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Thermodynamics of the lipase-catalyzed transesterification of (−)-menthol and dodecyl dodecanoate in organic solvents
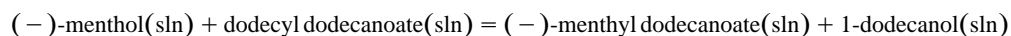
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Abstract

The thermodynamics of the lipase-catalyzed transesterification reaction

$$(−)\text{-menthol(sln)} + \text{dodecyl dodecanoate(sln)} = (−)\text{-menthyl dodecanoate(sln)} + \text{1-dodecanol(sln)}$$

have been studied. Equilibrium measurements were performed as a function of temperature with *n*-heptane, toluene and 2,2,4-trimethylpentane as solvents. The results of the equilibrium measurements were used to calculate the standard molar Gibbs energy $\Delta_r G_m^o$, enthalpy $\Delta_r H_m^o$ and entropy $\Delta_r S_m^o$ changes for the above reaction in these three solvents at the temperature $T = 298.15$ K. The values of the $\Delta_r G_m^o$ and $\Delta_r H_m^o$ in these solvents ranged, respectively, from 1.5 to 2.6 kJ mol^{-1} and from 0.2 to 4.0 kJ mol^{-1}. The (hexane + water) partition coefficients of the reactants and products were also determined at $T = 298.15$ K. A thermochemical cycle calculation was then used to calculate a value for the equilibrium constant $K = (2.4 \pm 0.7) \times 10^{-3}$ and $\Delta_r G_m^o = (14.9 \pm 0.7)$ kJ mol^{-1} for the above reaction in water. However, the average value of the equilibrium constant for reaction (1) in the organic solvents is remarkably constant, namely $\langle K \rangle = 0.372$ (estimated standard deviation of the mean = 0.014). Thus, the thermodynamics of this reaction in water are substantially different than in the organic solvents studied herein. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: 1-Dodecanol; Dodecyl dodecanoate; Equilibrium constants; Lipase; (−)-Menthol; (−)-Menthyl dodecanoate; Organic solvents; Partition coefficients; Solubility

1. Introduction

Biocatalysis in organic media is an important technique for the synthesis of stereoselective compounds [1–3]. In particular, lipase (EC 3.1.1.3) catalyzed reactions have been used for the selective acylation of the primary OH group in glycol [4] and glycerol [5], the stereoselective esterification of menthol [6,7] and ibuprofen [8], and for transesterification reactions [4,9] in organic solvents. An important features of biocatalysis in organic solvents are that it overcomes the difficulty of dissolving hydrophobic substances in aqueous media and it also essentially eliminates hydrolytic reactions.

There have been several earlier studies dealing with the thermodynamics of enzyme-catalyzed esterification reactions in non-aqueous solvents [5,10–15]. However, there have been no thermodynamic studies of transesterification

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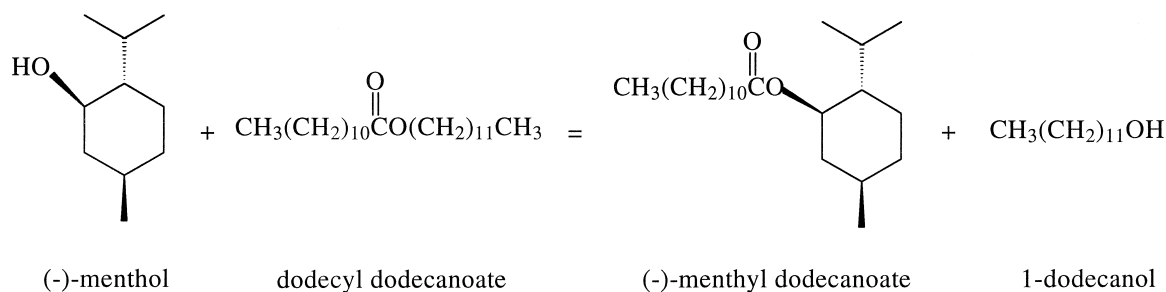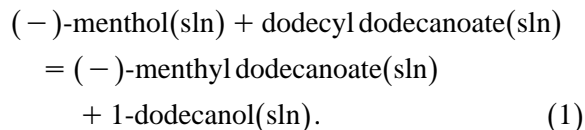
Fig. 1. Structures of the substances in reaction (1).

