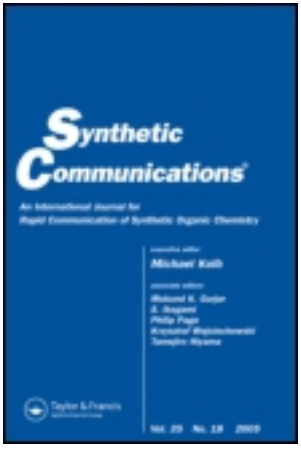

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A Simple and Efficient Procedure for Oxidation of Sulfides to Sulfoxides on Hydrated Silica Gel with Ceric Ammonium Nitrate (Can) In Methylene Chloride

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A SIMPLE AND EFFICIENT PROCEDURE FOR OXIDATION OF SULFIDES TO SULFOXIDES ON HYDRATED SILICA GEL WITH CERIC AMMONIUM NITRATE (CAN) IN METHYLENE CHLORIDE.

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Abstract: A simple, fast and efficient procedure for oxidation of sulfides to the corresponding sulfoxides with CAN mediated by hydrated silica gel in methylene chloride has been developed. To our knowledge, this is the first example of oxidation of sulfides with CAN in a non-aqueous media.

Sulfoxides are useful in organic synthesis as an activating group. They have been utilized extensively in carbon-carbon bond formation reactions.[1] Despite a number of alternative methods available for the synthesis of sulfoxides, oxidation of sulfides to the corresponding sulfoxides is the most favored method.[2] Popularity of this method is due to the availability of a wide variety of sulfides that can be utilized in the oxidation of sulfides to the corresponding sulfoxides.

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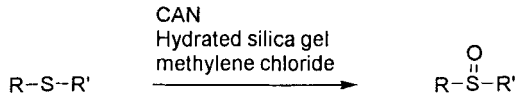
A number of oxidizing agents, including CAN, have been employed for this conversion.[3] However, the biggest difficulty associated with the oxidation of sulfides to sulfoxides is the susceptibility of sulfoxide to undergo further oxidation reaction in the reaction mixture to produce sulfones.[2] There is a need for an efficient and selective method that will oxidize sulfides to sulfoxides without complication from overoxidation.

Generally, it is expected that oxidation of sulfides with one equivalent of an oxidant will give sulfoxides, and with two or more equivalents of the oxidant sulfones will be produced. Controlling the reaction conditions for selective production of sulfoxide is difficult and often sulfone is produced along with sulfoxide even when only one equivalent of an oxidant is used. Ceric ammonium nitrate (CAN) had shown some promise in selective oxidation of sulfides to the corresponding sulfoxides in the past.[4] However, the reported procedures for oxidation of sulfides with CAN suffer from one or more of the following disadvantages: (a) Fails to oxidize sulfides containing α-hydrogen.[4] (b) Amount of CAN present in the reaction mixture must be controlled to prevent overoxidation.[5] (c) These procedures require aqueous media or a phase transfer conditions due to the limited solubility of CAN in organic solvents.[6]

We reported elsewhere that employment of hydrated silica gel in organic reactions offer a number of advantages including ability to

perform the reaction in organic solvents which previously required aqueous media in order to succeed.[7] In this paper, we report a facile procedure for oxidation of sulfides to the corresponding sulfoxides with ceric ammonium nitrate mediated by hydrated silica gel in methylene chloride, Scheme 1.

Scheme 1



1 **2**

To the best of our knowledge, this procedure is the first to employ an organic solvent in the oxidation reaction utilizing ceric ammonium nitrate as the oxidant. The results of this study have been presented in the Table. This newly developed method has the following advantages: (i) The process is mild, neutral and easy to carry out. (ii) No laborious aqueous work-up is involved in this method. The by-products of the oxidant are not soluble in methylene chloride and as a result a simple filtration can remove them easily. Removal of solvent from the filtrate produces the sulfoxide, which is often pure by TLC and NMR. However, impure products were purified by radial chromatography utilizing ethyl acetate/hexane as the eluent. (iii) This method utilizes methylene chloride as the solvent. (iv) This procedure is suitable for sulfides containing a wide range of functional groups such as ether, ester,

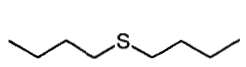
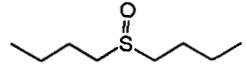
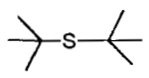
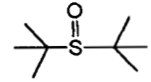
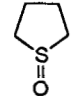
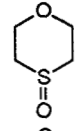
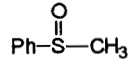
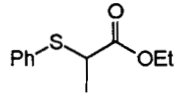
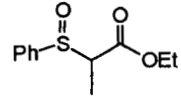
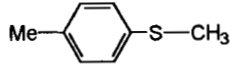
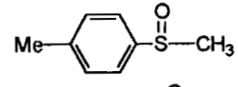
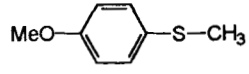
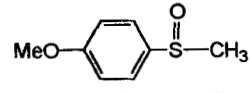
ketone, and nitro groups. (v) Presence of α-hydrogen does not have any detrimental effect on this procedure. (vi) This procedure produces excellent yields of sulfoxides and does not produce significant amounts of by-products including sulfone, and (vii) In this method, reaction time for most sulfides is very short.

