



Determination of descriptors for fragrance compounds by gas chromatography and liquid–liquid partition

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ABSTRACT

Retention factors on a minimum of eight stationary phases at various temperatures by gas–liquid chromatography and liquid–liquid partition coefficients for five totally organic biphasic systems were combined to estimate descriptors for 28 fragrance compounds with an emphasis on compounds that are known or potential allergens. The descriptors facilitated the estimation of several properties of biological and environmental interest (sensory irritation threshold, odor detection threshold, nasal pungency threshold, skin permeability from water, skin–water partition coefficients, octanol–water partition coefficients, absorption by air particles, adsorption by diesel soot particles, air–water partition coefficients, and adsorption by film water). The descriptors are suitable for use in the solvation parameter model and facilitate the estimation of a wide range of physicochemical, chromatographic, biological, and environmental properties using existing models.

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1. Introduction

Essential oils are liquids containing volatile aroma compounds obtained mainly from plant materials by steam distillation, infusion, extraction or cold-pressing [1]. They are widely used in the cosmetics, perfumery, pharmaceuticals, beverage, personal care, and food industries where their attractive odor and/or flavor is exploited to enhance the value of consumer products. Fragrances may also contain synthetic aroma compounds as well as compounds of natural origin. Several natural fragrances are terpene hydrocarbons and their oxygenated derivatives with high structural diversity. Some fragrance compounds are known or suspect allergens and subject to regulatory control [2]. These are the compounds emphasized in this report and are indicated in Table 1 together with their systematic chemical names. For perspective, when used as cosmetic products in the European Union it is required to inform consumers of the presence of potential allergenic compounds in cosmetic products if present at a concentration that exceeds 0.001% in leave-on products or 0.01% in rinse-off products [2] with similar regulations in force in other countries and trading blocks around the globe. Effective analytical methods employing headspace and/or extraction methods for isolation and gas chromatography for separation with mass spectrometric

detection have been developed for cosmetics to support compliance with regulatory requirements [3–6].

The use of properties that are easy to measure in order to estimate properties that are inaccessible, expensive or difficult to measure is a well established approach in chemistry and biology. This approach requires that some sort of empirical or theoretical model is established beforehand that provides a connection between the two sets of properties. Since a large number of transport-related processes can be described by equilibrium or rate approaches it is not surprising that free-energy related models are the most successful for these applications. Whether or not these studies involve the prediction of retention in separation systems, the distribution of compounds across biological membranes (e.g., skin permeation, nasal pungency, odor thresholds, etc.), environmental fate assessment (e.g., air–particulate, air–water distribution, octanol–water distribution, etc.) and so on: the ultimate goal is to establish a suitable quantitative structure–property relationship (QSPR) to facilitate the prediction of further system properties for compounds lacking experimental values [7–13].

Two general strategies are commonly employed in QSPR studies. The first approach starts with the generation of a large number of molecular descriptors using structure-based computational methods such as DRAGON, SYBYL, CODESSA (e.g., more than 800 descriptors can be calculated using CODESSA) [14]. Statistical tools are then used to reduce the number of descriptors to a manageable number while maximizing the experimental variance explained. The final output is usually a linear or non-linear model suitable for the prediction of properties for other compounds. The main weakness of this approach is that the selected descriptors may be

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Table 1
Plant-derived and synthetic fragrance compounds with those indicated as known or suspect allergens according to European Union regulations [2].

