Graphite-Catalyzed Acylative Cleavage of Ethers with Acyl Halides

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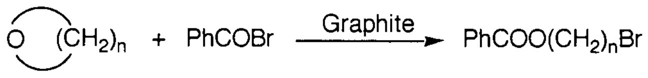
Graphite is found to catalyze acylative cleavage of ethers such as benzylic, allylic, *tert*-butylic and cyclic ethers with acyl halides to give the corresponding esters in good to excellent yields. Benzylic ether was cleaved chemoselectively, when a variety of other functional groups was present, to produce the corresponding ester along with benzyl halide.

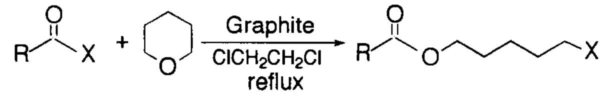
Conversion of alcohols into ethers is a widely used method for the protection of hydroxy groups in organic synthesis. A variety of reagents are available for the cleavage of the ethers but these are not always satisfactory for complex molecules containing sensitive functionalities and requiring selective deprotection. Ethers can also be cleaved by acylating agents such as acyl halide and acid anhydride in the presence of Lewis acid such as $ZnCl_2$[1] and $FeCl_3$[2] to the corresponding esters. Acylative cleavage of ethers also has been achieved by using $Mo(CO)_6$ [3] and palladium complexes[4]. Recently some new reagents for acylative cleavage have been reported (e. g., $CoCl_2$/acyl halide,[5] $SnBr_2$/acetyl bromide ,[6] and Zn/acyl chloride[7]). We here report a novel method involving graphite catalyzed acylative cleavage of a variety of ethers with acyl halides. To the best of our knowledge, it has not been reported that graphite, without any treatment, is effective as a catalyst for the acylative cleavage of ethers.

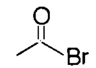
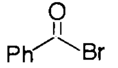
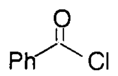
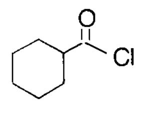
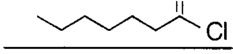
Cyclic ethers, tetrahydrofuran (THF) and tetrahydropyran (THP) were cleaved by acyl halides in the presence of graphite to give the corresponding halo esters.



The rate of THP opening is considerably slower than that of THF. Elevated temperature is necessary to affect cleavage in reasonable times. The reaction of THF with benzoyl bromide proceeded even at 30 ℃, whereas the reaction of THP required refluxing temperature of dichloroethane. In the acylative cleavage of THP by using $CoCl_2$[5], $MgBr_2$[8] and platinum complexes[9] as a catalyst, the yield of cleavage products does not exceed 60%. In contrast, THP reacted readily with acetyl bromide in the presence of graphite to form 5-bromopentyl acetate in 85% yield.The results of cleavage of THP with a variety of acid halides including acyclic, cyclic, and aromatic ones are shown in Table 1. The use of excess of the acyl halide gave higher yields and enhanced the reaction rate. In a general typical procedure, graphite[10] (1 g) was added to a mixture of tetrahydropyran (2 mmol) and acetyl bromide (4 mmol) in dichloroethane. The mixture was heated under reflux for 1 h. The products were isolated by a simple workup involving filtration of graphite,[11] washing the filtrate with aqueous sodium hydrogen carbonate, to remove the excess acetyl bromide, and evaporation of dichloroethane. Acyl chloride was less reactive than acyl bromide. The reaction of THP with benzoyl bromide gave 72% yield of the bromo ester after 1h, while benzoyl chloride reacted more slowly to produce the same yield of the chloro ester after 16 h. Aromatic chlorides were more reactive than cyclic and acyclic ones.

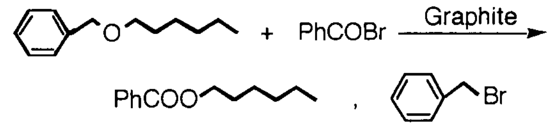
Table 1. Cleavage of tetrahydropyrane with graphite / acyl halide[a)]



Acyl halide	time (h)	yield (%)[b)]
	1	85
	1	72
	16	72
	24	36
	14	37

a) A mixture of THP (2 mmol), acyl halide (4mmol) and graphite (0.5 g) in 1,2-dichloroethane (5 mmol) was stirred under refulxing.
b) Yields were determined by GLC.

