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APPLICATION OF HEADSPACE GAS CHROMATOGRAPHY FOR THE INVESTIGATION OF KINETICS OF OXIDATION OF THIOLS BY DIMETHYL SULPHOXIDE IN AQUEOUS MEDIUM

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SUMMARY

The kinetics of the oxidation of thiols by dimethyl sulphoxide in the presence of water were investigated using headspace gas chromatography (HSGC). The rate constants for this reaction were determined and found to be considerably larger than those for oxidation in pure dimethyl sulphoxide. The applicability of HSGC to studies of reaction kinetics was examined. It was established that HSGC can be employed for the determination of rate constants provided that the rate of the equilibration process is high compared with the reaction rate. The relative standard deviations indicate that the precision of the determination of rate constants by HSGC is good.

INTRODUCTION

In addition to numerous analytical applications, headspace gas chromatography (HSGC) has also found extensive use for physico-chemical studies. The method has been employed for studying non-ideal solutions[1] and chemical equilibria in solutions[2,3]. Other uses include the determination of adsorption isotherms[4], gas–liquid distribution constants[5–7], aqueous solubilities[7] and vapour pressure[8,9].

During our studies on the determination of organic compounds by HSGC after sorption on solid sorbents and liquid desorption using dimethyl sulphoxide (DMSO)–water (1:1, v/v)[10], it has been observed that thiols undergo rapid oxidation with the formation of dimethyl sulphide and the respective disulphide. From the analytical point of view oxidation of thiols is undesirable, requiring special precautions when storing samples and standard solutions[11,12]. On the other hand, this reaction has been the subject of numerous investigations. DMSO oxidations have been widely utilized in organic synthesis[13,14] owing to the mild conditions and simple work-ups required and the high yields and selectivity. Oxidation of thiols by DMSO results in the formation of the corresponding disulphides with excellent yields and purity. This procedure is attractive not only for its simplicity and general applicability, but also because DMSO plays a double role as an oxidizing agent and a solvent. Various aspects of this reaction, such as the mechanism[15,16], reactivity of

thiols[16–18], kinetics[16,19,20] and yields[13,18,19] have been studied and reviewed[13].

No information has been published, however, on the oxidation of mercaptans by DMSO in the presence of water. As the rate of reaction is substantially increased in this case, it was decided to investigate the kinetics of conversion of thiols to disulphides by means of HSGC. This technique was selected for the following reasons:

(1) kinetic studies require a high sample throughput, which can be ensured by GC;

(2) the solvent (DMSO) peak is absent on a chromatogram of the headspace sample, which permits injections to be made in rapid succession;

(3) HSGC permits kinetic investigations of liquid systems containing aggressive species (*e.g.,* acids) or solids (*e.g.,* catalysts);

(4) large samples may be introduced into a GC column, thus allowing experiments to be carried out over a wide concentration range;

(5) automation of the HSGC process is simple and instruments offering this facility are commercially available.

It should be taken into account, however, that chemical reactions in two-phase systems can be upset by mass transfer between the phases, the reactions possibly occurring in one or both phases forming the system.

The purpose of this study was to examine the application of HSGC to the determination of the reaction order and rate constants of the oxidation of thiols in the liquid phase by DMSO in the presence of water.

EXPERIMENTAL

Apparatus

Headspace sample vials of 20 cm³ capacity were described in a previous paper[10]. Gas samples were withdrawn by means of a 1-cm³ gas-tight syringe and liquids were sampled using a 10-μl Hamilton syringe.

A Hewlett-Packard Model 5830 A gas chromatograph equipped with a flame-ionization detector was employed for GC analysis. The chromatographic conditions were as follows: column A (for separation of ethanethiol and methanethiol from dimethyl sulphide), 1.2 m × 2 mm I.D., stainless steel; packing, Tenax GC (60–80 mesh) (Enka, The Netherlands); column temperatures, 90 and 80°C; column B (for separation of dimethyl and diethyl disulphide), 2.4 m × 2 mm I.D., stainless steel; packing, 10% mixture of esters (1% phenyl neopentyl phosphite–33% DEGS–66% PEGA) on Chromosorb W AW DMCS (80–100 mesh): column temperature, 120°C; carrier gas, argon at 19 cm³/min; injector and detector temperatures, 150°C; sample volume, 0.25 or 0.5 cm³.

