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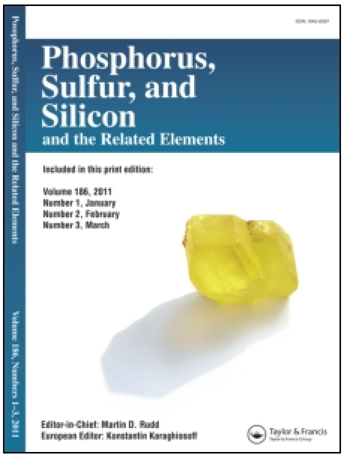

Phosphorus, Sulfur, and Silicon and the Related Elements

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1-BUTYL-4-AZA-1-AZONIABICYCLO[2.2.2]OCTANE DICHROMATE (BAAOD): AN EFFICIENT AND NOVEL REAGENT FOR OXIDATION OF SULFIDES TO THE CORRESPONDING SULFOXIDES

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This article describes an efficient and easy method for oxidation of sulfides ***1*** *to their corresponding sulfoxides* ***2*** *with 1-butyl-4-aza-1-azoniabicyclo[2.2.2]octane dichromate (BAAOD) under nonaqueous conditions in high yields.*

Keywords: DABCO; dichromate; oxidation; sulfides; sulfoxides

Sulfoxides play an important role in organic chemistry.[1–4] They have been utilized extensively in carbon-carbon bond formation reactions and as versatile building blocks in organic synthesis.[5,6] Oxidation of sulfides is a very useful route for preparation of sulfoxides. Several methods are available for conversion of sulfides to sulfoxides.[7–19] However, most of the existing methods use expensive or rare oxidizing reagents that are difficult to prepare. Many of these procedures also suffer from poor selectivity and also often suffer from lack of generality and economic applicability. Therefore, there is a need for a simple, inexpensive, general, and safer method for conversion of sulfides to sulfoxides.

RESULTS AND DICUSSION

In continuation of our ongoing program to develop efficient reagents for oxidizing organic compounds,[20] we now report a facile and selective

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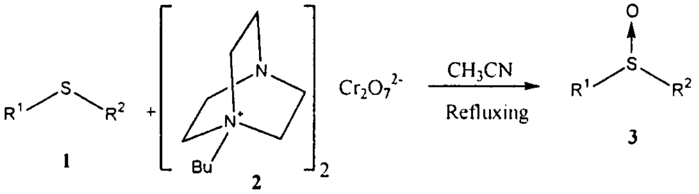
method for oxidation of sulfides **1** to their corresponding sulfoxides **3** with 1-butyl-4-aza-1-azoniabicyclo[2.2.2]octane dichromate **2** (BAAOD) in acetonitrile under nonaqueous conditions. This reagent is an orange powder, which is prepared by the dropwise addition of an aqueous solution of CrO_3 in 6 N HCl to an aqueous solution of 1-butyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide at room temperature. Filtration and drying of the precipitates produced an orange powder of 1-butyl-4-aza-1-azoniabicyclo[2.2.2]octane dichromate **2** (BAAOD). This reagent is a mild, efficient oxidizing agent, which can be stored for months without losing its oxidation ability. This reagent is quite soluble in methylene chloride, chloroform, acetone, and acetonitrile and insoluble in nonpolar solvents such as carbon tetrachloride, *n*-hexane, and diethyl ether.

We tried the reaction under nonaqueous conditions in different solvents, such as acetone, dichlormethane, chloroform, ethyl acetate, diethyl ether and acetonitrile under refluxing conditions. We discovered that acetonitrile was the best solvent for oxidation of sulfide to sulfoxide (Table I). The oxidations are carried out simply in a round-bottomed flask by stirring a mixture of this reagent and sulfides **1** in refluxing MeCN. After a given time (Table II), the sulfoxides **3** are isolated by straightforward procedure and overoxidation in this method was not a



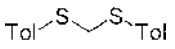
SCHEME 1

TABLE I Oxidation of Thioanisole to Methylphenyl Sulfoxide with **BAAOD 2** in Different Solvents under Refluxing Conditions

Entry	Solvent	Ratio of Oxidant/PhSMe	Reaction Time (h)	Yield (%)[a]
1	CH_2Cl_2	1.2:1	12	15
2	CH_3Cl	1.2:1	12	25
3	Et_2O	1.2:1	12	30
4	EtOAc	1.2:1	12	25
5	THF	1.2:1	10	40
6	Acetone	1.2:1	5	30
7	Acetonitrile	1.2:1	50 min	98

[a] Monitored by TLC analysis.

TABLE II Oxidation of Sulfides **1** to Sulfoxides **3** with **BAAOD 2** in Refluxing $CH_3CN^{a,b}$

Entry	R_1	R_2	Reaction time (min)	Yield (%)[c]
1	Ph	Me	50	98
2	Ph	*n*-Bu	62	98
3	Ph	$PhCH_2$	60	95
4	$PhCH_2$	Me	63	96
5	$PHCH_2$	*n*-Bu	55	92
6	$PhCH_2$	$PhCH_2$	55	93
7	$4\text{-}MeC_6H_4$	Me	50	95
8	$4\text{-}ClC_6H_4$	Me	65	85
9	C_4H_9	C_4H_9	85	83
10	1-Naphthyl	Me	50	93
11	Pr	Pr	85	82
12	Allyl	Allyl	65	84
13	Ph	CH_2Cl	65	89
14	$4\text{-}MeC_6H_4$	CH_2Cl	65	91
15	1-Napphtyl	$PhCH_2$	55	95
16	1-Napphtyl	CH_2Cl	55	86
17	$4\text{-}NO_2C_6H_4$	Me	50	90
18	$4\text{-}CHOC_6H_4$	Me	55	91
19	$4\text{-}OHCH_2C_6H_4$	Me	65	90
20	$4\text{-}NCC_6H_4$	Me	65	96
21	Ph	CH_2CH_2OH	70	88
22	$4\text{-}MeOC_6H_4$	CH_2Cl	55	95
23	$-(CH_2)_{4}-$	—	85	90
23	$-(CH_2)_{3}-$	—	80	92
24		—	60	89
25		—		
26		—	50	80[d]
27		—	60	78[e]
28		—	60	74[f]

