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Radical electrophilicities in solvent

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Abstract An electrophilicity scale for radicals in solution
is reported using the electrophilicity index, an important
quantity in conceptual density functional theory. Five dif-
ferent solvents were chosen, for which the static dielectric
constant covers the entire range of nonpolar to polar
solvents: n-hexane ($\varepsilon_r = 1.8819$), dichloromethane ($\varepsilon_r =
8.9300$), 2-propanol ($\varepsilon_r = 19.2640$), acetonitrile ($\varepsilon_r =
35.6880$) and water ($\varepsilon_r = 78.3553$). The calculations in
solution were carried out within the polarizable continuum
model through the Integral Equation Formalism (IEF-
PCM) approach. For water, also conductor-like screening
model (COSMO) calculations are reported. The electronic
chemical potential remains almost constant when going
from gas phase to solution. However, large decreases in
chemical hardness can be observed, resulting in more
electrophilic radicals compared to the gas phase, and even
influencing the overall order of the previously established
gas-phase scale. Both solvation models (COSMO and
IEF-PCM) lead to essentially the same results.

Keywords Electrophilicity index · Conceptual DFT ·
Solvent effects · Chemical hardness

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1 Introduction

Recently, we presented a radical electrophilic scale, global
as well as local, for a set of 35 organic radicals in the gas
phase (where the gas phase refers to calculations carried
out on isolated molecules without the presence of solvent)
[1]. This scale, based on the electrophilicity index as
introduced by Parr et al. [2] (for a recent review see
Chattaraj et al. [3]) and defined as the electronic chemical
potential squared over two times the chemical hardness,
has proven its value since assisting in classifying radical
systems [4–10], explaining reaction behavior and intro-
ducing other chemical concepts like radical stability
[11–14]. The question arises, though, as to whether the
order of this gas-phase electrophilicity scale still holds for
radicals in solution. Solvent effects can be very significant
when considering electrophile/nucleophile interactions
[15–17]. However, there is still a lot of debate about
whether or in which cases gas-phase properties could be
employed to describe concepts and reactions in solvent.
Parr et al. [2], for instance, stated that gas-phase properties
like the electrophilicity index can determine the reactivity
in the case of for instance "a close encounter between the
reacting species in a biological system," because "solvent
molecules have already been pushed out." Another
example is homolysis in solution where a caged radical pair
is formed, that is, solvent molecules surround the initially
formed radical pair, but none of the solvent molecules
interferes between the two radical fragments. In order to
escape the cage, one of the radicals needs to diffuse
through the solvent [18]. If the diffusion rate is higher than
the cage recombination rate, the radical fragments become
"free radicals." When such radicals approach each other
from a larger distance, they will feel the effect of each
other's global electrophilicity, although affected by the

presence of solvent molecules. Of course, not only can the presence of solvent alter the reactivity properties of the radical system; also, stronger radical–solvent interactions can come into play like radical addition to the solvent molecule, orbital interactions or the formation of a charge transfer complex [19].

Several studies have been performed to obtain more information about the effect of solvent on the properties and reactivity of different species. In 1986 Pearson estimated solution ionization potentials and electron affinities to obtain the effective electronic chemical potential and chemical hardness in solution for a set of neutral and charged species [20]. He concluded that the absolute electronegativity for small neutral molecules hardly changes going from gas phase to solvent, while the changes are much more pronounced for charged molecules. The chemical hardness values showed that neutral molecules become much softer in solution, although Pearson questioned their practical utility. De Luca et al. [21] applied three different approaches to compute the chemical hardness, already widely tested in gas phase, to species in solution, in order to evaluate the solvent effects on the chemical hardness. They found that for methods based on orbital energies (HOMO–LUMO gap and the internally resolved hardness tensor approach based on fractional occupation numbers), only a small dependency of the hardness on the solvent exists, in contradiction to the method based on total energy differences (from vertical electron affinity and vertical ionization potential) for which 50 % decreases in hardness values were detected.

Concerning the global electrophilicity index ω, Pérez et al. [22] looked into the effect of solvent on this particular

property for a set of 18 electrophiles, using Parr's formula [2], applied to the solution phase:

$$\omega_{\text{solv}} = \frac{\mu_{\text{solv}}^2}{2\eta_{\text{solv}}} \cong \frac{(IP_{\text{solv}} + EA_{\text{solv}})^2}{8(IP_{\text{solv}} - EA_{\text{solv}})} \tag{1}$$

where μ_{solv} is the electronic chemical potential [23] and η_{solv} the chemical hardness [24] in solvent. These two quantities were calculated by using the vertical ionization potential IP and electron affinity EA [20, 25], evaluated in solution. The electrophilicity index measures the energy stabilization when an optimal electronic charge transfer from the environment to the system occurs. Pérez et al. concluded that the electronic chemical potential for (most of) the series of neutral and more covalent electrophiles is almost unaffected by the solvent and that solvation makes the electrophile ligands softer than in the gas phase, again in agreement with Pearson's predictions. This means that for neutral systems, an enhancement of the electrophilicity is seen, controlled by changes in chemical hardness and the solvation energy, with a very small contribution from the electronic chemical potential of solvation. It also appears that μ_{solv} is dependent on the polarization charges induced in the environment within the reaction field approach, and according to that same approach, η_{solv} is independent of those charges [22, 26]. Meneses et al. [26] performed calculations using the continuum approach as well as the super-molecular approach to incorporate solvent effects. They discovered that "independent of the sign and magnitude of the charge, the chemical hardness always decreases upon solvation because the electrostatic potential decreases as the effective radius (solute radius plus a solvation layer) of the solute increases." However, there

Fig. 1 Correlation between the vertical electron affinity EA (in eV) and the reciprocal of the static dielectric constant ε_r^{-1} for the 2-hydroxyprop-2-yl radical. At $\varepsilon_r^{-1} = 1$, the *red point* is the computed gas-phase EA and the *black point* is the extrapolated one
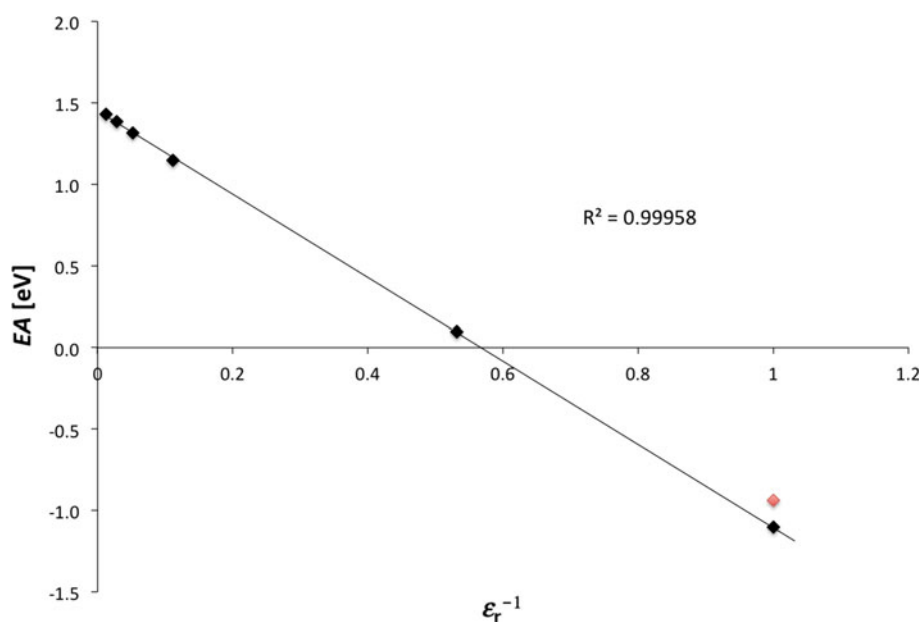
Table 1 The electronic chemical potential μ for the gas phase and 5 different solvents (using IEFPCM and COSMO) in eV