This reagent system is also very effective in the cleavage of acyclic ethers. As shown in Table 2 different types of ethers underwent cleavages by this procedure to produce the corresponding esters in good to excellent yields. If one of the alkyl groups is benzyl, allyl, and *tert*-butyl, the C-O bond attached to these moieties is cleaved selectively regardless of the nature of the other alkyl part. The cleavage of benzyl ether with benzoyl bromide gave the corresponding esters along with the formation of benzyl bromide.

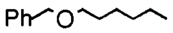
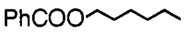
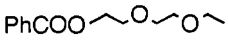
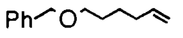
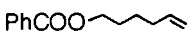
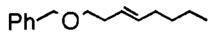
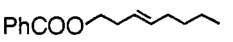
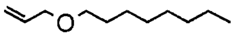
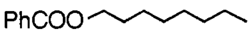
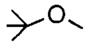
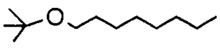
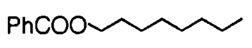
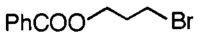


Benzyl ether was cleaved chemoselectively, when a variety of other functional groups (including double bond, triple bond and ether linkage) that are sensitive to reductive or acidic cleavage procedures, was present. For example, 1-benzyloxy-3,6-dioxaoctane and 1-benzyloxy-2-propyn were cleaved chemoselectively to produce the corresponding debenzylated ester in 80% and 93% yield, respectively (Run 3, 5). Allyl ether and *tert*-butyl ether were also cleaved to give deallylated and de-*tert*-butylated ester in high yields (Run 7~10).

In the reaction of benzylallyl ether with benzoyl bromide, the cleavage is selective to benzylic oxygen bond, producing allyl benzoate. *tert*-Butylalkyl ether was cleaved to tertiary carbon-

Table 2. Graphite catalyzed acylative clevage of ethers with benzoyl bromide[a]

$$\text{R-O-R'} + \text{PhCOBr} \xrightarrow[\text{ClCH}_2\text{CH}_2\text{Cl}]{\text{Graphite}} \text{PhCOOR} + \text{R'-Br}$$

Run	Ether	°C / h	Ester[b]	Yield(%)[c]
1		50/3		91
2		50/1		75
3		50/10		80
4		r.t./24		67
5		50/1		80
6		50/2		93
7		50/4		93
8		50/1.5		77
9		50/2	$PhCOOCH_3$	87
10		50/2		94
11		30/6		97

a) Conditions: ether (2 mmol), benzoyl bromide (4 mmol), graphite (0.5 g), 1,2-dichloroethane (5 mml). b) Characterized by IR, ^{1}H and ^{13}NMR and MS.
c) Yields were determined by GLC.

oxygen bond. Therefore, selective cleavage of *tert*-alkyl group in the presence of a secondary ones could be achieved straightforwardly and in good yield. Primary and secondary alkyl ether are inert to this reagent system. No ether cleavage was obtained in the phenolic ether such as anisol and phenylhexyl ether, however it underwent acylation to yield *p*-acylated phenolic ether in good yield.[12] The reaction of anisole with benzoyl bromide in the presence of graphite was carried out in refluxing benzene to yield *p*-methoxybenzophenone in 89% yield.

These results support a mechanism to similar to that proposed for the iron (III) chloride - acetic anhydride system[2] involving O-acylation of the ether followed by cleavage to give the most stable carbonium ion or nucleophlic displacement by acetate anion at the oxonium ion stage. The precise role of graphite is not clear to us . Presumably, acylinium cation and cationic intermediate are stabilized by graphite (cation - π interaction).

Further understanding of the catalysis by graphite and the application of graphite to other synthetic reaction are now under investigation.

References and Notes

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10 Graphite powder was from Aldrich (Catalogue no.28,286-3) and was employed without further purification.
11 The graphite used can be recovered by simple filtration of the reaction mixture and re-used. The recovered graphite was washed several times with ether and dichloroethane, followed by drying at 150 ℃ for 6 h. The activity of the graphite regenerated was lower than that of fresh graphite.
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