

DETERMINATION OF LOW CONCENTRATIONS OF DIBENZYL SULFOXIDE IN AQUEOUS SOLUTIONS

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Received July 13th, 1978

A spectrophotometric method was developed for the determination of low concentrations of sulfoxide in water, relying on the formation of a leuco-compound from the reaction of L-tryptophan with *p*-dimethylaminobenzaldehyde and its oxidation by sulfoxide in hydrochloric acid medium. The optimum conditions for the determination were found by using the simplex method. The calibration curve, measured at 620 nm, is linear up to the sulfoxide concentration $7.5 \cdot 10^{-5} \text{ mol l}^{-1}$ (i.e. 17.3 ppm), the limit of determination is 0.1 ppm, the reproducibility, expressed as the relative standard deviation (for $n = 6$) is 3–4%. Oxidants interfere with the determination. Nitrates can be removed by means of a strongly basic anion exchanger in the chloride form. Mixture water–acetone (6 + 1) passing with a low flow rate should be applied to the elution of the partly sorbed sulfoxide.

During the study of the extraction equilibria of dibenzyl sulfoxide (DBSO) the necessity emerged to determine the equilibrium contents of the sulfoxide in the aqueous and organic phases. Since the distribution constant of DBSO in the systems investigated (water–toluene or water–tetrachloromethane) is rather high (133.7 and 27.4, respectively), it is convenient to determine the content of the sulfoxide in the aqueous phase experimentally and that in the organic phase by calculation.

No suitable method has been so far suggested for the determination of small concentrations of sulfoxide in aqueous solutions. The procedures published are designed for the determination of higher sulfoxide concentrations, being based on oxidation–reduction^{1–9} or neutralization^{10,11} titrations. In fact, one photometric method has been worked out¹² for the determination of dimethyl sulfoxide in water, it requires, however, concentrations higher than 20 mg/ml. Recently, a procedure has been suggested for the photometric determination with aquopentacyanoferrate(II), where the water in the compound is replaced by a sulfoxide molecule¹³. This method, however, suits only for sulfoxides in which no steric hindrance operates (e.g., dimethyl sulfoxide, tetramethylene sulfoxide); neither the limit of determination nor the sensitivity of the method has been reported. Safronov¹⁴ has proposed a method of sulfoxide detection relying on the oxidation of the leuco-compound formed in the reaction of glyoxylic acid with L-tryptophan (1-amino-2-(3-indolyl)propionic acid) by sulfoxide in hydrochloric acid medium.

The reaction of tryptophan with aldehyde and the oxidation of the leuco-compound formed has been studied by several authors¹⁵⁻¹⁷, but unique conclusions concerning the composition and structure of the blue oxidation product have not been arrived at.

The aim of this work was to find the conditions for the photometric determination of low concentrations of sulfoxide relying on the aforesaid oxidation of the leuco-compound. The fractional factorial design $1/2 2^n$ (see^{18,19}) was used to select the factors that affect the determination of sulfoxide by this method, and the simplex method²⁰⁻²² was applied to the optimization of the determination conditions.

EXPERIMENTAL

Dibenzyl sulfoxide was purified by repeated crystallization from ethanol. Its m.p. ($^{\circ}\text{C}$) was in accordance with the published value²³. Its content, as determined by neutralization potentiometric titration¹¹, was 99.7%. L-Tryptophan (Koch-Light, England) and *p*-dimethylaminobenzaldehyde (Spolek pro chemickou a hutní výrobu, Czechoslovakia) were chemical grade purity, the other chemicals were reagent grade purity. The ion exchanger employed (Dowex 1X8) was washed with deionized water and converted to the Cl^- -form by using 2M-HCl.

The absorption spectra were scanned on an instrument Specord UV-VIS, the absorbances of the solutions were measured on a spectrophotometer VSU-2P (both Zeiss, Jena).