Common name	Systematic chemical name	Source ^a
<i>(i) Allergens</i>		
Amyl cinnamal	(Phenylmethylene)heptanal	TCI
Anise alcohol	4-Methoxybenzyl alcohol	CS
Benzyl alcohol		SA
Benzyl benzoate		ACROS
Benzyl cinnamate	Benzyl 3-phenylpropenoate	TCI
Benzyl salicylate	Benzyl 2-hydroxybenzoate	TCI
Cinnamyl alcohol	3-phenyl-2-propen-1-ol	ACROS
Citral (geranial)	3,7-Dimethylocta-2,6-dienal	(E-isomer) CS
Citral (neral)		(Z-isomer) CS
Coumarin	2H-1-Benzopyran-2-one	SA
Eugenol	2-Methoxy-4-prop-2-enylphenol	ACROS
Farnesol	3,7,11-trimethyldodeca-2,6,10-trien-1-ol	SA
Geraniol	3,7-Dimethylocta-2,6-dien-1-ol	TCI
Hydroxycitronellal	3,7-dimethyl-7-hydroxyoctanal	SA
α-Isomethyl ionone	3-Methyl-4(2,6,6-trimethyl-1-cyclohex-2-enyl)but-3-en-2-one	
Lilial	3-(4-tert-butylphenyl)butanal	TCI
Limonene	1-Methyl-4-(1-methethenyl)cyclohexene	CS
Linalool	3,7-Dimethyl-1,6-dien-3-ol	ACROS
Methyleugenol	1,2-Dimethoxy-4-prop-2-enylbenzene	TCI
<i>(ii) Not known to be allergens</i>		
Borneol	1,7,7-Trimethyl-bicyclo[2.2.1]heptan-2-ol	ACROS
Camphor	1,7,7-Trimethylbicyclo[2.2.1]heptan-2-one	CS
Carvone	2-Methyl-5-(1-methylethenyl)-2-cyclohexanone	ACROS
Citronellal	3,7-Dimethylocta-2,6-dienal	CS
2-Methoxycinnamaldehyde		SA
α-Pinene/β-pinene	4,7,7-Trimethylcyclo[3.1.1]hept-3-ene	CS
Terpinen-4-ol	4-Isopropyl-1-methyl-1-cyclohexen-4-ol	ACROS
Vanillin	4-Hydroxy-3-methoxybenzaldehyde	SA

^a ACROS = ACROS Organics, Morris Plains, NJ, USA; CS = Chem Services Inc., West Chester, PA, USA; SA = Sigma-Aldrich, Milwaukee, WI, USA; and TCI = TCI America, Portland, OR, USA

difficult to understand and the models may lack obvious chemical significance. The best set of reduced descriptors for the correlation of any given property is unlikely to be the same as the best set for the correlation of any other (often similar) property.

The above problems are circumvented by less flexible models that define a small number of descriptors in advance, and use just these descriptors to characterize all processes. The descriptors may be derived from theory [15], such as the five COSMOments (COSMO-RS is a model combining quantum theory, dielectric continuum models, surface interactions and statistical thermodynamics) or experimentally derived parameters, such as the six descriptors used in Abraham's solvation parameter model [16–18]. Theoretical models allow the calculation of descriptors for compounds that are unavailable or yet to be synthesized, but for accessible compounds, computational techniques can be slow and no faster than experimental methods for estimating descriptor values. The purpose of this report is the experimental determination of descriptor values for fragrance compounds to facilitate the estimation of a range of physicochemical and biological properties available through use of the solvation parameter model. These descriptors also provide chemical insight into how different compounds behave in transfer systems.

Many of the compounds in Table 1 have low water solubility and their descriptor values are difficult to determine by conventional methods based on aqueous liquid–liquid partitioning [17]. We encountered a similar problem in calculating descriptors for organosilicon compounds and developed an alternative procedure that uses a combination of gas chromatography and partitioning in totally organic solvent systems for this purpose [19,20]. In recent years the number of possible totally organic biphasic systems available for descriptor measurements has increased significantly [21] and advantage is taken of these developments to facilitate the determination of descriptors for fragrance compounds in this report. Abraham and co-workers have determined descriptor values for a several terpenes [13,22,23] based on a

combination of experimental and estimated property values with little overlap with the compounds in Table 1. By minimizing the use of estimated properties in the calculations it is hoped to provide improved values for all compounds including those in Table 1 previously estimated by Abraham and co-workers.

The solvation parameter model as generally used in studies of transfer properties takes two forms. For transfer from a gas phase to a condensed phase (for example, gas–liquid chromatography)

$$\log k = c + eE + sS + aA + bB + lL \quad (1)$$

and for transfer between condensed phases (for example, as in liquid–liquid partition)

$$\log K_p = c + eE + sS + aA + bB + vV \quad (2)$$

where the dependent variable is an experimental property such as a chromatographic retention factor, k , or a partition coefficient, K_p [16–18,24,25]. The capital letters in Eqs. (1) and (2) are descriptors that define the capability of a solute for electron lone pair interactions, E , dipole-type interactions, S , hydrogen-bonding interactions with the solute acting as a hydrogen bond acid, A , or base, B , the gas–liquid partition coefficient on *n*-hexadecane at 298.2 K, L , and McGowan's characteristic volume, V . The lower case letters are the complementary system properties to the solute descriptors with e determined by interactions with electron lone pairs, s dipole-type and induced dipole-type interactions, a hydrogen-bond basicity (because a hydrogen-bond acid solute will interact preferentially with a hydrogen-bond base solvent), b hydrogen-bond acidity, and l and v are determined by the difference in the work require to form a cavity in the receiving and donating phases and contributions from dispersion interactions that are not self-cancelling in the two phases. To determine the solute descriptors it is necessary to set up a series of equations similar to Eqs. (1) and (2) with known system constants that allow the convenient measurement of the partition or retention property for the solute. The descriptors are calculated by finding the unique values for each descriptor that

simultaneously minimizes the difference between the experimental solute properties and the model predicted properties across all equations [17,18,26].

