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An Efficient Conversion of Aromatic Fischer Carbene Complexes into Methylketones

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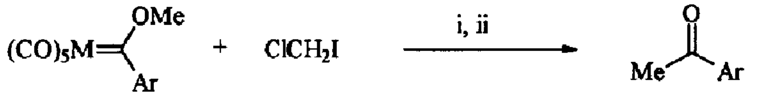
Abstract: Chloromethyllithium generated *in situ* is used to displace the metal from aromatic Fischer carbene complexes yielding, after hydrolysis, methylketones.

Since their initial preparation in the 1960's, Fischer carbene complexes have become a highly valuable tool for synthetically useful transformations[1], and they have been used as key intermediates in the total synthesis of natural and pharmacological products[1a,b]. Thus, they can serve as synthons for a variety of organic functional groups such as esters[2], aldehydes[3], ethers[4] or methyl vinyl ethers[5]. Enol ethers, in particular, can be prepared using diazomethane[6], a highly toxic and hazardous reagent[7], or from phosphorus ylides[8], involving tedious elimination of the generated phosphorus derivatives. For these reasons, alternative procedures for this transformation are of interest.

On the other hand, we have previously described the synthetic applications of chloromethyllithium[9]. In the present communication, we report a simple one-pot transformation of aromatic methoxycarbene complexes into aromatic methylketones, *via* enol ethers, using chloromethyllithium.

Thus, treatment of arylmethoxycarbene complexes 1 with chloromethyllithium generated *in situ*[10] at -78 °C gives, after hydrolysis, the corresponding methylketone 3 (Scheme 1 and Table).



1 2 3

Scheme 1. *Reagents and conditions*: i, MeLi / LiBr, -78 °C and then 20 °C; ii, H_2O, 20 °C.

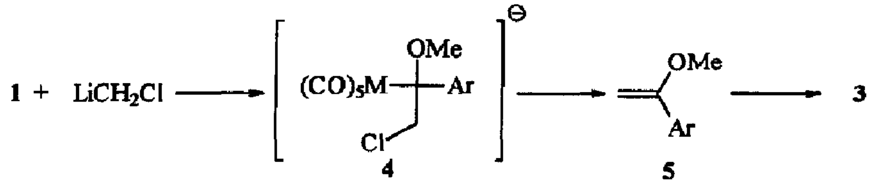
Table. Conversion of Fischer Carbene Complexes 1 into their corresponding Methylketones 3 with Chloromethyllithium.

Entry	M	Ar	Product[a]	Yield[b]
1	Mo	Ph	**3a**	80
2	Mo	2-Furyl	**3b**	78
3	Cr	Ph	**3a**	86
4	Cr	2-Furyl	**3b**	83
5	Cr	2-Thienyl	**3c**	75
6	Cr	4-Methoxyphenyl	**3d**	80
7	Cr	2-Naphtyl	**3e**	88

[a] All products were fully characterised by spectroscopic methods (IR, ^{1}H- and ^{13}C-NMR, and Mass spectrometry). [b] Isolated yield based on the starting Fischer carbene complex.

In a typical reaction, to a -78 °C stirred solution of metal-carbene complex 1 (3 mmol) and chloroiodomethane (6 mmol; 0.44 ml) in THF (30 ml) and diethylether (10 ml) was dropwise added, under nitrogen, methyllithium as a complex with lithium bromide (6 mmol; 4.0 ml of 1.5 mol.dm^{-3} solution in diethylether) over a period of 5 min. After stirring at -78 °C for 15 min, the mixture was allowed to reach room temperature. Then, the reaction was treated with H_2O and extracted with diethylether (3 x 10 ml). The combined ethereal layers were filtered over Celite® and dried (Na_2SO_4), the solvents were removed, and the resulting residue distilled to afford the corresponding methylketone 3.

The reaction may be viewed as proceeding by nucleophilic attack by the chloromethyllithium at the electron deficient carbene carbon to form the intermediate 4 which subsequently undergo spontaneous β-elimination yielding the corresponding enolether 5. Hydrolysis under the conditions described above of 5 affords the aromatic methylketone 3. (Scheme 2). This mechanism is supported by the isolating, before hydrolysis, of the enol ethers **5a** and **5e** from the carbene complexes **1a** and 1e.



Scheme 2

As expected, the reaction of chloromethyllithium with alkylmethoxycarbene complexes results in abstraction of the acidic H_α to the carbene-carbon atom, thus preventing the formation of alkyl vinyl ethers.

Otherwise, the reaction is very clean (no other products are detected), and general, since ketones 3 can be obtained from aromatic and heteroaromatic carbene complexes of molybdenum and chromium (see Table).

In conclusion, we believe that the methodology described in this paper represents a versatile procedure for the direct one-pot conversion of aromatic Fischer carbene complexes 1 into methylketones 3, thus constituting a simple and safer alternative to the use of the toxic diazomethane or phosphorus ylides.

Further studies of the reactivity of chloromethyllithium with α,β-insaturated Fischer carbene complexes are in progress.

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