Solubility of Butyl Paraben in Methanol, Ethanol, Propanol, Ethyl Acetate, Acetone, and Acetonitrile

Huaiyu Yang[†] and Åke C. Rasmuson*[,†,‡]

Department of Chemical Engineering and Technology, Royal Institute of Technology (KTH), SE-100 44 Stockholm, Sweden, and Department of Chemical and Environmental Sciences, Materials and Surface Science Institute, University of Limerick, Limerick, Ireland

The solubility of butyl paraben (butyl 4-hydroxybenzoate) have been determined in methanol, ethanol, propanol, acetone, ethyl acetate, and acetonitrile in the temperature range of (10 to 50) °C by the gravimetric method. The order of the solubility of butyl paraben in the different solvents as mass fraction at 20 °C is: methanol > ethanol > acetone > propanol > ethyl acetate > acetonitrile. In terms of mole fraction solubility, the corresponding order is acetone > propanol > ethanol > ethyl acetate > methanol > acetonitrile, which shows that both nonpolar and polar groups of the paraben molecule influence the solubility in the different solvents.

Introduction

Solid−liquid solubility plays a very important role in the design and operation of crystallization processes. The solubility relationship determines the method of supersaturation generation in crystallization and the yield and productivity of the process. For butyl paraben the data reported in the literature are quite scarce.[1,2] In the present work the solubility of butyl paraben in pure methanol, ethanol, propanol, acetone, ethyl acetate, and acetonitrile has been investigated at different temperatures from (10 to 50) °C.

Parabens, alkyl esters of *p*-hydroxybenzoic acid, are the most common preservatives in use today. Owing to their relatively low toxicity, parabens (or their salts) are found in many thousands of cosmetic, toiletries, food, and pharmaceutical products.[3−7] Antimicrobial activity and the octanol−water partition coefficient increase with the increase in molecular weight and the length of the alkyl side chain.[8−10] Methyl paraben alone, or more usually in combination with one or more of ethyl, propyl, and butyl paraben, is usually used as preservative.[11] Butyl paraben is used in advanced cosmetic formulas as a natural, nonirritating organically derived preservative. Butyl paraben increases the shelf life of cosmetics without oxidizing other ingredients. Butyl paraben is used for its antifungal properties, and parabens in general are said to have both antifungal and bactericidal properties. Butyl paraben has been used for many years as a preservative and is generally considered to be safe. Combinations of parabens have been proposed to have a synergistic effect on bacteria.[9,12]

Materials and Methods

Butyl paraben (CAS number: 94-26-8) of > 99.0 % purity was purchased from Aldrich and was used without further purification. Ethanol of 99.7 % purity was purchased from Solveco Chemicals, and methanol (≥ 99.9 %), 1-propanol (≥ 99.8 %), acetone (99.9 %), ethyl acetate (99.8 %), and acetonitrile (≥ 99.8 %) were from VWR International.

Procedures. The solubility of butyl paraben in a temperature range from (10 to 50) °C in methanol, ethanol, propanol, acetone, ethyl acetate, and acetonitrile have been determined by the gravimetric method. The temperature was controlled by thermostatic baths with an uncertainty of ± 0.01 °C, and the temperature was calibrated by a mercury thermometer (Precision, Arno Amavell, 6983 Kreuzwerthelm with uncertainty of ± 0.01 °C).

A bottle of 300 mL with about 50 mL of solvent was initially cooled to 10 °C at which an amount of solid butyl paraben was added. Saturation was reached by dissolution from a surplus of solid butyl paraben added to the solution, assuring there was a solid phase present in the solution at equilibrium. The solution was kept under agitation at 400 rpm by a magnetic stir bar for more than 12 h to ensure that equilibrium was reached. For sampling, a 10 mL syringe in its unbroken plastic bag was put into the water bath for several minutes to reach the same temperature as the solution. Then the syringe with a needle attached was used for sampling (2 to 4) mL solution in the bottles. A filter (PTFE 0.2 μm) was attached to the syringe through which the sample was transferred into two small preweighed plastic bottles ((1 to 2) mL solution per bottle). Each bottle was quickly covered to prevent evaporation and weighed with its content. Then the cover was removed, and the samples were dried in ventilated laboratory hoods at room temperature (about 25 °C). The solid sample mass was recorded repeatedly throughout the drying process to establish the point where the mass remained constant, which took more than one month to reach. The mass of the final dry sample was used for the calculation of the solubility, of course with appropriate correction for the mass of the covers. The balance (Mettler AE240) used had a resolution of ± 0.00001 g.

