SHORT PAPER

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Oxidative deprotection of oximes with peroxodisulfate under heterogeneous conditions[1]

Masao Hirano*, Kazuma Kojima, Shigetaka Yakabe and Takashi Morimoto

Department of Applied Chemistry, Faculty of Technology, Tokyo University of Agriculture and Technology (TUAT), Koganei, Tokyo 184-8588, Japan

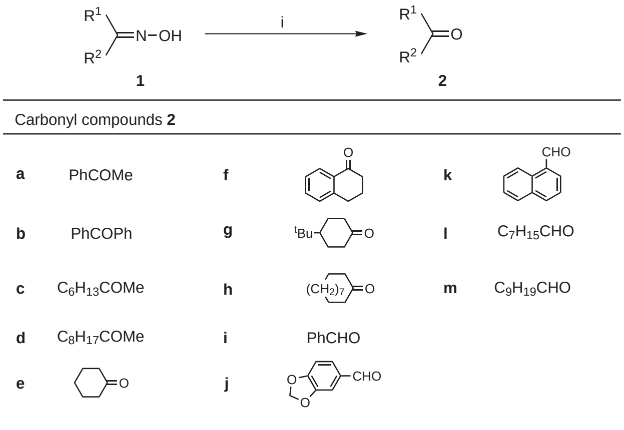
A reagent combination of $(NH_4)_2S_2O_8$, a catalytic amount of $AgNO_3$, in general, or $Cu(NO_3)_2$ in particular, and moist montmorillonite K10 clay in hexane regenerates the parent carbonyl compounds in high yields under relatively mild conditions.

Keywords: oxidative deprotection, oximes, perododisulfate

The protection of certain functional groups and the deprotection of the protected derivatives constitute important processes in the synthetic organic chemistry of polyfunctional molecules including the total synthesis of natural products. Thus large numbers of protective groups have been developed along with numerous methods for their removal.[2]

Oximes have been widely used not only as versatile reaction intermediates in organic syntheses,[3] but as carbonyl protecting groups and, therefore, considerable effort has been made for the development of new methods for their introduction and removal.[2] Of the many deprotection methodologies, use of supported reagents and catalysts[4] has recently attracted the attention of synthetic chemists, since these could give practically useful procedures. For example, Varma and his coworkers have shown that oximes,[5a,b] phenylhydrazones,[5c] semicarbazones,[5c] S,S-acetals,[5d] esters[5e] and silyl ethers[5f] can easily be deprotected with a variety of heterogeneous systems under microwave irradiation. We have recently observed that a reagent combination of ammonium peroxodisulfate, $(NH_4)_2S_2O_8$,[6] a catalytic amount of silver nitrate, $AgNO_3$, and montmorillonite clay K10 preloaded with the optimum amount of water (moist montmorillonite; *see* Experimental section) in hexane can favourably be used for the oxidation of a variety of aromatic alcohols and diols, giving the corresponding carbonyl compounds in excellent yields under relatively mild conditions.[1] As a part of our continued interest in the chemistry of supported reagents,[1,7] this paper describes an extension of the previous study[1] based on the use of the $(NH_4)_2S_2O_8/AgNO_3$ catalyst/montmorillonite clay system to the oxidative deprotection of oximes, since the heterogeneous system achieves a simple, high-yielding regeneration of the parent carbonyl compounds.

The present deprotection of oximes **1** can readily be carried out by efficiently stirring a heterogeneous mixture of **1**, $(NH4)_2S_2O_8$, a catalytic amount of $AgNO_3$ (5 mol% with respect to **1**) and hexane under an inert atmosphere in the presence of moist montmorillonite. Filtration of insoluble materials, washing of the filter cake with ether, followed by removal of the combined solvent, afforded the parent carbonyl compound **2**, which was able to be easily purified by a single chromatography. The applicability of the $(NH_4)_2S_2O_8/AgNO_3$ catalyst/moist montmorillonite system for typical aromatic, aliphatic and alicyclic ketoximes **1a–h** and aldoximes **1i–m** is summarised in Scheme 1 and Table 1. Thus, the oximes were, in general, efficiently deprotected to give **2** in over 90% yield from 2.5 to 3 h reactions under optimum conditions. The reaction of **1j** with the use of $AgNO_3$ catalyst failed to restore **2j** in a satisfactory yield (78%, run 10). This might in part be ascribed to the lability of the methylenedioxy linkage. Accordingly, we looked for other metal salts as catalysts. Of several Cu and Fe salts tested, we have found that copper(II) nitrate trihydrate, $Cu(NO_3)_2{\cdot}3H_2O$, favours the deprotection of **1j** to regenerate piperonal **2j** in excellent yield (run 11).



