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ARTICLE *in* JOURNAL OF MOLECULAR STRUCTURE THEOCHEM · SEPTEMBER 2008

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A further exploration of a nucleophilicity index based on the gas-phase ionization potentials

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ARTICLE INFO

Article history:
Received 28 April 2008
Received in revised form 17 June 2008
Accepted 24 June 2008
Available online 3 July 2008

Keywords:
Nucleophilicity
Gas-phase ionization potential
Electrophilicity
Electron-withdrawing group effects
Electron-releasing group effects

ABSTRACT

An empirical nucleophilicity index based on the gas-phase ionization potentials has been recently shown to be useful categorizing and settling the nucleophilicity power of a series of captodative ethylenes reacting in cycloaddition reactions (L.R. Domingo, E. Chamorro, P. Pérez, Journal of Organic Chemistry 73 (2008) 4615–4624). In the present work, the applicability of such model is tested within a broader series of substituted alkenes, substituted aromatic compounds and simple nucleophilic molecules. This index obtained within a Koopman's theorem framework has been evaluated here in both gas and solution phases for several well-known nucleophiles. These results are found to be linearly correlated. Finally, the feasibility of the predictive character of this index has been discussed in comparison to the available experimental nucleophilicities of some amines in water. These results further support and validate the usefulness of such approximation in the modeling of the global nucleophilicity.

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1. Introduction

Density functional theory (DFT) [1] provides a powerful framework for the development and exploration of chemical reactivity theory [2]. Within the complete hierarchy of DFT descriptors, global and local indexes have been shown to be powerful tools in the description of the polar character of cycloaddition reactions [3]. For instance, the electrophilicity index, ω, defined by Parr et al. [4] has been found useful to classify properly the global electrophilicity pattern along a series of reagents currently employed in Diels–Alder (DA) reactions [5]. In such context and when the electronic activation of the π system is achieved through only one type of electron-withdrawing (EW) or electron-releasing (ER) group, linear correlations between the difference in electrophilicity of the reagent pairs, $\Delta\omega$, and the polar character of the cycloaddition can be found. In this case, the electrophilicity index ω [4] categorizes on a unique theoretical scale, the electrophilic character of a series of reagents. However, when the substitution pattern is more complex, including more than one functional group with opposite electronic demand, the nucleophilic character cannot be straightforwardly associated to low values of the ω index. In these cases the difference in electrophilicities does not account for the polar character of the entire reaction. For instance, within this context it has been recently shown that the ω index of the captodative (CD) ethylenes appropriately describes its electrophilic character but not its nucleophilic proclivities [6]. The simplest approach to nucleophilicity is to consider it as the negative value of the gas-phase (intrinsic) ionization potentials, IPs, namely $N = -\mathrm{IP}$, from which high (low) nucleophilicities become naturally associated to low (high) ionization potentials. Within the general idea of this simplified model, the intrinsic nucleophilicity (i.e., associated to the negative of the gas-phase IPs) is thereafter corrected by differential solvation energies of species [7]. In the case of common reagents used on DA cycloaddition reactions this approximation is partially justified on the basis that most of them are neutral molecules and solvents have low dielectric constants. Recently, and in order to handle a working model descriptor for the nucleophilicity, we resort to the highest occupied molecular orbital (HOMO) energies obtained within the Kohn–Sham scheme, introducing thereafter an empirical (relative) nucleophilicity (N) index defined as [6]:

$$N = E_{\mathrm{HOMO(Nu)}}\ (\mathrm{eV}) - E_{\mathrm{HOMO(TCE)}}\ (\mathrm{eV}) \quad (1)$$

Note that this nucleophilicity scale is referred to tetracyanoethylene (TCE) taken as a reference, because it presents the lowest HOMO energy in a large series of molecules already investigated in the context of polar DA cycloadditions [6]. The above N scale is simply the negative of the ionization potential calculated within the framework of molecular orbital theory. Within the framework of Hartree–Fock, this is justified in terms of the Koopmans' theorem, yielding a scale with an arbitrary shifting of the origin. This choice allows us conveniently to handle a nucleophilicity scale of

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doi:10.1016/j.theochem.2008.06.022

positive values. Within the Kohn–Sham DFT scheme, the orbital energies do not have any physical meaning except to that implied from the Janak's theorem (e.g., the derivative of the total energy with respect to the orbital occupation number). However from the long-range behavior of electron density and being expected for the exact effective potential in a DFT theory, one could expect that the highest occupied molecular orbital energy be the exact ionization potential. Within approximate models of DFT we use the negative of the HOMO energy as an approximation to the ionization potential. The feasibility of such N index describing the nucleophilic behavior of an organic molecule has been previously tested in the context of the analysis of the nucleophilic nature of CD ethylenes [6]. The choice of $E_{\mathrm{HOMO(TCE)}}$ is completely arbitrary although it is justified in the context of comparing frontier molecular energies of common reagents used in polar organic reactions.