Radical	Gas phase	n-Hexane[a]	Dichloromethane[a]	2-Propanol[a]	Acetonitrile[a]	Water[a]	Water[b]
C(OH)(CH$_3$)$_2$	−3.0	−3.0	−3.0	−3.0	−3.0	−3.0	−3.0
C(CH$_3$)$_3$	−3.2	−3.2	−3.2	−3.2	−3.2	−3.2	−3.1
CH$_2$OH	−3.6	−3.6	−3.6	−3.6	−3.6	−3.6	−3.5
CH(CH$_3$)$_2$	−3.5	−3.5	−3.5	−3.5	−3.5	−3.5	−3.4
NO	−4.5	−4.4	−4.4	−4.4	−4.4	−4.4	−4.3
CH$_2$CH$_3$	−4.0	−4.0	−4.0	−4.0	−4.0	−4.0	−3.9
CH$_2$CH$_2$CH$_3$	−4.1	−4.0	−4.1	−4.1	−4.1	−4.1	−4.0
CH$_2$C$_6$H$_4$(OCH$_3$)	−3.6	−3.6	−3.7	−3.7	−3.7	−3.7	−3.7
CH$_3$C(O)	−4.3	−4.3	−4.2	−4.2	−4.2	−4.2	−4.2
CF$_2$CH$_3$	−4.6	−4.6	−4.6	−4.6	−4.6	−4.6	−4.6
CH$_2$C$_6$H$_4$(CH$_3$)	−3.8	−3.8	−3.9	−3.9	−3.9	−3.9	−3.9
CH$_2$CHCH$_2$	−4.2	−4.2	−4.2	−4.2	−4.2	−4.2	−4.2
HC(O)	−4.8	−4.7	−4.7	−4.7	−4.7	−4.6	−4.6
CH$_3$	−4.9	−4.8	−4.8	−4.8	−4.8	−4.8	−4.7
CH$_2$C$_6$H$_5$	−4.0	−4.0	−4.0	−4.1	−4.1	−4.1	−4.0
CHCH$_2$	−4.9	−4.9	−4.9	−4.9	−4.9	−4.9	−4.8
CH$_2$C$_6$H$_4$(F)	−4.0	−4.0	−4.0	−4.0	−4.1	−4.1	−4.0
C$_6$H$_4$(CH$_3$)	−4.8	−4.9	−5.0	−5.0	−5.0	−5.0	−5.0
C$_6$H$_4$(OCH$_3$)	−4.9	−4.9	−5.0	−5.1	−5.1	−5.1	−5.1
C$_6$H$_5$	−4.9	−4.9	−5.0	−5.0	−5.0	−5.1	−5.0
CCl$_3$	−4.9	−4.8	−4.8	−4.8	−4.8	−4.8	−4.8
C(CN)(CH$_3$)$_2$	−4.8	−4.7	−4.7	−4.7	−4.7	−4.7	−4.7
C$_6$H$_4$(F)	−5.2	−5.2	−5.3	−5.3	−5.3	−5.3	−5.2
CF$_3$	−6.0	−5.9	−5.9	−5.9	−5.9	−5.9	−5.8
NF$_2$	−6.6	−6.6	−6.6	−6.5	−6.5	−6.5	−6.5
C$_6$H$_4$(CN)	−5.6	−5.5	−5.4	−5.4	−5.4	−5.4	−5.3
NH$_2$	−6.7	−6.7	−6.7	−6.7	−6.7	−6.7	−6.5
CH$_2$C$_6$H$_4$(CN)	−4.8	−4.7	−4.6	−4.6	−4.6	−4.6	−4.5
OCH$_3$	−6.0	−6.1	−6.1	−6.1	−6.1	−6.1	−6.1
Tert-butoxycarbonylmethyl	−5.7	−5.7	−5.7	−5.7	−5.7	−5.7	−5.7
OCH$_2$CH$_3$	−5.9	−5.9	−6.0	−6.0	−6.0	−6.0	−6.0
OCH$_2$C(CH$_3$)$_3$	−5.7	−5.7	−5.9	−5.9	−5.9	−5.9	−5.9
CH$_2$CN	−5.9	−5.9	−5.8	−5.8	−5.8	−5.8	−5.7
SCH$_3$	−5.6	−5.6	−5.6	−5.6	−5.6	−5.6	−5.6
H	−7.3	−7.0	−6.8	−6.7	−6.7	−6.7	–
SCH$_2$CH$_3$	−5.5	−5.5	−5.6	−5.6	−5.6	−5.6	−5.5
NO$_2$	−6.6	−6.5	−6.5	−6.5	−6.5	−6.5	−6.3
OC$_6$H$_5$	−5.5	−5.5	−5.5	−5.5	−5.5	−5.5	−5.5
Tosyl	−5.6	−5.6	−5.7	−5.8	−5.8	−5.8	−5.8
Phenylsulfonyl	−5.7	−5.8	−5.9	−5.9	−5.9	−5.9	−5.9
OH	−7.5	−7.5	−7.5	−7.5	−7.5	−7.5	−7.4
SH	−6.4	−6.3	−6.3	−6.3	−6.3	−6.3	−6.2
2,2-Dimethyl-4,6-dioxo-1,3-dioxan-5-yl	−6.7	−6.7	−6.7	−6.7	−6.7	−6.7	−6.7
Br	−7.8	−7.7	−7.6	−7.6	−7.6	−7.6	−7.5
Cl	−8.4	−8.3	−8.3	−8.3	−8.3	−8.3	−8.2
F	−10.6	−10.6	−10.6	−10.6	−10.6	−10.6	−10.5
CN	−9.2	−9.1	−9.0	−9.0	−9.0	−9.0	−9.0

[a] Using IEF-PCM in Gaussian09

[b] Using COSMO in MOLPRO 2010.1

remains the problem of rigorously predicting the variations in chemical hardness for a system coupled to an external electric field.

