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N,N'-Dichlorobis(2,4,6-trichlorophenyl)urea (CC-2): an efficient reagent for conversion of oximes to ketones

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A method for the rapid conversion of oximes into the corresponding carbonyl compounds using *N,N'*-dichlorobis (2,4,6-trichlorophenyl)urea (CC-2) at room temperature is described. The method is economical as the solid by-product bis(2,4,6-trichlorophenyl)urea could be removed by filtration and recycled after re-chlorination.

Keywords: deoximation, oximes, carbonyls, CC-2, *N,N'*-Dichloro bis(2,4,6-trichlorophenyl) urea

The protection–deprotection of functional groups is a common sequence in organic synthesis. The carbonyl group is frequently protected by converting it to an oxime, hydrazone or semicarbazone. Oximes have been extensively used for the separation, purification and characterisation of aldehydes and ketones and in the preparation of amides *via* the Beckmann rearrangement.[1] They also serve as important synthetic intermediates for amines,[2] nitriles[3] and *gem* – chloronitroso compounds.[4] Oximes can also be prepared from non-carbonyl compounds and thus regeneration of carbonyl compounds from oximes represents a route for the synthesis of aldehydes and ketones.[5] A large number of methods have been reported for the deoximation of oximes using hydrolytic, reductive and oxidative reactions.[6-8] Many of the reagents employed for this purpose have disadvantages,[6,9-12] and are not chemoselective[6d,13] for deoximation in presence of alkene or alcohol.[13] Recently, deoximation using solid-supported reagents with microwave irradiation has also been reported.[14] However, the main drawback of this method was that it gave other oxidised products in the presence of other sensitive functions. Despite the many reagents available, there is scope for the development of clean, highly efficient process with newer reagents to overcome the difficulties of the reported methods.

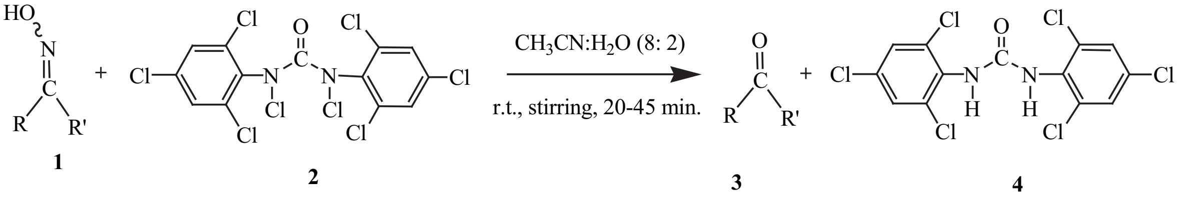
The development of recyclable reagents has received considerable interest for environmental reasons.[15] It prompted us to explore the possibility of using the stable, nontoxic and an efficient chlorine releasing reagent, *N,N'*-dichlorobis(2,4,6-trichlorophenyl)urea (CC-2).[16] CC-2 has been used as a reactive ingredient in a formulation developed in our laboratory to decontaminate the bis-(2-chloroethyl)sulfide (sulfur mustard) a cytotoxic, alkylating vesicant chemical warfare agent.[17] Having established a commercially viable synthetic procedure for CC-2, we have recently explored its applications to the synthesis of dialkyl chlorophosphates from dialkyl phosphites.[18] In continuation of our previous work,[19] we describe a more convenient, rapid, and economic, environmental friendly method using the reagent CC-2 for the synthesis of carbonyl compounds from their corresponding oximes at room temperature. The general synthetic method is given in Scheme 1.

Various reactions were performed to optimise the reaction conditions such as use of solvent, reaction temperature, time and number of equivalents of CC-2 to convert the oxime to the carbonyl compounds. The reaction was found to be complete at room temperature within 20–40 min. It was observed that substrate to reagent ratio of 2 : 1 was sufficient to completely convert oximes into corresponding carbonyl compounds. There was no increase in yield when the reaction was performed at equimolar ratio although the reaction was completed more quickly.

The choice of solvent also affects the yield and rate of reaction. The role of water is critical to hydrolyse the intermediate formed during the course of the reaction. The maximum yield (80–96%) was obtained when the reaction was performed in $CH_3CN–H_2O$ (8 : 2 v/v).