reactions in organic solvents or in water. These results are needed both to understand the energetics of these reactions and for process optimization calculations. Additionally, any practical conversion of reactants to products is helped by knowing the effect that the choice of solvent has on the position of equilibrium.

In this study, we have carried out an equilibrium investigation of the transesterification reaction

$$(-)\text{-menthol(sln)} + \text{dodecyl dodecanoate(sln)}$$
$$= (-)\text{-menthyl dodecanoate(sln)}$$
$$+ \text{1-dodecanol(sln).} \qquad (1)$$

Here, ''sln'' denotes an organic solvent. The structures of these substances are given in Fig. 1. In this study, the equilibrium constants for reaction (1) have been measured as a function of temperature using *n*-heptane, toluene and 2,2,4-trimethylpentane as solvents. These results are then used to calculate the standard molar enthalpy $\Delta_r H_m^o$ and Gibbs energy $\Delta_r G_m^o$ for reaction (1).

Since it is also of scientific interest to know the differences in thermodynamic driving forces in water vis a vis organic solvents, we also wanted to determine the value of the equilibrium constant for reaction (1) in water. However, because of the very low solubilities of the substrates in water and competing hydrolysis, this could not be done by direct measurement and a thermodynamic cycle had to be used to do this. Thus, the (*n*-hexane + water) partition coefficients of 1-dodecanol, and dodecyl dode-

canoate have also been measured at the temperature $T = 298.15$ K. These results in conjunction with earlier results from this laboratory [15] and the results for reaction (1) in *n*-hexane are then used to calculate the equilibrium constant for reaction (1) in water.

2. Experimental

The substances used in this study, their Chemical Abstract Service (CAS) numbers, empirical formulas, molar masses, source [1] and purities as determined by gas chromatography (GC) are given in Table 1. As discussed previously [15], the chiral mole fraction purities of (−)-menthol, and (−)-menthyl dodecanoate were 0.982 and 0.983, respectively. The lipase (EC 3.1.1.3) used for the biocatalysis was type II crude powder prepared from porcine pancreas.

The analysis of (−)-menthol, 1-dodecanol, (−)-menthyl dodecanoate and dodecyl dodecanoate, was carried out with a Hewlett–Packard (HP) 5890 gas chromatograph equipped with a flame ionization detector. The column was a fused silica HP 5 column (5% cross-linked

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Table 1
Principal substances used in this study with their Chemical Abstracts Service (CAS) registry numbers, empirical formulae, molecular weights M_r and supplier (A = Aldrich, B = Baker, F = Fluka M = Mallinckrodt, S = Sigma, Y = synthesized), mole fraction purity x as stated by supplier, and method used to determine the mole fraction purity [a]

Substance	CAS no.	Formula	M_r	Supplier	x	Method
(−)-Menthol[b]	2216-51-5	$C_{10}H_{20}O$	156.27	F	0.982	GC
Dodecyl dodecanoate	13945-76-1	$C_{24}H_{48}O_2$	368.64	S	0.987	GC
(−)-Menthyl dodecanoate[b]	57084-14-7	$C_{22}H_{42}O_2$	338.58	Y	0.982	GC
1-Dodecanol	112-53-8	$C_{12}H_{26}O$	186.32	S	0.99	GC
1-Decanol	112-30-1	$C_{10}H_{22}O$	158.28	S	0.99	GC
2,2,4-Trimethylpentane	540-84-1	C_8H_{18}	114.23	B	1.00	GC
Toluene	108-88-5	C_7H_8	92.14	M	0.99	GC
n-Hexane	110-54-3	C_6H_{14}	86.14	B	0.99	GC
n-Heptane	142-82-5	C_7H_{16}	100.20	M	0.997	GC
Lipase[c]	9001-62-1		5.0×10^4	S		

[a] These are the methods used by the vendor(s) to determine the purities of these substances.

