

Non-Catalyzed Cleavage Reactions of Ethers with Acyl Halides
under High-Pressure Conditions¹⁾

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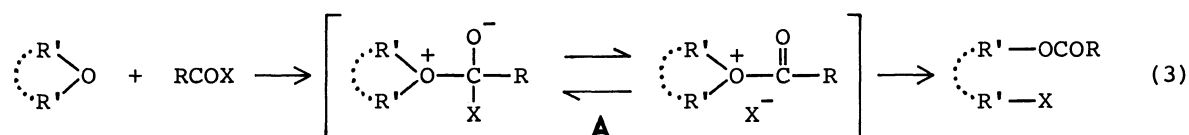
Various cyclic and acyclic ethers are efficiently cleaved with acyl chlorides or bromides to give ω -chloro- or ω -bromoesters under high-pressure conditions.

The utility of cleavage reactions of cyclic and acyclic ethers is well documented and several methods have been developed for this purpose.²⁾ Among these transformations the combination of acyl halides and Lewis acids has proved to be tremendously useful since its discovery in the beginning of this century. In this type of reactions RCO^+ ion derived from acyl halides and Lewis acids is generally considered to play an important role (Eqs. 1 and 2) and in the absence of Lewis



acids the reaction indeed is difficulty accessible except for highly reactive acyl iodides.³⁾










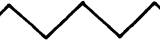

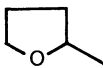






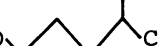
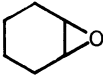
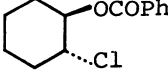
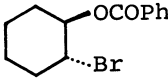
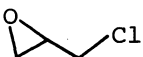
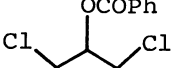
We anticipated that, if the reaction proceeds through an intermediate like A, such processes should be accelerated by using a high-pressure (Eq. 3), since

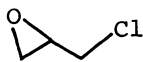
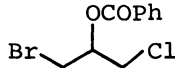
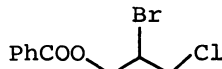
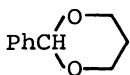



ionization and bond formation are both advantageous for this powerful technique.⁴⁾ In this paper we report that these expectations have been realized.

As summarized in Table 1, various ethers including some epoxides were

Table 1. Cleavage of Ethers with Acyl Halides at High-Pressure^{a)}

Run	Ether	RCOX	Temp/°C	Product	Yield/% ^{b)}
1	Et ₂ O	PhCOCl	62	PhCOOEt	(26)
2	n-Bu ₂ O	PhCOCl	62	PhCOOBu-n	(3)
3	"	PhCOBr	42	"	(13-17)
4		PhCOCl	62	PhCOO  Cl	95
5	"	4-MeOC ₆ H ₄ COCl	62	4-MeOC ₆ H ₄ COO  Cl	97
6	"	CH ₃ COCl	62	CH ₃ COO  Cl	81
7	"	 COCl	62	 COO  Cl	80
8	"	PhCOBr	42	PhCOO  Br	96
9		PhCOCl	62	PhCOO  Cl	57
10	"	PhCOBr	42	PhCOO  Br	89
11		PhCOCl	42	PhCOO  Cl PhCOO  Cl	36 ^{c)} 24 ^{c)}
12	"	 COCl	62	 COO  Cl  COO  Cl	46 ^{c)} 24 ^{c)}
13		PhCOCl	62		50
14	"	PhCOBr	42		71
15		PhCOCl	62		72 ^{d)}

16		PhCOBr	62		67 ^{c)}
					15 ^{c)}
17		PhCOCl	62		25
18	anisole	PhCOCl	62 ^{e)}	no reaction	

a) All reactions were performed employing 1.2 equiv. of ether and 1.0 equiv. of acyl halide in 1.5 ml of CH₃CN at 10 kbar for 24 h unless otherwise stated.

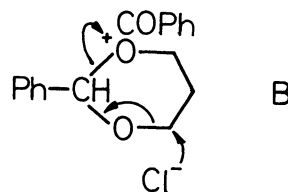
b) Isolated yield after distillation by Kugelrohr apparatus or purification by preparative TLC, values in parentheses were determined by GLC.

c) Ratio of regioisomers was determined by ¹H NMR and GLC.

d) Almost single isomer was obtained.

e) Reaction time was 48 h.

efficiently cleaved with acyl chlorides and bromides.⁵⁾ As expected, benzoyl bromide is better than benzoyl chloride for the present purpose.⁶⁾ The reactivity of ethers roughly depends on the basicity of ether oxygen: tetrahydrofuran ($pK_{HB} = 1.26$) and tetrahydropyran (1.23) are more basic than dibutyl ether (1.02) or diethyl ether (0.98) and the least basic anisole (0.02) was remarkably stable under these conditions.⁷⁾ The cleavage reactions of 2-methyltetrahydrofuran show no regioselectivity (runs 11 and 12). However, in both cases the major product is a primary chloride. This suggests that an S_N2-type cleavage reaction is preferentially occurred.⁸⁾ Interestingly, even acetal function was slowly reacted with benzoyl chloride (run 17). In this case the reaction probably proceeds through an acylated species B.



The presently discovered reaction can be conducted under almost neutral conditions without any Lewis acid catalysts. Therefore, we believe the procedure provides a new entry for the mild cleavage of ethers.

Further application of this reaction is currently under way.

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References

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- 5) All products were fully characterized by ^1H NMR, IR, and HRMS. For a description of our high-pressure apparatus and of the general procedure for high-pressure reactions, see H. Kotsuki, H. Nishizawa, S. Kitagawa, M. Ochi, N. Yamasaki, K. Matsuoka, and T. Tokoroyama, *Bull. Chem. Soc. Jpn.*, 52, 544(1979).
- 6) Although further experiments are necessary, it can not preclude a possibility that the following ionization process might be accelerated under the conditions used: $\text{RCOX} \rightleftharpoons \text{RCO}^+ + \text{X}^-$.
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