

ORGANIC SYNTHESIS  
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## Separation of 2,4'- and 4,4'-Dihydroxydiphenyl Sulfones

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**Abstract**—To develop a procedure for separating 2,4'- and 4,4'-dihydroxydiphenyl sulfones, their acidity and solubility in water were studied.

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Bisphenol S prepared by the reaction of 2 mol of phenol with 1 mol of sulfuric acid is a mixture of 4,4'- (**I**) and 2,4'-dihydroxydiphenyl sulfone (**II**) with small amounts of 2,4',4''-trihydroxytriphenyl disulfone (**III**) and unidentified colored and colorless impurities.

Previously crude bisphenol S was used for preparing macromolecular components of heat-developable mixtures and photoconductors. At present, only pure sulfones **I** and **II** are used for this purpose. Sulfone **III** does not find practical application so far. Most of the procedures for separating sulfones **I** and **II** are based on their different solubilities in organic solvents. Since only isomer **I** was used in practice, these methods consisted in its separation from concomitant impurities. Isolation of individual sulfones **I** and **II** by treatment of bisphenol S with a boiling mixture of *p*-xylene and isopropanol or methyl ethyl ketone was described in patent [1].

Procedures involving no organic solvents are more convenient for industrial applications. Components of bisphenol S were separated in the form of their monosodium salts [2] by the following procedure. An isomer mixture was dissolved in approximately 2 equiv of aqueous alkali to form the disodium salts readily soluble in water. Only the monosodium salt of **I** was precipitated after partial neutralization of the solution. As stated in patent [2], under these conditions isomer **II** is in the solution in the form of its disodium salt. The suspension was filtered. Monosodium salt of isomer **II** was crystallized after partial neutralization of the filtrate. The salt was separated from the solution. Acidification of an aqueous suspension of this salt gave pure sulfone **II**. Monosodium salts of sulfones **I** and **II** were recovered in 97 and 83% yields respectively, from a mixture containing 79 wt % sulfone **I**, 20 wt % sulfone **II**, and 1 wt % impurities [2].

The purity of both isolated salts was no less than 90%. Thus, this method seems promising for develop a high-performance industrial process for separating isomers **I** and **II** without using organic solvents.

We experimentally tested the procedure described in patent [2]. The results of separation of bisphenol S are presented in Table 1. Isomer **I** was isolated in a yield of 93 wt %, which is close to the yield reported in the patent. However, instead of pure isomer **II** we obtained only a mixture containing 48 wt % target product.

To exclude the possible influence of impurities which can be different in bisphenol used in [2] and in our sample, we prepared a model mixture containing pure isomers **I** and **II** in the ratio equal to that in the bisphenol described in patent [2] (Table 1, run no. 2). The results of separation of this mixture also differed from those reported in the patent.

Since, according to patent [2], monosodium salt of isomer **I** is formed and crystallizes in a solution in which isomer **II** is in the form the disodium salt, the acidity of sulfone **II** should be substantially higher

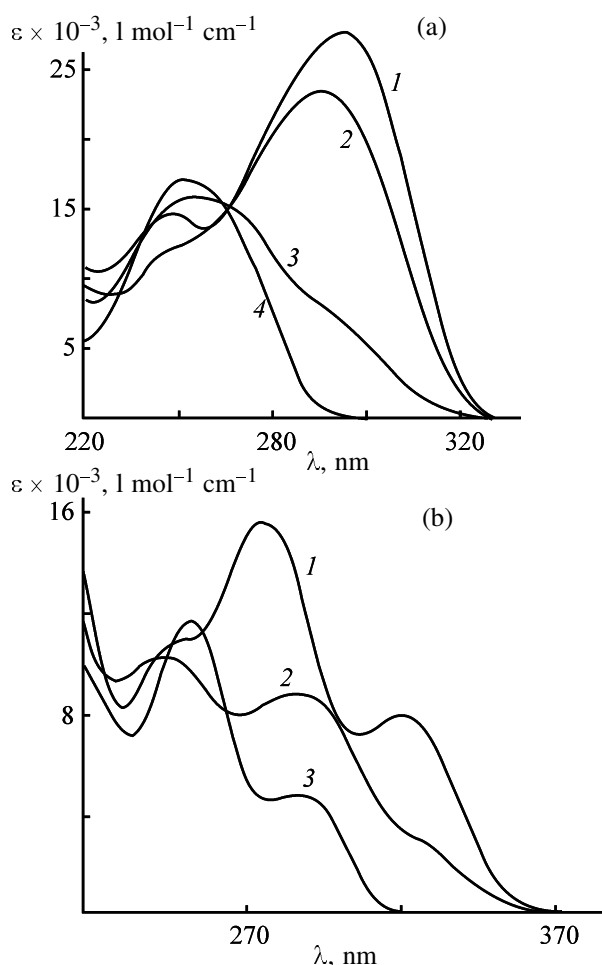
**Table 1.** Results of separation of a mixture of dihydroxydiphenyl sulfone isomers

