

## Oxidation of Methyl *p*-tolyl sulfide Mediated by 3-ethoxy-1, 2-benzisothiazole-1,1-dioxide using Various Bases in the Presence of Hydrogen peroxide

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### ABSTRACT

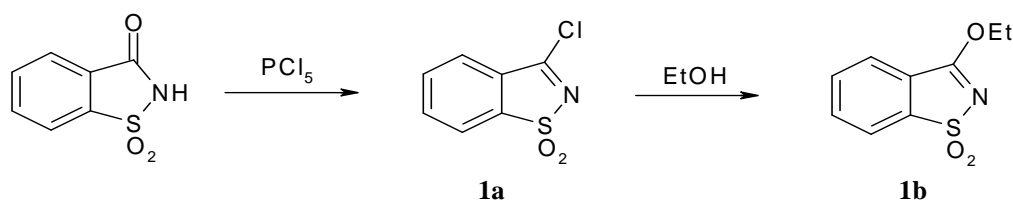
The oxidation of methyl *p*-tolyl sulfide to the corresponding sulfoxide is discussed using hydrogen peroxide which is very environmentally friendly primary oxidant by saccharin derivative, 3-ethoxy-1,2- benzisothiazole-1,1-dioxide. Meanwhile, the oxidation was examined in the presence of variety of organic bases.

**Keywords:** 3-Ethoxy-1,2-benzisothiazole-1,1-dioxide, Hydrogen peroxide, 1,5-Diazobicyclo[4.3.0]non-5-ene (DBN), 1,8-Diazabicyclo[5,4,0]undec-7-ene (DBU), *N, N*-Dimethylaniline, 4-Methylmorpholine.

### INTRODUCTION

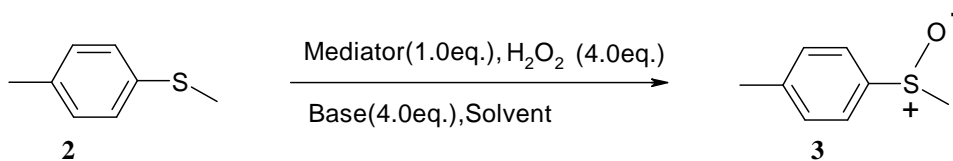
The use of sulfoxide as key intermediates for organic synthesis has drawn increasing interest in recent years [1-5]. Therefore, new methods and mediators for the preparation of sulfoxides continue to be developed [6-8]. The standard methods involve the oxidation of organic sulfides by various oxidizing reagents. The most common reagent to convert sulfides to sulfoxides is hydrogen peroxide alone or in the presence of various catalysts [9-15]. However, the major difficulty encountered in the preparation of sulfoxides by this method is over-oxidation to sulfones. Another drawback connected with the use of hydrogen peroxide is the relatively long reaction time which is needed for completion of the oxidation.

This article is concerned with the development of novel mediators for oxygen transfer to organic sulfides. The synthesis of 3-substituted-1,2-benzisothiazole-1,1-dioxides, **1a** was carried out from saccharin and phosphorus pentachloride. When **1a** was treated with ethanol, **1b** was obtained.



Scheme 1

The oxidation of methyl *p*-tolyl sulfide **2** was examined. The reactions were carried out by addition of a solution of hydrogen peroxide (35% w/v aqueous solution, 4.0 equiv.) to a stirred solution of base (4.0 equiv.) in the solvent, followed by the addition of mediator (1.0 equiv.).



Scheme 2

## MATERIALS AND METODS

Hydrogen peroxide (35 % w/v, 0.71 ml, 4.0 equiv.), was added to a stirred solution of base (4.0 equiv.) in dichloromethane (10 ml) at room temperature, followed by 3-ethoxy-1,2-benzisothiasole-1,1-dioxide (0.45 g, 2.13 mmol, 1.0 equiv.).

Methyl *p*-tolyl sulfide (0.29 ml, 2.17 mmol, 1.0 equiv.) was added, and the reaction mixture was stirred at room temperature for 2h, diluted with dichloromethane (10ml), washed with brine (10 ml) and saturated aqueous sodium sulfide (30ml), and dried over magnesium sulfate (2 g). Methyl *p*-tolyl sulfoxide was isolated as a white crystalline solid by evaporation to dryness followed by flash column chromatography using ethyl acetate (70 mg, 23 %), m.p. 39 - 40 °C (from DCM), FT-IR (nujol) /  $\text{cm}^{-1}$  1083 (S-O), 810, 3049;  $^1\text{H}$ NMR ( $\text{CDCl}_3$ );  $\delta_{\text{H}}$  2.42 (3H, s, Ar- $\text{CH}_3$ ), 2.70 (3H, s, S(O) $\text{CH}_3$ ), 7.28 (2H, d, *J*8, Ar), 7.50 (2H, d, *J*8, Ar); Ms,  $m/z$  = 154 (M+), 139, 91.