After taking the sample from the saturated solution at 10 °C, the solution was heated to the next temperature level, and a surplus of butyl paraben was added. Then the solubility at this temperature was measured as described above. These steps were repeated at every 10 °C until the highest temperature of 50 °C.

* To whom correspondence should be addressed. E-mail: rasmuson@ket.kth.se. Tel.: +46-8-7908227. Fax: +46-8-105228.
[†] Royal Institute of Technology.
[‡] University of Limerick.

10.1021/je1006289
Published on Web 09/20/2010

Table 1. Mass Fraction (Average of Two Measurements) Solubility of Butyl Paraben (*w*) in Methanol, Ethanol, Acetone, Propanol, Ethyl Acetate, and Acetonitrile and Standard Deviations

	100*w* (standard deviation)					
t/°C	in methanol	in ethanol	in acetone	in propanol	in ethyl acetate	in acetonitrile
9.9	63.747 (0.050)	59.644 (0.009)	60.032 (0.043)	56.450 (0.060)	42.415 (0.148)	27.470 (0.082)
19.9	72.337 (0.010)	67.228 (0.244)	66.623 (0.010)	63.368 (0.006)	50.085 (0.461)	44.874 (0.135)
29.9	79.107 (0.288)	75.540 (0.302)	72.983 (0.001)	70.603 (0.011)	59.077 (0.474)	60.998 (0.025)
39.9	85.382 (0.084)	82.420 (0.058)	79.436 (0.318)	77.721 (0.113)	68.848 (0.010)	75.275 (0.206)
49.9	91.161 (0.025)	89.321 (0.021)	86.062 (0.117)	84.955 (0.190)	78.087 (0.082)	85.689 (0.106)

Results and Discussion

Table 1 and Figure 1 present the mass fraction solubility data (g of solute/g of solution) of butyl paraben in methanol, ethanol, propanol, acetone, ethyl acetate, and acetonitrile from (10 to 50) °C, and the numbers in brackets in Table 1 give uncertainties estimated by the standard deviations of the two measurements at each temperature. Overall the solubility is very high—in the order of (1 to 10) g of solute per g of solvent. Figure 2 shows the corresponding van't Hoff plot. It is obvious that the solubilities in these solvents all increase with increasing temperature, but the van't Hoff enthalpy of solution differs. The solubility in acetonitrile is more sensitive to temperature. At 19.9 °C, the mass fraction solubility in these solvents changes from high to low in the order: methanol > ethanol > acetone > propanol > ethyl acetate > acetonitrile. However, at 29.9 °C the solubility in acetonitrile is higher than in ethyl acetate, and when the temperature increases to 49.9 °C, the solubility in acetonitrile is higher than in propanol and ethyl acetate. The solubility curves of butyl paraben in ethyl acetate, propanol, methanol, and ethanol are nearly parallel.

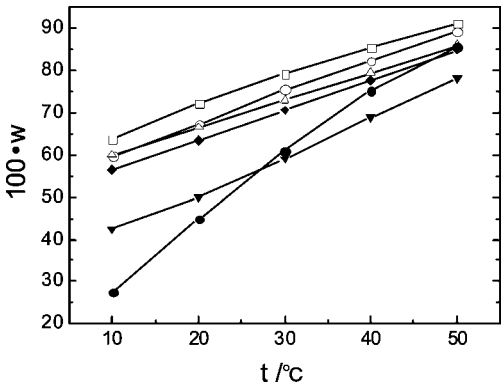

Figure 1. Solubility of butyl paraben in ethyl acetate, propanol, acetone, methanol, acetonitrile, and ethanol as mass fraction. □, methanol; ○, ethanol; △, acetone; ◆, propanol; ●, acetonitrile; ▼, ethyl acetate.

