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# SOLVENT EFFECTS IN THE OXIDATION OF THIOLS. IV. BASE CATALYZED OXIDATION OF THIOLS AND DISULFIDES TO SULFONIC ACIDS.

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IN the presence of strong oxidizing agents such as barium permanganate, boiling nitric acid, and hydrogen peroxide thiols are converted to sulfonic acids in yields varying from 30 to 90%[1-4]. The low temperature autoxidation of thiols in neutral media does not take place in the absence of added radical initiators such as peroxides, trace metals, or U.V. light and, in the absence of olefins, the primary oxidation products are disulfides[5]. The base-catalyzed autoxidation of thiols to disulfides occurs at low temperatures and the active species is the mercaptide ion ($RS^{\ominus}$)[6]. Some years ago, Xan and co-workers[7] studied the oxidation of thiols by molecular oxygen in alkaline solution. These workers reported that when oxidations were allowed to proceed to completion in the presence of an excess of strong alkali oxygen consumption in excess of that required for disulfide formation occurred. They attributed this finding to the formation of minor

$$2\ RSH + 0.5\ O_2 \longrightarrow RSSR + H_2O \qquad (1)$$

amounts of higher oxidation products (possibly sulfonic acids) but failed to establish the structure of such products. Previous studies in these laboratories have established that dipolar solvents markedly acclerate the low temperature anionic oxidation of thiols to disulfides at conversion levels of 25-30%[8,9,10]. Based on the observations of Xan et al., we have extended our earlier studies and now wish to report that at high levels of conversion mercaptide ions and disulfides can be oxidized to sulfonic acids at 23.5° in dipolar solvents such as dimethylformamide (DMF). To our knowledge, these are the first definitive examples of the low temperature oxidation of thiols and disulfides to sulfonic acids by molecular oxygen.

In a typical experiment, 25 mmoles of thiophenol were oxidized under a constant oxygen partial pressure of one atmosphere at 23.5°[11] for 22 hrs. in 75 ml. of a 1.3 molar solution of potassium hydroxide in DMF[12]. Potentiometric titration of the reaction mixture with standard silver nitrate solution indicated 96.5% of the thiol was converted to product. Reduction of a portion of the reaction mixture in a zinc/acetic acid solution and subsequent titration with silver nitrate indicated 0.3 g. of phenyl disulfide was present (4.7% yield, m.p. 60-62°, reported m.p.[13] 60-62°) The ion-exchange-spectrophotometric technique of Pobiner, Wallace, and Hofmann[14], which is both qualitative and quantitative, established that benzene sulfonic acid was formed (3.6 g., 91% yield, phenylhydrazinium salt, m.p. 178-180°, reported m.p.[15] 179°). 1-Butanethiol (25 mmoles) afforded n-butyl disulfide (9.3%) and 1-butane sulfonic acid (3.04 g., 88% yield, anilinium salt m.p. 159-161°, reported m.p.[16] 159-160°) when autoxidized under the above conditions for 17 hrs. para-Toluenethiol and ortho-toluenethiol gave better than 95% yields of their respective sulfonic acids[14] after 24 hrs. of oxidation in KOH/DMF. Thus, this reaction appears to be general and proceeds in high selectivity. Further, at temperatures of 80 to 100° reaction times of 3-4 hrs. suffice.

Experiments have also been carried out to determine the mode of formation of the acid. Both n-butyl disulfide and phenyl disulfide (12.5 mmoles) have been oxidized in KOH/DMF at 23.5° to their corresponding sulfonic acids in yields of 90% or better. Based on the moles of oxygen consumed/mole disulfide the aromatic disulfide was found to oxidize more rapidly than the aliphatic disulfide. In protic solvents such as water or alcohol anionic oxidation of these thiols at room temperature or 80° gives high yields of the disulfides[11] and the disulfides are not oxidized to any significant extent at 80° and 1 atmosphere pressure of oxygen. In the absence of added potassium hydroxide, thiol oxidations did not occur at 23.5° in DMF over a 20 hr. period. At 80°, long induction periods are observed. Addition of protic species to the dipolar solvent has a marked effect on the reaction. For example, in the presence of 30 volume % water autoxidation of 1-butanethiol ($KOH/1\text{-}C_4H_9SH = 4$) at 80° for 5 hrs. gave 42% of the disulfide and only 48% yield of 1-butane sulfonic acid. These results suggest that the reaction involves initial oxidation of the mercaptide ion to disulfide and subsequent nucleophilic attack on the disulfide linkage to produce a mercaptide ion and a sulfenate ion $(RSO)^{\ominus}$[17,18] which disproportionates to acid and disulfide. $RS^{\ominus}$ is reoxidized to the disulfide

$$RS^{\ominus} \xrightarrow{O_2} RSSR \xrightarrow{HO^{\ominus}} RS^{\ominus} + RSOH \qquad (2)$$

$$RSOH + HO^{\ominus} \longrightarrow RSO^{\ominus} + H_2O \qquad (3)$$

$$3\ RSO^{\ominus} \longrightarrow RSO_3^{\ominus} + RSSR \qquad (4)$$

and the cycle is repeated. Such a scheme is consistent with the greater ease of oxidation of phenyl disulfide and the deactivation of the base by protic species.

The above displacement reaction was further substantiated by adding phenyl disulfide (50 mmoles) to the base/dipolar solvent mixture under nitrogen. After 2 hrs., methyl iodide (50 mmoles) was added, the reaction mixture was diluted, neutralized with HCl, and extracted with ether. Distillation of the ether extract gave 2.89 g. of thioanisole, $C_6H_5\text{-}S\text{-}CH_3$, (theoretical, 2.85 g. based on disulfide converted) which was identified by its characteristic U.V. max. (235 mμ) and infrared comparison to an authentic sample.

At present, we would like to emphasize the use of KOH as the base. In the presence of stronger bases such as potassium *tert*-butoxide, a side reaction involving beta-proton abstraction from the disulfide to produce olefin and mercaptide ion occurs[19].

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