Materials

The dimethyl sulphoxide (DMSO) (Reachim, U.S.S.R.) and dimethylformamide (DMF) (POCh, Poland) solvents were purified by vacuum distillation. Methanethiol, ethanethiol, *n*-propanethiol, *tert.*-butanethiol and isopentanethiol (Fluka, Switzerland) (pure) were further purified by distillation. The thiol solutions investigated were prepared from stock solutions in methanol (*ca.* 3000 ppm, w/w) or pure thiols.

Procedure

The DMF, DMSO, water and DMSO–water (1:1) solvents were introduced into the headspace vials and left for 30 min to attain thermal equilibrium. Subsequently, pure thiols or methanol solutions of thiols were placed in the vial using a syringe and the volume of the gaseous phase was adjusted to 6 cm^3. The volume of the liquid phase was 10 cm^3. The headspace device was inverted several times to ensure complete mixing and the progress of attaining gas–liquid equilibrium or the progress of oxidation was followed by repeated injections of the gaseous (0.25 or 0.5 cm^3) or liquid phase (1 μl) into a gas chromatographic column. The chromatographic peak height was taken as a measure of decrease in concentration of thiol or increase in concentration of the reaction products.

RESULTS AND DISCUSSION

A schematic representation of the equilibria involved in the gas–liquid system in which chemical reactions may also occur is shown in Fig. 1, using as an example the oxidation of thiols by DMSO in the presence of water. The following types of equilibria can be distinguished:

(a) between the reactants (RSH, DMSO) and products (R$_2$S$_2$, DMS) in the gaseous (2) and liquid (8) phase–chemical reaction;

(b) distribution of the reactants (3, 4), products (5, 6) and solvents (4, 7) between the coexisting phases–mass transfer;

(c) between the reactants (RSH) and the contaminants (O$_2$) in the gaseous (1) and liquid (9) phases–side reaction.

Additionally, thermal equilibrium in the system should be considered. However, this equilibrium can be neglected, as the DMSO–water mixture was heated in advance. A mathematical description of all these equilibria for appropriate boundary conditions would in principle permit the determination of the resultant rate constant of the chemical reaction. In practice, however, an exact solution of this system of equations is usually impossible owing to both the mathematical complexity and the lack of information required for the formulation of all the equations and boundary conditions. For this reason, approximate solutions are generally sought in practice.
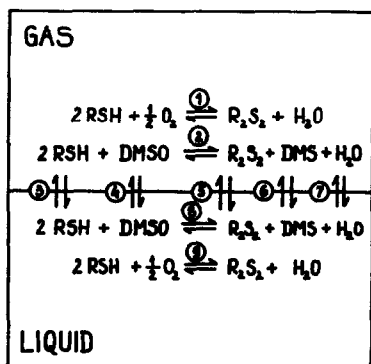

Fig. 1. Types of equilibria in two-phase system for headspace investigation of the oxidation of thiols by DMSO. DMS = dimethyl sulphide.

For the system presented in Fig. 1, equilibria 4, 5, 6 and 7 may be neglected *a priori* in further considerations, as according to literature data[19,20] in the presence of an excess of DMSO the oxidation of thiols is pseudo-first-order and virtually irreversible, which allows compounds not present in the kinetic equation to be disregarded.

In order to determine the effect of oxygen on the reaction rate, an experiment was carried out in which the concentration of ethanethiol in the headspace over DMF–water (1:1) solvent at 65°C was monitored. No measurable decrease in concentration was observed after 150 min. This observation and literature data[19] permit the conclusion that the rate of thiol oxidation by oxygen is slow compared with the DMSO oxidation in the presence of water and, hence, reactions 1 and 9 may be neglected. Finally, the oxidation reaction in the gaseous phase (2) was excluded from further consideration because the oxidation of aliphatic thiols by pure DMSO is very slow, *e.g.*, at 100°C the time for 50% conversion of 1-dodecanethiol is 100 h[17].

