Solvent Effects in the Base-Catalyzed Oxidation of Mercaptans with Molecular Oxygen[1]

THOMAS J. WALLACE AND ALAN SCHRIESHEIM

Esso Research & Engineering Co., Process Research Division, Exploratory Research Section, Linden, N. J.

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The homogeneous base-catalyzed oxidation of *n*-butyl mercaptan with molecular oxygen has been studied at 23.5° in solvents of low dielectric and high nucleophilicity and in dipolar, aprotic solvents of high dielectric. The rate of oxidation was found to be first order in the mercaptan. The rate of formation of the disulfide in solvents such as diglyme (diethylene glycol dimethyl ether), dioxane, and tetrahydrofuran (THF) is thirty-five to one hundred times faster than that in methanol. In solvents such as dimethylformamide (DMF) and dimethylacetamide (DMAc), the rate is about three hundred times faster than in methanol. In each case, sodium methoxide was used as the base. These results are rationalized on the basis of a specific solvation of the sodium cation associated with the incipient sodium mercaptide which is initially formed. In addition, a brief study on how various alkoxide bases affect the rate of oxidation of *n*-butyl mercaptan in alcoholic media was also carried out.

As part of a general program on solvent effects in anionic reactions, the oxidation of mercaptans to disulfides in various solvents is being studied. This oxidation in aqueous sodium hydroxide[2] has been investigated extensively in the past. Standard oxidation procedures utilize either molecular oxygen or iodine[3] to effect this reaction which usually proceeds almost quantitatively to the disulfide with alkyl and aromatic mercaptans. More potent oxidizing agents such as hydrogen peroxide[4] and lead tetraacetate[5] are also used, but these usually lead to a mixture of products.

In the base-catalyzed oxidation, the active species is the anion which is initially formed in an equilibrium step with the base (step 1). The resulting mercaptide ion apparently reacts with oxygen to give the thiyl radical which dimerizes to give the disulfide (steps 2 and 3). The peroxide ion generated can then decompose by reaction with the solvent to produce hydroxide ions and oxygen (step 4).

$$\mathrm{RSH} + \mathrm{B} \rightleftarrows \mathrm{RS}^- + \mathrm{BH}^+ \quad (1)$$

$$2\mathrm{RS}^- + \mathrm{O}_2 \longrightarrow 2\mathrm{RS}\cdot + \mathrm{O}_2^= \quad (2)$$

$$2\mathrm{RS}\cdot \longrightarrow \mathrm{R}_2\mathrm{S}_2 \quad (3)$$

$$\mathrm{O}_2^= + \mathrm{H}_2\mathrm{O} \longrightarrow 2\mathrm{OH}^- + 0.5\mathrm{O}_2 \quad (4)$$

Similar reaction schemes have been proposed for the oxidation of carbanions with molecular oxygen.[6,7] It is evident that such a scheme indicates an oxidation rate dependent on the amount and reactivity of the mercaptide ion. Any factor that enhances the formation of the ion should accelerate the reaction rate. Indirect proof that this is the situation is found in the work of Kharasch,[8] who reported that thioglycolic acid was oxidized about thirty times faster than *n*-propyl mercaptan and some 960 times faster than *tert*-butyl mercaptan. While the low rate of oxidation of the *tert*-butyl mercaptan could be due to steric effects, the differences between the first two mercaptans are undoubtedly due to electronic factors.

The purpose of the present investigation was to determine the effect of both (a) highly nucleophilic and low dielectric solvents, and (b) dipolar, aprotic solvents of high dielectric on the rate of the base-catalyzed oxidation of mercaptans to disulfides. A brief study was also made on how various alkoxide bases effect the rate of oxidation of mercaptans in alcoholic media.

Results

Little information is available concerning the effect of solvents on the rate of the base-catalyzed oxidation of mercaptans. Most experimental attempts to obtain reproducible kinetic data have been performed in an aqueous caustic media[2,9] where mercaptans have a limited solubility. Because of this solubility limitation, the mercaptan oxidations discussed in this paper were carried out in methanol, ethanol, *tert*-butyl alcohol, dipolar-aprotic, and ethereal solvents where the mercaptan is soluble over the concentration ranges used. Sodium methoxide was employed as the base in methanol and the dipolar-aprotic and ethereal solvents. Sodium ethoxide was used in ethanol while sodium potassium, rubidium, and cesium *tert*-butoxides were used in *tert*-butyl alcohol.

One tenth of a mole of the *n*-butyl mercaptan was oxidized in one hundred milliliters of methanol, ethanol, *tert*-butyl alcohol, THF, dioxane, diglyme, DMF, and DMAc at 23.5 ± 0.2° under a constant

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(1) Presented at the 140th Meeting of the American Chemical Society in Chicago, Ill., September, 1961.

