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Note

1-Benzyl-1-aza-4-azoniabicyclo[2.2.2]-octane periodate as new oxidant for oxidation of thiols and sulfides to the corresponding disulfides and sulfoxides under anhydrous conditions

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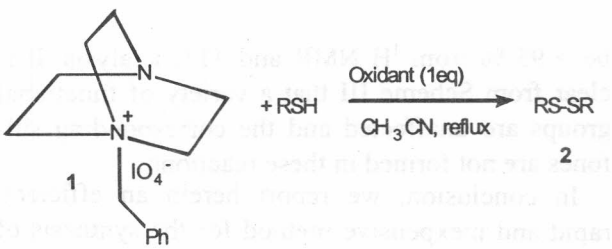
1-benzyl-1-aza-4-azoniabicyclo[2.2.2]octane periodate (BAABCOP) **1**, readily prepared as an orange solid from commercially available DABCO (1,4-diazobicyclo[2.2.2]octane) performs oxidation in anhydrous conditions. Under these conditions, thiols are selectively oxidised to disulfides. Sulfides are also oxidised to the corresponding sulfoxides under these conditions.

The conversion of mercaptans to disulfides is a useful transformation and is of importance both from a biological and practical point of view[1].

The reported reagents known to convert thiol to disulfide include, iodine-hydrogen iodide[2], thallium (III) acetate[3], bromine/aqueous potassium hydrogen carbonate[4], barium permanganate[5], zinc bismuthate[6], and lead tetraacetate[7]. These reagents suffer from either one or more of the following drawback such as availability of the reagent, preparation and stability of the reagent, cumbersome work up procedure, toxic or high cost of the reagent and oxidation of other functional groups in the presence of thiol group.

Sulfoxides find wide application in organic synthesis, particularly in carbon-carbon bond forming process[8]. These compounds are almost invariably prepared by oxidation of the corresponding sulfides, and several ways of achieving this transformation have been reported[9]. Unfortunately, many of these processes suffer major drawbacks, for example, where hazardous organic peracids are used, or in use of mixed phase reactions which lead to problems during work-up and also further oxidation of intermediate sulfoxides to the corresponding sulfone[10].

As part of an ongoing synthetic project we required an efficient and rapid method for the synthesis of a number of disulfides and sulfoxides from the corresponding thiols and sulfides respectively. We have found that reaction of 1-benzyl-1-aza-4-azoniabicyclo[2.2.2]octane periodate (BAABCOP) **1**, with thiols gave disulfides **2**, the reagent **1** was examined on a wide array of substrates such as aliphatic, aromatic and heterocyclic thiols (Scheme I), and we observed that the corresponding disulfides **2** were obtained in very high yields (95-99%), and in highly diminished reaction time (15-30 min) .

