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Ionization efficiency in electrospray ionization source and its relations to compounds' physico-chemical properties

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Institute of Chemistry, Faculty of Science and Technology, University of Tartu, Estonia

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II Oss, M.; Kruve, A.; Herodes, K.; Leito, I. Electrospray Ionization Efficiency Scale of Organic Compounds. *Anal. Chem.* **2010**, *82* (7), 2865–2872. https://doi.org/10.1021/ac902856t.

III Kruve, A.; Kaupmees, K.; Liigand, J.; Oss, M.; Leito, I. Sodium adduct formation efficiency in ESI source. *J. Mass Spectrom.* **2013**, 4*8*, 695–702. https://doi.org/10.1002/jms.3218.

IV Oss, M.; Tshepelevitsh, S.; Kruve, A.; Liigand, P.; Liigand, J.; Rebane, R.; Selberg, S.; Ets, K.; Herodes, K.; Leito, I. Quantitative Electrospray Ionization Efficiency Scale: 10 Years After. *Submitted to Rapid Commun. Mass Spectrom on 07.05.2021.*

Author's contribution

Paper I: Performed most of the experimental work. Contributed to writing the manuscript.

Paper II: Main person responsible for planning and writing the manuscript. Performed all the experimental work.

Paper III: Performed some of the experimental work.

Paper IV: Main person responsible for planning and writing the manuscript. Performed some of the experimental work.

ABBREVIATIONS

A	area
BP	Becke-Perdew
CEM	chain ejection model
COSMO-RS	COnductor like Screening MOdel for Real Solvents
CRM	charged residue mechanism
CV	cross validation
d	dipole moment
DFT	density-functional theory
ESI	electrospray ionization
GB	gas phase basicity
IE	ionization efficiency
IEM	ion evaporation model
LC	liquid chromatography
LOO	leave one out
M	molecular mass
MeCN	acetonitrile
MS	mass spectrometry
MV	molecular volume
O base	base with protonation center on oxygen
pK_a	negative base-10 logarithm of the acid dissociation constant (K_a)
pK_{aH}	pK_a of conjugate acid
$P_{oct/w}$	partition coefficient between octanol and water
$P_{s/h}$	partition coefficient between solvent and hexane
PSA	polar surface area
QSPR	Quantitative Structure Property Relationship
R^2	the square of the correlation coefficient
RIE	relative ionization efficiency
RF	radio frequency
RMSE	root mean square error
S	standard deviation
TM	target mass
TZVP	valence triple-zeta polarization basis set
WANS	weighed area of negative sigma

1. INTRODUCTION

Electrospray ionization (ESI) is a common and efficient ionization method, often used as interface between liquid chromatography and mass spectrometry. It has been applied to the analysis of a large variety of compound classes and due to its soft nature it can be used for compounds of wide range of molecular masses.[1–4] ESI is applicable for compounds of very different molecular sizes but it cannot be used for all compound groups (for example aromatic hydrocarbons, alkanes etc). Importantly, for different compounds with same concentrations in solution, the resulting signal intensities in MS spectra may be significantly, by orders of magnitude, different – i.e. the *ionization efficiencies* of compounds differ widely.

In spite of the extensive use of ESI there is still no full understanding of the relationships between the molecular parameters of a particular compound and its ionization efficiency. Advancement of reliable knowledge on electrospray ionization efficiency would be greatly aided by availability of quantitative ionization efficiency data of compounds with different chemical structures. If the data are to be compared, then the measurements have to be carried out under the same conditions. This means that defining a parameter for quantifying the effectiveness of from analytes in the ESI source, which could be measured for a large diversity of compounds under identical experimental conditions, would be very valuable. This parameters would enable composing a quantitative scale of ESI ionization efficiencies where all compounds on the scale can be compared to each other. Also, it would be beneficial if such measurements could be done using routine ESI-MS equipment, without the need of sophisticated apparatus or extensive rebuilding of commercial instruments.

The most obvious use of such ionization efficiency scale would be predicting ionization efficiency of compounds using their physico-chemical parameters. The scale could also lead to better understanding of the ESI mechanism at the molecular level. Relative ionization efficiency would enable calculating relative detection efficiency of compounds in LC-ESI-MS and would thus allow semi-quantitative analysis to be made without the need to calibrate with the analyte. The ionization efficiency parameter could also be used as a new molecular descriptor together with the well-established parameters, such as pK_a or octanol-water partition coefficient.

The general aim of this study was to gain fundamental knowledge on the relationships between compound's ionization in ESI source (positive ions, monoprotonation) and its physico-chemical properties. The technical objectives were compiling an extensive ionization efficiency scale containing ionization data of various compounds (with diverse physico-chemical property values) and finding quantitative relationships between compounds' ionization efficiency in the ESI source and its molecular properties.

2. LITERATURE OVERVIEW

2.1. The mechanism of ESI ionization

In the ESI interface there are two separate but interdependent parts (see Figure I in Paper I). The atmospheric pressure area includes the ESI spray needle and auxiliary hardware, and the vacuum interface provides a means for ion desolvation and transport into the mass spectrometer. The atmospheric pressure region commonly includes an electrospray needle at high electrical potential and means for providing one or several gas flows to aid nebulization and solvent evaporation. An interface into the vacuum area is accomplished using an entrance capillary and a skimmer or ion funnel. In this vacuum region excess gas and solvent molecules are removed by vacuum pump and ions are collisionally desolvated. Ions are transferred to high vacuum region of mass analyzer using ion guides.[5]

2.2. The formation of ions in ESI source

In electrospray process a fine mist consisting of small droplets is created when a high electric potential is applied to a needle containing a solution with a polar solvent. High electric potential applied to the sprayer capillary does not only affect the spraying process but also aids in the separation of positive and negative ions at the needle tip.[1] The spray process is often pneumatically assisted. A flow of heated drying gas is used facilitate solvent evaporation. An orifice or skimmer is used to introduce the ions into the vacuum region.

Positive and negative charges existing in the solution are separated by the electric field applied in atmospheric region of ESI source (Fig. 1). For instance, in positive ion mode, the electrospray needle has a relatively high positive potential relative to the vacuum orifice or skimmer. Anionic species are drawn to the needle tip, whereas cations dominate at the meniscus surface. The positive charges at the surface repulse each other, and the liquid surface distends away from the needle tip. When the electrostatic force and the surface tension are balanced, the cone-shaped liquid surface, referred to as a “Taylor cone” (Fig. 1) is formed. At even higher potential the excess positive charge overcomes the surface tension, and droplet is formed from the tip of the Taylor cone. The droplets in the formed mist carry an excess positive charge when the spray needle is at positive potential. As the solvent evaporates and the droplets shrink, the repulsion due to surface charge overcomes the surface tension and the droplet crumbles in so called Coulombic explosion. As a result a stream of smaller droplets evolves. The point at which the charge repulsion and the surface tension are balanced is the Rayleigh stability limit (Fig. 1).[1]

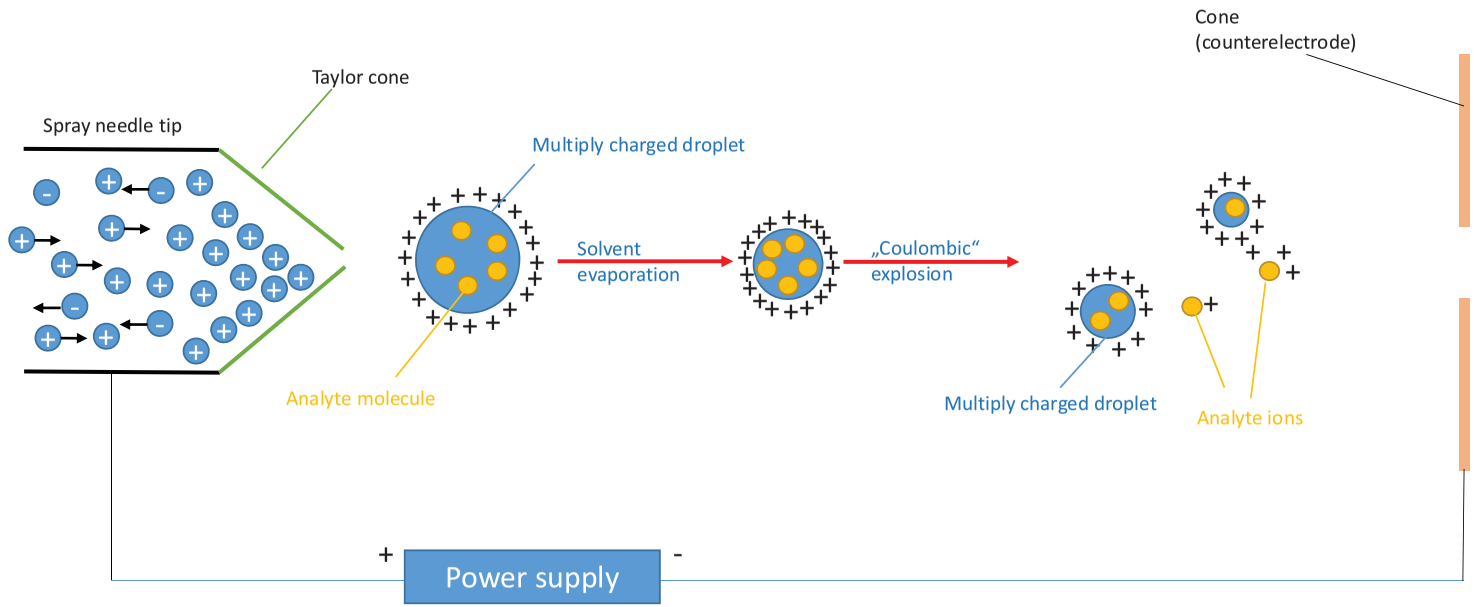

Figure 1. A schematic of the mechanism of ion formation.

Precise mechanism of ion formation from charged droplets has still not been fully explained in detail and there are different theories proposed.[5] The "charged residue mechanism" (CRM), proposed by Dole and coworkers and elaborated upon by Röllgen and coworkers[6,7], declares that the ions detected in ESI-MS are charged particles that remain after all of the solvent has evaporated from a droplet. The CRM believed to hold mainly for large globular molecules.[8] The "ion evaporation" model (IEM) proposed by Iribarne and Thomson [9] states that as a droplet reaches a radius of less than 10 nm, direct diffusion of solvated ions can take place from the droplet. IEM applies to low molecular mass molecules and small inorganic ions.[9] Chain ejection model (CEM)[10,11] is most convenient for long chained molecules like unfolded proteins. Due to their hydrophobicity they are believed to reside on the surface of the droplet. In principle, CEM is kindred to IEM , but due to its chain length the chain is ejected from surface of the droplet stepwise.[10]

In the case of low molecular weight compounds (as in present study), it is generally accepted that the ESI process proceeds via the ion evaporation mechanism.[12–14]

In the case of acidic conditions (as in this work) the charge of charged droplets is mostly due to solvated protons. It is useful to consider the droplet as consisting of two virtual "phases": the "bulk" and the "surface layer" (see figure 2). The charge of the droplet is predominantly localized in the surface layer (because of charge-charge repulsion). This means that there is excess of solvated protons in the surface layer and therefore it is expected to have much higher acidity than the interior.

In the case of ESI some (more basic) compounds are ionized (generally protonated) already in the initial solution. Their protonated forms simply diffuse into the surface layer and get ejected. There are, however numerous compounds that are, in the equilibrium sense, negligibly ionized in solution but nevertheless give ions with high efficiency.

The evidence from this work and from others[15–17] reveals that compounds with remarkably low basicity, but at the same time high lipophilicity/hydrophobicity (e.g. diphenylamine, phthalate esters, ...) can give ions via protonation with high efficiency from mildly acidic solutions.

The ionization mechanism that best agrees with these findings is the following: lipophilic/hydrophobic molecules diffuse to the droplet surface because of solvophobic/hydrophobic interaction. They get protonated for a short time only, because even with concentrating the solvated protons on the droplet surface the equilibrium acidity of the surface layer is most probably[18] nowhere near the pK_a of the protonated forms of the compounds. But during the short time while they are in protonated form there is high probability that these weakly solvated ions residing on the surface will be ejected from the droplet because of charge-charge repulsion.

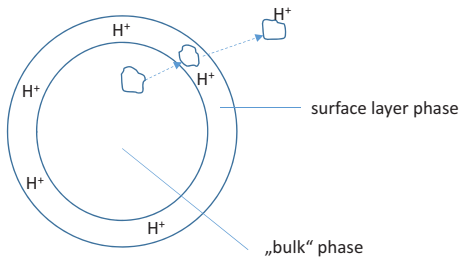

Figure 2. The rough schematic of how the particle withdraws from the droplet.

Efficiency of ESI for generating ions is strongly reliant on spray conditions, analyte and mobile phase properties. Ionization of some analytes may be highly efficient (even 100% efficiency has been discussed in case of nano-ESI[19]), but other analytes are not ionizable at all. In most cases only a part of the analyte molecules (or ions) in the liquid phase that is sprayed into the ESI source are finally converted to gas-phase ions (via protonation, adduct formation, deprotonation, etc.). The term ionization efficiency (IE) has been coined to denote the extent to which analyte molecules in liquid phase are converted to gas-phase ions and eventually detected in detector. Pursuant to that, IE includes the efficiency of generating gas-phase ions from analyte particles in the ESI source as well as efficiency ion transport and detection.

2.3. Ionization efficieny

In consideration of the wide usage of ESI, further development of the knowledge of predicting the ionization efficiency of a particular compound would be very useful. In qualitative terms it is known that the molecular properties that affect electrospray ionization efficiency are, for example, basicity (expressed as pK_{aH}, the pK_a value of conjugate acid), hydrophobicity, surface activity, etc.[20,21] Also, numerous quantitative studies on IE of molecules in the ESI source have been carried out (see Table 1).[13,20,22,23] In a fair share of them an aim has been to investigate how the response in ESI-MS depends on the molecular parameters of the analytes. Such information is of fundamental interest and is useful in LC-ESI-MS method development. Moreover, a highly practical application for reliable electrospray IE data would be calibration of LC-ESI-MS methods without chemical standards.[13] The following can be concluded from survey of literature (published before the present study):

1. In most studies a limited number of compounds have been included, often structurally similar. Many of the investigated compounds have been polyfunctional, which has often hindered finding relations between ionization efficiency and molecular structure.

2. In the majority of the published work the span of the studied compounds' ionization efficiencies has been limited.
3. Ionization in the electrospray source and its relation to molecular structure depend on the used solvent (mobile phase).[1] Therefore, ionization efficiencies measured using different solvent compositions are not directly comparable and thus the relations between compound's properties and ionization in ESI source found in various published studies are also usually not one-to-one comparable. For example, hydrophobicity of the ionized molecule (and thus the resulting ion) may be a very strong factor in water-rich mobile phases, but can be of limited importance in purely organic mobile phases (e.g. refs[21,24]).
4. Some of the studies have used rather narrow concentration ranges of analytes.
5. The measurement methodologies and the measurands used to describe ionization efficiency vary considerably. In some cases absolute MS responses are recorded[21,25]; in other cases different kinds of relative MS responses obtained using different experimental methodologies are recorded[26].

The main reasons for divergence of results of various published papers could be explained by observations 1, 3, 4 and 5. Due to the limited number of analytes and narrow span of the *IE* values it is not possible to derive reliable relationships between the ionization efficiency (under given experimental conditions) and molecular structure. To some degree, in ref[27] and in Paper IV these restricting aspects have been overcome: the range and the diversity of compounds is larger than in most of the previously published studies, analytes' concentration ranges have been by intentionally selected reasonably wide and in linear range of the signal-concentration plot.

Table 1 incorporates all the results containing ESI ionization studies (limited only to positive mode ESI via monoprotonation) known to us at the moment.

Table 1. Published studies of dependencies between ionization efficiency (ionization by monoprotonation) and compounds' parameters.

Compounds	**Concentration range**	**Compound's parameters investigated**	**Approximate *IE* span[a]**	**Ref[b]**
16 cations (metal cations, protonated alkaloids)	10^{-8}–10^{-2} M	surface activity, ion evaporation rate constant	10	25
6 tripeptides	10^{-7}–10^{-3} M	nonpolar surface area, surface activity	2.5	21
5 tetraalkylammonium salts	10^{-4} M	ion mobility relative to surface activity	35	26
7 esters, 3 aromatic amines	10^{-8}–10^{-3} M	hydrophobicity, chelating ability	10000	I
19 small bases with different structures	10^{-4} M	basicity in the solvent	300	22

Compounds	Concentration range	Compound's parameters investigated	Approximate *IE* span[a]	Ref[b]
58 metabolites, most of them amino acids and N-bases	10^{-3}–10^{-2} M	MV, log*P*, absolute ion mobility	70	13
62 compounds, most of them N-bases, esters and tetraalkyl-ammonium salts	10^{-8}–10^{-3} M	Molecular size, pK_a	1000000	II
10 diverse compounds	10^{-7}–10^{-5} M	hydrophobicity	100000	15
99 drugs and drug-like molecules	0.5 µg/mL	log*P*, log*D*, pK_a	1000	28
15 diverse compounds	10^{-8}–10^{-6} M	pK_a, log*P*, molecular size, chelating ability	10000	16
56 small N-bases	10^{-5} M	basicity, polarity, volatility, position of the substituent	1000	29
66 drugs and drug-like molecules	10^{-5} M	proton affinity and total molecular surface area	10000000	30
28 compounds, mainly anilines and aromatic N-heterocycles	10^{-6}–10^{-4} M	number of potential charge centers, hydrogen bonding acceptor capacity, polarity of the neutral form of the compound, pK_a, hydrophobicity, molecular volume	100000	17
9 esters, 8 diverse acids and bases	10^{-10}–10^{-7} M	compound affinities towards specific ionic species; excess surface charge; hydrophobicity of the formed species	1000	III
24 derivatized and un-derivatized amino acids	10^{-8} – 10^{-4} M	Molecular size	1000	31
57 diverse compounds	10^{-7} – 10^{-5} M	Molecular size, basicity	1000000	32
21 amino acids, 38 oligopeptides (consisting of up to 14 amino acid residues)	10^{-8} – 10^{-4} M	Hydrophobicity, molecular volume	100	33
353 diverse compounds incl. drugs, pesticides, amino acids, oligopeptides, small acids and bases, esters, etc	10^{-9} – 10^{-4} M	Hydrophobicity, size, basicity	10000000	27
334 diverse compounds incl. drugs, pesticides, amino acids, oligopeptides, small acids and bases, esters, etc	10^{-9} – 10^{-4} M	Hydrophobicity, size, basicity	10000000	IV

[a] Ratio between the highest and lowest *IE*. [b] References given in roman numeral are publications from present work.

