

Solvent-free Procedure for the Regeneration of Carbonyl Compounds from Nitrogenous Derivatives Using Dioxane-dibromide/SiO₂

Satinder K. Juneja, Monika Gupta, Satya Paul, and Rajive Gupta*

Department of Chemistry, University of Jammu, Jammu-180006, India. *E-mail: rajgupta5@rediffmail.com

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A solvent-free procedure is developed for the regeneration of carbonyl compounds from aldoximes or ketoximes by grinding at room temperature and from hydrazone, phenylhydrazone or semicarbazone derivatives under microwave irradiation using dioxane-dibromide/SiO₂. Products are obtained in excellent yields and are in a state of high purity.

Key Words : Solvent-free conditions, Oximes, Hydrazones, Semicarbazones, Dioxane-dibromide

Introduction

Nitrogenous derivatives serve as important synthetic intermediates as these are extensively used for purification, characterization and also for the protection of carbonyl compounds. Protection of carbonyl compounds as oximes, hydrazones, phenyl hydrazones, semicarbazones is of great interest to synthetic chemists since these can be readily prepared and cleaved. Among these nitrogenous derivatives, oximes received more attention because of their ready formation and deprotection to carbonyl compounds. Oximes also serve as intermediates for many reactions such as preparation of nitriles or amides *via* Beckmann rearrangement.¹ Numerous reagents are available for the regeneration of carbonyl compounds from their nitrogenous derivatives. Recently, Dowex (strongly acidic cation exchange resin),² silica chloride,³ mercuric nitrate,⁴ clay-supported ferric nitrate,⁵ *N,N'*-dibromo-1,3-propylene-bis[(4-ethylphenyl)sulphonamide],⁶ Co₂CO₈,⁷ bismuth nitrate on wet silica,⁸ microwave-assisted reaction,⁹ quinolinium dichromate,¹⁰ montmorillonite-K10,¹¹ K₅CoW₁₂O₄₀·3H₂O,¹² pyridinium chlorochromate,¹³ SnCl₂-SiO₂¹⁴ and acidic alumina¹⁵ have been reported for the regeneration of carbonyl compounds from their nitrogenous derivatives. However, some of these reported methods suffer from some disadvantages such as long reaction times, low yields, expensive reagents and over oxidation of products. Thus, there is still a scope for further development of mild, simple, environment-friendly and cost-effective method for the regeneration of carbonyl compounds from nitrogenous derivatives. In this paper, we wish to report a simple, fast and solvent-free method for the generation of carbonyl compounds from oximes, hydrazones, phenyl hydrazones and semicarbazones using dioxane-dibromide supported over silica gel under microwave irradiation.

Moreover, microwave enhanced reactions have gained popularity over the usual homogeneous and heterogeneous reactions as these accelerate a variety of synthetic transformations. Reactions that are facilitated by supported reagents on various solid inorganic surfaces have received attention in recent years. The advantages of these methods

over conventional heating include greater selectivity, enhanced reaction rates and cleaner products.

Results and Discussion

Dioxane-dibromide¹⁶ is a stable crystalline solid which can be used for several days if stored below 5 °C. It was prepared by adding bromine to dioxane at room-temperature and liberates bromine quantitatively. The proposed structure of dioxane-dibromide supported over silica gel is shown in Figure 1. Dioxane-dibromide when supported over silica gel becomes free flowing powder and the reaction can be carried out under microwave irradiation without evolution of fumes of bromine. Recently, we have reported the α -bromination of ketones using dioxane-dibromide over silica gel¹⁷ under microwave irradiation. In this paper, we report the regeneration of carbonyl compounds from oximes by simple grinding at room-temperature; and from hydrazones, phenylhydrazones and semicarbazones with microwave heating using dioxane-dibromide supported over silica gel. A series of aldoximes and ketoximes were subjected to deoxygenation with dioxane-dibromide/SiO₂ under microwave irradiation in solvent-free conditions. Firstly, deoxygenation was carried out under different set of conditions with respect to molar ratio of substrate, dioxane-dibromide/SiO₂. It was found that for 1 mmole of substrate, 1 mmole of dioxane-dibromide/SiO₂ was required. In a test reaction, cyclohexanone oxime (5 mmol), dioxane-dibromide (5 mmol) and silica (1 g) were grinded in a mortar with the help of pestle at room-temperature for 1 min, complete disappearance of oxime took place and cyclohexanone was isolated in 85% yield. Under these conditions, α -bromocyclohexanone (5%, as