[b] These are chiral mole fraction purities determined by GC [15].

[c] Type II crude powder obtained from porcine pancreas.

phenylmethylsilane, 30 m long × 0.53 mm i.d. with a film thickness of 0.80 μm). The head pressure of the helium carrier gas was 2.8 bar. The injector and detector temperatures were 250°C and 270°C, respectively. The initial column temperature of 100°C was held for 1 min and then raised to 225°C at a rate of 20°C min^{-1} and then held at the temperature $t = 225°C$ for 20 min. The substance 1-decanol was used as an internal standard for the analysis of (−)-menthol, 1-dodecanol, (−)-menthyl dodecanoate and dodecyl dodecanoate. The retention times of (−)-menthol, 1-decanol, 1-dodecanol, (−)-menthyl dodecanoate and dodecyl dodecanoate, were 2.3, 3.0, 4.3, 9.0 and 13.0 min, respectively.

The lipase used in this study was immobilized on glutaraldehyde-treated controlled-pore glass (CPG) beads using a procedure similar to that described previously [12]. Approximately 4 g of lipase was dissolved in 20 g of phosphate buffer {concentration $c(K_2HPO_4) = 0.1$ mol dm^{-3}, adjusted to pH = 7.0 with H_3PO_4}. The solution was centrifuged at 2000 rpm for 10 min to remove any insoluble materials. Then 10 g of silanized CPG beads were suspended in the enzyme solution and were stored overnight at $t = 4°C$. The next day, the solution was shaken at 25 rpm for an hour in a bath at $t = 25°C$. The

CPG beads with the enzyme immobilized on them were then filtered and washed with additional phosphate buffer and stored at 4°C using the aforementioned phosphate buffer. Just prior to use, most of the water on these beads was removed by vacuum filtration. Thus, by having a minimal amount of water present in the reaction mixture, the amount of any hydrolysis reaction is minimized.

Equilibrium measurements were carried out by approaching equilibrium from both directions of reaction. Dodecyl dodecanoate and (−)-menthol were used for the forward direction, and 1-dodecanol and (−)-menthyl dodecanoate were used for the reverse direction. After dissolving these substances in the organic solvents, ≈ 3 g of the CPG beads containing immobilized enzyme was added to each bottle. However, to minimize the loss of hexane and to reduce the equilibration time, mixtures containing the reactants and products were prepared so that the ratio {m(1-dodecanol) · m(−)-menthyl dodecanoate}/{m(−)-menthol · m(dodecyl dodecanoate)} was 0.22 for the forward direction of reaction and 0.53 for the reverse direction of reaction. Approximately 3 g of immobilized enzyme was then added to each of these bottles. Teflon stoppered glass bottles containing these solutions were then placed in a shaker bath

(≈ 25 rpm) and allowed to equilibrate. The temperature of the shaker bath was held constant to within $\pm 0.1°C$. The solutions were periodically analyzed to determine the extent of reaction and to see if the reaction quotients obtained from both directions of the reaction were equal and thus indicating that equilibrium had been achieved. In all cases, equilibrium was reached in 2 to 3 weeks. After completion of the equilibrium measurements, additional immobilized enzyme (≈ 1 g) was added to each bottle. The temperature of the bath was then changed and again allowed to equilibrate for 5 to 7 days.

