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A comparison of the solvation power of the green solvent 2,2,5,5-tetramethyloxolane versus toluene via partition coefficients

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ABSTRACT

2,2,5,5-tetramethyloxolane [previously published as 2,2,5,5-tetramethyltetrahydrofuran (TMTHF)] has recently been demonstrated as a greener and cleaner alternative to toluene in several applications. Assessing similarities in properties of toluene and 2,2,5,5-tetramethyloxolane is crucial for establishing this molecules potential to replace traditional non-polar organic solvents in the cleaner production of chemicals and materials. However, the Hansen solubility parameters (HSP) and Kamlet-Taft parameters (KT) give conflicting views on their similarities and differences, which necessitates a full comparative characterisation of the solvation environment of these two solvents. Such comparisons have been achieved through a direct and extensive determination of partition coefficients between each of the two solvents and water. The partition coefficients and Abraham's solvation parameter model have quantitatively clarified the similarities and differences in properties of 2,2,5,5-tetramethyloxolane and toluene. Solutes of high dipolarity and hydrogen-bond accepting ability tended to favour the aqueous phase in both systems, while large molar volume and high refractive indices favoured the organic phase. A significant difference between 2,2,5,5-tetramethyloxolane and toluene was observed for hydrogen-bond donating solutes. In general, such solutes strongly preferred the aqueous phase in the toluene/water system but preferred the organic phase in the 2,2,5,5-tetramethyloxolane/water system. This was due to the interaction of the protic solutes with the lone pairs of electrons on the ethereal oxygen of 2,2,5,5-tetramethyloxolane, a feature that is not present on toluene, and opens up new possibilities for applications of this sustainable solvent in liquid-liquid extraction, particularly in the isolation of natural products. As toluene is such an important solvent in the chemical industry, its replacement with a greener alternative such as 2,2,5,5-tetramethyloxolane would be hugely significant for cleaner synthesis, extractions and separations.

1. Introduction

Recent work has demonstrated several approaches to the development of greener or sustainable solvents that plays a key role towards cleaner production (Moity et al., 2014, 2016; Byrne et al., 2018). A variety of targets, including replacements for dipolar aprotic, chlorinated and Abraham's solvation parameter model is an indispensable tool which can be used to establish the similarity and difference between solvents such as 2,2,5,5-tetramethyloxolane (TMO) and toluene (Eq (1)) (Abraham et al., 2004).

Towards a cleaner production, replacing hydrocarbon solvents by greener solvent have been the focus of research (Alonso et al., 2013; Aycock, 2006; Byrne et al., 2017). However, significant gaps in the data sets of new greener solvents and their properties could potentially limit their widespread use. Therefore, it is essential to ensure that such gaps are filled and questions relating to the properties of new solvents are quickly addressed (Jin et al., 2017).

One such green solvent, 2,2,5,5-tetramethyloxolane (TMO) (or

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2,2,5,5-tetramethyltetrahydrofuran (TMTHF)), has recently been shown to be a greener alternative to toluene in several applications, including acylate polymerisation, a media for enzymatic esterifications and polycondensations, and solid-phase resin swelling (Byrne et al., 2017; Pellis et al., 2019; Ran et al., 2019), which crucially are a move towards a cleaner production. TMO has passed an Ames test for mutagenicity and although classed as an ether, it does not form peroxides like traditional ethers due to the absence of an α-hydrogen to the ethereal oxygen (Byrne et al., 2017). Instead, four bulky methyl groups surround the ethereal oxygen (Fig. 1), resulting in unusual solvent properties such as low binding affinity (Krieck et al., 2018) and basicity (Byrne et al., 2017).

For example, despite having Kamlet-Taft (KT) parameters (Kamlet et al., 1977; Kamlet and Taft, 1976; Taft and Kamlet, 1976) which are similar to traditional ethers (high β, low-medium π^*), TMO was shown to behave more like aromatic hydrocarbon solvents (low β, low-medium π^*), particularly toluene, in amidation, esterification, Grignard and radical polymerisations (Byrne et al., 2017). This was more consistent with the prediction of the Hansen solubility parameters (HSPs) (Hansen, 2012) which predicted the hydrogen-bonding ability of TMO to be low ($\delta_H = 2.1$), suggesting solvent behaviour that is more like toluene ($\delta_H = 2.0$) than other ethers (*e.g.* $\delta_H = 8$ for THF) (Byrne et al., 2017). Such contrasting descriptions of TMO's solvation power by HSP and KT parameters must be clarified to aid the uptake of TMO, and greener solvents in general.