In the context of our ongoing efforts in the field of conceptual DFT [27, 28], we will compute the electronic chemical potential, the chemical hardness and both the global and the local electrophilicity index for a set of uncharged radical systems in solvent. The resulting radical electrophilicity scales in solvent will be compared to the previously reported gas-phase scale. For water as a solvent, two different solvation methods (IEF-PCM and COSMO) will be applied to exclude artificial effects inherent to one of the two approaches.

2 Computational details

All calculations were performed within the Kohn–Sham framework. Geometries of all radical species were optimized in solvent at the B3LYP/6-311+G(d,p) level of theory [29–31] using both the polarizable continuum model through the integral equation formalism (IEF-PCM), as implemented in Gaussian09 [32], and the conductor-like screening model (COSMO), as implemented in MOLPRO 2010.1 [33]. The IEF-PCM method creates the solute cavity via a set of overlapping spheres [34–36]. The COSMO [37] model differs from the PCM model in that a scaled conductor boundary condition is used instead of the much more complicated dielectric boundary condition for the calculation of the polarization charges of a molecule in a continuum like with IEF-PCM. In the case of IEF-PCM, frequency calculations at the same level of theory were performed to ensure that all structures are minima on the potential energy surface.

3 Results and discussion

For this study, we use our extended database [11] of 47 radical systems, so 12 more than our previously published gas-phase radical electrophilicity scale [1], including C-, N-, O- and S-centered radicals, as well as some halogens, thus comprising a representative set of radicals for applications in organic chemistry. The structures can be retrieved from the Supporting Information. In order to compute the electrophilicity index, Parr's definition was applied to the solution phase as shown in Eq. 1, using IEF-PCM and—in the case of water—COSMO as the implicit solvation models. Five solvents were chosen, for which the static dielectric constant covers the entire range of nonpolar to polar solvents: n-hexane ($\varepsilon_r = 1.8819$), dichloromethane ($\varepsilon_r = 8.9300$), 2-propanol ($\varepsilon_r = 19.2640$), acetonitrile ($\varepsilon_r = 35.6880$) and water ($\varepsilon_r = 78.3553$).

3.1 Electronic chemical potential

The electronic chemical potential in solvent μ_{solv} is calculated using the finite difference approach as follows:

$$\mu_{\mathrm{solv}} \cong -\frac{IP_{\mathrm{solv}} + EA_{\mathrm{solv}}}{2}. \tag{2}$$

For 10 out of the 47 radical systems, negative electron affinities were found. Cardenas et al. [38] found that, despite the ongoing debate about using negative instead of zero EAs, in the case of the chemical hardness it makes no difference which approach is used for metastable anions, and we expect the same results for the electronic chemical potential. In this paper, we choose to use negative EAs instead of zero ones. However, electron affinity calculations of metastable anions, mainly found in the gas phase, are mostly unreliable using standard quantum chemical techniques due to the temporary nature of those ions. One reliable possibility is to extrapolate the gas-phase EA from a series of solvent-based EAs, since the EAs correlate linearly with the reciprocal of the dielectric constant ε_r [39]. In order to check the accuracy of our computed gas-phase negative EAs, we compared those values with the values extrapolated from the solvent-phase EA calculations using IEF-PCM. The average deviation was around 0.1 eV with a maximal deviation of around 0.15 eV for the 2-hydroxyprop-2-yl radical as shown in Fig. 1. These deviations on the (negative) EAs have a minor influence on the electronic chemical potential, the chemical hardness and the electrophilicity indices since these electronic properties are dominated by the much larger (in absolute value) IPs.

Table 1 contains both the gas-phase and solvent μ-values, using IEF-PCM as the solvation model. For water, also the COSMO values are listed since this model works best for solvents with a large dielectric constant value. The COSMO values are very close to the IEF-PCM values, on the average within 0.1 eV. We find that the electronic chemical potential remains almost constant (average change of 2 %) going from gas phase to water with the largest change, an increase of 7 %, observed for the hydrogen atom. When comparing the low-to-high value ranking of the gas phase and water data, no important shifts are observed, which is in line with the literature, which says that for uncharged species the electronic chemical potential is in most cases almost unaffected by the solvent [20, 22].

3.2 Chemical hardness

Much larger changes are seen for the chemical hardness values. The chemical hardness in solvent η_{solv} is computed as follows, again using the finite difference approach:

$$\eta_{\mathrm{solv}} \cong IP_{\mathrm{solv}} - EA_{\mathrm{solv}}. \tag{3}$$

Table 2 The chemical hardness η for the gas phase and 5 different solvents (using IEFPCM and COSMO) in eV

