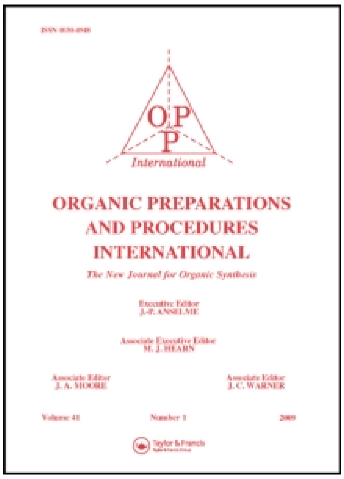

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REGENERATION OF CARBONYL COMPOUNDS FROM OXIMES, HYDRAZONES, SEMICARBAZONES, ACETALS, 1,1-DIACETATES, 1,3-DITHIOLANES, 1,3-DITHIANES AND 1,3-OXATHIOLANES

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INTRODUCTION

When a chemical reaction is to be carried out selectively at one site in a multifunctional compound, other reactive sites may have to be temporarily blocked. Many protective groups have been, and are being developed for this purpose. A protective group must fulfill a number of requirements. It must react selectively in good yield to give a protected substrate that is stable to the projected reactions. The protective group must be selectively removable in good yields with readily available, preferably non-toxic reagents that do not attack the regenerated functional group. The protective group should form a derivative that can be easily separated from side-products associated with its formation or cleavage. The protective group should have a minimum of additional functionality to avoid further sites of reaction (without the generation of new stereogenic centers). Greater control over the chemistry used in the synthesis of nature's architecturally beautiful and diverse molecular frameworks, as well as non-natural substances, is needed in view of the number of protection and deprotection steps often used to synthesize complex molecules.

Because of the order of reactivity of the carbonyl group [aldehydes (aliphatic > aromatic) > acyclic ketones and cyclohexanone > cyclopentanone > α,β-unsaturated ketones or α,α-disubstituted ketones >> aromatic ketones], it may be possible to protect a carbonyl group selectively in the presence of a less reactive one. The most useful protective groups are the acyclic and cyclic acetals and the acyclic and cyclic thioacetals. The protective group is introduced by treatment of the carbonyl compound in the presence of acid with an alcohol, diol, thiol, or dithiol. Cyclic and acyclic acetals and ketals are stable to aqueous and non-aqueous bases, to nucleophiles including organometallic reagents, and to hydride reductions. Protection of carbonyl groups as 1,3-dithiane or 1,3-dithiolane are quite often a necessary requirement in the synthesis of multifunctional organic molecules. Thioacetals are quite stable toward a wide variety of reagents and are also useful in organic synthesis as acyl carbanion equivalents in C-C bond-forming reactions. The carbonyl group forms a number of other very stable derivatives that are less useful as protective groups because of the greater difficulty involved in their removal. Such derivatives include cyanohydrins, hydrazones, imines, oximes, and semicarbazones. It is important that these groups be introduced easily be removed under mild conditions. The aim of this review is to describe recent methods for the regeneration of carbonyl compounds from oximes, hydrazones, semicarbazones, acetals, 1,1-diacetates, 1,3-dithiolanes, 1,3-dithianes and 1,3-oxathiolanes.

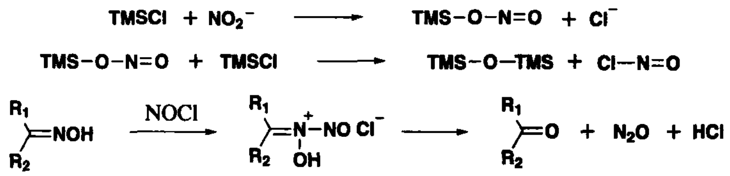
I. DEPROTECTION OF OXIMES

1. Deoximation With Organic Reagents

Oximes are used frequently to protect carbonyl compounds and hence considerable attention has been given to develop methods for their preparation from the carbonyl compounds and hydroxylamine.[1] Since oximes can also be obtained from non-carbonyl compounds, their conversion to carbonyl compounds constitutes a versatile synthesis of the latter compounds.[2] The classical method for deprotection of oximes by hydrolytic cleavage requires the use of strong mineral acids which often results in low yields. Hence a number of oxidative methods have been developed for cleavage of oximes. Pyridinium chlorochromate (PCC) was investigated as a deoximation reagent because of its convenience and selectivity in oxidation reactions. The reaction requires two equivalents of PCC, and more than 12 h at room temperature for maximum yields. A summary of results showed in *Table 1* (entries 1, 20 and 115).[3]

Another oxidative method for cleavage of oximes is I_2/CH_3CN. Iodine was found to be an effective and mild reagent for conversion of both ketoximes and aldoximes to their parent carbonyl compounds. The deoximation was carried out by mixing the oxime with iodine and refluxing in acetonitrile until the reaction was completed. The wide applicability of this reagent for the conversion of different oximes to the corresponding carbonyl compounds is summarized in *Table 1* (entries 2, 21, 95 and 116).[4]

Treatment of an oxime with a mixture of sodium nitrite or nitrate and chlorotrimethylsilane in carbon tetrachloride gave the parent carbonyl compound in nearly quantitative yields. To facilitate the solubilization of the inorganic sodium salts, about 5 mole % of benzyltriethylammonium chloride or Aliquat 336 was used (see *Table 1*, entries 3-5, 22-24, 52-54 and 96-98). The deoximation did not proceed with either sodium nitrite or nitrate or chlorotrimethylsilane alone, even after prolonged heating. The actual deoximating reagent is believed to be formed from the reaction of sodium nitrite with chlorotrimethylsilane as shown in *Scheme 1*.[5]



Scheme 1

Table 1. Deprotection of Oximes to the Carbonyl Compounds

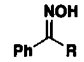
Entry	Oximes	R	Reagent	Solvent	Temp. /Time	Yield (%)	Ref
1		H	PCC	CH_2Cl_2	rt / 15h	56	*3*
2		H	I_2	CH_3CN	reflux / 3h	96	*4*
3		H	TMSCl+$NaNO_2$	CCl_4	rt / ---	95	*5*
4		H	TMSCl+$NaNO_3$	CCl_4	rt / ---	100	*5*
5		H	TMSCl+BuONO	CCl_4	rt / ---	94	*5*
6		H	$Ba(MnO_4)_2$	CH_3CN	reflux /3h	85	*8*
7		H	$Mn(OAc)_3$	Benzene	reflux /30min	89	*9*
8		H	$[(py)_2Ag]_2Cr_2O_7$	Benzene	reflux /10h	70	*10*
9		H	CPCC	CH_2Cl_2	reflux /1h	85	*11*
10		H	BPCP	Benzene	reflux /0.5h	80	*13*
11		H	BAABCPI	CH_3CN	reflux /15min	98	*16*
12		H	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	reflux /25min	89	*18*
13		H	BAABCPS	CH_3CN	reflux /20min	97	*19*
14		H	DOWEX50	H_2O	reflux /5h	32	*21*
15		H	$Zn(BiO_3)_2$	Toluene	reflux /1h	75	*24*
16		H	BTPPMS	CH_3CN	reflux /50min	94	*26*
17		H	Clayan	CH_2Cl_2	rt / 24h	80	*38*
18		H	$(NH_4)_2S_2O_8/SiO_2$	---	MW / 1.7 min	83	*42*
19		H	$Cu(NO_3)_2/SiO_2$	---	MW / 5 min	95	*44*
20		Me	PCC	CH_2Cl_2	rt / 15h	61	*3*
21		Me	I_2	CH_3CN	reflux /4h	98	*4*
22		Me	TMSCl+$NaNO_2$	CCl_4	rt / ---	97	*5*
23		Me	TMSCl+$NaNO_3$	CCl_4	rt / ---	93	*5*
24		Me	TMSCl+BuONO	CCl_4	rt / ---	96	*5*
25		Me	N_2O_4	THF	-35°C/10min	80	*7*
26		Me	N_2O_4	CH_2Cl_2	-35°C/10min	78	*7*
27		Me	$Ba(MnO_4)_2$	CH_3CN	reflux /4.5h	75	*8*
28		Me	$Mn(OAc)_3$	Benzene	reflux /1h	96	*9*

Table 1. Continued...

Entry	Oximes	R	Reagent	Solvent	Temp. /Time	Yield (%)	Ref
29		Me	$[(py)_2Ag]_2Cr_2O_7$	Benzene	reflux /8h	95	*10*
30		Me	CPPC	CH_2Cl_2	reflux /1h	90	*11*
31		Me	$(BnPPh_3)_2Cr_2O_7$	CH_3CN	reflux/15min	97	*12*
32		Me	BPCP	Benzene	reflux /0.25h	100	*13*
33		Me	DMP	CH_2Cl_2	rt/38min	92	*14*
34		Me	BAABCPI	CH_3CN	reflux /15min	100	*16*
35		Me	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	reflux /35min	96	*18*
36		Me	BAABCPS	CH_3CN	reflux /15min	100	*19*
37		Me	DOWEX50	H_2O	reflux /1h	90	*21*
38		Me	$Zn(BiO_3)_2$	Toluene	reflux /0.5h	80	*24*
39		Me	$Bi(NO_3)_3$	Acetone/H_2O	reflux /2h	88	*25*
40		Me	BTPPMS	CH_3CN	reflux /50min	99	*26*
41		Me	Ag_2CO_3/Bentonite	Benzene	reflux /3h	50	*33*
42		Me	Clayan	CH_2Cl_2	rt / 6h	95	*38*
43		Me	ACC/Alumina	Cyclohexane	60°C/5h	85	*39*
44		Me	$(BnPPh_3)_2Cr_2O_7/SiO_2$	----	Grinding/4min	97	*40*
45		Me	BAABCD	----	Grinding/20sec	91	*41*
46		Me	$(NH_4)_2S_2O_8/SiO_2$	----	MW / 1.5 min	65	*42*
47		Me	$Cu(NO_3)_2/SiO_2$	----	MW / 3 min	95	*44*
48		Me	$NaIO_4$/wet SiO_2	----	MW / 1.5 min	80	*43*
49		Me	CrO_3/SiO_2	----	MW / 45 sec	95	*45*
50		Me	$BiCl_3$	THF	MW / 5 min	80	*46*
51		Me	BAABCD	CH_2Cl_2	MW / 20 sec	91	*47*
52		Ph	TMSCl+$NaNO_2$	CCl_4	rt / ----	98	*5*
53		Ph	TMSCl+$NaNO_3$	CCl_4	rt / ----	97	*5*
54		Ph	TMSCl+BuONO	CCl_4	rt / ----	96	*5*
55		Ph	N_2O_4	THF	-35°C/10min	65	*7*
56		Ph	$Ba(MnO_4)_2$	CH_3CN	reflux /4.5h	80	*8*
57		Ph	$[(py)_2Ag]_2Cr_2O_7$	Benzene	reflux /8h	95	*10*
58		Ph	CPCC	CH_2Cl_2	reflux /1h	95	*11*
59		Ph	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	reflux/30min	95	*12*
60		Ph	DMP	CH_2Cl_2	rt/35min	94	*14*
61		Ph	BAABCPI	CH_3CN	reflux /15min	100	*16*
62		Ph	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	reflux /30min	97	*18*
63		Ph	BAABCPS	CH_3CN	reflux /15min	97	*19*

Table 1. Continued...

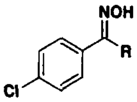
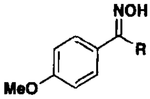
Entry	Oximes	R	Reagent	Solvent	Temp. /Time	Yield (%)	Ref
64		Ph	DOWEX50	H_2O	reflux /3h	85	*21*
65		Ph	$Zn(BiO_3)_2$	Toluene	reflux /1h	85	*24*
66		Ph	$Bi(NO_3)_3$	Acetone/H_2O	reflux /3h	80	*25*
67		Ph	BTPPMS	CH_3CN	reflux /120min	95	*26*
68		Ph	Ag_2CO_3/Bentonite	Benzene	reflux /4h	80	*33*
69		Ph	Clayan	CH_2Cl_2	rt / 8h	92	*38*
70		Ph	ACC/Alumina	Cyclohexane	60°C/6h	77	*39*
71		Ph	$(Bn_2PPh_3)_2Cr_2O_7/SiO_2$	----	Grinding/10min	97	*40*
72		Ph	BAABCD	----	Grinding/35sec	88	*41*
73		Ph	$Cu(NO_3)_2/SiO_2$	----	MW / 2 min	95	*44*
74		Ph	$NaIO_4$/wet SiO_2	----	MW / 1.5 min	89	*43*
75		Ph	CrO_3/SiO_2	----	MW / 45sec	91	*45*
76		Ph	$BiCl_3$	THF	MW / 2min	96	*46*
77		Ph	BAABCD	CH_2Cl_2	MW / 35sec	88	*47*
78		Me	N_2O_4	THF	-30°C/15min	75	*7*
79		Me	N_2O_4	CH_3CN	-30°C/15min	70	*7*
80		H	$Ba(MnO_4)_2$	CH_3CN	reflux /4h	80	*8*
81		H	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	reflux /15min	98	*12*
82		H	BPCP	Benzene	reflux /1h	85	*13*
83		H	BAABCPI	CH_3CN	reflux /15min	95	*16*
84		Me	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	reflux /40min	94	*18*
85		H	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	reflux /30min	87	*18*
86		H	BAABCPS	CH_3CN	reflux /20min	95	*19*
87		H	$Zn(BiO_3)_2$	Toluene	reflux /1h	65	*24*
88		Me	BTPPMS	CH_3CN	reflux /60min	90	*26*
89		H	$(BnPPh_3)_2Cr_2O_7/SiO_2$	----	Grinding/5min	98	*40*
90		H	$4\text{-}ClC_6H_4C{=}NOHR$	----	Grinding/40sec	93	*41*
91		H	$(NH_4)_2S_2O_8/SiO_2$	----	MW / 1.8 min	72	*42*
92		H	$NaIO_4$/wet SiO_2	----	MW / 1 min	75	*43*
93		H	$BiCl_3$	THF	MW / 8min	70	*46*
94		H	BAABCD	CH_2Cl_2	MW / 40sec	93	*47*
95		H	I_2	CH_3CN	reflux/3h	95	*4*
96		H	TMSCl+$NaNO_2$	CCl_4	rt / ----	97	*5*
97		H	TMSCl+$NaNO_3$	CCl_4	rt / ----	94	*5*

Table 1. Continued...

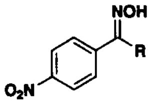
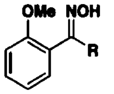
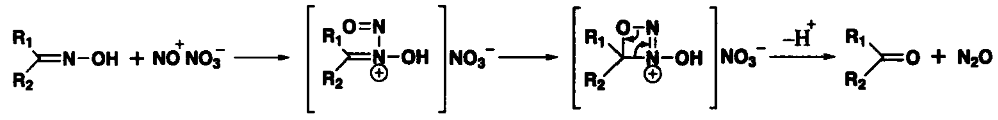
Entry	Oximes	R	Reagent	Solvent	Temp. /Time	Yield (%)	Ref
98		H	TMSCl+BuONO	CCl_4	rt / ----	97	*5*
99		H	$Mn(OAc)_3$	Benzene	reflux /2h	93	*9*
100		H	$[(py)_2Ag]_2Cr_2O_7$	Benzene	reflux /5h	65	*10*
101		H	CPCC	CH_2Cl_2	reflux /0.75h	97	*11*
102		H	DMP	CH_2Cl_2	rt/40min	83	*14*
103		H	Clayan	CH_2Cl_2	rt / 22h	82	*38*
104		H	ACC/Alumina	Cyclohexane	35°C/2h	79	*39*
105		Me	$(NH_4)_2S_2O_8/SiO_2$	----	MW / 1.5min	59	*42*
106		Me	$NaIO_4$/wet SiO_2	----	MW / 2min	93	*43*
107		H	$BiCl_3$	THF	MW / 4min	72	*46*
108		H	CPCC	CH_2Cl_2	reflux /4h	95	*11*
109		H	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	reflux /35min	80	*18*
110		Me	DMP	CH_2Cl_2	rt/40min	90	*14*
111		H	$Zn(BiO_3)_2$	Toluene	reflux/1h	72	*24*
112		H	ACC/Alumina	Cyclohexane	35°C/2.5h	20	*39*
113		H	$(NH_4)_2S_2O_8/SiO_2$	----	MW / 0.8min	66	*42*
114		H	CrO_3/SiO_2	----	MW / 120sec	57	*45*
115	Cyclohexanone oxime	----	PCC	CH_2Cl_2	rt / 18h	47	*3*
116	Cyclohexanone oxime	----	I_2	CH_3CN	reflux /3h	97	*4*
117	Cyclohexanone oxime	----	N_2O_4	THF	-30°C/15min	92	*7*
118	Cyclohexanone oxime	----	CPCC	CH_2Cl_2	reflux /2h	90	*11*
119	Cyclohexanone oxime	----	$(BnPPh_3)_2Cr_2O_7$	CH_3CN	reflux/15min	95	*12*
120	Cyclohexanone oxime	----	DMP	CH_2Cl_2	rt/48min	88	*14*
121	Cyclohexanone oxime	----	BAABCPI	CH_3CN	reflux /15min	95	*16*
122	Cyclohexanone oxime	----	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	reflux /45min	92	*18*
123	Cyclohexanone oxime	----	BAABCPS	CH_3CN	reflux /15min	95	*19*
124	Cyclohexanone oxime	----	DOWEX50	H_2O	reflux /2h	87	*21*
125	Cyclohexanone oxime	----	Amberlyst 15	Acetone/H_2O	rt/21h	92	*22*
126	Cyclohexanone oxime	----	$Zn(BiO_3)_2$	Toluene	reflux /3h	10-15	*24*
127	Cyclohexanone oxime	----	$Bi(NO_3)_3$	Acetone/H_2O	reflux /2h	80	*25*
128	Cyclohexanone oxime	----	BTPPMS	CH_3CN	reflux /20min	85	*26*
129	Cyclohexanone oxime	----	Ag_2CO_3/Bentonite	Benzene	reflux /2h	70	*33*
130	Cyclohexanone oxime	----	ACC/Alumina	Cyclohexane	60°C/5h	80	*39*
131	Cyclohexanone oxime	----	$(BnPPh_3)_2Cr_2O_7/SiO_2$	----	Grinding/4min	96	*40*
132	Cyclohexanone oxime	----	BAABCD	----	Grinding/35sec	85	*41*

Table 1. Continued...

