Selective, Convenient and Efficient Deprotection of Trimethylsilyl and Tetrahydropyranyl Ethers, Ethylene Acetals and Ketals with Oxone under Non-aqueous Conditions

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An efficient and selective method for the deprotection of trimethylsilyl (TMS) and tetrahydropyranyl (THP) ethers, ethylene acetals and ketals to their corresponding alcohols and carbonyl compounds using oxone in refluxing acetonitrile is described. Excellent chemoselectivity of this method makes it a useful and practical procedure in organic synthesis.

The selective introduction and removal of protecting groups is of great significance in the synthesis of complex organic molecules. The hydroxy group of alcohols is one of the most versatile functional groups, and its controlled manipulation is of practical value in organic synthesis. The protection of this functionality by conversion to the corresponding trimethylsilyl (TMS) and tetrahydropyranyl (THP) ethers is a common practice. Several reagents and methods are available for this purpose in the literature.[1—9] Deprotection of the above-mentioned ethers to the corresponding alcohols under mild conditions is also of practical importance.[9—13]

The protection of carbonyl compounds as their ethylene acetals and ketals has found wide applications in the multistep synthesis of organic molecules.[14—17] The deprotection of ethylene acetals and ketals to their carbonyl compounds is also of interest to synthetic organic chemists; a variety of methods have been reported in the literature.[18—20] However, some of the reported methods for deprotection of the above-mentioned ethers, ethylene acetals and ketals suffer from one or more disadvantages, such as long reaction times, low yields of the products, high cost or toxicity of the reagents, and a tedious work-up. Therefore, introducing a milder, more selective, and inexpensive reagent for such functional group transformations is of practical importance, and is still in demand.

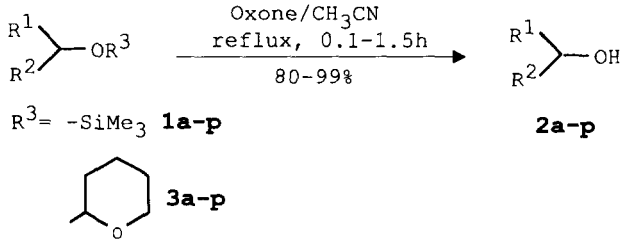
Recently, we have reported new methods for the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers, ethylene acetals and ketals.[21—23] In a continuation of our research in this area, we were interested to find a more efficient, more selective and inexpensive method for the deprotection and oxidative deprotection of the above-mentioned functional groups. In this respect, we wish to report that oxone in refluxing acetonitrile is able to transform trimethylsilyl and tetrahydropyranyl ethers, ethylene acetals and ketals to their corresponding alcohols and carbonyl compounds efficiently.

Results and Discussion

Oxone is a cheap and stable ternary composite of $KHSO_5$, $KHSO_4$ and K_2SO_4 in a 2 : 1 : 1 molar ratio. Several synthetically useful organic transformations using this reagent have been reported.[24—34]

The deprotection of trimethylsilyl and tetrahydropyranyl ethers, ethylene acetals and ketals with oxone, proceeds well in refluxing acetonitrile under non-aqueous conditions. Primary and secondary benzylic and saturated TMS **1a-i**, **1k-p** and THP **3a-i**, **3k-p** ethers are transformed to their corresponding alcohols **2a-i**, **2k-p** in high yields (Scheme 1, Table 1). Under the same reaction conditions, allylic TMS and THP ethers are transformed to the corresponding allylic alcohols **2j** without epoxidation of the carbon-carbon double bond (Entries **1j** and **3j**, Table 1). This observation is in contrast to that observed for oxone, which produces epoxides with double bonds.[29]