Table. Oxidation of methyl *p*-tolyl sulfide mediated by 1b at 25±1(°C)

| Entry | Base                        | Time  | Yield,% |
|-------|-----------------------------|-------|---------|
| 1     | DBU                         | 2h    | 08      |
| 2     | DBU                         | 2days | 13      |
| 3     | DBN                         | 2h    | 20      |
| 4     | DBN                         | 2days | 30      |
| 5     | 4-Methylmorpholine          | 2h    | 23      |
| 6     | 4-Methylmorpholine          | 2days | 04      |
| 7     | <i>N,N</i> -Dimethylaniline | 2h    | 37      |
| 8     | <i>N,N</i> -Dimethylaniline | 2days | 50      |
| 9     | $\text{K}_2\text{CO}_3$     | 2days | 33*     |

\*Methanol was used as solvent

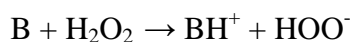
## RESULTS AND DISCUSSION

Oxidation of sulfide to sulfoxide in the presence of each intermediates can be carried out by hydroperoxy imine or oxaziridine and this reaction was reported by Davis [16] and Bulman Page [17], independently.

In sulfoxidation reaction, stronger bases increase the concentration of  $\text{OOH}^-$  (Scheme 3), and the concentration of hydroproxy amine or oxaziridine, therefore the efficiency of reaction for the oxidation proceeded. 4-Methylmorpholine ( $\text{pK}_a = 7.38$ ) [18], DBN ( $\text{pK}_a = 13.1$ ) [19] and DBU ( $\text{pK}_a = 13.4$ ) [20] are more basic than *N,N*-dimethylaniline ( $\text{pK}_a = 5.07$ ) [18] and the efficiency of sulfoxidation reactions in the presence of former bases should be more, while the reaction is

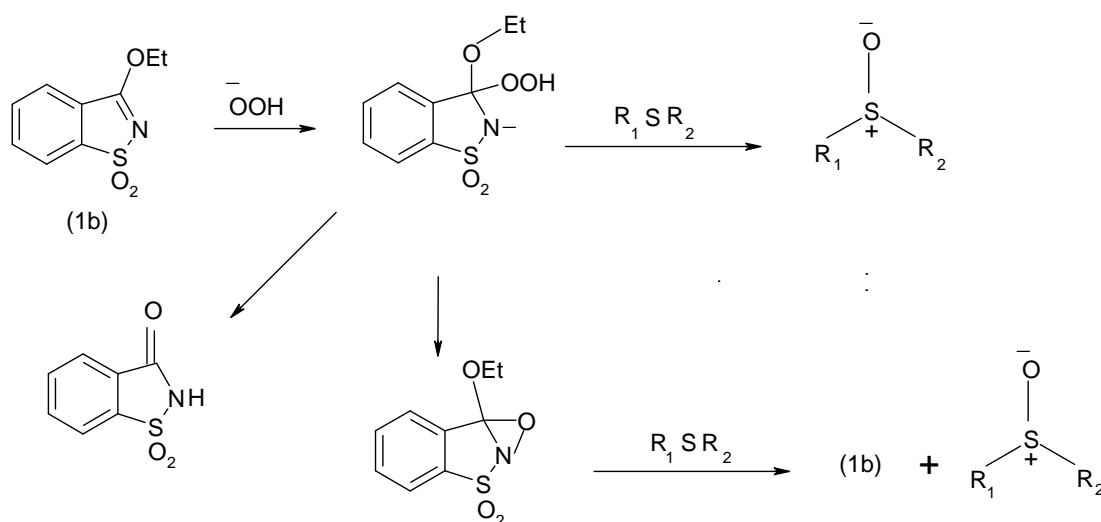
proceeded more efficiently with the latter base (Table, entry 2,4,6,8). It is obvious that the base should not be a good nucleophile, since it can react with sulfonylimine as it was reported [21]. *N,N*-Dimethylaniline is possibly less nucleophile than 4-methylmorpholine, DBN and DBU, and should be more efficient in the oxidation reaction.

Hydrogen peroxide (0.1-0.01 N aqueous solution) has a  $pK_a$  value of 11.62 [22]. The difference between the  $pK_a$  values of DBU, DBN and hydrogen peroxide indicates that in water the equilibrium lies >88% toward protonated DBU, DBN (Equation).



Mediation of O-transfer probably requires  $HOO^-$  attack on the sulfonylimine and this would necessitate transfer of  $HOO^-$  from water to dichloromethane.  $BH^+$  then assists this phase transfer process by pairing with  $HOO^-$  to preserve charge neutrality.

To assess the degree of sulfoxidation of methyl *p*-tolyl sulfide by direct oxidation by hydrogen peroxide itself, a control reaction was carried out using bases in dichloromethane from which the sulfonylimine was omitted. Analysis of the reaction mixture showed that hydrogen peroxide in basic media oxidises the sulfide only extremely slowly (Scheme 3).



**Scheme 3: The oxidation of methyl *p*-tolyl sulfide**

## CONCLUSION

Sulfoxidation was carried out using 3-ethoxy-1,2-benzisothiazole-1,1-dioxide and hydrogen peroxide, which for environmental point of view is the most attractive primary oxidant source for this process to date. Yields were generally lower using DBU, DBN, 4-methylmorpholine as base, except for the *N,N*-dimethylaniline, which showed good conversion of methyl *p*-tolyl sulfide to the corresponding sulfoxide. This is attributed to the less nucleophilicity of *N,N*-dimethylaniline than the other organic bases used.

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