RESULTS AND DISCUSSION

DETERMINATION OF THE SIGNIFICANT FACTORS AND THEIR OPTIMIZATION

The absorption spectra in the visible region of the oxidation products of the leuco-compound in the presence of DBSO exhibit the formation of two absorption maxima

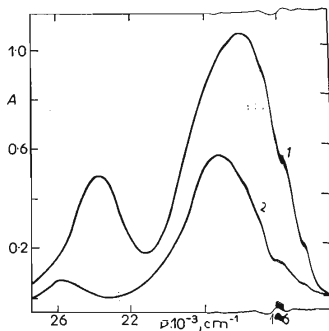


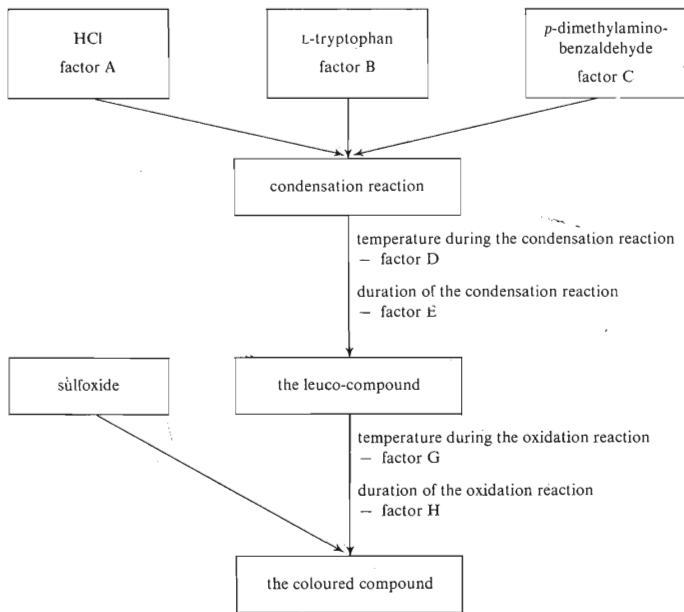
Fig. 1

Absorption Spectrum of the Product of Reaction of Dibenzyl Sulfoxide with the Leuco-Compound in Hydrochloric Acid Medium

Concentration of dibenzyl sulfoxide $5 \cdot 10^{-5} \text{ mol l}^{-1}$, cell 1 cm, measured against blanks; the leuco-compound prepared from 1 L-tryptophan and *p*-dimethylaminobenzaldehyde, 2 L-tryptophan and glyoxylic acid.

(at $25700-23700\text{ cm}^{-1}$ and $17500-16300\text{ cm}^{-1}$), whose positions depend on the kind of the aldehyde compound employed for the preparation of the leuco-compound (Fig. 1). It has been found that if *p*-dimethylaminobenzaldehyde is used instead of glyoxylic acid¹⁴, the reaction product possesses a higher absorption coefficient in otherwise identical conditions; the former compound was therefore employed for the preparation of the leuco-compound. The absorption maximum of the oxidation product of the leuco-compound with *p*-dimethylaminobenzaldehyde lies at 16130 cm^{-1} , where neither L-tryptophan nor the aldehyde itself exhibits any light absorption. The absorbance was found unaltered during 5–50 min after the finishing of the reaction (removing of the flask from the thermostat).

We considered the following scheme taking into account the significant factors involved:



In order to reduce the number of the requisite experiments, we considered the factors A–C significant and only tested the significance of the factors D–H. The factors A–C were then joined with the significant factors found by factorial experiment, and the optimum values of all the significant factors were sought by applying the simplex method.

