# Solubilities of Polyhydroxybenzophenones in an Ethanol + Water Mixture from (293.15 to 343.15) K

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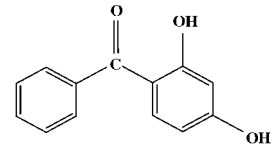
The solubilities of 2,4-dihydroxybenzophenone, 2,3,4-trihydroxybenzophenone, 2,3,4,4′-tetrahydroxybenzophenone, and 2,2′,4,4′-tetrahydroxybenzophenone in an ethanol + water mixture were determined in the temperature range from (293.15 to 343.15) K by a static analytical method. The concentrations of the investigated polyhydroxybenzophenones in saturated solution were analyzed by reverse-phase high-performance liquid chromatography. A semiempirical equation was proposed to correlate the experimental data and exhibited good agreement.

## Introduction

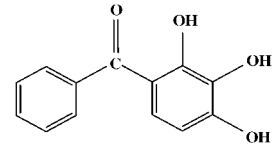
Polyhydroxybenzophenones are industrially important chemicals widely used in plastic, paint, and cosmetic industries as ultraviolet absorbers.[1] Another application extensively implemented for high purity polyhydroxybenzophenones is as an intermediate or component of photoresistive and light-sensitive materials, which are used in industries for photolithography and photoengraving to form patterned coatings on the surfaces.[2,3] The importance of polyhydroxybenzophenones has pushed forward the development of the manufacture and purification processes.[4,5] Generally, crystallization from a mixed solvent of water and ethanol is employed in the subsequent purification processes.[6–9] The solubilities of polyhydroxybenzophenones in an ethanol + water mixture are quite significant for the optimization of the purification process. Unfortunately, no related solubility data are currently available in the literature.[10]

In the present work, the solubilities of four important polyhydroxybenzophenones, i.e., 2,4-dihydroxybenzophenone, 2,3,4-trihydroxybenzophenone, 2,3,4,4′-tetrahydroxybenzophenone, and 2,2′,4,4′-tetrahydroxybenzophenone, in an ethanol + water mixture were determined in the temperature range from (293.15 to 343.15) K to provide important basic data for the development of the purification process.

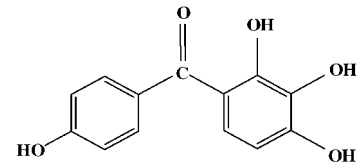
The four polyhydroxybenzophenones involved in this study are homologues with a different number of hydroxy groups, and the chemical structures of them are shown in Figure 1.



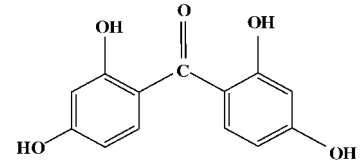

(a) 2,4-dihydroxybenzophenone




(b) 2,3,4-trihydroxybenzophenone




(c) 2,3,4,4'-tetrahydroxybenzophenone




(d) 2,2′,4,4'-tetrahydroxybenzophenone

**Figure 1.** Molecular formulas of 2,4-dihydroxybenzophenone, 2,3,4-trihydroxybenzophenone, 2,3,4,4′-tetrahydroxybenzophenone, and 2,2′,4,4′-tetrahydroxybenzophenone.

## Experimental Section

***Chemicals.*** 2,4-Dihydroxybenzophenone, 2,3,4-trihydroxybenzophenone, 2,3,4,4′-tetrahydroxybenzophenone, and 2,2′,4,4′-tetrahydroxybenzophenone (> 99.5 % purity) were obtained from the Shanghai Chemical Reagent Co., China. HPLC grade methanol and ethanol were from Merck. All chemicals were used as received.

***Apparatus and Procedure.*** The solubility determination in this study was carried out by a static analytical method similar to that described in our previous work.[10] The experimental setup is shown in Figure 2. The apparatus consisted of a three-necked round-bottom flask, which was placed in a water bath and maintained at a desired temperature by water circulated from a constant-temperature water bath with a thermoelectric controller (type CH1015, Cany Precision Instrument Co., Ltd.). The temperature could be maintained within ± 0.05 K of the required temperature. Continuous stirring was achieved with a magnetic stirrer. A condenser with a balloon at the top was connected to the vessels to prevent the solvents from evaporating. A mercury-in-glass thermometer with an uncertainty of ± 0.05 K was inserted into the flask for the measurement of the temperature.