Entry	Oximes	R	Reagent	Solvent	Temp. /Time	Yield (%)	Ref
133	Cyclohexanone oxime	----	$Cu(NO_3)_2/SiO_2$	----	MW / 1 min	95	*44*
134	Cyclohexanone oxime	----	$NaIO_4$/wet SiO_2	----	MW / 1 min	78	*43*
135	Cyclohexanone oxime	----	CrO_3/SiO_2	----	MW / 69sec	87	*45*
136	Cyclohexanone oxime	----	$BiCl_3$	THF	MW / 4min	82	*46*
137	Cyclohexanone oxime	----	BAABCD	CH_2Cl_2	MW / 35sec	85	*47*
138		H	BAABCPI	CH_3CN	Reflux / 20min	97	*16*
139		H	BAABCPI	CH_3CN	reflux / 15min	99	*19*
140		H	Amberlyst 15	H_2O	Reflux / 3h	88	22

Dinitrogen tetroxide reacts with several oximes at –40°C for short reaction times in aprotic solvents such as acetonitrile, tetrahydrofuran, chloroform, or carbon tetrachloride to afford the corresponding ketones in excellent yields (*Table 1*, entries 25, 26, 55, 78, 79 and 117). Dinitrogen tetroxide is known to be in equilibrium with NO^+ and NO_3^- ion.[6] The reaction appeared to be initiated by nitrosation on the nitrogen atom to form a cyclic azo intermediate, followed by ring cleavage as shown below to form the parent carbonyl compound.[7]



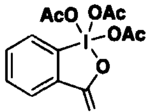
Scheme 2

Heavy metal reagents have been used as another chemical method for deoximation. The recovery of the parent carbonyl compounds from the corresponding oximes requires acid hydrolysis that removes the hydroxylamine from the equilibrium. This limits the reaction to exclude acid-sensitive ketones and aldehydes.

Barium permanganate [$Ba(MnO_4)_2$] is a stable, easily-prepared, inexpensive, non-explosive and mild oxidizing agent introduced for the efficient deoximation of aromatic oximes. The reaction is completed by refluxing the reaction mixture in acetonitrile (*Table 1* entries 6, 27, 56 and 80).[8] Manganese triacetate [$Mn(OAc)_3$] is another effective and mild oxidizing agent for the regeneration of carbonyl compounds from oximes in good yield and short time (*Table 1* entries 7, 28 and 99). The general procedure illustrates the simplicity of this method. A solution of the oxime in benzene with one equivalent of manganese triacetate was refluxed for 1-2 h. The precipitated manganese diacetate was removed by filtration and then washed with water. Purification afforded the pure aldehyde or ketone.[9]

Some deoximation reactions have been carried out by chromium(VI) reagents. For example, tetrakis(pyridine)silver dichromate ($[(Py)_2Ag]_2Cr_2O_7$) converts oximes to the corresponding carbonyl compounds in high yields and reacts selectively with aromatic oximes in the presence of aliphatic oximes (*Table* 1, entries 8, 29, 57 and 100).[10] 3-Carboxypyridinium chlorochromate (CPCC) is an inexpensive, stable (stored for months without losing its selectivity) and easily prepared reagent by the reaction of nicotinic acid with chromium trioxide in 6N hydrochloric acid for the conversion of the aliphatic and aromatic oximes to the carbonyl compounds in refluxing dichloromethane (*Table 1*, entries 9, 30, 58, 101, 108 and 118).[1] Another chromium-based reagent is benzyltriphenylphosphonium dichromate [$(PhCH_2PPh_3)_2Cr_2O_7$]. Ketoximes and benzaldoximes are easily deprotected in refluxing acetonitrile to produce the corresponding carbonyl compounds in high yields (*Table 1*, entries 31, 59, 81 and 119).[12] A noteworthy advantage of this reagent lies in its ability to selectively oxidize oximes in the presence of other oxidizable functions such as alcohols and double bonds. 2,2'-Bipyridylchromium peroxide (BPCP) converted different oximes to the carbonyl compounds. This reagent is prepared easily by the addition of concentrated hydrogen peroxide (60%) to an acidic solution of potassium dichromate at –10°C in ether. The reaction is carried out in dry benzene by refluxing a mixture of the oxime and of BPCP for 0.3-1 h. Work-up of the mixture afforded the oxidized product in 70-100% yield (*Table 1*, entries 10, 32 and 82).[13]

Dess-Martin's periodinane (1,1,1-triacetoxy)-1,1-dihydro-1,2-benziodoxol-3(1H)-one **1**) is one of the new reagents for the direct conversion of oximes to the corresponding carbonyl compounds (*Table 1* entries 33, 60, 102, 110 and 120).[14] The salient features of this method are the rapidity of reaction at room temperature in high yields, easy work-up and mild nature of DMP. Interestingly, the α,β-unsaturated oximes underwent deoximation very efficiently without affecting the C=C bond and the reaction is essentially chemoselective. In addition, it appears that electron withdrawing and electron-donating groups do not significantly affect the rate of reaction. The major drawback of this reagent was its explosiveness under impact or heating to >200°C.



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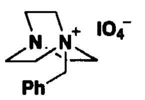

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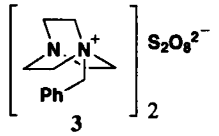
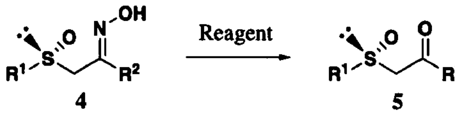


3

Another iodine-containing reagent is 1-benzyl-4-aza-1-azoniabicyclo[2.2.2] octane periodate (BAABCPI) **2**. This reagent can convert oximes to the corresponding carbonyl compounds (*Table 1*, entries 11, 34, 61, 83, 121 and 138) and α-sulfinyl oximes **4** to β-ketosulfoxides **5** respectively (*Scheme 3*, *Table 2*, entries 1, 4, 7, 10, 13 and 16).



a) R^1 = Phenyl, R^2 = Phenyl; b) R^1 = Phenyl, R^2 = 3,4-dimethoxyphenyl; c) R^1 = *p*-Tolyl, R^2 = Phenyl;
d) R^1 = *p*-Tolyl, R^2 = 3,4-dimethoxyphenyl; e) R^1 = 2-methoxy-1-naphthyl, R^2 = Phenyl;
f) R^1 = 2-methoxy-1-naphthyl, R^2 = 3,4-dimethoxyphenyl

Scheme 3

β-Ketosulfoxides are very important starting materials in asymmetric synthesis and can be obtained by the cleavage of C=N bonds of α-sulfinyl oximes. In this work, the C=N double bond cleavage of α-sulfinyl oximes had an interesting advantage over the earlier work,[15] since the reaction rate is rapid, proceeds in nearly quantitative yield and high optical purity.[16] Benzyltriphenylphosphonium peroxodisulfate [$(PhCH_2PPh_3)_2S_2O_8$], is another reagent which converts α-sulfinyl oximes **4** to β-ketosulfoxides **5** in high yields and high enantiomeric purity (*Scheme 3, Table 2* entries 2, 5, 8, 11, 14 and 17).[17] *n*-Butyltriphenylphosphonium peroxodisulfate $(Bu^nPPh_3)_2S_2O_8$ is a white, non-hygroscopic solid which is very stable and can be stored for months without losing its activity. It is readily and cheaply prepared by adding an aqueous solution of potassium peroxodisulfate to a solution of *n*-butyltriphenylphosphonium bromide in water-acetone (10:1). It is soluble in acetonitrile, dichloromethane and chloroform, and slightly soluble in CCl_4 and diethyl ether. The reaction with oximes carried out in acetonitrile under reflux, was complete in 20-60 minutes in nearly quantitative yield (*Table 1*, entries 12, 35, 62, 84, 85, 109 and 122).[18]

Table 2. Deprotection of α-Sulfinyl Oximes to β-Ketosulfoxides[a]

Entry	Substrate	Reagent	Time	Yield(%)	Ee (%)	Ref
1	**4a**	BAABCPI	15 min	98	95	*16*
2	**4a**	$(PhCH_2PPh_3)_2S_2O_8$	45 min	96	97	*17*
3	**4a**	BAABCPS	15 min	98	95	*19*
4	**4b**	BAABCPI	20 min	95	96	*16*
5	**4b**	$(PhCH_2PPh_3)_2S_2O_8$	45 min	95	99	*17*
6	**4b**	BAABCPS	20min	95	96	*19*
7	**4c**	BAABCPI	20 min	96	96	*16*
8	**4c**	$(PhCH_2PPh_3)_2S_2O_8$	58 min	98	100	*17*
9	**4c**	BAABCPS	20min	96	96	*19*
10	**4d**	BAABCPI	25 min	99	98	*16*
11	**4d**	$(PhCH_2PPh_3)_2S_2O_8$	55 min	95	100	*17*
12	**4d**	BAABCPS	25min	99	98	*19*
13	**4e**	BAABCPI	30 min	95	98	*16*
14	**4e**	$(PhCH_2PPh_3)_2S_2O_8$	45 min	99	100	*17*
15	**4e**	BAABCPS	30min	95	98	*19*
16	**4f**	BAABCPI	30 min	95	100	*16*
17	**4f**	$(PhCH_2PPh_3)_2S_2O_8$	65 min	97	99	*17*
18	**4f**	BAABCPS	30min	95	100	*19*

a) All reactions at reflux in CH_3CN

bis(1-Benzyl-4-aza-1-azoniabicyclo[2.2.2]octane) persulfate (BAABCPS, **3**) converts oximes to the corresponding carbonyl compounds (*Table* 1, entries 13, 36, 63, 86, 123 and 139) and α-sulfinyl oximes **4** to β-ketosulfoxides **5** (*Scheme 3*, *Table* 2, entries 3, 6, 9, 12, 15 and 18).[19] The C=N bond cleavage of optically active α-sulfinyl oximes by BAABCPS in acetonitrile at reflux is rapid (15-30 min) in nearly quantitative yield and high optical purity. This reagent is a mild and efficient reagent for synthesis of non-racemic chiral compounds. The advantage of this reagent is that it may be used under non-acidic and non-aqueous conditions.

However, many of the above reagents and/or the solvent systems used are toxic, corrosive or difficult to handle, especially on a large scale. With increasing environmental concerns, it is imperative that new "environment friendly" reagents be developed.[20] One example of such environmentally friendly reagent for the deprotection of oximes is a cation exchange resin, DOWEX 50W. Commercial Dowex 50 was soaked in 4N HCl overnight and then washed with distilled water until acid free, then used as an aqueous suspension. In a typical reaction, the oxime was heated at reflux with stirring in an aqueous suspension of Dowex 50. At the end of the reaction, the reaction mixture was steam distilled and the product was isolated in a pure state (*Table 1*, entries 14, 37, 64 and 124).[21] Ketones were obtained readily in high yield, whereas aldehydes were formed slowly and in lower yield. The results suggest that this procedure may show considerable selectivity for the regeneration of ketones over that of aldehydes.

Another environmentally friendly reagent is Amberlyst 15, a macrorecticular ion-exchange resin, which contains sulfonic groups. This procedure is carried out at room temperature or 80°C by simple dissolution of the oxime in acetone-water, with a given amount of Amberlyst 15 and stirring the mixture for 5-24 h; the yields are high and the work-up is straightforward. When acetone is used as exchange reagent, this resin is an excellent catalyst for conversion of oximes to the corresponding carbonyl compounds. (*Table 1*, entries 125 and 140).[22]

Recently, bismuth derivatives have become attractive candidates in organic synthesis because most bismuth compounds are relatively non-toxic, readily available at low cost and are fairly insensitive to small amounts of water.[23] Bismuth has an electron configuration of [Xe] $4f^{14}$ $5d^{10} 6s^2 6p^3$. Due to the weak shielding of the 4f electrons (Lanthanide contraction), bismuth (III) compounds exhibit Lewis acidity. Bismuth in the +5 state is an oxidizing agent. Recently zinc bismuthate has been reported as a mild, stable and easily prepared oxidant for the conversion of allylic and aromatic oximes to the corresponding aldehydes or ketones in refluxing toluene with high yields (*Table 1*, entries 15, 38, 65, 87, 111 and 126). Although $Zn(BiO_3)_2$, is not commercially available, it may be synthesized in high yield (99%) prior to use from zinc chloride and sodium bismuthate in water.[24]

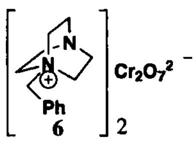
A more convenient reagent was recently reported. Bismuth nitrate pentahydrate is commercially available and requires no special handling. It is relatively non-toxic, insensitive to air and inexpensive. These features, coupled with the use of a relatively non-toxic solvent system (H_2O-acetone), make this method an attractive alternative to existing routes for deprotection of ketoximes (*Table 1* entries 39, 66 and 127),[25] especially in view of the particular advantage that the use of an inert atmosphere is not required for these reactions. The best yields were obtained when bismuth nitrate was mixed with montmorillonite K10. Presumably, montmorillonite K10 acts as a carrier to increase the surface area in the heterogeneous reaction. Catalytic amounts of $BiCl_3$ have been used for the deprotection of oximes with benzyltriphenylphosphonium peroxymonosulfate ($BnPPh_3^+HSO_5^-$, BTPPMS), (*Table* 1, entries 16, 40, 67, 88 and 128).[26]

2. Deoximation With Supported Reagents

Though some of the above reagents are satisfactory, several involve toxic metals, some are very expensive and/or their preparation require very rigorous precautions. Others are very efficient but lack selectivity in multistep synthesis. Furthermore, the high temperature required for some reagents leads to secondary reactions. In addition many popular oxidative reagents are based on chromium and lead, which are corrosive and toxic. Moreover, the derivatives of chromium (VI) are well known carcinogens.[27] Deoximation may be accomplished with Dowex 50 but gives poor yields in the case of aldehydes. Heterogeneous reactions facilitated by supported reagents on various solid inorganic surfaces have the advantage that they provide greater selectivity, enhanced reaction rates, cleaner products and procedural simplicity.[28-32]

Clay-supported metal salts such as bentonite-supported silver carbonate (Ag_2CO_3/ Bentonite) have been used in the oxidative deblocking procedures of ketoximes. The yields are comparable with the previously reported methods (*Table 1*, entries 41, 68 and 129). Facile reaction conditions, short reaction times, and straightforward work-up are typical.[33]

Ammonium nitrate is used as fertilizer[34, 35] and in textile finishing.[36] Since this reagent decomposes in the environment by microorganisms, ammonium nitrate is used as a green reagent.[37] For example, clay supported ammonium nitrate (clayan)[17] in dichloromethane has been used for the selective cleavage of aromatic oximes with electron-releasing groups on aromatic ring (*Table 1*, entries 17, 42, 69 and103).[38] Ammonium chlorochromate adsorbed on alumina (ACC/Alumina) is a convenient method for the oxidative cleavage of oximes to the corresponding aldehydes and ketones. However, the oxidation of aromatic aldoximes bearing electron-withdrawing groups gave poor yields (*Table 1*, entries 43, 70, 104, 112 and 130).[39] Oximes were converted to the corresponding aldehydes and ketones in cyclohexane or the cyclohexane-ether. Further oxidation of aldehydes to their carboxylic acids was not observed. In contrast, deoximation using PCC suffer from long reaction time (12-94 h) and low yields. The H_2O_2-PCC system is not suitable for aldoximes as over-oxidation products are usually formed. Simple grinding of silica gel supported benzyltriphenylphosphonium dichromate [$(PhCH_2PPh_3)_2Cr_2O_7$] and oxime in a mortar for a specified time at room temperature gave the corresponding carbonyl compounds in excellent yields (*Table 1*, entries 44, 71, 89 and 131).[40] Oxime with 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane dichromate (BAABCD) **6** in the presence of a catalytic amount of a Lewis acid such as aluminum chloride without support and solvent gave the aldehydes and ketones (*Table 1* entries 45, 72, 90 and 132).[41] Notably, aldehydes did not undergo further oxidation to the carboxylic acids under the reaction conditions. Another noteworthy advantage of the reagent is the selective oxidation of oximes, in the presence of semicarbazones. When a mixture of an equimolar amount of an oxime and semicarbazone was treated with reagent **6**, only the oxime was oxidized to the corresponding carbonyl compound and the semicarbazone remained unchanged. However, treatment of an oxime in the presence of benzyl alcohol led to the exclusive oxidation of benzyl alcohol to the corresponding aldehyde in 100% yield. Although these Cr(VI) derivatives are toxic, they are superior to the other methods from the standpoint of better yields, mild reaction conditions, straightforward work-up, short reaction time, and proceeding under non-aqueous and non-acidic conditions.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3. Deoximation Reaction Under Microwave (MW) Irradiation

Reagents impregnated on mineral supports, especially those that are efficient in dry media, have gained popularity in organic synthesis because of their selectivity and experimental simplicity. The salient features of the MW approach are the much-improved reaction rates and cleaner reactions. The microwave-assisted reactions in dry media are especially appealing as they provide an opportunity to work with open vessels, thus avoiding the risk of developing high pressure, and with good advantages for scale up.

Among the various solid supports examined, including alumina and montmorillonite K10 clay, silica gel has been found to be the best. Thus a facile deoximation procedure using silica gel doped with ammonium persulfate under microwave was reported (*Table 1*, entries 18, 46, 91, 105 and 113).[42] The use of recyclable silica gel support and the general applicability of this reaction to a variety of aldoximes and ketoximes under solvent-free conditions are other attractive features of this protocol. The neat oxime (or a solution in a minimum amount of dichloromethane) is combined with silica gel and the "dry" powder is mixed with ammonium persulfate. The contents are irradiated at full power in an alumina bath in a microwave oven. After completion of the reaction, the product is extracted into dichloromethane. Microwave irradiation of ketoximes on wet silica-supported sodium periodate under solvent-free conditions provided a rapid, efficient and simple method for regeneration of ketones (*Table 1*, entries 48, 74, 92, 106 and 134).[43] Copper(II) nitrate on silica gel has also been used for the deoximation reaction under microwave irradiation (*Table 1*, entries 19, 47, 73 and 133).[44] Silica gel supported chromium trioxide was also found to be an efficient reagent for the oxidative cleavage of oximes to the corresponding aldehydes and ketones in "dry media", under MW irradiation in a domestic microwave oven (*Table 1*, entries 49, 75, 114 and 135).[45]

In some cases, the cleavage of oximes has been carried out without any support in a small amount of solvent and in the presence of a catalytic amount of Lewis acid such as $BiCl_3$[46]

or reagent **6**.[47] One example was deoximation of ketoximes or aldoximes with bismuth trichloride in tetrahydrofuran under microwave irradiation (*Table 1*, entries 50, 76, 93, 107 and 136).[4] Similarly, oxime cleavage with 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane dichromate (BAABCD, **6**) in CH_2Cl_2 regenerates the corresponding carbonyl compounds in excellent yield (*Table 1*, entries 51, 47, 94 and 137).[47]

II. DEPROTECTION OF SEMICARBAZONES AND HYDRAZONES

1. Deprotection With Organic Reagents

Semicarbazones, hydrazones and their derivatives are important intermediates in organic synthesis because of their use in the protection[22, 48-55] and purification[50-52] of carbonyl compounds. Thus regeneration of carbonyl compounds from the corresponding *p*-nitrophenylhydrazones and semicarbazones under mild conditions is an important process. Extensive studies on the deprotection of these derivatives have been carried out using various methods. For example, treatment of hydrazones with dinitrogen tetroxide (N_2O_4) at low temperature in acetonitrile gave the corresponding ketones in excellent yields (*Table 3*, entries 1, 33, 103, 108 and 121).[7]

Table 3. Deprotection of Semicarbazones and Hydrazones Derivatives (ArC(NX)R)