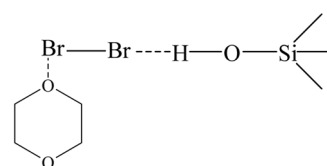
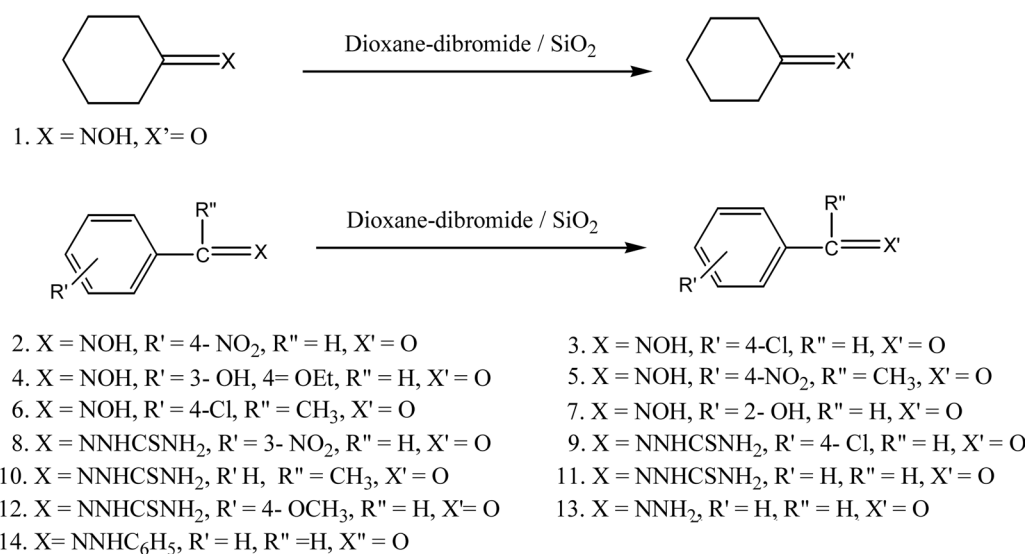


Figure 1. Proposed structure for dioxane-dibromide supported over silica gel.



Scheme 1

determined by ¹H NMR) was formed. Once we were able to cleave oximes, similar methodology was then extended for the regeneration of carbonyl compounds from hydrazones, phenylhydrazones and semicarbazones using the same optimum conditions but unfortunately, reaction did not go to completion even up to 1 h. Then hydrazones, phenylhydrazones and semicarbazones were subjected to irradiation under microwaves at 320 W. Complete conversion of starting material took place and carbonyl compounds were obtained in excellent yields. 320 W was selected as the optimum power level. For example, in case of hydrazone, phenyl hydrazone and semicarbazone of benzaldehyde, 95%, 65% and 83% of benzaldehyde was isolated after 10 min. of microwave heating respectively. It was found that little amount of α -brominated product was always formed together with carbonyl compound.

To explore the generality and scope of dioxane-dibromide/SiO₂ for the regeneration of carbonyl compounds from oximes, hydrazones, phenylhydrazones and semicarbazones, different substrates were chosen (shown in Scheme 1) and excellent yields were obtained (Table 1). Even the sterically hindered camphor oxime has been converted into camphor in good yield. Interestingly, α,β -unsaturated oximes underwent deoxygenation effectively without effecting C-C double bond and the reaction was essentially chemoselective.

The versatility of the reaction was also established by carrying out the reaction using 100% dioxane-dibromide and it was found that lot of fumes were evolved during the course of reaction which was very difficult to handle. Then it was tried with 100% wet silica gel, only 5% reaction was occurred. From this, it was inferred that dioxane-dibromide supported over silica gel is necessary.