3. METHOD FOR QUANTIFYING IONIZATION EFFICIENCIES

A method of quantifying relative ESI ionization efficiencies of analytes has been proposed and applied to a number of compounds under predefined ionization conditions,[Papers I and II] which provides a scale of relative ionization efficiencies of studied compounds against each other. The focus of this study comprises treatment only to positive ions and to ionization via protonation with a single proton.

Based on the IEM[9] and on the assumption that the rate of evaporation of protonated particle from a droplet is proportional to the concentration of the ion in the droplet, Tang and Kebarle[25,34] established the following relationship:

$$I(\mathrm{A}^+, \mathrm{ms}) = Pf \frac{k_\mathrm{A}[\mathrm{A}^+]}{k_\mathrm{A}[\mathrm{A}^+] + k_\mathrm{E}[\mathrm{E}^+]} I \tag{1}$$

where $I(\mathrm{A}^+,\mathrm{ms})$ is the intensity of MS signal of an ion A^+, $[\mathrm{A}^+]$ is the equilibrium concentration of the ion A^+ in the electrosprayed solution, k_A and k_E denote the rate constants of transferring the ions from the droplets to the gas-phase, $[\mathrm{E}^+]$ stands for the otal concentration tof all other cations in the droplet, f is the fraction of droplet charge that is converted into gas-phase ions, I is the total electrospray current, and P expresses the fraction of gas-phase ions formed in ESI source that get eventually detected by the mass spectrometer (ion transport efficiency). The parameters k, f and P all rely on the electrosprayed solvent composition. Absolute values of all these parameters would enable to gain highly valuable insight into ionization process but these are difficult to measure. For practical applications relative values enabling comparison of different compounds and different MS conditions are often sufficient. Relative values of k for some cations have been published.[25] Some estimates of f and P are also available.[25] There are, however, no comprehensive studies.

Enke[12] arrived at a similar equation using a different starting point: because of electrostatic repulsion, the excess charge of a droplet is wholly located on its surface. At the same time, the droplet's interior is neutral. In addition to this he introduced four assumptions: (1) the surface of the droplet and its interior are two distinct phases; (2) ions partition between these two phases, the partitioning is rapid and at any given moment the system can be considered to be at equilibrium; (3) the surface phase concentration of the ion is low compared to the interior and (4) the signal intensity of the ion in the mass spectrum is proportional to the concentration of the ion in the surface phase. All these put together led to the following equation:

$$R_\mathrm{A} = Pf \frac{K_\mathrm{A} C_\mathrm{A}}{K_\mathrm{A} C_\mathrm{A} + K_\mathrm{E} C_\mathrm{E}} [Q] \tag{2}$$

where R_A denotes the signal of the ion A^+ in the mass spectrum. K_A and K_E are the partition coefficients of A^+ and all other ions, respectively between the droplet interior and surface. C_A and C_E are the analytical concentrations of the respective species. [Q] is the concentration of the excess charge in the droplet. P and f have the same meaning as in Eqn. (1).

Equations (1) and (2) are very similar. At low A^+ concentrations (below 10^{-6} M) the relationship between concentration and signal is linear. The ionization efficiency parameter used in this work was defined on the basis of the Enke's model because it is more recent and physically more elaborate. Both models, however, lead to the same mathematical expressions.

On the basis of references [12] and [24] it can be shown that if the concentrations of A^+ and B^+ in the solution are significantly lower than concentration of the buffer electrolytes then their electrospray responses are independent of each other and the following holds:

$$\frac{R_A}{R_B} = \frac{K_A C_A}{K_B C_B} \tag{3}$$

The ratio K_A/K_B can be termed as the relative ESI ionization efficiency of ions A^+ and B^+. It can be obtained by spraying a solution containing known concentrations of the ions into the ESI-MS system under carefully defined experimental conditions and measuring their relative intensities R_A and R_B in the mass spectra:

$$\frac{K_A}{K_B} = \frac{R_A C_B}{R_B C_A} \tag{4}$$

Previous works[25,26] mostly examine behaviour of such compounds in the ESI source that are ions or predominantly ionized already in the solution phase. In practice, however, the ionization efficiency of such compounds that are weak bases (i.e. the pK_{aH} value is below 0) and are almost fully neutrals in solution of any realistic pH, or are weakly to moderately basic and are protonated only to a limited extent. Such compounds can nevertheless also be ionized by electrospray and many practically important analytes belong to this group. Such compounds are ionized by the excess charge in the droplets either by protonation or by metal cation adduct formation. Protonation is the only ionization type considered in this study. The relative ionization efficiency of neutrals B_1 and B_2 can be expressed by rewriting Eqn. (4) as follows:

$$\frac{K_1 \alpha_1}{K_2 \alpha_2} = \frac{K'_1}{K'_2} = \frac{R_1 C_2}{R_2 C_1} \tag{5}$$

Here K and R are the partition coefficient and response of the ions B_1H^+ and B_2H^+; C are the analytical concentrations of B_1 and B_2 and α are the protonation ratios of the compounds B_1 and B_2: α_1=[B_1H^+]/C_1 and α_2=[B_2H^+]/C_2. We define the *ionization efficiencies* of B_1 and B_2 as $IE(B_1)=R_1/C_1$ and $IE(B_2)=R_2/C_2$ under given conditions. The ratio K'_1/K'_2 is termed as *relative ionization efficiency* (*RIE*) of B_1 relative to B_2:

$$RIE(B_1/B_2) = \frac{IE(B_1)}{IE(B_2)} = \frac{K'_1}{K'_2} = \frac{R_1 C_2}{R_2 C_1} \tag{6}$$

The values of *RIE* can be determined according to Eqn. (6) by electrospraying solutions containing known concentrations of B_1 and B_2 and measuring the intensities of their signals in the mass spectrum. Ionization of a given compound is influenced by the presence of other compounds and ions in the solution. Moreover, there are several parameters that affect the efficiency of ion formation in the ESI source: source design and geometry; voltage between the spray needle and the MS entrance; pH, vapour pressure, viscosity and surface tension of the solution; flow rate and temperature of the involved nebulizing and drying gases. Some of the parameters are poorly controllable making measurement of absolute ionization efficiencies inaccurate. At the same time, the *relative* way of measurement enables cancelling of most of those influences. For verifying the relative measurement results the following *circular verification* was employed. Firstly, the measurements were carried out with compounds B_1 and B_2 (using several concentration ratios). Thereafter, the value $RIE(B_1, B_2)$ was verified by involving at least one additional compound B_3 and by determining the values $RIE(B_3, B_1)$ and $RIE(B_3, B_2)$. From Eqn. (5) it is easy to see that:

$$RIE(B_1, B_2) = RIE(B_3, B_2) \,/\, RIE(B_3, B_1) \tag{7}$$

Using logarithmic values is more convenient because the log*RIE* values are additive:

$$\log RIE(B_2, B_1) = \log RIE(B_3, B_1) - \log RIE(B_3, B_2) \tag{8}$$

When log*RIE* values for a number of compound pairs having common compounds are measured using the same conditions then it is possible to set up a self-consistent *quantitative scale of ionization efficiencies*. The log*IE* values of compounds on the scale can be found by selecting an anchor compound and fixing its log*IE* value, either by measuring or arbitrary assignment. This approach has worked for decades in acidity and basicity measurements in the gas phase[35] and in nonaqueous solvents.[36]

Slightly different approach measuring RIE values that implements the slopes of concentration-response plot has been simultaneously used.[27]

$$RIE(B_{1,}B_2) = \frac{slope(B_1)*IC(B_1)}{slope(B_2)*IC(B_2)} \quad (9)$$

where the linear regression in the linear range of the signal-concentration plot is used to estimate the slope of the signal versus concentration and the IC is the sum of relative abundances of isotopologues where highest abundance is taken equal to 100.

4. EXPERIMENTAL

All the measurements presented in Paper I, Paper II and Paper III were conducted on an Agilent XCT ion trap mass spectrometer. The MS and ESI parameters were not changed or optimized but the factory defaults were used: drying gas flow rate 7 L/min, nebulizer gas pressure 15 psi (103.4 kPa), drying gas temperature 300°C. Log*IE* data for Paper IV was obtained using mainly the mentioned Agilent XCT mass spectrometer but 4 additional MS setups were used: Agilent Single Quad 6100 single quadrupole mass spectrometer, Varian J-320 triple quadrupole mass spectrometer, Varian 910-FT-ICR mass spectrometer and Agilent 6495 Triple Quadrupole mass spectrometer.[16]

Although the scales obtained on different instruments are not identical, Liigand et al[16,27] have shown, that when the same solvent system is used, the log*IE* scales are transferable between instruments, since the differences between log*IE* scales are not statistically significant.

The use of equations (5) and (9) by default implies equal transmission efficiencies and ion detector sensitivities for the ions B_1H^+ and B_2H^+. With most of the conventional mass spectrometer designs (including the XCT used in present work) it is not utterly the case. Specifically, the efficiencies of ion transmission can be substantially different if the *m*/*z* ratios of ions are divergent. The ion transport and mass analyser parameters are in many contemporary mass spectrometers (also in the XCT) tuned to some *target mass* (TM). Several potentials in the apparatus that affect the transport and trapping of ions are linked and coordinated by TM. TM is "a smart parameter" that makes the tuning process easier. Regulating TM the actual MS parameters can be fine-tuned to specific *m*/*z* ratio (see Table 1 in Paper I).

It is also possible to regulate all the parameters linked to TM individually without using the TM parameter. Since in present work we deliberately aimed at reducing the number of variables TM was used without further optimization of the specific voltages. The intensities of peaks near the appointed TM are maximized as compared to the rest of the mass spectrum. Nevertheless, the decrease in the peak intensity when moving away from the TM is not steep especially towards lower *m*/*z* values (see figure 1 in Paper III). In order to assess the discrimination during ion transport, all RIE measurements were carried out using three different TM values: M+1 of the first compound, M+1 of the second compound and the *m*/*z* ratio 500. The log*RIE* value was found as average of the values obtained with the three target masses or average of two target masses, if one of the results was considerably different. The origin of the log*IE* values of the studied compounds is presented in Table 3.

Table 3. The ionization efficiencies (log*IE*) of the studied compounds together with CAS numbers and values of molecular parameters.[a]

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
1	N,N-dimethyl-4-[2-[4-[(phenyldi-1-pyrrolidinylphosphoranylidene)amino]-phenyl]diazenyl] benzenamine	[27]	*6.36*	29.18	-1.15	0	7.38	15.20	247	494.6	516.2	612.9	6.2	2.24	2097489-44-4
2	N,N-dimethyl-4-[2-[4-[(triphenylphosphoranylidene)amino]-phenyl]diazenyl] benzenamine	[27]	*6.27*	27.48	-1.19	0	6.65	14.55	253	501.6	528.1	625.4	6.0	1.90	33354-65-3
3	N-(diphenyl-1-pyrrolidinylphosphoranylidene)-4-(2-phenyldiazenyl) benzenamine	[27]	*6.23*	27.79	-1.32	0	6.86	14.46	244	451.5	467.9	556.1	12.6	1.96	2097489-37-5
4	4-(2-phenyldiazenyl)-N-(triphenylphosphoranylidene) benzenamine	[27]	*6.15*	28.83	-1.34	0	5.65	12.99	246	458.5	478.4	566.9	12.7	1.47	33341-95-6
5	N'-(2-chlorophenyl)-P,P-di-1-pyrrolidinyl-N-(tri-1-pyrrolidinylphosphoranylidene) phosphinimidic amide	II	*6.15*	24.10	-0.88	0	*17.55*	*25.4*[37]	263	553.1	459.7	675.1	10.4	7.13	417706-58-2
6	4-(2-phenyldiazenyl)-N-(phenyldi-1-pyrrolidinylphosphoranylidene) benzenamine	[27]	*6.17*	30.38	-1.25	0	7.55	15.07	243	444.5	459.9	563.1	13.0	2.87	2097489-38-6
7	4-(2-phenyldiazenyl)-N-(phenylbis-1-(dimethylamino)phosphoranylidene) benzenamine	[27]	*6.04*	30.23	-1.45	0	7.36	15.02	242	392.5	419.6	504.4	13.7	1.62	See Paper IV
8	N'''-(4-bromophenyl)-N,N',N''-tris(tri-1-pyrrolidinylphosphoranylidene)-phosphorimidic triamide	[27]	*5.97*	36.54	-0.55	0	23.43	31.32	278	968.0	664.4	1136.6	14.4	9.42	874220-63-0
9	N'''-(4-methoxyphenyl)-N,N',N''-tris(tri-1-pyrrolidinylphosphoranylidene)-phosphorimidic triamide	[27]	*5.83*	43.17	-0.53	0	25.32	34.39	279	919.1	675.5	1154.8	11.5	9.94	874220-62-9
10	((2,6-dinitrophenyl)imino)tris(pyrrolidino)-phosphorane	[16,17]	*5.68*	80.75	-1.47	0	*6.82*[16]	*13.79*	*238*	423.4	368.1	483.6	9.1	2.65	417706-63-9
11	(8S,9R)-(—)-N-benzylcinchonidinium chloride	[27]	*5.65*	24.32	-1.74	1	15.19	29.18	264	385.5	394.2	486.3	15.7	-1.47	69257-04-1
12	Tetrahexylammonium	II	*5.65*	0.00	-0.75	0	*39.0*	*51.48*	*292*	354.7	500.3	557.4	6.9	7.42	16436-29-6

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
13	N,N',N''- tripropylguanidine	[32]	*5.59*	31.40	-2.01	0	10.63	19.73	240	186.3	269.4	271.4	4.8	1.25	1020178-63-5
14	((4-((4-nitrophenyl)azo)phenyl)imino)-triphenyl-phosphorane	[27]	*5.56*	65.61	-1.26	0	3.67	10.99	235	503.5	508.7	593.6	25.6	-0.32	33341-94-5
15	tris(pyrrolidino)[[4-(trifluoromethyl)-phenyl]imino]phosphorane	II	*5.55*	13.40	-1.45	0	*10.65* [38]	*20.2*[37]	*245.4*[39]	401.4	365.8	461.1	14.1	3.38	417706-59-3
16	((2,5-dichlorophenyl)imino)tris-(pyrrolidino)-phosphorane	II	*5.52*	14.11	-1.28	0	*6.42*	*18.5*[37]	*248.3*[39]	402.3	371.9	473.9	9.7	4.10	300363-70-6
17	triphenylguanidine	[32]	*4.96*	131.86	-1.36	0	*9.13*[16]	16.27	226	607.7	588.0	744.4	6.9	-12.00	603-53-2
18	tris(dimethylamino)(phenylimino)-phosphorane	II	*5.22*	28.83	-2.26	0	*9.1*[40]	18.15	242	288.4	326.1	363.6	5.0	-0.42	35589-04-9
19	1,4-bis(dihydroquinidine)anthraquinone	[27]	*5.18*	14.29	-1.98	0	*10.64*[40]	*21*[37]	*246.1*[39]	255.3	281.3	341.8	7.6	2.34	176298-44-5
20	tetrabutylammonium	II	*5.14*	67.77	-0.67	0	9.16	17.33	239	858.1	789.0	1023.5	10.0	-2.42	1923-70-2
21	lidocaine	[27]	*5.13*	0.00	-1.34	0	*39.10*	*51.67*	*290*	242.5	341.3	383.0	6.9	4.87	137-58-6
22	quinine	[27]	*5.12*	26.74	-2.57	0	*7.95*[40]	15.84	227	235.3	282.8	323.1	6.0	-2.17	130-95-0
23	triisobutylphosphatrane	[27]	*5.05*	37.88	-2.22	0	*8.72*[40]	17.58	232	325.4	325.6	410.8	5.4	-3.97	331465-71-5
24	spiroxamine	IV	*5.04*	10.41	-1.50	0	3.09	9.71	216	343.5	344.8	462.1	2.7	-0.06	118134-30-8
25	dibenzylamine	[27]	*5.04*	21.42	-1.57	0	6.84	14.79	220	298.5	354.2	417.0	1.8	0.33	103-49-1
26	verapamil	[27]	*5.00*	15.75	-3.22	0	*8.43*[40]	16.76	225	198.3	259.3	270.2	1.6	-3.85	52-53-9
27	L-phenylalanyl-L-phenylalanyl-L-phenylalanyl-L-phenylalanine	[16,27]	*5.00*	49.17	-1.21	0	*8.6*[40]	16.62	229	455.6	513.9	590.5	10.2	-2.80	2667-02-9
28	atenolol	[27]	*4.95*	78.29	-2.65	0	*9.48*[40]	*17.59*[40]	223	267.3	323.6	345.9	9.5	-7.65	29122-68-7
29	4-[2-(4-nitrophenyl)diazenyl]-N-(phenyldi-1-pyrrolidinylphos-phoranylidene) benzenamine	[27]	*4.94*	69.84	-1.17	0	6.12	13.58	238	489.5	483.5	573.0	27.8	1.75	2097489-41-1
30	tetrapropylammonium	[15,16], II	*4.92*	0.00	-2.03	0	*37.2*	*49.58*	*286*	186.4	262.2	292.8	6.9	3.39	5810-42-4
31	Sudan II	[32]	*4.92*	31.29	-2.06	0	0.20	6.40	220	277.3	313.3	338.3	1.9	-2.01	3118-97-6

