Oxidative deprotection of tetrahydropyranyl and trimethylsilyl ethers in water using 1,4-dichloro-1,4-diazoniabicyclo[2,2,2]octane bis-chloride under neutral conditions

Mahmood Tajbakhsh* and Setareh Habibzadeh

Department of Chemistry, Mazandaran University, Babolsar, Iran

The oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers in water using 1,4-dichloro-1,4-diazoniabicyclo[2,2,2]octane bis-chloride as a new efficient reagent under neutral conditions is described. The DABCO was regenerated, rechlorinated and reused several times.

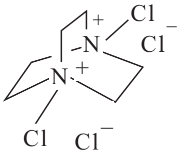
Keywords: tetrahydropyranyl ethers, trimethylsilyl ethers, 1,4-dichloro-1,4-diazoniabicyclo[2,2,2]octane bis-chloride, oxidation, deprotection.

Silyl and THP (tetrahydropyranyl) ethers are used as protecting groups for alcohols in synthetic chemistry because of their low cost, efficiency of preparation, stability under the intended reaction conditions and ease of removal.[1] A variety of methods for the selective removal of these groups have been developed,[2] but the direct synthesis of carbonyl compounds from tetrahydropyranyl or silyl ethers in water is not often described in the literature.[3] Such methods have limitations such as tedious work-up, long reaction times, low yields, high temperatures and also require the use of organic solvents, Lewis acid catalysts and expensive reagents. Thus, the introduction of new methods using inexpensive reagents and environmentally-friendly reaction conditions with water as solvent[4] for such functional group transformations is still required. In continuation of our investigations on oxidation reactions,[5] we explored the oxidation of THP and silyl ethers in water using 1,4-dichloro-1,4-diazoniabicyclo[2,2,2]octane bis-chloride. The analogous DABCO–bromine complex was previously prepared and employed as an oxidant for organic substrate, without regeneration of DABCO.[6,7]

Results and discussion

1,4-Dichloro-1,4-diazoniabicyclo[2,2,2]octane bis-chloride is easily and quantitatively prepared when a solution of DABCO in $CHCl_3$ was treated with a stream of chlorine gas at room temperature.[8] Similar behaviour was observed for 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2,2,2]octane bis-tetrafluoroborate (selectfluor),[9] and therefore we have proposed structure **1** for this reagent.

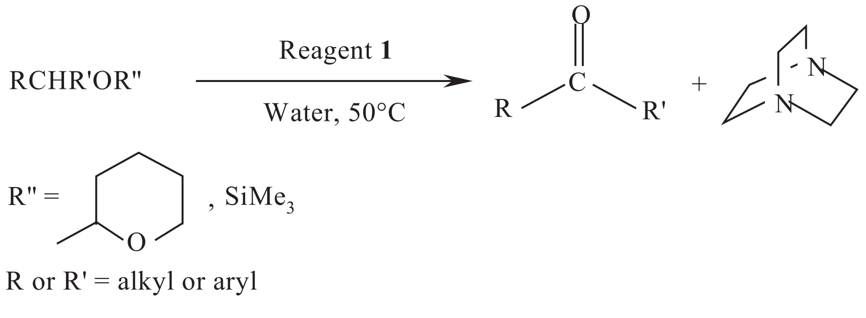
The high solubility of this reagent in water (pH = 7) makes it an efficient oxidant for organic substrates. It is inexpensive and DABCO is recovered, rechlorinated and reused several times in the oxidation reactions. Similar reactions with DABCO–bromine complex under heterogeneous conditions were carried out in 80°C without regeneration of DABCO.



1

To gain some preliminary information on this synthetically useful reaction, THP and silyl ethers of benzyl alcohol were chosen as model substrates. The optimum reaction conditions for oxidative deprotection of THP and silyl ethers to their carbonyl compounds involves a 1 : 0.6 molar ratio of substrate to reagent at 50°C in water (Scheme 1).

