

Bis(chlorine)-1,4-diazabicyclo[2.2.2]octane: a novel and reusable oxidising agent for conversion of alcohols into their carbonyl compounds under microwave irradiation

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Bis(chlorine)-1,4-diazabicyclo[2.2.2]octane was easily prepared by treatment of chlorine gas with 1,4-diazabicyclo[2.2.2]octane at room temperature. It is stable and can be used as an efficient oxidant for aliphatic and aromatic alcohols under microwave irradiation. In the oxidation reactions it is almost quantitatively converted into 1,4-diazabicyclo[2.2.2]octane which can be chlorinated and reused several times.

Keywords: oxidation; alcohols, bis(chlorine)-1,4-diazabicyclo[2.2.2]octane, carbonyl compounds, microwave

The oxidation of alcohols plays an important role in organic synthesis while the development of new oxidative processes continues to draw attention in spite of the availability of numerous oxidising reagents.¹ Many of these oxidising reagents used in stoichiometric amounts are often hazardous or toxic. Hence, in terms of economical and environmental concern, catalytic oxidation processes with inexpensive and environmentally benign oxidants are extremely valuable. Also forming aldehydes and ketones is a chemical transformation of primary industrial importance in the fine chemical industry as carbonyl compounds are precursors of a variety of valuable fine chemicals including fragrances, vitamins and drugs.² Reagents of choice for oxidation of alcohols to carbonyl compounds are pyridinium chlorochromate (PCC),³ Swern⁴ and Dess–Martin reagents,⁵ PCC catalysed oxidation with periodic acid,⁶ silica gel supported InBr_3 and InCl_3 ,⁷ H_2O_2 ,⁸ $\text{KBrO}_3/\text{ZrClO}_2$,⁹ ruthenium catalyst,¹⁰ *etc.*¹¹ In recent developments, the use of microwave irradiation has become a very popular tool to simplify and improve organic reactions, because the desired product is often obtained in high yield and in shorter reaction times. Furthermore, the reactions might be performed under solvent-free conditions and therefore be considered green chemistry.^{12,13}

Results and discussion

In our ongoing programme to find new oxidants for organic materials,^{14,15} we now report the preparation of bis(chlorine)-1,4-diazabicyclo[2.2.2]octane as a new efficient and reusable reagent for the oxidation of alcohols under microwave irradiation and under solvent-free conditions. This complex is easily prepared by treatment of 1,4-diazabicyclo[2.2.2]octane in CHCl_3 with chlorine gas at room temperature. The structure of this complex was determined by CHN analysis and a titration method.¹⁶ The Cl^+ content was measured by the titration method and the amount of Cl^+ and Cl^- together by the combustion analysis. The bis(chlorine)-1,4-diazabicyclo[2.2.2]octane is a homogenous solid, which can be kept for months in a vessel without losing its activity. It does not release chlorine during storage, as its analysis after two months showed no loss of chlorine. It had no offensive odour of chlorine or amine.

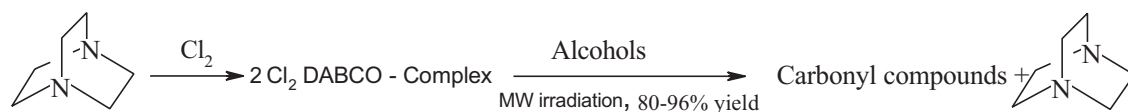
To gain some preliminary information on this synthetically useful reaction, benzyl alcohol was chosen as model substrate. We have studied the influence of mole ratio of oxidant to substrate and the reaction gave high yields with a molar ratio of 1:1 substrate: reagent under microwave irradiation (Scheme 1). In order to establish the generality of this method we have oxidised different alcohols with bis(chlorine)-1,4-diazabicyclo[2.2.2]octane without solvent, and the results are shown in Table 1.

As indicated in Table 1, primary aromatic (entries 1–6 and 13–15), primary aliphatic (entry 8), secondary aliphatic (entries 7 and 16) and allyl alcohols (entries 9 and 10) were successfully oxidised with this complex in high yield. The reaction works well with sterically hindered alcohols such as menthol (entry 11) or 2-adamantanol (entry 12). The 2-adamantanol required longer reaction times for the same amount of conversion than did other cyclic alcohols. In no reactions did we observe any over-oxidation products. Another 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 in industry, we have carried out the oxidation of benzyl alcohol under our optimum reaction conditions on large scale (30 mmol) and obtained almost the same yields as in the small-scale reaction.

Experimental

All the alcohols were purchased from Fluka and Merk companies. The reaction was monitored by TLC using silica gel plates and the products were identified by comparison of their spectra and physical data with those of the authentic samples. ^1H 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. IR spectra were recorded on Pye-unicam SP 1100 spectrophotometer. Elemental analysis was performed on a LECO 250 instrument. The microwave oven was a domestic National.