While the KT model uses two probe dyes to measure π^* and β (Kamlet et al., 1977; Kamlet and Taft, 1976; Taft and Kamlet, 1976), such a small number of model dyes (solutes) cannot represent solute-solvent interactions for a wide range of solutes from a variety of applications. Instead, direct experimental measurement of solute-solvent interactions over wide-ranging classes of solutes is required. A more direct and in-depth description of solvation properties of a solvent can only come from extensive partitioning data, and a model that considers the chemical properties of the solutes. Thus, a combination of partitioning measurements and the Abraham model leads to a superior characterisation of the solvation environment.

$$Log\ K_P = c + eE + sS + aA + bB + vV \qquad \text{(Eq. 1)}$$

K_P is the partition coefficient of a solute between two immiscible phases, the solute descriptors are shown in upper case letters (*S*, *A*, *B*, *E* and *V*) while the system constants are shown in lower case (*s*, *a*, *b*, *e*, *v* and *c*) (Abraham et al., 2004; Poole et al., 2009). *E* represents the excess molar refraction of a solute, which describes electron-pair interactions. *S* represents solute dipolarity, *A* and *B* represent hydrogen-bond donating and accepting respectively, and *V* represents the McGowan's volume (Abraham et al., 2004; Poole et al., 2009). By measuring the partitioning of a large set of solutes in a biphasic system and determining the system constants (s, *a*, *b*, *e*, *v* and *c*) by regression analysis, a solvation parameter model for that biphasic system can be generated (Abraham et al., 2004; Poole et al., 2009).

The solvation parameter model provides an accurate description and prediction of the separation of solutes between the two phases, which is vital in choosing the optimum solvent for liquid-liquid extraction and recrystallisation (Abraham et al., 2004; Poole et al., 2009). In addition, the system constants disclose information about specific solvent-solute interactions and the relative solvation power of two counter-solvents in a biphasic system. Furthermore, the system constants can be used to compare the solvation power of different solvents among biphasic systems containing a common counter-solvent (Karunasekara and Poole, 2011a, 2010; Poole et al., 2013). For example, the solvation parameter model has previously been used by Karunasekara and Poole to determine the system constants of three biphasic systems containing propylene carbonate as the common counter-solvent against the traditional solvents *n*-heptane, diisopentyl ether and 1-octanol (Karunasekara and Poole, 2011b). This allowed a detailed comparison of the solvents to be made in terms of the five solute descriptors (Karunasekara

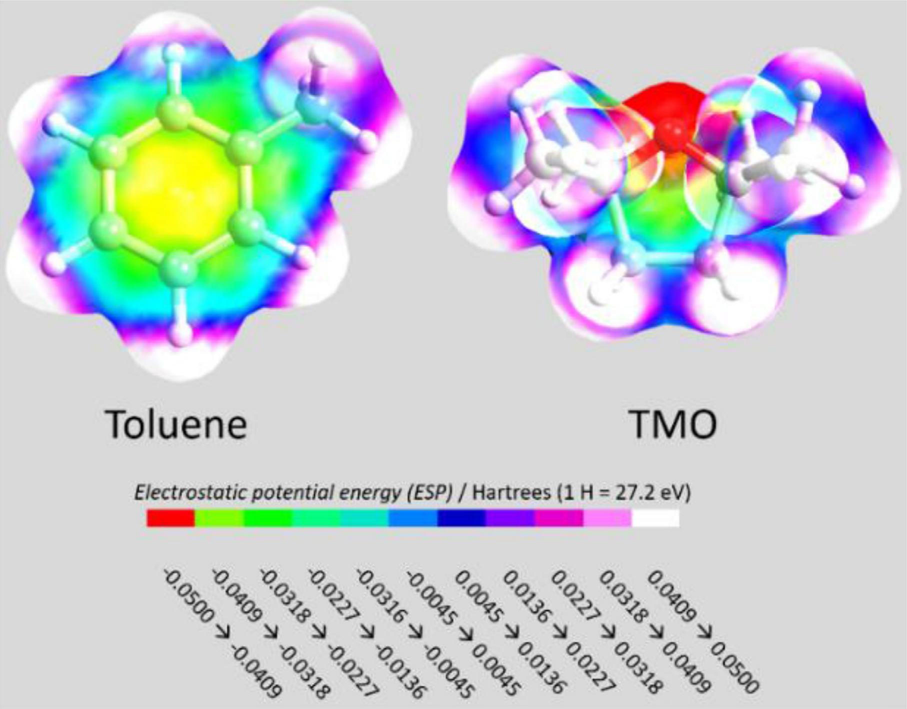

Fig. 1. Electrostatic potential (ESP) energy map of TMO and toluene.

and Poole, 2011b). Applied to green solvents, the suitability of a green solvent to replace a traditional solvent in specific niche applications can be identified.