Entry	Ar	R	X	Reagent	Solvent	Temp./Time	Yield (%)	Ref
1	Ph	Me	NH_2	N_2O_4	CH_3CN	-40°C/10min	91	*7*
2	Ph	Me	NHPh	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/8h	70	*10*
3	Ph	Me	4-NPH	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/10h	40	*10*
4	Ph	Me	2,4-DNPH	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/4h	65	*10*
5	Ph	Me	$NHC(O)NH_2$	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/10h	70	*10*
6	Ph	Me	NHPh	CPCC	CH_3CN	Reflux/1h	92	*11*
7	Ph	Me	4-NPH	CPCC	CH_3CN	Reflux/1.5h	83	*11*
8	Ph	Me	$NHC(O)NH_2$	CPCC	CH_3CN	Reflux/2.5h	87	*11*
9	Ph	Me	$NHC(O)NH_2$	$CuCl_2 \cdot 2H_2O$	CH_3CN	Reflux/30min	81	*57*
10	Ph	Me	NHTs	DMP	CH_2Cl_2	rt/80min	87	*14*
11	Ph	Me	NHPh	BAABCP	CH_3CN	Reflux/45min	98	*58*
12	Ph	Me	$N(Me)_2$	BAABCP	CH_3CN	Reflux/30min	95	*58*
13	Ph	Me	$NHC(O)NH_2$	BAABCP	CH_3CN	Reflux/120min	25	*58*
14	Ph	Me	NHPh	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	Reflux/45min	96	*18*
15	Ph	Me	4-NPH	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	Reflux/40min	93	*18*
16	Ph	Me	$NHC(O)NH_2$	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	Reflux/40min	83	*18*
17	Ph	Me	NHPh	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	Reflux/15min	98	*12*
18	Ph	Me	$N(Me)_2$	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	Reflux/20min	95	*12*

19	Ph	Me	$NHC(O)NH_2$	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	Reflux/40min	80	*12*
20	Ph	Me	$NHC(O)NH_2$	BTPPMS	CH_3CN	Reflux/60min	95	*26*
21	Ph	Me	2,4-DNPH	BTPPMS	CH_3CN	Reflux/360min	40	*26*
22	Ph	Me	$NHC(O)NH_2$	DOWEX-50	H_2O	Reflux/1h	96	*21*
23	Ph	Me	$NHC(O)NH_2$	ACC/Alumina	Acetone/H_2O	80°C/10h	90	*22*
24	Ph	Me	4-NPH	ACC/Alumina	CH_2Cl_2	35-40°C/4h	97	*59*
25	Ph	Me	4-NPH	ACC/Alumina	Ether/DMSO	Reflux/1h	90	*59*
26	Ph	Me	NHPh	$(PhCH_2PPh_3)_2Cr_2O_7$	----	Grinding/4min	98	*40*
27	Ph	Me	$N(Me)_2$	$(PhCH_2PPh_3)_2Cr_2O_7$	----	Grinding/8min	98	*40*
28	Ph	Me	$NHC(O)NH_2$	$(PhCH_2PPh_3)_2Cr_2O_7$	----	Grinding/10min	92	*40*
29	Ph	Me	$NHC(O)NH_2$	$(NH_4)_2S_2O_8$/clay	----	MW/0.6min	72	*67*
30	Ph	Me	$NHC(O)NH_2$	$(NH_4)_2S_2O_8$/clay	----	US/0.75h	77	*67*
31	Ph	Me	NHPh	$(NH_4)_2S_2O_8$/clay	----	MW/0.5min	71	*67*
32	Ph	Me	NHPh	$(NH_4)_2S_2O_8$/clay	----	US/1.50h	82	*67*
33	Ph	Ph	NH_2	N_2O_4	CH_3CN	-40°C/10min	85	*7*
34	Ph	Ph	NHPh	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/10h	50	*10*
35	Ph	Ph	4-NPH	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/10h	70	*10*
36	Ph	Ph	2,4-DNPH	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/6h	80	*10*
37	Ph	Ph	NHPh	CPCC	CH_3CN	Reflux/1h	98	*11*
38	Ph	Ph	4-NPH	CPCC	CH_3CN	Reflux/2h	85	*11*
39	Ph	Ph	$NHC(O)NH_2$	CPCC	CH_3CN	Reflux/2.5h	89	*11*
40	Ph	Ph	$NHC(O)NH_2$	$CuCl_2\cdot 2H_2O$	CH_3CN	Reflux/30min	64	*57*
41	Ph	Ph	NHPh	BAABCP	CH_3CN	Reflux/60min	98	*58*
42	Ph	Ph	4-NPH	BAABCP	CH_3CN	Reflux/120min	45	*58*
43	Ph	Ph	$N(Me)_2$	BAABCP	CH_3CN	Reflux/25min	98	*58*
44	Ph	Ph	NHPh	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	Reflux/30min	98	*18*
45	Ph	Ph	4-NPH	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	Reflux/45min	90	*18*
46	Ph	Ph	$NHC(O)NH_2$	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	Reflux/35min	89	*18*
47	Ph	Ph	NHPh	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	Reflux/30min	95	*12*
48	Ph	Ph	4-NPH	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	Reflux/30min	85	*12*
49	Ph	Ph	$N(Me)_2$	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	Reflux/20min	91	*12*
50	Ph	Ph	$NHC(O)NH_2$	BTPPMS	CH_3CN	Reflux/150min	85	*26*
51	Ph	Ph	$NHC(O)NH_2$	DOWEX-50	H_2O	Reflux/3h	90	*21*
52	Ph	Ph	4-NPH	ACC/Alumina	CH_2Cl_2	35-40°C/4h	97	*59*
53	Ph	Ph	NHPH	$(PhCH_2PPh_3)_2Cr_2O_7$/ SiO_2	----	Grinding/10min	92	*40*
54	Ph	Ph	4-NPH	$(PhCH_2PPh_3)_2Cr_2O_7$/ SiO_2	----	Grinding/10min	92	*40*
55	Ph	Ph	$N(Me)_2$	$(PhCH_2PPh_3)_2Cr_2O_7$/ SiO_2	----	Grinding/8min	96	*40*
56	Ph	Ph	$NHC(O)NH_2$	BAABCD	----	Grinding/35sec	90	*41*

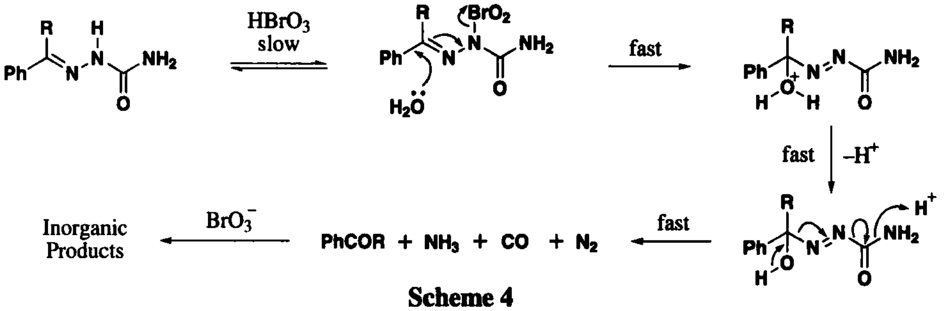
57	Ph	H	NHPh	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/8h	40	*10*
58	Ph	H	4-NPH	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/10h	60	*10*
59	Ph	H	NHPh	CPCC	CH_3CN	Reflux/1.5h	71	*11*
60	Ph	H	4-NPH	CPCC	CH_3CN	Reflux/1h	70	*11*
61	Ph	H	$NHC(O)NH_2$	CPCC	CH_3CN	Reflux/1h	80	*11*
62	Ph	H	$NHC(O)NH_2$	$CuCl_2 \cdot 2H_2O$	CH_3CN	Reflux/90min	51	*57*
63	Ph	H	$NHC(O)NH_2$	BAABCP	CH_3CN	Reflux/80min	35	*58*
64	Ph	H	$NHC(O)NH_2$	DOWEX-50	H_2O	Reflux/5h	20	*21*
65	Ph	H	$NHC(O)NH_2$	ACC/Alumina	CH_2Cl_2	Reflux/4h	72	*59*
66	Ph	H	4-NPH	ACC/Alumina	CH_2Cl_2	35-40°C/3h	79	*59*
67	Ph	H	NHTs	Clayfen	CH_2Cl_2	rt/?	79	*60*
68	Ph	H	NHPh	Clayfen	CH_2Cl_2	rt/?	83	*60*
69	Ph	H	2,4-DNPH	Clayfen	CH_2Cl_2	rt/?	69	*60*
70	Ph	H	4-NPH	$PhCH_2PPh_3)_2Cr_2O_7/ SiO_2$	----	Grinding/10min	97	*40*
71	$4\text{-}MeOC_6H_4$	H	NHPh	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/6h	45	*10*
72	$4\text{-}MeOC_6H_4$	H	4-NPH	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/8h	30	*10*
73	$4\text{-}MeOC_6H_4$	H	2,4-DNPH	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/5h	40	*10*
74	$4\text{-}MeOC_6H_4$	H	$NHC(O)NH_2$	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/5h	25	*10*
75	$4\text{-}MeOC_6H_4$	H	NHPh	CPCC	CH_3CN	Reflux/1h	80	*11*
76	$4\text{-}MeOC_6H_4$	H	4-NPH	CPCC	CH_3CN	Reflux/1h	75	*11*
77	$4\text{-}MeOC_6H_4$	H	$NHC(O)NH_2$	CPCC	CH_3CN	Reflux/0.75h	76	*11*
78	$4\text{-}MeOC_6H_4$	H	$NHC(O)NH_2$	$CuCl_2 \cdot 2H_2O$	CH_3CN	Reflux/90min	88	*57*
79	$4\text{-}MeOC_6H_4$	H	NHPh	BAABCP	CH_3CN	Reflux/45min	97	*58*
80	$4\text{-}MeOC_6H_4$	H	4-NPH	BAABCP	CH_3CN	Reflux/100min	45	*58*
81	$4\text{-}MeOC_6H_4$	H	$N(Me)_2$	BAABCP	CH_3CN	Reflux/25min	96	*58*
82	$4\text{-}MeOC_6H_4$	H	$NHC(O)NH_2$	BAABCP	CH_3CN	Reflux/100min	45	*58*
83	$4\text{-}MeOC_6H_4$	Me	NHPh	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	Reflux/25min	96	*12*
84	$4\text{-}MeOC_6H_4$	H	4-NPH	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	Reflux/30min	85	*12*
85	$4\text{-}MeOC_6H_4$	Me	$N(Me)_2$	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	Reflux/35min	98	*12*
86	$4\text{-}MeOC_6H_4$	Me	$NHC(O)NH_2$	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	Reflux/40min	85	*12*
87	$4\text{-}MeOC_6H_4$	Me	2,4-DNPH	BTPPMS	CH_3CN	Reflux/240min	20	*26*
88	$4\text{-}MeOC_6H_4$	H	4-NPH	ACC/Alumina	CH_2Cl_2	35-40°C/2.6h	82	*59*
89	$4\text{-}MeOC_6H_4$	H	4-NPH	$PhCH_2PPh_3)_2Cr_2O_7/ SiO_2$	----	Grinding/10min	90	*40*
90	$4\text{-}MeOC_6H_4$	Me	NHPh	$PhCH_2PPh_3)_2Cr_2O_7/ SiO_2$	----	Grinding/7min	98	*40*
91	$4\text{-}MeOC_6H_4$	Me	$N(Me)_2$	$PhCH_2PPh_3)_2Cr_2O_7/ SiO_2$	----	Grinding/15min	95	*40*
92	$4\text{-}MeOC_6H_4$	Me	2,4-DNPH	$PhCH_2PPh_3)_2Cr_2O_7/ SiO_2$	----	Grinding/15min	95	*40*
93	$4\text{-}MeOC_6H_4$	Me	$NHC(O)NH_2$	$(NH_4)_2S_2O_8$/clay	----	MW/0.9min	78	*67*
94	$4\text{-}MeOC_6H_4$	Me	$NHC(O)NH_2$	$(NH_4)_2S_2O_8$/clay	----	US/3h	88	*67*

95	3,4-$(MeO)_2C_6H_3$	H	NHC(O)NH_2	$CuCl_2{\cdot}2H_2O$	CH_3CN	Reflux/30min	88	*57*
96	3,4-$(MeO)_2C_6H_3$	Me	NHPh	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	Reflux/25min	95	*12*
97	3,4-$(MeO)_2C_6H_3$	Me	$N(Me)_2$	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	Reflux/25min	100	*12*
98	3,4-$(MeO)_2C_6H_3$	Me	NHC(O)NH_2	$(PhCH_2PPh_3)_2Cr_2O_7$	CH_3CN	Reflux/25min	70	*12*
99	3,4-$(MeO)_2C_6H_3$	H	NHPh	BTPPMS	CH_3CN	Reflux/210min	30	*26*
100	3,4-$(MeO)_2C_6H_3$	Me	NHPh	BTPPMS	----	Grinding/10min	95	*26*
101	3,4-$(MeO)_2C_6H_3$	H	NHPh	BTPPMS	----	Grinding/10min	100	*40*
102	3,4-$(MeO)_2C_6H_3$	H	NHPh	BTPPMS	----	Grinding/15min	80	*40*
103	4-$NO_2C_6H_4$	H	NH_2	N_2O_4	CH_3CN	0°C/30min	94	*7*
104	4-$NO_2C_6H_4$	H	NHC(O)NH_2	$CuCl_2{\cdot}2H_2O$	CH_3CN	Reflux/390min	7	*57*
105	4-$NO_2C_6H_4$	Me	NHC(O)NH_2	$CuCl_2{\cdot}2H_2O$	CH_3CN	Reflux/270min	82	*57*
106	4-$NO_2C_6H_4$	Me	4-NPH	ACC/Alumina	CH_2Cl_2	35-40°C/5h	80	*59*
107	4-$NO_2C_6H_4$	H	4-NPH	ACC/Alumina	CH_2Cl_2	35-40°C/3h	65	*59*
108	4-ClC_6H_4	H	NH_2	N_2O_4	CH_3CN	-40°C/10min	95	*7*
109	4-ClC_6H_4	Me	NHPh	CPCC	CH_3CN	Reflux/1.25h	90	*11*
110	4-ClC_6H_4	Me	4-NPH	CPCC	CH_3CN	Reflux/2h	84	*11*
111	4-ClC_6H_4	H	NHC(O)NH_2	$CuCl_2{\cdot}2H_2O$	CH_3CN	Reflux/240min	61	*57*
112	4-ClC_6H_4	Me	NHC(O)NH_2	$CuCl_2{\cdot}2H_2O$	CH_3CN	Reflux/60min	71	*57*
113	4-ClC_6H_4	Me	4-NPH	BAABCP	CH_3CN	Reflux/120min	10	*58*
114	4-ClC_6H_4	H	NHPh	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	Reflux/30min	77	*18*
115	4-ClC_6H_4	H	4-NPH	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	Reflux/35min	72	*18*
116	4-ClC_6H_4	H	NHC(O)NH_2	$(Bu^nPPh_3)_2S_2O_8$	CH_3CN	Reflux/45min	73	*18*
117	4-ClC_6H_4	Me	NHC(O)NH_2	$(NH_4)_2S_2O_8$/clay	----	MW/1.8min	82	*67*
118	4-ClC_6H_4	Me	NHC(O)NH_2	$(NH_4)_2S_2O_8$/clay	----	US/3h	90	*67*
119	4-MeC_6H_4	H	NHTs	Amberlyst 15	Acetone/H_2O	80°C/24h	86	*22*
120	4-MeC_6H_4	----	2,4-DNPh	Amberlyst 15	Acetone/H_2O	80°C/23h	61	*22*
121	4-MeC_6H_4	H	NH_2	N_2O_4	CH_3CN	-35°C/10min	94	*7*
122	4-MeC_6H_4	H	NHC(O)NH_2	$(NH_4)_2S_2O_8$/clay	----	MW/2min	69	*67*
123	4-MeC_6H_4	H	NHC(O)NH_2	$(NH_4)_2S_2O_8$/clay	----	US/3h	68	*67*
124	4-BrC_6H_4	----	2,4-DNPH	BTPPMS	CH_3CN	Reflux/300min	40	*26*
125	4-BrC_6H_4	----	NHC(O)NH_2	BTPPMS	CH_3CN	Reflux/120min	93	*26*
126	4-BrC_6H_4	----	4-NPH	ACC/Alumina	CH_2Cl_2	35-40°C/3h	70	*59*
127	4-BrC_6H_4	----	NHC(O)NH_2	BAABCD	----	Grinding/50sec	87	*41*
128	3-ClC_6H_4	Me	NHC(O)NH_2	BAABCD	----	Grinding/50sec	87	*41*
129	3-$NO_2C_6H_4$	Me	NHC(O)NH_2	BAABCD	----	Grinding/50sec	91	*41*
130	3-$MeOC_6H_4$	Me	NHC(O)NH_2	BAABCD	----	Grinding/50sec	92	*41*
131	-$(CH_2)_5$-	----	NHC(O)NH_2	$CuCl_2{\cdot}2H_2O$	CH_3CN	Reflux/15min	71	*57*
132	-$(CH_2)_4$-	----	NHTs	DMP	CH_2Cl_2	rt/90min	91	*14*

133	-$(CH_2)_5$-	----	$NHC(O)NH_2$	DOWEX-50	H_2O	Reflux/2h	90	*21*
134	-$(CH_2)_6$-	----	NHTs	Amberlyst 15	Acetone/H_2O	rt/23h	90	*22*
135	-$(CH_2)_5$-	----	$NHC(O)NH_2$	ACC/Alumina	CH_2Cl_2	Reflux/6h	72	*59*
136	-$(CH_2)_5$-	----	$NHC(O)NH_2$	ACC/Alumina	Ether	Reflux/0.5h	97	*59*
137	-$(CH_2)_4$-	----	4-NPH	ACC/Alumina	CH_2Cl_2	35-40°C/6h	90	*59*
138	-$(CH_2)_5$-	----	NHTs	Clayfen	CH_2Cl_2	rt/?	76	*60*
139	-$(CH_2)_5$-	----	NHPh	Clayfen	CH_2Cl_2	rt/?	87	*60*
140	-$(CH_2)_5$-	----	2,4-DNPH	Clayfen	CH_2Cl_2	rt/?	78	*60*
141	Fluorene	----	2,4-DNPH	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/6h	83	*10*
142	Fluorene	----	$NHC(O)NH_2$	$[(py)_2Ag]_2Cr_2O_7$	Benzene	Reflux/6h	55	*10*

NHTs = Tosylhydrazone, NHPh = phenylhydrazone, 4-NPH = *p*-nitrophenylhydrazone, 2,4-DNPH = 2,4-dinitrophenylhydrazone and $NH(CO)NH_2$ = semicarbazone

Oxidation of semicarbazones of benzaldehydes and acetophenones by potassium bromate [Br(V)] yields the respective aldehydes or ketones in good yield at ambient temperature. The rates of reaction are only slightly influenced by the change in substituents on the phenyl ring or by the polarity of the medium, suggesting that the intermediate is probably as polar as the reactants. The reaction possibly proceeds in the slow step *via* a *N*-bromate ester whose formation is generally less susceptible to electronic effects (*Scheme 4*).[56]