A standard solution containing (−)-menthol, 1-decanol, 1-dodecanol, (−)-menthyl dodecanoate and dodecyl dodecanoate was prepared in 2,2,4-trimethylpentane. The response factor ratios {(c'/(area of chromatographic peak)} for (−)-menthol, 1-decanol, (−)-menthyl dodecanoate and dodecyl dodecanoate with respect to 1-decanol were determined. Here, c' = composition expressed as mol (kg soln.$^{-1}$). For the analysis of (−)-menthol, 1-dodecanol, (−)-menthyl dodecanoate and dodecyl dodecanoate in the reaction mixture, 1.0 cm^3 of equilibrated organic phase and 100 μl of an internal standard solution (containing 1-decanol in 2,2,4-trimethylpentane) were gravimetrically added to a vial which was then capped tightly. Approximately 0.6 μl of this solution was then injected into the GC and analyzed. Values of c' for (−)-menthol, 1-dodecanol, (−)-menthyl dodecanoate and dodecyl dodecanoate were determined from the chromatographic peak areas of the reactants and products and their respective response factor ratios, and the chromatographic peak area and the known value of c' of the internal standard.

The procedure used for the measurement of the (*n*-hexane + water) partition coefficients $K_{h/w}$ of 1-dodecanol and dodecyl dodecanoate is now described. First, a known mass (≈ 0.5 g) of substance was dissolved in 15.0 cm^3 of *n*-hexane in a 125-cm^3 Erlenmeyer flask. Then, 70 g of water are added to the flask. A second flask containing nearly identical amounts of the same substances was also prepared. One of these flasks was placed in a constant temperature bath at $T = 283.15$ K, and the other flask was placed in another constant temperature bath set at $T = 308.15$ K. Both flasks were shaken at ≈ 25 rpm for ≈ 48 h. Then, both flasks were placed in the same constant temperature bath at $T = 298.15$ K, shaken at ≈ 25 rpm, and allowed to equilibrate for 6 days. The aqueous phase of each of these flasks was then analyzed as follows. A known mass (≈ 40 g) of the equilibrated aqueous phase was carefully transferred into a Teflon bottle and known masses of *n*-hexane (volume $V = 1.5$ cm^3) and the internal standard solution in 2,2,4-trimethylpentane ($V = 100$ μl) were quantitatively added to this bottle. The contents of this bottle were shaken and then centrifuged at 2000 rpm for 15 min. The value of c' of the solute extracted from the aqueous phase into the *n*-hexane phase was determined using the GC method described above. This analysis yields the value of c' of the solute in the original aqueous phase that had undergone equilibration. Since the total amount of the solute is well known, the value of c' in the *n*-hexane phase is readily calculated. The value of $K_{h/w}$ for a given solute is then calculated as the ratio of the values of c' of that solute in the *n*-hexane and aqueous phases. Values of c', which were used for sake of convenience in analyzing the experimental data, were later converted to molalities.

3. Results and discussion

The equilibrium constant K for reaction (1) is

$$K = m((-)\text{-menthyl dodecanoate})$$
$$\cdot m(1 - \text{dodecanol})/\{m((-)\text{-menthol})$$
$$\cdot m(\text{dodecyl dodecanoate})\}, \qquad (2)$$

where m is molality. It is important to note that this reaction is symmetrical, hence, the equilibrium constant is dimensionless. Thus, concentration (molarity), mole fraction, or any measure of

composition could be used and the numerical value of this equilibrium constant will be the same. Since $(-)$-menthol, 1-dodecanol, $(-)$-menthyl dodecanoate and dodecyl dodecanoate are all unionized in the organic solvents and their molalities are small ($m < 0.006$ mol kg^{-1}), it is reasonable to assume that their activity coefficients are close to unity. Therefore, the equilibrium constants reported in this study can also be identified with the thermodynamic equilibrium constants defined in terms of activities.