Run no.	Sample	Weight, g	Component content, wt %		
			I	II	III
1	Bisphenol S	50	82.0	16.5	1.5
	Isomer <b>I</b>	40.5	93.2	6.6	0.2
	Isomer <b>II</b>	7.9	45.6	48.0	6.4
2	Model mixture	50	80.0	20.0	0.0
	Isomer <b>I</b>	42.8	88.3	11.7	0.0
	Isomer <b>II</b>	6.9	61.9	38.1	0.0

**Table 2.** Acidity of isomers **I** and **II** in their 0.004 M aqueous solutions at 22°C

Isomer	Weighed portion, g	$V_{\text{equiv}}^*$ , ml	$\text{p}K_{\text{a}1}$	$\text{p}K_{\text{a}2}$
<b>I</b>	0.0991	6.13	7.52	8.65
	0.0946	5.87	7.50	8.51
	0.1003	6.21	7.53	8.57
Average	–	–	7.52	8.57
<b>II</b>	0.1043	6.47	7.57	8.79
	0.0915	5.55	7.53	8.83
	0.0974	6.05	7.54	8.86
Average	–	–	7.54	8.83

\*  $V_{\text{equiv}}$  is the equivalent volume of 0.1251 N NaOH.



**Fig. 1.** UV spectra of aqueous solutions of (a) isomer **I** at pH (1) 9.95, (2) 8.42, (3) 7.12, and (4) 5.16 and (b) isomer **II** at pH (1) 10.12, (2) 7.05, and (3) 5.24. ( $\epsilon$ ) Molar extinction coefficient and ( $\lambda$ ) wavelength.

than that of sulfone **I**.  $\text{p}K_{\text{a}1}$  and  $\text{p}K_{\text{a}2}$  of sulfone **I** in 71.9 wt % aqueous ethanol at 24°C is 9.01 and 9.93, respectively [3]; in water at 24°C, 7.57 and 8.53, respectively [3]; in 48% aqueous ethanol, 8.79 and 9.41, respectively [4]; and in 70 wt % aqueous ethanol, 8.87 and 10.44, respectively [5].

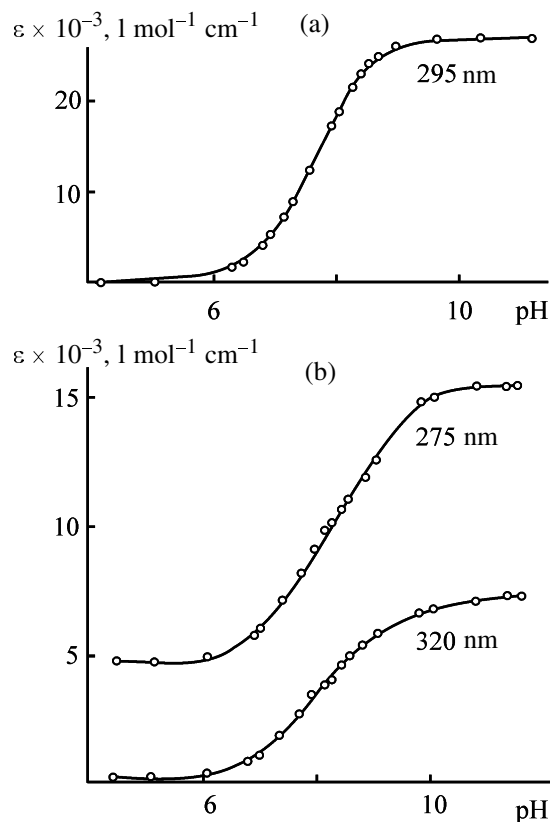
In addition, the acidity of chlorinated [5] and hydroxymethyl-substituted [6] 4,4'-dihydroxydiphenyl sulfone and 2,2'-dihydroxydiphenyl sulfone [4] is known. No data on acidity of sulfone **II** are reported.