2. Experimental

2.1. Materials

The solvents ethylene glycol, propylene carbonate, and formamide were obtained from Acros Organics (Morris Plains, NJ, USA) and n-heptane, isopentyl ether, and 2,2,2-trifluoroethanol from Sigma–Aldrich (Milwaukee, WI, USA). The solvents were dried over molecular sieves prior to use. The fragrance chemicals and their source are identified in Table 1. The columns used to determine retention factors by gas chromatography and their system constants over the temperature range 60–240 °C are identified in Table 2 [27–30]. Each compound was determined at several temperatures on each column selected to provide a reasonable range of retention factor values. The HP-5 column, Table 2, was used in the measurement of liquid–liquid partition coefficients.

2.2. Instrumentation

Gas chromatographic measurements were made with an Agilent Technologies (Palo Alto, CA, USA) HP6890 gas chromatograph fitted with a split/splitless injector and flame ionization detector using Chemstation software (rev. 8.04.01) for data acquisition. Nitrogen was used as the carrier gas at a constant velocity of 47 cm/s. The split ratio was set to 30:1, septum purge 1 mL/min, injector temperature 275 °C, and detector temperature 300 °C. Isothermal retention factors were determined at 20 °C intervals at several temperatures in the range 60–240 °C as dictated by the retention characteristics of each compound. For the measurement of liquid–liquid partition coefficients a temperature program was used starting at 150 °C for 1 min and then raised to 280 °C at 25 °C/min on the HP-5 column identified in Table 2. Occasionally, a slightly modified temperature program was required to handle co-elution of solutes with the internal standard or solvent peaks.

2.3. Determination of liquid–liquid partition coefficients

The method used to determine partition coefficients is described in detail elsewhere [31–33]. The 2.0 mL screw-capped sample vials with PTFE-lined caps (Supelco, Bellefonte, PA, USA) were charged by syringe with 0.75 mL of polar solvent, 0.75 mL of low polarity solvent, 1–10 µL of liquid sample, and 1 µL internal standard. Solid samples were dissolved in either solvent (depending on solubility) at a concentration of about 0.5–1.5 mg/mL and added to the vial as described for liquids. Smaller sample sizes were used in some cases to avoid saturation in one of the phases. The vials were shaken for 30 s and allowed to stand for 1 h or overnight at room temperature (22 ± 2 °C). Sample volumes of 1 µL from each phase were taken for calculation of the partition coefficients using the relationship

$$K_p = \left(\frac{S_{cs}}{S_{ps}} \right) \left(\frac{I_{ps}}{I_{cs}} \right) K_p^{IS} \quad (3)$$

where K_p is the partition coefficient for compound S , S_{sc} and S_{ps} the peak area for compound S in the counter solvent and polar solvent layers, respectively, I_{sc} and I_{ps} the peak area of the internal standard in the counter solvent and polar solvent layers, respectively, and K_p^{IS} the partition coefficient for the internal standard in the biphasic solvent system. The internal standards were anisole $K_p^{IS} = 0.725$ for n-heptane-2,2,2-trifluoroethanol [34], 4-nitrotoluene $K_p^{IS} = 0.968$ for n-heptane-formamide [31], biphenyl

$K_p^{IS} = 0.857$ for n-heptane-propylene carbonate [35], 5-chloro-2-nitroanisole $K_p^{IS} = 0.766$ for n-heptane-ethylene glycol [36], and 1,3-dinitrobenzene $K_p^{IS} = 0.950$ for isopentyl ether–ethylene glycol [36]. System constants for the biphasic systems were taken from [18,32,35,36].