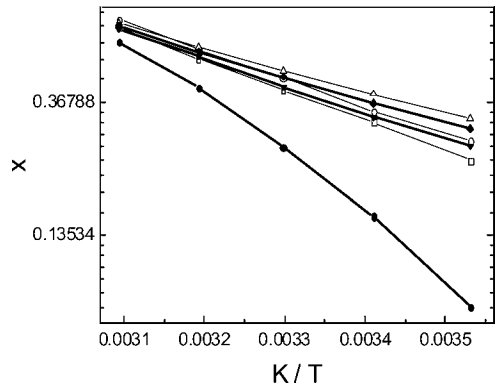

Figure 2. van't Hoff plot over the solubility of butyl paraben in ethyl acetate, propanol, acetone, methanol, acetonitrile, and ethanol. □, methanol; ○, ethanol; △, acetone; ◆, propanol; ●, acetonitrile; ▼, ethyl acetate.

In terms of mole fractions, the solubility at 19.9 °C changes according to acetone > propanol > ethanol > ethyl acetate > methanol > acetonitrile, the latter giving a significantly lower solubility than the others. The butyl paraben has an aromatic ring with a hydroxyl group in the para position to an ester group with a hydrocarbon chain tail. The hydroxyl function group is polar with a hydrogen-bond donating as well as accepting functionality. The ester group is hydrogen-bond accepting especially on the carbonyl oxygen. Out of the solvents, of course the alcohols have both hydrogen-bond donating and accepting functionalities, while acetone, ethyl acetate, and acetonitrile are only hydrogen-bond accepting. In the results of this work, the solubility appears to be influenced by the nonpolar aromatic ring and the hydrocarbon chain tail as well as by the polar hydroxyl and ester functionality, for example, as seen in how the solubility increases with increasing chain length of the alcohols. The empirical solvent polarity parameter, E_T, of Reichardt[13] is 0.762, 0.654, 0.617, 0.355, 0.228, and 0.460, of methanol, ethanol, propanol, acetone, ethyl acetate, and acetonitrile, respectively, which also show that the nonpolar groups of the paraben molecule are important for the solubility. Solubility in acetonitrile is more sensitive to temperatures than others, mainly since that the activity of −CN function group is more sensitive to temperatures than other function groups in other solvents.

The solubility data can be well-correlated by the nonlinear equation:

$$\ln x = A(T/\mathrm{K})^{-1} + B + C(T/\mathrm{K}) \qquad (1)$$

where x = mole fraction solubility (moles of solute/mole of solution), T is in kelvin, and A, B, and C are regression curve parameters which are listed in Table 2. Overall for all of the correlations, the correlation coefficients (R^2) exceed 0.999, and standard deviations are below 0.0321 in x.

From eq 1, the mole fraction solubility of butyl paraben at 25 °C is 0.338 in methanol and 0.372 in ethanol with standard deviations of about 0.03, which agrees well with the solubility data of Alexander et al.:[14] 0.336 in methanol and 0.355 in ethanol.

Conclusions

The solubility of butyl paraben in methanol, ethanol, propanol, acetone, ethyl acetate, and acetonitrile in the temperature range

