Experimental solubility for betulin and estrone in various solvents within the temperature range $T = (293.2$ to $328.2)$ K

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ABSTRACT

The solubility of complex triterpenes Lup-20(29)-ene-3β,28-diol (betulin) and (8R,9S,13S,14S)-3-hydroxy-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrocyclopenta[a]phenanthren-17-one (estrone) in numerous common solvents were determined by combined thermal gravimetry and digital thermal analysis (TGA/DTA). The measurements were conducted at atmospheric pressure and within the temperature range of $T = (293.2$ to $328.2)$ K. Melting point and enthalpy of fusion data of the solutes considered were also determined by DTA/TGA. The measured values were modelled using the Non-Random Two Liquid (NRTL) and Tsuboka–Katayama modified Wilson activity coefficient models which incorporated polynomial temperature dependence. The models provided a very good correlation of the experimental values in most cases.

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1. Introduction

The majority of separation processes employed in industry are based on promoting a mixture to form two phases, the compositions of which are generally different from the feed mixture. The conditions of temperature, composition, and pressure at which a certain phase will appear is governed by thermodynamic principles and the equilibrium condition. Crystallization is generally a (solid + liquid) separation process commonly employed in the petrochemical and pharmaceutical industries, in the production of waxes, polymers and pharmaceutical ingredients. Novel research, development, and optimisation are common in such industries, as the need for the exploration of alternate process routes and new product development is often required. To accomplish this, it is essential that the physical behaviour of the mixtures being considered is well described by either experimental data or accurate model predictions.

Betulin is a naturally occurring pentacyclic triterpene found in the bark of birch wood [1]. Recent studies have shown the effectiveness of betulin derivatives in the treatment of numerous cancers, including melanoma, neuroblastoma, lung carcinoma, and as a Human Immunodeficiency Virus inhibitor, [2–5]. There is, however, limited research available in the literature on the

(solid + liquid) behaviour of betulin in common solvents at equilibrium [6–8], which is imperative for the design of efficient betulin extraction processes.

Estrone is a common estrogenic hormone used mainly as a supplement drug in post-hysterectomy and post-menopausal women, to assist in regulating normal endocrine behaviour. Nevertheless, the physical behaviour of estrone in common solvents is not readily available in the literature [9–11].

The solubility behaviour of betulin and estrone was determined in more than 10 solvents at atmospheric pressure in the temperature range of $T = (293.2$ to $328.2)$ K in this study. The solvents used included: nonan-1-ol, pentan-1-ol, acetonitrile, 2-aminoethanol, n-dodecane, butan-2-ol, N,N-dimethylformamide, water, n-octane, octan-1-ol, morpholine-4-carbaldehyde, n-hexadecane, and 1-methyl-2-pyrrolidone. Furthermore, the experimental data measured were modelled using the Non-Random Two Liquid (NRTL) [12] and Tsuboka–Katayama modified Wilson [13] activity coefficient models which incorporated a polynomial temperature dependence.

2. Theory

2.1. Thermodynamic relationship

In the case of a eutectic system not undergoing (solid + solid) phase transitions, i.e. a single solid phase exists, Hildebrand and Scott [14] (also reported by Weidlich and Gmehling [15]) have shown that:

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TABLE 1
Chemical suppliers and purities.

Component	CAS no.	Supplier	Refractive index (RI) at T = 293.15 K and 0.101 MPa.[‡]		Minimum stated mass fraction purity	GC peak relative area (mass fraction purity)
			Exptl.	Lit.		
Solvents						
Nonan-1-ol	143-08-8	Sigma-Aldrich	1.4334	1.4333[a]	⩾0.99	0.9999[d]
Pentan-1-ol	71-41-0	Sigma-Aldrich	1.4098	1.4101[a]	⩾0.99	0.9970[d]
Acetonitrile	75-05-8	Sigma-Aldrich	1.3439	1.3442[b]	⩾0.999	0.9999
2-Aminoethanol	141-43-5	Sigma-Aldrich	1.4542	1.4541[a]	⩾0.99	0.9903[d]
n-Dodecane	112-40-3	Merck	1.4218	1.4210[a]	⩾0.99	0.9999
Butan-2-ol	78-92-2	Sigma-Aldrich	1.3983	1.3988[a]	⩾0.99	0.9916[d]
N,N-dimethylformamide	68-12-2	Aldrich	1.4304	1.4305[a]	⩾0.999	0.9999
n-Octane	111-65-9	Merck	1.3978	1.3974[b]	⩾0.99	0.9999
Octan-1-ol	111-87-5	Reidel-de Haën	1.4291	1.4295[a]	⩾0.995	0.9950[d]
Morpholine-4-carbaldehyde	4394-85-8	Merck	1.4849	1.4845[a]	⩾0.99	0.9999
n-Hexadecane	544-76-3	Sigma-Aldrich	1.4346	1.4345[a]	⩾0.99	0.9999
1-Methyl-2-pyrrolidone	872-50-4	Merck	1.4690	1.4684[a]	⩾0.995	0.9999
Water[c]	7732-18-5		1.3329	1.3330		
Solutes						
Lup-20(29)-ene-3β,28-diol (betulin)	473-98-3	Sigma-Aldrich			⩾0.99	⩾0.99[e]
(8R,9S,13S,14S)-3-hydroxy-13-methyl- 6,7,8,9,11,12,13,14,15,16-decahydrocyclopenta[a] phenanthren-17-one (estrone)	53-16-7	Sigma-Aldrich			⩾0.99	⩾0.99[e]
(3β,25R)-Spirost-5-en-3-ol (diosgenin)	512-04-9	Sigma-Aldrich			⩾0.93[f]	⩾0.99[e]