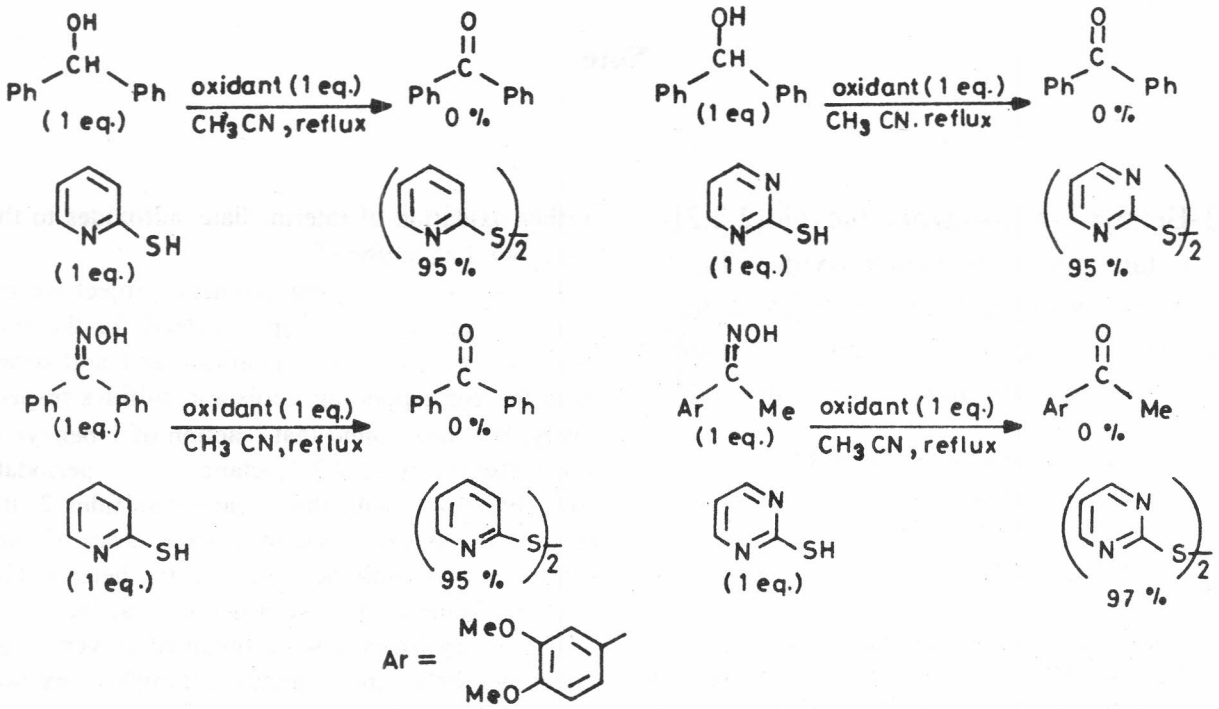


R= a) 2-benzimiazoyl b) 2-pyridyl
c) *p*-tolyl d) *p*-nitrophenyl
e) *p*-chlorophenyl f) phenyl
g) 2-naphthyl h) *o*-nitrophenyl
i) *o*-chlorophenyl j) *o*-chlorophenyl
k) n-butyl

Scheme I

Another noteworthy of the reagent lies in the exclusive formation of the disulfides irrespective of the presence of other oxidisable function (oxime and alcohol). When we treated one equivalent of thiol in the presence of very reactive benzyl alcohol or oxime only the thiol selectively oxidised (**Scheme II**).

We have also found that by oxidation of sulfides **3** with **1** to the corresponding sulfoxides **4** (Scheme III), the oxidation is rapid (15-30 min.), and almost quantitative from ^{1}H NMR analysis. In all cases, the yield of crude product was judged to

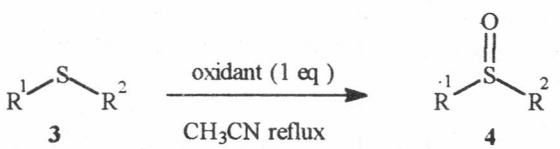


Scheme II

be > 95 % from ^{1}H NMR and TLC analysis. It is clear from Scheme III that a variety of functional groups are unaffected and the corresponding sulfones are not formed in these reactions.

In conclusion, we report herein an efficient, rapid and inexpensive method for the synthesis of disulfides and sulfoxides that is superior to previously reported methods in terms of selectivity, yields and purity of products and also rapid and easy workup.

Preparation of 1-benzyl-1-aza-4-azoniabicyclo[2.2.2]octane periodate (BAABCOP) 1: General procedure. The reagent was prepared in two steps, in step one, to a solution of 1,4-diazobicyclo[2.2.2]octane (DABCO) (0.1 mole, 11.22g) in acetone (200 mL) was added benzyl bromide (0.1 mole, 17.1 g) dropwise, the white solid of 1-benzyl-1-aza-4-azoniabicyclo[2.2.2]-octane bromide was precipitated, the crystals were collected, washed with acetone (20 mL) and then dried under high vacuum (0.01 mm Hg), yield 25.5 g (90 %). In step two, to a solution of 1-benzyl-1-aza-4-azoniabicyclo[2.2.2]octane bromide (0.05 mole, 14.15 g) was added a solution of $NaIO_4$ (0.05 mole, 10.70 g) in H_2O (20 mL) dropwise, the orange solid of 1-benzyl-1-azo-4-azoniabicyclo[2.2.2]octane periodate (BAABCOP)



R^1	R^2
Ph	Me
Ph	$PhCH_2$
Ph	Et
Ph	CH_2CO_2Me
Ph	CH_2CO_2tBu
Ph	$Ar'COCH_2$
Ph	$Ph\ COCH_2$
p-Tolyl	Me
p-Tolyl	$PhCH_2$
p-Tolyl	Et
p-Toly	CH_2CO_2Me
p-Toll	CH_2CO_2tBu
p-Toyl	$Ar'COCH_2$
p-Tlyl	$Ph\ COCH_2$
2-pyridyl	$PhCH_2$
p-Tolyl	*n*-butyl
2-pyridyl	*n*-butyl
Ph	$PhSCH_2$
p-Tolyl	*p*-$C_6H_4SCH_2$

Ar'=3,4-$(MeO)_2C_6H_3COCH_2$

Scheme III

1 was precipitated. The reaction mixture was stirred at -5°C for 30 min., the crystals were collected, washed with water (20 mL) and then dried under high vacuum (0.01 mm Hg), yield 19.90 g (80 %).

Preparation of disulfide 2. The thiol (2 mmoles) was added to a stirred solution of oxidant **1**, (2 mmoles, 0.79 g) in acetonitrile (15 mL). The mixture was heated at reflux until TLC showed complete disappearance of starting material, which required 15-30 min, depending on the substrate. The mixture was cooled and 3 g silica gel was added to the reaction mixture and was stirred for 5 min, the solid was then separated by filtration through Celite and washed with acetonitrile (2×10mL) and the filtrate was then evaporated under reduced pressure to dryness to give disulfide **2**.

Preparation of sulfoxide 4. The sulfide **2**, (2 mmoles) was added to a stirred solution of oxidant **1** (3 mmoles, 1.20 g) in acetonitrile (15 mL). The mixture was refluxed and worked-up as reported for disulfide **2** to give sulfoxide **4**.

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