(2) E. E. Reid, "Organic Chemistry of Bivalent Sulfur, I," Chemical Publishing Co., Inc., New York, 1958.

(3) A. I. Vogel, "A Textbook of Practical Organic Chemistry," Longmans, Green and Co., London, England, 1959.

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(8) M. S. Kharasch, unpublished work. Reported in "Vistas in Free Radical Chemistry," Pergamon Press, New York, 1959, p. 101.

(9) N. H. Horton *et al.*, *J. Am. Chem. Soc.*, **63**, 1139 (1941).

oxygen pressure of one atmosphere. Two tenths of a mole of alkoxide base were used in each run, giving a 2:1 mole ratio of base to mercaptan. Each oxidation was carried out to about 40 to 50% completion. The amount of mercaptan converted to the disulfide at any given time was determined by the amount of oxygen consumed since it was determined experimentally that the stoichiometry for disulfide formation involves a 4:1 mole ratio of mercaptan to oxygen. This method was found to be accurate to within 2% and is in agreement with the results of Horton.[9]

The first-order rate constants for the oxidation of *n*-butyl mercaptan to the disulfide in each solvent along with the rates relative to that in methanol appear in Table I. In the ether solvents, the rate of oxidation is thirty-five to one hundred times faster than in methanol. In the dipolar-aprotic solvents, the rate is some three hundred times faster than in methanol.

TABLE I

OXIDATION OF *n*-BUTYL MERCAPTAN IN NONHYDROXYLIC SOLVENTS

Solvent	$k \times 10^3$, Min.$^{-1}$	k Relative to Methanol
Methanol	3.22	1
THF	116	36
Dioxane	989	90
Diglyme	323	100
DMAc	936	291
DMF	1077	334

These results suggested that the sodium cation associated with the incipient mercaptide ion is being solvated more readily in the ethereal and dipolar solvents than in methanol. In order to investigate this, a brief study of the oxidation of *n*-butyl mercaptan in ethanol and *tert*-butyl alcohol was carried out under the previously described conditions. In these experiments, a 2:1 mole ratio of base to the mercaptan was also used and the cation of the base was kept constant (sodium). The results appear in Table II. As the medium changes and becomes less hydroxylic, the rate of oxidation of *n*-butyl mercaptan increases. In addition, there appears to be a rough correlation between the pK of the solvent and the rate of oxidation.

TABLE II

OXIDATION OF *n*-BUTYL MERCAPTAN IN HYDROXYLIC SOLVENTS

Solvent	pK^a	Base	$k \times 10^3$, Min.$^{-1}$
Methanol	16	NaOMe	3.22
Ethanol	18	NaOEt	5.75
tert-Butyl alcohol	19	NaOtBu	21.00

[a] See ref. 10.

A second phase of this research was concerned with the effect of various alkoxide bases on the rate of oxidation of *n*-butyl mercaptan in methanol and *tert*-butyl alcohol. These results are summarized in Table III.

TABLE III

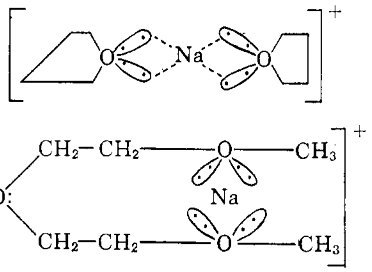
RATE CONSTANTS FOR THE OXIDATION OF *n*-BUTYL MERCAPTAN IN THE PRESENCE OF VARIOUS ALKOXIDE BASES

Solvent	Base	$k \times 10^3$, Min.$^{-1}$
Methanol	NaOMe	3.22
Methanol	KOMe	31.3
tert-Butyl alcohol	NaO*t*Bu	21.0
tert-Butyl alcohol	KO*t*Bu	34.7
tert-Butyl alcohol	RbO*t*Bu	193
tert-Butyl alcohol	CsO*t*Bu	479

As one proceeds from sodium to cesium *tert*-butoxide the oxidation rate is about twenty-three times greater in *tert*-butyl alcohol. Use of potassium methoxide in place of sodium methoxide gives a ten fold increase in the methanol system.

Discussion of Results

The acceleration of the rate of oxidation of *n*-butyl mercaptan in the various nucleophilic and dipolar solvents employed in this study is best rationalized as being due to a solvation of the sodium cation associated with the mercaptide ion in an ion-pair intermediate. In the case of the ether solvents, an sp^3-complex between the solvent and the sodium cation is most likely formed by *sp*-orbital overlap between the electron pairs of the ether oxygen atom and the empty 3*s*-orbital of the sodium cation. The complex formed in diglyme is probably most stable, since it is of a cyclic nature. The THF complex would require two molecules of the solvent and would tend to be least stable.