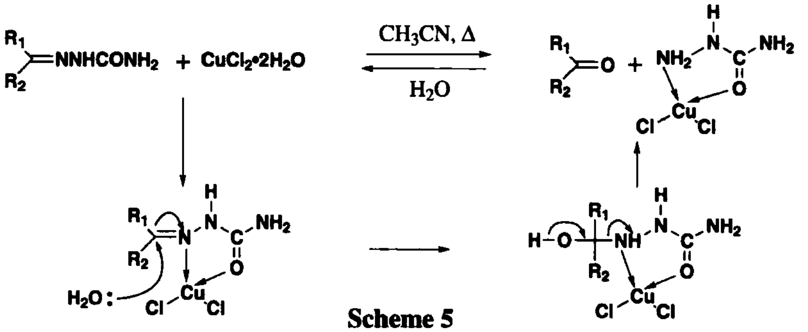


Scheme 4

Some deprotection reactions of semicarbazones and hydrazones may be carried out by Cr(VI) based reagents. Phenylhydrazones, 4-nitrophenylhydrazones, 2,4-dinitrophenylhydrazones and semicarbazones were converted to the corresponding carbonyl compounds with tetrakis(pyridine)silver dichromate in benzene ($[Py)_2Ag]_2Cr_2O_7$) (*Table 3*, entries 2, 34, 57 and 71 for phenylhydrazones; 3, 35, 58 and 72 for 4-nitrophenylhydrazones; 4, 36, 73 and 141 for 2,4-dinitrophenylhydrazones and 5, 74 and 142 for semicarbazones).[10]

3-Carboxypyridinium chlorochromate (CPCC) is a convenient reagent for conversion of phenylhydrazones, *p*-nitrophenylhydrazones and semicarbazones to the corresponding carbonyl compounds (*Table 3*, entries 6, 37, 59, 75 and 109 for phenyl-hydrazones, 7, 38, 60, 76 and 110 for 4-nitrophenylhydrazones, 8, 39, 61 and 77 for semicarbazones).[11] Benzyltriphenylphosphonium dichromate [$(PhCH_2PPh_3)_2Cr_2O_7$] is able to oxidize substituted hydrazones and semicarbazones to the corresponding carbonyl compounds (*Table 3* , entries 17, 47, 83 and 96 for phenylhydrazones, 48 and 84 for 4-nitrophenylhydrazones, 18, 49, 85 and 97 for *N,N*-dimethylhydrazones and 19, 86 and 98 for semicarbazones).[12]

A suspension of semicarbazones and hydrated Cu(II) chloride in acetonitrile affords carbonyl compounds in high yields after reflux (*Table 3*, entries 9, 40, 62, 78, 95, 104, 105, 111, 112 and 131). No additional amount of water is required; the water of hydration was sufficient to accomplish the hydrolysis. It was suggested that Cu(II) ion forms monocyclic chelates with semicarbazones and semicarbazides through the imino/terminal amino nitrogen and the carbonyl oxygen. Thus, in light of these indications, it is believed that Cu(II) ion would exert a favorable effect on the hydrolysis of semicarbazones *via* chelation at the imino nitrogen by making the latter more electrophilic as well as by stabilizing the leaving group in the transition state (*Scheme 5*).[57]



Scheme 5

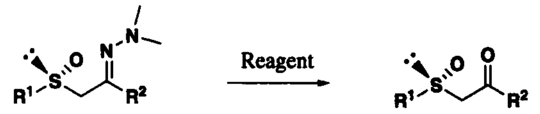
Dess-Martin's periodinane **1** (DMP) is an iodine-based reagent for the regeneration of carbonyl compound from tosylhydrazones (*Table 3*, entries 10 and 132).[14] This reagent is a mild and selective oxidizing compound for the oxidation of primary and secondary alcohols to aldehydes and ketones and for direct conversion of oximes and tosylhydrazones to the corresponding carbonyl compounds. It is noteworthy that, unlike other oxidative hydrolytic methods, the major drawback of over-oxidation of the resulting aldehydes is not observed under the reaction conditions and thus this reagent possesses significant advantages over the existing methods such as simple procedure, high yields, reduced reaction times and mild conditions.

Another iodine-based reagent is 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane periodate (**2**, BAABCPI). This reagent converts phenylhydrazones, *p*-nitrophenylhydrazones and semicarbazones to the corresponding carbonyl compounds (*Table 3*, entries 11, 41 and 79 for phenylhydrazones; entries 42, 80 and 113 for 4-nitrophenylhydrazones; entries 12, 43 and 81 for *N,N*-dimethylhydrazones and 13, 63 and 82 for semicarbazones) and β-ketosulfoxide hydrazones **7** to β-ketosulfoxides **4** respectively (*Scheme 6*, *Table 4*, entries 1, 3, 5, 7, 9 and 11).[58] Benzyltriphenylphosphonium peroxodisulfate [$(PhCH_2PPh_3)_2S_2O_8$] can also convert β-ketosulfoxide hydrazones **7** to the corresponding β-ketosulfoxides **4** (*Scheme 6*, *Table 4*, entries 2, 4, 6, 8, 10 and 12).[17]

Table 4. Deprotection of β-Ketosulfoxide Hydrazones to β-Ketosulfoxides[a]

Entry	Substrate	Reagent	Time	Yield(%)	Ee (%)	Ref
1	**7a**	BAABCPI	20 min	98	95	*58*
2	**7a**	$(PhCH_2PPh_3)_2S_2O_8$	60 min	98	95	*17*
3	**7b**	BAABCPI	20 min	100	96	*58*
4	**7b**	$(PhCH_2PPh_3)_2S_2O_8$	65 min	98	96	*17*
5	**7c**	BAABCPI	25 min	96	96	*58*
6	**7c**	$(PhCH_2PPh_3)_2S_2O_8$	60 min	95	98	*17*
7	**7d**	BAABCPI	25 min	99	98	*58*
8	**7d**	$(PhCH_2PPh_3)_2S_2O_8$	60 min	97	98	*17*
9	**7e**	BAABCPI	30 min	95	98	*58*
10	**7e**	$(PhCH_2PPh_3)_2S_2O_8$	65 min	97	100	*17*
11	**7f**	BAABCPI	30 min	95	100	*58*
12	**7f**	$(PhCH_2PPh_3)_2S_2O_8$	80 min	99	100	*17*

a) All reactions at reflux in CH_3CN



7 4

a) R^1 = Phenyl, R^2 = Phenyl; b) R^1 = Phenyl, R^2 = 3,4-dimethoxyphenyl; c) R^1 = *p* = Tolyl, R^2 = Phenyl;
d) R^1 = *p*-Tolyl, R^2 = 3,4-dimethoxyphenyl; e) R^1 = 2-methoxy-1-naphthyl, R^2 = Phenyl;
f) R^1 = 2-methoxy-1-naphthyl, R^2 = 3,4-dimethoxyphenyl

Scheme 6

n-Butyltriphenylphosphonium peroxodisulfate $[(nBuPPh_3)_2S_2O_8]$ is another peroxodisulfate-based reagent which provides an efficient and general method for the cleavage of the C=N bond of phenylhydrazones, *p*-nitrophenylhydrazones and semicarbazones under non-aqueous and aprotic conditions (*Table 3*, entries 14, 44 and 114 for phenylhydrazones; 15, 45 and 115 for 4-nitrophenylhydrazones and 16, 46 and 116 for semicarbazones).[18] Benzyltriphenylphosphonium peroxymonosulfate ($BnPPh_3^+HSO_5^-$, BTPPMS), in the presence of $BiCl_3$ is an efficient reagent for the conversion of phenylhydrazones, 2,4-dinitrophenylhydrazones and semicarbazones to the corresponding carbonyl compounds (*Table 3*, entries 99 for phenylhydrazone; 21, 87 and 124 for 2,4-dinitrophenylhydrazones and 20, 50 and 125 for semicarbazones).[26]

An aqueous suspension form of cation exchange resin Dowex-50 has been used for the deprotection of semicarbazones (*Table 3*, entries 22, 51, 64 and 133).[21] This procedure shows impressive selectivity for the regeneration of ketones in preference to aldehydes (*Table 3*, entries 22, 51, 64 and 133).[21]. Treatment of a mixture of an equal amount of the acetophenone semicarbazone and benzaldehyde semicarbazone with Dowex-50 for 1 h, gave a quantitative yield of acetophenone with only a trace of benzaldehyde.[21] This technique of selective deblocking of a ketone in the presence of an aldehyde can serve as an alternative to the Luche reaction.[21]

Various tosylhydrazones, 2,4-dinitrophenylhydrazones and semicarbazones were converted into the corresponding carbonyl compounds in mostly quantitative yields by Amberlyst 15, a macroreticular ion-exchange resin that contains sulfonic acid, *via* equilibrium exchange with aqueous acetone (*Table 3*, entries 119 and 134 for tosylhydrazones; 120 for 2,4-dinitrophenylhydrazone and 23 for semicarbazones).[22] In this method, groups which are acid-sensitive such as furyl derivatives, esters or ethers survive and, above all, excellent results are obtained in aldehyde regeneration. Combination of Amberlyst 15 with acetone is one of the most convenient of existing methods for carbonyl regeneration from nitrogenous derivatives, on the basis of its simplicity and cheapness and the high yields obtained (>85%) with a large variety of derivatives, under mild conditions.

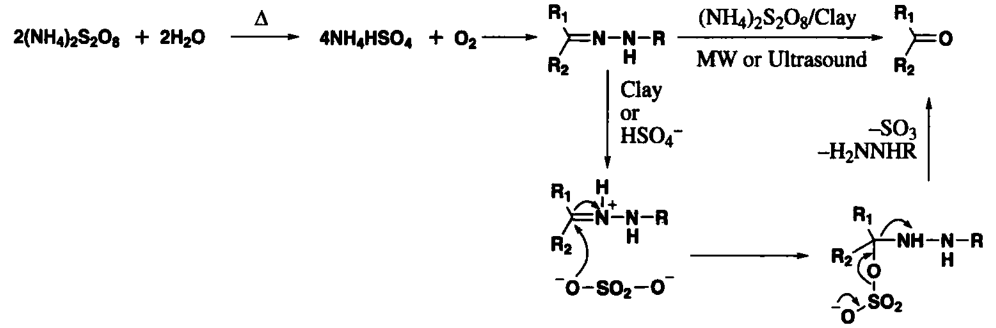
Deprotection of *p*-nitrophenylhydrazones and semicarbazones in good yields has been carried out with ammonium chlorochromate adsorbed on alumina (ACC/alumina) under mild conditions (*Table 3*, entries 24, 52, 66, 88, 106, 107, 126 and 137 for 4-nitrophenylhydrazones and 25, 65, 135 and 136 for semicarbazones).[59] Tosylhydrazones, phenylhydrazones, 2,4-dinitrophenylhydrazones and semicarbazones could be cleanly cleaved in good yields (*Table 3*, entries 67 and 138 for tosylhydrazones; 68 and 139 for phenylhydrazones and 69 and 140 for 2,4-dinitrophenylhydrazones) with an extremely inexpensive clay-supported ferric nitrate ("Clayfen") under very mild conditions.[60]

2. Deprotection With Supported Reagents and/or Microwave Irradiation

In recent years, organic reactions on solid support and those that are assisted by microwave, especially under solvent-less conditions, have attracted attention because of their enhanced selectivity, milder reaction conditions and associated ease of manipulation. In continuation of the efforts in this area, some simple oxidative cleavages of semicarbazones and derivatives of hydrazones have been reported. Benzyltriphenylphosphonium dichromate [$(PhCH_2PPh_3)_2Cr_2O_7$] supported on silica gel converts substituted hydrazones to the corresponding carbonyl compounds in excellent yields (*Table 3*, entries 26, 53, 90 and 100 for phenylhydrazones; 27, 55, 91 and 101 for *N,N*-dimethylhydrazones; 54 and 70 for 4-nitrophenylhydrazone; 92 for 2,4-dinitrophenylhydrazones and 28, 93 and 102 for semicarbazones).[40]

1-Benzyl-4-aza-1-azoniabicyclo[2.2.2]octane dichromate (**6**, BAABCD) is another Cr(VI)-based reagent for selective conversion of semicarbazones to the corresponding carbonyl compounds, under solvent-free conditions and without any support but in the presence of a catalytic amount of aluminum chloride (*Table 3*, entries 56 and 127-130).[41]

Semicarbazones and phenylhydrazones were also deprotected *via* simple oxidation with ammonium persulfate and montmorillonite K10 clay and accelerated by microwave or ultrasonic irradiation. Ammonium persulfate is an inexpensive and readily accessible oxidizing agent. It is commonly used in industry for bleaching [61] and for wastewater treatment.[62] However, only scant literature is available that describes its applications in organic synthesis.[61-66] In view of the established beneficial effects of reagents on solid supports, a variety of mineral supports such as alumina, clay and silica for ammonium persulfate have been examined and it was soon discovered that montmorillonite K10 clay provides the clean regeneration of the corresponding ketones (*Table 3*, entries 31 and 32 for phenylhydrazones using microwave and ultrasonic irradiation respectively, 29, 93, 117 and 122 for semicarbazones using microwave irradiation and 30, 94, 118 and 123 for semicarbazones using ultrasonic irradiation). The mechanism of the above transformation probably involves the decomposition of ammonium persulfate on clay (which is acidic and contains water) under the influence of microwaves, as shown in *Scheme 7*.[67]



Scheme 7

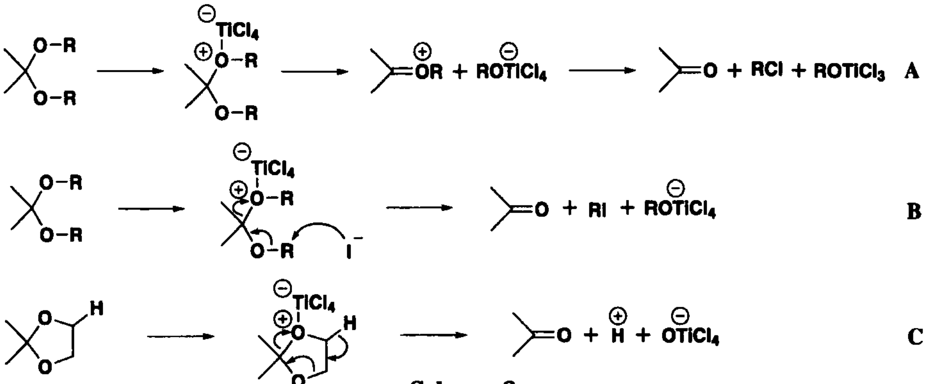
III. DEPROTECTION OF ACETALS

Acetals are among the most useful and versatile protecting groups in organic synthesis. They find widespread application in the protection of carbonyl, hydroxy and diol functions. For this reason, the protection and deprotection of the carbonyl functional group remains a crucial challenge to organic chemists. Experience shows that the critical parameters are generally the stability and the cleavage of the protecting group rather than its introduction. Therefore regeneration of the parent carbonyl group from the masked form is a useful synthetic process. There are several methods for the deprotection of acetals and ketals such as aqueous acid hydrolysis.[1] However, very often this method is incompatible with the presence of some other functional group in the molecule such as a protected hydroxyl group.

To overcome the problem, several non-acidic cleaving methods for acetals have been employed. Partial hydrolysis has been occasionally mentioned as an inconvenience in the chromatography of acetals on silica gel or alumina columns. Indeed, it has been shown that, hydrolysis on wet silica is a very convenient procedure for the regeneration of carbonyl compounds from corresponding acetals (*Table 5*, entries 1, 2, 33 and 34).[68] The results show that, when acetals are simply shaken with a small amount of wet silica gel or acidic wet silica gel, they readily convert to the corresponding carbonyl compounds; the later are easily isolated from the silica gel by filtration, solvent washing and evaporation. The rate of hydrolysis is rapid for dialkylacetal or α,β-unsaturated carbonyl compounds with wet silica gel only (0.25-3 h); α,β-unsaturated dioxolanes are hydrolyzed to the corresponding carbonyl compounds using wet silica gel with small amount of oxalic acid in 0.5-3 h; finally, acetals of saturated ketones equally need wet silica gel with oxalic acid or even sulfuric acid. The usefulness of such a deacetalization method, particularly for acetal of α,β-unsaturated carbonyl compounds consists of a) simplicity of operation, b) possibility of selective deacetalization of unsaturated over saturated acetals; c) straightforward isolation of pure carbonyl product; and d) obtaining the carbonyl compounds which are unstable in acidic medium.

An aqueous method utilizing phosphorous triiodide and diphosphorous tetraiodide has been reported for deprotection of acetals. The reactions were particularly easy with 1,1-dimethoxyalkanes, on stirring at room temperature for about 15 minutes in dichloromethane with approximately 0.3 or 0.4 molar equivalent, respectively, of P_2I_4 or PI_3.[69] These data are summarized in *Table 5* (entries 26, 28, 35 and 59 for P_2I_4 and entries 27, 29, 36 and 60 for PI_3). This method failed to deprotect the dioxolane moiety even under these conditions.