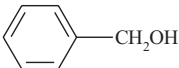
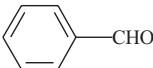
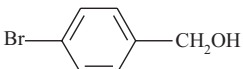
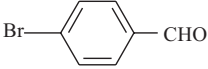
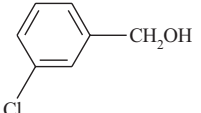
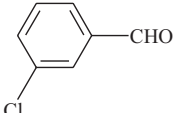
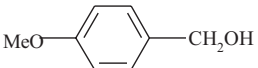
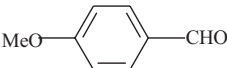
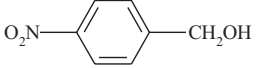

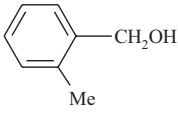
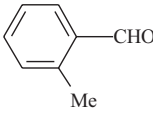
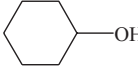
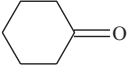
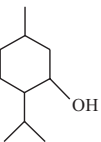
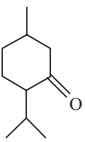
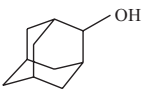
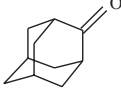
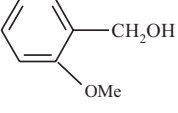
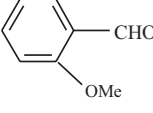
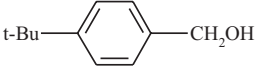

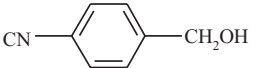
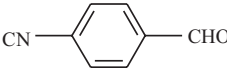
Preparation of bis(chlorine)-1,4-diazabicyclo[2.2.2]octane: Chlorine gas was bubbled for 1 h at room temperature through a solution of 1,4-diazabicyclo[2.2.2]octane (6.72 g, 60 mmol) in chloroform (100 ml). The solvent was evaporated under reduced pressure to afford almost pure product (98%), m.p.: decomp. 125–130°C. Anal. Calcd for $\text{C}_6\text{H}_{12}\text{N}_2\text{Cl}_4$: 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. ^1H NMR (D_2O) δ 3.2 (s, 12H, 6 CH_2). ^{13}C NMR (D_2O) δ 91.3. IR 2800, 1500, 1380, 1000 and 750 cm^{-1} .



Scheme 1

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Table 1 Oxidation of alcohols to aldehydes and ketones with the bis(chlorine)-1,4-diazabicyclo[2.2.2]octane

Entry	Substrate	Reaction time/min	Product ^a	Yield/% ^b	Ref.
1		2		95	17a
2		4		93	17b
3		4		95	17c
4		3		87	17d
5		6		90	17e
6		3		96	17f
7		2		80	17g
8	$\text{CH}_3(\text{CH}_2)_4\text{CH}_2\text{OH}$	2	$\text{CH}_3(\text{CH}_2)_4\text{CHO}$	90	17h
9	$\text{H}_2\text{C}=\text{CHCH}_2\text{OH}$	3	$\text{H}_2\text{C}=\text{CHCHO}$	92	17i
10	$\text{PhCH}=\text{CHCH}_2\text{OH}$	4	$\text{PhCH}=\text{CHCHO}$	88	17j
11		5		85	18k
12		4		86	18l
13		3		90	17m
14		4		88	17n
15		6		80	17o
16	$\text{CH}_3\text{CHOCCH}_2\text{CH}_3$	3	$\text{CH}_3\text{COCH}_2\text{CH}_3$	87	17p

^aAll products were characterised spectroscopically (¹H NMR, IR) and showed physical and spectroscopic data in accordance with their expected structure and by comparison with authentic sample.

^bThe yields refer to isolated products.

General procedure for oxidation of alcohols

An appropriate alcohol (5 mmol) was mixed with bis(chlorine)-1,4-diazabicyclo[2.2.2]octane (5.2 mmol) in a watch glass. The mixture was transferred into a small beaker and placed in a microwave oven (600 W, 180°C) for the indicated time. After completion of the reaction (TLC), ether was added to the reaction mixture and the resulting mixture was washed with solution of 1% HCl. The aqueous layer (**1**) was separated and the organic layer was washed with 3% sodium bicarbonate solution and water respectively. The organic phase was dried over MgSO₄, filtered and evaporated to dryness under reduced pressure to afford the corresponding carbonyl compound in a pure form.

Regeneration of 1,4-diazabicyclo[2.2.2] octane

The aqueous layer (**1**) from above procedure was further treated with 10% sodium bicarbonate solution and 1,4-diazabicyclo[2.2.2]octane was extracted with ether (3 × 10). The ether layer was dried over MgSO₄, and evaporated to give pure 1,4-diazabicyclo[2.2.2]octane (95%) which can be chlorinated and reused several times.

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