Radical	Gas phase	n-Hexane[a]	Dichloromethane[a]	2-Propanol[a]	Acetonitrile[a]	Water[a]	Water[b]
$C(OH)(CH_3)_2$	8.0	5.8	3.8	3.4	3.3	3.2	3.0
$C(CH_3)_3$	7.9	5.8	3.8	3.5	3.3	3.3	3.0
CH_2OH	9.2	6.6	4.1	3.8	3.6	3.5	3.3
$CH(CH_3)_2$	8.4	6.1	4.0	3.6	3.5	3.4	3.2
NO	11.6	8.7	6.0	5.6	5.4	5.3	4.9
CH_2CH_3	9.1	6.5	4.2	3.8	3.7	3.6	3.3
$CH_2CH_2CH_3$	8.6	6.2	4.0	3.7	3.6	3.5	3.2
$CH_2C_6H_4(OCH_3)$	6.1	4.2	2.5	2.2	2.1	2.1	1.9
$CH_3C(O)$	8.7	6.3	4.0	3.7	3.6	3.5	3.3
CF_2CH_3	9.6	7.2	4.9	4.6	4.5	4.4	4.1
$CH_2C_6H_4(CH_3)$	6.2	4.3	2.6	2.3	2.2	2.1	2.0
CH_2CHCH_2	7.8	5.4	3.3	3.0	2.9	2.8	2.6
$HC(O)$	9.9	7.1	4.6	4.2	4.1	4.0	3.7
CH_3	10.0	7.2	4.6	4.2	4.0	3.9	3.6
$CH_2C_6H_5$	6.4	4.5	2.6	2.4	2.3	2.2	2.0
$CHCH_2$	9.5	6.9	4.5	4.1	4.0	3.9	3.6
$CH_2C_6H_4(F)$	6.5	4.5	2.7	2.4	2.3	2.2	2.1
$C_6H_4(CH_3)$	8.3	6.2	4.2	3.9	3.8	3.7	3.5
$C_6H_4(OCH_3)$	8.4	6.3	4.3	4.0	3.9	3.8	3.6
C_6H_5	8.5	6.3	4.3	4.0	3.8	3.7	3.5
CCl_3	8.0	5.8	3.8	3.5	3.4	3.3	3.2
$C(CN)(CH_3)_2$	7.6	5.5	3.5	3.2	3.1	3.0	2.8
$C_6H_4(F)$	8.7	6.5	4.4	4.1	4.0	3.9	3.7
CF_3	10.8	8.2	5.7	5.4	5.2	5.2	4.9
NF_2	11.9	9.1	6.5	6.2	6.0	5.9	5.6
$C_6H_4(CN)$	8.4	6.3	4.4	4.1	4.0	3.9	3.7
NH_2	12.1	9.1	6.3	5.9	5.7	5.6	5.1
$CH_2C_6H_4(CN)$	6.0	4.2	2.5	2.2	2.1	2.0	1.9
OCH_3	9.5	6.8	4.3	3.9	3.7	3.6	3.2
Tert-butoxycarbonylmethyl	8.3	6.2	4.1	3.8	3.7	3.6	3.4
OCH_2CH_3	8.9	6.4	4.0	3.7	3.5	3.4	3.1
$OCH_2C(CH_3)_3$	8.2	6.0	3.9	3.5	3.4	3.3	3.0
CH_2CN	8.8	6.3	4.1	3.8	3.6	3.5	3.3
SCH_3	7.5	5.0	2.6	2.3	2.2	2.1	1.9
H	12.8	9.1	5.7	5.2	5.0	4.9	–
SCH_2CH_3	7.2	4.9	2.6	2.3	2.1	2.1	2.0
NO_2	10.3	7.6	5.1	4.8	4.6	4.5	4.1
OC_6H_5	6.7	4.6	2.7	2.4	2.3	2.2	2.1
Tosyl	6.8	4.8	3.0	2.7	2.6	2.5	2.4
Phenylsulfonyl	7.0	5.0	3.1	2.8	2.7	2.6	2.5
OH	11.6	8.3	5.3	4.9	4.7	4.6	3.9
SH	8.1	5.3	2.8	2.4	2.3	2.2	2.1
2,2-Dimethyl-4,6-dioxo-1,3-dioxan-5-yl	7.5	5.5	3.7	3.4	3.3	3.2	3.0
Br	8.4	5.6	3.1	2.7	2.6	2.5	2.2
Cl	9.4	6.4	3.7	3.3	3.2	3.1	2.8
F	14.3	10.7	7.5	7.1	6.9	6.8	6.3
CN	10.2	7.4	4.9	4.5	4.4	4.3	4.0

[a] Using IEF-PCM in Gaussian09

[b] Using COSMO in MOLPRO 2010.1

Fig. 2 The chemical hardness for a total of 47 radicals in gas phase and different solvents
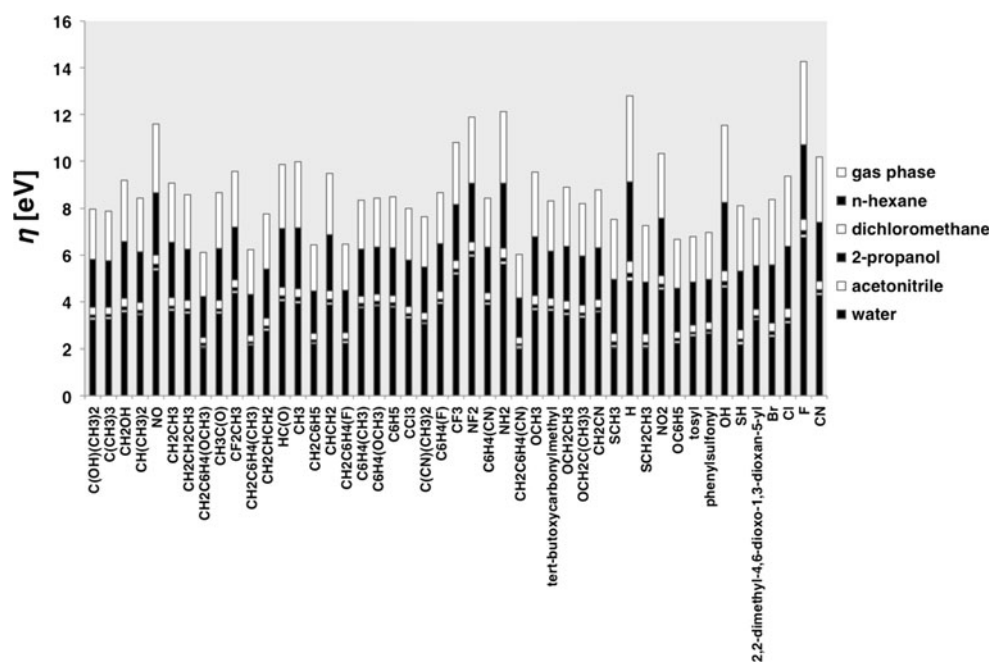
All gas phase, IEF-PCM and COSMO values can be retrieved from Table 2. Again, for water, the COSMO values do not differ much from the IEF-PCM values, with the COSMO values on the average being 0.2–0.3 eV lower than the PCM values but with a correlation of more than 99 %. Figure 2 lists η for all radical systems ordered according to the gas-phase electrophilicities, starting with the values for water and adding up until the gas-phase values. All radicals become much softer in solvent, with changes from 50 to 73 % when gas-phase and water values are compared. The biggest changes are observed for the aliphatic thiyl radicals (R–S$^{\cdot}$), the para-substituted benzyl radicals, the phenoxy radical, chlorine and bromine, so radicals including highly polarizable (soft) atoms or groups. The smallest changes are observed for the para-substituted phenyl radicals, the N- and F-centered radicals as well as those radicals containing fluorine atoms (with the exception of *p*-fluorobenzyl). The first strong decrease (46.5 % of the overall difference is due to the gas phase/*n*-hexane change) can be linked to the actual solvation. This agrees with the findings of Meneses et al. [26]. The second strong decrease of 43.0 % (going from *n*-hexane to the more polar dichloromethane) is due to the increasing polarity of the solvent. Further changes are 6.0 % going from dichloromethane to 2-propanol, 2.4 % to acetonitrile and finally 1.5 % to water. These changes, in terms of percentage (100 % being the percentage when going from gas phase to water), are constant for every radical in the database and can be traced back to the estimation for

changes in η upon solvation, derived from the approximate (generalized) reaction field Born's model: [22, 26, 40]

$$\Delta E_{\text{solv}} = -\frac{1}{2}\left(1 - \frac{1}{\varepsilon_r}\right)\sum_A \sum_B Q_A Q_B \Gamma_{AB} \tag{4}$$

where Q_A and Q_B are the net charges of atoms A and B in the molecule and Γ_{AB} is a solute–solvent interaction integral. To get the estimation for the changes in chemical hardness in solution, we differentiate Eq. 4 twice with respect to the net charge:

$$\Delta\eta_{\varepsilon_r \leftarrow 1} = -\left(1 - \frac{1}{\varepsilon_r}\right)\sum_A \Gamma_{AA}. \tag{5}$$

