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Selective Oxidation of Sulfides to Sulfoxides and Sulfones by Microwave Thermolysis on Wet Silica-Supported Sodium Periodate§

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Abstract: A variety of symmetrical and unsymmetrical sulfides have been selectively and expeditiously oxidized to either sulfoxides or sulfones in good yields using wet silica-supported sodium periodate under microwave thermolysis conditions. © 1997 Elsevier Science Ltd.

In synthetic organic chemistry, the selective oxidation of sulfides to sulfoxides or sulfones has been a challenge for many years. Various oxidizing reagents used for this purpose include nitric acid,[1] hydrogen peroxide,[2] dinitrogen tetroxide,[3] chromic acid,[4] manganese dioxide,[4a] ozone,[5] peracids,[6] selenium dioxide,[7] sodium periodate,[8] hypervalent iodine reagents,[9] sodium perborate,[10] and some recently introduced reagent systems.[11] Among the increasingly popular category of supported reagents, the use of sodium metaperiodate on alumina[12] in ethanolic solution (room temp. 0.5-48 h) and sodium metaperiodate supported on silica gel[13] in methylene chloride (20 °C, 48 h) has also been documented. The reaction, however, remains incomplete in the latter case and requires intermittent addition of extra reagent and longer reaction time. Besides extended reaction period, most of these processes suffer from drawbacks, such as the use of corrosive acids, hazardous peracids, and toxic metallic compounds that generate waste streams. Consequently, there is a need for the development of environmentally benign solventless method.

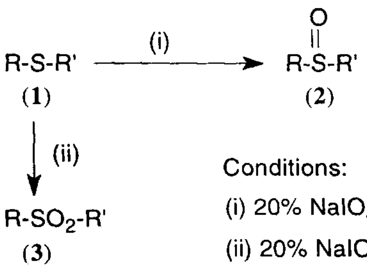
The reagents impregnated on inorganic solid supports and specially that are efficient under solvent-free conditions,[14,15] have gained popularity in organic synthesis because of their enhanced reactivity, selectivity, and associated ease of manipulation. During the course of our investigations on organic manipulations that are accelerated by microwaves in solventless processes,[15] we have observed a pronounced microwave effect.[16,17] The reactions in dry media condition[14,15] are specially appealing as they provide an opportunity to work with open vessels, thus avoiding the risk of high pressure development and with a possibility of upscaling the reactions on preparative scale. Recently described utility of wet silica-supported sodium periodate reagent for the efficient cleavage of glycols,[18] prompts us to report our own results on the selective oxidation of sulfides to sulfoxides and sulfones under solvent-free conditions using microwaves.

The supported reagent is prepared by evaporation to dryness a solution of sodium periodate (2 part by weight) in water in presence of silica (8 parts). The reagent is obtained as a free flowing solid containing 0.94 mmol of sodium periodate per gram of reagent (20%) after drying at 120 °C for 12h. The oxidation is conducted by adsorbing the sulfide substrate on wet silica supported sodium periodate and exposing the solid mixture to microwave irradiation in an unmodified microwave oven. The reaction is monitored by thin layer chromatography and upon completion, the products are isolated by extraction with ethyl acetate. Systematic studies with various solid supports have revealed that the silica and acidic clays are the most effective.

Dedicated to Dr. Christopher Baldwin, a strong proponent of science, on the occasion of his 50th birthday

Wetting of silica supported reagent also plays an important role in these reactions as the absence of moisture slows down the oxidation process considerably and invariably the reaction remains incomplete. Therefore, the addition of water during the course of reaction is often required especially for oxidation to the sulfone stage. This observation has also been corroborated by recent reports.[18,19]

The optimum ratio of sulfide to periodate (1:1.7 equivalents) is found to be ideal for complete conversion of sulfides to sulfoxides (<5% contamination of sulfone) while the reaction remains incomplete with lesser amounts i.e. 1:1 and 1:1.5. The use of excess reagent (1:3 equivalents) affords the corresponding sulfones (*via* sulfoxides) in a clean reaction. The generality of this approach has been demonstrated by a facile and effortless oxidation of a wide variety of alkyl, aryl and aromatic sulfides as shown in the Table. In an anomalous case, dibenzothiophene, however, undergoes rapid oxidation into a mixture of sulfoxide and sulfone and consequently is converted to sulfone directly using 3.0 equivalent of the catalyst (entry 8). A noteworthy feature of this protocol is its applicability to long chain aliphatic sulfides (entry 6) which are normally insoluble in polar solvents and are difficult to oxidize.



