethyl iodide (25 mmol) was added and the reaction solution was stirred further at the same reaction conditions. After 12 hr, the solution was diluted with diethyl ether, washed three times with brine, dried, and filtered, and the ether was removed with a rotary evaporator. The residue was placed on a short column (silica gel) and washed free of the colored iron compounds with hexane, and the product removed with benzene. Fractional distillation gave 2.1 g (72%) of ethyl phenyl ketone.

$$\text{R-MgBr} \xrightarrow[\text{ii) R'I}]{\text{i) Fe(CO)}_5} \text{R-CO-R'} \qquad \text{[Eq. 1]}$$

Representative results are listed in the Table. The yields were improved by the addition of 20 ml of 1-methylpyrrolidine-2-one to the reaction solution (Run 5 and 9).

Table. Synthesis of ketones from Grignard reagents

Run	RMgBr R	R'I R'	Solvent	Yield of R-CO-R' (%)
1	$CH_3CH_2CH_2-$	CH_3CH_2-	THF	78
2	$CH_3CH_2CH_2-$	$CH_3(CH_2)_3-$	THF	75
3	$CH_3(CH_2)_3-$	CH_3-	THF	70
4	$CH_3(CH_2)_3-$	$CH_3(CH_2)_3-$	THF	75
5			THF-NMP[a]	82 (91)[b]
6	$CH_3(CH_2)_7-$	CH_3-	THF	74
7	C_6H_5-	CH_3-	THF	65 (79)[b]
8	C_6H_5-	CH_3CH_2-	THF	72
9			THF-NMP[a]	78
10	C_6H_5-	$CH_3(CH_2)-$	THF	73

a) 1-Methylpyrrolidine-2-one. b) Yields in parentheses were determined by g.l.c. using internal standards.

In these reactions, acyltetracarbonylferrates [I] are assumed to be an intermediate [Eq. 2]; infrared spectra of the reaction mixtures of Grignard reagents and pentacarbonyliron have bands characteristic of [I].[3)]

$$\text{R-MgBr} \xrightarrow{Fe(CO)_5} \left[\underset{\underset{O}{\|}}{RC}\text{-Fe(CO)}_4\right]^- \xrightarrow{R'I} \text{R-CO-R'} + \text{[Fe compounds]} \quad \text{[Eq. 2]}$$

[I]

The main advantages of our method are the facility of the reaction procedure (this reaction is able to be carried out without cooling and/or heeting) and the high yields of the products (alcohols and alkanes which are frequently produced by the reaction of Grignard reagents with carboxylic acid derivatives are negligible). Other applications are currently explored in our laboratory.

References

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