

Cobalt(II) Chloride Catalysed Acylative Cleavage of Ethers

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
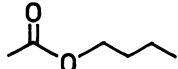
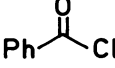
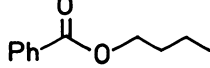
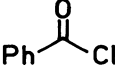
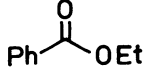


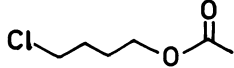
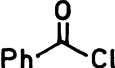
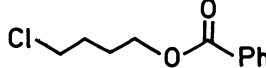
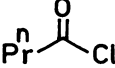
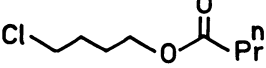


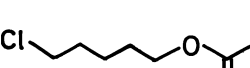
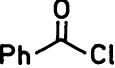
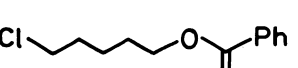

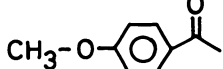

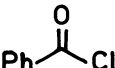

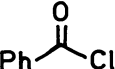
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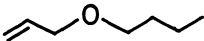

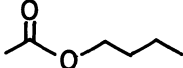
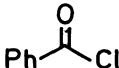
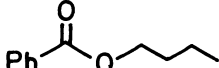
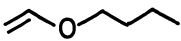

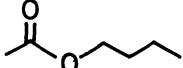
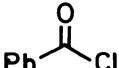
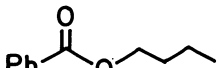
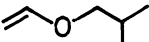

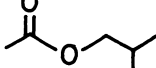
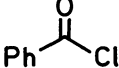
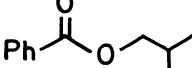
In the presence of catalytic amount of cobalt(II) chloride in acetonitrile, a wide variety of ethers are cleaved with acyl chlorides, to the corresponding esters in good to excellent yield.

Masking of alcohols as aliphatic, benzylic or allylic ethers is now very routinely applied in organic synthesis because they have proved to be quite indispensable, particularly during multistep syntheses where selective protection or deprotection of alcohols¹⁾ via these ethers is very often desired for other functional group manipulations. Unmasking of ethers to the parent alcohol has multifarious routes, although the success of this transformation very largely depends upon a judicious choice of the deblocking²⁾ reagent which is compatible with the other functional groups present in the ether molecule. This consideration for selectivity during ether cleavage has paved way to the development of new deblocking reagents and as a consequence to this concerted effort, organic chemist is now endowed with a plethora of new methods for cleaving variety of ethers to the corresponding alcohols. Besides the classical mode of cleavage, which involves the use of HI or HBr the modern variation consists of boron,³⁾ Aluminium,⁴⁾ and silicon⁵⁾ based reagents and a recent review on the cleavage of ethers has highlighted⁶⁾ the merits and demerits of these reagents.

On the other hand, ethers can also be cleaved by acylating agent like anhydrides or acyl chlorides to the corresponding esters in the presence of transition metal complexes as demonstrated by Ganem,⁷⁾ Apler,⁸⁾ and recently by Stille,⁹⁾ and their coworkers. Similarly Karger,¹⁰⁾ and Mazur had shown the cleavage of aliphatic and benzylic ethers with acetyl tosylate without a catalyst to the corresponding esters. These methods, though encompasses an efficient acylative cleavage of a wide variety of ethers, are marred by the harsh reaction conditions because often they require higher temperature and longer reaction periods for a successful reaction. Moreover, the usage of expensive transition metal complexes of Mo, W and even Pd as demonstrated by Apler and Stille, respectively, may pose some limitation for these methods to be of any preparative significance. Furthermore, none of these methods alone is suitable for the cleavage of acyclic aliphatic, benzylic, allylic, and vinylic ethers. In order to dispense with these shortcomings, we envisioned a catalyst which can mediate the cleavage of ethers