Thus, the published data on isomer **I** are contradictory. This can be due to the influence of the solution composition of the acid properties. Since the acidity of compound **I** in water [3] was measured using an insufficiently pure sample (a mixture of isomers with mp 236–238°C was studied, whereas the mp (melting point) of pure **I** was 249.5°C [7]) and no data on the acidity of sulfone **II** under the comparable conditions were reported, in this study we performed parallel measurements of the acidity of isomers **I** and **II** in an aqueous solution. The potentiometric titration curves of ~0.004 M aqueous solutions of these compounds are similar and typical of dibasic acid. The acidity constants calculated by the Neues procedure [8] are presented in Table 2.

The  $\text{p}K_{\text{a}1}$  (negative logarithm of the dissociation constant for the first step) values of isomers **I** and **II** are almost the same (7.52 and 7.54, respectively). Since the structure of the aromatic ring of the  $\text{ArSO}_2$  groups insignificantly affects the acidity of the 4-hydroxy group [3], the first dissociation step of compounds **I** and **II** is deprotonation of the 4-hydroxy group. At the same time, the  $\text{p}K_{\text{a}2}$  values of isomers **I** and **II** differ substantially (8.57 and 8.83, respectively). This is due to the fact that the second dissociation step of isomer **I** involves deprotonation of the 4-hydroxy group whereas the second dissociation step of isomer **II** is deprotonation of the 2-hydroxy group.

We found that  $\text{p}K_{\text{a}2}$  of isomer **II** is somewhat larger than that of isomer **I**. This is consistent with the ratio of acidities of other *o*- and *p*-substituted phenols. For example, *o*-nitrophenol is weaker acid than *p*-nitrophenol ( $\text{p}K_{\text{a}}$  7.23 and 7.15, respectively [8]).

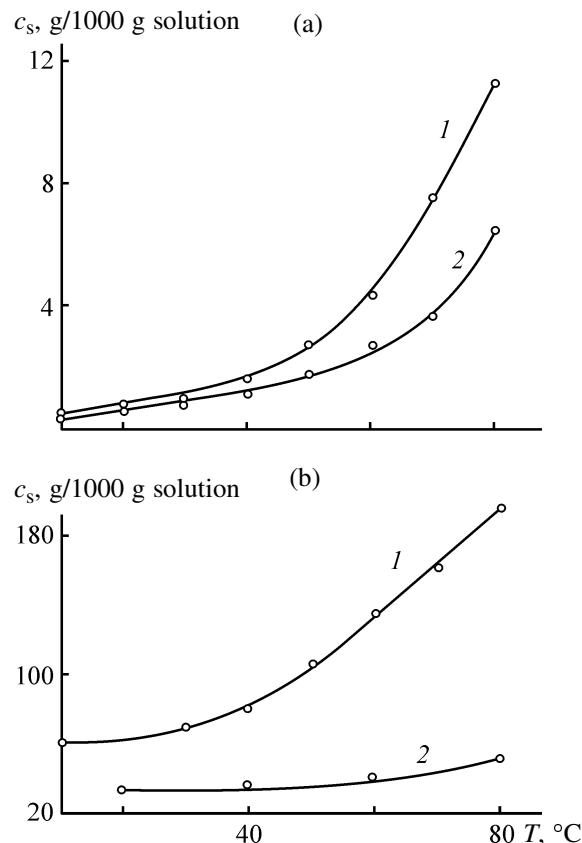
Our experiments on the influence of the pH on the absorption spectra of aqueous solutions of compounds **I** and **II** additionally confirmed their similar acid properties. Unlike the spectra of the molecular compounds [9], dianions of **I** and **II** strongly absorb in the relatively long-wave range (Fig. 1). The spectrum of dianion **I** contains a band with a maximum at  $\lambda = 295 \text{ nm}$  ( $\epsilon = 27400 \text{ l mol}^{-1} \text{ cm}^{-1}$ ); two



**Fig. 2.** Molar extinction coefficient  $\epsilon$  as a function of pH of solutions of (a) **I** and (b) **II** (analytical wavelengths are indicated).