The development of quantitative scales of nucleophilicity has been a common subject from the thirties [8]. Swain and Scott [9] introduced the first nucleophilicity scale based on linear free energy relationships including the rate constants for a S_N2 reporting a four-parameter equation in order to improve the nucleophilicity description. Later on, the explicit consideration of additional factors contribute to rationalize a better quantitative description of nucleophilicity [10,11]. Legon and Millen [12] proposed an experimental model to probe the gas-phase nucleophilicities and electrophilicities in hydrogen-bonded B-HX dimers, where B is the nucleophile and HX is the electrophile, using the low-frequency hydrogen bond stretching modes as a measure of the nucleophilicity power. The model has been successfully applied to several nucleophilic systems [13]. The availability of empirical scales of electrophilicity and nucleophilicity has been very useful rationalizing for instance selectivity, reaction mechanisms, solvent and substituent effects in many chemical problems [14,15]. In this context, the usefulness of these scales has been illustrated by Mayr and Patz [16] who have provide a quantitative criteria to choose whether a given electrophile-nucleophile combination reaction will take place. These authors [16] have stressed the idea to use different scales of nucleophilicity and electrophilicity that are independent of the reaction partner. They have first observed that the reactions rates of many carbocations with uncharged nucleophiles follow a linear free energy relationship, namely $\log k = s(N + E)$, with E and N parameters defining the electrophilicity and nucleophilicity powers of reacting species, respectively, and where s describes the sensitivity of the nucleophile involved in the reaction. With this equation, these authors have established a basis for building experimental scales of relative electrophilicity and nucleophilicity for a large variety of electrophile-nucleophile combinations [16–19].

Understanding that electrophilicity/nucleophilicity are useful concepts invoked in chemistry to rationalize electronic aspects of reactivity, selectivity, substituent effects, solvent effects, etc., the establishment of such scales becomes strongly justified. Within this perspective, the electrophilicity index ω defined by Parr et al. [4] in terms of the electronic chemical potential [1] and the chemical hardness [1], has shown to be a powerful tool. For instance, it has been successfully applied to classify diene and dienophile reagents participating in DA reactions at both global [5] and local levels [20], and for dipole and dipolarophile pairs in 1,3-dipolar cycloadditions [21]. It has also been an important device giving further understanding on the reactivity of singlet carbenes and their electrophilic pattern [22]. Solvent effects on the electrophilicity of ions and neutral molecules have been already reported [23].

On the other hand, it has been many attempts to define a nucleophilicity index. For instance, Roy et al. [24] proposed the local hardness and local softness based on DFT [1] reactivity descriptors to predict both intramolecular an intermolecular nucleophilic attacks on carbonyl compounds. Chattaraj et al. [25] have stressed the idea of using a generalized index of philicity, which can be applied to electrophilic, nucleophilic, and radical reactions [26,27]. The local philicity has been demonstrated to be a useful tool to describe chemical reactivity and selectivity [28]. A multiphilic descriptor has been also introduced to describe simultaneously the electrophilicity and nucleophilicity of the given atomic sites in the molecule [29]. Recently, an empirical nucleophilicity index for soft–soft interactions has been also introduced [13]. This new nucleophilicity index is obtained in terms of both nucleophile and electrophile frontier orbitals. Such index has been applied and validated with experimentally available kinetic data for amines, diimines, anilines, alcohols, ethers, alkenes, and π- and n-nucleophiles [13,30]. Also recently, Cedillo et al. [31] have introduced a nucleophilicity index derived from a perturbation model for the interaction between a nucleophile and a positive test charge. The model was validated for a series of neutral nucleophiles with a known nucleophilicity pattern [31]. Nucleophilicity and electrophilicity for radicals have been recently explored using a variety of models proposed in the literature [32]. The appealing linear correlation found between the global electrophilicity and the nucleophilicity scales suggested in some cases that these concepts are indeed inversely related [32] along related series of systems.

In this work, we further explore if such N index introduced in Eq. (1) could be suitable for a wider range of molecular systems. Our aim intends to extend the applicability of this approach by examining the nucleophilicity ability of a series of substituted alkenes, substituted aromatic compounds and simple nucleophilic molecules. The proposed nucleophilicity index is compared with the experimental IPs and with those obtained in solution (i.e., $CHCl_3$ and DMSO) phase. Finally, in order to explore the reliability of the empirical nucleophilicity descriptor of Eq. (1), it has been compared with the experimental nucleophilicity index (in water) for a short series of substituted amines.

2. Computational methods

The HOMO energies for all systems at their ground states were obtained at the B3LYP/6-31G(d) level of theory using the GAUSSIAN03 [33] package of programs. Understanding our aim is just the study of qualitative trends, this level of theory provides an enough suitable structure and electronic description of selected systems. Solvent effects calculations were conducted at within the polarizable continuum model PCM [34] using DMSO and $CHCl_3$ as medium.