The levels of the factors for the factorial design used are given in Table I. The factorial design was conducted according to the scheme apparent from Table II, where the average absorbances are also given. For the various sources of absorbance variability, the following values of the *F* criterion were calculated:

Factor	D	E	G	H	DE(GH)	DG(BD)	DH(EG)
<i>F</i> -criterion	2.84	56.96	725.0	128.0	15.47	–	–

TABLE I
Factor Levels of the Fractional Factorial Design

Factor	Lower level	Upper level
D Temperature of the condensation reaction	20°C	60°C
E Duration of the condensation reaction	50 min	100 min
G Temperature of the oxidation reaction	30°C	60°C
H Duration of the oxidation reaction	30 min	60 min

TABLE II
The Design Matrix for the Factorial Experiment $1/2 \cdot 2^4$ and the Measured Absorbance Values
 $c_{\text{DBSO}} = 5 \cdot 10^{-5} \text{ mol l}^{-1}$, $c_{\text{HCl}} = 9 \text{ mol l}^{-1}$, $c_{\text{tryptophan}} = 4 \cdot 10^{-4} \text{ mol l}^{-1}$,
 $c_{\text{dimethylaminobenzaldehyde}} = 1 \cdot 10^{-3} \text{ mol l}^{-1}$, λ 620 nm, cell 1 cm.

Factor					Absorbance	Factor					Absorbance
D	E	G	H	D		E	G	H			
a	a	a	a		0.312	a	a	b	b		0.966
b	a	a	b		0.614	b	a	b	a		0.849
a	b	a	b		0.440	a	b	b	a		0.719
b	b	a	a		0.240	b	b	b	b		0.845

^a Lower level, ^b upper level.

From a comparison with the critical value $F_{crit} = 18.51$ (for $\alpha = 0.05$, $\nu_1 = 1$, $\nu_2 = 2$) the duration of the condensation reaction (factor E) and the duration and temperature of the oxidation reaction (factors G and H) emerge as the significant factors. Inasmuch as the temperature of the condensation reaction does not affect the absorbance of the reaction mixture, the condensation was conducted at ambient temperature.

The simplex method was employed to find the optimum values of the factors A, B, C, E, G, and H. A constant concentration of DBSO ($5 \cdot 10^{-5} \text{ mol l}^{-1}$) was applied during the measurements of the mixture. The lower and upper levels of the factors examined are given in Table III. The factors were normalized as given in²², where the procedure for the determination of the first simplex and derivation of the higher order simplexes is also discussed. The factors and absorbances for the various simplex vertices are given in Table IV. For the vertices 9 (simplex 3) and 12 (simplex 6) the absorbance dropped below their maximum values from the preceding simplexes (*i.e.* 2 and 5, vertices 8 and 11, respectively), they were, however, higher than those for the skipped vertices (4 and 3, respectively). A modified step ($\alpha = -0.5$) was therefore used for the subsequent simplexes (see²²). The maximum absorbance value was found for the vertex 14 (simplex 8). In order to localize the maximum of the dependence of the absorbance on the experimental conditions more precisely, the step was lowered in the subsequent simplexes ($\alpha = +0.5$). A slightly greater absorbance value was obtained with this shortened step. Additional step lowering and refining of the conditions for the maximum absorbance was dropped, as the difference between two successive absorbance values (1.347 and 1.365) was practically insignificant.

TABLE III

Lower and Upper Levels of the Factors Followed During the Simplex Method Optimization of the Dibenzyl Sulfoxide Determination

Factor	Lower level	Upper level
A Volume of concentrated HCl ($\rho = 1.18 \text{ g cm}^{-3}$), ml	6.00	8.00
B Concentration of L-tryptophan, $10^{-4} \text{ mol l}^{-1}$	3.00	8.00
C Concentration of <i>p</i> -dimethylaminobenzaldehyde, $10^{-3} \text{ mol l}^{-1}$	1.50	4.00
E Duration of the condensation reaction, min	50	100
G Temperature of the oxidation reaction, °C	35	60
H Duration of the oxidation reaction, min	35	60

The optimum conditions of the determination, found as the average of the values of the various factors corresponding to all the vertices of the simplex with the highest response (simplex 15) (see²²) are as follows: 9M-HCl (this is 7.5 ml of concentrated

TABLE IV

Optimization of the Conditions of the Determination of Dibenzyl Sulfoxide by Means of the Simplex Method

$c_{\text{DBSO}} = 5 \cdot 10^{-5} \text{ mol l}^{-1}$, λ 620 nm, cell 1 cm, measured against a blank.