bands at  $\lambda = 275 \text{ nm}$  ( $\epsilon = 15\,400 \text{ l mol}^{-1} \text{cm}^{-1}$ ) and  $\lambda = 320 \text{ nm}$  ( $\epsilon = 8000 \text{ l mol}^{-1} \text{cm}^{-1}$ ) are observed in the spectrum of dianion **II**. When pH of solutions of these compounds increases from 6 to 9, the absorption in these ranges increases (Fig. 2). The pH dependence of the molar absorption coefficient has a usual S-shape and reflects an increase in the degree of dissociation with pH. Since the absorption spectra of conjugated acids **I**, **II**, and their mono- and dianions overlap in the whole range, it is impossible to determine  $\text{p}K_{\text{a}1}$  and  $\text{p}K_{\text{a}2}$  from the spectra data. However, the pH of half-neutralization of isomer **I**, calculated from the spectral data, is 7.71. For isomer **II**, this value calculated from the absorption at  $\lambda = 275 \text{ nm}$  and  $\lambda = 320 \text{ nm}$  was 8.09 and 8.05, respectively. Thus, these results also show that the acidity of isomer **II** is noticeably lower than that of isomer **I**. Therefore, the statement [2] that monosodium salt of **I** precipitates and the readily water-soluble disodium salt of **II** remains in the solution after acidification of solutions containing disodium salts of **I** and **II** is incorrect.

Selective crystallization of one of the isomers may also be due to its lower solubility. The data on solu-



**Fig. 3.** Solubility  $c_s$  of (a) (1) sulfone **I** and (2) **II** and (b) their monosodium salts as a function of temperature  $T$ .

bility of isomers **I** and **II** are contradictory. Zehenter and Fauzer reported [10] that the solubility of isomer **II** (0.32 g in 100 g of water) at 22°C is higher by a factor of approximately 1.5 than that of isomer **I** (0.24 in 100 g of water). At the same time, isomer **I** was recrystallized from an aqueous solution to remove less soluble isomer **II** [7]. To clarify this point, we studied the solubility of sulfones **I** and **II** in water in a wide temperature range. As seen from Fig. 3, the solubility of isomer **II** at 10–80°C is lower by a factor of 2 than that of isomer **I**. Hence, although the content of isomer **I** in its mixture with isomer **II** is high, it is difficult to isolate isomer **I** by recrystallization from water.

Crystallization of monosodium salt of **I** from an acidified aqueous solution of a mixture of disodium salts of **I** and **II**, described in patent [2], could be due to substantial difference in the solubilities of the monosodium salts of these isomers. Since no data on the solubilities of monosodium salts of **I** and **II** are reported, we determined the concentrations of their saturated aqueous solutions at different temperatures (Fig. 3). As seen from Fig. 3, the solubility of mono-

sodium salt of **II** is lower than that of monosodium salt of **I** in the whole temperature range. These data clarify the experimental results on separation of mixtures of isomers **I** and **II**.

Since separation of sulfone **I** from impurities of isomer **II** was performed by treatment of their ammonium salts [11], we studied the solubility of monoammonium salt of **I** in water at different temperatures. The solubility of this salt in water is noticeably lower than that of the monosodium salt, with the difference being the most pronounced at low temperatures. The solubility  $c_s$  (wt %) of the sodium salt at 10, 30, 40, 50, 60, 70, and 80°C is 6.0, 7.0, 8.2, 11.1, 14.6, 16.6, and 20.1, respectively; the solubility of the ammonium salt at 20, 30, 40, 50, 60, and 70°C is 3.4, 3.6, 4.8, 7.1, 11.0, and 15.0, respectively. Thus, isomer **I** can be purified more efficiently in the form of monoammonium salt as compared to its sodium analog.

Thus, separation of isomers **I** and **II** in the form of their monosodium salts based on the difference both in their acidities and in solubilities in water at a usual content of isomer **II** in the mixture (15–20 wt %) is ineffective. However, if the content of isomers **I** and **II** in the mixture substantially differs (~85 and ~2 wt %, respectively), the salts of these compounds can be separated by the procedure described in [11]. This procedure is unsuitable for isolation of pure **II**.