Herein, a structural basis of the solvation power of the new green solvent, TMO, in comparison with the traditional solvent, toluene, will be clarified through an extensive determination of the partition constants of TMO/water and toluene/water systems. The solvation parameter model was also used to predict the partitioning of solutes between the two phases in each biphasic system tested. This allowed a rational approach to identifying applications where TMO could replace toluene, and thus encourages its uptake into industrial processes, such as the extraction of fatty acids and alcohols in a biorefinery.

2. Experimental

2.1. Materials

TMO was synthesised according to the method of Byrne et al. (2017). Toluene was bought from VWR chemicals. All other chemicals were obtained from Sigma Aldrich and were used without any further purification. The 5-HT and Stabilwax GC columns were obtained from Restek.

2.2. Methods

Gas chromatographic measurements were made with an Agilent Technologies HP 6890 gas chromatograph, with a with a flame ionisation detector (GC-FID), fitted with a Rxi-5HT capillary column (30 m × 250 μm x 0.25 μm nominal, max temperature 400 °C) or a Stabilwax capillary column (30 m × 250 μm x 0.25 μm nominal, max temperature 260 °C). Helium was used as the carrier gas at a flow rate of 2 mL min^{-1} with a split ratio of 30:1. The initial oven temperature was 40 °C which was held for 4 min at which point it was increased at a rate of 10 °C min^{-1} to 250 °C, at which temperature it was held for 2 min. Injection temperature was 250 °C and the detector temperature was 250 °C.

Partition coefficients were determined using a similar method to that reported by Poole et al. (Karunasekara and Poole, 2011a). 2 mL of organic solvent, 2 mL water, 10 μL internal standard and 30 μL (liquid solutes) or 20 mg (solid solutes) of test solute was added to a 5 mL screw-capped vial. Vials were shaken and allowed to stand for 24 h, after which time, 1 mL of each phase was transferred to a 1.5 mL GC vial for analysis.

$$K_P = \left(\frac{S_{org}}{S_{aq}}\right)\left(\frac{IS_{aq}}{IS_{org}}\right)K_P^{IS} \qquad \text{(Eq. 2)}$$

Equation (2) (Eq. (2)) was used to calculate the partitioning of solutes between the two phases, where K_P is the partition coefficient for solute S, S_{org} and S_{aq} are the peak area for solute S in the organic and aqueous layers respectively, I_{org} and I_{aq} are the peak areas for the internal standard in the organic and aqueous layers respectively, and K_P^{IS} is the partition coefficient of the internal standard in the given system. The internal standard was diglyme, $K_P = 0.651 \pm 0.124$ ($n = 10$) in the toluene/water system and $K_P = 0.141 \pm 0.014$ ($n = 10$) in the TMO/water system. The standard deviation of each solvent system was measured by taking 1,4-dioxane as a representative solute and carrying out five repeats in each system. The standard deviation of the toluene water system was found to be ±0.047 and the TMO/water system was found to be ±0.115.

Regression analysis was undertaken using IBM SPSS Statistics 24. Solute descriptors were taken from the literature. To test the predictability of the partition models, training and test datasets were selected at random.

3. Results and discussion

Using Eq. (1), regression analysis was performed using the Log K_P of 65 solutes between two liquid phases as the independent variables and the corresponding known solute descriptors (S, A, B, E and V) as the dependent variables, to determine the system constants (s, a, b, e, v and c) of two biphasic systems (TMO/water and toluene/water). The solute descriptors and Log K_P values of each of the 65 solutes are shown in Table 1. The 65 solutes were chosen specifically to be representative across a broad area of the “solute space” (Figures S1, S2 and S3, ESI). Molecules containing different heteroatoms and functionality were included in the solute list resulting in a broad range of S, A, B, E and V values and combinations thereof, as shown in Figs. S1–3 in the ESI. As gas chromatography was the method of analysis used to determine K_P values, the solutes also had to be sufficiently volatile. Solute descriptor values were obtained from the literature.

Regression analysis using the solute descriptors and partition coefficients from Table 1 gave the system constants (s, a, b, e, v and c) shown in Table 2. In the organic/aqueous systems, molecular descriptors with negative system constants indicate a preference for the aqueous phase while those with positive values indicate a preference for the organic phase. As water was common to both systems, a direct comparison could be made between TMO and toluene. In this comparison, positive values indicate a preference for TMO and negative values indicate a preference for toluene. The negative s (dipolarity) of both organic/aqueous systems shows that a solutes dipolarity is a driver towards the aqueous phase. In the hypothetical TMO/toluene system, s is almost negligibly and negative, indicating that solute dipolarity would be a very weak driver towards toluene. A comparison of the observed Log K_P versus the predicted Log K_P based on the values in Table 2 can be seen in Figs. S4 and S5 in the ESI.