The results are shown in the Table 1. Aliphatic THP ethers (Table 1, entries 1 and 5), aromatic THP ethers (Table 1, entries 2–4 and 6–9) and α,β-unsaturated THP ether (Table 1, entry 10) were efficiently cleaved to the corresponding carbonyl compounds in good yields. The yield was reduced when a NO_2 group was present on the aromatic ring (Table 1, entry 9). Longer reaction times had no effect on the yield. A THP ether containing a double bond (Table 1, entry 10) was also oxidised with no chlorination of the double bond. Similarly, aliphatic and aromatic silyl ethers (Table 1, entries 11–19) were also cleaved to the corresponding carbonyl compounds. No overoxidation products were detected in the case of aldehydes. Note that both THP and silyl ethers were not just hydrolysed by the reaction but only carbonyl compounds were obtained. An interesting feature of this method was the recovery of 1,4-diazabicyclo[2,2,2]octane in nearly quantitative amount which can easily be chlorinated and reused several times. In order to investigate the applicability of this procedure, we have also carried out the oxidation THP and silyl ether of benzyl alcohol under our optimum reaction conditions on a larger scale (60 mmol) and obtained the same yields as in small-scale reaction.



Scheme 1

---

* Correspondent. E-mail: tajbaksh@umz.ac.ir

Table 1 Oxidative deprotection of tetrahydropyranyl and silyl ethers with 1,4-dichloro-1,4-diazoniabicyclo[2,2,2]octane bis-chloride in water

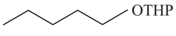
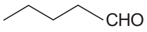
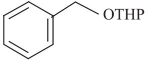
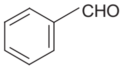
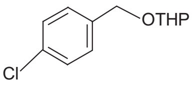
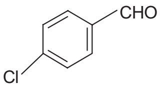
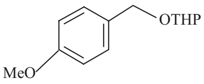
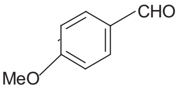
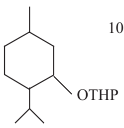
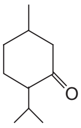
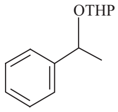
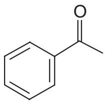
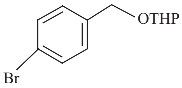
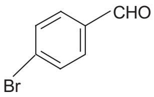
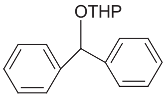
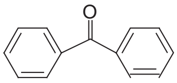
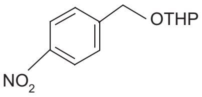
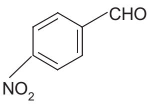
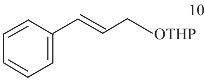
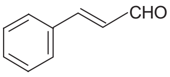
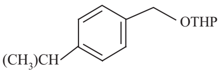
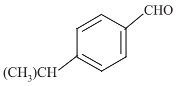
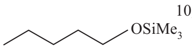
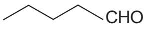
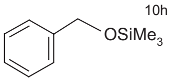
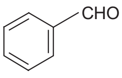
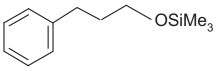
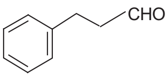
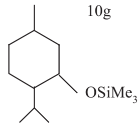
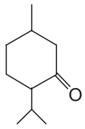
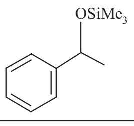
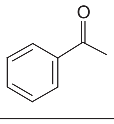
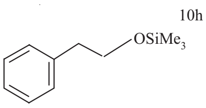
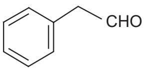
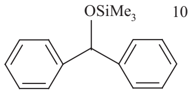
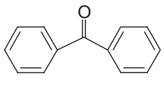
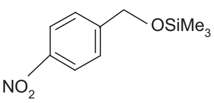
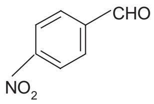
Entry	Substrate[a]	Product[b]	Time/min	Yield/%[c]	M.p./°C or bp/°C/Torr	
					Found	Reported[11]
1	 [10a]		20	90	99–101/760	100–103/760
2	 [10a]		25	92	175–176/760	178–179/760
3			25	90	44	45–47
4	 [10b]		30	93	121–122/12	118–121/12
5	 [10c]		30	89	85–87/12	85–88/12
6	 [10d]		35	87	199–201/760	202/760
7	 [10e]		35	88	54	55–57
8			35	84	49–51	49–50
9	 [10f]		40	74	103–105	104–106
10	 [10d]		30	91	246	248
11			15	88	230–231/760	232–235/760
12	 [10g]		20	95	99–100/760	100–103/760
13	 [10h]		30	95	174–176/760	178–179/760
14			25	89	101–103/13	104–105/13
15	 [10g]		35	86	85–86/12	85–88/12
16	 [10g]		35	90	200–202	201–202

Table 1 *Continued*

Entry	Substrate[a]	Product[b]	Time/min	Yield/%[c]	M.p./°C or bp/°C/Torr	
					Found	Reported[11]
17			40	87	56	55–57
18			40	85	49–51	49–50
19			55	77	103–105	104–106

[a]The tetrahydropyranyl and trimethyl silyl ethers prepared are known compounds and were characterised by comparison of their physical and spectral data with those reported in the literature.