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**Table 1. HPLC Conditions for 2,4-Dihydroxybenzophenone, 2,3,4-Trihydroxybenzophenone, 2,3,4,4′-Tetrahydroxybenzophenone, and 2,2′,4,4′-Tetrahydroxybenzophenone**

| | solute | | | |
|---|---|---|---|---|
| conditions | 2,4-dihydroxybenzophenone | 2,3,4-trihydroxybenzophenone | 2,3,4,4′-tetrahydroxybenzophenone | 2,2′,4,4′-tetrahydroxybenzophenone |
| mobile phase[a] | 65:35 | 60:40 | 70:30 | 42:58 |
| wavelength/nm | 288 | 315 | 320 | 340 |
| temperature/K | 303.15 | 303.15 | 303.15 | 303.15 |
| linear range/mg·mL$^{-1}$ | 0.03∼1.09 | 0.04∼0.87 | 0.05∼0.89 | 0.01∼0.50 |
| correlation coeff, $R^2$ | 0.9998 | 0.9999 | 0.9998 | 0.9991 |
| rsd ($n = 6$) | 0.20 % | 0.15 % | 0.18 % | 0.13 % |

[a] Methanol: 0.2 % (wt %) perchloric acid aqueous solution in volume ratio.

**Table 2. Solubilities of 2,4-Dihydroxybenzophenone, 2,3,4-Trihydroxybenzophenone, 2,3,4,4′-Tetrahydroxybenzophenone, and 2,2′,4,4′-Tetrahydroxybenzophenone in Ethanol ($\omega$) + Water (1 − $\omega$) from (293.15 to 343.15) K ($\omega$ = Mass Fraction)**