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
32	N,N-diphenylbispidine	[41]	*4.88*	7.17	-2.14	0	*5.84*	*13.15*	*232*	279.4	303.4	358.6	5.3	1.26	531-91-9
33	phenyl tetramethylguanidine	II	*4.86*	11.56	-1.77	0	*11.77*[39]	*20.8*[37]	*240.4*[37]	192.3	239.5	263.3	6.0	0.66	2556-43-6
34	tributylamine	[27]	*4.83*	5.98	-1.87	0	*9.9*[38]	*18.39*	*231.3*[42]	186.4	279.5	294.7	0.9	2.17	102-82-9
35	buprofezin	[27], IV	*4.80*	20.62	-1.91	0	5.36	12.69	232	306.4	329.9	386.6	4.5	1.41	69327-76-0
36	pirimiphos-ethyl	[27]	*4.79*	43.30	-1.84	0	3.57	11.16	226	320.4	335.2	388.8	4.6	-0.84	23505-41-1
37	N-isopropylbenzylamine	[27]	*4.77*	15.21	-3.93	0	9.10	17.42	224	150.2	209.7	214.0	1.6	-3.22	102-97-6
38	bupirimate	[27]	*4.76*	73.41	-1.74	0	6.31	14.81	231	317.4	334.8	387.4	7.3	-1.97	58694-46-5
39	Sudan I	[32]	*4.69*	33.06	-2.58	0	0.20	6.51	217	249.3	279.6	297.0	1.4	-3.55	842-07-9
40	reserpine	[27]	*4.66*	92.84	-1.11	0	*9.97*[40]	17.42	232	609.7	578.3	708.1	7.3	-5.25	50-55-5
41	biquinoline	[27]	*4.66*	14.73	-2.26	0	*3.66*[40]	*11.28*[43]	233	257.3	287.6	308.2	0.0	0.58	119-91-5
42	hexyl-methylimidazolium	II	*4.66*	2.61	-1.45	0	30.9	47.00	*367*	167.3	242.1	245.1	6.9	1.10	382150-50-7
43	diphenylguanidine	II	*4.61*	42.39	-3.29	0	*10*[38]	*19.32*	*239*	212.3	252.8	268.7	3.8	-3.52	102-06-7
44	1-[2-(diphenylmethoxy)ethyl]-4-(3-phenylpropyl)piperazine	[27]	*4.61*	15.40	-1.40	0	7.81	16.13	228	415.6	474.3	552.1	0.8	-0.29	76778-22-8
45	fenpropimorph	[27]	*4.60*	12.75	-1.59	0	6.74	14.54	226	304.5	372.6	427.5	1.6	0.27	67564-91-4
46	tripropylamine	II	*4.56*	5.97	-2.60	0	*10.7*[38]	*18.2*[39]	*229.5*[39]	144.3	225.5	230.9	0.8	1.30	102-69-2
47	N,N-diethylnicotinamide	[27]	*4.46*	25.66	-3.35	0	4.11	13.07	*217.3*[42]	179.2	220.3	238.7	5.9	-5.98	59-26-7
48	quino[7,8-h]quinoline	[27]	*4.43*	11.06	-2.46	0	*12.00*[43]	*19.61*[43]	249	231.3	249.3	269.8	3.5	0.51	195-41-5
49	mepanipyrim	[27], IV	*4.36*	25.51	-2.63	0	2.96	10.12	223	224.3	279.5	284.8	3.0	-4.00	110235-47-7
50	cybutryne	[27]	*4.34*	42.44	-2.19	0	3.96	11.31	227	254.4	294.2	320.3	4.5	0.26	28159-98-0
51	Mianserin	[27]	*4.33*	8.54	-2.64	0	7.53	15.56	223	265.4	290.7	337.9	1.7	-3.50	24219-97-4
52	Acridine	[17,27], II	*4.28*	10.45	-3.30	0	*5.6*[44]	*13.83*	*224.8*[42]	180.2	213.3	222.4	3.4	-1.64	260-94-6

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
53	Thiabendazole	IV	*4.23*	30.90	-3.48	0	*4.64*[43]	*12.42*[43]	225	202.3	221.5	228.4	4.0	-3.99	148-79-8
54	Febantel	[27]	*4.20*	84.36	-1.61	0	-5.67	3.94	232	447.5	445.1	508.9	6.2	-0.62	58306-30-2
55	Diphenylamine	II	*4.18*	16.04	-4.17	0	*0.79*[38]	*6.0*[37]	*208*	170.2	214.7	224.0	1.5	-5.67	122-39-4
56	N-[3-(dimethylamino)propyl]-N',N''-dipropyl-guanidine	[32]	*4.12*	30.41	-1.61	0	13.88	23.46	247	229.4	321.7	334.0	5.4	1.36	1020178-65-7
57	3-methoxy-N,N-dimethylaniline	[41]	*4.11*	13.28	-3.88	0	*4.74*[40]	*11.21*[40]	*218*	152.2	201.8	206.4	1.3	-3.44	15799-79-8
58	Imazalil	[27]	*4.10*	18.12	-2.40	0	6.38	15.77	228	298.2	306.0	339.9	5.7	-3.28	35554-44-0
59	7,8-benzoquinoline	[27]	*4.10*	9.28	-3.56	0	*4.25*	*10.86*[43]	224	180.2	210.2	218.8	2.8	-2.74	230-27-3
60	Tetraethylammonium	[15,16], II	*4.08*	0.00	-3.62	0	*38.83*	*52.61*	*286*	130.3	184.8	203.5	6.7	1.33	66-40-0
61	centralite I	[32]	*4.07*	23.42	-2.21	1	-5.04	3.44	219	269.4	304.3	350.1	4.1	0.41	85-98-3
62	tetraphenylphosphonium	[27]	*4.01*	0.00	-1.75	0	32.91	45.34	292	339.4	360.3	426.4	10.5	2.65	18198-39-5
63	R(-)-propylnorapomorphine	[27]	*3.99*	42.95	-2.55	0	7.71	15.56	230	295.4	313.8	356.4	4.3	-4.65	18426-20-5
64	paclobutrazol	[27], IV	*3.97*	40.45	-2.43	0	1.04	9.27	213	294.8	308.6	369.5	4.3	-5.46	76738-62-0
65	quinoxyfen	[27]	*3.97*	15.40	-2.34	0	4.41	12.21	223	309.1	294.2	324.7	3.5	-2.59	124495-18-7
66	DBU	II	*3.96*	11.43	-3.20	0	*12.4*[45]	*24.3*[37]	*242.7*[37]	153.2	188.7	203.2	5.2	0.71	6674-22-2
67	epoxiconazole	[27], IV	*3.93*	33.46	-2.61	0	1.04	9.76	216	330.8	320.6	377.3	6.6	-5.96	135319-73-2
68	crimidine	[27]	*3.92*	17.57	-3.32	0	3.18	11.07	225	172.6	202.8	203.8	9.0	-1.03	535-89-7
69	1-naphthylamine	[15–17], II	*3.92*	28.68	-6.03	0	*3.92*[37]	*9.77*[37]	*209.2*[42]	144.2	182.1	185.0	2.4	-9.86	134-32-7
70	strychnine	[27]	*3.91*	28.39	-2.45	0	*8.26*[46]	17.54	223	335.4	306.2	384.2	6.9	-5.50	57-24-9
71	2,4,6-trimethylpyridine	II	*3.90*	10.20	-3.80	0	*7.45*[37]	*14.98*[37]	*229*	122.2	176.0	171.6	3.2	-0.82	108-75-8
72	tetramethylguanidine	II	*3.89*	23.60	-4.12	0	*13.6*[39]	*23.3*[39]	*238.4*[39]	115.2	165.4	165.8	4.3	-0.57	80-70-6
73	quinoline	[41]	*3.88*	10.71	-4.79	0	*4.93*[40]	*12.4* [47]	*220.2*[40]	130.2	166.3	164.5	3.3	-3.54	91-22-5

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
74	flusilazole	[27]	*3.88*	24.02	-2.55	0	2.01	10.72	220	302.4	311.0	357.8	4.4	-5.01	96827-34-8
75	4-dimethylamino-N,N-dimethylaniline	[41]	*3.87*	7.33	-3.31	0	7.11	14.79	227	165.3	220.6	231.5	0.0	-2.10	100-22-1
76	triethylamine	[15,16], II	*3.86*	6.09	-4.48	0	*10.7*[37]	*18.8*[37]	*227*[37]	102.2	165.6	164.3	0.9	-0.43	121-44-8
77	4-pyridinepropionic acid	[27]	*3.86*	45.46	-4.62	0	6.23	15.03	218	152.2	190.1	188.8	3.2	-8.25	6318-43-0
78	Gly-Gly-Gly-Phe-Phe-NH_2	[27]	*3.85*	172.56	-1.85	0	5.53	14.41	208	499.5	498.1	597.8	8.5	-20.57	2108020-29-5
79	2,2-bipyridine	[32]	*3.84*	14.95	-3.71	0	*4.49*[40]	*12.26*[43]	*223.1*[48]	157.2	193.6	194.3	0.0	-1.69	366-18-7
80	N,N'-bis[3-(dimethylamino)propyl]-N''-propyl-guanidine	[32]	*3.83*	32.97	-1.36	0	13.39	22.82	246	272.5	372.6	395.4	4.9	0.92	1020178-64-6
81	2-aminobenzimidazole	[41]	*3.83*	48.82	-6.20	0	*7.54*[40]	*16.08*[40]	*230*	134.2	166.9	161.2	3.5	-8.29	934-32-7
82	diphenyl phthalate	[15,16], II	*3.79*	38.86	-2.01	1	*-11.90*	*-3.84*	*214*	319.3	334.1	370.5	7.8	0.71	84-62-8
83	glycyl-L-prolylglycylglycine	[27]	*3.79*	122.91	-3.00	0	7.14	17.38	221	287.3	312.2	328.9	7.2	-15.98	13054-03-0
84	pyrimethanil	[27]	*3.78*	25.49	-3.04	0	3.77	11.00	223	200.3	246.7	253.5	2.9	-3.68	53112-28-0
85	ethoxyquin	[27]	*3.76*	22.41	-2.57	0	3.37	10.55	221	218.3	266.7	289.4	2.4	-2.33	91-53-2
86	Ac-Gly-Lys-OMe	[16,27]	*3.73*	101.58	-2.69	0	*10.5*[49]	*18.80*	214	260.3	315.3	329.6	7.8	-14.50	10236-44-9
87	N,N-dimethylaniline	[15–17], II	*3.72*	6.46	-4.83	0	*5.1*[39]	*11.4*[37]	*217.3*[39]	122.2	172.9	173.7	3.1	-3.55	121-69-7
88	8-aminoquinaldine	[41]	*3.71*	33.38	-3.97	0	*10.28*	*11.54*[43]	237	159.2	196.4	198.9	5.9	-3.30	18978-78-4
89	propamocarb	[27]	*3.71*	31.14	-2.64	0	9.17	18.47	236	189.3	242.0	256.9	2.6	-0.09	24579-73-5
90	carbendazim	[27], IV	*3.70*	52.82	-4.00	0	*4.53*[43]	*12.24*[43]	222	192.2	219.1	218.6	4.6	-5.64	10605-21-7
91	sebuthylazine	[27]	*3.70*	45.79	-2.57	0	1.25	8.50	215	230.7	270.6	279.7	6.9	-2.63	7286-69-3
92	tetraconazole	[27]	*3.70*	29.33	-2.63	0	1.68	10.77	215	373.2	333.6	383.3	6.7	-7.63	112281-77-3
93	ethyl-methylimidazolium	II	*3.68*	1.20	-4.42	0	*35.16*	*46.96*	*274*	111.2	162.2	155.8	6.9	-1.00	145022-44-2
94	triphenylamine	II	*3.67*	5.63	-2.57	0	-6.4	*1.28*[50]	*209.5*[42]	246.3	283.4	320.1	0.1	-0.71	603-34-9

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
95	Sudan III	[32]	*3.66*	46.24	-1.65	0	0.43	7.03	229	353.4	385.2	415.2	1.8	-0.43	85-86-9
96	2-pyridinepropionic acid	[27]	*3.65*	45.05	-4.59	0	5.45	13.82	217	152.2	190.3	188.3	3.9	-7.67	15197-75-8
97	guanfacine	[27]	*3.65*	68.73	-3.86	0	9.35	18.93	226	247.1	249.0	264.8	2.3	-9.13	29110-47-2
98	simazine	[27]	*3.65*	46.28	-3.19	0	*1.65*[40]	8.09	214	202.7	237.3	236.4	7.4	-3.71	122-34-9
99	4-fluoro-3-nitroaniline	II	*3.65*	68.54	-7.01	0	*2.4*[37]	*7.7*[37]	*189*	157.1	171.4	167.4	9.3	-14.24	364-76-1
100	ampicillin	[27]	*3.63*	101.25	-2.85	0	*2.55*[40]	13.46	219	350.4	334.7	408.0	6.4	-13.10	69-53-4
101	1,3-bis(phenylmethyl) 2-(ethoxymethylene)propanedioate	[27]	*3.63*	42.95	-1.81	1	-4.45	4.89	227	341.4	376.2	413.1	9.6	1.69	56606-21-4
102	vamidothion	III, IV	*3.62*	51.71	-2.25	1	-1.02	9.58	234	288.3	289.8	327.8	2.4	-0.28	2275-23-2
103	atrazine	[27]	*3.61*	45.84	-2.85	0	*1.68*[40]	8.21	214	216.7	254.7	259.4	6.7	-3.02	1912-24-9
104	scopolamine	[27]	*3.61*	53.45	-2.59	0	*7.75*[40]	17.22	224	304.4	312.5	362.2	4.3	-5.08	51-34-3
105	4-methylaniline	[27]	*3.60*	29.54	-6.85	0	*5.08*[46]	11.08	*206.70*[42]	108.2	156.9	149.8	1.9	-9.69	106-49-0
106	acetylcholine	[27]	*3.59*	20.81	-3.97	0	33.85	49.54	275	146.2	199.8	203.5	7.9	-3.03	51-84-3
107	danofloxacin	[27]	*3.59*	51.20	-1.83	0	3.23	14.54	244	358.4	344.8	401.9	15.3	-1.38	112398-08-0
108	propiconazole	[27]	*3.53*	36.42	-2.08	0	1.30	10.30	217	343.2	334.7	386.5	5.7	-4.66	60207-90-1
109	myclobutanil	[27], IV	*3.53*	38.10	-2.44	0	0.62	9.51	215	289.8	314.2	358.4	8.3	-7.04	88671-89-0
110	tetraethylthiuram disulfide	[27]	*3.52*	2.67	-1.78	0	-11.02	-5.22	211	297.6	304.6	363.7	1.9	2.83	97-77-8
111	Sudan IV	[32]	*3.52*	43.73	-1.45	0	0.55	7.10	230	381.5	414.7	456.6	2.1	0.51	85-83-6
112	heptylamine	[27]	*3.51*	29.82	-3.78	0	*10.67*[46]	*18.35*[40]	*212.5*[42]	116.2	194.5	186.8	1.9	-7.52	111-68-2
113	2,6-dimethylpyridine	[17], II	*3.50*	10.14	-4.60	0	*6.7*[37]	*14.1*[37]	*222.5*[42]	108.2	157.4	150.0	2.4	-1.83	108-48-5
114	methiocarb	[27], II	*3.49*	36.44	-3.19	0	*-8.78*	*-0.75*	*194*	226.3	263.2	279.1	5.8	-7.47	2032-65-7
115	4-amino-N,N-dimethylaniline	[41]	*3.49*	31.18	-4.86	0	6.65	14.88	*221.9*[42]	137.2	186.8	189.5	2.2	-4.59	99-98-9