[b]All products showing physical and spectral data in accordance with expected structures.

[c]The yields refer to isolated products.

In conclusion, we report here an efficient and simple method for oxidation of THP and silyl ethers under aqueous and neutral conditions. The positive features of the present method are: (1) ease of operation; (2) facile recycling of the DABCO; (3) excellent yields; (4) environmental consciousness: no organic solvent is used in the reaction and only a small amount is needed for the workup.

Experimental

All the starting materials were purchased from Fluka and Merck. All trimethylsilyl and tetrahydropyranyl ethers were known compounds and were prepared according to described procedures.[12] The oxidation products were known compounds and they were identified by comparison of their physical data, IR and NMR spectra with those of authentic samples. Yields refer to isolated products or to their 2,4-dinitrophenyl hydrazones. Melting points were determined using a Mettler FP 5 apparatus and were uncorrected. ^{1}H NMR spectra were measured at 300 MHz on a JEOL spectrometer with tetramethylsilane (Me_4Si) as an internal reference and $CDCl_3$ as the solvent for aldehydes and ketones. IR spectra were recorded on Pye-Unicam SP 1100 spectrophotometer. Elemental analysis was performed on a LECO 250 instrument.

Preparation of 1,4-dichloro-1,4-diazoniabicyclo[2,2,2]octane bis-chloride

Chlorine gas was bubbled for 10 minutes through a solution of 1,4-diazabicyclo[2,2,2]octane (DABCO) (6.72 g, 60 mmol) in chloroform (100 cm^3). The solvent was evaporated under reduced pressured to afford the product (14.94 g, 98%), m.p. decomp. 125–130°C. Anal. Calcd for $C_6H_{12}N_2Cl_4$: C, 28.3; H, 4.7; N, 11.0; Cl, 55.9. Found: C, 27.9; H, 4.6; N, 11.2; Cl, 55.6. ^{1}H NMR (D_2O) δ 3.2 (s, 12H, 6CH$_2$). ^{13}C NMR (D_2O) δ 91.3. IR 2800, 1500, 1380, 1000 and 750 cm^{-1}.

General procedure for oxidative cleavage of THP and silyl ethers

The substrate (THP ether or silyl ether, 5 mmol) and 1,4-dichloro-1,4-diazoniabicyclo[2,2,2]octane bis-chloride (0.76 g, 3 mmol) was added to H_2O (15 cm^3) in a flask. The reaction mixture (pH = 7) was warmed to 50°C and stirred. After completion of the reaction (TLC), Et_2O (10 cm^3) was added to reaction mixture and was washed with solution of 1% aq. HCl (1 × 10 cm^3). The aqueous layer **1** was separated and the organic layer was washed with 3% aq. $NaHCO_3$ (1 × 10 cm^3) and water (1 × 10 cm^3) respectively. The organic layer was dried over $MgSO_4$, filtered and evaporated to dryness under reduced pressure to afford the corresponding carbonyl compound.

Regeneration of 1,4-diazabicyclo[2,2,2]octane

The aqueous layer **1** from the above procedure was further treated with 10% sodium bicarbonate solution (2 × 10 cm^3) and 1,4-diazabicyclo[2,2,2]octane (DABCO) was extracted with ether (3 × 10 cm^3). The ether layer was dried over $MgSO_4$, and evaporated to give pure 1,4-diazabicyclo[2,2,2]octane (0.31 g, 95%), which can be chlorinated and reused several times.

THP ether of 4-chlorobenzyl alcohol (entry 3): Colourless viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.54–1.89 (m, 6 H, CH$_2$), 3.52 (d, J = 11.2 Hz, 1 H, OCH$_2$), 3.87 (t, J = 8.4 Hz, 1 H, OCH$_2$), 4.44 (d, J = 12.0 Hz, 1 H, ArCH), 4.67 (br s, 1 H, OCHO), 4.72 (d, J = 12.4 Hz, 1 H, ArCH), 7.29 (br s, 4 H, ArH) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 19.4, 25.5, 30.6, 62.1, 68.0, 97.7, 128.3 (2 C), 128.9 (2 C), 133.0, 136.65 ppm; IR (neat): ν = 2943, 2867, 1592, 1464, 1358, 1132, 1075, 1038 cm^{-1}.