[‡] Standard uncertainties u are $u(RI) = 0.0001$, $u(T) = 0.01$ K, $u(P) = 0.002$ MPa.
[a] Lide at T = 293.15 K [16].
[b] James and Lord at T = 293.15 K [17].
[c] Water conductivity = 27.6 μS · m^{-1}.
[d] Purified by molecular sieving.
[e] GC–MS fraction relative abundance.
[f] Purified by recrystallization with acetone.

$$\ln(x_i^{sat}\gamma_i^{sat}) = -\frac{\Delta_{fus}H_i({}_{fus}T_i)}{R_{fus}T_i}\ln\left(\frac{{}_{fus}T_i}{T}\right) \qquad (1)$$

In equation (1), x_i^{sat} is the liquid mole fraction of the solute at the saturation condition, γ_i^{sat} is the activity coefficient of the solute in the saturated solution, $\Delta_{fus}H_i$ is the enthalpy of fusion at the melting temperature ${}_{fus}T_i$, R is the Universal Gas Constant, and T is the temperature of the system. In this expression, the difference between the solid heat capacity and sub-cooled liquid heat capacity is estimated by the entropy of fusion at the triple or melting point.

γ_i^{sat} is a function of composition at a given temperature and can be calculated using a Gibbs excess energy model.

2.2. Activity coefficient models

The NRTL [12] and T–K–Wilson [13] models were used to correlate the experimental results. A brief description of the models is presented below.

2.2.1. The Non-Random Two-Liquid (NRTL) model
The activity coefficient expression of the NRTL model [12] for a binary mixture is given by:

$$ln\gamma_i = x_j^2\left[\tau_{ji}\left(\frac{G_{ji}}{x_i + x_jG_{ji}}\right)^2 + \left(\frac{\tau_{ij}G_{ij}}{(x_j + x_iG_{ij})^2}\right)\right] \qquad (2)$$
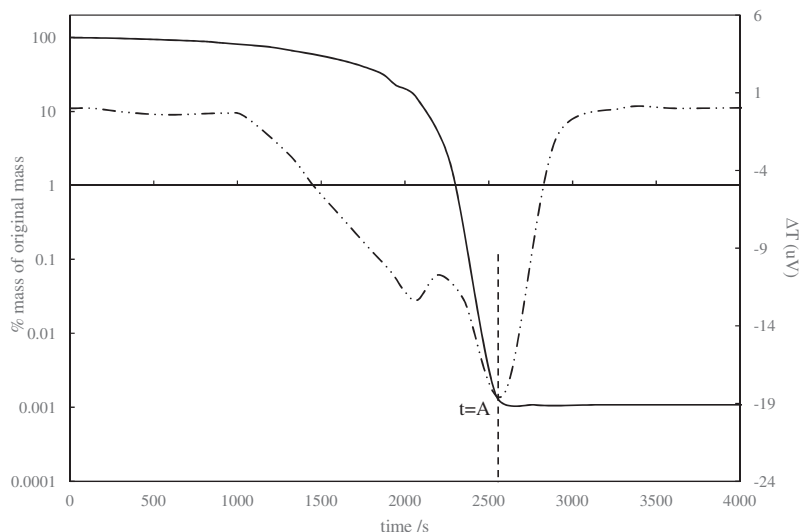

FIGURE 1. A generic combined TG-DTA plot; (−−) TG, (⎯·⎯·⎯) DTA.