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
116	pyridoxine	[27]	*3.49*	62.21	-4.41	0	*4.98*[40]	15.01	230	170.2	195.5	198.3	7.5	-7.44	65-23-6
117	3-aminobenzoic acid	[41]	*3.47*	63.26	-6.89	0	*3.09*[40]	11.16	*198.9*[42]	138.1	*169.3*[51]	163.5	7.2	-14.85	99-05-8
118	benzamidine	[27]	*3.47*	47.19	-6.21	0	11.18	20.91	231	121.2	162.1	157.1	4.3	-6.51	618-39-3
119	2-methylaniline	[27]	*3.46*	28.39	-6.99	0	*4.44*[46]	9.91	*205.30*[4]$_2$	108.2	154.4	149.7	2.6	-9.20	95-53-4
120	4-methoxypyridine	[27]	*3.45*	17.96	-5.51	0	*6.62*[40]	*14.23*[40]	*222.20*[4]$_2$	110.1	147.5	139.4	4.8	-4.41	620-08-6
121	thiacloprid	IV	*3.45*	32.55	-3.08	0	-1.01	6.40	204	253.7	264.0	284.2	9.8	-7.80	111988-49-9
122	benzylamine	II	*3.43*	29.89	-7.05	0	*9.3*[37]	*16.9*[37]	*210.2*[42]	108.2	157.1	151.1	2.1	-9.30	100-46-9
123	2-aminophenol	[41]	*3.41*	47.59	-8.61	0	*4.7*[40]	11.13	*207.2*[42]	110.1	*146.3*[51]	137.8	1.8	-11.97	95-55-6
124	thiamine	[27]	*3.40*	56.89	-2.53	0	16.26	30.81	262	265.4	287.9	314.4	14.6	-5.32	70-16-6
125	benalaxyl	[27]	*3.38*	31.34	-1.95	1	-6.53	2.82	224	326.4	331.6	410.3	6.9	1.96	71626-11-4
126	9(10H)acridanone	[27]	*3.34*	30.62	-3.94	0	-15.34	-8.48	186	196.2	220.2	231.3	8.6	-8.20	578-95-0
127	azoxystrobin	[27]	*3.34*	86.36	-1.70	0	-1.15	7.27	227	404.4	409.3	460.9	9.4	-5.06	131860-33-8
128	piperidine	[15,16], II	*3.34*	17.11	-6.44	0	*11.1*[39]	*19.3*[39]	*220*[39]	86.2	131.4	125.6	1.8	-5.10	110-89-4
129	phthalazine	[27]	*3.30*	23.35	-5.13	0	*3.47*[40]	*11.55*[43]	223	131.2	161.9	160.8	7.9	-4.86	253-52-1
130	isoproturon	[27]	*3.29*	29.94	-2.87	0	-2.50	5.72	206	207.3	265.0	280.2	6.3	-1.95	34123-59-6
131	benzimidazole	[27]	*3.29*	24.03	-6.39	0	*5.56*[40]	*14.3*[40]	*220.0*[42]	119.1	151.8	145.9	5.2	-6.90	51-17-2
132	chlormequat	[27]	*3.29*	0.00	-5.24	0	34.08	48.83	273	122.6	163.3	166.5	6.7	-2.93	999-81-5
133	3-nitroaniline	[17], II	*3.29*	68.68	-6.98	0	*2.5*[37]	*7.7*[37]	*193.9*[51]	139.1	165.8	159.5	8.2	-13.44	99-09-2
134	aniline	[17], II	*3.27*	29.52	-8.71	0	*4.6*[39]	*10.6*[37]	*203.3*[42]	94.1	138.0	128.1	2.4	-10.42	62-53-3
135	2-aminopyridine	[41]	*3.25*	35.54	-7.38	0	*6.71*[52]	*14.7*[53]	*218.8*[42]	95.1	133.0	122.5	3.0	-6.44	504-29-0
136	metribuzin	[27]	*3.25*	60.98	-3.34	0	0.18	8.58	218	215.3	236.6	255.8	3.4	-3.94	21087-64-9

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
137	benzyl ethylethoxymethylenemalonate	[32]	*3.24*	43.07	-2.10	1	-3.33	5.95	226	279.3	322.5	343.4	5.2	1.57	1884453-39-7
138	hexylamine	[27]	*3.24*	29.82	-4.48	0	*10.64*[40]	*18.34*[40]	*213.60*[42]	102.2	174.6	164.8	1.9	-7.83	111-26-2
139	sulfamethoxazole	[27]	*3.23*	99.06	-3.86	0	-1.44	5.01	190	254.3	257.8	276.5	9.1	-15.89	723-46-6
140	1,10-phenantroline	[27], III	*3.23*	16.23	-3.38	0	*4.86*[54]	*13.68*[43]	*>217*[43]	181.2	207.2	216.0	5.5	-1.69	66-71-7
141	2-chloroaniline	[27,32]	*3.20*	28.59	-6.96	0	*2.62*[40]	*7.86*[40]	199	128.6	154.6	149.6	2.7	-9.82	95-51-2
142	metamitron	[27]	*3.20*	61.23	-4.26	0	1.36	10.50	219	203.2	226.6	235.5	5.3	-6.23	41394-05-2
143	sulphanilamide	[27], II	*3.19*	98.80	-6.31	0	*2.1*[38]	*6.69*	193.8	173.2	190.1	190.7	7.7	-15.75	63-74-1
144	pyridoxamine	[27]	*3.17*	67.55	-4.12	0	*8.08*[40]	16.45	231	169.2	199.4	204.3	6.1	-6.71	85-87-0
145	methomyl	II, IV	*3.17*	46.67	-4.38	0	*-7.00*	*1.10*	222.2	163.2	200.2	197.5	5.0	-8.03	16752-77-5
146	leucine	[31]	*3.15*	61.78	-5.75	0	*2.34*[40]	13.48	*210.5*[42]	132.2	177.4	179.6	8.2	-11.47	61-90-5
147	tetracycline	[27]	*3.15*	140.42	-2.13	0	10.66	20.88	241	445.4	382.9	479.7	11.1	-6.03	64-75-5
148	5-nitrobenzimidazole	[27]	*3.14*	63.10	-5.73	0	*3.48*[40]	*10.39*[40]	209	164.1	178.7	176.3	11.5	-10.06	94-52-0
149	trifloxystrobin	[27]	*3.14*	46.52	-1.56	0	-1.68	5.97	225	409.4	398.4	470.3	5.3	1.23	141517-21-7
150	cyromazine	[27]	*3.13*	97.51	-4.78	0	14.23	25.61	245	170.2	196.9	209.7	11.2	-11.08	66215-27-8
151	4-aminopyridine	[27]	*3.11*	35.46	-7.23	0	*9.17*[40]	*18.40*[40]	*226.50*[42]	95.1	132.6	121.9	6.3	-5.86	504-24-5
152	3-aminopyridine	[32]	*3.09*	35.37	-7.08	0	*6.09*[40]	*14.17*[40]	*220.5*[42]	95.1	132.8	122.2	4.9	-6.13	462-08-8
153	4-chloroaniline	[27]	*3.07*	29.52	-7.20	0	*4.15*[40]	*9.89*[40]	*201.20*[42]	128.6	157.7	151.2	5.0	-11.25	106-47-8
154	phenylalanine	[31]	*3.05*	60.23	-5.67	0	*2.2*[40]	13.21	*212.5*[42]	166.2	200.6	207.1	7.8	-11.60	63-91-2
155	histidine	[31]	*3.04*	78.18	-7.77	0	*1.77*[40]	16.07	*227.1*[42]	142.1	164.4	159.5	13.8	-12.86	71-00-1
156	indazole	[27]	*3.04*	28.90	-6.41	0	*1.25*[43]	*7.61*[43]	*207.7*[42]	119.1	151.3	145.7	2.6	-7.68	271-44-3

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
157	arginine	[31]	*3.03*	117.56	-5.35	0	*1.82*[46]	12.70	*240.58*[42]	175.2	220.3	220.0	12.7	-18.91	74-79-3
158	triazophos	[27]	*3.03*	46.90	-2.23	0	-2.25	5.08	217	314.3	328.7	354.9	2.4	-3.43	24017-47-8
159	4-aminobenzoic acid	[17]	*3.02*	64.39	-7.40	0	*2.42*[40]	3.42	*198.9*[42]	138.1	169.1	163.8	6.7	-15.47	150-13-0
160	quinazoline	[27]	*3.02*	18.20	-5.38	0	*3.51*[40]	*9.19*[43]	215	131.2	162.1	158.4	4.7	-6.05	253-82-7
161	2-methylpyridine	II	*3.02*	10.56	-5.69	0	*5.94*[37]	*13*[37]	*219.2*[42]	94.1	137.9	128.3	2.8	-3.54	109-06-8
162	N-methylpiperidine	II	*3.01*	6.92	-4.92	0	*10.1*[39]	*18.25*[39]	*224.7*[42]	100.2	148.9	148.2	0.9	-2.01	626-67-5
163	dimethyl phthalate	[15,16], II, III	*3.01*	36.76	-3.03	1	*0.58*	*10.36*	*206.2*[51]	195.2	219.9	223.2	9.4	0.87	131-11-3
164	4-phenylazophenol	[27]	*2.99*	38.09	-3.30	0	2.39	9.28	223	199.2	239.0	242.1	2.7	-5.36	1689-82-3
165	pyridine	[15–17], II	*2.99*	10.93	-7.51	0	*5.3*[39]	*12.5*[37]	*214.7*[39]	80.1	118.8	106.7	3.3	-5.42	110-86-1
166	pyrrolidine	[15,16], II	*2.99*	17.73	-7.79	0	*11.3*[37]	*19.6*[37]	*218.8*[37]	72.1	117.6	106.3	1.6	-5.86	123-75-1
167	3-hydroxypyridine	[41]	*2.97*	30.57	-7.69	0	*8.6*[40]	14.77	*214.6*[42]	96.1	128.7	117.6	2.0	-8.98	109-00-2
168	pyridate	[27]	*2.95*	42.08	-1.39	0	-2.19	5.36	220	379.9	413.1	466.3	8.2	-0.44	55512-33-9
169	pyrazophos	[27]	*2.94*	63.37	-1.67	0	-0.90	6.67	218	374.4	389.1	424.3	3.7	-2.83	13457-18-6
170	dopamine	[27]	*2.93*	67.70	-6.11	0	*9.05*[40]	18.95	213	154.2	194.6	193.4	3.9	-13.81	51-61-6
171	2-aminobenzoic acid	[41]	*2.93*	57.46	-6.59	0	*2.12*[40]	7.80	*207.7*[42]	138.1	165.3	161.1	1.9	-10.60	118-92-3
172	6-aminocaproic acid	[27]	*2.90*	64.46	-5.05	0	10.05	19.28	210	132.2	187.9	179.9	1.6	-12.19	60-32-2
173	ditalimfos	[27]	*2.89*	61.56	-2.35	1	-9.93	-0.67	218	284.2	288.9	316.5	8.8	0.49	5131-24-8
174	1,3-diethyl-2-[[(2-carboxyethyl)amino]-methylene]propanedioate	[31]	*2.89*	78.14	-2.57	1	-2.84	6.13	217	260.3	293.2	305.7	3.5	-4.63	303120-73-2
175	adenine	[27]	*2.88*	63.81	-6.77	0	*4.22*[40]	13.20	*218.10*[42]	136.1	155.9	148.8	3.6	-10.72	73-24-5
176	acetamiprid	[27], IV	*2.86*	32.14	-3.10	0	-0.53	7.02	206	223.7	251.9	267.7	9.4	-7.60	135410-20-7

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
177	indoxacarb	[27]	*2.84*	73.10	-1.54	1	-8.05	0.82	216	528.8	446.2	535.6	6.2	-0.19	173584-44-6
178	bitertanol	[27]	*2.83*	46.73	-2.08	0	0.81	9.16	213	338.4	367.3	429.4	5.2	-6.16	55179-31-2
179	nicotinamide	[27]	*2.81*	49.00	-6.68	0	*3.40*[40]	*10.93*[40]	*211.90*[42]	123.1	154.1	147.1	2.9	-9.74	98-92-0
180	2-(2,2-di(ethoxycarbonyl)vinylamino)-acetic acid	[31]	*2.80*	84.35	-3.15	1	-12.03	-3.66	201	246.2	277.4	277.3	2.6	-8.38	54132-81-9
181	benzalazine	[27]	*2.79*	19.18	-2.85	0	1.60	8.94	223	209.3	264.9	268.4	0.0	-2.41	588-68-1
182	glycyl-glycyl-L-α-aspartyl-L-Alanine	[27]	*2.78*	163.47	-3.06	0	7.25	17.52	224	319.3	335.8	365.0	7.2	-18.16	103972-83-4
183	4-aminophenol	[27]	*2.77*	49.34	-8.81	0	*5.50*[40]	12.46	206	110.1	147.2	138.7	2.9	-13.52	123-30-8
184	benzanilide	[27]	*2.76*	28.91	-3.61	0	-12.12	-5.29	197	198.2	239.5	250.5	5.5	-6.00	93-98-1
185	isoleucine	[31]	*2.75*	59.79	-5.85	0	*2.32*[46]	14.08	*211.2*[42]	132.2	173.9	178.1	8.0	-10.65	73-32-5
186	4-nitroaniline	[17], II	*2.72*	68.69	-6.90	0	*1.00*[38]	*6.2*[37]	*199.4*[42]	139.1	166.1	159.7	12.5	-13.48	100-01-6
187	3-aminophenol	[41]	*2.71*	49.29	-8.71	0	*4.25*[40]	10.52	*207.2*[42]	110.1	147.5	139.1	1.6	-13.88	591-27-5
188	methionine	[31]	*2.70*	59.32	-5.68	0	*2.13*[40]	13.90	*215.5*[42]	150.2	181.0	183.6	9.5	-9.83	59-51-8
189	valine	[31]	*2.70*	60.98	-7.18	0	*2.32*[55]	14.31	*209.5*[42]	118.2	157.9	157.3	8.0	-2.80	72-18-4
190	3-dimethylaminobenzoic acid	[41]	*2.69*	39.18	-4.32	0	1.78	9.39	206	166.2	204.0	209.3	7.7	-9.16	99-64-9
191	4-nitroimidazole	[27]	*2.69*	60.76	-10.78	0	-4.48	3.41	191	113.1	131.0	118.2	3.3	-10.97	3034-38-6
192	chloridazon	[27]	*2.68*	50.52	-3.65	1	-3.96	4.42	215	222.7	231.4	243.0	7.8	-5.34	1698-60-8
193	D-homocysteinethiolactone	[27]	*2.68*	43.31	-7.86	0	5.51	14.29	205	118.2	143.2	137.9	4.3	-11.21	130548-06-0
194	phenylalanine Fmoc	[27], IV	*2.67*	68.87	-2.17	0	-7.64	0.23	212	388.4	401.1	466.6	5.2	-5.77	35661-40-6
195	diethylamine	II	*2.66*	16.78	-7.02	0	*10.7*[38]	*18.8*[37]	*219.7*[42]	74.1	129.8	120.7	1.5	-5.10	109-89-7
196	aldicarb	II, IV	*2.66*	44.48	-2.55	1	-5.74	2.45	207	191.3	229.1	239.0	7.3	-4.24	116-06-3

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
197	fenhexamid	[27], IV	*2.65*	47.07	-2.35	1	-4.74	1.03	202	303.2	293.6	345.8	1.5	-9.81	126833-17-8
198	vinclozolin	[27]	*2.65*	41.79	-2.73	1	-13.49	-7.47	188	287.1	277.8	305.9	3.6	-7.46	50471-44-8
199	butylamine	[27]	*2.65*	29.81	-6.85	0	*10.77*[46]	19.96	*211.9*[42]	74.1	134.9	121.1	1.9	-8.48	109-73-9
200	L-homocysteinethiolactone	[27]	*2.65*	43.24	-7.93	0	5.47	14.26	205	118.2	142.9	137.5	4.3	-11.24	31828-68-9
201	ethoprophos	[27]	*2.64*	30.36	-2.09	1	-8.71	-1.65	209	243.3	281.3	303.4	0.4	-0.98	13194-48-4
202	tris(hydroxymethyl)aminomethane	[41]	*2.63*	82.13	-7.38	0	*8.07*[56]	18.3	217	122.1	152.8	150.8	5.2	-10.26	77-86-1
203	pyridoxal	[27]	*2.63*	57.25	-4.67	0	3.07	11.87	218	168.2	190.6	193.0	4.7	-6.61	65-22-5
204	proline	[31]	*2.63*	49.45	-7.14	0	*1.952*[46]	12.60	*211.8*[42]	116.1	148.1	143.0	3.4	-10.10	147-85-3
205	2-nitroimidazole	[27]	*2.63*	64.17	-9.48	0	-2.69	5.76	199	114.1	132.4	119.7	8.6	-9.94	527-73-1
206	tryptophan	[31]	*2.62*	74.82	-5.63	0	*2.38*[57]	13.66	*219*[42]	191.2	216.3	227.6	7.3	-14.29	73-22-3
207	hexythiazox	[27], IV	*2.60*	36.47	-1.71	1	-8.58	-1.12	207	352.9	354.8	401.4	2.7	0.02	78587-05-0
208	lysine	[31]	*2.58*	87.92	-5.09	0	*2.16*[46]	13.44	*227.3*[42]	147.2	198.1	195.2	8.4	-13.98	56-87-1
209	Gly-bAla-bAla	[27]	*2.57*	113.59	-3.94	0	9.14	18.76	207	218.2	263.6	261.7	5.7	-18.62	78677-27-7
210	fluquinconazole	[27], IV	*2.56*	42.51	-2.35	0	-1.48	6.52	207	377.2	333.7	386.7	2.3	-7.92	136426-54-5
211	boscalid	[27]	*2.55*	31.20	-2.26	0	-1.56	6.01	208	344.2	339.3	383.1	3.5	-5.65	188425-85-6
212	pentylamine	[27]	*2.55*	29.82	-5.46	0	*10.63*[46]	19.93	*212.6*[42]	88.2	154.8	143.0	1.9	-8.14	110-58-7
213	thiophanate-methyl	[27]	*2.52*	73.13	-2.25	0	-6.14	2.76	229	343.4	336.4	375.7	14.8	-2.95	23564-05-8
214	tyrosine	[27]	*2.51*	80.16	-5.73	0	*2.20*[46]	13.63	215	182.2	210.4	220.4	8.8	-14.51	60-18-4
215	validamycin A	[27]	*2.50*	228.66	-2.18	0	3.61	13.62	233	498.5	441.2	556.9	10.9	-19.36	37248-47-8
216	cytosine	[27]	*2.50*	61.52	-8.38	0	*4.45*[57]	15.45	*219.00*[42]	112.1	138.2	127.3	9.9	-10.88	71-30-7
217	benzophenone	II, III	*2.48*	17.39	-3.29	1	*-6.18*	*0.69*	*203.8*[42]	183.2	220.9	230.7	4.9	-3.10	119-61-9