After optimisation of the reaction conditions, the scope of the reaction was explored with structurally diverse oximes. With CC-2 in $CH_3CN–H_2O$ they afforded the corresponding carbonyl compounds without any side products. The insoluble byproduct (**4**) was removed by filtration and washed with acetonitrile. The compound **4** could be reused for the preparation of CC-2 by the reported procedure.[19] Removal of the solvent from the filtrate under reduced pressure gave the crude product. Solid products were crystallised from diethyl ether and liquid products were obtained by vacuum distillation after evaporation of solvent. The results of this study are given in Table 1. It is evident from the Table 1 that even the sterically hindered ketoximes such as camphor oxime and fenchone oxime (Entries 14 and 15) were successfully converted to their corresponding ketone in high yields. The by-product bis (2, 4, 6-trichlorophenyl) urea (**4**) is insoluble in most of the organic solvents. Hence (**4**) can be filtered off and recycled just by re-chlorination to give the CC-2. This makes the process simple, economical and reduces waste. Another advantage of this method is that reaction is clean with shorter reaction times and easy work-up. The rate of the deoximation reactions were fast as all the reactions were completed within 20–45 min. including those oximes that have either electron-donating (entry 6) or electron-withdrawing (entry 13) groups at *para* position of phenyl ring.

The aldoximes were also converted to the corresponding aldehydes and no carboxylic acid was formed due to the over-



Scheme 1

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Table 1 Deoximation of oximes using CC-2

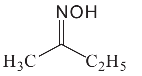
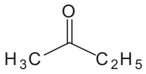
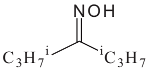
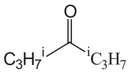
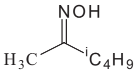
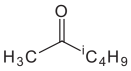
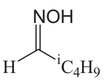
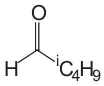
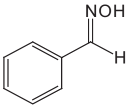
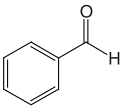
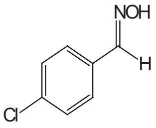
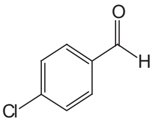
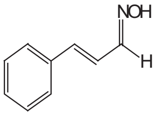
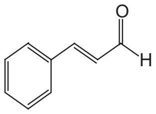
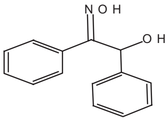
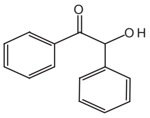
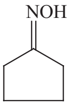
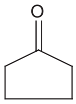
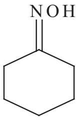
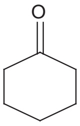
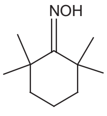
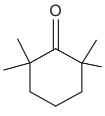
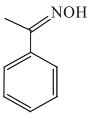
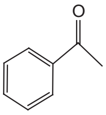
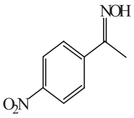
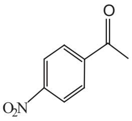
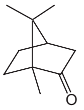
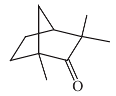
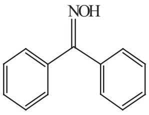
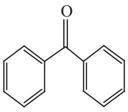
Entry	Substrate	Product	Time/min	B.P./°C)		Yield[a]
				Obsd	Lit	
1			20	78–80	80	96
2			25	124–126	124	94
3			20	116–118	117–118	95
4			25	88–90	90	96
5			25	176–177	178–179	90
6			25	92–94/10[c]	45–50[b]	92
7			35	140–142/3[c]	248	88
8			35	135–136[b]	134–138[b]	86
9			20	128–130	130–131	92
10			20	155–157	155	94
11			40	70–72/12[c]	50–53/3[c]	89
12			25	122–124/24[c]	202	92
13			25	77–78[b]	75–78[b]	88
14			35	174–177[b]	175–177[b]	89

Table 1 *Continued*

Entry	Substrate	Product	Time/min	B.P./°C)		Yield^a
				Obsd	Lit	
15			40	60–62/15^c	192–194^c	82
16			35	48–50^b	47–51^b	85