## EXPERIMENTAL

**Crude bisphenol S** was prepared by sulfonation of phenol in the presence of *o*-dichlorobenzene. A 250-ml three-necked flask equipped with a thermometer, a mechanical stirrer with a seal, and a Würtz adapter with a descending condenser was loaded with phenol (120 g) and dichlorobenzene (80 ml). To this solution, 92% sulfuric acid (68 g) was added with stirring at 100–110°C within 10 min. The mixture was kept at 100–110°C for 1 h and then was heated to boil at 140–145°C. The aqueous azeotrope of *o*-dichlorobenzene was separated and the organic layer was returned to the reaction mixture. The temperature of the reaction mixture increased to 180°C within 5 h. Then the reaction mixture was cooled, and *o*-dichlorobenzene was decanted. A solution of sodium hydroxide (51 g) in water (150 ml) was added to the residue. The resulting suspension was heated at 90–95°C with stirring until a solution was formed. The residual organic solvent was separated, and the solution was diluted to 600 ml with distilled water and acidified with 70% sulfuric acid to pH ~3. After cooling of the reaction mixture, the precipitate was filtered off,

washed with distilled water, and dried at 110–120°C. The yield of crude bisphenol S containing 82, 16.5, and 1.5 wt % of sulfones **I**, **II**, and **III**, respectively, was 143 g (90%).

**Individual isomers I and II** were obtained by separation of crude bisphenol using a benzene–acetone mixture by the procedure described in [7]. The melting points of isomer **II** and **I** recrystallized from 5% aqueous ethanol were 185–186 and 248–249°C, respectively, which is close to the published data (186.7 and 249.5°C, respectively [7]).

**Monosodium salts of sulfones I and II and monoammonium salt of I** were prepared by dissolution of these sulfones in 1 equiv of aqueous solution of the appropriate base on heating. The precipitates of these salts formed on cooling were filtered off and dried at 105–110°C. As determined by UV spectroscopy, the content of the target product was no less than 99.5%.

Chromatographic analysis of crude bisphenol S and the isomer mixtures was performed on a Milikhrom chromatograph using columns packed with Sil 600. A mixture of hexane (40 ml), ethyl acetate (20 ml), acetic acid (2 ml), and trifluoroacetic acid (0.5 ml) was used as the eluent. The wavelength used for detection was  $\lambda = 260$  nm.

The content of individual isomers in aqueous solutions was determined by their absorption measured in 1-cm quartz cells on an SF-26 spectrophotometer. The molar extinction coefficient of isomers **I** ( $\lambda = 295$  nm) and **II** ( $\lambda = 275$  nm) measured in solution with pH 11.0–11.5 was 27400 and 15450  $\text{l mol}^{-1} \text{cm}^{-1}$ , respectively.

Crude bisphenol S was separated by the procedure in [2]. Crude bisphenol S (50 g) was placed in a 250 ml three-necked flask equipped with a thermometer, a mechanical stirrer, and a reflux condenser. A solution of NaOH (17 g) in water (75 ml) was added. The resulting suspension was refluxed until a solution was formed. 72% sulfuric acid (12.6 g) was added. The suspension was slowly cooled to 40°C. A precipitate of monosodium salt of isomer **I** was filtered off and the liquid phase was thoroughly removed by pressing. The filtrate was heated to 90–95°C with stirring and acidified to pH 3–4. After cooling, the precipitate of isomer **II** was filtered off, washed with distilled water, and dried at 105–110°C. Isolated monosodium salt of isomer **I** was suspended in distilled water (120 ml). The suspension was heated to 90–95°C with stirring and acidified to pH 4–5. After cooling, the precipitate of isomer **I** was filtered off, washed with distilled water, and dried at 105–110°C.

A mixture containing 80 wt % isomer **I** and 20 wt % isomer **II** was separated similarly.

To determine the solubility of sulfones **I** and **II** and their salts in water, weighed portions of these compounds were mixed with water in a flask equipped with a thermometer and a reflux condenser. The resulting suspensions were heated to a temperature higher by 5–10°C than the required temperature. The system was thermostated with an accuracy of  $\pm 0.2^\circ\text{C}$  for 5–6 h with stirring. Samples of the saturated solution were taken with a sampler equipped with a glass frit, placed in a weighing bottle, cooled to room temperature, weighed on an analytical balance with an accuracy of  $\pm 0.00005$  g, and analyzed spectrophotometrically.

### CONCLUSION

The relative acidities of 2,4'- and 4,4'-dihydroxydiphenyl sulfones and the solubilities of their salts do not allow isolation of the pure 2,4'-isomer by precipitation of its monosodium salt but allow removal of impurities of the 2,4'-isomer from 4,4'-dihydroxydiphenyl sulfone.

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