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Mild and efficient method for the cleavage of cyclic and acyclic ethers by iodine under solvent-free conditions☆

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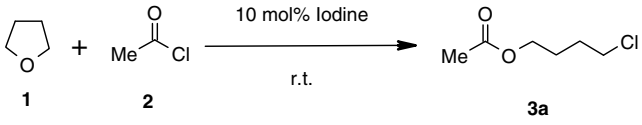
Abstract—Ethers undergo smooth cleavage with acyl chlorides in the presence of a catalytic amount of elemental iodine under extremely mild conditions to give the corresponding halo esters. This new procedure offers significant advantages such as high conversions, short reaction times and enhanced selectivity together with mild reaction conditions, which makes it an attractive strategy.

The cleavage of ethers is a versatile reaction in organic synthesis, mainly in degradation or transformation of complex molecules especially in biologically active natural products such as carbohydrates and macrolide antibiotics. Additionally, aliphatic, benzylic and allylic ethers are frequently used as protecting groups for hydroxyl functions,[1] which then require subsequent cleavage to release polyfunctional molecules useful in organic synthesis.[2] The cleavage of ethers with acyl chlorides has been reported using Lewis acids such as SmI_2,[3] $ZnCl_2$,[4] $FeCl_3$,[5] $Mo(CO)_6$,[6] $MoCl_5$,[7] $PdCl_2(PPh_3)_2$,[8] $CoCl_2$,[1] NaI,[9] lanthanide salts,[10] Zn,[11] graphite,[12] aluminium complexes[13] and others.[14] However, many of these methods often involve the use of toxic or expensive reagents and the formation of mixtures of products resulting in low yields. Therefore, the development of simple, convenient and practical procedures for the cleavage of cyclic and acyclic ethers continues to be a challenge. Recently, iodine[15] has been used in acid mediated and other organic transformations. However, there have been no reports on the use of elemental iodine for the cleavage of ethers with acyl chlorides.

In continuation of our interest on the catalytic application of elemental iodine,[16] we disclose herein a mild, efficient and practical methodology for the cleavage of cyclic and acyclic ethers with acyl chloride using iodine as the catalyst under solvent-free conditions.[17] Firstly, we attempted the cleavage of tetrahydrofuran with acetyl chloride in the presence of elemental iodine. The reaction went to completion within 2 h and the product was obtained in 91% yield (Scheme 1).



1 2 3a

Scheme 1.

Encouraged by this result, we examined benzoyl chloride, 3-methylbenzoyl chloride, 2-chlorobenzoyl chloride and the acid chloride derived from cyhalothrin, again using tetrahydrofuran, and obtained the corresponding halo esters in good to excellent yields (Table 1, entries b–e). Like tetrahydrofuran, several other cyclic and acyclic ethers were cleaved with a range acyl chlorides to afford the corresponding halo esters in good yields (Table 1, entries f–m). In the cases of entries f and h (Table 1), 10% and 20%, respectively, of the regioisomers were observed, which was confirmed by GC analysis. Using 10 mol % of iodine under solvent free-conditions afforded higher yields with reduced reaction times as compared to some other cheap reagents such as $FeCl_3$,[5] $ZnCl_2$[4] and NaI[9] for the cleavage of cyclic and acyclic ethers.

In summary, we have described a simple, convenient, efficient and practical method for the cleavage of cyclic and acyclic ethers with acyl chlorides using

Keywords: Ethers; Acyl chloride; Iodine.
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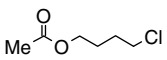
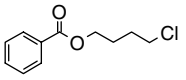
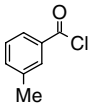
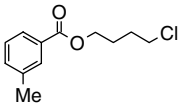
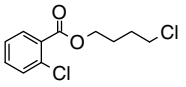
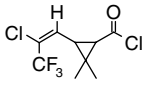
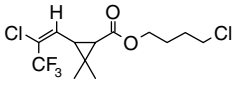
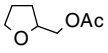
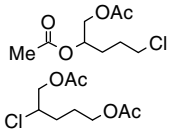
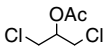
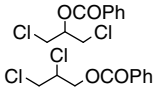
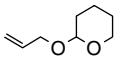
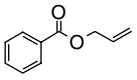
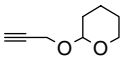
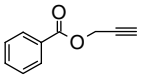
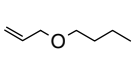
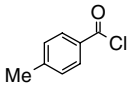
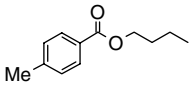
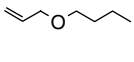
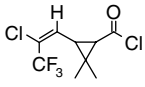
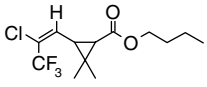
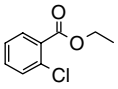
Table 1. Iodine catalyzed cleavage of cyclic and acyclic ethers by aryl chlorides under solvent-free conditions