Constant a (hydrogen-bond donating ability), is the main difference between toluene and TMO as solvents. The large negative a in the toluene/water system indicates a strong driver towards the aqueous phase, whilst the positive a in the TMO/water system indicates a driver towards the organic phase. Hydrogen-bond donating solutes can interact with TMO but not toluene, due to the ethereal oxygen on TMO, which can accept hydrogen-bonds of protic solutes. As such, TMO has a stronger affinity for protic organic solutes than water, particularly more lipophilic hydrogen-bond donating solutes. The large positive a value in the hypothetical TMO/toluene system clearly illustrates the difference between TMO and toluene.

Excess molar refraction, e, is a measure of the polarisable electrons in a solute. Almost no polarisability is observed in water, whilst a high degree of polarisability can be observed in aromatic molecules. As such, the e constant greatly favoured the organic layer in toluene/water system, but only demonstrated a slight preference for TMO in the TMO/water system. The hypothetical TMO/toluene system shows a strong preference for toluene. This is perhaps due to the electronegative oxygen atom of TMO more rigidly holding the molecules' electrons in place, resulting in weak polarisability. As the electronegativity of the oxygen atom is hidden by the four bulky methyl groups, the overall polarity of the molecule is also low (illustrated in Fig. 1 and indicated by its low π^* (KT) and δ_P (HSP) parameters). Thus, the polar water molecules can compete for the dissolution of polarisable solutes with the weakly polar and weakly polarisable TMO but cannot compete with the highly polarisable toluene.

The large positive v constant favours the less self-associating phase, as less energy is required to form a large cavity to

Table 1
Descriptor values and Log K_P's for 59 solutes tested for partitioning in two biphasic water/organic solvent systems.