3. Results and discussion

The nucleophilicity N values obtained from Eq. (1) for a series of nucleophilic organic molecules are displayed in Table 1. It may be seen three families of nucleophiles (a) substituted alkenes, (b) substituted aromatic compounds and (c) simple nucleophilic molecules. Note that while the family (a) participates in electrophilic addition reactions to alkenes, the family (b) participates in aromatic electrophilic substitution reactions of aromatic compounds. The corresponding HOMO energies are also reported in Table 1. From Table 1a it may be seen the most nucleophilic species within the substituted alkene series is dimethylvinylamine (N = 4.28 eV), while acetylene presents the lowest nucleophilic character (N = 1.45 eV). The ER character of the CH_3O-group is clearly incorporated in the proposed nucleophilicity model. Note in general that the substituent effect may be rationalized through the N values. For instance, tetrasubstituted ethylene by this group is noticeably more nucleophilic than the monosubstituted one (e.g., compare N = 3.97 eV and N = 3.17 eV, respectively). Note also from the calculated nucleophilicity in alkyl substituted ethylenes: nucleophiles

Table 1
Gas-phase HOMO energy calculated at B3LYP/6-31G(d) and nucleophilicity (N) values calculated using Eq. (1)

Nucleophiles	HOMO energy (au)	HOMO energy (eV)	N (eV)
(a) Substituted alkenes			
$CH_2{=}CHN(CH_3)_2$	−0.1779	−4.84	4.28
$(CH_3O)_2C{=}C(OCH_3)_2$	−0.1892	−5.15	3.97
$CH_3OCH{=}C(OCH_3)_2$	−0.1987	−5.41	3.71
$CH_2{=}C(OCH_3)_2$	−0.2060	−5.61	3.51
$(CH_3)_2C{=}C(CH_3)_2$	−0.2119	−5.77	3.35
$CH_2{=}CHOCH_3$	−0.2188	−5.95	3.17
$CH_3CH{\equiv}C(CH_3)_2$	−0.2256	−6.14	2.98
$HC{=}COCH_3$	−0.2347	−6.39	2.73
$CH_3CH{=}CHCH_3$	−0.2350	−6.39	2.72
$CH_2{\equiv}C(CH_3)_2$	−0.2395	−6.52	2.60
$CH_3C{=}CCH_3$	−0.2406	−6.55	2.57
$CH_2{\equiv}CHCH_3$	−0.2498	−6.80	2.32
$HC{=}CCH_3$	−0.2595	−7.06	2.06
$CH_2{\equiv}CH_2$	−0.2667	−7.26	1.86
$HC{=}CH$	−0.2819	−7.67	1.45
(b) Substituted aromatic compounds			
$C_6H_5{-}NH_2$	−0.1982	−5.39	3.72
$p{-}C_6H_4$ (OH) (CH_3)	−0.2109	−5.74	3.38
$C_6H_5(OH)$	−0.2189	−5.96	3.16
$C_6H_5(NHCHO)$	−0.2294	−6.24	2.88
$p{-}C_6H_4(OH)(COCH_3)$	−0.2332	−6.34	2.77
$C_6H_5{-}CH_3$	−0.2353	−6.40	2.71
C_6H_6	−0.2463	−6.70	2.42
$C_6H_5{-}Cl$	−0.2464	−6.71	2.41
$C_6H_5(COCH_3)$	−0.2471	−6.72	2.39
$C_6H_5(CHO)$	−0.2552	−6.94	2.17
$C_6H_5(CO_2H)$	−0.2603	−7.08	2.03
$p{-}C_6H_4(Cl)(CHO)$	−0.2628	−7.15	1.97
$C_6H_5{-}NO_2$	−0.2789	−7.59	1.53
(c) Simple nucleophilic molecules			
NH_2NH_2	−0.2009	−5.47	3.65
$N(CH_3)_3$	−0.2073	−5.64	3.48
$NH(CH_3)_2$	−0.2151	−5.85	3.26
NH_2CH_3	−0.2236	−6.09	3.03
CH_3SCH_3	−0.2150	−5.85	3.27
CH_3OOCH_3	−0.2299	−6.26	2.86
CH_3SH	−0.2364	−6.43	2.69
CH_3OOH	−0.2367	−6.44	2.68
CH_3OCH_3	−0.2452	−6.67	2.45
H_2O_2	−0.2464	−6.70	2.41
NH_3	−0.2523	−6.86	2.25
NH_2OH	−0.2546	−6.93	2.19
H_2S	−0.2615	−7.12	2.00
CH_3OH	−0.2645	−7.20	1.92
CH_3CO_2H	−0.2754	−7.49	1.62
H_2O	−0.2911	−7.92	1.20
Reference compound			
$(CN)_2C{=}C(CN)_2$	−0.3351	−9.12	0.00

See the text or details.

yielding tertiary carbenium ions as $(CH_3)_2C{=}C(CH_3)_2$ (N = 3.35 eV) and $CH_3CH{=}C(CH_3)_2$ (N = 2.98 eV) are clearly more reactive than those without this chance as $CH_2{=}CHCH_3$ (N = 2.32 eV) and $CH_2{=}CH_2$ (N = 1.86 eV). The inductive effect of alkyl groups on the nucleophilicity trends are in agreement with experimental results [16].