Entry	Ether	Acyl chloride	Product[a]	Time (h)	Yield (%)[b]
a				2.0	91
b				2.0	93
c				3.5	83
d				3.0	88
e				4.5	92
f				7.0	65 (9:1)[c]
g				4.0	85
h				6.0	71 (8:2)[c]
i				2.5	80
j				4.5	78
k				3.5	88
l				4.5	87
m				5.0	80

[a] All products were characterized ^{1}H NMR and IR spectra and mass spectrometry.
[b] Yields obtained after column chromatography.
[c] By GC analysis.

elemental iodine as the catalyst, under solvent free-conditions.

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17. *General procedure for cleavage of THF, ethers and epoxides*: To a mixture of (6.90 mmol) of cyclic/acyclic ether and (0.69 mmol) of acyl chloride, a catalytic amount of iodine (10 mol %) was added. The reaction mixture was stirred at room temperature under a nitrogen atmosphere for an appropriate time (Table 1). After completion of the reaction as indicated by TLC, the reaction mixture was quenched with saturated aq sodium bicarbonate solution (15 ml) and extracted with ethyl acetate (2×15 ml). Evaporation of the solvent followed by purification on silica gel (Merck, 100–200 mesh, ethyl acetate–hexane, 0.5:9.5) afforded the pure ester derivative. Spectroscopic data for selected products: **3d**: 4-Chlorobutyl 2-chlorobenzoate: Liquid. IR (KBr): ν_{max} 3070, 2959, 1731, 1592, 1472, 1436, 1293, 1250, 1120, 1050, 771, 749 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.77 (d, $J = 8.7$ Hz, 1H), 7.45–7.23 (m, 3H), 4.35 (t, $J = 5.8$ Hz, 2H,), 3.58 (t, $J = 5.8$ Hz, 2H), 1.94 (quin, $J = 5.8$ Hz, 4H). LCMS: *m/z*: 247 (M^+, 10%), 230 (7), 221 (5), 156 (8), 149 (5), 139 (10), 116 (5), 91 (7). HRMS calcd for $C_{11}H_{13}Cl_2O_2$: 247.0292. Found: 247.0294. Compound **3e**: 4-Chlorobutyl 3-[(*E*)-2-chloro-3,3,3-trifluoro-1-propenyl]-2,2-dimethyl-1-cyclopropanecarboxylate: Liquid, IR (KBr): ν_{max} 3079, 2961, 1727, 1654, 1453, 1416, 1275, 1201, 1140, 1087, 955, 772 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ: 6.90 (d, $J =$ 9.4 Hz, 1H), 4.10 (t, $J = 5.8$ Hz, 2H), 3.55 (t, $J = 5.8$ Hz, 2H), 2.14 (t, $J = 9.4$ Hz, 1H), 1.95–1.82 (m, 5H), 1.30 (d, $J = 3.6$ Hz, 6H). LCMS: *m/z*: 334 (M+1, 5%), 301 (89), 279 (68), 205 (15), 149 (28), 116 (12), 107 (5), 69 (5), 57 (5). HRMS calcd for $C_{13}H_{18}Cl_2F_3O_2$: 333.0635 $(M+H)^+$. Found: 333.0642. Compound **3m**: Ethyl 2-chlorobenzoate: Liquid, IR (KBr): ν_{max} 3072, 2983, 2935, 2873, 1731, 1593, 1473, 1436, 1389, 1366, 1293, 1252, 1116, 1051, 854, 748 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.76 (d, $J = 7.2$ Hz, 1H), 7.43–7.22 (m, 3H), 4.39 (q, $J = 7.2$ Hz, 2H), 1.40 (t, $J = 7.2$ Hz, 3H). LCMS: *m/z*: 185 (M+1, 78%), 177 (25), 157 (58), 149 (18), 139 (40), 127 (10), 116 (8), 103 (5), 88 (10). HRMS calcd for $C_9H_{10}ClO_2$: 185.0369 $(M+H)^+$. Found: 185.0371.