Solute	*S*	*A*	*B*	*E*	*V*	Log K_P (Tol./water)	Log K_P (TMO/water)	Log K_P (TMO/Tol.)
Benzoic Acid (Jover et al., 2004)	0.900	0.590	0.400	0.730	0.932	1.272	2.248	1.486
Butyric Acid (Zissimos et al., 2002)	0.620	0.600	0.450	0.210	0.747	−0.033	0.830	1.688
Acetic Acid (Zissimos et al., 2002)	0.650	0.610	0.440	0.265	0.465	−2.461	−0.276	1.677
Diethyl Carbonate (Zissimos et al., 2002)	0.560	0.000	0.530	0.061	0.946	1.886	1.494	−0.328
Cyclopentanol (Zissimos et al., 2002)	0.540	0.320	0.560	0.427	0.763	−0.124	0.782	0.617
2-propanol (Zissimos et al., 2002)	0.360	0.330	0.560	0.212	0.590	−0.822	−0.301	0.716
1-Butanol (Zissimos et al., 2002)	0.420	0.370	0.480	0.224	0.731	−0.149	0.793	0.882
t-Butanol (Stephens et al., 2011b)	0.360	0.370	0.530	0.200	0.731	−0.712	0.096	0.880
Ethanol (Zissimos et al., 2002)	0.420	0.370	0.480	0.246	0.449	−1.305	−0.673	0.846
1-Propanol (Zissimos et al., 2002)	0.420	0.370	0.480	0.236	0.590	−0.591	0.009	0.864
Methanol (Zissimos et al., 2002)	0.440	0.430	0.470	0.278	0.308	−1.459	−0.967	1.030
Benzaldehyde (Zissimos et al., 2002)	1.000	0.000	0.390	0.820	0.873	2.006	1.899	−0.590
Vanillin (Stephens et al., 2011b)	1.300	0.310	0.680	0.990	1.131	0.833	1.037	0.372
Octane (Zissimos et al., 2002)	0.000	0.000	0.000	0.000	1.258	6.156	5.739	−0.145
Cyclohexene (William E Acree and Abraham, 2006)	0.200	0.000	0.100	0.395	0.802	3.576	3.681	−0.362
1-Hexene (Zissimos et al., 2002)	0.080	0.000	0.070	0.078	0.911	4.393	4.057	−0.225
Dimethylacetamide (Zissimos et al., 2002)	1.330	0.000	0.780	0.363	0.788	−1.597	−1.621	−0.523
Pyridine (Zissimos et al., 2002)	0.840	0.000	0.520	0.631	0.675	0.499	−0.065	−0.568
Triethylamine (Zissimos et al., 2002)	0.150	0.000	0.790	0.101	1.054	1.295	0.949	−0.388
Dipropylamine (Zissimos et al., 2002)	0.300	0.080	0.690	0.124	1.054	1.435	1.907	−0.099
Dibutylamine (Zissimos et al., 2002)	0.300	0.080	0.690	0.107	1.336	2.380	1.945	−0.065
Butylamine (Zissimos et al., 2002)	0.350	0.160	0.610	0.224	0.772	0.183	0.060	0.131
Hexylamine (Zissimos et al., 2002)	0.350	0.160	0.610	0.197	1.054	1.841	1.530	0.169
Naphthylamine (Stephens et al., 2011b)	1.260	0.200	0.570	1.670	1.185	2.366	2.292	−0.230
Aniline (Zissimos et al., 2002)	0.960	0.260	0.410	0.955	0.816	0.937	1.197	0.248
Benzene (Zissimos et al., 2002)	0.520	0.000	0.140	0.610	0.716	3.185	2.507	−0.464
Xylenes (mix of *o*, *m* and *p*) (Zissimos et al., 2002)	0.560	0.000	0.160	0.663	0.998	4.453	3.663	−0.461
Fluorene (Stephens et al., 2011b)	1.060	0.000	0.240	1.588	1.357	5.246	3.320	−0.795
Propylene Carbonate (Zissimos et al., 2002)	1.300	0.000	0.640	0.319	0.697	0.025	−0.840	−0.482
n-Butyl Acetate (Stephens et al., 2011b)	0.600	0.000	0.450	0.071	1.028	2.326	2.304	−0.305
t-Butyl Acetate (Zissimos et al., 2002)	0.540	0.000	0.470	0.025	1.028	2.129	–	−0.292
Butyl Benzoate (Poole et al., 2009)	0.850	0.000	0.460	0.668	1.495	4.004	3.539	−0.487
Ethyl Acetate (Stephens et al., 2011b)	0.620	0.000	0.450	0.106	0.747	1.283	0.882	−0.346
Propyl Acetate (Poole et al., 2009)	0.573	0.000	0.452	0.092	0.888	1.969	1.557	−0.327
t-Butyl Methyl Ether (Stephens et al., 2011b)	0.110	0.000	0.630	0.024	0.872	1.272	1.340	−0.339
t-Butyl Ethyl Ether (Stephens et al., 2011b)	0.180	0.000	0.590	0.020	1.013	1.796	1.929	−0.316
Anisole (Poole et al., 2009)	0.768	0.000	0.311	0.712	0.916	2.945	2.784	−0.525
Diethyl Ether (Zissimos et al., 2002)	0.250	0.000	0.450	0.041	0.731	1.415	1.264	−0.319
1,4-Dioxane (Stephens et al., 2011b)	0.750	0.000	0.640	0.329	0.681	0.150	−0.418	−0.481
Methyl Formate (Zissimos et al., 2002)	0.680	0.000	0.380	0.192	0.465	0.134	−0.971	−0.390
Chlorocyclohexane (Stephens et al., 2011a)	0.480	0.000	0.100	0.448	0.968	3.502	3.296	−0.369
Iodomethane (Stephens et al., 2011b)	0.430	0.000	0.120	0.676	0.508	2.522	2.506	−0.503
1,2-Dichloroethane (Jover et al., 2004)	0.490	0.100	0.100	0.322	0.635	2.510	2.269	−0.009
Chloroform (Zissimos et al., 2002)	0.490	0.150	0.020	0.425	0.617	2.770	3.156	0.142
Bromobenzene (Poole et al., 2009)	0.723	0.000	0.089	0.882	0.891	3.039	2.679	−0.538
Chlorobenzene (Zissimos et al., 2002)	0.650	0.000	0.070	0.718	0.839	3.277	3.116	−0.477
1,2-Dichlorobenzene (Zissimos et al., 2002)	0.750	0.000	0.020	0.825	0.961	3.942	2.728	−0.494
Iodobenzene (Poole et al., 2009)	0.784	0.000	0.135	1.182	0.975	3.862	3.482	−0.653
3-pentanone (Zissimos et al., 2002)		0.660	0.000	0.510	0.154	0.829	1.121	1.105
Acetophenone (Poole et al., 2009)	1.026	0.000	0.503	0.806	1.014	2.377	1.875	−0.598
2-Butanone (Zissimos et al., 2002)	0.700	0.000	0.510	0.166	0.688	0.709	0.397	−0.389
3-Hexanone (Zissimos et al., 2002)	0.660	0.000	0.510	0.136	0.970	2.232	1.619	−0.350
Propionitrile (Stephens et al., 2011b)	0.900	0.020	0.360	0.162	0.545	0.638	0.162	−0.300
Acetonitrile (Zissimos et al., 2002)	0.430	0.000	0.120	0.676	0.508	−0.060	−0.453	−0.159
Nitrobenzene (Zissimos et al., 2002)	0.784	0.000	0.135	1.182	0.975	3.001	2.055	−0.583
Nitroethane (Zissimos et al., 2002)	0.660	0.000	0.510	0.154	0.829	1.121	0.669	−0.332
Nitromethane (Zissimos et al., 2002)	1.026	0.000	0.503	0.806	1.014	0.413	0.117	−0.219
4-Nitroaniline (Stephens et al., 2011b)	0.700	0.000	0.510	0.166	0.688	–	1.913	0.861
m-Cresol (Stephens et al., 2011b)	0.660	0.000	0.510	0.136	0.970	0.591	2.827	1.396
p-Cresol (Stephens et al., 2011b)	0.900	0.020	0.360	0.162	0.545	0.612	2.728	1.403
Phenol (Zissimos et al., 2002)	0.900	0.070	0.320	0.237	0.404	0.425	2.122	1.501
3-Fluorophenol (Stephens et al., 2011b)	0.950	0.060	0.310	0.313	0.424	0.595	2.479	1.603
4-Fluorophenol (Zissimos et al., 2002)	1.110	0.000	0.280	0.871	0.891	0.215	2.320	1.672
3-Hydroxybenzaldehyde (Zissimos et al., 2002)	1.720	0.820	0.260	1.070	0.949	−0.046	1.745	1.902
4-Nitrophenol (Stephens et al., 2011b)	1.920	0.460	0.350	1.220	0.990	−0.207	2.268	2.180
Resorcinol (Stephens et al., 2011b)	0.950	0.020	0.330	0.270	0.565	−1.946	0.360	3.081
Ethylene glycol (Zissimos et al., 2002)	0.760	0.600	0.690	0.460	0.508	−3.932	−2.219	1.514