The results of the equilibrium measurements are given in Table 2. The molalities of $(-)$-menthol from the forward direction of reaction have been corrected for the $(+)$-menthol impurity (mole fraction $x = 0.018$). Similarly, the presence of the $(+)$-menthyl dodecanoate impurity ($x = 0.017$) in the reverse reaction mixture has also been corrected for. The average of the corrections in the reported molalities of $(-)$-menthol due to the presence of $(+)$-menthol (forward direction of reaction only) was $2.5 \times$

Table 2

Results of equilibrium measurements for the transesterification reaction (1) in the organic solvents 2,2,4-trimethylpentane, n-hexane, n-heptane and toluene. $C_{10}H_{20}O$ is $(-)$-menthol, $C_{24}H_{48}O_2$ is dodecyl dodecanoate, $C_{22}H_{42}O_2$ is $(-)$-menthyl dodecanoate and $C_{12}H_{26}O$ is $1 -$ dodecanol. The molalities of these substances in solution at equilibrium are given in columns 3–6. The quantity $K_{\text{(combined)}}$ was calculated from the equilibrium constants which were measured from both directions of the reaction. Each result is the average of five measurements. The uncertainties are based on two estimated standard deviations of the mean

Direction	T (K)	$m(C_{10}H_{20}O) \times 10^3$ (mol kg^{-1})	$m(C_{24}H_{48}O_2) \times 10^3$ (mol kg^{-1})	$m(C_{22}H_{42}O_2) \times 10^3$ (mol kg^{-1})	$m(C_{12}H_{26}O) \times 10^3$ (mol kg^{-1})	K	$K_{\text{(combined)}}$
2,2,4-Trimethylpentane							
Forward	287.85	3.136	1.629	0.962	1.763	0.332 ± 0.004	0.333 ± 0.005
Reverse	287.85	2.731	1.854	0.958	1.765	0.334 ± 0.009	
Forward	293.55	3.596	1.381	0.905	2.042	0.372 ± 0.016	0.368 ± 0.011
Reverse	293.55	2.983	1.709	0.947	1.942	0.361 ± 0.009	
Forward	298.05	2.730	1.362	0.760	1.808	0.370 ± 0.019	0.359 ± 0.013
Reverse	298.05	3.436	1.294	0.775	1.993	0.347 ± 0.009	
Forward	303.30	3.137	1.009	0.565	1.940	0.346 ± 0.016	0.345 ± 0.008
Reverse	303.30	3.268	1.377	0.688	2.247	0.344 ± 0.006	
n-Hexane							
Forward	298.15	3.659	4.045	1.647	3.277	0.365 ± 0.006	0.362 ± 0.007
Reverse	298.15	3.833	4.394	1.881	3.217	0.359 ± 0.013	
n-Heptane							
Forward	282.95	5.590	3.311	1.596	4.395	0.379 ± 0.015	0.378 ± 0.008
Reverse	282.95	4.263	2.318	1.093	3.416	0.378 ± 0.007	
Forward	288.15	5.550	3.487	1.720	4.370	0.388 ± 0.007	0.387 ± 0.005
Reverse	288.15	4.136	2.323	1.134	3.260	0.385 ± 0.005	
Forward	293.15	5.767	3.138	1.600	4.591	0.406 ± 0.010	0.407 ± 0.006
Reverse	293.15	4.414	2.139	1.066	3.612	0.408 ± 0.009	
Forward	298.15	3.541	1.582	0.825	2.799	0.412 ± 0.012	0.410 ± 0.010
Reverse	298.15	3.460	1.355	0.664	2.868	0.406 ± 0.017	
Toluene							
Forward	282.95	3.430	3.127	2.025	1.889	0.357 ± 0.008	0.359 ± 0.007
Reverse	282.95	3.617	3.350	2.218	1.961	0.359 ± 0.007	
Forward	288.15	3.586	3.170	2.065	2.026	0.368 ± 0.008	0.365 ± 0.006
Reverse	288.15	3.652	3.374	2.213	2.016	0.362 ± 0.010	
Forward	293.15	3.574	3.213	2.003	2.029	0.354 ± 0.003	0.356 ± 0.003
Reverse	293.15	3.636	3.266	2.062	2.059	0.358 ± 0.004	
Forward	298.15	3.039	2.590	1.580	1.796	0.361 ± 0.006	0.364 ± 0.006
Reverse	298.15	3.354	2.859	1.814	1.938	0.367 ± 0.010	

10^{-5} mol kg^{-1} in the four solvents studied; the average correction in the molality of (−)-menthyl dodecanoate due to the presence of (+)-menthyl dodecanoate (reverse direction of reaction only) was 7.2×10^{-5} mol kg^{-1}. The reported equilibrium constants $K_{(combined)}$ are the averages of all of the results obtained from the forward and the reverse directions of reaction. The uncertainties reported in Table 2 are equal to two estimated standard deviations of the mean.