Titanium(IV) chloride in diethyl ether at room temperature can effectively deprotect acetals, including dioxolanes, under mild conditions (*Table 5*, entries 3, 4, 37, 38 and 42), sometimes in the presence of lithium iodide; with regard to the mechanism of these conversions of acetals to carbonyl compounds, different processes can be proposed depending on the structure of starting acetals (*Scheme 8*). The first process (A) would be operative with an acetal of an aromatic aldehyde where an intermediate cationic species is stabilized, the second case (B) concerns the aliphatic acetals that require lithium iodide to be converted to the parent ketone and process (C) was proposed in the case of ethylene ketals.[70]



Scheme 8

These processes have been used for the selective deprotection of ethylene acetal groups in the presence of THP ethers. The dimethylacetal of benzaldehyde is rapidly cleaved at room temperature by treatment with a 0.5 molar equivalent of $TiCl_4$. However, the same conditions failed with the dimethylacetal of saturated aldehydes or ketones after 4 h. The rate of conversion of the dimethylacetal of saturated aldehydes or ketones is greatly increased by addition of one equivalent of lithium iodide, and the corresponding carbonyl compounds is subsequently obtained in good yield. Other results show that the first process is also effective for dioxolanes, which are rapidly deprotected in the presence of a slight molecular excess of $TiCl_4$. An efficient and versatile approach for the cleavage of acetals under non-acidic and aprotic conditions uses the dropwise addition of a CH_2Cl_2 solution of either dimethylboron bromide or diphenylboron bromide to a cold (-78°C), stirred solution of acetals in dry methylene chloride (*Table 5*, entries 5, 6, 39 and 40).[71]

Table 5. Deprotection of Acetals Derivatives to their Parent Carbonyl Compounds

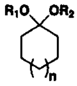
Entry	Cmpd	Reagent	Solvent	Temp./Time	Yield (%)	Ref
1	$R_1 = R_2 = -(CH_2)-_2$, n=0	Wet silica gel	CH_2Cl_2	rt/3h	98	*68*
2	 $R_1 = R_2 = -(CH_2)-_2$, n=1	Wet silica gel	CH_2Cl_2	rt/1h	82	*68*
3	$R_1 = R_2 = -(CH_2)-_2$, n=1	$TiCl_4$	Et_2O	rt/20h	75	*70*
4	$R_1 = R_2 = CH_3$, n=1	$CuCl_2{\bullet}2H_2O$	CH_3CN	rt/30min	85	*88*
5	$R_1 = R_2 = CH_3$, n=3	Me_2BBr	CH_2Cl_2	-78°C/1h	93	*71*
6	$R_1 = R_2 = -(CH_2)-_2$, n=3	Me_2BBr	CH_2Cl_2	-78°C/1h	92	*71*
7	$R_1 = R_2 = -(CH_2)-_2$, n=0	$PdCl_2(CH_3CN)_2$	Acetone	rt/0.33h	100	*72*
8	$R_1 = R_2 = -(CH_2)-_2$, n=1	$PdCl_2(CH_3CN)_2$	Acetone	rt/30h	90	*72*
9	$R_1 = R_2 = -(CH_2)-_2$, n=7	$PdCl_2(CH_3CN)_2$	Acetone	rt/1h	96	*72*
10	$R_1 = R_2 = C_2H_5$, n=1	AlI_3	CH_3CN	rt/10min	90	*79*
11	$R_1 = R_2 = C_2H_5$, n=1	SiH_2I_3	$CDCl_3$	-42°C /1min	99	*80*
12	$R_1 = R_2 = -(CH_2)-_2$, n=1	SiH_2I_3	$CDCl_3$	-42°C /1min	56	*80*
13	$R_1 = R_2 = C_2H_5$, n=1	$SmCl_3$/ CH_3COCl	pentane	rt/15min	95.1	*82*
14	$R_1 = R_2 = CH_3$, n=1	$SmCl_3$/ CH_3COCl	pentane	rt/30min	95.7	*82*
15	$R_1, R_2 = -(CH_2)-_2$, n=1	$SmCl_3$/ CH_3COCl	pentane	rt/24h	6.4	*82*
16	$R_1, R_2 = -(CH_2)-_2$, n=1	$CeCl_3{\bullet}7H_2O$	CH_3CN	rt/12h	85	*86*
17	$R_1, R_2 = -CH(n\text{-}Bu)\text{-}CH_2-$, n=1	$CeCl_3{\bullet}7H_2O$	CH_3CN	Refluxt/3h	91	*86*
18	$R_1, R_2 = -(CH_2)-_2$, n=1	$AgBrO_3/AlCl_3$	CH_3CN	Refluxt/2h	95	*89*
19	$R_1, R_2 = -(CH_2)-_2$, n=1	$NaBrO_3/AlCl_3$	CH_3CN	Refluxt/5h	93	*89*
20	$R_1, R_2 = -(CH_2)-_2$, n=1	DMD	CH_2Cl_2/Acetone	0°C/24h	35	90
21	$R_1, R_2 = -(CH_2)-_2$, n=1	MTFMD	CH_2Cl_2/TFP	0°C/2h	98	*90*
22	$R_1, R_2 = -(CH_2)-_2$, n=1	$PBGSiCl/CH_3COCl$	----	rt/4h	73	*91*
23	$R_1 = R_2 = CH_3$, n=1	Montmorillonite K10	CH_2Cl_2	rt/5min	95	*94*
24	$R_1, R_2 = -(CH_2)-_2$, n=1	Montmorillonite K10	CH_2Cl_2	rt/2h	71	*94*
25	$R_1, R_2 = -(CH_2)-_3$, n=1	Montmorillonite K10	CH_2Cl_2	rt/2h	76	*94*
26	$R_1 = R_2 = CH_3$, R = *t*-Bu	PI_3	CH_2Cl_2	rt/0.25h	78	*69*

Table 5. Continued...

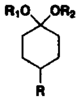
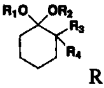
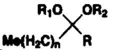
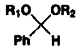
Entry	Cmpd	Reagent	Solvent	Temp./Time	Yield (%)	Ref
27	 $R_1 = R_2 = CH_{3,}$, R = *t*-Bu	P_2I_4	CH_2Cl_2	rt/0.25h	81	*69*
28	$R_1 = R_2 = CH_{3,}$, R = *t*-Bu	PI_3	CH_2Cl_2	60°C/6h	65	*69*
29	$R_1 = R_2 = CH_{3,}$, R = *t*-Bu	P_2I_4	CH_2Cl_2	60°C/4h	58	*68*
30	$R_1 = R_2 = CH_{3,}$, R = *t*-Bu	DDQ	CH_3CN/H_2O	rt/1h	92	*81*
31	$R_1 = R_2 = CH_{3,}$, R= (=O)	DDQ	CH_3CN/H_2O	rt/3h	95	*81*
32	$R_1, R_2 = -(CH_2)-_2$, R= (=O)	$CuCl_2{\bullet}2H_2O$	CH_3CN	rt/30min	95	*88*
33	$R_1 = R_2 = CH_3$, R_3; R_4 = (=CH_2) 	Wet silica gel	CH_2Cl_2	rt/0.5h	91	*68*
34	$R_1 = R_2 = CH_3$, R_3; R_4 = 	Wet silica gel	CH_2Cl_2	rt/3h	60	*68*
35	$R_1 = R_2 = C_2H_5$,R= CH_3, n = 8 	P_2I_4	CH_2Cl_2	60°C/4h	85	*69*
36	$R_1 = R_2 = C_2H_5$, R= CH_3, n = 8	PI_3	CH_2Cl_2	60°C/4h	79	*69*
37	$R_1 = R_2 = CH_3$,R= CH_3, n = 6	$TiCl_4$/LiI	Et_2O	rt/3h	85	*70*
38	$R_1 = R_2 = C_2H_5$,R= CH_3, n = 6	$TiCl_4$/LiI	Et_2O	rt/6h	85	*70*
39	$R_1, R_2 = -(CH_2)-_2$, R= CH_3, n = 8	Me_2BBr	CH_2Cl_2	-78°C /1h	97	*71*
40	$R_1, R_2 = -(CH_2)-_2$, R= CH_3, n = 8	Ph_2BBr	CH_2Cl_2	-78°C /1h	90	*71*
41	$R_1, R_2 = -(CH_2)-_2$, R= CH_3, n = 6	Clayan	----	MW/3min	90	*96*
42	 $R_1 = R_2 = CH_3$	$TiCl_4$	Et_2O	rt/10min	90	*70*
43	$R_1 = R_2 = C_2H_5$	AlI_3	CH_3CN	rt/10min	80	*79*
44	$R_1, R_2 = -(CH_2)-_2$	AlI_3	CH_3CN	rt/10min	82	*79*
45	$R_1 = R_2 = CH_3$	DDQ	CH_3CN/H_2O	rt/1h	75	*81*
46	$R_1 = R_2 = C_2H_5$	$SmCl_3/CH_3COCl$	pentane	rt/15min	93.5	*82*
47	$R_1, R_2 = -(CH_2)-_2$	$SmCl_3/CH_3COCl$	pentane	rt/1h	88.7	*82*
48	$R_1 = R_2 = C_2H_5$	WCl_6	CH_2Cl_2	rt/5min	93	*87*
49	$R_1 = R_2 = CH_3$	WCl_6	CH_2Cl_2	rt/5min	92	*87*
50	$R_1 = R_2 = CH_3$	$CuCl_2{\bullet}2H_2O$	CH_3CN	rt/30min	85	*88*
51	$R_1, R_2 = -(CH_2)-_2$	$CuCl_2{\bullet}2H_2O$	CH_3CN	rt/30min	95	*88*
52	$R_1, R_2 = -(CH_2)-_2$	$AgBrO_3/AlCl_3$	CH_3CN	Reflux/0.75h	90	*89*
53	$R_1, R_2 = -(CH_2)-_2$	$NaBrO_3/AlCl_3$	CH_3CN	Reflux/1h	95	*89*
54	$R_1 = R_2 = CH_3$	DMD	CH_2Cl_2/Acetoe	18°C/96h	50	*90*
55	$R_1 = R_2 = CH_3$	PBGSiCl/CH_3COCl	----	rt/1h	90	*91*
56	$R_1 = R_2 = CH_3$	Montmorillonite K10	CH_2Cl_2	rt/5min	95	*94*
57	$R_1 = R_2 = CH_3$	Clayan	----	MW/3.5min	86	96

Table 5. Continued...

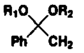
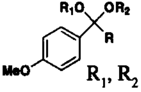
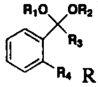
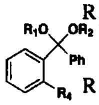
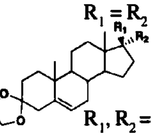
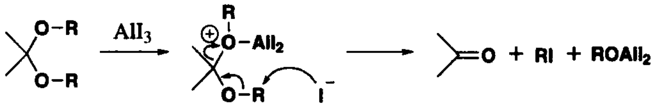
Entry	Cmpd	Reagent	Solvent	Temp./Time	Yield (%)	Ref
58	$R_1, R_2 = -(CH_2)-_2$	BAABCD	----	MW/3min	83	97
59	 $R_1 = R_2 = CH_3$	P_2I_4	CH_2Cl_2	rt/0.25h	67	*69*
60	$R_1 = R_2 = CH_3$	PI_3	CH_2Cl_2	rt/0.25h	75	*69*
61	$R_1 = R_2 = CH_3$	AlI_3	CH_3CN	rt/10min	86	*79*
62	$R_1, R_2 = -(CH_2)-_2$	AlI_3	CH_3CN	rt/30min	83	*79*
63	$R_1 = R_2 = CH_3$	DDQ	CH_3CN/H_2O	rt/1h	90	*81*
64	$R_1, R_2 = -(CH_2)-_2$	WCl_6	CH_3CN	rt/10min	94	*87*
65	$R_1, R_2 = -(CH_2)-_2$	$CuCl_2 \cdot 2H_2O$	CH_3CN	rt/30min	96	*88*
66	$R_1, R_2 = -(CH_2)-_2$	$AgBrO_3/AlCl_3$	CH_3CN	Reflux/0.65h	90	*89*
67	$R_1, R_2 = -(CH_2)-_2$	$NaBrO_3/AlCl_3$	CH_3CN	Reflux/0.75h	89	*89*
68	$R_1 = R_2 = CH_3$	$PBGSiCl/CH_3COCl$	----	rt/6h	63	*91*
69	$R_1, R_2 = -(CH_2)-_2$	$BnPh_3P^+ HSO_5^-$	CH_3CN	Reflux/35min	90	*92*
70	$R_1 = R_2 = CH_3$	Montmorillonite K10	CH_2Cl_2	rt/5min	100	94
71	$R_1, R_2 = -CH_2-C(CH_3)_2-CH_2-$	Montmorillonite K10	CH_2Cl_2	rt/30min	95	94
72	$R_1, R_2 = -(CH_2)-_2$	KmnO4/alumina	----	Grinding/5mn	98	95
73	$R_1, R_2 = -(CH_2)-_2$	KmnO4	----	Grinding/25in	68	95
74	$R_1, R_2 = -(CH_2)-_2$	BAABCD	----	MW/3:20min	95	97
75	 $R_1, R_2 = -(CH_2)-_2 R = H$	SiH_2I_2	$CDCl_3$	-42°C/1min	100	*80*
76	$R_1 = R_2 = CH_3, R = H$	SiH_2I_2	$CDCl_3$	-42°C/1min	100	*80*
77	$R_1, R_2 = -(CH_2)-_2 R = CH_3$	SiH_2I_2	$CDCl_3$	-42°C/10min	20	*80*
78	 $R_1, R_2 = -(CH_2)-_{2,} R = H$	SiH_2I_2	$CDCl_3$	-42°C/10min	100	*80*
79	$R_1 = R_2 = CH_{3,} R = H$	DDQ	CH_3CN/H_2O	rt/1h	91	*81*
80	$R_1 = R_2 = CH_{3,} R = H$	$SmCl_3/CH_3COCl$	Pentane	rt/0.5h	98	*82*
81	$R_1, R_2 = -(CH_2)-_{2,} R = H$	WCl_6	CH_2Cl_2	rt/5min	89	*87*
82	$R_1, R_2 = -(CH_2)-_2 R_3 = H, R_4 = Ome$	$BnPh_3P^+ HSO_5$	CH_3CN	Reflux/60min	87	*92*
83	 $R_1, R_2 = -(CH_2)-2, R_3 = H, R_4 = NO_2$	$BnPh_3P^+ HSO_5$	CH_3CN	Reflux/80min	78	*92*
84	$R_1, R_2 = -(CH_2)-2, R_3 = H, R_4 = Cl$	$BnPh_3P^+ HSO_5$	CH_3CN	Reflux/75min	80	*92*
85	$R_1, R_2 = -(CH_2)-_2, R_3 = H, R_4 = OMe$	$KmnO_4$/alumina	----	Grinding/15min	92	*95*
86	$R_1, R_2 = -(CH_2)-_2, R_3 = H, R_4 = OMe$	$KmnO_4$	----	Grinding/35min	70	*95*
87	$R_1, R_2 = -(CH_2)-_2, R_3 = H, R_4 = NO_2$	$KmnO_4$/alumina	----	Grinding/15min	75	*95*
88	$R_1, R_2 = -(CH_2)-_2, R_3 = H, R_4 = OMe$	$KmnO_4$/	----	Grinding/35min	55	*95*
89	$R_1, R_2 = -(CH_2)-_2, R_3 = H, R_4 = Cl$	$KmnO_4$/alumina	----	Grinding/15min	85	*95*

Table 5. Continued...

Entry	Cmpd	Reagent	Solvent	Temp./Time	Yield (%)	Ref
90	$R_1, R_2 = -(CH_2)-_2, R_3 = H, R_4 = Cl$	$KmnO_4/$	----	Grinding/40min	55	*95*
91	$R_1, R_2 = -(CH_2)-_2, R_3 = H, R_4 = NO_2$	BAABCD	----	MW/3x2min	89	*97*
92	$R_1, R_2 = -(CH_2)-_2, R_3 = H, R_4 = OMe$	BAABCD	----	MW/3x20min	90	*97*
93	 $R_1, R_2 = -(CH_2)-_2$	$CeCl_3•7H_2O$	CH_3CN	Reflux/5h	91	*86*
94	$R_1, R_2 = -(CH_2)-_2$	$CuCl_2•2H_2O$	CH_3CN	rt/30min	98	*88*
95	$R_1 = R_2 = CH_3$	$PBGSiCl/CH_3COCl$	----	rt/3h	88	*91*
96	 $R_1, R_2 = -(CH_2)-_2$	$CuSO_4$/Silica	$CHCl_3$	60°C/3h	82	*93*
97	$R_1, R_2 = -(CH_2)-_2$	$CuSO_4$/Silica	$CHCl_3$	60°C/4h	61	*93*
98	$R_1 = R_2 = CH_3$	$CuSO_4$/Silica	$CHCl_3$	60°C/2h60°C/	81	93
99	$R_1 = C(O)CH_3, R_2 = H$	$CuSO_4$/Silica	$CHCl_3$	24h	85	*93*

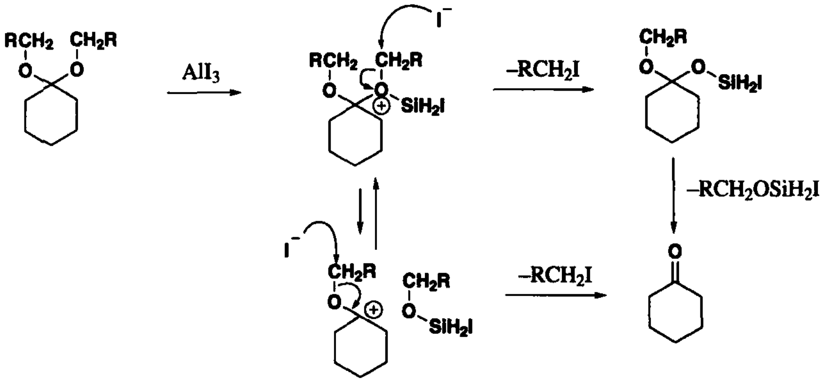
The use of catalytic quantities of $PdCl_2(CH_3CN)_2$ in acetone represents an attractive and simple technique for removing ethylene acetals. The conditions are compatible with other functionalities, including a number of routinely employed alcohol protecting groups. Initially, the reactivity patterns of several ketals were examined in CH_3CN. Upon treatment with $PdCl_2(CH_3CN)_2$, yields are often excellent; however, these hydrolyses were not consistently reproducible. Modifications, such as freshly prepared catalyst, other sources of Pd (II) and standardized amounts of H_2O did little to improve the situation. Ultimately, simply switching to acetone as solvent, which favors transketalization, gave excellent results as summarized in *Table 5* (entries 7, 8 and 9).[72]

Aluminum triiodide is a useful reagent for effecting a variety of synthetic transformations.[73-78] It was observed that AlI_3 has a greater affinity towards ethereal oxygen and forms a weak complex with it. Ketals, on treatment with this reagent in an aprotic solvent, would form a complex and release the parent carbonyl compound (*Scheme 9*). A freshly prepared pale yellow solution of AlI_3 in dry benzene was added to a solution of the substrate in acetonitrile with continuous stirring at room temperature. Within a short time, the deprotected carbonyl compound was formed in good yield (*Table 5*, entries 10, 43, 44, 61 and 62).[7]



Scheme 9

Diiodosilane (SiH_2I_2) is a mild reagent for cleavage of ketals hydrolytically to give the carbonyl compounds. At low temperature (-42°C) and short reaction time (a few minutes), catalytic amounts (5-10 mol%) of diiodosilane provide clean deprotection of various ketals to yield ketones and aldehydes, with no apparent reduction of the latter (*Table 5*, entries 11, 12 and 75-78). At temperatures above 0°C, diiodosilane effectively converts ketals to the carbonyl compound and the iodoalkanes.

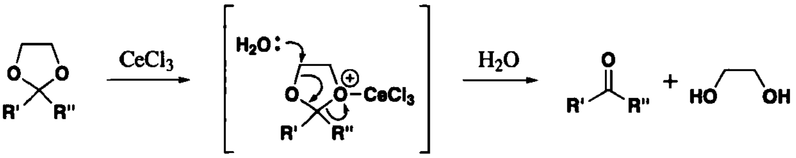


Scheme 10

In the presence of a catalytic amount of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ), acetals are readily hydrolyzed to the corresponding aldehydes or ketones in aqueous acetonitrile. Reactions using neutral DDQ have the advantage over the conventional methods using acidic catalysts, because of mildness of the reaction conditions (*Table 5*, entries 30, 31, 45, 63 and 79).[81]

The non-acidic deprotection of acetals is a desirable goal and the acetyl chloride-samarium trichloride system is simple and convenient. To a solution of the acetal in anhydrous *n*-pentane, samarium trichloride was added under a nitrogen atmosphere at room temperature. Upon addition of freshly distilled acetyl chloride after the specified time, the carbonyl compound was isolated in good to excellent yields (*Table 5*, entries 13-15, 46, 47 and 80).[82]

Many of these procedures suffer from one or more drawbacks: lack of selectivity, unsatisfactory yields, cost or toxicity of the reagent, or the necessity of anhydrous conditions. These limitations led to further investigations of new reagents able to perform the selective cleavage of acetals in good yields. Recently, several synthetically useful organic reactions using trivalent lanthanide salts have been reported[83-85] and the use of $CeCl_3$ in methanol is a well-known method for this purpose. The deprotection of 1,3-dioxolanes was carried out in acetonitrile in the presence of $CeCl_3$ as reagent. To a stirred suspension of acetal and sodium iodide in acetonitrile was added $CeCl_3 \cdot 7H_2O$, and the resulting mixture was stirred for the specified time at the reported temperature (*Table 5*, entries 16, 17 and 93). The mechanism for these transformations of 1,3-dioxolanes to carbonyl compounds is unclear. A reasonable explanation may be that the combination of a Lewis acid and the presence of water effects the deprotection (*Scheme 11*).[86]

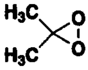


Scheme 11

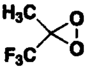
Tungsten hexachloride (WCl_6) in dichloromethane or acetonitrile at room temperature is a mild and efficient method for deprotection of a variety of ketals and rapidly converted them to their corresponding carbonyl compounds (*Table 5*, entries 48, 49, 64 and 81).[87] A variety of acetals were efficiently cleaved in short times and in high yields using $CuCl_2 \cdot 2H_2O$ in acetonitrile at room temperature. The results are summarized in *Table 5*, entries 32, 50, 51, 65 and 94. The deprotection reaction worked even with a catalytic amount of copper chloride, but the reaction time was longer. The pH 2-3 of the reaction mixture indicated that the reaction is probably acid-catalyzed. This method was effectively used in the synthesis of diols important in asymmetric syntheses.[88]

Ethylene ketals are transformed to ketones with $AgBrO_3/AlCl_3$ in refluxing acetonitrile. $AgBrO_3/AlCl_3$ is also able to transform ethylene acetals to aldehydes in refluxing carbon tetrachloride in high yields (*Table 5*, entries 18, 52 and 66 for $AgBrO_3/AlCl_3$ and entries 19, 53 and 67 for $NaBrO_3/AlCl_3$). Both sodium bromate and silver bromate are effective under non-aqueous conditions when catalyzed with $AlCl_3$.[89]

An alternative method is deprotection of ketals *via* oxidation. Compared to oxidation methods which use metal oxides stoichiometrically or metal complexes catalytically, oxidations employing either *in-situ* or isolated dioxiranes, **8a** or **8b** (a new class of powerful oxidants) often have the advantage of simple procedures, mild reaction conditions, ease of product isolation and increased yields. Thus dimethyldioxirane (DMD) **8a** and methyl(trifluoromethyl)dioxirane (MTFMD) **8b** have been applied to perform an impressive variety of useful synthetic transformations, such as oxidative cleavage of acetals and hemiacetals to carbonyl containing products. Addition of a solution of **8a** in acetone or **8b** in 1,1,1-trifluoropropane (TFP) to the acetals in dry CH_2Cl_2 kept at 0°C, affords the carbonyl compounds in 35-90% yields (*Table 5*, entries 20, 21 and 54).