Solute descriptors obtained from the literature sources shown for each solute. Solutes marked with a hyphen (–) were not tested.

Table 2
Regression data showing the system constants, *s*, *a*, *b*, *e* and *v*, as well as the R^2, *SE*, *p*-value and number of tested solutes, n_s, in each model.

Property	Toluene/water	TMO/water	TMO/Toluene
s	−0.755	−0.766	−0.011
a	−3.180	0.275	3.455
b	−4.945	−5.178	−0.233
e	0.430	0.057	−0.373
v	4.298	4.396	0.098
c	0.642	0.374	−0.268
R^2	0.965	0.927	–
SE	0.367	0.424	–
p-value	<0.001	<0.001	–
n_s	65	65	65

R^2 is the square of the multiple correlation coefficient, SE is the standard error, the p-value indicates the likelihood of the correlation being due to random noise, and n_s is the number of solutes considered in the model.

solubilise the solute. Due to hydrogen-bonding in water, its self-association is much higher than the non-polar organic solvents, toluene and TMO, demonstrated by its larger Hildebrand parameter (32.8 $MPa^{0.5}$ for water, compared to 18.2 $MPa^{0.5}$ and 15.7 $MPa^{0.5}$ for toluene and TMO respectively). As such, larger solutes were more readily solubilised in the organic phase of both organic/water systems. TMO was shown to be marginally less self-associating than toluene based on the small positive *v* constant in the hypothetical TMO/toluene system.