Note that within the continuum model of solvent effects, the changes in η are predicted to be negative. For the changes in percentage in η going from one solvent to another, Eq. 5 can be rewritten as follows:

$$\frac{\Delta\eta_{\varepsilon_{r,2} \leftarrow \varepsilon_{r,1}}}{\Delta\eta_{\varepsilon_{r,\max} \leftarrow 1}} = \frac{\left(\frac{1}{\varepsilon_{r,2}} - \frac{1}{\varepsilon_{r,1}}\right)}{\left(1 - \frac{1}{\varepsilon_{r,\max}}\right)} \tag{6}$$

where $\varepsilon_{r,\max}$ stands for the maximal dielectric constant in our list, namely for water. The chemical hardness change in percentage is not a function of the type of radical within the solvent models applied in this study. This implies that for any solvent with a certain dielectric constant, the chemical hardness of any radical system listed in this work can be interpolated from the values in Table 2 with a good accuracy.

Table 3 The global electrophilicity index ω for the gas phase [1] and 5 different solvents (using IEFPCM and COSMO) in eV

Radical	Gas phase	n-Hexane[a]	Dichloromethane[a]	2-Propanol[a]	Acetonitrile[a]	Water[a]	Water[b]
$C(OH)(CH_3)_2$	0.581	0.774	1.217	1.339	1.395	1.434	1.492
$C(CH_3)_3$	0.651	0.870	1.336	1.459	1.516	1.556	1.632
CH_2OH	0.717	0.969	1.535	1.686	1.756	1.804	1.834
$CH(CH_3)_2$	0.720	0.978	1.530	1.675	1.742	1.787	1.842
NO	0.876	1.139	1.607	1.712	1.759	1.789	1.876
CH_2CH_3	0.891	1.220	1.925	2.108	2.191	2.248	2.313
$CH_2CH_2CH_3$	0.980	1.311	2.035	2.225	2.313	2.373	2.475
$CH_2C_6H_4(OCH_3)$	1.033	1.533	2.750	3.102	3.269	3.385	3.521
$CH_3C(O)$	1.083	1.443	2.224	2.428	2.521	2.585	2.681
CF_2CH_3	1.113	1.458	2.136	2.301	2.375	2.425	2.516
$CH_2C_6H_4(CH_3)$	1.157	1.685	2.946	3.307	3.477	3.595	3.722
CH_2CHCH_2	1.161	1.646	2.730	3.023	3.158	3.251	3.386
$HC(O)$	1.172	1.565	2.353	2.547	2.634	2.694	2.816
CH_3	1.209	1.632	2.524	2.751	2.854	2.924	3.046
$CH_2C_6H_5$	1.239	1.798	3.111	3.482	3.656	3.777	3.914
$CHCH_2$	1.252	1.711	2.661	2.902	3.011	3.086	3.210
$CH_2C_6H_4(F)$	1.265	1.807	3.046	3.391	3.552	3.663	3.781
$C_6H_4(CH_3)$	1.384	1.886	2.919	3.182	3.302	3.383	3.533
$C_6H_4(OCH_3)$	1.398	1.909	2.953	3.216	3.335	3.416	3.556
C_6H_5	1.405	1.913	2.946	3.207	3.325	3.406	3.553
CCl_3	1.480	1.999	3.028	3.280	3.393	3.470	3.573
$C(CN)(CH_3)_2$	1.495	2.051	3.179	3.463	3.592	3.680	3.857
$C_6H_4(F)$	1.579	2.101	3.120	3.370	3.482	3.559	3.694
CF_3	1.672	2.159	3.016	3.207	3.292	3.348	3.445
NF_2	1.849	2.391	3.287	3.478	3.560	3.615	3.795
$C_6H_4(CN)$	1.857	2.384	3.366	3.602	3.707	3.778	3.897
NH_2	1.871	2.468	3.543	3.786	3.893	3.964	4.216
$CH_2C_6H_4(CN)$	1.878	2.630	4.319	4.787	5.005	5.157	5.346
OCH_3	1.918	2.720	4.413	4.848	5.047	5.182	5.872
Tert-butoxycarbonylmethyl	1.930	2.607	3.949	4.283	4.434	4.537	4.750
OCH_2CH_3	1.940	2.747	4.483	4.939	5.148	5.290	5.921
$OCH_2C(CH_3)_3$	1.959	2.754	4.449	4.895	5.099	5.239	5.761
CH_2CN	2.003	2.715	4.100	4.435	4.585	4.686	4.921
SCH_3	2.054	3.103	5.939	6.849	7.295	7.611	7.915
H	2.063	2.662	4.001	4.346	4.503	4.610	–
SCH_2CH_3	2.078	3.121	5.935	6.838	7.279	7.593	7.791
NO_2	2.118	2.821	4.096	4.388	4.517	4.603	4.898
OC_6H_5	2.236	3.245	5.577	6.234	6.542	6.756	7.267
Tosyl	2.283	3.273	5.501	6.096	6.377	6.571	7.021
Phenylsulfonyl	2.358	3.345	5.514	6.094	6.361	6.545	6.959
OH	2.462	3.420	5.319	5.785	5.994	6.135	6.943
SH	2.520	3.755	7.054	8.101	8.612	8.973	9.345
2,2-Dimethyl-4,6-dioxo-1,3-dioxan-5-yl	3.017	4.078	6.095	6.582	6.799	6.947	7.279
Br	3.614	5.295	9.405	10.610	11.182	11.581	12.672
Cl	3.772	5.439	9.224	10.265	10.749	11.083	11.884
F	3.954	5.238	7.424	7.899	8.106	8.244	8.762
CN	4.119	5.607	8.397	9.050	9.339	9.534	10.156