Scheme 1 i, $(NH_4)_2S_2O_8$, $AgNO_3$ or $Cu(NO_3)_2$, moist montmorillonite, hexane

The earlier study employed $(NH_4)_2S_2O_8$ for the deprotection of a steroidal oxime in aqueous sulfuric acid.[8] When recent environmental constraint is taken into consideration,[4a,9] this procedure is no longer attractive since it produces highly acidic waste or may requires a large volume of a neutralising base. Thus, as suggested above, Varma *et al.*[‡] have investigated deprotection of a number of ketoximes and aldoximes with a $(NH_4)_2S_2O_8$/silica gel/microwave system under solvent free conditions, in which the products were removed from the reaction mixtures by eluting with a large volume of dichloromethane (4 × 30 ml per mmol of **1**).[5b] Although the reactions were very rapid being completed within a few minutes in every case, the current method can favourably be compared to their reactions in terms of smaller quantities of the oxidant ($[Oxime]/[(NH_4)_2S_2O_8]$= 1/5 and 1/2.5 in the former[5b] and the present cases, respectively) and, especially, of the improved yield of the products. Indeed, the carbonyl

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* To receive any correspondence. Fax: +81-423-88-7033.

[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

[‡] They also utilised $(NH_4)_2S_2O_8$ for the deprotection of phenylhydrazones and semicarbazones in combination with montmorillonite K10 and microwave or ultrasonic irradiation.[5c]

Table 1 Regeneration of carbonyl compounds from the oximes

		Conditions[a]		Yield
Run	Carbonyl compound	Temp/°C	Time/h	(%)[b]
1	**2a**	50	2.5	98
2[c]	**2b**	60	3.0	>99[d]
3	**2c**	50	2.5	99
4	**2d**	50	2.5	92
5	**2e**	50	2.5	91
6	**2f**	50	2.5	>99
7	**2g**	50	2.5	97[e]
8	**2h**	50	2.5	95[f]
9	**2i**	50	2.5	91
10[c]	**2j**	60	2.5	78
11[c,g]	**2j**	60	2.5	95[h]
12	**2k**	50	2.5	95
13	**2l**	50	2.5	94
14	**2m**	50	2.5	90

[a] Under argon; oxime 1 mmol, $(NH4)_2S_2O_8$ 2.5 mmol, $AgNO_3$ 0.05 mmol (5 mol% with respect to oxime), moist montmorillonite (H_2O content, 14 wt %) 1 g, hexane 10 ml. [b] Isolated yield of chromatographically purified carbonyl compound. [c] Moist montmorillonite (H_2O content, 17 wt %) 1 g. [d] M.p. 47–48 °C (lit, 48.5–49 °C; *Ref.* 11, p. 637). [e] Mp 47–48 °C (lit, 49–50 °C; *Ref.* 11, pp. 1168). [f] Mp 58–59 °C (lit, 59 °C; Ref. 11, p. 1612). [g] $Cu(NO_3)_2·3H_2O$ (0.1 mmol) was used instead of $AgNO_3$ as the catalyst. [h] M.p. 32–34.5 °C (lit, 37 °C; Ref. 11, p. 4349).

compounds **2a**, **f**, **i** and **k** were given in 98 (run 1), >99 (run 6), 91 (run 9) and 95% yield (run 12), respectively, whereas the former system gave 65, 64, 83 and 76% of **2a**, **f**, **i** and **k**, respectively. In addition, the present method is devoid of the use of a highly hazardous solvent, CH_2Cl_2, and a microwave generator. Consequently, it could reasonably be concluded that a combination of $(NH_4)_2S_2O_8$, $AgNO_3$ catalyst in general or $Cu(NO_3)_2$ in particular, and moist montmorillonite in hexane demonstrated here constitutes a mild, easily accessible and high-yielding deoximation procedure.