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
218	methiocarb-sulfoxide	[27]	*2.48*	52.78	-2.73	1	-2.03	7.26	222	242.3	270.0	287.9	6.4	-5.83	2635-10-1
219	dimethyl glutarate	[27], II, III	*2.47*	35.86	-3.65	1	*-0.41*	*10.69*	*207.3*[51]	161.2	198.8	196.4	10.7	0.02	1119-40-0
220	diphenylhydantoin	[27]	*2.44*	56.13	-3.75	1	-14.32	-6.58	192	253.3	262.1	294.7	3.9	-9.19	57-41-0
221	demeton-S-methyl sulfoxide	[27]	*2.44*	46.38	-2.88	1	-2.88	7.55	226	247.3	250.9	276.1	6.2	-2.16	919-86-8
222	benzamide	II, III	*2.42*	41.92	-6.41	0	*-3.56*	*3.8*[44]	*205.8*[42]	122.1	158.1	152.5	5.6	-8.02	55-21-0
223	penicillin G	[27]	*2.41*	73.25	-2.57	1	-8.37	1.16	211	335.4	333.5	389.0	6.8	-6.97	69-57-8
224	glyceryl tributyrate	[27], III	*2.40*	54.81	-1.68	1	-16.84	-8.30	208	303.4	356.7	387.9	3.1	1.08	60-01-5
225	mecarbam	[27]	*2.39*	49.07	-1.98	1	-7.98	-0.08	213	330.4	340.4	374.3	11.4	0.30	2595-54-2
226	glutamic acid	[31]	*2.39*	89.51	-6.96	0	*2.13*[46]	14.86	*210.1*[42]	148.1	172.4	169.9	10.4	-12.86	56-86-0
227	parathion	[27], IV	*2.37*	66.20	-2.30	1	-11.45	-5.31	200	292.3	302.0	321.7	9.9	-4.66	56-38-2
228	imidacloprid	[27], IV	*2.36*	71.21	-3.15	0	-0.57	7.02	205	256.7	261.4	274.7	9.5	-7.64	138261-41-3
229	aclonifen	[27]	*2.36*	68.77	-3.43	0	-6.51	0.58	198	265.7	266.0	283.9	6.6	-6.92	74070-46-5
230	threonine	[31]	*2.35*	79.90	-8.84	0	*2.09*[46]	12.36	*212.4*[42]	120.1	149.0	146.3	6.2	-13.40	72-19-5
231	4-chloro-2-nitroaniline	II	*2.32*	63.30	-5.97	0	*-1.0*[40]	*3.8*[37]	190.5	173.6	180.5	178.5	7.9	-10.47	121-87-9
232	oxamyl	[27], IV	*2.31*	59.18	-2.83	0	-5.49	3.62	218	220.3	249.4	262.5	9.1	-3.14	23135-22-0
233	glutamine	[31]	*2.31*	93.55	-6.42	0	*2.17*[46]	18.00	*215*[42]	147.2	176.3	174.0	10.2	-10.98	184161-19-1
234	tebufenozide	[27]	*2.27*	35.74	-1.45	1	-7.66	1.17	224	353.5	393.4	461.2	9.9	2.85	112410-23-8
235	(S)-3-anilino-5-methyl-5-phenylimida-zolidine-2,4-dione	[27]	*2.26*	57.03	-2.98	0	-9.12	-1.37	205	282.3	297.3	336.3	4.6	-7.66	332855-88-6
236	2-nitroaniline	[17], II	*2.26*	63.29	-6.73	0	*-0.26*[46]	*4.8*[37]	*193.5*[51]	139.1	161.4	156.3	7.6	-9.93	88-74-4
237	GlyFmoc	[32]	*2.25*	69.04	-3.18	1	-8.49	-2.18	188	298.3	313.6	346.8	3.9	-16.08	29022-11-5
238	phthalic acid	[27]	*2.22*	70.02	-5.52	1	-7.62	-0.95	199	167.1	182.3	184.8	7.6	-14.98	88-99-3

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
239	tolylfluanid	[27]	*2.22*	41.26	-2.37	0	-9.58	-2.31	204	348.3	300.3	363.5	7.4	-1.22	731-27-1
240	dazomet	[27]	*2.22*	8.04	-5.34	0	1.53	9.89	206	163.3	186.0	194.1	10.6	-9.05	533-74-4
241	aspartic acid	[31]	*2.21*	93.36	-9.26	0	*1.99*[40]	11.26	*209*[42]	134.1	155.5	149.2	7.2	-15.92	56-84-8
242	metanephrine	[31]	*2.20*	59.76	-3.92	0	8.81	18.05	223	198.2	234.5	249.3	3.9	-8.04	5090-31-3
243	pyridazine	[27]	*2.20*	23.36	-8.88	0	*2.33*[40]	*10.07*[43]	*209.60*[42]	81.1	115.3	102.3	6.1	-6.83	289-80-5
244	linuron	[27]	*2.20*	33.28	-2.91	1	-6.93	0.19	201	250.1	256.8	267.2	9.3	-3.87	330-55-2
245	propoxur	[27]	*2.19*	34.27	-2.68	1	-6.95	1.71	216	210.3	249.4	261.9	5.6	0.12	114-26-1
246	hypoxanthine	[27]	*2.18*	57.73	-7.69	0	1.26	11.21	*210.4*[42]	137.1	151.8	143.7	7.8	-12.33	68-94-0
247	α-alanine	[27]	*2.17*	61.13	-10.47	0	*9.87* [58]	14.56	208	90.1	125.2	113.0	8.1	-13.03	56-41-7
248	dichlofluanid	[27]	*2.17*	42.65	-2.74	0	-6.22	1.12	204	334.2	283.2	344.8	7.6	-3.95	1085-98-9
249	triasulfuron	[27]	*2.17*	95.29	-1.92	0	-0.78	8.66	233	402.8	371.3	420.1	11.6	-2.75	82097-50-5
250	β-alanine	[27]	*2.15*	60.35	-10.26	0	*10.24*[58]	19.93	217	90.1	125.1	112.2	3.7	-11.98	107-95-9
251	tetramethylammonium	II	*2.15*	0.00	-6.13	0	*34.91*	*51.07*	279.5	74.1	127.6	122.7	7.3	-1.62	75-57-0
252	terephthalic acid	[27]	*2.15*	71.16	-5.46	1	-8.92	-3.95	183	167.1	186.5	184.8	0.0	-18.73	100-21-0
253	serine	[31]	*2.14*	80.91	-10.78	0	*2.21*[57]	13.61	*210.5*[42]	106.1	134.8	124.7	6.2	-15.40	56-45-1
254	anthraquinone	[32]	*2.13*	40.53	-4.31	1	*-8.2*[59]	-7.86	180	211.2	230.4	244.4	0.0	-18.74	84-65-1
255	dimethyl succinate	[27], II, III	*2.12*	37.32	-4.39	1	*-1.93*	*8.91*	*205.5*[51]	147.1	182.4	174.8	2.5	-1.13	106-65-0
256	asparagine	[31]	*2.12*	96.58	-8.46	0	*2.17*[46]	15.94	*213.1*[42]	133.1	159.3	152.7	9.2	-13.66	70-47-3
257	quinoxaline	[27]	*2.11*	17.99	-5.26	0	*0.60*[60]	*7.4*[43]	*208.8*[42]	131.2	162.4	160.0	0.9	-5.57	91-19-0
258	diethyl (ethoxymethylene)malonate	[32]	*2.10*	42.96	-2.50	1	-3.11	6.49	223	217.2	261.2	266.8	4.9	1.86	87-13-8
259	caffeine	[27]	*2.10*	40.68	-3.83	0	*0.60*[61]	*7.51*[43]	209	195.2	210.6	221.2	5.5	-6.70	58-08-2

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
260	clofentezine	[27]	*2.07*	37.99	-2.39	0	-5.86	0.99	215	304.2	291.5	319.0	0.6	-1.53	74115-24-5
261	tri-allate	[27]	*2.06*	17.78	-2.16	0	-8.33	-1.80	205	305.7	293.8	348.3	5.4	-0.22	2303-17-5
262	drazoxolon	[27]	*2.04*	55.08	-3.19	0	-4.68	2.75	211	238.7	244.7	256.9	10.0	-3.80	5707-69-7
263	cyanophenphos	[27]	*2.04*	33.24	-2.13	0	-12.50	-6.14	200	304.3	326.1	359.7	8.5	-3.96	13067-93-1
264	alachlor	[27]	*2.00*	20.34	-2.25	1	-8.02	0.01	212	270.8	291.1	341.7	7.6	0.28	15972-60-8
265	pymetrozin	[27], IV	*1.97*	58.53	-3.28	0	4.44	13.18	221	218.2	249.2	255.4	5.7	-7.50	123312-89-0
266	phenylbenzoate	II, III	*1.97*	25.22	-3.40	1	*-8.89*	*-2.22*	*199.6*[51]	199.2	229.2	244.2	6.5	-4.67	93-99-2
267	guanidine	II	*1.95*	74.00	-13.89	0	*13.6*[39]	*24.97*	*226.9*[39]	60.1	97.3	79.2	4.6	-9.42	50-01-1
268	thiamethoxam	III	*1.92*	70.41	-3.06	0	-4.60	4.90	203	292.7	271.2	307.2	11.1	-5.81	153719-23-4
269	Gly-Gly-Gly-NH_2	[27]	*1.91*	123.13	-4.72	0	4.71	15.30	221	205.2	236.5	231.6	12.2	-15.40	556-33-2
270	azelaic acid	[27]	*1.91*	73.43	-3.34	1	-9.23	-3.20	184	189.2	246.4	246.4	4.5	-15.40	123-99-9
271	dimethylmaleate	[27], III	*1.89*	39.13	-4.37	1	-6.93	2.26	211	147.1	182.6	174.8	1.9	-1.11	624-48-6
272	phenthoate	[27]	*1.88*	35.74	-2.03	1	-12.16	-5.23	212	321.4	320.9	366.3	8.4	1.16	2597-03-7
273	aldicarb-sulfone	[27]	*1.86*	80.51	-3.52	1	-8.59	-1.20	209	223.3	244.8	259.5	5.7	-11.56	1646-88-4
274	methiocarb-sulfone	[27]	*1.84*	66.65	-2.95	1	-7.81	-1.09	193	258.3	271.6	297.4	10.8	-8.69	2179-25-1
275	salicylic acid	[27]	*1.84*	55.13	-6.80	1	*-6.8*[40]	*0.06*[62]	180	139.1	162.7	157.9	3.2	-16.98	69-72-7
276	trifluraliin	IV	*1.84*	75.27	-2.24	0	-7.04	0.37	207	336.3	318.2	366.6	4.7	-0.49	1582-09-8
277	aldicarb-sulfoxide	[27]	*1.83*	60.76	-3.21	0	-6.43	2.84	212	207.3	237.0	250.4	2.6	-4.33	1646-87-3
278	trimethylamine	[27]	*1.81*	7.12	-7.79	0	*9.78*[40]	*17.61*[40]	*219.4*[42]	60.1	113.5	101.2	1.0	-4.38	75-50-3
279	procymidone	[27]	*1.79*	33.06	-2.48	1	-11.21	-4.23	194	285.1	283.2	313.9	5.7	-5.46	32809-16-8
280	methamidophos	[27]	*1.79*	58.73	-6.34	0	-4.21	4.19	200	142.1	165.2	161.5	5.1	-9.59	10265-92-6

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
281	2-nitrobenzoic acid	[27]	*1.78*	72.48	-4.26	1	*-7.00*[40]	*0.30*[40]	196	168.1	176.2	174.5	6.3	-7.53	552-16-9
282	6-nitroindazole	[27]	*1.78*	67.93	-5.67	0	*-0.97*[40]	5.21	198	164.1	178.8	174.9	4.8	-10.63	7597-18-4
283	glyphosate	[27]	*1.69*	112.85	-8.49	0	*0.78*[40]	10.09	200	170.1	184.3	177.9	9.1	-23.03	1071-83-6
284	4-hydroxybenzoic acid	[27], III	*1.67*	57.26	-6.62	1	*-6.67*[40]	-0.45	196	139.1	164.3	158.9	5.0	-16.92	99-96-7
285	glyceryl triacetate	[27], III	*1.61*	67.30	-3.38	1	-10.56	-3.03	*202*	219.2	252.2	263.3	2.9	-8.59	102-76-1
286	phorate	[27]	*1.59*	15.43	-2.20	1	-12.74	-6.93	208	261.4	282.0	309.0	2.8	0.86	298-02-2
287	cysteine	[16,27]	*1.56*	61.67	-9.06	0	*1.98*[40]	13.23	*207.8*[42]	122.2	148.9	143.2	7.1	-13.63	52-90-4
288	normetanephrine	[31]	*1.54*	71.10	-4.84	0	8.19	17.07	219	184.2	214.3	224.6	5.2	-10.28	97-31-4
289	myristic acid	[32]	*1.52*	38.22	-1.75	1	-7.91	-1.77	185	229.4	331.9	339.1	2.2	-9.97	544-63-8
290	p-anisaldehyde	[27]	*1.46*	26.17	-4.61	1	-3.97	3.46	*203*[42]	137.2	175.8	171.2	7.7	-6.66	123-11-5
291	ethyl paraben	[27]	*1.46*	42.25	-4.14	1	-7.81	-0.86	203	167.2	202.4	199.5	2.1	-7.37	120-47-8
292	ethofumesate	[27]	*1.43*	62.71	-2.55	1	-15.58	-9.22	191	287.4	299.2	332.5	3.0	-7.48	26225-79-6
293	dimethyl malonate	II, III	*1.43*	39.13	-5.37	1	*-6.02*	*3.65*	*200*[51]	133.1	166.0	154.4	6.7	-2.57	108-59-8
294	thiram	[27]	*1.38*	2.92	-2.47	0	-9.87	-3.45	211	241.4	245.6	279.9	2.3	0.10	137-26-8
295	glycine	[16,27]	*1.33*	64.25	-14.75	0	*7.86*[40]	17.18	*203.7*[42]	76.1	108.1	91.9	2.7	-15.77	56-40-6
296	2,4,6-trinitroaniline	[27]	*1.32*	134.97	-5.41	0	*-9.41*[40]	-6.88	184	229.1	212.4	214.5	5.0	-10.18	489-98-5
297	fenvalerate	[27]	*1.32*	45.46	-1.66	1	-14.10	-9.26	191	420.9	423.4	513.9	10.1	-4.69	51630-58-1
298	p-methoxybenzoic acid	[27], III	*1.32*	44.56	-4.87	1	-4.40	2.07	*208.1*[51]	153.2	183.9	180.2	9.3	-12.94	100-09-4
299	cholic acid	[27]	*1.30*	96.39	-1.76	1	-7.51	-1.72	188	381.5	381.0	477.2	5.9	-16.00	81-25-4
300	ethylene glycol diacetate	[27], III	*1.28*	45.45	-4.82	1	-9.62	-2.52	183	147.1	191.8	180.3	3.1	-9.33	111-55-7
301	2-cyanophenol	II, III		37.99	-5.94	0	*-10.31*	*-4.35*	*194*	120.1	156.0	148.0	4.7	-8.04	611-20-1