Table 2. Values of Parameters in $\ln x = A(T/\mathrm{K})^{-1} + B + C(T/\mathrm{K})$

	methanol	ethanol	acetone	propanol	ethyl acetate	acetonitrile
A	−1145.19	−1430.23	339.8378	187.9712	−698.157	−13800.4
B	−1.0869	1.3469	−8.6206	−8.1433	−3.24275	74.6545
C	0.01289	0.00826	0.02208	0.0220	0.01525	−0.1007

of (10 to 50) °C is overall very high—in the order of (1 to 10) g of solute per g of solvent on a solute-free basis. In all solvents the solubility increases with temperature, a dependence that is well-captured by a three-parameter regression equation. The solubility of butyl paraben in the different solvents at 19.9 °C as mass fraction is methanol > ethanol > acetone > propanol > ethyl acetate > acetonitrile. In terms of mole fractions solubility, the corresponding order is acetone > propanol > ethanol > ethyl acetate > methanol > acetonitrile, which shows that both nonpolar and polar groups of the molecule influence the solubility of paraben in the different solvents.

Literature Cited

(1) Grant, D.; Mehdizadeh, M.; Chow, A. H. L.; Fairbrother, J. E. Non-linear van't Hoff solubility-temperature plots and their pharmaceutical interpretation. *Int. J. Pharm.* **1984**, *18*, 25–38.

(2) Perlovich, G.; Rodionov, S. V.; Bauer-Brandl, A. Thermodynamics of solubility, sublimation and solvation processes of parabens. *Eur. J. Pharm. Sci.* **2005**, *24*, 25–33.

(3) Andersen, F. Final Report on the Safety Assessment of Methylparaben, Ethylparaben, Propylparaben, and Butylparaben. *Int. J. Toxicol.* **1984**, *3*, 147–209.

(4) Andersen, F. Final Report on the Safety Assessment of Isobutylparaben and Isopropylparaben 1. *Int. J. Toxicol.* **1995**, *14*, 364–372.

(5) Soni, M.; Burdock, G. A.; Taylor, S. L.; Greenberg, N. A. Safety assessment of propyl paraben: a review of the published literature. *Food Chem. Toxicol.* **2001**, *39*, 513–532.

(6) Soni, M.; Taylor, S. L.; Greenberg, N. A.; Burdock, G. A. Evaluation of the health aspects of methyl paraben: a review of the published literature. *Food Chem. Toxicol.* **2002**, *40*, 1335–1373.

(7) Andersen, F. Final Amended Report on the Safety Assessment of Methylparaben, Ethylparaben, Propylparaben, Isopropylparaben, Butylparaben, Isobutylparaben, and Benzylparaben as used in Cosmetic Products. *Int. J. Toxicol.* **2008**, *27*, 1–82.

(8) Murrell, W.; Vincent, J. The esters of 4-hydroxybenzoic acid and related compounds. IV. The bacteriostatic action of *n*-alkyl 4-hydroxybenzoates. *J. Soc. Chem. Ind. London* **1950**, *69*, 109–113.

(9) Doron, S.; Friedman, M.; Falach, M.; Sadovnic, E.; Zvia, H. Antibacterial effect of parabens against planktonic and biofilm *Streptococcus sobrinus*. *Int. J. Antimicrob. Agents* **2001**, *18*, 575–578.

(10) Golden, R.; Gandy, J.; Vollmer, G. A review of the endocrine activity of parabens and implications for potential risks to human health. *Crit. Rev. Toxicol.* **2005**, *35*, 435–458.

(11) Charnock, C.; Finsrud, T. Combining esters of para-hydroxy benzoic acid (parabens) to achieve increased antimicrobial activity. *J. Clin. Pharm. Ther.* **2007**, *32*, 567–572.

(12) Ma, Y.; Marquis, R. Irreversible paraben inhibition of glycolysis by *Streptococcus mutans* GS-5. *Lett. Appl. Microbiol.* **2008**, *23*, 329–333.

(13) Reichardt, C. *Solvents and solvent effects in organic chemistry*; Wiley-VCH: Germany, 2002.

(14) Alexander, K. S.; John, W. M.; Harol, P., Jr.; Anthony, N. P. Solubility profiles and thermodynamics of parabens in aliphatic alcohols. *Indian J. Pharm. Sci.* **1977**, *66*, 42–48.

Received for review June 16, 2010. Accepted September 7, 2010.

JE1006289