The equilibrium constants, standard molar Gibbs energies, and standard molar enthalpies for reaction (1) at $T = 298.15$ K were then calculated using the Clarke and Glew equation [16] with all of the measured data. It was also assumed that the standard molar heat-capacity change $\Delta_r C_{p,m}^o$ was equal to zero for reaction (1) in all of the solvents. These calculated values are: $K = (0.353 \pm 0.019)$, $\Delta_r G_m^o = (2.58 \pm 0.14)$ kJ mol^{-1} and $\Delta_r H_m^o = (1.5 \pm 6.7)$ kJ mol^{-1} for reaction (1) in 2,2,4-trimethylpentane; $K = (0.412 \pm 0.008)$, $\Delta_r G_m^o = (2.20 \pm 0.05)$ kJ mol^{-1} and $\Delta_r H_m^o = (4.0 \pm 1.6)$ kJ mol^{-1} for reaction (1) in n-heptane; and $\Delta_r G_m^o = (2.53 \pm 0.07)$ kJ mol^{-1}, $K = (0.361 \pm 0.010)$ and $\Delta_r H_m^o = (0.2 \pm 2.0)$ kJ mol^{-1} for reaction (1) in toluene. The temperature dependency of reaction (1) in n-hexane was not studied. Here, we have $K = (0.362 \pm 0.007)$ and $\Delta_r G_m^o = (2.52 \pm 0.05)$ kJ mol^{-1} at $T = 298.15$ K. All of these uncertainties are equal to two estimated standard deviations of the mean.

The aqueous saturation molalities $m(sat)$ and the (n-hexane + water) partition coefficients $K_{h/w}$ of (−)-menthol, 1-dodecanol, (−)-menthyl dodecanoate and dodecyl dodecanoate are given in Table 3. The values of $m(sat)$ for 1-dodecanol and for dodecyl dodecanoate are from Tewari [14], and the values of $m(sat)$ and the values of $K_{h/w}$ of (−)-menthol, and (−)-menthyl dodecanoate are from Tewari et al. [15]. The (n-hexane + water) partition coefficients $K_{h/w}$ of 1-dodecanol and dodecyl dodecanoate were determined in this study. The reported $K_{h/w}$ values are the averages of the

Table 3
Saturation molalities $m(sat)$ in water and (n-hexane + water) partition coefficients $K_{h/w}$ of (−)-menthol, 1-dodecanol, 1-dodecyl dodecanoate and (−)-menthyl dodecanoate at $T = 298.15$ K. The uncertainties are based on two estimated standard deviations of the mean. Final uncertainties are given in the text (see Section 3)

Substance	$m(sat)$ (mol kg^{-1})	$K_{h/w}$
(−)-Menthol[a,b]	$(2.34 \pm 0.12) \times 10^{-3}$	732 ± 7
1-Dodecanol[c]	$(3.91 \pm 0.26) \times 10^{-5}$	$(5.53 \pm 0.60) \times 10^{4}$
Dodecyl dodecanoate[c]	$(3.90 \pm 0.08) \times 10^{-6}$	$(2.12 \pm 0.40) \times 10^{5}$
(−)-Menthyl dodecanoate[a]	$(9.83 \pm 0.78) \times 10^{-6}$	$(4.18 \pm 0.52) \times 10^{5}$

[a] The value of the saturation molality $m(sat)$ and of the (n-hexane + water) partition coefficient $K_{h/w}$ for this substance are from Tewari et al. [15].