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
302	benzoic acid	II	*1.22*	37.51	-6.57	1	*-7.70*	*-2.61*	*188.8*[42]	123.1	155.4	148.7	3.0	-14.27	65-85-0
303	methyl paraben	[27]	*1.22*	42.52	-4.75	1	-8.04	-1.06	*199.0*[42]	153.2	184.3	180.4	2.3	-8.18	99-76-3
304	2-methoxybenzaldehyde	[27]	*1.18*	20.12	-4.44	1	-4.37	3.25	209	137.2	171.6	169.1	7.4	-2.71	135-02-4
305	cinnamic acid	[27]	*1.18*	38.59	-4.94	1	-5.77	0.73	201	149.2	190.1	185.0	3.7	-10.53	140-10-3
306	captafol	[27]	*1.17*	34.50	-2.72	1	-12.00	-5.90	194	350.1	286.7	345.3	6.6	-6.90	2425-06-1
307	thymine	[27]	*1.16*	55.94	-7.30	1	*-3.08*[40]	*2.70*[43]	*203.2*[42]	127.1	151.9	144.6	6.4	-13.30	65-71-4
308	4-hydroxybenzaldehyde	[27]	*1.13*	38.88	-6.27	1	-3.61	3.68	203	123.1	156.2	149.1	7.0	-11.14	123-08-0
309	2,6-dimethoxy pyridine	II	*1.12*	25.17	-4.25	0	*1.6*[37]	*7.6*[37]	218.1	140.2	177.2	172.1	5.4	-1.83	6231-18-1
310	ethylamine	II	*1.12*	29.80	-12.64	0	*10.6*[37]	*18.4*[37]	*210.6*[42]	46.1	94.6	76.9	1.9	-9.34	75-04-7
311	hydrazinecarboxylic acid, 2-(phenyl-methylene)-, 1,1-dimethylethyl ester	[27]	*1.07*	42.16	-2.70	0	-2.55	5.56	216	221.3	272.1	282.2	5.1	-2.67	24469-50-9
312	3-methoxycatechol	[27]	*1.00*	47.71	-5.99	1	-12.44	-8.57	183	141.1	170.5	166.1	4.6	-15.58	934-00-9
313	3-chloropyridine	II	*1.00*	10.87	-6.52	0	*2.84*[63]	*10.0*[37]	*208.3*	114.6	138.5	129.5	3.0	-6.07	626-60-8
314	2-methoxypyridine	II	*0.99*	18.03	-5.46	0	*3.06*[37]	*10.0*[37]	*215.8*[42]	110.1	148.1	139.7	4.7	-3.42	1628-89-3
315	2-chloropyridine	II	*0.97*	10.96	-6.36	0	*0.49*[37]	*7.5*[37]	*208*[42]	114.6	138.6	129.7	5.0	-4.70	109-09-1
316	2,4-dinitroaniline	[17], II	*0.95*	102.48	-6.37	0	*-4.53*[38]	*-2.50*	*180.1*[39]	184.1	188.9	186.9	10.6	-12.76	97-02-9
317	α-amino-2,3-dihydro-5-methyl-3-oxo-4-isoxazolepropanoic acid	[31]	*0.94*	97.52	-5.78	0	2.16	11.10	209	187.2	198.2	213.6	14.3	-18.13	74341-63-2
318	taurocholic acid	[27]	*0.91*	135.48	-1.44	1	-4.71	4.61	216	516.7	477.2	619.7	3.8	-11.50	81-24-3
319	PheDeemm	[31]	*0.85*	84.56	-2.22	1	-13.46	-5.81	204	336.4	359.2	417.5	2.0	-6.88	1222062-76-1
320	2-acetamido-5-nitrothiazole	[27]	*0.82*	74.74	-5.19	0	-4.26	3.23	197	188.2	193.4	190.7	11.1	-10.74	140-40-9
321	etofenprox	IV	*0.80*	23.49	-1.58	1	-9.60	-3.68	204	377.5	434.8	475.3	2.7	-2.60	80844-07-1
322	bifenthrin	[27]	*0.79*	22.49	-1.68	1	-9.43	-4.10	197	423.9	408.9	501.6	6.3	-4.25	82657-04-3

No.	Compound	log*IE* origin[b]	log*IE*	PSA	WANS	O base	pK_{aH} (H_2O)	pK_{aH} (MeCN)	GB	M+1	A	MV	d	log$P_{s/h}$	CAS
323	2-nitrobenzaldehyde	[27]	*0.78*	56.54	-5.61	1	-9.62	-3.38	186	152.1	170.9	168.7	7.0	-10.62	552-89-6
324	heptyl paraben	[27]	*0.75*	42.26	-2.06	1	-7.88	-1.01	204	237.3	301.8	313.0	5.2	-5.49	1085-12-7
325	uracil	[27]	*0.68*	56.60	-9.35	1	*-2.35*[40]	*3.38*[43]	*201.2*[42]	113.1	133.9	122.6	6.5	-13.23	66-22-8
326	ethyl benzoate	II	*0.53*	25.22	-4.17	1	*-6.91*	*0.85*	194.1	151.2	193.2	191.2	6.8	-4.46	93-89-0
327	propyl paraben	[27]	*0.53*	42.24	-3.45	1	-8.04	-1.07	203	181.2	222.3	222.0	5.2	-6.85	94-13-3
328	3-nitro-1H-1,2,4-triazole	[27]	*0.50*	77.66	-12.10	0	-6.71	1.21	190	115.1	128.6	114.4	9.5	-13.00	24807-55-4
329	pyrazine	[27]	*0.17*	18.20	-9.22	0	*0.6*[40]	*7.74*[43]	*202.4*[42]	81.1	115.1	102.3	0.0	-8.28	290-37-9
330	2-(trifluoromethane) sulfonylbenzoic acid	[27], III	*0.10*	63.18	-3.64	1	-10.69	*-3.66*	*202*	255.2	218.7	239.2	9.0	-6.14	142994-06-7
331	3-nitrobenzaldehyde	[27]	*0.09*	58.33	-5.78	1	-9.21	-2.80	185	152.1	174.8	169.5	3.0	-11.45	99-61-6
332	methyl benzoate	II	*0.00*	25.49	-4.93	1	*-7.16*	*0.59*	*195.7*[42]	137.2	172.9	170.0	6.7	-5.53	93-58-3
333	4-methylcatechol	[27]	*-0.07*	41.86	-6.75	1	-11.88	-7.98	177	125.1	161.0	154.5	3.8	-16.91	452-86-8
334	4-nitrobenzaldehyde	[27]	*-0.09*	58.28	-5.66	1	-9.24	-2.90	*182.4*[42]	152.1	174.3	169.4	3.4	-11.46	555-16-8

[a] The physico-chemical parameters are Polar Surface Area, Weighted Absolute Negative Sigma, descriptor whether a base protonates on oxygen or not, negative base-10 logarithm of the acid dissociation constant of conjugate acid in aquous solution, and in acetonitrile, Gas phase Basicity, molecular Mass, Area, Molecular Volume, dipole moment and partition coefficient between solvent and hexane of the protonated compound. Molecular parameter values were calculated in this work, unless stated otherwise. References are given for literature values. Log*IE* values from multiple sources were averaged. [b] References given in roman numeral are publications from present work.

The solvent composition for all measurements resulting in log*IE* values presented in Table 3 was acetonitrile (Chempure, assay ≥99.5 by GC)/ 0.1% aqueous formic acid (Riedel-de Haën, 98–100% puriss. p.a.) in volume ratio 80:20. For each RIE measurement solutions of two compounds in the solvent were prepared and these were infused in either of the two ways. One way was using two syringe pumps connected with a 'T'-piece with around 1 mm^3 of dead volume (for enabling the solutions to mix). The concentration ratio of the compounds can be simply varied by changing the ratio of infusion rates of the two pumps. Another way was preparing mixed solutions prior to introducing them using a single syringe pump. The majority of the experiments were conducted using setup with two pumps although both ways provided equal results.

The range of the concentrations of compounds in the sprayed mixture was from $n \cdot 10^{-8}$ mol/L to $n \cdot 10^{-3}$ mol/L. Thus the mentioned change in concentration is in the linear range of the concentration to signal ratio[12] and the obtained log*RIE* values were reasonably constant at different concentrations (see more detailed info in Paper I). All measurements were done at solution flow rate of 8.3 µL/min (0.5 mL/h). The log*RIE* dependence on the solution flow rate (in the range of 8.3 to 20 µL/min) was studied in early stage of this work and the results are presented in Paper I.

The mass spectra were gained averaging ca 250 spectra that were registered over a time span of ca 100 s. Two different measurement methods in agreement with eq 6 and 9 were used for gaining relative values of ionization efficiencies. One consisted in measuring the RIE of two compounds being together in the sprayed mixture and the second one consisted in registering the signals in mass spectra separately for each compound and using the slopes of the chart of signals in mass spectrum versus concentrations.[17,41]

5. COMPUTATIONAL METHODS

5.1. The studied properties of compounds

One of the main purposes of this study was to analyse correlations between compound properties and IE in ESI source. Taking into account the ESI mechanism, the following 11 molecular parameters were included in data analysis:

a. Basicity (the ability to be protonated and become a cation) descriptors: pK_{aH} in acetonitrile (pK_{aH}(MeCN)), in water (pK_{aH}(H_2O)) and the gas phase basicity (GB);
b. molecular size descriptors of the protonated compound: molecular mass (M+1), molecular area (A) and molecular volume (expressed as logMV);
c. polarity and charge localization/delocalization descriptors of the protonated molecule: polar surface area (PSA), dipole moment (*d*), weighed area of negative sigma (WANS) [64];
d. hydrophobicity (distribution coefficient of the protonated forms between a polar and a nonpolar medium) descriptor: partition coefficient of the protonated molecule between the used solvent and hexane (log$P_{s/h}$);
e. type of basicity center (O base): equal to 1 if the compound is an oxygen-protonated base, otherwise 0.

Logarithmic values (e.g. log*P* instead of P, pK_a instead of K_a) are often used because it reduces the division of values into groups due to the differences in these values.

Partition coefficient between the used solvent and hexane (log$P_{s/h}$) was used as one of the hydrophobicity parameters, instead of the more common log$P_{oct/w}$. There are no experimental log$P_{s/h}$ values available, but this parameter has been chosen because of the following:

1. Polarity of hexane is significantly lower than octanol. Therefore this value better describes hydrophobicity;
2. Experimental log$P_{oct/w}$ data for a number of compounds in our scale are available[65], but their usefulness is often limited, because of different (or even undefined) pH values that were used for determining them. This leads to poorly defined meaning of many literature values in terms of what are the actual species in solution. At the same time, the COSMO-RS computation enables computing the parameter just the the protonated form of the compound.

5.2. Computational methods

The density-functional theory (DFT) Becke-Perdew (BP) valence triple-zeta polarization basis set (TZVP) and/or COnductor like Screening MOdel for Real Solvents (COSMO-RS)[66–68] approach were used to obtain the computational values for all the mentioned compounds' parameters. For every studied compound various tautomers (different protonation centers) and conformations (different molecular geometries) were considered. For MV, A and *d* values the most stable tautomer and conformation (with the lowest free energy in the conductor continuum) was used. With all of the other compounds' parameters all of considered configurations were statistically weighted and accounted for by COSMO-RS software.

Full geometry optimization of the ions was carried out at DFT BP TZVP level with the Turbomole software package (version 7.2[69]). The COSMO-RS computations were performed applying the COSMOtherm[70] software (version C3.0 Release 17.05[71]). The solvent phases for the log*P* calculations were the water-acetonitrile mixture 20:80 (corresponding to mole fractions 0.42 and 0.58) and pure hexane. Volume quotient value VQ = V1/V2 = 0.29 was used in log$P_{s/h}$ calculations. Mutual mixing of the phases was not considered.

5.3. Multilinear regression analysis

In order to detect relationships between compounds' properties and the ionization efficiency all the above mentioned physico-chemical properties were included in the data analysis. In order to analyze the influence of these diverse parameters all of the included parameters, along with log*IE* values, were scaled. For the molecular volume of the cation it was found that instead of just molecular volume, its logarithm should be used in the model. For high basicity values thresholds were used (7 for pK_{aH} in H_2O, 20 for pK_{aH} in MeCN and 230 for GB), i.e. a threshold value was used instead of the real basicity in the case where the basicity was higher than the respective threshold value. The use of such thresholds was based on the assumption that the number of protonated molecules in the solution is determined by the pH of the solution as well as by the pK_{aH}. Basicities above the threshold values are not expected to give any additional advantage in terms of ionization when acidic solution is used, as basically all molecules are protonated in such solutions. Confidence level 95% was used for the statistical analysis.

Starting with all above-mentioned parameters multilinear regression analysis was performed repeatedly using step by step backward elimination i.e. eliminating parameters that had low statistical significance and/or correlated strongly with one another. The correlation matrix between the parameters is given in Table 4.

Table 4. Correlations between analysed compounds' parameters. Values are scaled and thresholds are used as described in text.

	GB	**pK_{aH}(MeCN)**	**A**	**M+1**	***d***	**PSA**	**WANS**	**O base**	**log$P_{s/h}$**	**logMV**	**pK_{aH}(H_2O)**
GB		0.5386	0.1202	0.0809	0.0172	0.0343	0.1297	0.1513	0.3216	0.1097	0.4641
pK_{aH}(MeCN)			0.0000	0.0019	0.0063	0.0090	0.0099	0.3169	0.0226	0.0046	0.9302
A				0.9346	0.1040	0.0204	0.6194	0.0011	0.2066	0.9317	0.0011
M+1					0.1371	0.0403	0.5169	0.0015	0.1637	0.8724	0.0050
d						0.1134	0.0242	0.0000	0.0008	0.0928	0.0008
PSA							0.0138	0.0006	0.3774	0.0135	0.0157
WANS								0.0179	0.3849	0.7794	0.0172
O base									0.0002	0.0048	0.3830
log$P_{s/h}$										0.2298	0.0117
logMV											0.0102
pK_{aH}(H_2O)											

Several paths for data analysis using multilinear regression (see Table 5 below and Figure 1 in Paper IV) were adopted and the reached models were evaluated by the standard deviation (S) and R^2 values of the obtained relationships between log*IE* and compound parameters. Three most significant models containing three most substantial parameters affecting compound's ionization efficiency in ESI source each were obtained. Table 5 demonstrates the sequence of excluding the parameters, the weight of the parameters included in final models with corresponding S values in parentheses. Additionally number of different paths changing the order of elimination steps were considered. Obtained results were identical or worse (comparing R^2 values) than the models presented in Tabel 5. The statistical models obtained were validated by a leave-one-out test (LOO) and 5-fold cross-validation (CV). The corresponding root mean square errors (RMSE) are presented in Paper IV in Table 3.

Table 5. Paths of three statistically most significant models obtained via the multilinear regression analysis (correlation between log*IE* and compounds' parameters).

Parameter	Path 1	Path 2	Path 3	All In
pK_{aH}(H_2O)	0.60(0.03)	0.63(0.03)	0.64(0.03)	0.78(0.13)
A	0.36(+/-0.04)	eliminated 5.	eliminated 1.	-0.036(0.167)
log$P_{s/h}$	0.27(0.04)	0.24(0.03)	eliminated 8.	0.14(0.07)
logMV	eliminated 1.	0.41(0.03)	0.55(0.03)	0.96(0.20)
M+1	eliminated 2.	eliminated 1.	eliminated 4.	-0.33(0.13)
GB	eliminated 3.	eliminated 3.	eliminated 2.	0.044(0.066)
O base	eliminated 4.	eliminated 4.	eliminated 6.	-0.10(0.04)
WANS	eliminated 5.	eliminated 2.	eliminated 5.	-0.18(0.10)
pK_{aH}(MeCN)	eliminated 6.	eliminated 6.	eliminated 3.	-0.26(0.13)
d	eliminated 7.	eliminated 7.	eliminated 7.	0.031(0.033)
PSA	eliminated 8.	eliminated 8.	-0.23(0.03)	-0.15(0.05)
R^2	0.678	0.701	0.711	0.732
S^b	0.57	0.55	0.54	0.53

Coefficient and standard deviation values of the retained parameters are presented in columns "Path 1" to "Path 3". The step at which the parameter was excluded from the model is indicated for the remaining parameters. Column "All In" presents the model where all considered parameters are included. [b] *S* values are scaled. The corresponding unscaled values range from 0.69 to 0.75 (scaling factor 1.31).

6. RESULTS AND DISCUSSION

6.1. The log*IE* scale

The main results of the work are presented as the scale of log*IE* values in Table 3. This comprehensive log*IE* scale was obtained by collecting and bringing to the same scale the log*IE* data for 334 compounds spanning over 6 log*IE* units. As the reference compound for the scale, methyl benzoate with log*IE* value arbitrarily set to zero was assigned (Paper I and Paper II).

The ionization efficiency scale of log*IE* values presented in Table 3 was obtained by assembling the results of various studies of different researchers from our workgroup (authors of Paper IV) over the period of approximately 15 years. In the case that data is obtained only form this study, the log*IE* values in Table 3 are obtained by minimizing the sum of squared differences (SS) between the assigned log*IE*(B_i) and log*IE*(B_j) values and directly measured log*RIE*(B_i, B_j) values. SS is minimized by following equation (see Paper II for details):

$$SS = \sum_{k=1}^{n_m} \{\log RIE_k(B_i, B_j) - [\log IE(B_i) - \log IE(B_j)]\}^2 \rightarrow \min \quad (10)$$

where logRIE_k(B_i, B_j) is the result of k-th experiment that has been carried out between compounds B_i and B_j and n_m is the number of measurements. Relative ionization efficiency (RIE) of compounds B_i and B_j is specified in Eq. 6.

Consistency of the scale (presented in Table 3) is expressed by the pooled standard deviation (s_{pooled}) of the log*IE* values obtained from measurements reflected in published studies integrated with the consistency standard deviation of the log*IE* scale presented in Paper II:

$$s_{\text{pooled}} = \sqrt{\frac{(df_1 \times {s_1}^2 + df_2 \times {s_2}^2 + \cdots + df_n \times {s_n}^2)}{(df_1 + df_2 + \cdots + df_n)}} \quad (11)$$

where df_i denotes the degrees of freedom of individual data sets, s_i is the standard deviation of the corresponding data set and n is the number of pooled standard deviations. The consistency parameter s = 0.30 of the scale from the Paper II was taken as one of the standard deviations included in pooling (df = 346). With all the data included in this study, the pooled consistency standard deviation of the scale is s_{pooled} = 0.33 log*IE* units with overall df = 421. As can be seen, in broad terms the consistency of the overall scale in Table 3 is similar to the one published in Paper II.