The decrease in the concentration of ethanethiol in the headspace over pure DMSO at 45°C observed in a preliminary experiment was less than 5% after 270 min. On the other hand, the times for 50% conversion of the investigated thiols oxidized in DMSO–water (1:1) were of the order of 14–120 min in the temperature range 45–65°C. Thus, water increases the reaction rate considerably, presumably owing to the formation of a more favourable transition state for protonation of the DMSO through hydrogen bonding or hydration. However, this process can occur only in the liquid phase and, consequently, oxidation in the gaseous phase is very slow. Hence, the concentration of thiols in the headspace over the solution depends on two factors: the rate of mass transfer between the coexisting phases (3) and the rate of oxidation in the liquid (8). The determination of correct rate constants of chemical reaction requires that the rate of mass transfer be high compared with the rate of reaction.

The studies of the dynamics of mass transfer between gas and liquid were performed by introducing the investigated thiol into the liquid phase (DMSO or water) in a manner ensuring uniform distribution throughout the liquid (the solution was agitated) and monitoring the dependence of the gaseous phase concentration, c_G, on time. As the rates of oxidation in pure DMSO or water are very low, the changes in concentration of thiols in the headspace reflect the dynamics of mass transfer in the system. The results of these investigations for ethanethiol in water are shown in Fig. 2.

It follows from Fig. 2 that doubling the concentration essentially does not change the time necessary to attain equilibrium, whereas increasing the temperature by 10°C roughly halved this time, in accordance with the Van 't Hoff rule. The oscillations in concentration in Fig. 2 presumably occur because under predominantly diffusion conditions the system is adequately described by a second-order differential equation with respect to time, the solution of which contains a cosine term. At 45°C, the equilibration time for ethanethiol was of the order of 60 min and was short compared with the time of reaction (see Fig. 3). Similar results were obtained for DMSO as the solvent.

Subsequently, the rate of oxidation of thiols in DMSO–water was followed by determining the rate of change of concentration with time in both liquid (DMSO–water) and gaseous phases. This dependence for ethanethiol is shown in Fig. 3, where the rate of equilibration of EtSH between water and air is also shown.
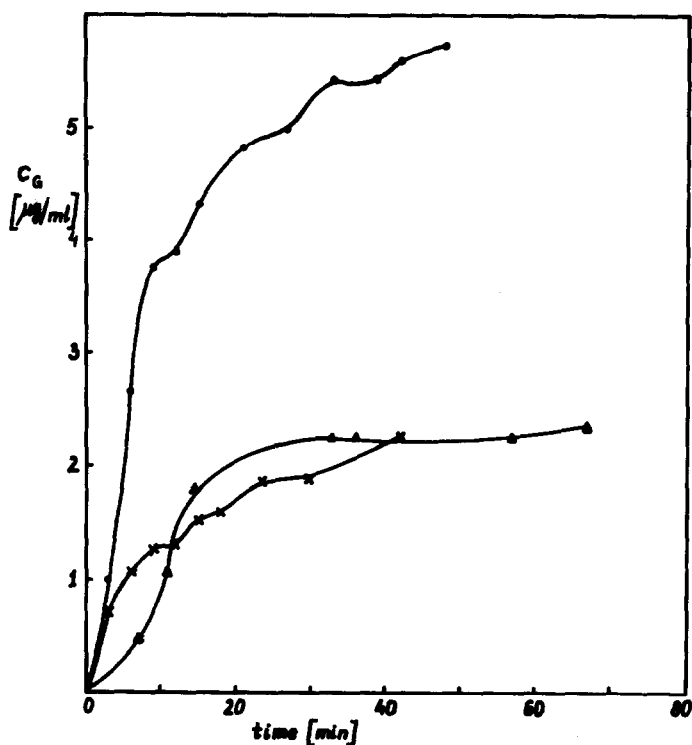
Fig. 2. Dynamics of mass transfer between gaseous and aqueous phases for ethanethiol. ●, c_L = 20 μg/ml, t = 45°C; ×, c_L = 10 μg/ml, t = 45°C; ▲, c_L = 8 μl/ml, t = 55°C (c_L = concentration of ethanethiol in the liquid phase).
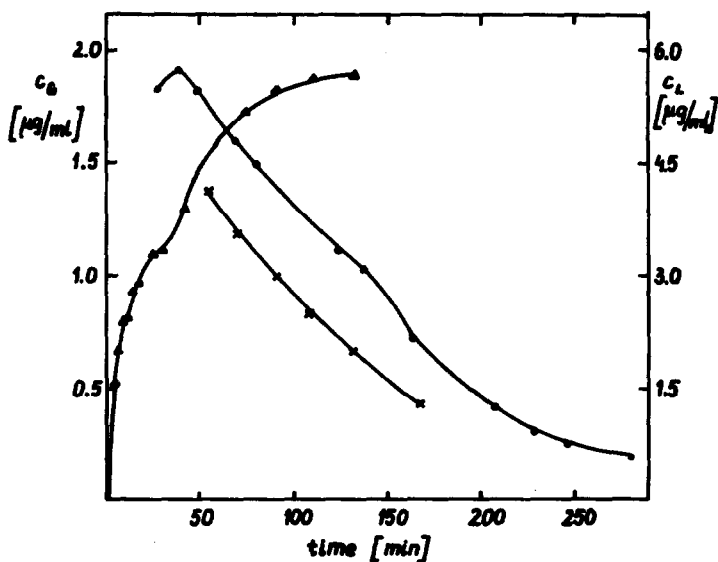

