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Methyl Triphenylphosphonium Peroxydisulfate (MTPPP): A Mild and Inexpensive Reagent for the Cleavage of Oximes, Phenylhydrazones and 2,4-Dinitro phenylhydrazones to the Corresponding Carbonyl Compounds Under Non-Aqueous Conditions

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We have dedicated this paper to Prof. H. Firouzabadi on the occasion of his 65th birthday and also his retirement

Methyltriphenylphosphonium peroxydisulfate (MTPPP) was synthesized by treating methyltriphenylphosphonium bromide with potassium peroxydisulfate in aqueous solution. This reagent was used as a suitable and efficient reagent for the cleavage of oximes, phenylhydrazones and 2,4-dinitro phenylhydrazones to their corresponding carbonyl compounds under non-aqueous condition.

Keywords: Deprotection, Oxidative cleavage, Carbonyl compounds, Phosphonium salts.

INTRODUCTION

Protection and deprotection of functional groups are important aspects in organic chemistry [1]. Nitrogen derivatives of aldehydes and ketones are crystalline and so they can constitute an effective method for the isolation, purification, and characterization of carbonyl compounds [2]. Despite of protecting role of oximes, these compounds can be used in the preparation of nitriles [3], amides through Beckmann rearrangement [4] or to activate the carbonyl groups [5]. Since oximes can also be prepared from non-carbonyl compounds [6a–b], transformation of oximes to their corresponding carbonyl compounds is an important reaction. Reported oxidative or reductive methods in order to deprotect oximes [7,8], suffer form low yields or over oxidation [8,9]. In addition to their frequent use as protecting groups, phenylhydrazones and 2,4-dinitro phenylhydrazones are stable and have had an important role in synthesis and analysis [10-11]. Several oxidative deprotection methods for oximes have been developed which have some advantages over the classical hydrolysis methods [12–25]. However, little attention has been paid to the oxidative cleavage of phenylhydrazones and 2,4-dinitro phenylhydrazones [26–33].

EXPERIMENTAL

General

Chemicals were purchased from Fluka, Merck, and Aldrich chemicals companies. All reactions were carried out in refluxing acetonitrile. Yields refer to the isolated products after purification. The products were characterized by comparing their spectral (IR, ^{1}H NMR) data, TLC and

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physical data with those of authentic samples [34]. All ^{1}H NMR spectra were recorded at 300 MHz in $CDCl_3$ relative to TMS as an internal standard and IR spectra were recorded on Shimadzu 435 IR spectrometer.

Preparation of Methyltriphenylphosphonium peroxydisulfate (MTPPP)

To an aqueous solution of methyltriphenylphosphonium bromide (10 mmol, 3.57 g) was added an aqueous solution of potassium peroxydisulfate (5 mmol, 1.35 g) under stirring at room temperature. A white precipitate was formed after 30 min stirring. The mixture was filtered, washed with water (2x15 ml), and dried at room temperature (3.78 g, 96% Yield), which decomposed at 210-212 °C to a dark-brown material. IR (KBr) 3100, 2980, 1600, 1495, 1480, 1260, 1190, 1050, 860, 750, 690 cm^{-1}. ^{1}H NMR (DMSO-d$_6$) δ, ppm: 7.9-7.7 (m, 15 H), 3.19 (d, J=14.6, P-$\underline{CH_3}$). ^{13}C NMR: δ 134.5, 134.4, 132.5, 132.3, 129.7, 129.3, 116.4. Elemental analysis Calculated for $C_{38}H_{36}O_8P_2S_2$; C: 61.13%, H: 4.83%, N: 0.00%; Found C: 61.18%, H: 4.90%, N: 0.01%.