Experimental

General: Commercial $(NH_4)_2S_2O_8$ (Wako), $AgNO_3$ (Kojima Chemical, Japan) and $Cu(NO_3)_2·3H_2O$ (Kokusan Chemical Works, Japan) were used as received. Aldehydes and ketones are commercial chemicals, most of which were used as received from suppliers, but impure materials were purified by distillation or recrystallisation just prior to use. Oximes **1a**–**m** were prepared by the reaction of the carbonyl compounds with hydroxylamine hydrochloride ($NH_2OH·HCl$) in ethanol in the presence of a hydrotalcite clay as the base catalyst.[10] Deionized water (0.16 or 0.2 g) was added to commercial montmorillonite K10 (Aldrich; 1 g) in several portions, followed by vigorous shaking of the mixture on every addition for a few min until a free-flowing powder was obtained, to afford moist montmorillonite (loading 14 or 17 wt % of water, respectively), 1.0 g of which was immediately used for the deoximation. Hexane was dried ($CaCl_2$), distilled, and stored over molecular sieves. Melting points were determined on a Yanagimoto MP-S3 melting point apparatus and are uncorrected. Mass spectra were determined on a JEOL SX-102A mass spectrometer coupled to a Hewlett Packard GC5890 Series II GC apparatus *via* a heated capillary column. GLC was performed on a Shimadzu GC-14B instrument equipped with a FID through a 2 m×5 mm diameter glass column packed with 5% PEG-20M on Chromosorb WAW-DMCS, and interfaced with a Shimadzu Chromatopac C-R6A integrator, with temperature programming. ^1H NMR spectra were recorded with a JEOL PMX-60 (60 MHz) spectrometer for solutions in $CDCl_3$ using Me_4Si as an internal standard.

Deoximation Procedure: The following procedure for benzophenone oxime **1b** is representative. A 30 ml, two-necked, round bottom flask, equipped with a 1.5 cm long Teflon-coated stirrer bar, a 25 cm long condenser, and a glass gas-inlet tubing connected to an argon-filled balloon, was arranged in order to perform the reaction under inert atmosphere by linking the top of the condenser to a liquid paraffin trap *via* a flexible silicone rubber tubing. The flask was charged with **1b** (0.197 g, 1 mmol) and hexane (10 ml), to which freshly prepared moist montmorillonite (H_2O content, 17 wt %; 1 g), $AgNO_3$ (8.5 mg, 0.05 mmol; 5 mol% with respect to **1b**) and $(NH4)_2S_2O_8$ (0.571 g, 2.5 mmol) were added, and it was then deaerated by gently passing a stream of dry argon throughout the system. The flask was kept at 60 °C in a thermostatted oil-bath while efficient stirring was continued in order to ensure smooth reaction and to attain reproducible results. After 3 h, the reaction mixture was cooled rapidly to room temperature by external cooling and was then filtered through a sintered glass funnel. The filter cake was washed thoroughly with portions of dry ether (in total *ca*. 50 ml). Rotary evaporation of the combined solvent, followed by chromatography on a silica gel column (Merck silica gel 60, hexane–AcOEt, 8:2 v/v), gave pure (GLC, TLC and NMR) benzophenone **2b** in over 99% yield (0.182 g): m.p. 47–48 °C (lit,[11] m.p. 48.5–49°C).

Deoximation of the other substrates **1a** and **1c**–**m** was carried out as above, except for the case of run 11 where $Cu(NO_3)_2·3H_2O$ (0.0242g, 0.1 mmol) was used as the catalyst. The reaction conditions (reaction temperature and time, the concentration of the metal salts and H2O content of montmorillonite K10) were determined on the basis of the reactivity of the oximes and the yields of the carbonyl compounds. The products thus obtained were identified by the comparison of NMR,[12] MS and IR[13] spectra with those of commercial samples.

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