Fig. 3. Variation of concentration of ethanethiol with time in the liquid (×) and gaseous (●) phases. Liquid phase, 10 cm³ of DMSO–water (1:1, v/v); temperature, 45°C. The equilibration of ethanethiol between the aqueous and gaseous phases is also shown (▲).
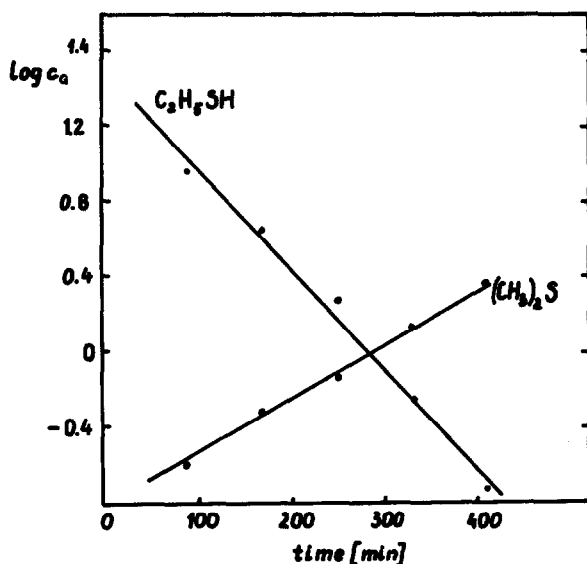
Fig. 4. Plot of log c_G vs. time for the determination of the rate constant of oxidation of ethanethiol by DMSO in the presence of water at 45°C.

It follows from Fig. 3 that after an initial transition period the dependence on time of concentration changes of thiol in the liquid is reflected with good accuracy by the variation of concentration with time in the gaseous phase. For example, the rate constant determined from the slope of the curve ln c_L = f(t) was 0.0124, which is in agreement with the k values obtained from the dependence ln c_G = f(t) (see Tables II and III). Similar results were obtained for other thiols investigated. Hence, HSGC may be utilized for the investigation of reaction mechanisms and rates provided that the rate of equilibration of one of reactants or products between the two phases is at least several times higher than the reaction rate. This condition is met for small molecules with high diffusion coefficients. Hence, the rate of oxidation of thiols could be reliably determined on the basis of concentration changes of thiols or dimethyl sulphide with time (Fig. 4), but with disulphides the fluctuations in concentration were too large to permit the direct determination of the rate constants and a mathematical analysis would be required to separate the effect of mass transfer. This problem will be dealt with in a separate paper.

The HSGC investigation of the oxidation of thiols by DMSO in aqueous medium confirmed that the only products formed were the respective disulphides and dimethyl sulphide. The reaction was rapid and virtually irreversible, and consequently it is suitable for preparative purposes. The order of the oxidation reaction was determined by fitting the experimental data to kinetic equations of various orders. The disappearance of thiols adhered to good pseudo-first-order kinetics in the presence of excess of DMSO and water. This is illustrated by the data in Table I and Fig. 4. The values of the coefficient of determination (r^2) indicate that the best fit was obtained for the first-order dependence. The values of rate constants were determined from the slope of the dependence ln c_G = f(t). Either the disappearance of thiol or the formation of dimethyl sulphide may be employed for the determination of rate

