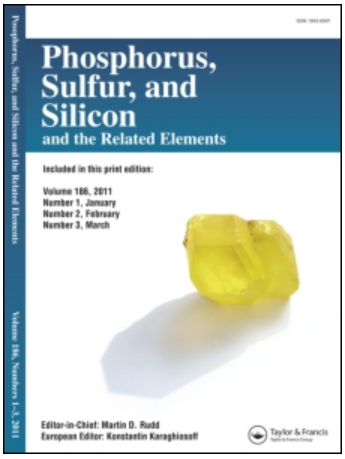

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Oxidation of Thiols Using $K_2S_2O_8$ in Ionic Liquid

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A green, straightforward, and novel method for oxidation of thiols to the corresponding disulfides is reported using $K_2S_2O_8$ in the ionic liquid 1-butyl-3-methylimidazolium bromide [(bmim)Br] at 65–70°C. The corresponding disulfides were obtained in excellent yield and short reaction time.

Keywords Disulfides; ionic liquid; $K_2S_2O_8$; oxidation; thiols

INTRODUCTION

Oxidation of thiols to the corresponding disulfides under mild conditions is a useful reaction from the point of view of biological and industrial applications.[1] Since thiols can be over-oxidized, extensive research has been performed to control their oxidation at the disulfide stage.[2]

The oxidation coupling of thiols to disulfides is an essential reaction in the synthesis of natural products, and further oxidation to disulfide S-oxides (thiosulfinates), 1,1-dioxides (thiosulfonates), and sulfonic acids is possible. Weak S-S bonds in these compounds impart high reactivity,[3] and in natural products, these moieties and related cyclic analogues are associated with interesting biological activity.[4]

Ionic liquids (IL) have frequently been used as green solvents in place of conventional organic solvents,[5–9] being superior due to their

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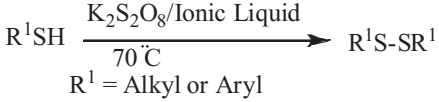
extremely low vapor pressure, excellent thermal stability, reusability, and ability to dissolve many organic and inorganic substrates.[10] The application of ionic liquids as solvents and catalysts has been reported for a variety of functional group transformations, but their use as acid catalysts under solvent-free conditions deserves more attention.[11]

RESULTS AND DISCUSSION

In connection with our ongoing program on developing new methods for organic functional groups transformation,[12–17] we wish to report the applications of potassium persulfate, $K_2S_2O_8$, in ionic liquid, 1-butyl-3-methylimidazolium [(bmim)Br] and the use of this efficient, inexpensive, and mild reagent for oxidizing a variety of aliphatic and aromatic thiols.

This method is effective for coupling of aliphatic and aromatic thiols to the corresponding disulfides. It was found that only traces of further oxidation products such as S-oxides (thiosulfinates), 1,1-dioxides (thiosulfonates), and sulfonic acids are formed. A series of thiols was oxidized to disulfides rapidly using this reagent. Primary alcohol, amine, carboxylic acid, ester, and methoxy functional groups were unaffected during the oxidation (Scheme 1 and Table I).



SCHEME 1

In conclusion, this is a new and green method for oxidation of thiols to the corresponding disulfides. The green chemistry, straightforward workup, mild reaction conditions, high yields of the products, and short reaction time make this a useful method for oxidation of thiols to disulfides.

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.[15] All $_1$H NMR spectra were recorded at 300 MHz in $CDCl_3$ relative to TMS (0.00 ppm), and IR spectra were recorded on Shimadzu 435 IR spectrometer.