Experimental Section

General. All the melting points were determined on Perfit melting point apparatus and are uncorrected. ¹H and ¹³C

NMR spectral data were registered on Bruker DPX-200 NMR spectrometer (200 MHz) in CDCl₃ using tetramethylsilane as an internal standard. The IR spectra were recorded using KBr disc on Perkin-Elmer FTIR spectrophotometer. Mass spectral data was recorded on Jeol JMS D-300 mass spectrometer at 70 eV. The elemental analysis was performed on CHNS-932 Analyser (Leco). For the microwave irradiation experiments described below, a conventional (unmodified) household microwave oven equipped with a turn table was used (LG Smart Chef MS 255 R having maximum output power of 900 W).

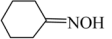
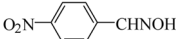
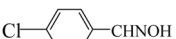
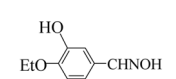
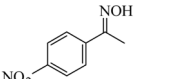
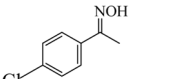
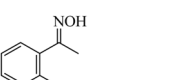
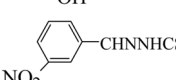
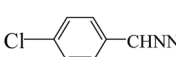
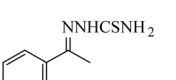

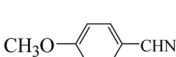


General procedure for the regeneration of carbonyl compounds from oximes. To a mixture of an aldoxime or ketoxime (5 mmol) and dioxane-dibromide (1.24 g, 5 mmol), silica gel (1 g) was added and grinded well in a mortar with the help of pestle for an appropriate time (monitored by TLC, Table 1). The product was extracted with diethyl ether (3 × 10 mL) followed by crystallization or passing through a column of silica gel and elution with ethylacetate: pet. ether (1:9).

The structures of the products were confirmed by ¹H and ¹³C NMR, IR, mass spectral data and comparison with authentic samples available commercially or prepared according to the literature methods.

General procedure for the regeneration of carbonyl compounds from hydrazones, phenylhydrazones and semicarbazones. To a mixture of hydrazone, phenyl hydrazone or semicarbazone (5 mmol) and dioxane-dibromide (1.24 g, 5 mmol), silica gel (1 g) was added and grinded well in a mortar with the help of pestle and then subjected to microwave irradiation for an appropriate time (monitored by TLC, Table 1) at 320 W. After completion of the reaction, the product was extracted with diethyl ether (3 × 10 mL) followed by crystallization or passing through a column of silica gel and elution with ethylacetate: pet. ether (1:9).

The structures of the products were confirmed by ¹H and ¹³C NMR, IR, mass spectral data and comparison with authen-

Table 1. Results of regeneration of carbonyl compounds from nitroeneous derivatives using dioxane-dibromide supported over silica gel under microwave irradiation (Power = 320W)

Entry	Substrate ^a	Time ^b (s)	Isolated Yield ^c (%)	Mp or Bp/Lit. Mp or Bp (°C)
1		60	85	Liq./155(bp) ¹⁸
2		51	89	104-06/106 ¹⁸
3		20	77	46-48/47 ¹⁸
4		21	75	75-77/76 ¹⁸
5		90	63	79-81/78 ¹⁸
6		53	83	Liq./232(bp) ¹⁸
7		20	82	Liq./213(bp) ¹⁸
8		70	72	56-58/57 ¹⁸
9		20	88	46-48/47 ¹⁸
10		391	87	Liq./200(bp) ¹⁸
11		610	78	Liq./178(bp) ¹⁸
12		680	83	Liq./248(bp) ¹⁸
13		60	93	Liq./178(bp) ¹⁸
14		90	60	Liq./178(bp) ¹⁸

^aIn case of oximes, the reaction was performed by simple grinding (manually) in a mortar at room temperature, while for hydrazones, phenylhydrazones and semicarbazones, the reaction was performed under microwave irradiation. ^bTime at which maximum yield was obtained. ^cIsolated yields from three experimental runs. In each experimental run, the condition remains the same.

tic samples available commercially or prepared according to the literature methods.

Conclusion

In conclusion, we have developed a mild, efficient and selective reagent for the regeneration of carbonyl compounds from oximes by grinding at room-temperature; and from hydrazones, phenylhydrazones and semicarbazones under microwave irradiation.

The major advantages of this new reagent over other reported reagents are that it requires lesser reaction time,

promote higher yields and can be prepared easily. Moreover, over oxidation of the products is also avoided. In addition to it, this reagent requires only grinding in case of oximes and microwave irradiation for seconds in case of hydrazones, phenyl hydrazones and semicarbazones.