[a] Using IEF-PCM in Gaussian09

[b] Using COSMO in MOLPRO 2010.1

Fig. 3 Correlation of the global electrophilicity index in water, calculated with IEF-PCM in Gaussian09 and with COSMO in MOLPRO 2010.1
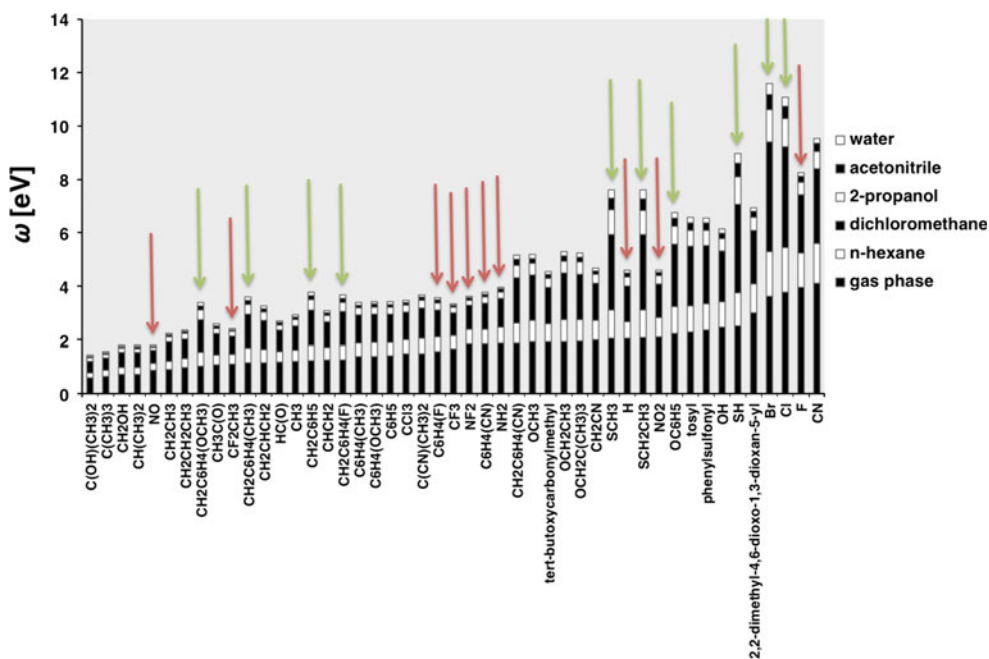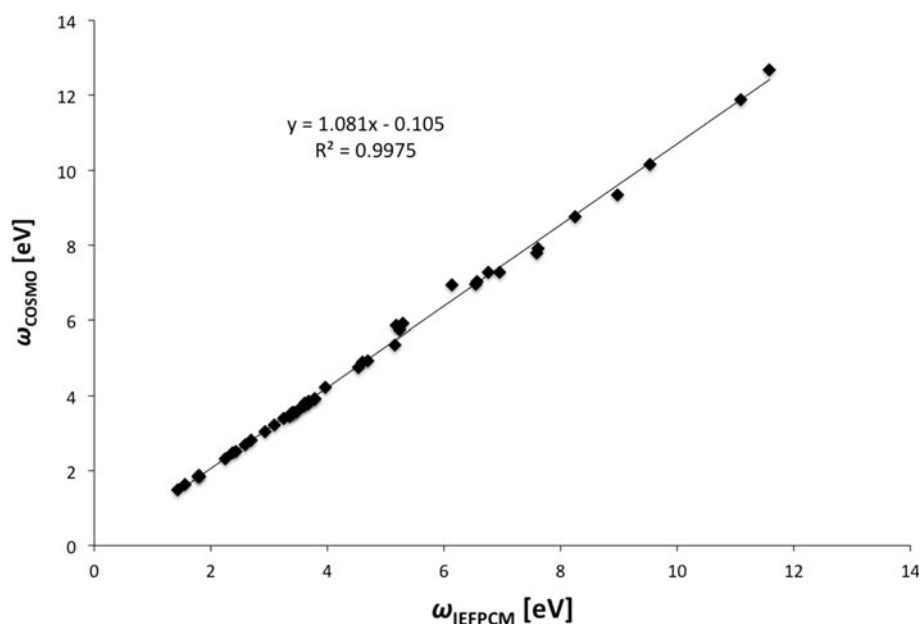

$$y = 1.081x - 0.105$$
$$R^2 = 0.9975$$

Fig. 4 Global electrophilicity index ω for a total of 47 radicals in gas phase and different solvents. *Green arrows*: radicals with the biggest increase in η. *Red arrows*: radicals with the lowest increase in η, going from gas phase to water

3.3 Global electrophilicity index

Combining the solvent effects on μ and η, we can determine the effect on the radical electrophilicity index ω. The values for ω in gas phase and solvent (IEF-PCM and COSMO) can be found in Table 3. In Fig. 3 the correlation between the IEF-PCM and COSMO electrophilicity values

is depicted. The agreement between the two implicit solvation models is excellent with a correlation coefficient of 0.9975 and an almost perfectly linear 1-to-1 correspondence (slope of 1.081 and intercept of −0.105 eV). On the basis of this correlation, artifacts induced by the use of one of the two solvation models can be excluded. Figure 4 shows the global electrophilicity index for all radicals,

Table 4 The local electrophilicity index, condensed to the radical center, ω_{rc}^+, for the gas phase and 5 different solvents (using IEFPCM) in eV

Radical	Gas phase	n-Hexane[a]	Dichloromethane[a]	2-Propanol[a]	Acetonitrile[a]	Water[a]
$C(OH)(CH_3)_2$	0.254	0.387	0.697	0.786	0.829	0.858
$C(CH_3)_3$	0.376	0.544	0.849	0.923	0.964	0.993
CH_2OH	0.447	0.705	1.348	1.519	1.609	1.672
$CH(CH_3)_2$	0.460	0.717	1.285	1.440	1.509	1.556
NO	0.499	0.655	1.074	1.187	1.240	1.276
CH_2CH_3	0.502	0.763	1.423	1.618	1.710	1.775
$CH_2CH_2CH_3$	0.537	0.766	1.292	1.435	1.501	1.547
$CH_2C_6H_4(OCH_3)$	0.546	0.818	1.495	1.693	1.786	1.851
$CH_3C(O)$	0.555	0.735	1.059	1.133	1.165	1.187
CF_2CH_3	0.559	0.756	1.220	1.321	1.378	1.417
$CH_2C_6H_4(CH_3)$	0.571	0.843	1.503	1.693	1.782	1.844
CH_2CHCH_2	0.594	0.928	1.716	1.938	2.042	2.114
$HC(O)$	0.611	0.893	1.439	1.568	1.627	1.668
CH_3	0.621	0.955	1.707	1.920	2.019	2.087
$CH_2C_6H_5$	0.653	0.949	1.636	1.828	1.917	1.980
$CHCH_2$	0.654	0.887	1.391	1.520	1.578	1.618
$CH_2C_6H_4(F)$	0.693	1.015	1.709	1.891	1.975	2.033
$C_6H_4(CH_3)$	0.693	0.961	1.516	1.655	1.718	1.761
$C_6H_4(OCH_3)$	0.698	0.998	1.702	1.900	1.993	2.058
C_6H_5	0.699	0.960	1.484	1.615	1.675	1.715
CCl_3	0.712	1.000	1.631	1.797	1.872	1.924
$C(CN)(CH_3)_2$	0.767	1.037	1.540	1.657	1.709	1.744
$C_6H_4(F)$	0.781	1.164	1.995	2.218	2.321	2.391
CF_3	0.808	1.192	2.036	2.259	2.362	2.432
NF_2	0.811	1.189	2.015	2.235	2.336	2.405
$C_6H_4(CN)$	0.824	1.176	1.952	2.157	2.250	2.314
NH_2	0.929	1.323	2.149	2.363	2.460	2.527
$CH_2C_6H_4(CN)$	1.062	1.455	2.268	2.472	2.564	2.627
OCH_3	1.183	1.544	2.200	2.349	2.415	2.460
Tert-butoxycarbonylmethyl	1.188	1.612	2.523	2.757	2.864	2.936
OCH_2CH_3	1.208	1.653	2.553	2.779	2.881	2.951
$OCH_2C(CH_3)_3$	1.257	1.651	2.316	2.459	2.522	2.563
CH_2CN	1.286	1.755	2.682	2.908	3.011	3.080
SCH_3	1.311	1.942	3.295	3.656	3.819	3.931
H	1.330	1.945	3.259	3.607	3.766	3.876
SCH_2CH_3	1.416	2.034	3.377	3.724	3.882	3.990
NO_2	1.423	1.959	3.016	3.276	3.393	3.472
OC_6H_5	1.715	2.665	5.277	6.117	6.529	6.821
Tosyl	1.754	2.713	5.341	6.189	6.605	6.900
Phenylsulfonyl	1.822	2.410	3.488	3.734	3.843	3.915
OH	2.063	2.662	4.001	4.346	4.503	4.610
SH	2.378	3.314	5.185	5.645	5.851	5.991
2,2-Dimethyl-4,6-dioxo-1,3-dioxan-5-yl	2.475	3.702	6.999	8.049	8.560	8.923
Br	2.687	3.737	5.777	6.265	6.482	6.629
Cl	3.614	5.295	9.405	10.610	11.182	11.581
F	3.772	5.439	9.224	10.265	10.749	11.083
CN	3.954	5.238	7.424	7.899	8.106	8.244