Overall, it can be seen in the hypothetical TMO/toluene system (Table 3) that the differences between toluene and TMO in terms of *s* and *v* was marginal, *a* was a powerful driver towards TMO and was the most striking difference between the two organic solvents, while *b* and *e* were drivers towards toluene. Fig. 2, which shows the partitioning in the toluene/water system compared to the TMO/water system, illustrates these findings. The dashed line through the origin represents the interface between TMO and toluene. Deviations from the dashed line show the magnitude of the preference of certain solutes for one organic phase over the other. Greater distance from the dashed line indicates a stronger preference for that phase. Solutes placed above/left of the dashed line would partition more towards the TMO layer in a hypothetical TMO/toluene and vice versa. Protic solutes such as lipophilic carboxylic acids, alcohols and phenols were more solubilised in the weakly basic TMO solvent where they can hydrogen-bond with the lone pairs on TMO's ethereal oxygen. This suggests that TMO could be a useful solvent for the extraction of natural products from plant waxes. Plant waxes are known to contain many useful lipophilic compounds such as fatty acids, β-diketones, wax esters, polycosanols and sterols to name but a few (Sin et al., 2014). Yields of certain molecules, such as fatty acid or alcohols, may be increased as a result of improved separation from water in a TMO/water system compared to traditional hydrocarbon solvents, such as toluene or hexane. In contrast, lone pair donating solutes such as amines, ethers, aromatics, ketones and carbonates tended to favour toluene over TMO, due to the greater polarisability of toluene compared to TMO. Propylene carbonate has a strong preference for toluene over TMO which suggests mutual repulsion of the lone pairs between propylene carbonate and TMO. Karunasekara and Poole previously demonstrated lone pair repulsion in propylene carbonate using the Abraham solvation parameter model in a propylene carbonate/heptane system, which is consistent with the observations of this work (Karunasekara and Poole, 2011b). Finally, alkenes, alkanes, amides and haloaromatics tended to partition similarly in both systems due to the lack of any significant hydrogen-bonding in these classes of molecules.

The predictability of the model was tested using a training set and test set of solutes which were chosen by random selection. ~80% of the entire data set was used in the training set and the remaining ~20% of the data was used in the test set. The model was generated using the training set and its predictability was tested using the test set. Some changes in the training model (Table 3) compared to the original model (Table 1) were observed as expected, as the data used was different and the number of solutes is reduced. However, the relative differences between the toluene/water system and the TMO/water system remained similar. When the training set model was used to predict the system constants (s, *a, b, e, v* and *c*) of the test solutes, an R^2 of 0.958 was obtained in the toluene/water system, and an R^2 of 0.925 was obtained in the TMO/water system, indicating good model predictability in both systems (coefficients shown in Table S2, ESI).

The system constants (s, *a, b, e, v* and *c*) obtained for the toluene/water system in this work were compared with those of Abraham et al. (Table 3) and Acree et al. (Abraham et al., 2004; Stephens et al., 2011a). The slight differences between each model are likely due to the different test sets used between each research group, as well as some slight differences in the measured partitioning of solutes between different research groups (shown in Table S1, ESI). Indeed, the partition coefficients reported by Acree et al. were obtained from the literature by a wide range of research groups so variation in experimental methods is likely. However, it can be seen that despite these differences, partition coefficient values are similar in all cases, indicating a good comparison between each research group and a robust model for this work.

4. Conclusions

TMO is a non-polar green solvent with the potential to replace toluene, however, questions relating to its properties as a solvent have hindered its potential in the development of new cleaner production methods. This manuscript offers important new insights and enhances the data set of a potentially greener solvent, thus encouraging its further use in the cleaner production of chemicals, polymers and materials. In the event that data on solvents properties is missing, incomplete or contradictory, the widespread use and application of this solvent in industry is likely to be limited. In order to encourage cleaner production, it is vital to complete data sets and resolve any contradictory properties.

To assess quantitatively the similarity (replaceability) and

Table 3
Comparison of the toluene/water system constants from this work and the work of Abraham et al. (2004) Acree et al. (Stephens et al., 2011a).

Property	Toluene/water system constants		
	This work	Abraham (Abraham et al., 2004)	Acree (Stephens et al., 2011a)
s	−0.755	−0.720	−0.644
a	−3.180	−3.010	−3.002
b	−4.945	−4.824	−4.748
e	0.430	0.527	0.431
v	4.298	4.545	4.524
c	0.642	0.143	0.125