The method reported in this paper for oxidation of sulfides to the corresponding sulfoxides with CAN is superior to the existing procedures. This procedure oxidizes sulfides selectively in the presence of a variety of other functional groups (see Table). Unlike others,[4] this method can oxidize dialkyl sulfides without any complication from Pummerer rearrangement. In contrast to a previously reported procedure,[6] oxidation of cyclic sulfides under these reaction conditions does not require any special care. The limitations of this method, we are aware of, are that this procedure fails to produce clean oxidation reaction for diphenyl sulfide **1m** and sulfides containing olefin functional group such as compounds **1o** and **1p**. These sulfides produced mixture of products which are difficult to separate. After laborious separation, we obtained unacceptable yields of the sulfoxides from these reactions. Others reported difficulties in oxidation of diphenyl sulfides[6,8] and reaction of CAN with alkenes functional group complicate the sulfide oxidation process.

Experimental Section

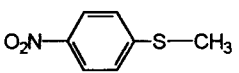
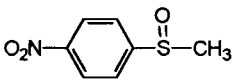
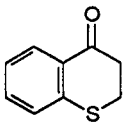
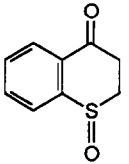
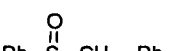
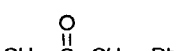
All reactions were magnetically stirred. Methylene chloride was

Table : Oxidation of sulfides to sulfoxides

	Sulfide (1)	Sulfoxide (2)	Yield%	Rxn. time min.	mp/bp °C	(reported)[18]
a.			90	40	30-31	32
b.			100	40	102-104 (3 mm)	104-105 (3 mm)
c.			100	50	102-105 (12 mm)	105-107 (12 mm)
d.			100	50	40-42	41-43
e.	Ph—S—CH_3		100	60	28-30	29-30
f.			80	120	oil	oil
g.			95	15	70-73	73-75
h.			100	10	oil	oil

(*continued*)

Table (Contd.): Oxidation of sulfides to sulfoxides

	Sulfide (1)	Sulfoxide (2)	Yield%	Rxn. time min.	mp/bp °C	(reported)[18]
i.			97	40	148-150	150-151
j.			85	80	46-48	47-50
k.	Ph—S—CH_2CH_3		96	20	oil	oil
l.	Ph—S—CH_2—Ph		96	45	122-124	122-123
m.	Ph—S—Ph	Mixture of products	–			
n.	CH_3—S—CH_2—Ph		93	20	52-54	53-54
o.		Mixture of products	–			
p.		Mixture of products	–			

used as received from the supplier without any further purification. Sulfides **1a-e**, **1g-k, 1m-p** were purchased from Aldrich Chemical Company, U. S. A. and used without further purification. Sulfides **1f** and **1l** were prepared according to a known procedure.[7] Ceric ammonium nitrate was purchased from Aldrich Chemical Company, U. S. A. The silica gel used in the oxidation reactions as solid support was MN-Kieselgel 60 (0.04-0.063 mm mesh size) supplied by Fisher Scientific. NMR spectra were recorded on a Hitachi-Perkin Elmer R24A 60 MHz NMR instrument. Samples for NMR were dissolved in $CDCl_3$. ^1H chemical shifts are expressed as ppm relative to tetramethylsilane. IR spectra were recorded on an Analect RFX-30 FT-IR instrument and are reported in wavenumbers (cm^{-1}). Chromatographic separations were carried out by preparative centrifugal thin-layer chromatography with silica gel (Merck #7749) on a Chromatotron Model 7924T. Analytical thin-layer chromatography was done on precoated silica gel plates with 254 nm fluorescent indicator (Merck # 5715) and developed in the indicated solvent systems. Compounds were visualized under uv lamp and/or by staining either with a *p*-anisaldehyde/sulfuric acid or phosphomolybdic acid.

Oxidation of dibutyl sulfide to the dibutyl sulfoxide: a general procedure for sulfides (1a-p) oxidation.

The following oxidation procedure for butyl sulfide is representative of *all* sulfides presented in the Table.

Dry silica gel (5 g) was placed in a 100 mL round bottom flask containing a magnetic stirring bar and a loosely fitted rubber septum. Water (2.5 g) was added dropwise to the vigorously stirred silica gel. After complete addition of the water, stirring continued until a free flowing powder was obtained (5 min). Ceric ammonium nitrate (2.74 g, 5 mmol) was added to the above hydrated silica gel. The contents of the above flask was stirred for 5 minutes followed by the addition of methylene chloride (25 mL). A solution of butyl sulfide **1a** (365 mg, 2.50 mmol) in methylene chloride (5 mL) was added slowly to the stirred heterogeneous mixture. The orange color of the CAN disappeared instantly. The reaction mixture was stirred at room temperature for 10 minutes. During this period, complete disappearance of the butyl sulfide was evident by thin-layer chromatography using ethyl acetate:hexane (1:1) as the developing solvent and *p*-anisaldehyde/sulfuric acid as the staining agent. The reaction mixture was then filtered through a sintered glass funnel, the solid residue was washed with methylene chloride (40 mL) and the washings were added to the filtrate. Removal of solvent from the methylene chloride solution under vacuum produced a colorless thick oil. Radial chromatography of the crude product using ethyl acetate:hexane (1:1) as the eluent produced butyl sulfoxide **2a** as a colorless thick oil (405 mg, 100% yield).