[a] Using IEF-PCM in Gaussian09

Fig. 5 Local electrophilicity index, condensed on the radical center, ω_{rc}^+, for a total of 47 radicals in gas phase and different solvents. The *arrows point* to those radicals for which the Fukui function for a nucleophilic attack f_{rc}^+ shows the biggest increase, going from gas phase to water
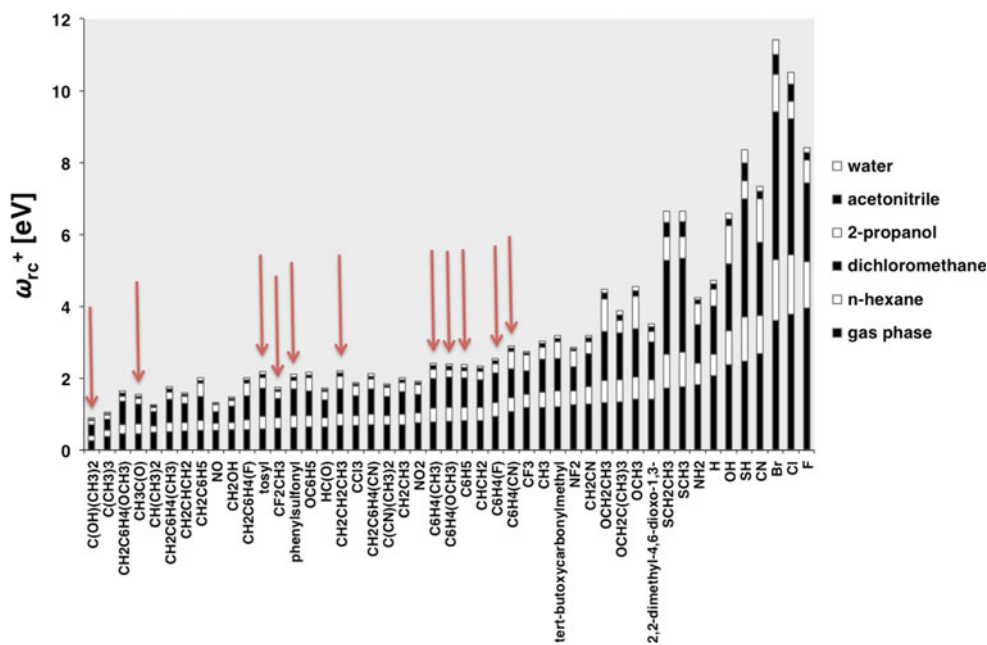
starting with the gas-phase values and increasing up to the water values. Again, the radical systems are ordered according to the gas-phase electrophilicity. All radicals become more electrophilic as the solvent gets more polar. This enhancement in electrophilic power for neutral systems was already highlighted by Pérez et al. [22]. The differences in electrophilicity between the gas phase and the different solvents are following the hardness trend to a great extent. Increasing polarity of the solvent, however, plays a bigger role in the electrophilicity variations, because of the influence of μ_{solv} (squared property in Eq. 1), making the electrophilicity changes not as constant as is the case for the chemical hardness (all in terms of percentage). The overall change ($\omega_{water} - \omega_{gas}$) consists of the following average increases: 24.6 % from gas phase to *n*-hexane, 51.6 % to dichloromethane, 13.4 % to 2-propanol, 6.1 % to acetonitrile and finally 4.2 % to water, showing that increasing polarity has a bigger influence on the electrophilicity index than on the chemical hardness. We see that strong electrophilic and strong nucleophilic radicals are also in solution listed at the ends of the electrophilicity scale. The aliphatic thiyl radicals (R–S·), the benzyl radicals, chlorine and bromine shift toward more electrophilicity because of their softer character in solvent. Fluorine and the radicals with fluorine substituents shift to a less electrophilic place in the table (except for *p*-fluorobenzyl). This confirms that all shifts of importance in the electrophilicity scales can be attributed to the changes in η (as visualized with the green and red arrows in Fig. 4). This also means that for any solvent with a certain dielectric constant, the global electrophilicity of any radical system listed in this work can be calculated from the values in

Tables 1 and 2, using for instance an average value for the electronic chemical potential and an interpolated value (using Eq. 6 as mentioned in the previous section) for the chemical hardness.