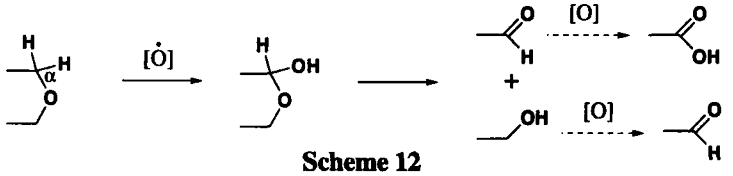


8a



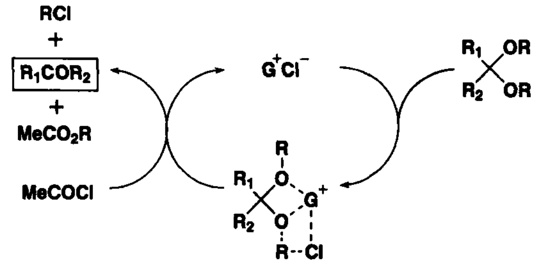
8b

The oxidation-cleavage is initiated by O-atom insertion into the C-H bonds of the 1,3-dioxolane or into the methyne C-H of the dimethyl moiety of acetals, and followed by rearrangement shown in *Scheme 12*.[90]



Scheme 12

Acetals have been treated at room temperature with stoichiometric amounts of acetyl chloride in the presence of catalytic amounts of a silica-supported guanidinum chloride (PBGSiCl) to produce the corresponding aldehydes and ketones in good yields under neutral conditions after moderate reaction times (*Table 5*, entries 22, 55, 68 and 95). The mechanism is viewed as the tight association of guanidinum cation (G^+) with the oxygen lone pair of the acetals. Thus, the chloride anion induces dealkylation on the less-substituted carbon center in the α-position to the oxonium-like intermediate (*Scheme 13*).[91] These results were attributed to the high nucleophilicity of the chloride anion associated with the guanidinum cation, related to the weakness of the ion pair derived from steric effect and charge stabilization by the guanidinum ion (*Scheme 13*). Consequently, the interaction of an ether linkage with guanidinum chloride would induce the dealkylation of acetals, while acetyl chloride could act as a source of chloride anion. Therefore in a typical procedure, freshly distilled acetyl chloride was added dropwise to a suspension of PBGSiCl in the acetal in the absence of solvent. The reaction mixture was stirred until the end of methyl chloride evolution. The catalyst was recovered by dilution of the reaction mixture with chloroform and filtration, washed with chloroform, dried under vacuum and reused in another experiment.



Scheme 13

Benzyltriphenylphosphonium peroxomonosulfate ($BnPh_3P^+HSO_5^-$) was used as a new reagent for oxidative deprotection of ethylene acetals in refluxing acetonitrile in the presence of bismuth chloride (*Table 5*, entries 69 and 82-84). Although several Lewis acids such as $ZnCl_2$, $FeCl_3$, $AlCl_3$ and $BiCl_3$ were examined, surprisingly only $BiCl_3$ was found to be an effective catalyst during this investigation.[92]

Most of the methods used for the cleavage of ketals employ aqueous reaction media acidified with mineral acids or non-aqueous media acidified with organic acids. There are few examples that make use of non-aqueous neutral reaction conditions. Even lower are the cases of cleavage methods performed with the reagent deposited on an inorganic support. Copper(II) sulfate supported on silica gel in organic solvents promotes the cleavage of acetals to the corresponding carbonyl compounds under mild conditions (*Table 5*, entries 96-99).[93]

The inexpensive, commercially available, acidic and activated clay, montmorillonite K10 in dichloromethane, provided a mild and efficient procedure for effecting the transformation of sensitive ketals into ketones in the total synthesis of anticancer agents, bromoxone and harveynone. As with many deprotection methods employing heterogeneous reagents, the reaction is operationally straightforward and the reagent is easily removed by filtration when the transformation is complete. Several general reactions were carried out to define the scope and limitation of this deprotection procedure. *Table 5*, entries 23-25, 56, 70 and 71 gives data on representative results.[94]

Potassium permanganate in the presence or absence of alumina was used to transform ethylene acetals to the corresponding carbonyl compounds under solvent-free conditions, a manipulatively simple and rapid method for oxidative deprotection of ethylene acetals. The yield of transformation of ethylene acetals to the corresponding carbonyl compounds with potassium permanganate without using alumina was lower and the rate was slower. The data for $KMnO_4$, in the presence and absence of alumina, are summarized in *Table 5*, entries 72, 85, 87 and 89 and entries 73, 86, 88 and 90 respectively.[95]

Reagents impregnated on mineral solid supports are efficient in solvent free conditions under microwave irradiation and have attained importance because of their enhanced reactivity, selectivity and ease of manipulation. Clay supported ammonium nitrate "Clayan", converts acetals into the parent carbonyl compounds under microwave irradiation. The eco-friendly nature of the reagent and non-solvent conditions are the important features of the procedure. Clayan was prepared by the impregnation of ammonium nitrate on montmorillonite K10. Mixing clayan with acetals and then subjecting to MW irradiation gave the corresponding carbonyl compounds in good yield (*Table 5*, entries 41 and 57).[96]

1-Benzyl-4-aza-1-azoniabicyclo[2.2.2]octane dichromate (BAABCD) is a useful reagent for the selective cleavage of ethylene ketals. This very simple and efficient method has been carried out under microwave irradiation. The reaction was complete within 3-4 minutes and the pure aldehydes and ketones obtained by a simple work-up (*Table 5*, entries 58, 74, 91 and 92).[97]

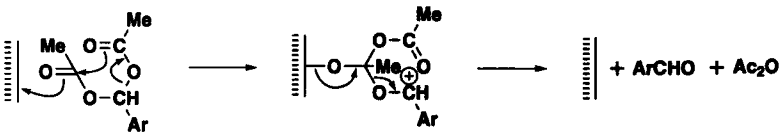
IV. DEPROTECTION OF 1,1-DIACETATES

Acetals are the most common derivatives utilized for selective protection and deprotection of carbonyl compounds. However, in many cases different strategies are desirable where selective protection of aldehydes in the presence of keto groups are desired. In this context, protection as the 1,1-diacetate can be successfully utilized. A number of methods employed for the preparation of 1,1-diacetates from aldehydes include the use of strong protic acids such as sulfuric acid, phosphoric acid and methanesulfonic acid [98] or Lewis acids such as zinc chloride, ferric chloride [99] and phosphorus trichloride.[100] Although these methodologies can afford 1,1-diacetates in good yields, the forcing reaction conditions limit more widespread applications. To this end, different heterogeneous and environmentally friendly catalysts have been utilized. These include Nafion-H,[101] tungestosilic acid,[102] B-Y and HZSM-5 zeolite,[103,104] sulfated zirconia[105] and expensive graphite.[106] Since 1,1-diacetates are stable to oxidants,[107,108] easily prepared and can serve as starting materials for Diels-Alder cycloaddition reactions,[109,110] they have received increased attention over the last decade.

Complete conversion of 1,1-diacetates to the corresponding aldehydes is accomplished with either sodium hydroxide or potassium carbonate in aqueous THF overnight. Consequently, cleavage of this protecting group is possible under very mild conditions. This method in which no detailed procedures are given has, however, the substantial drawback of requiring long reaction times.[111]

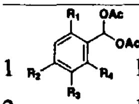
The boron triiodide (BI_3)-*N,N*-diethylaniline complex, generated *in situ* from boron, *N,N*-diethylaniline and I_2, regenerated carboxaldehydes from the corresponding geminal diacetate derivatives under mild condition in good yields. The reaction was carried out by adding a solution of the diacetate in benzene to the BI_3 complex in benzene under argon atmosphere and at room temperature, stirring for the specified time give the aldehyde in good yields (*Table 6*, entries 1-3 and 29).[112] Ceric ammonium nitrate (CAN) coated on silica gel in dichloromethane selectively converts benzaldehydediacetates to the corresponding benzaldehydes. For this deprotection reactions, CAN has proved to be an ideal reagent because of the mild conditions involved (*Table 6*, entries 4-8).[113] Expensive graphite has been previously used as an efficient and convenient catalyst for preparation of 1,1-diacetates from aldehydes.[106] In addition this reagent could deprotect same diacetates to their parent aldehyde in refluxing dichloromethane or benzene with excellent yields (*Table 6*, entries 9-13).[114]

A number of 1,1-diacetates are easily cleaved in good to excellent yields under catalysis by montmorillonite clays in refluxing dichloromethane and/or under microwave irradiation.[115, 116] However, the reagent was used for only one compound and no general study is available. In this work, montmorillonite K10 or KSF for the time indicated in *Table 6* regenerated carbonyl derivatives without the use of an additional microwave oven (*Table 6*, entries 14, 16, 18, 20 and 22 for Montmorillonite K10 (MMK10) and entries 15, 17, 19, 21 and 23 for Montmorillonite KSF (MMKSF). The mechanism of this reaction was different from the mechanism of hydrolysis of diacetates in aqueous hydrochloric acid. The hydroxamate test identifies the presence of acetic anhydride in the reaction products. Furthermore, neither additional nor anhydrous conditions affect the reaction rate. These results show that the reaction undergoes a unimolecular decomposition of 1,1-diacetates to give an aldehyde and acetic anhydride and in this method the supposed-clay functions as a Lewis acid (*Scheme 14*).[117]



Scheme 14

Table 6. Deprotection of 1,1-Diacetates

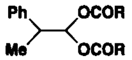
Entry	Cmpd	R_1	R_2	R_3	R_4	Reagent	Solvent	Temp./ Time	Yield (%)	Ref
1		H	H	H	H	BI_3/N,N-diethylaniline	C_6H_6	rt/3h	65	*112*
2		H	CH_3	H	H	BI_3/N,N-diethylaniline	C_6H_6	rt/3h	66	*112*
3		H	Br	H	H	BI_3/N,N-diethylaniline	C_6H_6	rt/3h	65	*112*
4		OCH_3	H	OCH_3	H	CAN/SiO_2	CH_2Cl_2	rt/15min	92	*113*
5		H	OCOMe	H	H	CAN/SiO_2	CH_2Cl_2	rt/15min	98	*113*
6		H	OCOMe	OCH_3	H	CAN/SiO_2	CH_2Cl_2	rt/15min	90	*113*
7		OCH_3	NO_2	OCH_3	H	CAN/SiO_2	CH_2Cl_2	rt/15min	94	*113*
8		OCH_3	H	OCH_3	NO_2	CAN/SiO_2	CH_2Cl_2	rt/15min	95	*113*
9		H	H	H	H	Expansive Graphite	CH_2Cl_2	Reflux/15mi	98	*114*
10		H	CH_3	H	H	Expansive Graphite	CH_2Cl_2	Reflux/10mi	99	*114*
11		H	OCH_3	H	H	Expansive Graphite	CH_2Cl_2	Reflux/10min	99	*114*
12		H	OCH_3	Cl	H	Expansive Graphite	CH_2Cl_2	Reflux/30min	95	*114*
13		H	OCH_3	NO_2	H	Expansive Graphite	CH_2Cl_2	Reflux/30min	96	*114*
14		H	H	H	H	MMK10	CH_2Cl_2	Reflux/20min	98	*117*
15		H	H	H	H	MMKSF	CH_2Cl_2	Reflux/20min	96	*117*
16		H	CH_3	H	H	MMK10	CH_2Cl_2	Reflux/20min	99	*117*
17		H	CH_3	H	H	MMKSF	CH_2Cl_2	Reflux/15min	98	*117*
18		H	OCH_3	H	H	MMK10	CH_2Cl_2	Reflux/20min	98	*117*
19		H	OCH_3	H	H	MMKSF	CH_2Cl_2	Reflux/20min	96	*117*
20		H	H	Cl	H	MMK10	CH_2Cl_2	Reflux/30min	95	*117*
21		H	H	Cl	H	MMKSF	CH_2Cl_2	Reflux/40min	93	*117*
22		H	H	NO_2	H	MMK10	CH_2Cl_2	Reflux/20min	98	*117*
23		H	H	NO_2	H	MMKSF	CH_2Cl_2	Reflux/25min	95	*117*
24		H	Ph	H	H	Zeolite HSZ-360	----	MW/20min	99	*119*
25		H	NO_2	H	H	Zeolite HSZ-360	----	MW/20min	93	*119*
26		H	OCH_3	H	H	Zeolite HSZ-360	----	MW/20min	94	*119*
27		H	CH_3	H	H	Zeolite HSZ-360	----	MW/20min	86	*119*
28		H	H	H	H	Zeolite HSZ-360	----	MW/20min	94	*119*
29	$Me(CH_2)_nCH(OAc)_2$	N = 4				BI_3/N,N-diethylaniline	C_6H_6	rt/2.5h	60	*119*
30		N = 10				Zeolite HSZ-360	----	MW/20min	88	*119*

Zeolite HSZ-360 can generate 1,1-diacetate from aldehyde in the presence of acetic anhydride in good to high yields (85-98%). Next the ability of this catalyst for the production of aldehydes from 1,1-diacetate was investigated. Microwave irradiation of 1,1-diacetate/zeolite

HSZ-360mixture for 20 minutes provide clean regeneration of the corresponding aldehydes in high yields (88-99%) (*Table 6*, entries 24-28 and 30).[118]

Hydrolytic enzymes, especially esterases and lipases, are among the most broadly used classes of enzymes in organic synthesis. Their great catalytic abilities, broad substrate specificity, stability and low cost make them attractive for chemical transformation. A new and convenient method for the optical resolution of aldehydes, which bear an asymmetric carbon adjacent to the carbonyl carbon, has been developed through lipase-catalyzed resolution of the corresponding acylals. Thus substrates were chosen to test the enzymatic hydrolysis with the following commercially available hydrolytic enzymes: *Pig Liver Esterase* (PLE), *Pig Pancreatic Lipase* (PPL), P-*Fluorescens* Lipase (PFL) and *Candida Rugosa Lipase* (CRL). The results are summarized in *Table 7*. *Candida Rugosa* Lipase (CRL) showed the best stereoselectivity.[119]

Table 7. Asymmetric Enzymatic Hydrolysis of 1,1-Diacylates of 2-Phenylpropanal[a]

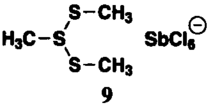
Entry	Substrate	R=	Enzyme	Time (min)	Conversion	Ee	Ref
1		Me	PLE	30	30	2	118
2		Me	PPL	40	18	14	118
3		Me	CRL	70	25	72	118
4		Me	PFL	360	5	-	118
5		Et	CRL	90	23	40	118
6		Pr	CRL	90	20	35	118

a) All configurations are R except for entry 4.

V. DEPROTECTION OF 1,3-DITHIOLANES AND 1,3-DITHIANES

Cyclic thioacetals and ketals have been widely used as carbonyl protecting groups and indeed, considerable effort has been made for the development of new methods for their introduction and removal.[1] Their primary use, however, involves the protection of the carbonyl function, exemplified by numerous useful applications in organic synthesis and the total synthesis of natural products.[120-123] 1,3-Dithiolanes are usually obtained by acid-catalyzed condensation of carbonyl compounds with 1,2-ethanedithiol. Lewis acid catalysts used for this purpose include boron trifluoride etherate,[124] zinc(II) chloride,[125] aluminum(III) chloride,[126] titanium(IV) chloride,[127] lanthanum(III) chloride,[128] tellurium chloride,[129] tetrachlorosilane[130] and organotin triflates.[131] 1,3-Dithianes are usually obtained by acid-catalyzed condensation of carbonyl compounds with 1,3-dithiols. Lewis acid catalysts used for this purpose include boron trifluoride etherate,[132-134] $SOCl_2$-SiO_2,[135] tellurium chloride,[129] Montmorillonite KSF clay without solvent[136] samarium iodide.[137] Of the many dithioacetalization methodologies, chemical procedures are more widely used than others, based on photolytic and electrolytic processes.

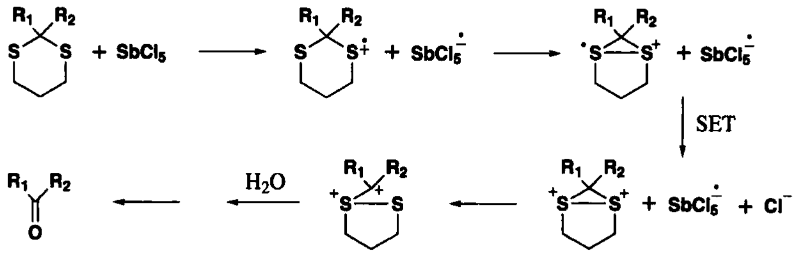
A mixture of aqueous hydrochloric acid and dimethyl sulfoxide is presumably in equilibrium with small amounts of the chlorodimethylsulfonium ion, a positive halogen donor which has been used as mild chlorinating agent.[138] Chlorination of dithianes in aqueous media has been used to regenerate the carbonyl function.[139, 140] On the basis of this fact, the cleavage may be performed by using a positive sulfur donor such as methylbis[methylthio]sulfonium hexachloroantimonate **9**.[141] The reaction was carried out in dichloromethane and at –77°C (*Table 8*, entries 1 and 46).[142]



9

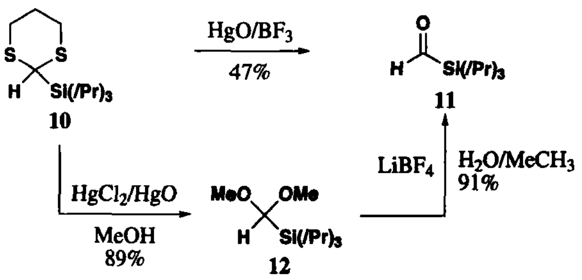
Conversion of thioacetals to the corresponding carbonyl compounds can be performed under a variety of reaction conditions, one of them being the oxidative method. When diethyl and diphenyl dithioacetals were treated with a mixture of *m*-chloroperbenzoic acid and trifluoroacetic acid in dichloromethane, the corresponding carbonyl compounds were regenerated in high yield (*Table 8*, entries 78-80, 87 and 88).[143] The application of some oxidative methods to polyfunctional molecules is limited due to the drastic conditions required, and to the difficulty to obtain reproducible yields. Thus, chemical methods often require the use of heavy metal reagents, antimony pentachloride ($SbCl_5$) being one of them.