2.4. Partition coefficients from the literature sources

Liquid–liquid partition coefficients in n-hexane-acetonitrile for α -pinene, β -pinene, limonene, linalool, borneol, camphor, neral, geraniol, farnesol, and eugenol were taken from [37] and used with the system constants given in [20,38]. Partition coefficient for vanillin in 1,2-dichloroethane–water [39] and chloroform–water [40] were used with the system constants given in [18]. Partition coefficients for vanillin [39,41], eugenol [42,43], carvone [43], terpinen-4-ol [43], α -pinene [44,45], β -pinene [45], limonene [44,45], linalool [44,46], geraniol [46], anise alcohol [47], borneol [47], camphor [47], and benzyl salicylate [48] in octanol–water were used for verification of the descriptor values with the system constants given in [18]. Henry's law constants for α -pinene [45], β -pinene [45,49], limonene [45,49,50], linalool [50,51], and carvone [51] were converted to gas–water partition coefficients and used with the system constants given in [18].

2.5. Calculations

All calculations were performed on a Dell Dimension 9200 computer (Austin, TX, USA) using the Solver add-in module in Excel 2007 (Microsoft Corporation, Redmond, WA). The V descriptor was calculated from the molecular formula by summing atom constants and correcting for the number of bonds in the molecule as described in [52]. It has units of $\text{cm}^3 \text{mol}^{-1}/100$. The E descriptor was calculated by

$$E = 10V \left[\frac{\eta^2 - 1}{\eta^2 + 2} \right] - 2.832V + 0.526 \quad (4)$$

where η is the refractive index at 20 °C for the sodium D-line [53]. It has units of $\text{cm}^3 \text{mol}^{-1}/10$. For the seven solid compounds in Table 1, and only these compounds, refractive index values were initially estimated using ChemSketch v.10 (ACD Labs, Toronto, Ontario, Canada). These were used as initial estimates for the calculation of the E descriptor, which was then optimized by the Solver method along with the other descriptor values [19,26,28,54]. Solver is an optimization package that adjusts selected changing cells (descriptors) to minimize the value in a target cell (standard deviation of the residuals).

$$\text{Standard deviation} = \left[\frac{\sum (\log k_{\text{exp}} - \log k_{\text{cal}})^2}{n - 1} \right]^{1/2} \quad (5)$$

where $\log k_{\text{exp}}$ is the experimental retention factor (or partition coefficient), $\log k_{\text{cal}}$ the model predicted retention factor (or partition coefficient) using Eqs. (1) or (2), and n the number of experimental retention factors for each solute on all columns and temperatures and liquid–liquid partition coefficient for all biphasic partition systems.

3. Results and discussion

Retention factors at temperatures appropriate for the compounds indicated in Table 1 on the columns identified in Table 2 were measured and combined with liquid–liquid partition coefficients for the calculation of descriptor values using the Solver method [18,19,26,28,54]. The descriptors are summarized in Table 3. The V descriptor, for all compounds, and the E descriptor,

Table 2

Wall-coated open-tubular columns used for descriptor calculations by gas chromatography. Columns are calibrated for use over the temperature range 60–240 °C.

Column	Source ^a	Dimensions	Film thickness (μm)	Reference
SPB-Octyl	A	30 m × 0.25 mm	0.25	[27,28]
HP-5	B	30 m × 0.32 mm	0.25	[27,28]
Rtx-440	C	30 m × 0.25 mm	0.50	[28,29]
DB-225	B	15 m × 0.32 mm	0.25	[28,30]
HP-88	B	25 m × 0.25 mm	0.20	[29,30]
Rtx-OPP	C	30 m × 0.32 mm	0.15	[28,30]
Rtx-5Sil MS	C	30 m × 0.25 mm	0.50	[26]
HP-Innowax	B	60 m × 0.53 mm	1.00	[8,30]

^aA = Supelco, Bellefonte, PA, USA; B = Agilent Technologies, Folsom, CA, USA; and C = Restek Corporation (Bellefonte, PA, USA).

for compounds that are liquid at 20 °C, are available by calculation [52,53]. The other descriptors, and the *E* descriptor for solids, are experimental values. The standard deviation of the residuals supports the conclusion that the descriptors for each compound in Table 3 adequately define the properties of the compounds across the experimental systems used for their determination. In the case of farnesol two isomers were observed by gas chromatography on several stationary phases. Since farnesol has four possible structural isomers and individual standards are not available, we were unable to establish the identity of the two peaks observed by gas chromatography, or determine whether each peak is a single isomer or mixture of at least two of the possible structural isomers. Descriptors for the two peaks are indicated in Table 3 as isomer 1 and isomer 2 in the elution order observed on columns of low polarity. To estimate physicochemical properties for farnesol, Section 3.1, an average value for the two isomers was used. For a few compounds ($n > 100$ in Table 3) additional data from an earlier study [18] by gas chromatography for additional stationary phases to those shown in Table 2, and retention factors by reversed-phase liquid chromatography and micellar electrokinetic chromatography were included in the descriptor calculations.