4-Chlorobenzaldehyde (entry 3): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.7 (s, 1 H, CHO), 7.3–7.6 (m, 4H, ArH) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 129.4 (2 C), 129.9 (2 C), 135.89, 140.1, 192.0 ppm.

THP ether of benzhydrol (entry 8): White solid; m.p. 50–51°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.52–1.97 (m, 6 H, CH$_2$), 3.47–3.52 (m, 1 H, OCH$_2$), 3.85–3.91 (m, 1 H, OCH$_2$), 4.66 (t, J = 3.2 Hz,1 H, OCHO), 5.79 [s, 1 H, (Ar) 2C*H*], 7.17–7.36 (m, 10 H, ArH) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 19.3, 25.65, 30.7, 62.0, 78.1, 95.4, 126.7 (2 C), 126.9 (2 C), 127.4 (2 C), 127.5 (2 C), 128.0 (2 C), 128.3 (2 C) ppm; IR (KBr): ν = 2942, 2903, 2877, 1490, 1199, 1121, 1025, 977, 916 cm^{-1}.

Benzophenone (entry 8): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.2–7.7 (m, 10 H, ArH) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 129.1 (4 C), 130.5 (4 C), 131.5 (2 C), 138.1(2 C), 196.81 ppm.

TMs ether of 3-phenylpropanol (entry 14): Colourless liquid, ^{1}H NMR ($CDCl_3$): δ = 7.22–7.18 (5H, m), 3.60 (2H, t, J = 6.5 Hz), 2.68 (2H, t, J = 8 Hz), 1.85(2H, m), 0.11 (9H, s) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 33.1, 34.2, 62.5, 127.6, 129.1 (2 C), 129.2 (2 C), 142.5 ppm; IR (KBr): ν = 1251, 1100, 841 cm^{-1}.

3-phenylpropanal (entry 14): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.61 (d, J = 1.79, 1 H, CHO), 7.3 (m, 5 H, ArH), 2.9 (t, J = 7.08 Hz, 2 H, CH$_2$), 2.5 (m, J = 7.08, 1.79 Hz, 2 H, CH$_2$) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 45.6, 127.1, 129.1 (2 C), 129.3 (2 C), 141.0, 201.4 ppm.

TMS ether of 4-nitrobenzyl alcohol (entry 19): Colourless liquid, ^{1}H NMR ($CDCl_3$): d 7.31–7.19 (4H, m), 4.72 (2H, s), 0.10 (9H, s) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 66.1, 120.4 (2 C), 128.1 (2 C), 144.2, 171.2 ppm; IR (KBr): ν = 1253, 1095,844 cm^{-1}.

4-nitrobenzaldehyde (entry 19): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.1 (s, 1 H, CHO), 7.2–7.9 (m, 4 H, ArH) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 131.4 (2 C), 133.2 (2 C), 139.7, 146.8, 192.5 ppm.

Received 16 April 2007; accepted 23 April 2007
Paper 07/4596 doi: 10.3184/030823407X209723

References

1 (a) T.W. Green and P.G.M. Wuts, *Protective Groups in Organic Synthesis,* 3rd edn; John Wiley and Sons: New York, 1999, p. 49; (b) P.J. Kocienski, In *Protective Groups;* D. Enders, R. Noyori and B.M. Trost, eds., Georg Thieme: Stuttgart, 1994, pp. 83; (c) P.J. Kocienski, *Protecting Groups,* Thieme: Stuttgart, 1994, pp. 28; (d) A.J. Pearson and W.R. Roush, in *Handbook of Reagents for Organic Synthesis: Activating Agents and Protecting Groups,* Wiley: New York, 1999, p. 84.

2 (a) N.S. Krishnaveni, K. Surendra, M.A. Reddy, Y.V.D. Nageswar and K.R. Rao, *J. Org. Chem.,* 2003, **68,** 2018; (b) M.A. Reddy, K. Surendra, N. Bhanumathi and K.R. Rao, *Tetrahedron,* 2003, **58,** 6003; (c) M.A. Reddy,

N. Bhanumathi and K.R. Rao, *Tetrahedron,* 2002, **43,** 3237; (d) M.A. Reddy, N. Bhanumathi and K.R. Rao, *Synlett,* 2000, 339; (e) A. Hajipour, S. Malakpour, I. Mohammadpoor-Baltork and M. Malakoutihah, *Tetrahedron,* 2002, **58,** 143; (f) A. Khan, S. Islam, L.H. Choudhury and S. Ghosh, *Tetrahedron Lett.,* 2004, **45,** 9617.