Conversion of Oximes, Phenyl hydrazones and 2,4-dinitro phenylhydrazones to the Corresponding Carbonyl Compounds using MTPPP

A General procedure:

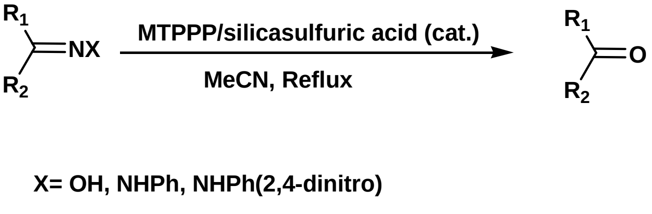
A mixture of acetophenone oxime **1a** (1mmol, 0.135 g) and silicasulfuric acid (0.02 g, 0.16 mmol) in acetonitrile (5 ml) was prepared. To this solution, 0.75 g (1mmol) of **MTPPP** was added and the reaction mixture was refluxed for 20 sec. When TLC showed no more progress (n-hexane:EtOAc 80:20), the mixture was allowed to reach at room temperature and then was filtered. The solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel with (EtOAc:n-hexane; 1:5) to give pure acetophenone (0.17 g, 95%), bp 200-202 °C/760 mmHg (Lit.[34] bp 200-202 °C/760 mmHg).

RESULTS AND DISCUSSION

As part of our ongoing project to develop the synthesis of quaternary ammonium and phosphonium salts [35], we now wish to report the synthesis of **MTPPP** as an efficient and novel reagent for the oxidative cleavage of oximes, phenylhydrazones and 2,4-dinitrophenylhydrazones to their corresponding carbonyl compounds under non-aqueous conditions.

Using **MTPPP** in the presence of 0.16 molar ratio of silicasulfuric acid [36], various oximes, phenylhydrazones and 2,4-dinitrophenylhydrazones have been successfully deprotected to afford the corresponding aldehydes and ketones in good to excellent yields. The reactions are performed in acetonitrile under reflux conditions and the results are summarized in Table 1. Notably the regenerated aldehydes did not undergo further oxidation to carboxylic acids under the reaction condition. **MTPPP** is a mild, efficient, stable and inexpensive reagent, which has been used for our studies under non-aqueous conditions. This reagent is a white powder, which is prepared by the dropwise addition of an aqueous solution of potassium peroxydisulfate to an aqueous solution of methyltriphenylphosphonium bromide at room temperature. Filtration and drying of the precipitates produced a white powder, which could be stored for months without losing its oxidation ability [37].

In order to establish the optimum reaction conditions, we have examined the effects of the solvent for deprotection. After a series of experiments on acetophenone oxime poor results were obtained with all solvents investigated other than acetonitrile. Deprotection of acetophenone oxime to its corresponding acetophenone with **MTPPP** in the presence of various Lewis acids such as $FeCl_3$, $AlCl_3$, $BiCl_3$ and silicasulfuric acid were examined in refluxing acetonitrile. Surprisingly only silicasulfuric acid was shown to be effective catalyst for this purpose (0.16 molar ratio). Higher molar ratio of the oxidant had no effect. This reagent in the presence of catalytic amount of silicasulfuric acid (0.16 molar ratio) is an efficient reagent for oxidative cleavage of oximes, phenylhydrazones and 2,4-dinitro phenylhydrazones to their corresponding carbonyl compounds in moderate to excellent yields (Scheme 1 and Table 1).



Scheme 1

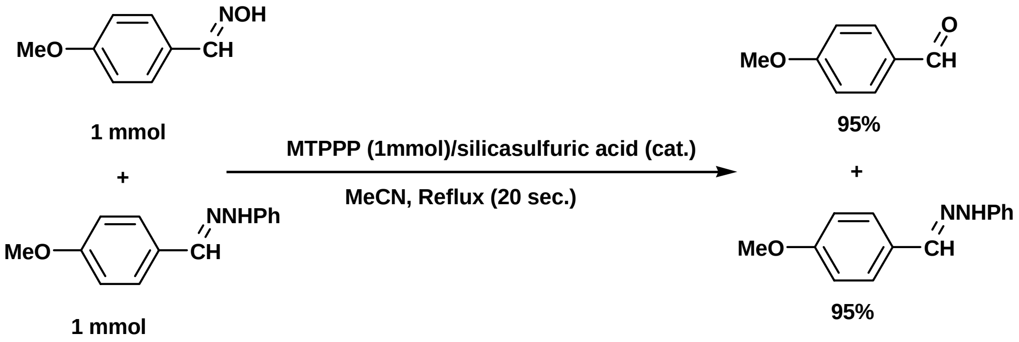
Table 1. [a]Conversin of oximes **1a-j**, phenylhydrazones **1k-m** or 2,4-dinitro phenylhydrazones **1n-q** with **MTPPP** in the presence of catalytic amount of silicasulfuric acid in refluxing acetonitrile.