Activation of organic molecules through single electron transfer (SET) affords ion-radical intermediates that participate in many oxidation and reduction processes. Antimony pentachloride has been successfully used for the generation of organic cation radicals.[144] Since the dithioacetalization is recognized as an important reaction in synthetic organic chemistry, the SET reactions of dithioacetals with antimony pentachloride became of interest. The reaction of several 1,3-dithianes with $SbCl_5$ in methylene chloride under nitrogen at 0°C, produced carbonyl compounds in good yields (*Table 8*, entries 2, 9, 17 and 32-34). [145] The proposed reaction pathway is depicted on *Scheme 15*.



Scheme 15

The reaction of 2-lithio-1,3-dithiane with triisopropylsilyl chloride (TIPSCl) led to **10** cleanly. The solvolysis of **10** in a mixture of $HgCl_2$, HgO, MeOH afforded **12** in 89% yield. The hydrolysis of **12** in refluxing aqueous acetonitrile and in the presence of $LiBF_4$ provided **11** in 91% yield. In contrast, even the mild Vedejs-Fuchs hydrolysis conditions[146] gave **11** in significantly lower yield and purity (*Scheme 16*).[147]



Scheme 16

Reaction of 1,3-dithiolanes with SeO_2 in acetic acid at room temperature regenerates the corresponding carbonyl compounds in good yields (*Table 8*, entries 47, 57, 72 and 81).[148] The full account of the reagent (silver salt-I_2) system for deprotection of dithioacetals and its application for the synthesis of α-hydroxyaldehyde has been described.[149] Among silver perchlorate, silver acetate, silver carbonate and silver nitrite, the latter was the most effective for deprotection of 1,3-dithianes and 1,3-dithiolanes (*Table 8*, entries 10, 20, 21 and 48).

Table 8. Deprotection of 1,3-Dithianes and 1,3-Dithiolanes

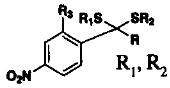
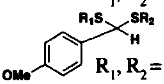
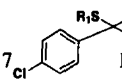
Entry	Cmpd	Reagent	Solvent	Temp./Time	Yield (%)	Ref
1	 $R_1, R_2 = -(CH_2)-_3$, R= CH_3, R_3 = H	$(CH_3)_3S_3{}^+SbCl_5{}^-$	CH_2Cl_2	-77°C/1min	100	*142*
2	$R_1, R_2 = -(CH_2)-_3$, R, R_3 = H	$SbCl_5$	CH_2Cl_2	0°C/10min	66	*145*
3	$R_1, R_2 = -(CH_2)_2$-R=H, $R_3 = NO_2$	Nitrogen oxides	CH_2Cl_2	0-5°C/---	87	*153*
4	$R_1, R_2 = -(CH_2)-_3$, R, R_3 = H	$Fe(NO_3)_3$	hexane	50°C/10min	100	*155*
5	$R_1, R_2 = -(CH_2)-_2$, R, R_3 = H	$Fe(NO_3)_3$	hexane	50°C/10min	100	*155*
6	$R_1, R_2 = -(CH_2)-_3$, R, R_3 = H	$Fe(NO_3)_3$/silica	hexane	40-50°C/10min	100	*159*
7	$R_1, R_2 = -(CH_2)-_2$, R, R_3 = H	clayfen	---	MW/40sec	97	*164*
8	$R_1, R_2 = -(CH_2)-_3$, R, R_3 = H	clayfen	---	rt	97	*164*
9	$R_1, R_2 = -(CH_2)-_3$	$SbCl_5$	CH_2Cl_2	0°C/10min	76	*145*
10	 $R_1, R_2 = -(CH_2)-_3$	$AgClO_4/I_2$	THF	rt/5min	95	*149*
11	$R_1, R_2 = -(CH_2)-_2$	Amberlyst 15	Acetone/H_2O/CHO	80°C/96h	60	*154*
12	$R_1, R_2 = -(CH_2)-_2$	$Fe(NO_3)_3$	hexane	50°C/5min	89	*155*
13	$R_1, R_2 = -(CH_2)-_3$	$Fe(NO_3)_3$	hexane	50°C/5min	93	*155*
14	$R_1, R_2 = -(CH_2)-_3$	$Fe(NO_3)_3$/silica	hexane	40-50°C/10min	100	*159*
15	$R_1 = R_2$ = Et	Clayan	CH_2Cl_2	40-50°C/18h	83	*160*
16	$R_1, R_2 = -(CH_2)-_2$	Clayfen	---	rt	97	*164*
17	 $R_1, R_2 = -(CH_2)-_3$, R= CH_3	$SbCl_5{}^-$	CH_2Cl_2	0°C/10min	81	*145*
18	$R_1, R_2 = -(CH_2)-_2$, R = H	$Fe(NO_3)_3$	hexane	50°C/10min	93	*159*

Table 8. Continued...

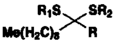
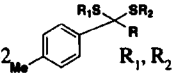
Entry	Cmpd	Reagent	Solvent	Temp./Time	Yield (%)	Ref
19	$R_1, R_2 = -(CH_2)-_3$, $R = H$	$Fe(NO_3)_3$	hexane	50ºC/10min	95	*155*
20	 $R_1, R_2 = -(CH_2)-_2$, $R= H$	$AgNO_3/I_2$	THF	rt/2.5h	73	*149*
21	$R_1, R_2 = -(CH_2)-_3$, $R = H$	$AgNO_3/I_2$	THF	rt/5.5h	88	*149*
22	$R_1, R_2 = -(CH_2)-_3$, $R = H$	H_5IO_6	Ether/THF	rt/5min	91	*150*
23	$R_1, R_2 = -(CH_2)-_3$, $R = CH_3$	H_5IO_6	Ether/THF	rt/5min	94	*150*
24	$R_1, R_2 = Et$, $R = CH_3$	Isoamyl nitrite	CH_2Cl_2	rt/0.5h	89	*151*
25	$R_1, R_2 = -(CH_2)-_3$, $R = H$	Nitrogen oxides	CH_2Cl_2	0-5ºC/---	96	*153*
26	$R_1 = R_2 = Et$, $R = H$	Clayfen	CH_2Cl_2	rt/3h	87	*157*
27	$R_1 = R_2 = Et$, $R = H$	Claycop	CH_2Cl_2	rt/3h	88	*157*
28	$R_1, R_2 = -(CH_2)-_3$, $R = H$	Clayfen	CH_2Cl_2	rt/4h	99	*157*
29	$R_1, R_2 = -(CH_2)-_3$, $R = H$	Claycop	CH_2Cl_2	rt/4h	91	*157*
30	$R_1, R_2 = -(CH_2)-_3$, $R = CH_3$	Clayfen	CH_2Cl_2	rt/4h	99	*157*
31	$R_1, R_2 = -(CH_2)-_3$, $R = CH_3$	Claycop	CH_2Cl_2	rt/4h	98	*157*
32	 $R_1, R_2 = -(CH_2)-_3$, $R= Ph$	$SbCl_5^-$	CH_2Cl_2	0ºC/10min	81	*145*
33	$R_1, R_2 = -(CH_2)-_3$, $R = H$	$SbCl_5$	CH_2Cl	0ºC/10min	63	*1559*
34	$R_1, R_2 = -(CH_2)-_3$, $R = CO_2Me$	$SbCl_5$	CH_2Cl_2	0ºC/10min	63	*145*
35	$R_1, R_2 = -(CH_2)-_2$, $R = H$	$Fe(NO_3)_3$	hexane	50ºC/10min	100	*155*
36	$R_1, R_2 = -(CH_2)-_3$, $R = H$	$Fe(NO_3)_3$	hexane	50ºC/10min	100	*155*
37	$R_1, R_2 = -(CH_2)-_3$, $R = p\text{-}MeC_6H_4$	$TCPPClO_4$	CH_2Cl_2	hn/120min	95	*161*
38	$R_1, R_2 = -(CH_2)-_3$, $R = CH_3$	$TCPPClO_4$	CH_2Cl_2	hn/100min	72	*161*
39	$R_1, R_2 = -(CH_2)-_3$, $R = CO_2Me$	$TCPPClO_4$	CH_2Cl_2	hn/240min	59	*161*
40	$R_1, R_2 = -(CH_2)-_3$, $R = H$	$TCPPClO_4$	CH_2Cl_2	hn/90min	68	*161*
41	$R_1, R_2 = -(CH_2)-_2$, $R = p\text{-}MeC_6H_4$	$TCPPClO_4$	CH_2Cl_2	hn/30min	90	*161*
42	$R_1, R_2 = -(CH_2)-_2$, $R = CH_{34}$	$TCPPClO_4$	CH_2Cl_2	hn/60min	50	*161*
43	$R_1, R_2 = -(CH_2)-_2$, $R = CH_{34}$	$TCPPClO_4$	CH_2Cl_2	hn/18min	39	*161*
44	$R_1, R_2 = -(CH_2)-_2$, $R = H$	$TCPPClO_4$	CH_2Cl_2	hn/18min	96	*161*
45	$R_1 = R_2 = Ph$, $R = H$	$TCPPClO_4$	CH_2Cl_2	hn/12min	83	*161*
46	$R_1, R_2 = -(CH_2)-_3$	$(CH_3)_3S_3^+SbCl_6^-$	CH_2Cl_2	-77ºC/5min	97	*142*
47	 $R_1, R_2 = -(CH_2)-_2$	SeO_2	AcOH	rt/50min	96	*148*
48	$R_1, R_2 = -(CH_2)-_3$	$AgNO_2/I_2$	THF	rt/20min	89	*149*
49	$R_1, R_2 = -(CH_2)-_2$	Amberlyst 15	Acetone/H_2O/CHO	80ºC/15h	80	*154*
50	$R_1, R_2 = -(CH_2)-_2$	$Fe(NO_3)_3$	hexane	50ºC/10min	95	*155*
51	$R_1, R_2 = -(CH_2)-_3$	$Fe(NO_3)_3$	hexane	50ºC/10min	96	*155*

Table 8. Continued...

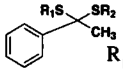
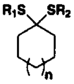
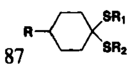
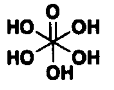
Entry	Cmpd	Reagent	Solvent	Temp./Time	Yield (%)	Ref
52	$R_1, R_2 = -(CH_2)-_3$	Clayfen	CH_2Cl_2	rt/5h	100	*157*
53	$R_1, R_2 = -(CH_2)-_3$	Claycop	CH_2Cl_2	rt/5h	100	*157*
54	$R_1, R_2 = -(CH_2)-_3$	$Fe(NO_3)_3$/silica	hexane	40-50°C/15min	99	*159*
55	$R_1 = R_2 = Et$	Clayan	CH_2Cl_2	40-50°C/20h	86	*160*
56	$R_1, R_2 = -(CH_2)-_2$	Clayfen	---	RT	95	*164*
						
57	$R_1, R_2 = -(CH_2)-_2$	SeO_2	AcOH	rt	91	*148*
58	$R_1, R_2 =- (CH_2)-_3$	H_5IO_6	Eherr/THF	rt/120min	99	*150*
59	$R_1, R_2 = -(CH_2)-_3$	Isoamyl nitrite	CH_2Cl_2	reflux/2.5h	5	*151*
60	$R_1 = R_2 = Et$	Isoamyl nitrite	CH_2Cl_2	rtC/0.5h	84	*151*
61	$R_1, R_2 = -(CH_2)-_3$	Nitrogen oxides	CH_2Cl_2	0-5°C/---	97	*153*
62	$R_1, R_2 = -(CH_2)-_2$	$Fe(NO_3)_3$	hexane	50°C/10min	94	*155*
63	$R_1, R_2 = -(CH_2)-_3$	$Fe(NO_3)_3$	hexane	50°C/10min	98	*155*
64	$R_1 = R_2 = Et$	Clayfen	CH_2Cl_2	rt/2.5h	99	*157*
65	$R_1, R_2 = -(CH_2)-_2$	Clayfen	CH_2Cl_2	rt/3h	100	*157*
66	$R_1, R_2 = -(CH_2)-_3$	Clayfen	CH_2Cl_2	rt/2.5h	98	*157*
67	$R_1 = R_2 = Et$	Claycop	CH_2Cl_2	rt/4h	99	*157*
68	$R_1, R_2 = -(CH_2)-_2$	Claycop	CH_2Cl_2	rt/6h	100	*157*
69	$R_1, R_2 = -(CH_2)-_3$	Claycop	CH_2Cl_2	rt/5h	97	*157*
70	$R_1, R_2 = -(CH_2)-_3$	$Fe(NO_3)_3$/silica	Hexane	40-50°C/10min	99	*155*
71	$R_1 = R_2 = Et$	Clayfen	---	RT	92	*164*
						
72	$R_1, R_2 = -(CH_2)-_2$	SeO_2	AcOH	rt/25min	98	*148*
73	$R_1, R_2 = - (CH_2)-_3$	Nitrogen oxides	CH_2Cl_2	0-5°C/---	40	*153*
74	$R_1, R_2 = -(CH_2)-_2$	$Fe(NO_3)_3$	hexane	50°C/30min	82	*155*
75	$R_1, R_2 = -(CH_2)-_3$	$Fe(NO_3)_3$	hexane	50°C/30min	84	*155*
76	$R_1, R_2 = -(CH_2)-_3$	$Fe(NO_3)_3$/silica	hexane	40-50°C/30min	97	*159*
77	$R_1, R_2 = -(CH_2)-_2$	Clayfen	---	RT	86	*164*
						
78	$R_1, R_2 = -(CH_2)-_3$, n = 7	mCPBA	CH_2Cl_2	0°C/1h	0	*143*
79	$R_1, R_2 = Et$, n = 7	mCPBA	CH_2Cl_2	0°C/1h	95	*143*
80	$R_1, R_2 = Ph$, n = 7	mCPBA	CH_2Cl_2	0°C/1h	98	*143*
81	$R_1, R_2 = -(CH_2)-_2$, n = 1	SeO_2	AcOH	rt/120min	92	*148*
82	$R_1, R_2 = -(CH_2)-_2$, n = 3	Amberlyst 15	Acetone/H_2O/CHO	80°C/10h	92	*148*
83	$R_1, R_2 = -(CH_2)-_3$, n = 7	Amberlyst 15	Acetone/H_2O/CHO	80°C/48h	73	*154*
84	$R_1, R_2 = -(CH_2)-_3$, n = 1	$Fe(NO_3)_3$/silica	Hexane	40-50°C/3min	98	*154*

Table 8. Continued...

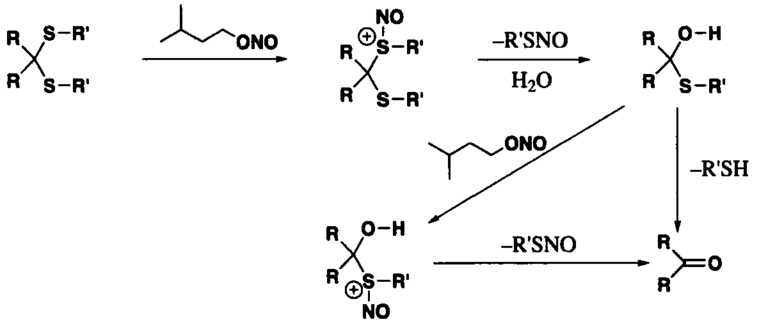
Entry	Cmpd	Reagent	Solvent	Temp./Time	Yield (%)	Ref
85	$R_1, R_2 = -(CH_2)-_3$, n = 7	$Fe(NO_3)_3$/silica	Hexane	40-50°C/10min	88	*159*
86	$R_1, R_2 = Et$, n = 1	Clayan	CH_2Cl_2	rt/16h	????	*160*
87	 $R_1, R_2 = Et$, R = *t*Bu	mCPBA	CH_2Cl_2	0°C/1h	96	*143*
88	R_1, R_2 = Pht, R = *t*Bu	mCPBA	CH_2Cl_2	0°C/1h	95	*143*
89	$R_1, R_2 = -(CH_2)-_3$, $R = -O(CH_2)_2O-$	H_5IO_6	Ether/THF	rt/20min	86	*150*
90	$R_1, R_2 = -(CH_2)-_3$, R=Ph	$TCPPClO_4$	CH_2Cl_2	hn/420min	63	*161*

Periodic acid **13** under non-aqueous conditions has been used for the deprotection of the dithio derivatives to the corresponding carbonyl compounds. This simple high-yield transformation is conveniently carried out in non-aqueous medium and works well with complex sensitive aldehydes and in the presence of other protective groups (*Table 8*, entries 22, 23, 58 and 89).[150]



13

However, chemical methods often require the use of reagents of elements such as Hg^{2+}, Ag^{+}, Se^{4+}, Tl^{3+}, Cd^{2+}, which are inherently toxic and/or expensive to use. In view of economical, practical and recent environmental demands, there is a significant advantage in using non-toxic and inexpensive metal salts. The use of nitrosonium and nitronium ion sources for regenerating carbonyl compounds from protected derivatives under various conditions has had some early successes. For example, an interesting method for dethioacetalization with isoamyl nitrite has been proposed.[151] The corresponding carbonyl compounds were obtained by stirring a mixture of thioacetal and isoamyl nitrite in dichloromethane at room temperature for a specified time (*Table 8*, entries 24, 59 and 60). The proposed mechanism is shown in *Scheme 17*.