V^a	S^b	Vertices retained	Values of the factors						A
			A ml ^c	B 10^{-4} M	C 10^{-3} M	E min	G °C	H min	
1	1		6.30	3.80	1.67	53	37	37	0.191
2	1		7.50	4.00	2.00	60	40	40	0.754
3	1		6.50	8.00	2.00	60	40	40	0.533
4	1		6.50	4.00	4.00	60	40	40	0.365
5	1		6.50	4.00	2.00	100	40	40	0.379
6	1		6.50	4.00	2.00	60	60	40	0.594
7	1		6.50	4.00	2.00	60	40	60	0.429
8	2	2,3,4,5,6,7	7.00	6.00	3.00	80	50	50	0.869
9	3	2,3,5,6,7,8	7.00	6.00	0.33	80	50	50	0.395
9'	3	2,3,5,6,7,8	6.90	5.50	1.24	75	47	47	0.745
10	4	2,3,6,7,8,9'	7.10	6.50	2.08	32	53	53	1.012
11	5	2,3,6,8,9',10	7.30	7.30	2.11	62	57	30	1.086
12	6	2,6,8,9',10,11	7.60	3.20	2.14	63	62	47	0.940
12'	6	2,6,8,9',10,11	7.30	4.30	2.01	62	57	45	0.993
13	7	2,8,9',10,11,12'	7.90	7.20	2.15	64	41	48	1.334
14	8	2,8,10,11,12',13	7.90	6.30	3.22	49	52	41	1.347
15	9	2,8,10,11,12',14	6.80	4.30	2.65	51	51	38	0.752
15'	9	2,8,10,11,12',14	7.60	6.40	2.27	61	46	46	1.177
16	10	2,8,10,12',14,15'	7.50	3.90	2.75	52	43	61	0.812
16'	10	2,8,10,12',14,15'	7.40	6.50	2.27	60	51	38	0.983
17	11	2,8,12',14,15',16'	7.80	4.70	2.84	92	47	34	0.853
17'	11	2,8,12',14,15',16'	7.30	6.00	2.27	47	51	48	0.892
18	12	2,8,14,15',16',17'	7.50	7.40	2.98	56	41	43	1.091
19	13	2,14,15',16',17',18	8.00	6.20	2.00	31	44	35	1.207
20	14	14,15',16',17',18,19	7.80	8.90	3.00	41	56	43	1.342
21	15	14,15',16',18,19,20	8.10	7.80	2.97	52	46	34	1.365
22	16	15',16',18,19,20,21	7.60	8.10	1.94	51	44	38	1.003
22'	16	15',16',18,19,20,21	6.80	6.80	2.90	50	50	40	1.220

^a Vertex; ^b simplex; ^c volume of conc. hydrochloric acid ($\rho = 1.18 \text{ g cm}^{-3}$).

HCl, $\rho = 1.18 \text{ g cm}^{-3}$, in 10 ml of the reaction mixture), $7.07 \cdot 10^{-4} \text{ M}$ L-tryptophan, $2.67 \cdot 10^{-3} \text{ M}$ *p*-dimethylaminobenzaldehyde, duration of the condensation reaction 50 min, its temperature $20 \pm 3^\circ \text{C}$, duration of the oxidation reaction 40 min, its temperature 50°C .

SENSITIVITY, LIMIT OF DETERMINATION, AND REPRODUCIBILITY OF THE METHOD

The calibration dependence $A = f(c_{\text{DBSO}})$ was measured and found linear in the region of $c_{\text{DBSO}} 0.15 \cdot 10^{-5} - 7.4 \cdot 10^{-5} \text{ mol l}^{-1}$, obeying the regression straight line equation $A = 0.849 + 2.44 \cdot 10^4 c_{\text{DBSO}}$ when measured at 620 nm in 1 cm cell against water (c_{DBSO} in mol l^{-1}). The reproducibility of this calibration dependence determination is given by the corresponding standard deviations of the equation $y = a + bx$: $s_a = 0.014$, $s_b = 6.2 \cdot 10^2$, $s_{xy} = 0.013$. The sensitivity of the method is determined by the slope of the calibration plot ($2.44 \cdot 10^4 \text{ l mol}^{-1}$).