substrate	R_1	R_2	time	yield (%)[b]	mp/°C or bp/°C/Torr (lit.[34])
1a	Ph	Me	20 sec	95	200-202/760 (202)
1b	3,4-$(MeO)_2C_6H_3$	Me	15 sec	98	45-46 (46-49)
1c	4-BrC_6H_4	CH_2Br	30 sec	40	108 (107-110)
1d	2-ClC_6H_4	H	30 sec	85	214-216/760 (214)
1e	[c]4-ClC_6H_4	H	5 sec	95	43-44 (44-47)
1f	2-$MeOC_6H_4$	H	20 sec	98	34 (34-37)
1g	4-$MeOC_6H_4$	H	50 min	95	250/760 (247-249)
1h	2,5-$(MeO)_2C_6H_3$	H	40 sec	40	48-50 (49-51)
1i	3,4-$(MeO)_2C_6H_3$	H	30 sec	40	82 (81-83)
1j	2-HO-5-$NO_2C_6H_3$	H	5 sec	95	126 (123-126)
1k	4-$MeOC_6H_4$	H	20 sec	90	250/760 (247-249)
1l	3,4-$(MeO)_2C_6H_3$	H	40 sec	50	82 (81-83)
1m	2-ClC_6H_4	H	40 min	60	214-216/760 (214)
1n	Ph	Me	30 min	55	200-202/760 (202)
1o	4-BrC_6H_4	Me	20 min	50	49 (49-52)
1p	4-$MeOC_6H_4$	Me	30 min	10	36 (36-38)
1q	3,4-$(MeO)_2C_6H_3$	H	30 min	15	82 (81-83)

[a]Confirmed by comparison with authentic samples (IR, TLC and ^1H NMR) [34]. [b]Yield of isolated pure product after purification. [c]Substrate/eagent (1:0.5)

In this method, oxidative cleavage is achieved by treating oximes **1a-j**, phenylhydrazones **1k-m** or 2,4-dinitro phenylhydrazones **1n-q** (1 mmol) with **MTPPP** (1 mmol) in the presence of catalytic amount of silicasulfuric acid (0.16 molar ratio) in refluxing acetonitrile. The reaction time is usually short (5-30 sec for oximes and 20-240 sec for phenylhydrazones and 2,4-dinitro phenylhydrazones) and the isolation of the products is straightforward (Table 1 and Scheme 1). It is very important to note that the procedure is effective for the selective cleavage of oximes. This methodology offers a simple, inexpensive and a selective route for converting oximes and phenylhydrazones to their corresponding carbonyl compounds (Scheme 2).

In order to evaluate the synergy between silicasulfuric acid and this reagent we tried several experiments. When we used acetophenone oxime with silicasulfuric acid in the absence of



Scheme 2

this reagent, no deprotection was occurred. We also tried the reaction of acetophenone oxime with **MTPPP** in refluxing acetonitrile in the absence of silicasulfuric acid and found that the reaction proceeded in 25% yield after 2 h. We also investigated the use of potassium peroxydisulfate in the presence of silicasulfuric acid in refluxing acetonitrile and observed that the reaction does not complete after 4 h and the corresponding ketone was obtained in 60% yield. This reaction in the presence of $AlCl_3$ as an acid catalyst proceeds 5% after 20 sec (the same time applied in use of silicasulfuric acid).

In conclusion, silica sulfuric acid was found to act as a good, inexpensive and insoluble proton source in all organic solvents. The low cost and availability of the reagents and simple procedure make this method attractive. At the same time, silica sulfuric acid can serve as an efficient catalyst for the conversion of oximes, phenylhydrazones and 2,4-dinitrophenylhydrazones derivatives into their corresponding carbonyl compounds under heterogeneous conditions. The yields are good to excellent and the procedure is simple and convenient. The reactions carried out in a short reaction time by using **MTPPP** in the presence of 0.16 molar ratio of silica sulfuric acid. Moreover, the oxidative cleavage of these derivatives takes place in refluxing acetonitrile and no over oxidation observed under the reaction conditions.

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