TABLE I Oxidation of Thiols to Disulfides[a,b,c]

Reactant	Product	Reaction (min)	Time Yield (%)	Mp or Bp/mmHg °C (Lit) [15]
C_6H_5SH	$(C_6H_5S)_2$	10	94	59–61 (59–61)[15]
4-MeC_6H_4SH	(4-$MeC_6H_4S)_2$	15	93	47–48 (47–48)[15]
4-$MeOC_6H_4SH$	(4-$MeOC_6H_4S)_2$	20	88	44–45 (44–45)[15]
4-$NH_2C_6H_4SH$	(4-$NH_2C_6H_4S)_2$	20	84	76–77 (75–77) [15]
3-MeC_6H_4SH	(3-$MeC_6H_4S)_2$	10	94	–21 (–21)[15]
4-ClC_6H_4SH	(4-$ClC_6H_4S)_2$	20	90	72–73 (72–73)[15]
2-$Me_2OCC_6H_4SH$	(2-$MeOOCC_6H_4S)_2$	10	91	197–198 (198–199) [15]
$C_6H_5CH_2SH$	(C_6H_5 $CH_2S)_2$	20	90	69–70 (69–70)[15]
4-$NO_2C_6H_4SH$	(4-$NO_2C_6H_4S)_2$	20	90	177–178 (172–178)[15]
2-PyridylSH	(2-PyridylS)$_2$	20	92	52–53 (52–53)[15]
4-PyridylSH	(4-PyridylS)$_2$	25	92	76–77 (76–77)[15]
CyclopentylSH	(CyclopentylS)$_2$	20	98	105–106 (105–106)[15]
CyclohexylSH	(CyclohexylS)$_2$	25	84	124 129 (124–129)[15]
HO-CH_2CH_2SH	(HO-$CH_2CH_2S)_2$	25	84	Thick oil (156–1148/2)[15]
$H_2OCCH_2CH_2SH$	($HOOCCH_2CH_2S)_2$	20	86	157–159 (157–159)[15]
$HOOCCH_2SH$	($HOOCCH_2S)_2$	25	90	139–141 (138–139)[15]
$CH_3(CH_2)_3SH$	($CH_3(CH_2)_3S)_2$	30	80	94–96/6 (94–96/6)[15]
$CH_3(CH_2)_4SH$	($CH_3(CH_2)_4S)_2$	30	84	oil (117–119/6)[15]
$CH_3(CH_2)_6SH$	($CH_3(CH_2)_6S)_2$	30	83	oil (152–154/6)[15]
$CH_3(CH_2)_7SH$	($CH_3(CH_2)_7S)_2$	20	92	Semi solid (143–147/5)[15]
1-$(HSCH_2)_2C_6H_4$	(-$SCH_2C_6H_4CH_2S$-)$_n$	25	84	–

[a]Confirmed by comparison with authentic samples (IR, TLC, and NMR).
[b]Oxidant/thiol/ionic liquid (1.0:1.0:1.0).
[c]Yield of isolated pure product after chromatography or distillation.

All reactions were carried out at room temperature in a hood with strong ventilation.

Procedure for Oxidation of Thiols to the Corresponding Disulfide: Typical Procedure

A mixture of thiophenol (10 mmol, 1.1 g) , $K_2S_2O_8$(2.7 g, 10 mmol), and [bmim]Br (2.7 g, 10 mmol) was ground for 1 min with a mortar and pestle. The mixture was transferred to a round-bottomed flask and kept at 65–70°C for the time specified in Table I. The progress of the reaction was followed by TLC/GC. After the reaction was completed (Table I), 20 mL of diethyl ether was added and the reaction mixture was filtered through a sintered glass funnel, the filtrate was transferred to a separatory funnel and washed with $NaHCO_3$ (5%). The organic layer was dried over anhydrous Na_2SO_4, and the solvent was removed in vacuo. The residue was purified through a short column of silica gel

(cyclohexane:EtOAc, 3:1) to obtain diphenyl disulfide in 94% yield, mp 59–61°C [Lit.[16] mp 58–61°C]. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.62–7.48 (m, 4H), 7.42–7.20 (m, 6H). IR (KBr): 459, 470, 687, 734, 1435, 1474, 1572, 3050 cm^{-1}.

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