3 (a) P.E. Sonnet, *Org. Prep. Proc. Int.,* 1978, **10,** 91; (b) E.J.S. Parish, A. Kizito and R.W. Heidepriem, *Synth. Commun.,* 1993, **23,** 223; (c) I. Mohammadpoor-Baltork, P. Shirvani, *Synthesis,* 1997, 756; (d) I. Mohammadpoor-Baltork, B. Kharamsh, *J. Chem. Res. (S),* 1998, 146; (e) M. Lalonde, T.H. Chan, *Synthesis,* 1985, 817 and references cited therein.

4 (a) M. Narender, M.S. Reddy, P. Kumar, Y.V.D. Nageswar and K.R. Rao, *Tetrahedron Lett.,* 2005, **46,** 1971; (b) H. Tohama, T. Maegawa, S. Takizawa and Y. Kita, *Adv. Synth. Catal.,* 2002, **344,** 328.

5 (a) M.M. Heravi, M. Tajbakhsh and M. Ghassemzadeh, *Z. Naturforsch,* 1999, **54B,** 396; (b) M. Tajbakhsh, M.M. Heravi, S. Habibzadeh and M. Ghassemzadeh, *J. Chem. Res. (S),* 2001, 39; (c) M. Tajbakhsh, M.M. Heravi and S. Habibzadeh, *Phosphorus, Sulfur,* 2001, **176,** 191; (d) M. Tajbakhsh, I. Moammadpoor-Baltork and F. Ramzanian, *J. Chem. Res. (S),* 2001, 182; (e) M. Tajbakhsh, M.M. Heravi, S. Habibzadeh and M. Ghassemzadeh, *Phosphorus, Sulfur,* 2001, **176,** 151; (f) M.M. Lakouraj, M. Tajbakhsh, V. Khojasteh and M.H. Golabi, *Phosphorus, Sulfur,* 2004, **179,** 2645.

6 (a) L.K. Blair, J. Baldwin and W.C. Smith, *J. Org. Chem.,* 1977, **42,** 1816; (b) M.M. Heravi, F. Derikvand, M. Ghassemzadeh and B. Neumüller, *Tetrahedron Lett.,* 2005, **46,** 6243.

7 M. Tajbakhsh, M.M. Heravi and S. Habibzadeh, *Synth. Commun.,* in press.

8 M. Tajbakhsh and S. Habibzadeh, *J. Chem. Res. (S),* 2006, 539.

9 (a) R.E. Banks, M.K. Besheesh, S.N. Mohialdin and I. Sharif, *J. Chem. Soc., Perkin Trans. 1,* 1996, 2069; (b) J. Liu and C. Wong, *Tetrahedron Lett.,* 2002, **43,** 4037.

10 (a) M.M. Heravi, F.K. Behbahani, H.A. Oskooie, and R. Hekmat Shoar, *Tetrahedron Lett.,* 2005, **46,** 2543; (b) A.T. Khan, E. Mondal, B.M. Borah and S. Ghosh, *Eur. J. Org. Chem.* 2003, 4113; (c) Y.S. Hon, C.F. Lee, R.J. Chen and P.H. Szu, *Tetrahedron,* 2001, **57,** 5991; (d) Y.J. Kim and R.S. Varma, *Tetrahedron Lett.,* 2005, **46,** 1467; (e) B. Karimi and M. Khalkhali, *J. Molecular Catalysis A: Chemical,* 2005, **232,** 113; (f) A.T. Khan, S. Ghosh and H.L. Choudhury, *Eur. J. Org. Chem.,* 2005, 4891; (g) M.M. Mojtahedi, H. Abbasi and M.S. Abaee, *J. Molecular Catalysis A: Chemical,* 2006, **250,** 6; (h) J.S. Yadav, B.V.S. Reddy, A.K. Basak, G. Baishya and A.V. Narsaiah, *Synthesis,* 2006, 3831.

11 *Aldrich Catalogue/Handbook of Fine Chemicals*, 1992–1993.

12 (a) G. Maity and S.C. Roy, *Synth. Commun.,* 1993, **23,** 1667; (b) G. Neille, *J. Org. Chem.*, 1960, **25,** 1063.