| $T$/K | $\omega = 0$ | $\omega = 0.1$ | $\omega = 0.2$ | $\omega = 0.3$ |
|---|---|---|---|---|
| | | 2,4-dihydroxybenzophenone | | |
| 293.15 | 0.0071 ± 0.0003 | 0.0178 ± 0.0007 | 0.049 ± 0.002 | 0.182 ± 0.010 |
| 298.15 | 0.0092 ± 0.0004 | 0.0201 ± 0.0007 | 0.072 ± 0.003 | 0.305 ± 0.011 |
| 303.15 | 0.0104 ± 0.0004 | 0.0254 ± 0.0008 | 0.102 ± 0.003 | 0.51 ± 0.02 |
| 308.15 | 0.0123 ± 0.0003 | 0.0333 ± 0.0009 | 0.141 ± 0.004 | 0.84 ± 0.03 |
| 313.15 | 0.0161 ± 0.0005 | 0.047 ± 0.001 | 0.209 ± 0.006 | 1.25 ± 0.04 |
| 318.15 | 0.0189 ± 0.0006 | 0.063 ± 0.003 | 0.294 ± 0.007 | 1.85 ± 0.07 |
| 323.15 | 0.0258 ± 0.0007 | 0.087 ± 0.002 | 0.43 ± 0.01 | 2.85 ± 0.10 |
| 328.15 | 0.0332 ± 0.0008 | 0.125 ± 0.004 | 0.62 ± 0.02 | 4.22 ± 0.15 |
| 333.15 | 0.043 ± 0.001 | 0.161 ± 0.006 | 0.88 ± 0.03 | 6.01 ± 0.22 |
| 338.15 | 0.058 ± 0.001 | 0.219 ± 0.008 | 1.25 ± 0.04 | 8.30 ± 0.31 |
| 343.15 | 0.081 ± 0.002 | 0.314 ± 0.009 | 1.85 ± 0.05 | 11.23 ± 0.50 |
| | | 2,3,4-trihydroxybenzophenone | | |
| 293.15 | 0.0112 ± 0.0005 | 0.032 ± 0.001 | 0.113 ± 0.003 | 0.45 ± 0.01 |
| 298.15 | 0.0134 ± 0.0005 | 0.042 ± 0.002 | 0.151 ± 0.003 | 0.61 ± 0.02 |
| 303.15 | 0.0189 ± 0.0007 | 0.057 ± 0.002 | 0.224 ± 0.005 | 0.95 ± 0.03 |
| 308.15 | 0.0248 ± 0.0008 | 0.078 ± 0.003 | 0.327 ± 0.01 | 1.45 ± 0.04 |
| 313.15 | 0.0331 ± 0.0010 | 0.119 ± 0.003 | 0.51 ± 0.01 | 2.23 ± 0.06 |
| 318.15 | 0.044 ± 0.001 | 0.173 ± 0.005 | 0.74 ± 0.02 | 3.73 ± 0.08 |
| 323.15 | 0.063 ± 0.002 | 0.241 ± 0.01 | 1.15 ± 0.03 | 5.33 ± 0.17 |
| 328.15 | 0.086 ± 0.003 | 0.354 ± 0.01 | 1.81 ± 0.05 | 7.55 ± 0.31 |
| 333.15 | 0.122 ± 0.003 | 0.51 ± 0.01 | 2.89 ± 0.06 | 9.86 ± 0.39 |
| 338.15 | 0.165 ± 0.006 | 0.78 ± 0.02 | 4.35 ± 0.10 | 12.60 ± 0.50 |
| 343.15 | 0.219 ± 0.008 | 1.15 ± 0.03 | 6.44 ± 0.15 | 15.80 ± 0.78 |
| | | 2,3,4,4′-tetrahydroxybenzophenone | | |
| 293.15 | 0.0114 ± 0.0005 | 0.0381 ± 0.0009 | 0.152 ± 0.007 | 0.90 ± 0.04 |
| 298.15 | 0.0153 ± 0.0006 | 0.051 ± 0.002 | 0.244 ± 0.008 | 1.12 ± 0.05 |
| 303.15 | 0.0222 ± 0.0008 | 0.078 ± 0.003 | 0.369 ± 0.010 | 1.51 ± 0.06 |
| 308.15 | 0.0305 ± 0.0010 | 0.124 ± 0.005 | 0.55 ± 0.02 | 2.12 ± 0.09 |
| 313.15 | 0.044 ± 0.001 | 0.183 ± 0.006 | 0.86 ± 0.03 | 3.07 ± 0.11 |
| 318.15 | 0.060 ± 0.003 | 0.261 ± 0.008 | 1.31 ± 0.05 | 4.78 ± 0.16 |
| 323.15 | 0.086 ± 0.003 | 0.378 ± 0.009 | 1.93 ± 0.06 | 6.86 ± 0.24 |
| 328.15 | 0.133 ± 0.005 | 0.54 ± 0.01 | 2.86 ± 0.10 | 9.11 ± 0.31 |
| 333.15 | 0.179 ± 0.006 | 0.77 ± 0.02 | 4.15 ± 0.13 | 11.81 ± 0.46 |
| 338.15 | 0.262 ± 0.011 | 1.13 ± 0.03 | 6.31 ± 0.15 | 15.04 ± 0.65 |
| 343.15 | 0.364 ± 0.013 | 1.56 ± 0.05 | 9.01 ± 0.35 | 19.10 ± 1.09 |
| | | 2,2′,4,4′-tetrahydroxybenzophenone | | |
| 293.15 | 0.0071 ± 0.0004 | 0.0262 ± 0.0008 | 0.077 ± 0.003 | 0.282 ± 0.011 |
| 298.15 | 0.0089 ± 0.0005 | 0.0313 ± 0.0008 | 0.112 ± 0.004 | 0.45 ± 0.02 |
| 303.15 | 0.0113 ± 0.0005 | 0.0364 ± 0.0012 | 0.171 ± 0.006 | 0.75 ± 0.03 |
| 308.15 | 0.0155 ± 0.0007 | 0.045 ± 0.002 | 0.254 ± 0.009 | 1.25 ± 0.05 |
| 313.15 | 0.0212 ± 0.0008 | 0.065 ± 0.003 | 0.348 ± 0.011 | 1.90 ± 0.08 |
| 318.15 | 0.0273 ± 0.0009 | 0.114 ± 0.005 | 0.55 ± 0.01 | 2.85 ± 0.10 |
| 323.15 | 0.0380 ± 0.0011 | 0.161 ± 0.008 | 0.91 ± 0.03 | 4.05 ± 0.14 |
| 328.15 | 0.057 ± 0.002 | 0.248 ± 0.011 | 1.50 ± 0.06 | 5.61 ± 0.25 |
| 333.15 | 0.088 ± 0.004 | 0.41 ± 0.02 | 2.30 ± 0.07 | 7.72 ± 0.32 |
| 338.15 | 0.123 ± 0.005 | 0.60 ± 0.03 | 3.31 ± 0.10 | 10.52 ± 0.44 |
| 343.15 | 0.159 ± 0.006 | 0.91 ± 0.04 | 5.02 ± 0.18 | 14.12 ± 0.65 |