The agreement between the assigned log*IE* values (gained by aforementioned minimization procedure) and directly measured log*RIE* values is analyzed and discussed in Paper II. The conclusions on the factors that can be ruled out as cause of disagreements causing the pooled standard deviation were: (a)

relatively broad span of the molecular masses measured against one another; (b) the differences of concentrations of compounds measured together in infused solution; (c) differences in the two compounds' concentration – signal ratios and the slopes of those plots. For specific data on the disagreements between measurements, see Paper II. Some of the later studies[27] (carried out using approach of equation 9) that are also represented in the log*IE* scale of Table 3 already have canceled out such influence by conducting measurements with only one analyte in solution at time.

6.2. Additional ions in mass spectra

The presented ionization efficiency scale was based on the efficiency of ionization via mono-protonation. However, some side-processes occurred during ionization (e.g. Na-adduct formation and fragmentation). This is discussed in Papers I, II and III. The general conclusions are that fragmentation occurs after the protonation process but formation of Na-adducts occurs simultaneously with protonation. Therefore the calculations of log*RIE* values did not include the $[B+Na]^+$ ions but ions formed from the $[B+H]^+$ ions via fragmentation were considered as daughter ions of the $[B+H]^+$ ions and their abundances were included into the MS responses by adding the intensities of the fragment ions' peaks in mass spectra to the $[B+H]^+$ peak of the compound. In most of the cases the intensities of $[B+H]^+$ peaks were much more intensive than additional fragments' peaks. Some examples are presented in Figures 3 and 4. More details are given in Papers I, II and III.

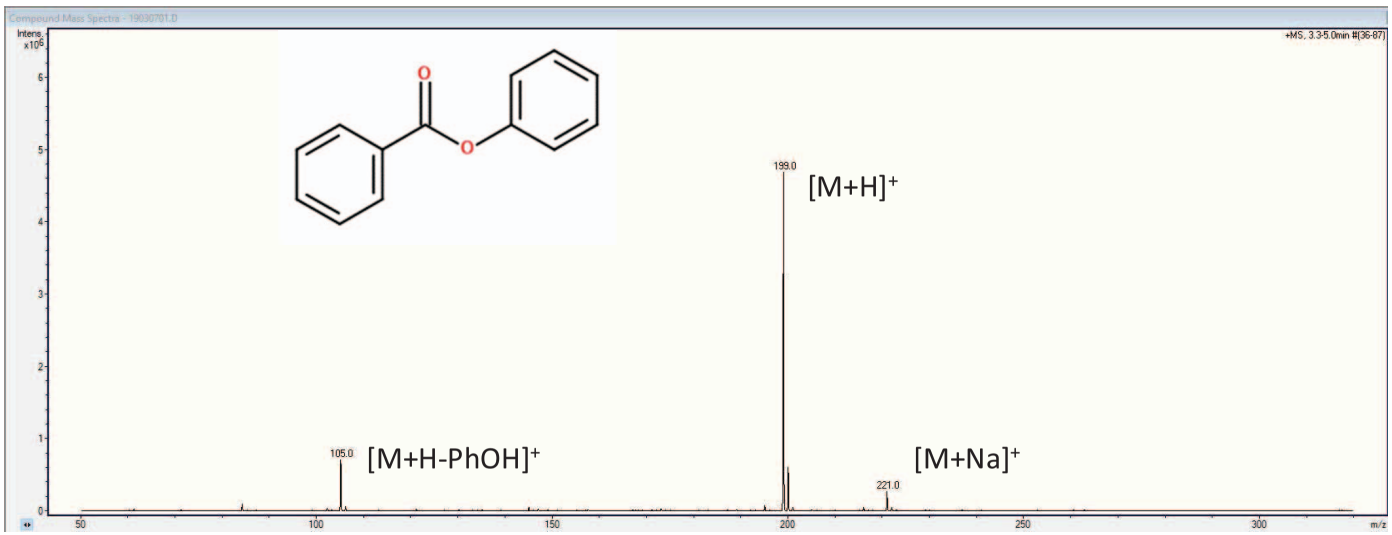

Figure 3. Mass spectrum of phenyl benzoate.

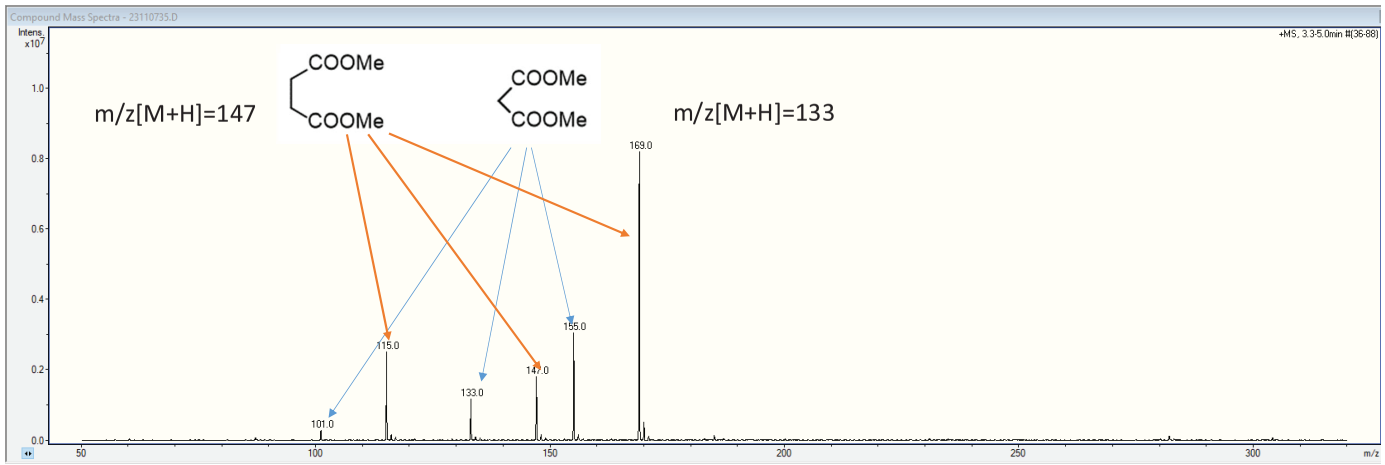

Figure 4. Mass spectrum of dimethylsuccinate vs dimethylmalonate. Concentration of the compounds in sprayed solution was correspondingly $1.58 \cdot 10^{-5}$ and $1.54 \cdot 10^{-5}$ M.

6.3. Correlation of log*IE* values to molecular properties.

Since there is no complete experimental data of all the afore mentioned parameters of the studied compounds a considerable part of the data used in multilinear regression is computational.

As can be seen from the models in Table 5, all studied multilinear regression analysis paths led to similar results. The most significant parameters affecting the ionization in ESI source (in the studied solvent system), are the basicity of the compound (best expressed via pK_{aH} in water) as the descriptor characterizing the ability to be protonated and become a cation; the size of the molecule (expressed via A or logMV) as the descriptor characterizing the stabilization of the protonated form of the molecule in the gas phase (besides basicity, the sheer size of the formed ion is an important stabilizing factor in the gas phase[72]) and hydrophobicity ($\log P_{s/h}$) or charge (de)localization in the protonated molecule (PSA) as the descriptors characterizing the affinity of the protonated forms towards the drop surface. R^2 values of models obtained by different paths are so similar that there is no justification for preferring one model to another. With different sets of compounds, the rank order of R^2 values may moderately change but the chemical insight into the factors affecting ionization remains the same. More detailed discussion about the mentioned analysis paths is available in Paper IV.

Having only one of the three basicity-related parameters in the model is justified, because the three basicity parameters, p$K_{aH}(H_2O)$, pK_{aH}(MeCN) and GB, are significantly correlated to one another. As expected, the models containing p$K_{aH}(H_2O)$ were favorable (comparing R^2 values). The used solvent contains more acetonitrile than water, but water solvates ions stronger. Moreover, acetonitrile, as the more volatile solvent, evaporates preferentially from the droplet during the ESI process. Therefore, the actual formation of the gas-phase ion (according to IEM) takes place from a significantly more water-rich medium than the initial solvent.

The three models in Table 5 have similar performance, as evidenced by the R^2 and S values (see Figure 1 in Paper IV), as well as by the scatter plots in Figure 3 in Paper IV. The RMSE of prediction in the range of 0.7 to 0.8 log*IE* units means that, in addition to helping elucidate the molecular parameters that determine the ionization efficiency, the models have also practically useful prediction accuracy. In all three models, all three parameters have high and similar statistical significance. This can be considered as indirect evidence of the importance of the aforementioned three factors and the stability of the models. As an additional strong point in favor of the three-parameter models, their performance is similar to the model containing all parameters (last column of Table 5).

Most of the compound families studied in present work have a rather wide span of log*IE* values and there are no distinguished differences of log*IE* values between those. However, some compound families (e.g. phosphazenes and tetraalkylammonium salts) enable drawing conclusions that ionization in a

group of similar compounds is indeed determined by the size and basicity of those compounds. Conversely – small molecular size and low basicity leads to relatively low ionization efficiencies. It can be seen from Table 3 that increasing the number of alkyl chains or expanding of alkyl chain within a compound family increases the ionization efficiency. This is largely due to the corresponding increase in molecular size, lipophilicity and a moderate increase of basicity. Family-based correlations are studied and presented in Papers II and IV.

SUMMARY

The main purpose of this study has been gaining a better understanding of the relations between different molecular properties of compounds and the signal intensities of their monoprotonated ions in electrospray ionization MS. A large number of ionization efficiency (log*IE*) values have been obtained from different studies carried out by the present author and others, leading to log*IE* data of 344 compounds of high structural diversity. Eleven molecular parameters deemed to be important for ionization in ESI – p$K_{aH}(H_2O)$, pK_{aH}(MeCN), GB, PSA, A, M+1, MV, d, WANS, log$P_{s/h}$, O base – have been found from literature or via computations (if experimental values were not available from literature). Using multiple linear regression model all the parameters were taken account for estimating the importance of these properties for evaluating compounds ionization efficiency in ESI source. Three slightly different but essentially coherent models for estimating compounds log*IE* have been obtained. It was found that in the studied solvent system, a compound's ionization in ESI source (via monoprotonation) is determined by its basicity (expressed by pK_{aH} in water), molecular size (expressed by A or logMV) and hydrophobicity/ lipophilicity (expressed by log$P_{s/h}$). The RMSE of prediction of the models are in the range of 0.7 to 0.8 log*IE* units, which is insufficient for accurate quantitative estimation of compounds log*IE* but the models can be used for approximate prediction of the relative abundance of analytes.

REFERENCES

(1) *Applied Electrospray Mass Spectrometry*; Pramanik, B. N., Ganguly, A. K., Gross, M. L., Eds.; Practical spectroscopy series; Marcel Dekker: New York, 2002.

(2) Whitehouse, C. M.; Dreyer, R. N.; Yamashita, Masamichi.; Fenn, J. B. Electrospray Interface for Liquid Chromatographs and Mass Spectrometers. *Anal. Chem.* **1985**, *57* (3), 675–679. https://doi.org/10.1021/ac00280a023.

(3) Bruins, A. P.; Covey, T. R.; Henion, J. D. Ion Spray Interface for Combined Liquid Chromatography/Atmospheric Pressure Ionization Mass Spectrometry. *Anal. Chem.* **1987**, *59* (22), 2642–2646. https://doi.org/10.1021/ac00149a003.

(4) Van Berkel, G. J.; Glish, G. L.; McLuckey, S. A. Electrospray Ionization Combined with Ion Trap Mass Spectrometry. *Anal. Chem.* **1990**, *62* (13), 1284–1295. https://doi.org/10.1021/ac00212a016.

(5) Hoffmann, E. de; Stroobant, V. *Mass Spectrometry: Principles and Applications*, 3rd ed.; J. Wiley: Chichester, West Sussex, England ; Hoboken, NJ, 2007.

(6) Dole, M.; Mack, L. L.; Hines, R. L.; Mobley, R. C.; Ferguson, L. D.; Alice, M. B. Molecular Beams of Macroions. *The Journal of Chemical Physics* **1968**, *49* (5), 2240–2249. https://doi.org/10.1063/1.1670391.

(7) Mack, L. L.; Kralik, P.; Rheude, A.; Dole, M. Molecular Beams of Macroions. II. *The Journal of Chemical Physics* **1970**, *52* (10), 4977–4986. https://doi.org/10.1063/1.1672733.

(8) Fenn, J. B. Ion Formation from Charged Droplets: Roles of Geometry, Energy, and Time. *Journal of the American Society for Mass Spectrometry* **1993**, *4* (7), 524–535. https://doi.org/10.1016/1044-0305(93)85014-O.

(9) Iribarne, J. V. On the Evaporation of Small Ions from Charged Droplets. *J. Chem. Phys.* **1976**, *64* (6), 2287. https://doi.org/10.1063/1.432536.

(10) Konermann, L.; Ahadi, E.; Rodriguez, A. D.; Vahidi, S. Unraveling the Mechanism of Electrospray Ionization. *Anal. Chem.* **2013**, *85* (1), 2–9. https://doi.org/10.1021/ac302789c.

(11) Konermann, L.; Rodriguez, A. D.; Liu, J. On the Formation of Highly Charged Gaseous Ions from Unfolded Proteins by Electrospray Ionization. *Anal. Chem.* **2012**, *84* (15), 6798–6804. https://doi.org/10.1021/ac301298g.

(12) Enke, C. G. A Predictive Model for Matrix and Analyte Effects in Electrospray Ionization of Singly-Charged Ionic Analytes. *Anal. Chem.* **1997**, *69* (23), 4885–4893. https://doi.org/10.1021/ac970095w.

(13) Chalcraft, K. R.; Lee, R.; Mills, C.; Britz-McKibbin, P. Virtual Quantification of Metabolites by Capillary Electrophoresis-Electrospray Ionization-Mass Spectrometry: Predicting Ionization Efficiency Without Chemical Standards. *Anal. Chem.* **2009**, *81* (7), 2506–2515. https://doi.org/10.1021/ac802272u.

(14) Kebarle, P. A Brief Overview of the Present Status of the Mechanisms Involved in Electrospray Mass Spectrometry. *J Mass Spectrom* **2000**, *35* (7), 804–817. https://doi.org/10.1002/1096-9888(200007)35:7<804::AID-JMS22>3.0.CO;2-Q.

(15) Liigand, J.; Kruve, A.; Leito, I.; Girod, M.; Antoine, R. Effect of Mobile Phase on Electrospray Ionization Efficiency. *J. Am. Soc. Mass Spectrom.* **2014**, *25* (11), 1853–1861. https://doi.org/10.1007/s13361-014-0969-x.

(16) Liigand, J.; Kruve, A.; Liigand, P.; Laaniste, A.; Girod, M.; Antoine, R.; Leito, I. Transferability of the Electrospray Ionization Efficiency Scale between Different Instruments. *J. Am. Soc. Mass Spectrom.* **2015**, *26* (11), 1923–1930. https://doi.org/10.1007/s13361-015-1219-6.

(17) Liigand, J.; Laaniste, A.; Kruve, A. PH Effects on Electrospray Ionization Efficiency. *J. Am. Soc. Mass Spectrom.* **2017**, *28* (3), 461–469. https://doi.org/10.1007/s13361-016-1563-1.
(18) Liigand, P.; Heering, A.; Kaupmees, K.; Leito, I.; Girod, M.; Antoine, R.; Kruve, A. The Evolution of Electrospray Generated Droplets Is Not Affected by Ionization Mode. *J. Am. Soc. Mass Spectrom.* **2017**, *28* (10), 2124–2131. https://doi.org/10.1007/s13361-017-1737-5.
(19) Smith, R. D.; Shen, Y.; Tang, K. Ultrasensitive and Quantitative Analyses from Combined Separations−Mass Spectrometry for the Characterization of Proteomes. *Acc. Chem. Res.* **2004**, *37* (4), 269–278. https://doi.org/10.1021/ar0301330.
(20) Kostiainen, R.; Kauppila, T. J. Effect of Eluent on the Ionization Process in Liquid Chromatography–Mass Spectrometry. *Journal of Chromatography A* **2009**, *1216* (4), 685–699. https://doi.org/10.1016/j.chroma.2008.08.095.
(21) Cech, N. B.; Enke, C. G. Relating Electrospray Ionization Response to Nonpolar Character of Small Peptides. *Anal. Chem.* **2000**, *72* (13), 2717–2723. https://doi.org/10.1021/ac9914869.
(22) Ehrmann, B. M.; Henriksen, T.; Cech, N. B. Relative Importance of Basicity in the Gas Phase and in Solution for Determining Selectivity in Electrospray Ionization Mass Spectrometry. *J Am Soc Mass Spectrom* **2008**, *19* (5), 719–728. https://doi.org/10.1016/j.jasms.2008.01.003.
(23) Kamel, A. M.; Brown, P. R.; Munson, B. Effects of Mobile-Phase Additives, Solution PH, Ionization Constant, and Analyte Concentration on the Sensitivities and Electrospray Ionization Mass Spectra of Nucleoside Antiviral Agents. *Anal. Chem.* **1999**, *71* (24), 5481–5492. https://doi.org/10.1021/ac9906429.
(24) Constantopoulos, T. L.; Jackson, G. S.; Enke, C. G. Challenges in Achieving a Fundamental Model for ESI. *Analytica Chimica Acta* **2000**, *406* (1), 37–52. https://doi.org/10.1016/S0003-2670(99)00600-5.
(25) Kebarle, P.; Tang, L. From Ions in Solution to Ions in the Gas Phase - the Mechanism of Electrospray Mass Spectrometry. *Anal. Chem.* **1993**, *65* (22), 972A-986A. https://doi.org/10.1021/ac00070a001.
(26) Bökman, C. F.; Bylund, D.; Markides, K. E.; Sjöberg, P. J. R. Relating Chromatographic Retention and Electrophoretic Mobility to the Ion Distribution within Electrosprayed Droplets. *J Am Soc Mass Spectrom* **2006**, *17* (3), 318–324. https://doi.org/10.1016/j.jasms.2005.11.006.
(27) Liigand, J.; Wang, T.; Kellogg, J.; Smedsgaard, J.; Cech, N.; Kruve, A. Quantification for Non-Targeted LC/MS Screening without Standard Substances. *Sci Rep* **2020**, *10* (1), 5808. https://doi.org/10.1038/s41598-020-62573-z.
(28) Mandra, V. J.; Kouskoura, M. G.; Markopoulou, C. K. Using the Partial Least Squares Method to Model the Electrospray Ionization Response Produced by Small Pharmaceutical Molecules in Positive Mode: Modelling Positive Electrospray Ionization Response. *Rapid Commun. Mass Spectrom.* **2015**, *29* (18), 1661–1675. https://doi.org/10.1002/rcm.7263.
(29) Kiontke, A.; Oliveira-Birkmeier, A.; Opitz, A.; Birkemeyer, C. Electrospray Ionization Efficiency Is Dependent on Different Molecular Descriptors with Respect to Solvent PH and Instrumental Configuration. *PLoS ONE* **2016**, *11* (12), e0167502. https://doi.org/10.1371/journal.pone.0167502.
(30) Cramer, C. J.; Johnson, J. L.; Kamel, A. M. Prediction of Mass Spectral Response Factors from Predicted Chemometric Data for Druglike Molecules. *J. Am. Soc.*

Mass Spectrom. **2017**, *28* (2), 278–285. https://doi.org/10.1007/s13361-016-1536-4.