The cleavage of ethylene acetals and ketals was also in-



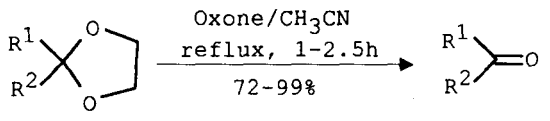
1,2,3	R^1	R^2	1,2,3	R^1	R^2
a	Ph	H	**i**	n-C_6H_{13}	H
b	2-$MeOC_6H_4$	H	**j**	PhCH=CH	H
c	2-$NO_2C_6H_4$	H	**k**	Ph	Me
d	3-$MeOC_6H_4$	H	**l**	4-ClC_6H_4	Me
e	3-$NO_2C_6H_4$	H	**m**	$PhCH_2$	Ph
f	4-$MeOC_6H_4$	H	**n**	4-PhC_6H_4	Me
g	4-$NO_2C_6H_4$	H	**o**		
h	$Ph(CH_2)_2$	H	**p**		

Scheme 1.

Table 1. Deprotection of TMS and THP Ethers with Oxone

Substrate	Product[a)]	Time /h	Yield /%	Substrate	Product[a)]	Time /h	Yield /%	Mp (°C) or Bp (°C) /Torr[b)] Found	Reported[35]
1a	**2a**	0.25	99	**3a**	**2a**	1	90	204—205/760	205/760
1b	**2b**	0.25	99	**3b**	**2b**	1	85	247—249/760	248—250/760
1c	**2c**	0.25	98	**3c**	**2c**	1	94	71—72	70—72
1d	**2d**	0.4	98	**3d**	**2d**	1.5	80	248—249/723	250/723
1e	**2e**	0.4	96	**3e**	**2e**	1.5	90	176—179/3	175—180/3
1f	**2f**	0.35	92	**3f**	**2f**	1.5	80	258/760	259/760
1g	**2g**	0.25	97	**3g**	**2g**	1	94	93—95	92—94
1h	**2h**	0.1	97	**3h**	**2h**	1	81	234—235/760	235/760
1i	**2i**	0.15	95	**3i**	**2i**	1.25	82	175—176/760	176/760
1j	**2j**	0.25	95	**3j**	**2j**	1.5	83	248—250/760	250/760
1k	**2k**	0.15	98	**3k**	**2k**	1	95[c)]	202—204/745	204—745
1l	**2l**	0.15	97	**3l**	**2l**	1	88	117—119/10	119/10
1m	**2m**	0.25	98	**3m**	**2m**	1	95	67—68	67
1n	**2n**	0.25	90	**3n**	**2n**	1.5	80	84—86	85—86
1o	**2o**	0.4	96	**3o**	**2o**	1.5	81	159—161/760	160—161/760
1p	**2p**	0.15	98	**3p**	**2p**	1	93	101—103/2	102—104/2

a) All products were identified by comparison of their physical and spectral data with those of authentic samples. b) 1 Torr = 133.322 Pa. c) In refluxing CH_2Cl_2 and $CHCl_3$, 53 and 67% of 1-phenylethanol were obtained after 1 h, respectively.



4a-m **5a-m**

4,5	R^1	R^2	4,5	R^1	R^2
a	Ph	H	**h**	Ph	Me
b	2-$MeOC_6H_4$	H	**i**	4-ClC_6H_4	Me
c	2-$NO_2C_6H_4$	H	**j**	$PhCH_2$	Ph
d	4-$MeOC_6H_4$	H	**k**	4-PhC_6H_4	Me
e	4-$NO_2C_6H_4$	H	**l**		
f	$Ph(CH_2)_2$	H	**m**		
g	PhCH=CH	H			

Scheme 2.