^{a}Isolated yields; ^{b}melting point of compounds; ^{c}boiling point under reduced pressure at mm Hg.
All the products were compared with authentic sample and gave satisfactory IR, NMR and MS data
The purity of the products which have different boiling points to their literature values, were checked by GC and TLC. R_f value and retention time was matched with authentic samples. On distillation of these compounds at atmospheric pressure, it was observed that yields of the products were reduced by 8–15%.

oxidation of the regenerated aldehydes. The method showed chemo-selectivity. The oxidative deoximation of benzoin (entry 8) and the unsaturated oxime (cinnamaldoxime, entry 7) proceeded without affecting the hydroxyl group and double bond respectively. In order to examine the chemo-selectivity of the method further, two sets of experiments were performed under similar reaction conditions. In the first set of experiments, an equimolar mixture of benzophenone oxime and styrene were allowed to react with CC-2. The benzophenone oxime under went chemo-selective deoximation giving 85% benzophenone without any observable oxidation of styrene. Similarly in another experiment, an equimolor mixture of benzophenone oxime and benzyl alcohol, were allowed to react with CC-2 at room temperature. The benzophenone oxime underwent chemoselective oxidative deoximation giving (85%) benzophenone, whereas benzyl alcohol was recovered almost quantitatively. It indicated non-competitive oxidation of oximes in the presence of hydroxyl group as well as with a double bond.

In conclusion, we describe a simple, mild, convenient and chemo-selective method for the oxidative deoximation of oximes by the use of CC-2. The hydroxyl and alkene groups are not affected. Finally the dechlorinated product (**4**) can be converted to (**2**) by rechlorination and could be reused several times making it recyclable.

Experimental

All the oximes were synthesised by reported methods. The chemicals required for synthesis of oximes and CC-2 was purchased from Aldrich Chemical Company USA. Solvents and other chemicals such as pyridine, NaOH, hydroxylamine hydrochloride, acetic acid, and acetonitrile were obtained from S.D. Fine Chemicals, Mumbai, India.

IR spectra were recorded on Bruker FT-IR spectrometer model Tensor 27 as KBr disks.^{1} H NMR spectra were recorded on Bruker DPX Avance FT- NMR in $CDCl_3$ or DMSOd6 using tetramethylsilane as an internal standard at 400 MHz. A Chemito GC model 1000 instrument was used with flame ionisation detector (FID). A capillary column (30 m × 0.25 mm I.D-BP5) packed with 5% phenyl and 95% dimethyl polysiloxane (SGE) coated on fused silica was employed. The injection port and detector block were maintained at 280°C and 260°C respectively and the column oven was at programmed temperature profile started at 50°C, ramped up to 280°C at 25°C/min. Nitrogen was used as a carrier gas (at a flow rate of 30 ml/min). Air for FID was supplied at 300 ml/min and hydrogen at 30 ml/min. In all analysis, 1 μl sample were injected and peaks recorded on computerized data acquisition station. The GC–MS analyses were performed in EI (70 eV) in full scan mode with an Agilent 6890 GC equipped with a model 5973 mass selective detector (Agilent Technologies, USA). An SGE BPX5 capillary column with 30 m length × 0.32 mm internal diameter × 0.25 μm film thickness was used at temperature program of 80°C (2 min)–20°C/min–280°C (3 min). Helium was used as the carrier gas at a constant flow rate of 1.2 ml/min. The samples were analysed in the splitless mode at injection temperature of 250°C, EI source temperature 230°C and quadrupole analyser at 150°C.

Typical experimental procedure

In a typical experimental procedure, a solution of benzophenone oxime, 9.85 g (0.05 mol) in 50 ml acetonitrile was added slowly to a suspension of CC-2, 12.2 g (0.025 mol) in 25 ml acetonitrile–H_2O mixture (8:2) with stirring at room temperature. The progress of the reaction was monitored by TLC. The completion of reaction was also indicated by ceasing the precipitation of bis-(2,4, 6-trichlorophenyl) urea. The reaction mixture was filtered by suction and washed with acetonitrile (4 × 10 ml). The solvent was evaporated and the residue was cooled under ice cold which gave crude solid product followed by recrystallisation from diethyl ether to afford pure crystals of benzophenone; yield: 7.74 g (85%), m.p. 47–48°C (lit 46–48°C).

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