Spectral data of some selected compounds

Entry 1. Cyclohexanone. ¹H NMR (CDCl₃) δ: 2.45-2.68 (m, 4H), 2.82-2.94 (m, 2H), 4.34-4.62 (m, 4H). IR (KBr, ν_{max} in cm⁻¹): 1690, 2800. ¹³C NMR (CDCl₃) δ: 211.3 (C=O), 41.9 (C-2, C-6), 27.1 (C-3, C-5), 25.1 (C-4). Mass: m/z (M⁺): 98

Entry 6. 4-Chloroacetophenone. ¹H NMR (CDCl₃) δ: 2.50 (s, 3H, COCH₃), 6.80-6.84 (d, 2H, Harom), 7.45-7.56 (d, 2H, Harom). IR (KBr, ν_{max} in cm⁻¹): 3300, 2800, 1690. ¹³C NMR (CDCl₃) δ: 197.6 (C=O), 130 (C-Cl), 129.5 (C-6), 128.2 (C-3, C-5), 134.5 (C-4). Mass: m/z (M⁺): 154.5

Entry 7. 2-Hydroxyacetophenone. ¹H NMR (CDCl₃) δ: 2.35 (s, 3H, CH₃), 5.01 (bs, 1H, OH), 6.75-6.80 (m, 1H, Harom), 6.85-6.92 (m, 1H, Harom), 7.62-7.35 (d, 1H, Harom), 7.89-7.95 (d, 1H, Harom). IR (KBr, ν_{max} in cm⁻¹): 3500, 3300, 2800, 1690. ¹³C NMR (CDCl₃) δ: 197.6 (C=O), 129.5 (C-6), 128.9 (C-3, C-5), 134.2 (C-4), 115 (C-OH). Mass: m/z (M⁺): 136.

Entry 10. Acetophenone. ¹H NMR (CDCl₃) δ: 2.35 (s, 3H, COCH₃), 6.62-6.75 (m, 1H, Harom), 6.92-7.10 (m, 1H, Harom), 7.75-7.92 (d, 2H, Harom). IR (KBr, ν_{max} in cm⁻¹): 3300, 2800, 1690. ¹³C NMR (CDCl₃) δ: 197.6 (C=O), 137.1 (C-1), 129.5 (C-2, C-6), 128.9 (C-3, C-5), 134.2 (C-4). Mass; m/z (M⁺): 120.

Entry 11. Benzaldehyde. ¹H NMR (CDCl₃) δ: 6.60-6.70 (m, 1H, Harom), 6.92-7.15 (m, 2H, Harom), 7.68-7.72 (d, 2H, Harom), 9-10 (s, 1H, CHO). IR (KBr, ν_{max} in cm⁻¹): 3300, 1710. ¹³C NMR (CDCl₃) δ: 192.4 (C=O), 136.4 (C-1), 129.5 (C-2, C-6), 128.5 (C-3, C-5), 135.2 (C-4). Mass: m/z (M⁺): 106.

Entry 12. Anisaldehyde. ¹H NMR (CDCl₃) δ: 3.40-4.01 (s, 3H, OCH₃), 6.85-6.95 (d, 2H, Harom), 7.80-7.90 (d, 2H, Harom), 9-10 (s, 1H, CHO). IR (KBr, ν_{max} in cm⁻¹): 3300, 1720, 1275. ¹³C NMR (CDCl₃) δ: 192.4 (C=O), 136.4 (C-1), 129.8 (C-2, C-6), 127.5 (C-3, C-5), 134.0 (C-4), 51.0 (C-OCH₃). Mass: m/z (M⁺): 120.

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 16. Dioxane-dibromide was prepared by adding bromine dropwise (8 mL) to dioxane (5 mL) until a yellow solid product was obtained. It was filtered, dried in a vacuum desiccator and stored in a refrigerator (Yield 10 g, mp = 61-62 °C). It was orange coloured crystalline solid. The orange colour was due to charge transfer transitions between dioxane and bromine. The structure of dioxane-dibromide was confirmed by elemental analysis. Anal. Calcd. for dioxane-dibromide (C₄H₈O₂Br₂): C, 19.5; H, 3.25; O, 13.008; Br, 64.2. Found: C, 19.3; H, 3.30; O, 12.98; Br, 64.0.
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