(31) Gornischeff, A.; Liigand, J.; Rebane, R. A Systematic Approach toward Comparing Electrospray Ionization Efficiencies of Derivatized and Non-Derivatized Amino Acids and Biogenic Amines. *J Mass Spectrom* **2018**, *53* (10), 997–1004. https://doi.org/10.1002/jms.4272.

(32) Rebane, R.; Kruve, A.; Liigand, J.; Liigand, P.; Gornischeff, A.; Leito, I. Ionization Efficiency Ladders as Tools for Choosing Ionization Mode and Solvent in Liquid Chromatography/Mass Spectrometry. *Rapid Commun Mass Spectrom* **2019**, *33* (23), 1834–1843. https://doi.org/10.1002/rcm.8545.

(33) Liigand, P.; Kaupmees, K.; Kruve, A. Influence of the Amino Acid Composition on the Ionization Efficiencies of Small Peptides. *J Mass Spectrom* **2019**, *54* (6), 481–487. https://doi.org/10.1002/jms.4348.

(34) Tang, Liang.; Kebarle, Paul. Effect of the Conductivity of the Electrosprayed Solution on the Electrospray Current. Factors Determining Analyte Sensitivity in Electrospray Mass Spectrometry. *Anal. Chem.* **1991**, *63* (23), 2709–2715. https://doi.org/10.1021/ac00023a009.

(35) Koppel, I. A.; Taft, R. W.; Anvia, F.; Zhu, S.-Z.; Hu, L.-Q.; Sung, K.-S.; DesMarteau, D. D.; Yagupolskii, L. M.; Yagupolskii, Y. L. The Gas-Phase Acidities of Very Strong Neutral Bronsted Acids. *J. Am. Chem. Soc.* **1994**, *116* (7), 3047–3057. https://doi.org/10.1021/ja00086a038.

(36) Kütt, A.; Tshepelevitsh, S.; Saame, J.; Lõkov, M.; Kaljurand, I.; Selberg, S.; Leito, I. Strengths of Acids in Acetonitrile. *Eur. J. Org. Chem.* **2021**, *2021* (9), 1407–1419. https://doi.org/10.1002/ejoc.202001649.

(37) Kaljurand, I.; Kütt, A.; Sooväli, L.; Rodima, T.; Mäemets, V.; Leito, I.; Koppel, I. A. Extension of the Self-Consistent Spectrophotometric Basicity Scale in Acetonitrile to a Full Span of 28 p K_a Units: Unification of Different Basicity Scales. *J. Org. Chem.* **2005**, *70* (3), 1019–1028. https://doi.org/10.1021/jo048252w.

(38) Perrin, D. D. *Dissociation Constants of Organic Bases in Aqueous Solution*; Butterworths: London, 1965.

(39) Rõõm, E.-I.; Kütt, A.; Kaljurand, I.; Koppel, I.; Leito, I.; Koppel, I. A.; Mishima, M.; Goto, K.; Miyahara, Y. Brønsted Basicities of Diamines in the Gas Phase, Acetonitrile, and Tetrahydrofuran. *Chem. Eur. J.* **2007**, *13* (27), 7631–7643. https://doi.org/10.1002/chem.200700097.

(40) Yang, J.-D.; Cheng, J.-P. *Internet Bond-Energy Databank (*pK_a *and BDE) – IBonD*; v2.0.

(41) Liigand, P.; Kaupmees, K.; Haav, K.; Liigand, J.; Leito, I.; Girod, M.; Antoine, R.; Kruve, A. Think Negative: Finding the Best Electrospray Ionization/MS Mode for Your Analyte. *Anal. Chem.* **2017**, *89* (11), 5665–5668. https://doi.org/10.1021/acs.analchem.7b00096.

(42) Hunter, E. P. L.; Lias, S. G. Evaluated Gas Phase Basicities and Proton Affinities of Molecules: An Update. *J. Phys. Chem. Ref. Data* **1998**, *27* (3), 413–656. https://doi.org/10.1063/1.556018.

(43) Lõkov, M.; Tshepelevitsh, S.; Heering, A.; Plieger, P. G.; Vianello, R.; Leito, I. On the Basicity of Conjugated Nitrogen Heterocycles in Different Media: On the Basicity of Conjugated Nitrogen Heterocycles in Different Media. *Eur. J. Org. Chem.* **2017**, *2017* (30), 4475–4489. https://doi.org/10.1002/ejoc.201700749.

(44) Izutsu, K. *Acid-Base Dissociation Constants in Dipolar Aprotic Solvents*; Chemical data series; Blackwell Scientific Publications ; Distributors, USA, Publishers' Business Services: Oxford ; Boston : Brookline Village, Mass, 1990.
(45) Kaupmees, K.; Trummal, A.; Leito, I. Basicities of Strong Bases in Water: A Computational Study. *Croatica Chemica Acta* **2014**, *87* (4), 385–395. https://doi.org/10.5562/cca2472.
(46) http://www.zirchrom.com/organic.htm.
(47) Zevatskii, Yu. E.; Samoilov, D. V. Empirical Method for Description of Solvent Effect on the Ionization Constants of NH Acids. *Russ. J. Org. Chem.* **2008**, *44* (12), 1737. https://doi.org/10.1134/S1070428008120026.
(48) Oresmaa, L.; Haukka, M.; Vainiotalo, P.; Pakkanen, T. A. Ab Initio Calculations and Mass Spectrometric Determination of the Gas-Phase Proton Affinities of 4,4'-Disubstituted 2,2'-Bipyridines. *J. Org. Chem.* **2002**, *67* (23), 8216–8219. https://doi.org/10.1021/jo026126r.
(49) Lehninger, A. L.; Nelson, D. L.; Cox, M. M. *Lehninger Principles of Biochemistry*, 4th ed.; W.H. Freeman: New York, 2005.
(50) Tshepelevitsh, S.; Kütt, A.; Lõkov, M.; Kaljurand, I.; Saame, J.; Heering, A.; Plieger, P. G.; Vianello, R.; Leito, I. On the Basicity of Organic Bases in Different Media: On the Basicity of Organic Bases in Different Media. *Eur. J. Org. Chem.* **2019**, *2019* (40), 6735–6748. https://doi.org/10.1002/ejoc.201900956.
(51) https://webbook.nist.gov/chemistry/.
(52) Bellobono, I. R.; Favini, G. Ultraviolet Absorption and Protonation Equilibria of Amino- and Nitro-Substituted Pyridines. *J. Chem. Soc. B* **1971**, No. 0, 2034–2037. https://doi.org/10.1039/J29710002034.
(53) Augustin-Nowacka, D.; Chmurzyński, L. A Potentiometric Study of Acid–Base Equilibria of Substituted Pyridines in Acetonitrile. *Analytica Chimica Acta* **1999**, *381* (2), 215–220. https://doi.org/10.1016/S0003-2670(98)00771-5.
(54) *CRC Handbook of Chemistry and Physics, 97th Edition*, 97th edition.; Haynes, W. M., Ed.; CRC Press, 2016.
(55) Dawson, R. M. C. *Data for Biochemical Research*; Clarendon Press: Oxford, 1959.
(56) Perrin, D. D.; International Union of Pure and Applied Chemistry; Commission on Electroanalytical Chemistry. *Dissociation Constants of Organic Bases in Aqueous Solution: Supplement 1972*; Butterworths: London, 1972.
(57) Wood, E. Data for Biochemical Research (Third Edition). *Biochemical Education* **1987**, *15* (2), 97. https://doi.org/10.1016/0307-4412(87)90110-5.
(58) Rumble, J. R.; Lide, D. R.; Bruno, T. J. *CRC Handbook of Chemistry and Physics: A Ready-Reference Book of Chemical and Physical Data.*; 2017.
(59) Tanabe, K.; Misono, M.; Hattori, H.; Ono, Y. *New Solid Acids and Bases: Their Catalytic Properties.*; Elsevier Science: Amsterdam, 2014.
(60) Nachod, F. C.; Zuckerman, J. J. *Determination of Organic Structures by Physical Methods. Vol. 4 Vol. 4*; Academic Press: New York; London (24 Oval Rd, N.W.1), 1971.
(61) Avdeef, A. *Absorption and Drug Development: Solubility, Permeability, and Charge State*; Wiley-Interscience: Hoboken, N.J, 2010.
(62) Kolthoff, I. M.; Chantooni, M. K. Protonation Constants of Very Weak Uncharged Bases in Acetonitrile. *J. Am. Chem. Soc.* **1973**, *95* (26), 8539–8546. https://doi.org/10.1021/ja00807a007.

(63) Bryson, A. The Effects of Substituents on the pK_a Values and N-H Stretching Frequencies of 1- and 2-Naphthylamines. *J. Am. Chem. Soc.* **1960**, *82* (18), 4862–4871. https://doi.org/10.1021/ja01503a029.
(64) Kaupmees, K.; Kaljurand, I.; Leito, I. Influence of Water Content on Basicities in Acetonitrile. *J Solution Chem* **2014**, *43* (7), 1270–1281. https://doi.org/10.1007/s10953-014-0201-4.
(65) *Exploring QSAR*; Hansch, C., Leo, A., Hoekman, D. H., Eds.; ACS professional reference book; American Chemical Society: Washington, DC, 1995.
(66) Klamt, A. *COSMO-RS: From Quantum Chemistry to Fluid Phase Thermodynamics and Drug Design*, 1. ed.; Elsevier: Amsterdam, 2005.
(67) Klamt, A. Conductor-like Screening Model for Real Solvents: A New Approach to the Quantitative Calculation of Solvation Phenomena. *J. Phys. Chem.* **1995**, *99* (7), 2224–2235. https://doi.org/10.1021/j100007a062.
(68) Klamt, A.; Jonas, V.; Bürger, T.; Lohrenz, J. C. W. Refinement and Parametrization of COSMO-RS. *J. Phys. Chem. A* **1998**, *102* (26), 5074–5085. https://doi.org/10.1021/jp980017s.
(69) TURBOMOLE V7.2 2017, a Development of University of Karlsruhe and Forschungszentrum Karlsruhe GmbH, 1989–2007, TURBOMOLE GmbH, since 2007; Available from Http://Www.Turbomole.Com.
(70) Eckert, F.; Klamt, A. Fast Solvent Screening via Quantum Chemistry: COSMO-RS Approach. *AIChE J.* **2002**, *48* (2), 369–385. https://doi.org/10.1002/aic.690480220.
(71) COSMOtherm, Version C3.0, Release 17.05; COSMOlogic GmbH & Co. KG, http://www.Cosmologic.De.
(72) Leito, I.; Koppel, I. A.; Koppel, I.; Kaupmees, K.; Tshepelevitsh, S.; Saame, J. Basicity Limits of Neutral Organic Superbases. *Angew. Chem. Int. Ed.* **2015**, *54* (32), 9262–9265. https://doi.org/10.1002/anie.201503345.
(73) University of Tartu, “UT Rocket.” Share.Neic.No, Doi: 10.23673/PH6N-0144.

SUMMARY IN ESTONIAN

Ionisatsiooni efektiivsus elektropihustusionisatsiooni allikas, seosed analüüdi füüsiko-keemiliste omadustega

Käesoleva uurimistöö peamisteks eesmärkideks oli (a) analüüsida ainete ioniseerumise efektiivsust elektropihustusionisatsiooni allikas (keskendudes monoprotoniseerumisele); (b) koostada ulatuslik skaala ainete suhteliste ionisatsiooniefektiivsuste andmetega; (c) hinnates erinevate aine füsikokeemiliste omaduste mõju ionisatsiooniefektiivsusele elektropihustusionisatsiooni allikas teha sisulisi järedusi ionisatsiooniefektiivsuse ja ainete omaduste vahel (antud solvendis).

On välja töötatud meetod suhteliste ionisatsiooniefektiivsuste mõõtmiseks, mis võimaldas koostada ulatusliku (kokku 344 erinevat ühendit erinevatest aineklassidest) ionisatsiooniefektiivsuste skaala (uuritud solvendis). Multilineaarset regressiooni kasutades analüüsiti valitud 11 parameetri (ühendi aluselisus vees – pK_{aH}(H_2O), ühendi aluselisus atseetonitriilis – pK_{aH}(MeCN), gaasifaasiline aluselisus – GB, protoneeritud molekuli pinna polaarse ala suurus – PSA, protoneeritud molekuli pindla – A, protoneeritud molekuli ruumala – MV, protoneeritud molekuli molekulmass – M+1, molekuli dipoolmoment – d, laengu (de)lokaliseerumine protoneeritud molekuli pinnal – WANS, protoneeritud osakse jaotumine solvendi ja heksaani vahel – log$P_{s/h}$, parameter, mis iseloomustab, kas protoneerumine toimub eelistatult hapnikule – O base) ja ionisatsiooniefektiivsuse seoseid ning jõuti kolme üksteisest veidi erineva mudelini, mis sisuliselt kinnitavad kõik samu seoseid. Võib järeldada, et antud solvendis on aine ionisatsioon (monoprotoneerumisena) elektropihustusionisastiooni allikas määratud peamiselt aine aluselisuse, (pK_{aH}(H_2O)), molekuli suuruse (A või logMV) ja hüdrofoobsuse/lipofiilsuse (log$P_{s/h}$) väärtusega. Saadud mudelite headuse hindamiseks leitud ruutkeskmise hälbe väärtus jääb vahemikku 0.7 kuni 0.8 log*IE* ühikut, mis ei ole piisav täpsete kvantitatiivsete ennustuste tegemiseks, aga võimaldab analüüdi ionisatsiooniefektiivsust elektropihustusionisatsiooni allikas ligikaudselt hinnata.

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PUBLICATIONS

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II **Oss, M**.; Kruve, A.; Herodes, K.; Leito, I. Electrospray Ionization Efficiency Scale of Organic Compounds. *Anal. Chem.* **2010**, *82* (7), 2865–2872. https://doi.org/10.1021/ac902856t.

III Kruve, A.; Kaupmees, K.; Liigand, J.; **Oss, M**.; Leito, I. Sodium adduct formation efficiency in ESI source. *J. Mass Spectrom.* **2013**, 4*8*, 695–702. https://doi.org/10.1002/jms.3218.

IV **Oss, M.**; Tshepelevitsh, S.; Kruve, A.; Liigand, P.; Liigand, J.; Rebane, R.; Selberg, S.; Ets, K.; Herodes, K.; Leito, I. Quantitative Electrospray Ionization Efficiency Scale: 10 Years After. Submitted on 07.05.2021 to *Rapid Commun. Mass Spectrom*.

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Publikatsioonide loetelu

I Leito, I.; Herodes, K.; **Huopolainen, M**.; Virro, K.; Künnapas, A.; Kruve, A.; Tanner, R. Towards the Electrospray Ionization Mass Spectrometry Ionization Efficiency Scale of Organic Compounds. *Rapid Commun. Mass Spectrom.* **2008**, *22* (3), 379–384. https://doi.org/10.1002/rcm.3371.

II **Oss, M**.; Kruve, A.; Herodes, K.; Leito, I. Electrospray Ionization Efficiency Scale of Organic Compounds. *Anal. Chem.* **2010**, *82* (7), 2865–2872. https://doi.org/10.1021/ac902856t.

III Kruve, A.; Kaupmees, K.; Liigand, J.; **Oss, M**.; Leito, I. Sodium adduct formation efficiency in ESI source. *J. Mass Spectrom.* **2013**, 4*8*, 695–702. https://doi.org/10.1002/jms.3218.

IV **Oss, M.**; Tshepelevitsh, S.; Kruve, A.; Liigand, P.; Liigand, J.; Rebane, R.; Selberg, S.; Ets, K.; Herodes, K.; Leito, I. Quantitative Electrospray Ionization Efficiency Scale: 10 Years After. Submitted on 07.05.2021 to *Rapid Commun. Mass Spectrom.*

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