TABLE I

DETERMINATION OF THE ORDER OF REACTION OF OXIDATION OF THIOLS IN DMSO–WATER (1:1) AT 45°C

Kinetic equation	Parameter	Compound			
		CH_3SH		C_2H_5SH	
		t (min)	c (μg/ml)	t (min)	c (μg/ml)
		55	2.181	90	9.249
		85	1.027	170	4.304
		115	0.551	250	1.822
		145	0.271	330	0.539
		175	0.128	410	0.169
$\ln c = -k\,t + a$	k (min^{-1})	0.0233		0.0126	
(first order)	a	2.05		3.53	
	$r^{2\star}$	0.9989		0.9900	
$\dfrac{1}{c} = k\,t + a$	k (ml μg^{-1} min^{-1})	0.0579		0.0166	
(second order)	a (ml μg^{-1})	-3.72		-2.41	
	$r^{2\star}$	0.8447		0.7361	

* r^2 = coefficient of determination.

constants (see Fig. 4) if the stoichiometry of the reaction is accounted for.

The precision of the headspace determination of rate constants was good, as indicated by the exemplary results for ethanethiol at three temperatures (Table II). The higher values of the relative standard deviation (s_r) at higher temperatures may be explained by the increase in the reaction rate with temperature and, consequently, larger experimental errors. The rate constants roughly double when the temperature increases by 10°C (Table II), in accordance with the Van 't Hoff rule. Hence, it is possible to calculate the reaction rates at temperatures other than those for which the k values were determined.

The rate constants for the oxidation reactions of several volatile thiols determined by HSGC are listed in Table III. It follows from the results that the rate constants decrease with increase in carbon chain length and are highest for meth-

TABLE II

TEMPERATURE DEPENDENCE AND PRECISION OF DETERMINATION OF RATE CONSTANTS FOR OXIDATION OF ETHANETHIOL IN DMSO–WATER (1:1)

Initial concentration of C_2H_5SH: 0.112 mg/ml.

Temperature (°C)	k (min^{-1})					k (min^{-1})	s_r (%)	Confidence interval ($\pm\ t \cdot \bar{s}$)
	1	2	3	4	5			
45	0.0126	0.0126	0.0125	0.0124		0.0125	0.76	0.0002
55	0.0230	0.0240	0.0227			0.0232	2.9	0.0017
65	0.0526	0.0488	0.0568	0.0506	0.0514	0.0514	6.8	0.0043

TABLE III

COMPARISON OF RATE CONSTANTS (k) AND HALF-LIVES (τ) FOR THE OXIDATION RE-
ACTION OF SELECTED THIOLS

Compound	Temperature (°C)					
	45		55		65	
	k (min^{-1})	τ (min)	k (min^{-1})	τ (min)	k (min^{-1})	τ (min)
Methanethiol	0.0233	29.7	—		—	
Ethanethiol	0.0125	55.3	0.0232	29.9	0.0514	13.5
n-Propanethiol	—		—		0.0294	23.6
tert.-Butanethiol	—		—		0.0060	116
Isopentanethiol	—		—		0.0145	47.8

anethiol. The rate constants are roughly halved when the carbon chain increases by a methylene group in the C_1–C_3 range. The higher rate constant for isopentanethiol than tert.-butanethiol is probably due to steric effects.

CONCLUSIONS

Aliphatic thiols undergo oxidation in DMSO–water mixture with the formation of the respective disulphide and dimethyl sulphide. In the presence of excess of DMSO the reaction is pseudo-first order and the rate constants are substantially larger than for oxidation in pure DMSO. The rate of reaction decreases with increase in carbon chain length. The rate constants roughly halve with the introduction of a methylene group in the carbon chain.

HSGC is suitable for the kinetic studies owing to the absence of peaks of non-volatile solvents on the chromatograms of headspace samples, which permits rapid successive injections. Reactions in aggressive media or those containing a solid phase may be investigated. HSGC can be employed for the determination of the rate constants of reactions occurring in the liquid phase if the rate of the equilibration process is high compared with the reaction rate that occurs with volatile compounds.

The k values determined on the basis of the investigation of concentration changes in the gaseous phase are in good agreement with the values obtained directly from studies in the liquid phase, thus demonstrating the good accuracy of the method. The precision of the determination of rate constants is good, as shown by the standard deviations.

Large samples may be introduced, thus increasing the sensitivity of the method.

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