Table 3

Descriptors for fragrance compounds.

Compound	Descriptor						Statistics SD	n
	<i>E</i>	<i>S</i>	<i>A</i>	<i>B</i>	<i>L</i>	<i>V</i>		
<i>(i) Allogens</i>								
Amyl cinnamal	1.212	1.050	0	0.736	7.133	1.8163	0.051	60
Anise alcohol	0.899	0.967	0.537	0.778	5.328	1.1156	0.036	69
Benzyl alcohol	0.803	0.871	0.410	0.558	4.248	0.9160	0.038	372
Benzyl benzoate	1.264	1.316	0	0.582	7.499	1.6804	0.044	143
Benzyl cinnamate	1.311	1.542	0	0.612	8.963	1.9192	0.032	40
Benzyl salicylate	1.413	1.338	0.012	0.433	8.000	1.7391	0.038	47
Cinnamyl alcohol	1.096	0.994	0.489	0.592	5.424	1.1548	0.040	300
Citral (geranial)	0.610	0.938	0	0.659	5.463	1.4473	0.051	58
Citral (neral)	0.589	0.901	0	0.650	5.391	1.4473	0.048	68
Coumarin	1.288	1.620	0	0.522	6.015	1.0619	0.048	241
Eugenol	0.946	0.865	0.353	0.540	5.785	1.3544	0.042	70
Farnesol (isomer 1)	0.675	0.591	0.375	0.791	7.511	2.1518	0.038	57
Farnesol (isomer 2)	0.757	0.576	0.372	0.834	7.628	2.1518	0.041	55
Geraniol	0.493	0.625	0.282	0.606	5.434	1.4903	0.033	72
Hydroxycitronellal	0.262	1.006	0.379	1.100	6.039	1.5920	0.028	37
α-Isomethyl ionone	0.762	1.007	0	0.710	6.402	1.9023	0.052	59
Lilial	0.775	0.995	0	0.594	6.654	1.8593	0.037	59
Limonene	0.497	0.336	0	0.174	4.693	1.3230	0.043	62
Linalool	0.391	0.482	0.244	0.745	4.803	1.4903	0.028	124
Methyleugenol	0.939	1.050	0	0.781	5.942	1.4653	0.041	61
<i>(ii) Not known to be allogens</i>								
Borneol	0.757	0.714	0.158	0.653	5.091	1.3591	0.036	139
Camphor	0.506	0.829	0	0.671	5.043	1.3161	0.046	146
Carvone	0.638	0.929	0	0.610	5.402	1.3387	0.039	132
Citronellal	0.287	0.680	0	0.758	5.071	1.4903	0.044	76
2-Methoxycinnamaldehyde	1.219	1.522	0	0.623	6.313	1.3114	0.035	58
α-Pinene	0.441	0.190	0	0.225	4.348	1.2574	0.034	55
β-Pinene	0.525	0.233	0	0.200	4.584	1.2574	0.047	46
Terpinen-4-ol	0.553	0.584	0.147	0.651	5.226	1.4247	0.033	160
Vanillin	1.107	1.392	0.382	0.664	5.673	1.1313	0.028	59

Table 4
Comparison of estimated and experimental octanol–water partition coefficients for fragrance compounds.

Compound	Octanol–water partition coefficient (log K_{ow})	
	Estimated ^a	Experimental ^b
<i>(i) Allegens</i>		
Amyl cinnamal	4.16	
Anise alcohol	1.11	1.10
Benzyl alcohol	1.16	1.10
Benzyl benzoate	3.87	3.97
Benzyl cinnamate	4.44	
Benzyl salicylate	4.67	4.31
Cinnamyl alcohol	2.00	1.70
Citral (geranial)	2.72	
Citral (neral)		2.78
Coumarin	1.34	1.39
Eugenol	3.02	2.99
Farnesol	5.35	
Geraniol	3.31	3.47
Hydroxycitronellal	1.41	
α -Isomethyl ionone	4.32	
Lilial	4.57	
Limonene	4.52	4.48 (av)
Linalool	2.95	2.97
Methyleugenol	2.59	
<i>(ii) Not known to be allegens</i>		
Borneol	2.74	2.72
Camphor	2.24	2.13 (av)
Carvone	2.50	2.71
Citronellal	2.65	
2-Methoxycinnamaldehyde	2.03	
α -Pinene	4.23	4.66
β -Pinene	4.30	4.22
Terpinen-4-ol	3.02	2.86 (av)
Vanillin	1.21	1.19 (av)

^a Estimated using $\log K_{ow} = 0.083 + 0.684E - 1.209S - 0.185A - 3.355B + 3.846V$ [18].