The limit of determination was found by measuring the absorbances of five blank samples against water. The average of the absorbance values was $\bar{A} = 0.822$, variation range $R_0 = 0.029$. The minimum measurable absorbance of a sample was calculated from the relation $A_{\text{min}} = \bar{A}_0 + ks_0$, where $k = 3$ (see²⁴) and the standard deviation was calculated from the variation range. The value $A_{\text{min}} = 0.859$ was obtained, and from the regression straight line coefficients, the c_{min} was calculated to be $4.2 \cdot 10^{-7} \text{ mol l}^{-1}$, hence 0.1 ppm.

The reproducibility of the determination was considered for two determination procedures: one relied on the preparation of a stock solution of the leuco-compound and use of its aliquots for the sulfoxide determination (procedure A), in the other the components affording the leuco-compound were mixed for each determination separately (procedure B). The determination of the same concentration of DBSO ($2.00 \cdot 10^{-5} \text{ mol l}^{-1}$) was repeated five times (measured against a blank); the rel. standard deviations 3.0 and 4.3% were obtained for the procedures A and B, respectively. The F-test showed that the difference in the precision of the two procedures was statistically insignificant ($F = 2.14$, $F_{\text{crit}} = 5.05$ for $\nu_1 = \nu_2 = 5$ and $\alpha = 0.05$). The procedure A was further applied for practical reasons.

EFFECT OF FOREIGN COMPONENTS ON THE DETERMINATION OF SULFOXIDE

The effect of the components that may accompany the sulfoxide in a sample was examined. This applies to sulfide or sulfone, which may be present as impurities in the chemical; and since the method was worked out for analytical monitoring of sulfoxide extraction in the presence of strong mineral acids, the effect of nitrates and sulfates was investigated as well. Chlorides do not interfere; on the contrary, their presence is prerequisite.

Sulfides and sulfones were found not to interfere with the determination. Sulfates virtually do not exert an interfering effect either (Table V). This, however, is not

TABLE V

Effect of Sulfate and Sulfuric Acid on the Absorbance of the Solution Analyzed
 λ 620 nm, cell 1 cm, measured against water.

c_{DBSO} $10^{-5} \text{ mol l}^{-1}$	Absorbance for the concentration, mol l^{-1}								
	K_2SO_4					H_2SO_4			
	0	0.1	0.5	1.0	1.5	0	0.1	0.2	0.6
0.5	0.969	0.975	0.981	0.992	1.009	0.969	0.981	0.999	1.199
1.5	1.190	1.194	1.202	1.215	1.235	1.187	1.195	1.227	1.445
3.0	1.581	1.594	1.601	1.613	1.637	1.583	1.598	1.629	1.879

TABLE VI

Separation of Nitrates from Dibenzyl Sulfoxide on the Ion Exchanger Dowex 1X8

Absorbance measured after washing the column with water-acetone mixture, volume of the elution solution 40 ml, flow rate $0.5 \text{ ml cm}^{-2} \text{ min}^{-1}$; λ 620 nm, cell 1 cm, measured against a blank.