Scheme 17

Thioacetals derived from aldehydes and ketones can be unmasked to the corresponding carbonyl compounds in high yield on exposure to a solution of oxides of nitrogen in dichloromethane. Nitrogen oxides were prepared according to literature procedure [152] by treating arsenious oxide with concentrated HNO_3 and the resulting gaseous mixture was bubbled through dichloromethane cooled in an ice-bath (0-5°C). The green solution obtained could be stored at 0-5°C for several months without loss of activity. The oxides of nitrogen are usually regarded as a mixture of N_2O_4, N_2O_3 and NO_2. The deprotection of thioacetals was carried out in stirring dichloromethane, at 0-5°C and was completed between 5-20 min (*Table 8*, entries 3, 25, 61 and 73).[153]

In continuation of the investigation on new cleaner chemical processes, carbonyl compounds were regenerated from corresponding 1,3-dithiolanes *via* equilibrium exchange with aqueous acetone, paraformaldehyde and Amberlyst 15, as an acidic catalyst, at 80°C (*Table 8*, entries 11, 49, 82 and 83).[154] As mentioned in the deoximation section, Amberlyst 15 is an excellent and far superior catalyst for regeneration of carbonyl compounds from nitrogenous derivatives when wet acetone is used as the exchange reagent. This has led to the development of a new method for the deprotection of dithioacetals. This procedure, which is a modification of the standard method for the hydrolyses of thioacetals, is carried out at 80°C by dissolving the appropriate dithioacetals in acetone/water/paraformaldehyde in the presence of catalytic amounts of Amberlyst 15 and stirring the reaction mixture at 80°C for 15-20 h. After a straightforward work-up, the corresponding pure carbonyl compounds are obtained in satisfactory to good yields.[154]

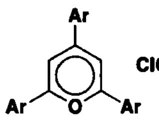
In order to simplify the method, to increase reagent utility and to avoid non-selective hydrolysis, a method based on dry conditions has been developed to convert S,S-acetals efficiently into the parent carbonyl compounds by simply adding an inorganic support material to a reaction mixture in an aprotic solvent. The efficiency of a heterogeneous system based upon iron(III) nitrate oxidation has been established in some investigations. In view of economical, practical and recent environmental demands, significant advantage was observed in using the non-toxic and inexpensive iron(III) nitrate as metal salt and Montmorillonite K10 as an inorganic support material.[155] For dethioacetalization of 1,3-dithiolanes, see *Table 8*, entries 5, 12, 18, 35, 50, 62 and 74 and for dethioacetalization of 1,3-dithianes see *Table 8*, entries 4, 13, 18, 36, 51, 63 and 75.

As mild and convenient sources of nitrosonium cations which are innocuous towards the carbonyl group (even of benzaldehyde), both clay-supported ferric nitrate ("Clayfen") and clay-supported cupric nitrate ("Claycop"), are reagents of choice for this hydrolysis. No external source of water is needed since it is provided by the internal structure of the clay. "Clayfen" and "Claycop" were prepared by mixing the K10 bentonite clay with iron (III) nitrate nonahydrate and copper (II) nitrate trihydrate respectively in acetone.[156] Stirring the thioacetals with clayfen or claycop in dichloromethane for a few hours, at room temperature, results in rapid evolution of nitrogen oxides. Stirring was maintained until full disappearance of the oxides (*Table 8*, entries 26-31, 52, 53 and 64-69).[157, 158]

1,3-Dithianes derived from aromatic, aliphatic and cyclic ketones or aldehydes can be conveniently converted to the parent carbonyl compounds with a combination of ferric nitrate and silica gel in hexane in excellent to quantitative yields. Simple efficient stirring of a mixture of ferric nitrate, silica gel, 1,3-dithianes in hexane as the solvent at 40-50°C for 3-30 minutes can readily carry out this deprotection reaction. The resulting carbonyl compounds are obtained by a simple work-up procedure (*Table 8*, entries 6, 14, 54, 70, 76, 84 and 85).[159]

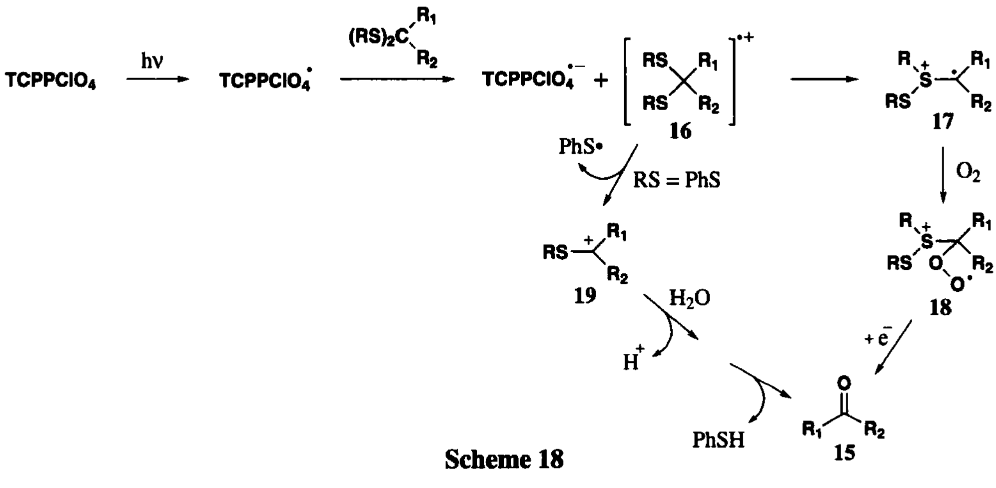
Clay supported ammonium nitrate ("clayan") is another clay supported reagent for dethioacetalization of thioacetals and dithianes. To a solution of thioacetal derivatives of carbonyl compounds in dry dichloromethane, clay supported ammonium nitrate ("clayan") was added and the mixture was stirred at room temperature under nitrogen atmosphere for the stipulated period (*Table 8*, entries 15, 55 and 86).[160]

Based on the results from the electrochemical studies and the photo-induced electron-transfer (PET) reactions of organosulfur compounds, it was expected that PET process could be useful for the deprotection of dithioacetals and ketals. This prediction proved to be correct by the studies reported on the photoreactions of various dithioacetals and ketals using *tris*(*p*-chlorophenyl)pyryliumperchlorate (TCPPClO$_4$) **14** as a sensitizer. Irradiation of dichloromethane solutions containing dithioacetals or ketals and pyrylium salt **14** at $\lambda > 360$nm afforded the corresponding carbonyl compound in good to excellent yields in the presence of molecular oxygen (*Table 8*, entries 37-45 and 90).[161]



Ar = p-ClC$_6$H$_4$
14

On the basis of the results obtained in this study, the reaction mechanism in *Scheme 18* was proposed. Single electron-transfers from the substrate to the excited state of TCPPClO$_4$ gives the cation radical intermediate **16**. The formed cation radical **16** undergoes carbon-sulfur bond cleavage in dual fashion depending on the structure of **16**. Usually, bond cleavage of **16** gaves a sulfonium and a carbon radical moieties as shown in **17**. The radical portion of **17** is captured by molecular oxygen to give the peroxy radical **18** which rearranges to the carbonyl compound **15** through another electron transfer step. In the case of diphenyldithioacetal, it is also probable that the cation radical **16** can release phenylthio radical (PhS•) to form the carbocation **19**. The formed cation **19** is attacked by water and finally converted to the carbonyl compound **15** (*Scheme 18*).



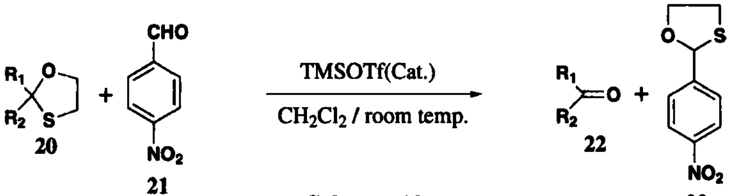
Scheme 18

The use of inexpensive supported reagents appears to be an attractive option because of selectivity and the ease of manipulation. In this context, clay supported reagents have found widespread utility in a variety of heterogeneous reactions. Recently, reactions under solvent-free conditions have received increasing attention.[162, 163] A facile conversion of thioacetal carbonyl compounds using ("Clayfen") in the solid state under microwave irradiation was reported (*Table 8*, entries 7, 8, 16, 56, 71 and 77). The reaction presumably proceeds *via* the nitrosonium ions and no-side products were formed during the deprotection reaction. This method is environmentally benign, with cleavage of the thioacetal to the carbonyl compounds in a short reaction time and in high yield without using toxic organic solvents.[164]

VI. DEPROTECTION OF 1,3-OXATHIOLANES

Among the various functional groups, the protection of the carbonyl group as an 1,3-oxathiolane is an important one due to the following applications; they are used as acyl carbanion equivalents[165] for the formation of carbon-carbon bonds. They also serve as valuable starting materials for the enantioselective synthesis of tertiary α-hydroxy aldehydes, α-hydroxy acids and glycols, first demonstrated by Eliel and his co-workers.[165] Later on, Utimoto and his group had also shown[166] the application of chiral 1,3-oxathiolane in organic synthesis. In addition, the use of *O,S*-acetals is more straightforward than the corresponding *O,O*-acetals or *S,S*-acetals. Although a large number of methods have been developed for the preparation of dithioacetals and their deprotection to carbonyl compounds,[1] only a few methods are known for oxathioacetals.[1] The existing methods for protection available are: either refluxing carbonyl compounds with 2-mercaptoethanol in benzene in the presence of catalytic amount of *p*-toluenesulfonic acid[167] or equimolar boron trifluoride etherate, [168] or $ZnCl_2$,[169] or a catalytic amount of $CF_3SO_3SiMe_3$ (TMSOTf).[170]All these methods have some drawbacks such as harsh reaction conditions,[167, 168] long reaction times,[169] expensive reagent (TMSOTf)[170] as well as difficulty in handling. Similarly, only a few methods are known for deprotection of 1,3-oxathiolanes into the corresponding carbonyl compounds.[149-151]

Isoamyl nitrite is one of the efficient reagents applied for the deprotection of 1,3-oxathiolanes in reasonable yields, by simply stirring a solution of 1,3-oxathiolanes in dichloromethane with isoamyl nitrite (*Table 9*, entries 12, 16, and 22).[151] Development of mild protocols for protection and deprotection of carbonyl compounds has been the focus of increased current interest. Recently, *p*-nitrobenzaldehyde/TMSOTf was introduced as a useful reagent for deprotection of 1,3-oxathiolanes. Thus when 1,3-oxathioacetals were treated with an equivalent amount of *p*-nitrobenzaldehyde in the presence of catalytic amounts of TMSOTf in dichloromethane at room temperature, the corresponding carbonyl compounds were obtained readily *via* transoxathioacetalization (*Scheme 19, Table 9*, entries 1, 6, 13, 17, 18 and 20).[171]



Scheme 19

Table 9. Deprotection of 1,3-Oxathiolanes

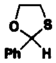
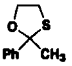
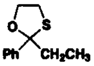
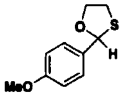
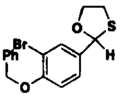
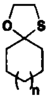
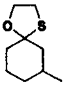
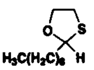
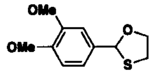
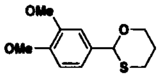
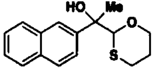
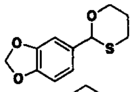
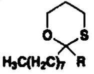
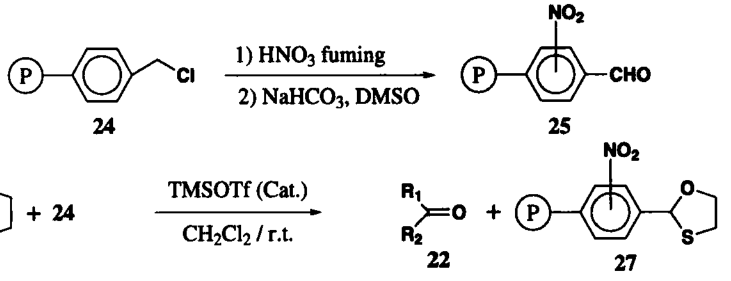
Entry	Cmpd	Reagent	Solvent	Temp./Time	Yield (%)	Ref
1		TMSOTf/4-nitrobenzaldehyde	CH_2Cl_2	rt/5min	94	*171*
2		TMSOTf	Not reported	rt/10min	82	*170*
3		$AgNO_2$	THF	rt/0.5h	96	*149*
4		$H_2MoO_4 \bullet H_2O$-H_2O_2	CH_2Cl_2/ H_2O	0-5°C/2.5h	80	*176*
5		TMSOTf	Not reported	rt/12h	50	*170*
6		TMSOTf/4-nitrobenzaldehyde	CH_2Cl_2	rt/5min	86	*171*
7		TMSOTf/PSB[a]	CH_2Cl_2	rt/3h	89	*174*
8		TMSOTf	Not reported	rt/10min	72	*170*
9		$H_2MoO_4 \bullet H_2O$-H_2O_2	CH_2Cl_2/ H_2O	0-5°C/2.25h	72	*176*
10		TMSOTf/PSB[a]	CH_2Cl_2	rt/2h	96	*174*
11		TMSOTf	Not reported	rt/15min	69	*170*
12		Isoamyl nitrite	CH_2Cl_2	rt/1.2h	93	*151*
13		TMSOTf/4-nitrobenzaldehyde	CH_2Cl_2	rt/5min	93	*171*
14		TMSOTf/PSB[a]	CH_2Cl_2	rt/3h	83	*174*
15		$H_2MoO_4.H_2O$-H_2O_2	CH_2Cl_2/ H_2O	0-5°C/2.5h	92	*176*
16		Isoamyl nitrite	CH_2Cl_2	rt/1.25h	70	*151*
17		n = 2 TMSOTf/4-nitrobenzaldehyde	CH_2Cl_2	rt/5min	78	*171*
18		n = 7 TMSOTf	CH_2Cl_2	rt/5min	90	*171*
19		n = 7 $H_2MoO_4 \bullet H_2O$-H_2O_2	CH_2Cl_2/ H_2O	0-5°C/4h	96	*176*
20		TMSOTf/4-nitrobenzaldehyde	CH_2Cl_2	rt/5min	83	*171*
21		TMSOTf/PSB[a]	CH_2Cl_2	rt/3h	96	*174*

Table 9. Continued...

Entry	Cmpd	Reagent	Solvent	Temp./Time	Yield (%)	Ref
22		Isoamyl nitrite	CH_2Cl_2	rt/1.5h	64	*151*
23		H_2MoO_4•H_2O-H_2O_2	CH_2Cl_2/ H_2O	0-5°C/1.5h	90	*175*
24		$AgNO_3$	THF	rt/5h	83	*149*
25		$AgNO_3$	THF	rt/5h	94	*149*
26		$AgNO_3$	THF	rt/1h	61	*149*
27		H_5IO_6	Ether/THF	rt/10	98	*150*
28		R=H H_5IO_6	Ether/THF	rt/10min	90	*150*
29		R=Me H_5IO_6	Ether/THF	rt/10min	95	*150*

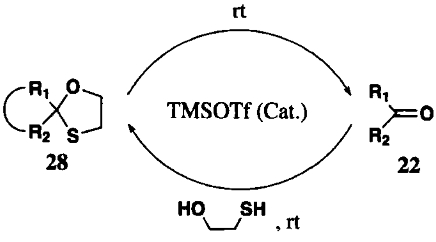
a) Polymer-supported benzaldehyde (PSB)

Based on successful use of *p*-nitrobenzaldehyde as efficient acceptor in deprotection of oxathioacetals, it seems that if nitrobenzaldehyde were to be supported on a polymer, the polymer-supported nitrobenzaldehyde by-product would be insoluble, thus facilitating straightforward work-up and recovery of the carbonyl compounds. Thus polymer-supported nitrobenzaldehyde **25** was prepared from 20% chloromethylated polystyrene (4% cross-linked) by nitration,[172] followed by oxidation (*Scheme 20*).[173] When oxathioacetals were treated with the functionalized polymer **25** in the presence of TMSOTf as the catalyst in dichloromethane at room temperature, the corresponding carbonyl compounds were obtained cleanly in excellent yields (*Table 9*, entries 7, 10, 14 and 21).[174]



Scheme 20

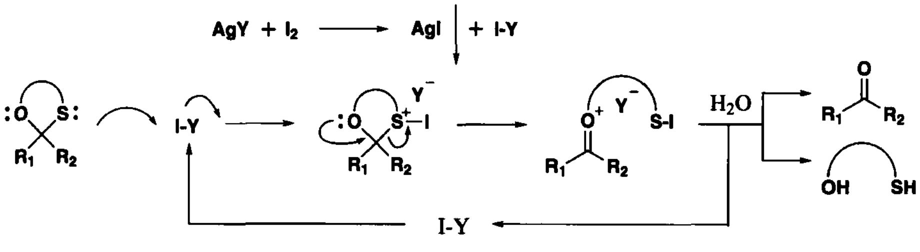
TMSOTf alone has been also employed as a mild, efficient and versatile catalyst to effect the facile conversion of carbonyl compounds to oxathiolanes and vice-versa under essentially identical conditions (*Scheme 21*). Oxathiolanes were prepared by stirring the mixture of



Scheme 21

carbonyl compounds and mercaptoethanol in the presence of TMSOTf (cat.), at room temperature. Interestingly, it was observed that activated oxathiolanes (R_1 or R_2 = aryl group), when subjected to the treatment of the same catalyst (TMSOTf), could be converted to carbonyl compounds in high yields. It is obvious that the presence of an aryl ring seems to be an essential factor for successful transformation of oxathiolanes to carbonyl compounds (*Table 9*, entries 2, 5, 8 and 11).[170] Surprisingly, some of these methods have serious drawbacks such as difficulties in removing the by-product of 1,3-oxathiolanes derived from 4-nitrobenzaldehyde[171] which requires expensive polymer supported reagents[174] and sometimes they fail to deprotect the oxathioacetals of non-aromatic compounds, in addition to requiring long reaction times.[170]

Some other methods are also well known based on halonium ion sources such as I_2-silver salts. Silver perchlorate, silver nitrite, silver nitrate, silver acetate or silver carbonate-iodine system are effective for demonothioacetalization. Among these reagents, a silver nitrite-iodine system was commendable from the points of efficiency and safety (*Table 9*, entries 3 and 24-26). The combination of a silver salt and iodine was essential. This fact suggests that the active species of this reagent system would be I^+. A possible mechanism for this reaction is illustrated in *Scheme 22*. An application of this deprotective reagent system was demonstrated in the synthesis of optically active α-hydroxy aldehydes using chiral 1,3-oxathianes.[149]



Scheme 22

Unfortunately, these methods also suffer because of a large molar excess of expensive reagents such as the silver salts. Therefore there is still a need to develop alternative methods for the protection as well as deprotection of carbonyl compounds. Periodic acid in non-aqueous solution is an efficient method to convert oxathioacetals to the corresponding carbonyl compounds under mild conditions (*Table 9*, entries 27-29). A notable advantage of this method is its simplicity and ease of work-up of the reaction. An additional benefit is that after the reaction is complete, there is no smell of thiol, which makes this method very attractive, particularly for large-scale preparations.[150]

The ability of diperoxomolybdate(VI) to oxidize bromide ion,[175] led to the idea that a $H_2MoO_4.H_2O$-H_2O_2 catalyzed oxidation of ammonium bromide could be utilized for cleavage of 1,3-oxathiolanes. A wide variety of carbonyl compounds can be easily protected to the corresponding 1,3-oxathiolanes in good yields, in the presence of catalytic amounts of perchloric acid in dry CH_2Cl_2 at 0-5°C. On the other hand, various 1,3-oxathiolanes can be selectively deprotected to the parent carbonyl compounds in very good yields by H_2MoO_4 H_2O-H_2O_2 catalyzed oxidation of ammonium bromide in the presence of perchloric acid in CH_2Cl_2/H_2O solvent system (*Table 9*, entries 4, 9, 15, 19 and 23). Mild conditions, high selectivity, efficiency and relatively good yields are some of the major advantages of the procedure. In addition, these chemicals are environmentally acceptable.[176]

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