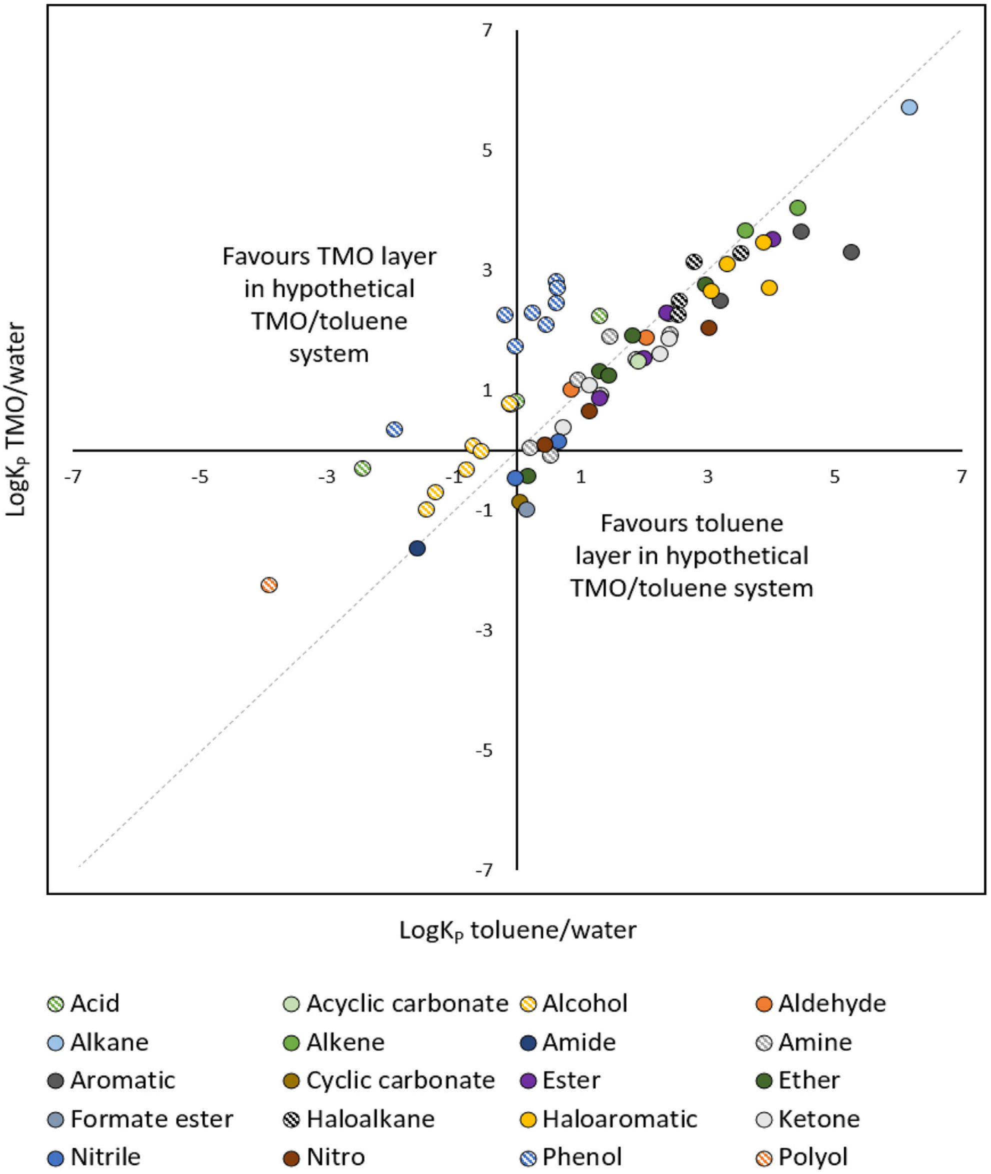

Fig. 2. Comparison of the partitioning of solutes in the TMO/water and toluene/water systems.

difference between the two solvents, an extensive and systematic measurement of partition coefficients, using a wide variety of solutes in organic/water biphasic systems has been performed. The partitioning data have been modelled by the five-parameter Abraham model, which can directly summarise how solvation is determined by a solutes' chemical properties and can help identify the difference between TMO and toluene, unlike KT and HSP models. As water is common to both systems, a direct comparison between TMO and toluene can be achieved. In addition, the solubility of solutes outside the test set in TMO can be predicted using the newly generated solvation parameter model. These measurements have highlighted opportunities and insights into how the unique properties of TMO could be an advantage over traditional non-polar solvents in certain applications.

Such a comprehensive comparison between toluene and TMO has led to the following new insights: dipolar (s), hydrogen-bond accepting (b) and polarisable (e) solutes were all shown to favour toluene over TMO. However, the lone pairs on TMO were demonstrated to be a powerful driver for the dissolution of protic solutes (a) by TMO in comparison with toluene. In addition, large (v) solutes marginally favoured TMO over toluene. This revealed that TMO contains slight basicity, consistent with ether solvents, which could improve the extraction yields of lipids including fatty acids and alcohols from plant waxes compared to toluene, and likely other aliphatic hydrocarbon solvents such as hexane. In addition, many cleaning applications could benefit from the use of TMOs interesting affinity for protic solutes.

Importantly, the steric hindrance prevents TMO's basicity from adversely influencing the rate for amidation, esterification and Grignard reactions; therefore allowing this solvent to behave like toluene. These results demonstrate that TMO could be both a suitable greener alternative to toluene and other non-polar volatile organic solvents in a wide range of synthetic applications, whilst also possessing a specific advantage (basicity) in the dissolution of protic solutes in extractions and cleaning applications.

Conflicts of interest

There are no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclepro.2019.118175.

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