3.4 Local electrophilicity index, condensed to the radical center

To describe the electrophilic character of a reactive site within a molecule, a local electrophilicity index $\omega^+(\mathbf{r})$ has been proposed [41, 42]. The condensed-to-atom k variant is defined as: [3]

$$\omega_k^+ = \omega f_k^+ \tag{7}$$

with f^+ the Fukui function for nucleophilic attack [43]. For the computation of f^+, the Finite Differences Approximation (FDA) has been used. In this paper, atomic populations were obtained with the NPA method [44]. For the analysis of electrophile–nucleophile interactions, $\omega^+(\mathbf{r})$ is a better reactivity descriptor than the corresponding Fukui function, because the local electrophilicity index is a product of a global (ω) and a local index ($f^+(\mathbf{r})$). In this paper we solely report values for the local electrophilicity index condensed to the radical center, ω_{rc}^+ (with rc = radical center). The values for ω_{rc}^+ in gas phase and solvents (using IEF-PCM) can be retrieved from Table 4. A mixed influence on ω_{rc}^+ is observed: on the one hand, the variations in chemical hardness (or in global electrophilicity) and on the other hand, the variations in the Fukui function f^+. The largest changes in f^+ are encountered for the phenyl radicals, 2-hydroxyprop-2-yl, *n*-propyl, acetyl, 1,1-difluoroethyl, tosyl and sulfonyl (Fig. 5). They vary

Fig. 6 The influence of the electronic chemical potential and the chemical hardness on the global electrophilicity differences between water and gas phase (*first bar* of each radical) as well as the influence of the global electrophilicity and the Fukui function f^+ on the local electrophilicity differences (*second bar*)
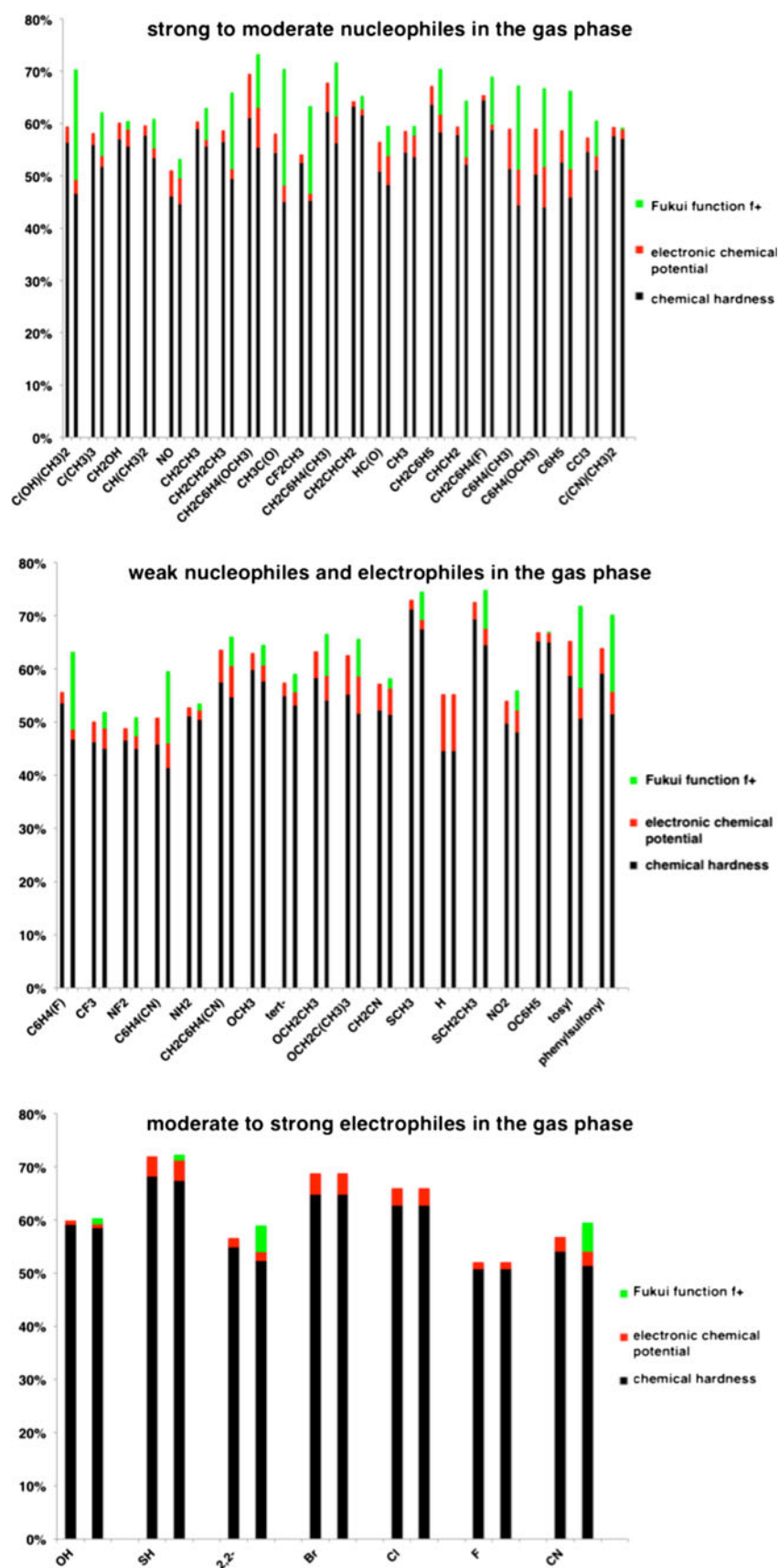
from 0 % for the atomic radicals and the phenoxy radical to as much as 30 % for acetyl. The average increase is 9 %, much smaller than the change in chemical hardness (average decrease of 60 %), but much more pronounced than the change in electronic chemical potential (average change of 2 %). So the local descriptors are affected less by the solvent used, in agreement with Padmanabhan et al. [45]. The local electrophilicity index, however, is a combination of a local and a global descriptor so both local and global changes are combined. As both the local and the global descriptors change upon solvation, it is advisable to use ω_{rc}^+ instead of f_{rc}^+ when investigating and analyzing (intermolecular) electrophile–nucleophile interactions locally. Even though the changes in chemical hardness for any solvent can be predicted from the values in both gas phase and water and from the dielectric constants of those media using Eq. 6, the changes in Fukui function f_{rc}^+ cannot be predicted straightforwardly and therefore require additional calculations in solution.

4 Conclusions

In summary, the global and local electrophilicity scales for radical systems in the gas phase, as introduced by De Vleeschouwer et al. [1], have been extended to electrophilicity scales for a larger set of radical systems in five different solvents, with a dielectric constant ranging from nonpolar to polar solvent situations. Both the global and local electrophilicity indices follow the trend in chemical hardness changes to a great extent, when going from the gas phase to solution, whereas the electronic chemical potential is found to be almost constant over all solvents and in the gas phase. In addition, it is shown that the chemical hardness changes in percentage are not a function of the type of radical, within the solvent models applied in this study, as can be derived from the approximate (generalized) reaction field Born's model. Figure 6 shows the division into portions due to η, μ and f^+, for the changes in ω and ω_{rc}^+ between the gas phase and water. From these plots it can be seen which radicals are affected more by which property, concerning their change in electrophilicity index value. These new radical electrophilicity scales for solvents can be of great importance to organic chemists in the study of radical reactivity and selectivity in the solvents considered here or for other solvents through interpolation, in case of the global electrophilicity index.

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