[a] Confirmed by comparison with authentic samples.[14–19]
[b] Substrate/oxidant (1:1.2 mmol).
[c] Yield of isolated pure products.
[d] 10% disulphoxide.
[e] 20% disulphoxide.
[f] 22% disulphoxide.

problem. This method offers a simple, general, selective and highly efficient route for converting sulfides **1** to the corresponding sulfoxides **3**.

The generality of the method was examined using alkyl aryl, dialkyl, diaryl, cyclic sulfide, and aryl disulfide. It was discoverd that a wide variety of sulfides can be selectivly oxidized by this inexpensive reagents under mild conditions (Table II). The rates of reactions of arylalkyl and diaryl sulfides are not dependent on the subtituents on the aromatic ring. The reagent was chemoselective, tolerating various functional groups, such as, methoxy, carbonyl, hydroxy, nitro, nitrile, C=C double bonds, and halide. This method is a versatile procedure for synthesis of α-chloro sulfoxides from their corresponding sulfides (Table II, entries 13 and 14).

In conclusion, we report an easy and versatile method for converting sulfides to their corresponding sulfoxides with the following advantages:

(a) Our reagent is inexpensive and easily handed, which can be stored on the bench for months without losing its activity.
(b) The procedure is simple and occurs under non-aqueous conditions in refluxing acetonitrile.
(c) The yield of sulfoxide is high and the reaction time is short.
(d) The isolation of product is straightforward.

EXPERIMENTAL

General

Yields refer to isolated pure products after column chromatography. The products were characterized by comparison of their spectral (IR, ^{1}H NMR) and physical data with those of authentic samples.[14–19] All ^{1}H NMR spectra were recorded at 300 and 500 MHz in $CDCl_3$ relative to TMS (0.00 ppm) and IR spectra were recorded on Shimadzu 435 IR spectrometer. All reactions were carried out in refluxing acetonitrile.

Preparation of 1-Butyl-4-aza-1-azoniabicyclo[2.2.2]-octane Bromide

A solution of 1,4-diazoniabicyclo[2.2.2]octane (11.2 g, 100 mmol) and 1-bromo-butane (27.4 g, 200 mmol) in 100 mL of acetone was was refluxed for 30 min to afford a white powder. After cooling the reaction moxure, the resulting white precipitate was removed by filtration and washed with ether (2 × 50 mL), to afford **1**-butyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide as an white powder (22.90 g, 92% yield).

Preparation of 1-Butyl-4-aza-1-azoniabicyclo[2.2.2]-octane Dichromate (BAAOD) (1)

To a solution of 1-butyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide (24.90 g, 100 mmol) in 100 mL of water was added dropwise a solution of CrO_3 (10 g, 100 mmol) in 100 mL of HCl (3 N). The above solution was stirred for 20 min at room temperature. The resulting orange precipitate was removed by filtration and washed with cooled distilled water (2 × 50 mL), and dried in a desiccator under vacuum over calcium chloride to afford an orange powder (26.3 g, 95% yield), which decomposed at 117–118°C to a dark brown material. ^{1}H-NMR (d_6-DMSO, 500 MHz): $\delta = 3.66$ (m, 24 H), 1.48 (m, 10 H), 0.92 (m, 8 H). ^{13}C-NMR (d_6-DMSO, 75 MHz) $\delta = 64.74, 51.86, 44.93, 41.95, 41.45, 40.95, 40.79, 24.69, 20.42, 14.83$; Anal calcd for $C_{20}H_{42}N_4Cr_2O_7$: C, 39.41; H, 6.95; N, 9.19%. Found: C, 39.56; H, 6.73; N, 9.25%.

Typical Procedure for Oxidation of Sulfides 2 to Sulfoxides 3 with Reagent 1

To a solution of thioanisole (1 mmol, 0.124 g) in acetonitrile (5 mL) in a 25 mL round-bottomed flask which was equipped with a condenser and a magnetic stirrer, reagent **1** (1.2 mmol, 0.66 g) was added. The reaction mixture was refluxed for 50 min. After disappearance of the starting sulfide monitored by TLC using EtOAc/cyclohexane (2:8), the mixture was filtered through a sintered glass funnel, the solid residue was washed with acetonitrile (10 × 2 mL). The solvent was removed under reduced pressure. The residue was purified by column chromatography using silica gel (EtOAc/cyclohexane, 2:8) to afford methyl phenyl sulfoxide as a colorless oil in 98% yield as revealed from ^{1}H NMR analysis, mp 30–32°C [Lit.[16] m.p. 32–33°C]. ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 2.7$ (s, 3H), 7.48–7.56 (m, 3H), 7.64–7.67 (m, 2H). IR (film): $\upsilon = 692, 754, 954, 1046, 1092, 1415, 1446, 1477, 2915, 3000, 3062$ cm^{-1}.

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