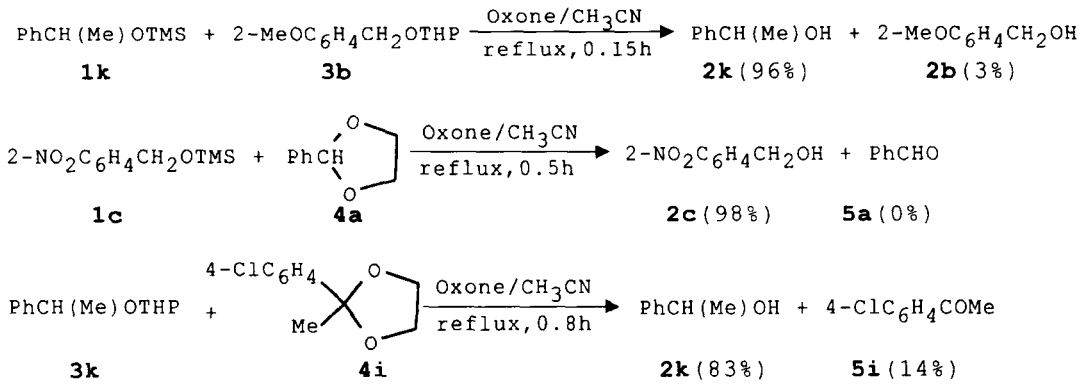
vestigated with this reagent. Ethylene acetals and ketals **4a-m** were transformed to their corresponding carbonyl compounds **5a-m** in refluxing acetonitrile efficiently (Scheme 2, Table 2). The cleavage of ethylene acetal in a conjugated enal system occurred without exploiting the double bond (Entry **4g**, Table 2).

We have also investigated the chemoselectivity of the deprotection method of substrates under our studies. The results are shown in Scheme 3 and Tables 3, 4, and 5. As can be seen, interesting selectivities were observed; TMS ethers are deprotected in the presence of THP ethers and ethylene acetals or ketals with high selectivity (Tables 3 and 4); THP ethers are also transformed to their corresponding alcohols selectively in the presence of ethylene acetals or ketals (Table 5). These selectivities are useful practical achieve-

Table 2. Deprotection of Ethylene Acetals and Ketals with Oxone

Substrate	Product[a)]	Time/h	Yield/%	Mp (°C) or Bp (°C) /Torr Found	Reported[35]
4a	**5a**	2	85[b)]	176—178/760	178—179/760
4b	**5b**	2	90	237—238/760	238/760
4c	**5c**	2.5	73	152—153/23	153/23
4d	**5d**	2	90	247—248/760	248/760
4e	**5e**	2.5	77	106—108	105—108
4f	**5f**	2.5	72	96—97/12	97—98/12
4g	**5g**	2	76	247—248/760	248/760
4h	**5h**	1	98[b)]	200—202/760	202/760
4i	**5i**	1	99	231—233/760	232/760
4j	**5j**	2.5	84	55—56	55—56.5
4k	**5k**	2.5	74	117—118	116—118
4l	**5l**	2	77[b)]	153—155/760	155/760
4m	**5m**	1	98	113—115/6	113—116/6

a) All products were identified by comparison of their physical and spectral data with those of authentic samples. b) Yield based on the isolation of its 2,4-dinitrophenylhydrazone derivative.



Scheme 3.

Table 3. Competitive Deprotection of TMS and THP Ethers with Oxone

Substrate	Product (Yield/%)	Time/h
1b +**3a**	**2b** (91)+**2a** (9)	0.25
1a +**3b**	**2a** (92)+**2b** (7)	0.25
1k +**3b**	**2k** (96)+**2b** (3)	0.15
1b +**3k**	**2b** (93)+**2k** (5)	0.15
1m+**3k**	**2m** (90)+**2k** (9)	0.25
1k +**3m**	**2k** (94)+**2m** (3)	0.15

Table 4. Competitive Deprotection of TMS Ethers and Ethylene Acetals (Ketals) with Oxone

Substrate	Product (Yield/%)	Time/h
1a+**4a**	**2a** (100)+**5a** (0)	0.4
1a+**4b**	**2a** (97)+**5b** (2)	0.4
1b+**4a**	**2b** (98)+**5a** (0)	0.33
1a+**4c**	**1a** (99)+**5c** (0)	0.4
1c+**4a**	**2c** (98)+**5a** (0)	0.5
1a+**4h**	**2a** (90)+**5h** (10)	0.4
1l +**4h**	**2l** (90)+**5h** (8)	0.4
1k+**4h**	**2k** (91)+**5h** (7)	0.4
1k+**4a**	**2k** (95)+**5a** (3)	0.4
1k+**4i**	**2k** (92)+**5i** (7)	0.4