Spectral data for Compounds (2a-p):

Products 2a-p are known compounds and their identities were

established by comparison of their NMR and IR data with the data reported in the literature reference.

Dibutyl Sulfoxide 2a[9]

^{1}H NMR 0.974 (t, 6H, J=7.32 Hz), 1.20-1.8 (m, 8H), 2.70 (t, *J*=7.2 Hz, 4H). IR 1022, 1270, 1406, 1415, 1449, 2887, 2940, 2974.

***Ditert*-Butyl sulfoxide 2b**[10]

^{1}H NMR 1.35 (s). IR 826, 1029, 1045, 1186, 1226, 1378, 1485, 2876, 2941, 2973.

Tetrahydrothiophene oxide 2c[9]

^{1}H NMR 1.80-2.50 (m, 4H), 2.55-2.90 (m, 4H). IR 1028, 1225, 1236, 1618, 1775, 1735, 2887, 2952.

4-oxo-1,4-thioxane 2d[11]

^{1}H NMR 2.40-3.10 (m, 4H), 3.50-4.50 (m, 4H). IR 1025, 1038, 1081, 1124, 1234, 1289, 1398, 1409, 1485, 1665, 2871, 2936, 2980.

Methyl phenyl sulfoxide 2e[9]

^{1}H NMR 2.68 (s, 3H), 7.40-7.70 (m, 4H). IR 692, 754, 954, 1046, 1092, 1415, 1446, 1477, 2915, 3000, 3062.

Ethyl α-sulfinylphenyl propionate 2f[12]

^{1}H NMR 1.00-1.50 (m, 6H), 3.40- 4.50 (m, 3H), 7.45 (m, 5H). IR 701, 759, 1060, 1094, 1180, 1232, 1325, 1385, 1464, 1741, 2873, 2920, 2954, 2988, 3070.

Methyl 4-methylbenzene sulfoxide 2g[13]

^{1}H NMR 2.40 (s, 3H), 2.70 (s, 3H), 7.30 (d, *j*=8.5 Hz, 2H), 7.50 (d, *j*=8.5

Hz, 2H); IR 820, 962, 1049, 1093, 1420, 1507, 1605, 2882, 2936, 3000, 3056.

4-methoxybenzene methyl sulfoxide 2h[13]

^{1}H NMR 2.60 (s, 3H), 3.80 (s, 3H), 7.00 (d, *j*=9 Hz, 2H), 7.50 (d, *j*=9 Hz, 2H). IR 824, 977, 986, 1026, 1103, 1185, 1267, 1321, 1474, 1517, 1615, 2860, 2915, 2969, 2990, 3078, 3100.

Methyl 4-nitrobenzene sulfoxide 2i[14]

^{1}H NMR 2.80 (s, 3H), 7.75 (d, *j*=9 Hz, 2H), 8.30 (d, *j*=9 Hz, 2H). IR 748, 863, 967, 1048, 1094, 1348, 1533, 2868, 2925, 3029, 3110.

Thiooxochroman-4-one s-oxide 2j[15]

^{1}H NMR 2.90 (m, 1H), 3.44 (m, 3H), 7.67 (t, *J*=7.4, 7.6 1H), 7.70 (t, *J*=7.4, 7.6 1H), 7.91 (d, *J*=7.6, 1H), 8.10 (d, *J*=7.6, 1H). IR 786, 1054, 1185, 1294, 1338, 1447, 1589, 1698, 2909, 2942, 2985, 3028, 3072.

Ethyl phenyl sulfoxide 2k[16]

^{1}H NMR 1.02 (t, *j*=8 Hz, 3H), 2.50-3.01 (m, 2H), 7.40 (m, 5H). IR 692, 749, 965, 1022, 1040, 1078, 1412, 1446, 1488, 2954, 2976, 3056.

Benzyl phenyl sulfoxide 2l[17]

^{1}H NMR 3.97 (d, *J*=12.5 Hz, 1H), 4.07 (d, *J*=12.5 Hz, 1H), 6.88-7.00 (m, 2H), 7.20-7.37 (m, 3H), 7.38-7.50 (m, 5H). IR 696, 753, 1042, 1089, 1447, 1500, 2914, 2972, 3064.

Diphenyl sulfoxide 2m[12]

^{1}H NMR 7.40-7.45 (m, 6H), 7.60-7.64 (m, 4H). IR 708, 766, 1049, 1104, 1453, 1485, 3067.

Benzyl methyl sulfoxide 2n[13]

^{1}H NMR 2.46 (s, 3H), 4.00 (s, 2H), 7.10-7.40 (m, 5H). IR 1010, 1285, 1368, 1450, 1505, 3060.

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