^b Where multiple experimental values for log K_{ow} were reported an average value (av) is indicated. The literature sources cited in Section 2.4.

the octanol–water partition coefficients using the descriptors in Table 3. The relative absolute error of 0.127 suggests that the descriptors are suitable for the prediction of the partition coefficients with no greater uncertainty than is anticipated in the measurement of experimental partition coefficients. The latter is unknown in absolute terms, of course, but from the general agreement between independently determined experimental partition coefficients is not expected to be less than about 0.2–0.3 log units [57].

In Table 5 are assembled estimated values for sensor irritation threshold, log(1/SIT) [23], odor detection threshold, log(1/ODT) [13,23], nasal pungency threshold (log 1/NPT) [13,23,58], skin permeability coefficient from water (log k_p) [59,60], skin–water partition coefficient (log K_{sc}) [59,60], absorption to ambient air particles (log K_A) [11,61] or adsorption to diesel soot particles (log K_{DS}) [11,62], air–water partition coefficients (log K_W) [18], and film water adsorption (log K_{AW}) [63,64]. These measurements are generally made according to a specific protocol that has to be followed to obtain comparable results (see cited sources above). The sensory impact of volatile chemicals in humans results predominantly from the stimulation of the olfactory nerve (odor detection) and the trigeminal nerve (eye irritation and pungency detection) [23,58]. The independently derived models for eye irritation and nasal pungency are almost equivalent and can be combined into a more general model for sensory irritation thresholds [23]. Underlying these models is that sensory perception can be predicted from the transfer of volatile chemicals from the gas phase to a receptor phase area. The models do not account for selective interactions that some compounds might have with specific receptors in the receptor phase area but can be helpful in identifying the

contribution of specific receptor interactions to the overall sensory stimulation caused by volatile chemicals. The estimated values for the volatile fragrance compounds in Table 5 (estimates are not given for solid compounds of low volatility because these may not be compatible with the experimental protocol) indicate a wide range of sensitivities covering 5–6 orders of magnitude. A distinguishing feature of the different measures of odor responsiveness is the a/b system constant ratio at 2.43 for the sensory irritation threshold, 1.78 for the nasal pungency threshold, and 0.97 for the odor detection threshold. The ratios are obtained by dividing the a system constant for each model by the b system constant for the same model. For example, for sensory irritation the hydrogen-bond basicity of the receptor area makes a more significant contribution to the observed sensory response than its hydrogen-bond acidity ($a/b=2.43$) while for the odor detection threshold the hydrogen-bond acidity and basicity of the receptor area are about equally important ($a/b=0.97$). The capability of a compound to participate in hydrogen-bonding interactions (A and B descriptors) is important for odor responsiveness, as well as its capability to produce vapors soluble in low-polarity regions of the receptor (L descriptor). Interactions of a dipole-type also contribute to sensory thresholds but vary less among the three sensory threshold models (s varies from 1.3 to 1.6). There are a few experimental values for the odor detection threshold (log 1/ODT) for linalool (experimental=0.02 and estimated=0.85), geraniol (experimental=1.05 and estimated=1.48), limonene (experimental=−0.99 [R-enantiomer] and −0.66 [S-enantiomer] and estimated=−0.70), α -pinene (experimental=−1.28 and estimated=−1.18), and β -pinene (experimental=−1.07 and estimated=−0.93) [23]. There is good agreement for geraniol, limonene (the solvation parameter model contains no term to distinguish individual enantiomers), α -pinene, and β -pinene but poor agreement for linalool. There are too few experimental values for the odor detection threshold for the fragrance compounds in Table 1 to comment in a general sense on the difference between the experimental and predicted threshold values. The agreement, accept for perhaps linalool, is quite good given the difficulty of the experimental measurements and the understandably wide standard deviations for the experimental values [13,23].