Conditions:
(i) 20% $NaIO_4$-Silica (1.7 eq.), MW
(ii) 20% $NaIO_4$-Silica (3.0 eq.), MW

Table: Oxidation of sulfides to sulfoxides and sulfones using wet $NaIO_4$-Silica system

Entry	R	R'	Sulfoxides		Sulfones	
			Time[a] (sec)	Yield[b] (%)	Time[a] (sec)	Yield[b] (%)
1	$C_6H_5CH_2$	C_6H_5	150	83	150	87
2	C_6H_5	C_6H_5	120	85	140	93
3	$C_6H_5CH_2$	$C_6H_5CH_2$	150	80	180	80
4	C_6H_5	CH_3	120	80	150	82
5	$CH_3(CH_2)_3$	$CH_3(CH_2)_3$	40	76	60[c]	72
6	$C_{12}H_{25}$	CH_3	80	80	150	80
7	$-CH_2-CH_2-CH_2-CH_2-$		30	82	60[c]	72
8	Dibenzothiophene		-	-	180	74

[a] The temperature of the alumina bath (heat sink) inside a Sears Kenmore microwave oven (2450 MHz) equipped with a turntable at full power (900 Watts) found to be ~140 °C after 150 seconds of irradiation. [b] Unoptimized yields of isolated products that exhibited physical and spectral properties in accord with the assigned structures. [c] Irradiated twice for a maximum period of 30 sec. each after a time interval of 10 min.

The benzyl phenyl sulfide is converted to the corresponding sulfoxide by simple mixing of wet sodium periodate on silica (20%) (1:1.7 equivalents) and allowing it to stand at room temperature for 3 hours. The sulfoxide product is isolated in pure form without any sulfone formation even in trace amounts. The same sulfide substrate when admixed with dry reagent (ratio 1:1.7) requires 15 hours for completion of the reaction indicating that the wet conditions facilitate the reaction. This mixture stored for extended period of time did not produce sulfone even after 2 days.

The role of microwave irradiation in the acceleration of these oxidation reactions is examined for benzyl pheny sulfide (entry 1) by conducting the reaction using an alternate heating medium (oil bath) at a comparable temperature of 140 °C (the temperature attained by alumina bath after irradiation time of 150 sec). It is found that the sulfide is converted to sulfoxide in about 5 min. using 1:1.7 equivalent of the reagent indicating that it may be a purely thermal effect. The conversion of sulfide to sulfone, however, requires 40 min. for completion of reaction in an oil bath at the same temperature (140 °C) and with the similar ratio of substrate to reagent (1:3) in contrast to 150 sec in the microwave oven. We find the use of microwave oven more convenient and clean with the added benefit that it does not require mixing; microwaves are neither absorbed nor their transmission restricted by the solid support.

General procedures

Preparation of sodium periodate-supported silica gel:

Silica gel (230-400 mesh, Baxter) for column chromatography (40 g) is added to a stirred solution of sodium periodate (10 g, 46.7 mmol) in 60 mL of warm water. The mixture is stirred for 30 min and water is removed under reduced pressure on a rotary evaporator. After removal of most of the water benzene is added and evaporated similarly to eliminate last traces of water. The resulting white powder is heated at 120 °C for 12h to get a constant weight. The reagent contains 0.94 mmol of sodium periodate per gram of the reagent system.

Preparation of sulfoxides:

The sulfide (**1**, 0.75 mmol.) is dissolved in dichloromethane (2-3 mL) and adsorbed over silica supported sodium periodate (20%, 1.36 g, 1.28 mmol.) that is wetted with 0.3 mL of water by thoroughly mixing on a vortex mixture. The adsorbed powdered material is transferred to a glass test tube and is inserted in an alumina bath (alumina: 100 g, mesh 65-325, Fisher scientific; bath: 5.7 cm diameter) inside the microwave oven. The compound is irradiated for the time specified in the table and the completion of the reaction is monitored by TLC examination. After completion of the reaction, the product is extracted into ethyl acetate (2 x 15 mL). The removal of solvent at reduced pressure affords crude sulfoxide (**2**) that contains less than 5% sulfone (**3**) (by ^{1}H NMR analysis of the crude product). The final purification is achieved by column chromatography over silica gel column or a simple crystallization.

Preparation of sulfones:

The sulfide (**1**, 0.75 mmol.) is dissolved in dichloromethane (2-3 mL) and adsorbed over silica supported sodium periodate (20%, 2.39 g, 2.25 mmol.) that is wetted with 0.5 mL of water by thoroughly mixing on a vortex mixer. The dry powder is transferred to a test tube and subjected to microwave irradiation. The reaction is monitored by TLC, the time required for each substrate is given in the table. The product is extracted into ethyl acetate (2 x 15 mL) and removal of the solvent at reduced pressure affords pure sulfones (**3**).

In conclusion, we have developed a facile, manipulatively easy, and solvent-free method for the oxidation of sulfides to either sulfoxides or sulfones that requires mild microwave thermolysis using wet silica supported sodium periodate.

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