First, binary (ethanol + water) mixtures were prepared by mass with an uncertainty of ± 0.1 mg. Next, excess solute and about 200 mL of binary solvent were put into the flask. Then, the contents of the flask were stirred at 200 rpm. After 2 h of stirring, the solution was kept still for at least 6 h allowing undissolved solid to settle. Finally, samples were taken through a sampling line which is very thin to ensure small dead volume and analyzed by reverse-phase high-performance liquid chromatography (HPLC). The time required to establish solid−liquid equilibrium was experimentally determined by repetitively measuring the solubilities at certain time intervals until reproducible data were obtained. The reproducibility was found to be within 0.5 % after 6 h of settling time.

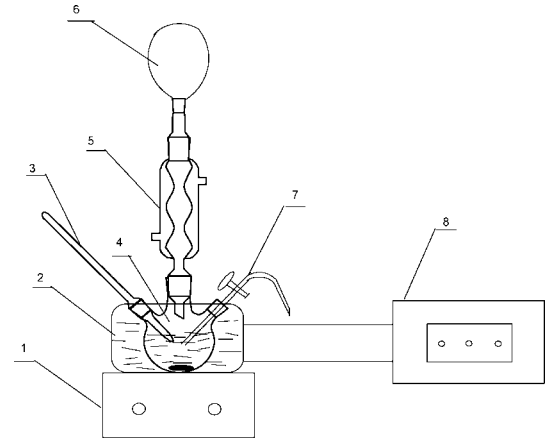


**Figure 2.** Experimental setup for solubility measurement: 1, magnetic stirrer; 2, water bath; 3, mercury-in-glass thermometer; 4, three-necked round-bottom flask; 5, condenser; 6, balloon; 7, sampling line; 8, constant-temperature water bath.

***Analysis.*** After disregarding the first (2 to 3) mL solution received from the sampling line, about 2 g of saturated solution was collected, weighed, and diluted with 1:1 (volume ratio) methanol−water solution to a certain volume. Then, the composition of the pretreated samples was directly determined by reverse-phase HPLC (Agilent 1100 series). The HPLC column was a DIAMONSIL C18 (Dikma Technologies, 250 × 4.6 mm, 5 $\mu$m). Methanol−perchloric acid solution was used as the mobile phase at a flow rate of 0.8 mL·min$^{-1}$. Other conditions are shown in Table 1. The analytical method was found to be simple, fast, accurate, and reliable.

## Results and Discussion

Six samples were taken and analyzed for each experimental point. The experimental data for the solubilities of 2,4-dihydroxybenzophenone, 2,3,4-trihydroxybenzophenone, 2,3,4,4′-tetrahydroxybenzophenone, and 2,2′,4,4′-tetrahydroxybenzophenone in an ethanol + water mixture are listed in Table 2, with error limits using the 95 % confidence level. The units for solubility are grams per 100 g of solvent. Solubilities of 2,2′,4,4′-tetrahydroxybenzophenone in an ethanol + water mixture at different concentrations are shown in Figure 3, and similar behavior was exhibited by 2,4-dihydroxybenzophenone, 2,3,4-trihydroxybenzophenone, and 2,3,4,4′-tetrahydroxybenzophenone. From the results, we can see that the solubilities of the four polydyxoxybenzophenones

**Table 3. Parameters in Equation 1 for Polyhydroxybenzophenones**

| solute | *a* | *b* | *c* | *d* | *σ* |
|---|---|---|---|---|---|
| 2,4-dihydroxybenzophenone | 22.42 | 7.47 | −8738.91 | 3703.14 | 0.06 |
| 2,3,4-trihydroxybenzophenone | 38.27 | −55.80 | −13259.40 | 22767.37 | 0.31 |
| 2,3,4,4′-tetrahydroxybenzophenone | 33.28 | −41.48 | −11374.12 | 17489.04 | 0.45 |
| 2,2′,4,4′-tetrahydroxybenzophenone | 35.27 | −39.99 | −12364.85 | 17627.29 | 0.16 |

in an ethanol + water mixture increase as the temperature and the concentration of ethanol in the mixture solvent increase. Figure 4 depicts the solubilities of 2,4-dihydroxybenzophenone, 2,3,4-trihydroxybenzophenone, 2,3,4,4′-tetrahydroxybenzophenone, and 2,2′,4,4′-tetrahydroxybenzophenone in pure water. Generally, the molecule with more −OH groups in the polyhydroxybenzophenone has larger solubility as the molecular polarity increases. However, 2,2′,4,4′-tetrahydroxybenzophenone is an exception as it is a wholly symmetry molecule which decreases its polarity.