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The intermediate acceleration of the rate in dioxane could possibly be due to some 1,4-complex formation in the boat form of the molecule. However, one would not expect this contribution to be very large because of the increased steric strain that is introduced into the six-membered ring by carbon-carbon angle deformation and carbon-hydrogen repulsion.

In the case of the dipolar solvents, the further enhancement of the rate is probably due to two factors: (1) complex formation between the sodium cation and the electron pair of the dimethylamino group, and (2) weak ion-pair formation between the sodium cation and the dipole of the carbonyl group. In addition to the cation-solvent stabilization, some stabilization of the anion by orbital

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(10) M. K. McEwen, *J. Am. Chem. Soc.*, **58**, 1124 (1936).

overlap with the dipolar group might occur.[11-13] The relative contributions of the two modes of stabilization are difficult to assess and we are doing more work in this area.

These results are in agreement with the results of Wilkinson,[14] who found that potassium metal could be dissolved by complex formation in THF and ethylene glycol dimethyl ether, the latter being the more effective. The sodium cation with its empty 3*s*-orbital should be complexed even more readily in solvents of this type. In addition, Atherton and Weissman[15] have recently found that the ESR spectrum of sodium naphthalenide in THF shows splitting which they have attributed to dissociation of an intimate ion pair and an interaction of the solvent with the sodium ion.

The enhanced rate of oxidation in DMF and DMAc is also in accord with the work of Zaugg,[16,17] who found that DMF and dimethyl sulfoxide (DMSO) were superior to THF and monoglyme as solvents for the alkylation of enolate ions with *n*-butyl bromide. Further support of these conclusions can be derived from the work in hydroxylic solvents, since the rate of oxidation in *tert*-butyl alcohol is about seven times faster than that in methanol. As the basicity of the hydroxylic media increases, specific cation solvation becomes more facile and there is less competition between solvent and mercaptan for base. This parallels the effect found in the nonhydroxylic solvents.

The variation of the rate of oxidation with different alkoxide bases is somewhat difficult to interpret. However, the results do suggest that as the size of the alkali metal cation increases, there is a greater degree of dissociation of the alkoxide base due to decreased solvent-base aggregation. If this is the case, the concentration of alkali metal mercaptide should increase. Such a sequence seems reasonable since the cesium *tert*-butoxide–*tert*-butyl alcohol system is midway in activity between the sodium methoxide–methanol and sodium methoxide–DMF systems. We are hopeful that conductivity measurements in these and similar solvent-base systems will shed more light on this aspect of the work.

Experimental

Purification of Solvents.—The solvents were distilled through a 20-plate column in a nitrogen atmosphere. They were then stored over nitrogen and Drierite. One exception was the dioxane, which was obtained from Matheson, Coleman and Bell as the spectral grade reagent.

Preparation of Reaction Mixtures.—All base-solvent systems were made up to the appropriate molarity in a nitrogen drybox. Each solvent contained 0.20 mole of base. One tenth of a mole of *n*-butyl mercaptan was then added to the reaction flask which was sealed and transferred to the oxidation apparatus. If the amount of base is increased, the system becomes rather complex and the kinetic order changes from first to zero, since the medium is no longer homogeneous. In addition, the rate is stirring dependent indicating diffusion is rate-controlling under nonhomogeneous conditions.

Oxidation Experiments.—Actual oxidation experiments were carried out in a Pyrex glass flask attached to a water-cooled condenser which was attached to the source of oxygen. The oxygen was stored in a balloon under 1 atm. of pressure and passed through a wet-test meter and into a calcium chloride drying tube before entering the glass reaction vessel containing the reaction mixture. After an equilibrium pressure was established, the reaction mixture was stirred continuously at 1100 r.p.m. by a large magnetic stirrer. The volume of oxygen consumed at any given time was read off the wet-test meter which was graduated in liters. In this manner, a constant oxygen pressure of about one atmosphere was maintained above the solution throughout the entire experiment.

The oxidation of *n*-butyl mercaptan was carried out eight times in sodium methoxide–methanol. The stoichiometry of the reaction indicated 4 moles of oxygen are consumed per mole of mercaptan. This agreed with the results of previous workers.[9] The reaction could be stopped at any given time and analysis of the reaction mixture indicated that the amount of disulfide formed corresponded to that calculated by oxygen consumption to within 2%.

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