[b] Stephen and Stephen [19] give the solubility of ''menthol'' as 0.42 g dm^{-3}. This corresponds to $m(sat) = 0.0027$ mol kg^{-1}, a value that can be considered to be in agreement with the value obtained by Tewari et al. [15].

[c] The value of the saturation molality $m(sat)$ for this substance is from Tewari [14].

values obtained from two different approaches to equilibrium. These results will be used subsequently in a thermodynamic cycle calculation (see below).

The reported uncertainties in Tables 2 and 3 are the random errors in the measurements expressed as two estimated standard deviations of the mean and do not include possible systematic errors in the measurements. It is judged that reasonable estimates of the standard uncertainties [17] due to possible systematic errors in the values of the equilibrium constant K for reaction (1) are: $0.05K$ in the GC measurements of the molalities of the reactants and products and $0.01K$ due to sample impurities. Estimates of the standard uncertainties in the values of the (n-hexane + water) partition coefficients $K_{h/w}$ are: $0.03K_{h/w}$ in the measurements of the molalities of the substances and $0.01K_{h/w}$ due to sample impurities.

These estimated uncertainties are then combined in quadrature together with the statistical uncertainties in the measured values of these quantities expressed as one estimated standard deviation of the mean to obtain combined standard uncertainties [17]. These combined uncertainties are then multiplied by two to obtain the

final uncertainties. Thus, the final values at $T = 298.15$ K are $K = (0.353 \pm 0.052)$ for reaction (1) in 2,2,4-trimethylpentane; $K = (0.362 \pm 0.038)$ for the reaction in n-hexane; $K = (0.412 \pm 0.045)$ for the reaction in n-heptane; and $K = (0.361 \pm 0.042)$ for the reaction in toluene. Similarly, the final uncertainties in the (n-hexane + water) partition coefficients are $K_{h/w} = (2.12 \pm 0.40) \times 10^5$ for dodecyl dodecanoate and $K_{h/w} = (5.53 \pm 0.60) \times 10^4$ for 1-dodecanol. Since the aforementioned systematic errors do not depend on the temperature and since $\Delta_r H_m^o$ is essentially determined from the slope of $\ln K$ vs. $(1/T)$, the uncertainties in the values of $\Delta_r H_m^o$ obtained by using the Clarke and Glew [16] are unchanged from those obtained above.
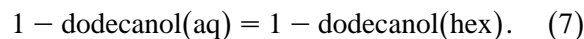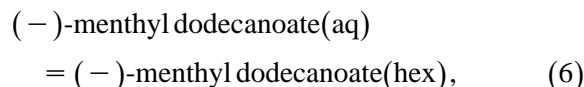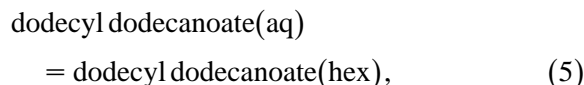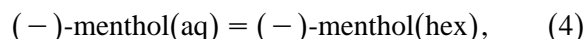
We now consider reaction (1) in aqueous media.

$$(-)\text{-menthol(aq)} + \text{dodecyl dodecanoate(aq)}$$
$$= (-)\text{-menthyl dodecanoate(aq)}$$
$$+ \text{1-dodecanol(aq)}. \qquad (3)$$
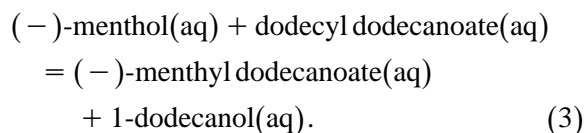
The equilibrium constant for this reaction is of the same form as Eq. (2). Since, all the substances involved in this reaction will be in a non-ionized form unless placed in extremely alkaline solution, the charge numbers of these species are zero except under extreme conditions of pH. Therefore, it makes sense to also select reaction (3) as the chemical reference reaction [18]. Because of low the saturation molalities of the reactants and products (see Table 3) and hydrolytic reaction, a direct measurement of the equilibrium constant K for

reaction (3) in water would be very difficult. However, it can be calculated with a thermochemical cycle by using our knowledge of the (n-hexane + water) partition coefficients $K_{h/w}$ and the value of the equilibrium constant for reaction (1) in n-hexane.