Table 1. Cobalt (II) chloride catalysed cleavage of ethers with acyl chlorides

Entry	Ether	Acyl chloride ^{b)}	Time/h	Products	Yield/ ^{a)} %
1	Bu ⁿ ₂ O		6		70 ^{c)}
2	"		8		65 ^{c)}
3	Et ₂ O		8		49 ^{c)}
4			2		90
5	"		3		89
6	"		3		78
7			12		55
8	"		14		30
9	PhOMe		12		50
10	Ph-CH ₂ -OMe		4	Ph-CH ₂ -Cl + Ph-CH ₂ -NHCOCH ₃	59 ^{c)} / 33
11	"		4	Ph-CH ₂ -Cl + Ph-CO-OCH ₃ + Ph-CH ₂ -NHCOCH ₃	45 / 87 / 21
12	Ph-CH ₂ -O-CH ₂ -Ph		4	Ph-CH ₂ -Cl + Ph-CH ₂ -O-CO-CH ₃ + Ph-CH ₂ -NHCOCH ₃	40 / 87 / 25
13	"		5	Ph-CH ₂ -Cl + Ph-CH ₂ -O-CO-Ph + Ph-CH ₂ -NHCOCH ₃	51 / 89 / 20

14			4		89 ^{c)}
15	"		4		87 ^{c)}
16			1 ^{d)}		79 ^{c)}
17	"		1.5		85 ^{c)}
18			1 ^{d)}		77 ^{c)}
19	"		1.5		81 ^{c)}

- a) Isolated yields of the compounds properly characterized by IR and ^1H NMR.
 b) All the reactions were carried out with 1.5 equiv. of acyl chloride at room temperature in dry acetonitrile.
 c) No attempt was made to trap the volatile chlorides or esters.
 d) Reaction was carried out at 0 °C.

under mild conditions and our endeavours in this direction culminated into some useful findings which are disclosed here.

Our recent observation on cobalt(II) chloride catalysed acylation¹¹⁾ of thiols and alcohols encouraged us to gauge the scope of this reaction towards the related system like ethers. Accordingly, when a catalytic amount (5 mol%) of anhydrous cobalt(II) chloride in dry acetonitrile was stirred with a mixture of an ether (1 equiv.) and an acyl chloride (1.5 equiv.) at ambient temperature under nitrogen atmosphere for few hours, after usual work-up and chromatographic separation, esters were obtained in good to excellent yield (see Table 1). The superiority of this method is characterized by: (a) low temperature and short reaction time, (b) facile cleavage of aliphatic, benzylic, allylic and vinylic ethers and (c) low cost of cobalt catalyst. Thus, aliphatic ethers like dibutyl ether and diethyl ether and cyclic ether like tetrahydrofuran, tetrahydropyran (entries 1-8) were cleaved by acyl chlorides to the corresponding esters and chloro esters, respectively, in very good yields. However in the case of diethyl ether and tetrahydropyran the yields were moderate. Similarly allylic ether (entries 14 and 15) underwent smooth cleavage to the corresponding esters in excellent yield. No ether cleavage was observed in case of anisole, however it underwent acylation to yield p-methoxyacetophenone in moderate yield (entry 9). In case of benzylic ether cleavage, besides the usual product, benzyl acetamide was also obtained as a by-product (entries 10 to 13).

This product may result from the attack of acetonitrile (solvent) on oxonium ion, presumably formed during the reaction. Surprisingly alkyl vinyl ethers were also cleaved under these conditions to give only alkyl esters (entries 16 to 19) in very good yields, as no product(s) arising due to the reaction of vinyl moiety could be obtained under these conditions. This reaction is rather unusual as it involves the cleavage of an sp^2 hybridised carbon-oxygen bond—an observation unprecedented in literature. The preparative usefulness of this method over the existing ones, resides in its versatility as it cleaves aliphatic, benzylic, allylic and vinylic ethers with remarkable ease and efficiency under very mild conditions. Mechanistically this reaction may have some similarity with the $Co(I)H(CO)_4$ induced cleavage of cyclic ethers¹²⁾ as reported by Heck. Cleavage of vinyl ethers in this unusual manner is rather perplexing and therefore, currently we are studying the generality and the mechanism of this reaction.

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(Received January 12, 1987)