Table 5. Competitive Deprotection of THP Ethers and Ethylene Acetals (Ketals) with Oxone

Substrate	Product (Yield/%)	Time/h
3a+**4a**	**2a** (78)+**5a** (19)	0.8
3a+**4b**	**2a** (79)+**5b** (19)	1
3b+**4a**	**2b** (80)+**5a** (20)	1
3a+**4c**	**2a** (90)+**5c** (8)	1
3c+**4a**	**2c** (81)+**5a** (18)	1
3l +**4h**	**2l** (82)+**5h** (12)	0.75
3k+**4h**	**2k** (79)+**5h** (20)	1
3k+**4i**	**2k** (83)+**5i** (14)	0.8

ments in deprotected the above-mentioned derivatives.

Even though the reaction mechanism is interesting, at the present time it is obscure to us, and we have not been able to assign any reasonable mechanism for them in our studies.

Conclusion

In this study, we have developed a simple, mild, selective and efficient procedure for the deprotection of TMS and THP ethers, ethylene acetals and ketals to their corresponding alcohols and carbonyl compounds, respectively. In addition, the commercial availability of the reagent, short reaction times, high yields of the products, easy work-up, low cost and non-toxicity of the reagent are other advantages of the present method, which makes this procedure a useful and attractive addition to the currently available methods.

Experimental

General. Trimethylsilyl and tetrahydropyranyl ethers, ethylene acetals and ketals were prepared according to described procedures.[3,5,14] All of the oxidation products were characterized by comparisons of their spectral and physical data with those of authentic samples. The yields refer to isolated products or their 2, 4-dinitrophenylhydrazones. The melting points were determined using a Mettler FP5 apparatus, and are uncorrected. The IR spectra were run on a Philips PU9716 spectrophotometer. ^{1}H NMR spectra were recorded in a $CDCl_3$ solution on a Bruker AM 80 MHz spectrometer using TMS as an internal standard. A GC analysis was performed with a Shimadzu 16A gas chromatograph with a flame-ionization detector using a column of 15% Carbowax® 20M chromosorb-W 60-80 mesh.

Deprotection of Trimethylsilyl 1a-p and Tetrahydropyranyl 3a-p Ethers; General Procedure. In a round-bottomed flask (50 mL) equipped with a magnetic stirrer and a condenser, a solution of trimethylsilyl **1** or tetrahydropyranyl **3** either (1 mmol) in CH_3CN (15 mL) was prepared. After oxone (0.615 g, 1 mmol) was added to the solution, the mixture was refluxed for 0.1—1.5 h. The progress of the reaction was monitored by GC or TLC (eluent: hexane/EtOAc: 10/1). The reaction mixture was filtered and the solid material was washed with CH_3CN (15 mL). The filtrate was evaporated and the resulting crude material was purified on a silica-gel plate or silica-gel column with an appropriate eluent. Pure alcohols **2a-p** were obtained in 80—99% yields (Table 1).

Deprotection of Ethylene Acetals and Ketals 4a-m; General Procedure. To a solution of ethylene acetal or ketal **4** (1 mmol) in CH_3CN (15 mL) in a 50 mL round-bottomed flask equipped with a magnetic stirrer and a condenser, oxone (0.615 g, 1 mmol) was added and the mixture was refluxed for 1—2.5 h. The progress of the reaction was monitored by GC or TLC (eluent: hexane/EtOAc:10/1). The mixture was filtered and the solid mate-

rial was washed with CH_3CN (15 mL). The filtrate was evaporated and the resulting crude material was purified on a silica-gel plate or silica-gel column with an appropriate eluent. Pure carbonyl compounds **5a-m** were obtained in 72—99% yields (Table 2).

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