The skin permeability coefficients and partition coefficients provide useful information on the rate (permeability) and uptake (partition) by dermal absorption from exposure to fragrance chemicals in aqueous solution [59,60]. Most fragrance compounds are expected to transfer from water to skin relatively quickly (intermediate to large permeability coefficients) and accumulate in the skin (intermediate to high partition ratios). The permeability coefficient (log k_p) covers the range from about −6 to −3 and the partition coefficient (log K_{sc}) from 0.8 to 3. The driving force for the rate and extent of solute transfer is size (V descriptor) with the property that favors slower transfer and distribution to the aqueous phase hydrogen-bond basicity (B descriptor). Thus compounds like benzyl alcohol and anise alcohol are poorly absorbed by skin compared with the terpene derivatives and benzyl esters. For benzyl alcohol the prediction (log $k_p = -5.69$) is in good agreement with the experimental value −5.30 [59]. This is the only experimental value we are aware of for the compounds in Table 1.

Absorption by air particles [11,61] and adsorption by diesel soot particles [11,62] provide insight into particle phase deposition of volatile chemicals in atmospheric aerosols. In both cases the capacity for polar interactions (S , A , and B descriptor) favors particle sorption processes as well as non-polar interactions represented by the L descriptor. For the fragrance compounds log K_A covers the range −2.5 to 3.3 and log K_{DS} the range −3.5 to 3. These are wide ranges and indicate that there is no general conclusion that can be made for fragrance compounds as a group and it is necessary to consider compounds individually to assess the ability of air

Table 5
Estimated properties for biological and environmental processes calculated with the solvation parameter model. Sensory irritation threshold, odor detection threshold and nasal pungency threshold have units of parts per million, skin permeability coefficients from water cm²/s, absorption to air particulates m³/g, adsorption to diesel soot m⁻¹, and adsorption to film water m⁻¹.

	Biological ^a					Environmental ^a			
	log(1/SIT)	log(1/ODT)	log(1/NPT)	log <i>k_p</i>	log <i>K_{SC}</i>	log <i>K_A</i>	log <i>K_{DS}</i>	log <i>K_W</i>	log <i>K_{AW}</i>
<i>(i) Allegens</i>									
Amyl cinnamal	0.17	3.69	0.73	-4.09	2.30	1.20	0.61	4.15	-1.08
Anise alcohol				-6.01	0.80	0.94	0.54	6.51	-0.002
Benzyl alcohol	-1.09	1.38	-1.12	-5.69	0.90	-0.58	-1.45	4.99	-2.04
Benzyl benzoate	0.66	4.27	1.16	-4.07	2.34	1.67	1.04	4.18	-1.23
Benzyl cinnamate				-3.72	2.69	3.22	2.97	4.60	0.04
Benzyl salicylate				-3.52	2.82	2.04	1.30	3.54	-1.58
Cinnamyl alcohol	0.29	2.79	0.33	-5.37	1.35	0.76	0.05	5.62	-1.01
Citral (geranial)	-1.35	1.84	-1.03	-4.59	1.60	-0.35	-0.94	3.65	-2.02
Citral (neral)	-1.48	1.69	-1.16	-4.54	1.62	-0.45	-1.05	3.51	-2.12
Coumarin	-0.03	3.71	0.25	-5.46	1.27	0.57	-0.45	3.27	-1.85
Eugenol	-0.19	2.44	-0.02	-4.61	1.81	0.62	-0.04	5.26	-2.13
Farnesol	1.13	3.51	1.50	-3.45	2.67	2.25	2.41	4.22	0.86
Geraniol	-0.99	1.48	-0.81	-4.30	1.81	0.03	-0.37	4.15	0.79
Hydroxycitronellal	1.11	3.45	1.16	-5.75	0.76	1.57	2.02	6.98	1.84
α-Isomethyl ionone	-0.47	2.81	-0.06	-3.75	2.37	0.57	0.14	7.05	1.60
Lilial	-0.47	2.80	-0.04	-3.49	2.55	0.71	0.23	3.27	-1.60
Limonene	-3.58	-0.70	-3.22	-3.12	2.51	-1.93	-3.09	-0.22	-5.00
Linalool	-1.62	0.85	-1.43	-4.62	1.50	-0.66	-1.07	3.67	-1.53
Methyleugenol	-0.64	2.76	-0.24	-4.93	1.51	0.21	-0.42	4.57	-1.41
<i>(ii) Not known to be allegens</i>									
Borneol				-4.76	1.54	-0.53	-1.27	3.72	-2.11
Camphor				-4.86	1.32	-0.80	-1.41	3.44	-2.26
Carvone	-1.48	1.72	-1.16	-4.69	1.52	-0.45	-1.12	3.43	-2.29
Citronellal	-1.92	1.04	-1.61	-4.63	1.40	-0.81	-1.19	3.27	-1.84
2-Methoxycinnamaldehyde				-5.13	1.51	0.83	0.01	5.31	-1.57
α-Pinene	-4.01	-1.18	-3.63	-3.35	2.29	-2.33	-3.52	-0.36	-5.12
β-Pinene	-3.79	-0.93	-3.40	-3.30	2.36	-2.11	-3.32	-0.37	-5.10
Terpinen-4-ol	-1.60	1.15	-1.32	-4.51	1.62	-0.52	-1.08	3.14	-2.02
Vanillin				-5.78	1.07	1.15	0.52	6.69	-0.52