$c_{\text{NO}_3^-}$ mol l^{-1}	Absorbance for the water-acetone mixture						
	1 : 1	2 : 1	3 : 1	4 : 1	5 : 1	6 : 1	7 : 1
	$0.5 \cdot 10^{-5} \text{ M dibenzyl sulfoxide}^b$						
0.01	0.859 ^c	0.301	0.275	0.153	0.125	0.110	0.095
	0.317 ^c	0.277	0.181	0.130	0.119	0.115	0.101
0.60	1.119 ^c	0.982	0.614	0.215	0.139	0.109	0.100
	0.752 ^c	0.453	0.473	0.196	0.107	0.117	0.109
	$4.0 \cdot 10^{-5} \text{ M dibenzyl sulfoxide}^b$						
0.01	1.295 ^c	1.203	1.175	1.152	0.946	0.926	0.863
	0.805 ^c	1.126	1.017	1.095	0.919	0.917	0.954
0.60	> 2 ^c	1.517	1.358	1.251	0.984	0.915	0.895
	1.147 ^c	1.273	1.125	1.199	0.932	0.930	0.972

^a Concentration in the initial solution; ^b absorbances of the $0.5 \cdot 10^{-5}$ and $4.0 \cdot 10^{-5}$ M dibenzyl sulfoxide solutions without NO_3^- and without passing through the ion exchanger $A = 0.105$ and 0.905 , respectively; ^c results of parallel measurements.

true of sulfuric acid (Table V), since the acidity of the solution affects the absorbance, as has been found previously. Oxidants such as Fe(III) , NO_2^- , NO_3^- do interfere. Since the method of determination should be applicable also in the presence of nitric acid, the possibility to remove nitrates by means of an anion exchanger (Dowex 1X8) was tested. It is possible to remove them by ion exchange (for chloride ions); however, an amount of the sulfoxide is simultaneously sorbed. When the ion exchanger column is washed with water or a water-ethanol mixture (1 + 4 to 6 + 1), the nitrate is eluted together with the sulfoxide, and if ethanol is applied in excess, the ion exchanger contracts appreciably. The most suitable agent for washing out the sorbed sulfoxide is water-acetone mixture (6 : 1) (Table VI).

The appropriate flow rate for the washing of the column was established to be $0.5 \text{ ml cm}^{-2} \text{ min}^{-1}$; the washing is complete with 10 to 13 V_c (V_c is the total volume of the exchanger column). With a smaller volume of the washing solution the sulfoxide is not eluted perfectly, with a larger volume break-through of the nitrate occurs, as proved by the reaction of the eluate with brucine and also by an increase of the sample absorbance after the developing of the colouration.

Working Procedure

In a ground-in flask is placed ($t < 15^\circ\text{C}$) a quantity of concentrated hydrochloric acid such that its resulting concentration in the mixture for the condensation reaction be 10.2M; $n \cdot 0.5 \text{ ml}$ of 0.23% solution of L-tryptophan in water (n is the expected number of determinations) and $n \cdot 0.5 \text{ ml}$ of 0.8% solution of *p*-dimethylaminobenzaldehyde in 2M-HCl are added, and the mixture is allowed to stand at room temperature for 50 min.

In a 10 ml volumetric flask are placed 1 ml of the sample and 8.8 ml of the leuco-compound solution prepared as described above, and made up to the mark with water. After shaking, the content of the flask is heated in a thermostat at 50°C for 40 min. After cooling (10 to 30 min after the removing from the thermostat), the absorbance is measured in a 1 cm cell at 620 nm against a blank prepared analogously. The calibration curve is plotted in the same manner. The sulfoxide standard solution has to be added up to the maximum of 1 ml with the necessary accuracy.

In the presence of nitrate, the sample containing less than 0.6 mmol NO_3^- is allowed to pass through a column ($15 \times 0.5 \text{ cm}$) of the anion exchanger Dowex 1X8 (50—100 mesh) in the chloride form, and the column is washed with 40 ml or so of a mixture water-acetone (6 : 1) applying the flow rate 0.1 ml min^{-1} . The solution is evaporated under a lamp to the volume $\sim 0.5 \text{ ml}$, and after cooling is transferred into a 10 ml volumetric flask; for the rinsing of the beaker, the prepared solution of the leuco-compound is used up to the volume 8.8 ml. The content of the flask is diluted to volume, and further proceeded as in the foregoing case.

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Translated by P. Adámek.