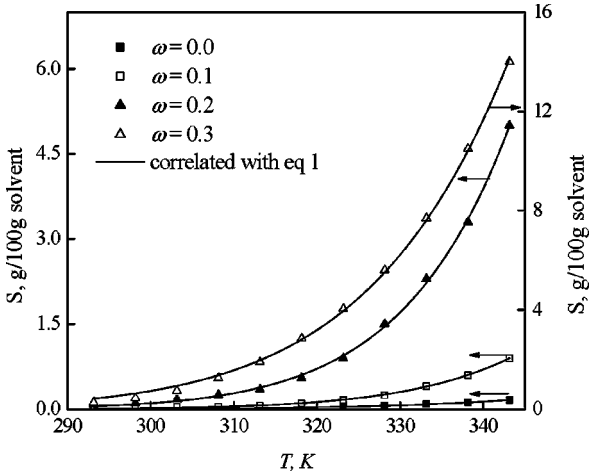


**Figure 3.** Solubilities of 2,2′,4,4′-tetrahydroxybenzophenone in an ethanol + water mixture at different concentrations.

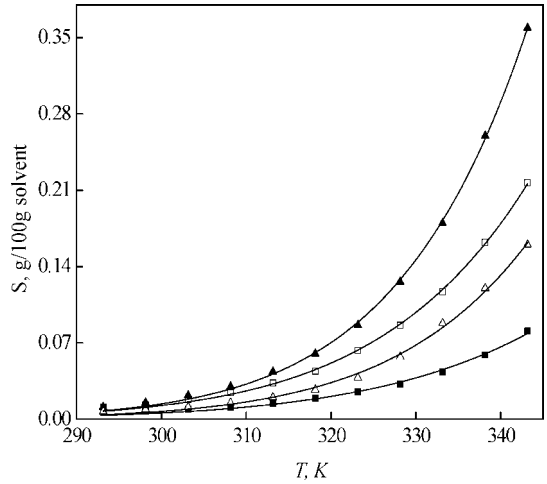


**Figure 4.** Solubilities of 2,4-dihydroxybenzophenone, 2,3,4-trihydroxybenzophenone, 2,3,4,4′-tetrahydroxybenzophenone, and 2,2′,4,4′-tetrahydroxybenzophenone in pure water. ■, 2,4-dihydroxybenzophenone; □, 2,3,4-trihydroxybenzophenone;▲, 2,3,4,4′-tetrahydroxybenzophenone; Δ, 2,2′,4,4′-tetrahydroxybenzophenone; —, correlated with eq 1.

A semiempirical equation shown in eq 1 was proposed to correlate the experimental data

$$S = \exp(a + b\omega + c/T + d\omega/T) \quad (1)$$

where $S$ refers to solubility; $T$ is temperature; $\omega$ is the mass fraction of ethanol in the solvent mixture; and $a$, $b$, $c$, and $d$ are parameters. The values of parameters $a$, $b$, $c$, and $d$ are presented in Table 3, with the root-mean-square deviations (rmsd) defined by

$$\sigma = \left[\sum_{i-1}^{n} (S_{ci} - S_i)^{2/n}\right]^{1/2} \quad (2)$$

where $S_i$ is experimental solubility; $S_{ci}$ is the calculated solubility; and $n$ is the number of experimental points. Plots of the correlated results are also shown in Figures 3 and 4, suggesting that the equation fits the data well.

## Conclusion

The solubilities of 2,4-dihydroxybenzophenone, 2,3,4-trihydroxybenzophenone, 2,3,4,4′-tetrahydroxybenzophenone, and 2,2′,4,4′-tetrahydroxybenzophenone in an ethanol + water mixture were determined in the temperature range from (293.15 to 343.15) K by a static analytical method. A semiempirical equation was employed to correlate the experimental data with good agreement. The information yielded from this work is essential for the industrial development of purification processes of the four polyhydroxybenzophenones.

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