^a Models employed for property estimations.

log(1/SIT) = -7.839 + 1.620S + 3.431A + 1.413B + 0.759L; SD = 0.36, n = 643 [23].

log(1/ODT) = -5.27 + 0.51E + 1.96S + 1.48A + 1.53B + 0.723L; SD = 0.46, n = 64 [13].

log(1/NPT) = -7.89 + 0.20E + 1.32S + 2.71A + 1.52B + 0.823L; SD = 0.359, n = 48 [13].

log *k_p* = -5.426 - 0.106E - 0.473S - 0.473A - 3.000B + 2.296V; SD = 0.464, n = 119 [59].

log *K_{SC}* = 0.341 + 0.341E - 0.206S - 0.024A - 2.178B + 1.850V; SD = 0.216, n = 45 [59].

log *K_A* = -6.515 - 0.209E + 0.958S + 2.534A + 0.680B + 0.906L; SD = 0.115, n = 53 [11].

log *K_{DS}* = -8.61 - 1.02E + 1.10S + 3.19A + 1.49B + 1.15L; SD = 0.195, n = 84 [11].

log *K_W* = -0.929 + 0.474E + 3.042S + 3.819A + 4.531B - 0.286L; SD = 0.177, n = 88 [18].

log *K_{AW}* = -8.63 - 0.95E + 1.06S + 3.49A + 4.01B + 0.65L; SD = 0.117, n = 73 [63].

particulates to remove fragrance compounds from the atmosphere. The mechanism is less efficient for the small low polarity terpenes (for example, limonene, α-pinene, etc.) and efficient mechanism for larger and polar terpene derivatives and related compounds (for example, benzyl cinnamate, farnesol, hydroxycitronellal, etc.)

The partition of trace volatile compounds from air to water (log *K_W*) demonstrates efficient absorption of most fragrance compounds by bulk water (such as rain droplets). The exception is weakly polar terpenes, such as α-pinene, β-pinene and limonene which are only poorly absorbed compared to the more polar compounds in Table 5. The predicted partition coefficients cover a wide range from -0.2 to about 7 with small molecules that are capable of strong hydrogen-bonding interactions having the most favorable partition coefficients. Except for carvone there is good agreement between experimental and predicted air-water partition coefficients for the seven compounds with experimental values [benzyl alcohol = 4.86 (predict 4.99), camphor = 3.44 (predict 3.44), carvone = 4.24 (predict 3.43), limonene = -0.20 (predict -0.22), linalool = 3.72 (predict = 3.67), α-pinene = -0.40 (predict -0.36), and β-pinene = -0.44 (predict -0.37)]. Adsorption to film water shows significant characteristic differences to absorption by bulk water accounted for largely by the difference in cavity formation and dispersion interactions for immersion of a compound into bulk water and interactions of a compound with the surface layer of

water molecules as well as a significant contribution from electron lone pair repulsion for adsorption on film water. Also, interactions of a dipole-type contribute less to adsorption by film water compared with absorption by bulk water. Compounds such as anise alcohol and vanillin have favorable partition coefficients for absorption by bulk water but are only weakly adsorbed by film water. The predictions in Table 5 provide an indication that for a number of fragrance compounds the efficiency of removal from aerosols by bulk water and film-supported water are expected to be quite different.

4. Conclusions

Chromatographic and liquid-liquid partition methods facilitate the calculation of descriptors for use in the solvation parameter model for a wide range of compounds. The use of gas chromatography and totally organic liquid-liquid partition systems are particularly useful for compounds of low water solubility and facilitate the calculation of transfer properties in aqueous systems that are challenging to measure directly. Descriptors for the 28 fragrance compounds determined in this study should allow the prediction of a wide range of chromatographic, physicochemical, biological and environmental properties for these compounds using established models.

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