The partition coefficients $K_{h/w}$ pertain to the following equilibria:

$$(-)\text{-menthol(aq)} = (-)\text{-menthol(hex)}, \qquad (4)$$

$$\text{dodecyl dodecanoate(aq)}$$
$$= \text{dodecyl dodecanoate(hex)}, \qquad (5)$$

$$(-)\text{-menthyl dodecanoate(aq)}$$
$$= (-)\text{-menthyl dodecanoate(hex)}, \qquad (6)$$

$$\text{1-dodecanol(aq)} = \text{1-dodecanol(hex)}. \qquad (7)$$

Here, ''hex'' denotes n-hexane. A value of $\Delta_r G_m^o$ for reaction (3) can then be calculated as:

$$\Delta_r G_m^o(3) = \Delta_r G_m^o(1) + \Delta_r G_m^o(4) + \Delta_r G_m^o(5)$$
$$- \Delta_r G_m^o(6) - \Delta_r G_m^o(7). \qquad (8)$$

The values of $K_{h/w}$ in Table 3 were used to calculate values of $\Delta_r G_m^o$ for reactions (5), (6) and (7); the value of $\Delta_r G_m^o(1)$ for reaction (1) in n-hexane was calculated from the measured value of its equilibrium constant (see above). The thermochemical cycle calculation gives $\Delta_r G_m^o(3) = (14.9 \pm 0.7)$ kJ mol^{-1} for reaction (3). This corresponds to K $= (2.4 \pm 0.7) \times 10^{-3}$ for reaction (1) in water.

The results obtained for reaction (1) are summarized in Table 4. These appear to be the only thermodynamic results in the literature for any transesterification reaction either in organic sol-

Table 4

Summary of results for the equilibrium constant K, standard molar Gibbs energy change $\Delta_r G_m^o$, standard molar enthalpy change $\Delta_r H_m^o$ and standard molar entropy change $\Delta_r S_m^o$ at $T = 298.15$ K for the reaction: $(-)$-menthol(sln) + dodecyl dodecanoate(sln) = $(-)$-menthyl dodecanoate(sln) + 1-dodecanol(sln). The uncertainties are discussed in the text (see Section 3)

Solvent	K	$\Delta_r G_m^o$ (kJ mol^{-1})	$\Delta_r H_m^o$ (kJ mol^{-1})	$\Delta_r S_m^o$ (kJ mol^{-1})
n-Heptane	0.412 ± 0.045	2.20 ± 0.27	4.0 ± 1.6	6 ± 5
n-Hexane	0.362 ± 0.038	2.52 ± 0.26		
Toluene	0.361 ± 0.042	2.53 ± 0.03	0.2 ± 2.0	$-(8 \pm 7)$
2,2,4-Trimethylpentane	0.353 ± 0.052	2.58 ± 0.37	1.5 ± 6.7	$-(4 \pm 23)$
H$_2$O	0.0024 ± 0.0007	14.9 ± 0.7		

vents or in water. Thus, these results can prove useful for the estimation of thermodynamic quantities for structurally related reactions. It is seen that the enthalpies of reaction are small (≤ 4 kJ mol^{-1}). Also, the standard molar entropy changes $\Delta_r S_m^o$ are either zero or very close to zero.

The average value of the equilibrium constants for reaction (1) in the organic solvents is remarkably constant, namely $\langle K \rangle = 0.372$ with an estimated standard deviation of the mean of only 0.014. The most significant difference is seen in the value of $\Delta_r G_m^o$ for reaction (1) in water as compared to this reaction in the four organic solvents studied. Clearly water is substantially different in many of its properties (relative permittivity, octanol water partition coefficient and ability to hydrogen bond) from the organic solvents used in this study.

Acknowledgements

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