For the aromatic series (see Table 1b), ER groups like NH_2, OH, NHCHO and CH_3 on the aromatic system enhance the nucleophilicity power compared with that observed for benzene (C_6H_6) (N = 2.42 eV), taken as reference. The most nucleophilic species is aniline with N = 3.72 eV. Note that the EW $COCH_3$ group at the para position of phenol (N = 3.16 eV) produces a decrease nucleophilicity value in $p{-}C_6H_4(OH)(COCH_3)$ (N = 2.77 eV). This result is consistent with the EW ability of the $COCH_3$ group able to delocalize charge from the oxygen of the OH group through the aromatic ring. On the other hand, EW groups (e.g., $COCH_3$, CHO, Cl, NO_2) decrease the nucleophilicity values of the aromatic molecules with respect to benzene.

For simple nucleophilic molecules, it may be seen that amines and derivatives are on the top of Table 1c. In the methylamine series the order of nucleophilicity in gas phase is predicted to be $NMe_3 > NHMe_2 > NH_2Me > NH_3$. This order is again in agreement with gas-phase experimental results [35]. The electronic inductive effect of the methyl group can be also observed along the substituted peroxide series: CH_3OOCH_3 (N = 2.86 eV) > CH_3OOH (N = 2.68 eV) > H_2O_2 (N = 2.41 eV). Clearly this effect is manifested enhancing the nucleophilicity values when the number of methyl groups increases in the substitution pattern. Thiols show the same behavior in presence of the methyl groups, e.g., $CH_3SCH_3 > CH_3SH > H_2S$. The methanol and acetic acid are predicted to be poor nucleophiles by the N index, in agreement with experimental data [36]. Note that H_2O is the less nucleophilic species of the three series, in the chosen relative scale given by Eq. (1).

The series of nucleophiles given in Table 1 may be classified into three general groups. Group I of strong nucleophiles which include molecules with a nucleophilicity power larger than 3.00 eV. A second group of moderate nucleophiles (group II) including molecules with nucleophilicity values comprised within the range 3.00 eV–2.00 eV, and a third group III of marginal nucleophiles including compounds with nucleophilicity values less than 2.00 eV.

In Table 2 are collected the gas-phase nucleophilicity values and those in $CHCl_3$ and DMSO as solvents for some molecules which the IPs [37] are available. From the N values, it may be seen that the nucleophilicity is attenuated in the presence of polar solvent. More polar nucleophiles are more slightly attenuated in DMSO, ε = 46.7 D, than in $CHCl_3$, ε = 4.9 D. Despite our simple nucleophilicity model in Eq. (1) is based directly on the HOMO energy of the nucleophiles it is interesting to see if exist correlation of the calculated N values with the experimental ionization potentials. In this framework, Fig. 1, reports an excellent linear relationship between these quantities for the series of molecules in Table 1, given by $IP_{exp} = 13.64 - 1.60N$, with an R = 0.95. For the alkylamine subseries given in Table 1, this relationship is improved considerably, R = 1.00. Note also that water, which is predicted to be the poorest nucleophile in Table 1, presents the largest IP value of the molecules given in Table 2. Furthermore, there also exists a good linear trend relating the gas-phase N values and those obtained in $CHCl_3$ and DMSO by using Eq. (1). This correlation is shown in Fig. 2. The correlation in $CHCl_3$ is $N_{CHCl_3} = -0.23 + 0.97N$ with R = 0.99 and in DMSO is $N_{DMSO} = -0.32 + 0.96N$ with R = 0.98. It can be seen that the nucleophilicity trend obtained for these 32 systems in $CHCl_3$ and DMSO respect to the gas-phase N values is very similar. It may be seen that the slope, in both cases, is very closer to the unit. These results validate the gas-phase nucleophilicity values, obtained from our model of Eq. (1) categorizing the nucleophilicity reactive proclivity of molecular systems. It can be observed that the solvent effects, considered by the PCM, on the nucleophilicity are linearly proportional to that calculated gas-phase N values, as previously emphasized.

As a final example of validation of our proposed model in Eq. (1), Table 3 reports the calculated nucleophilicity values and the experimental N values for a series of primary and secondary amines, both of them were measured in water as solvent. Although the relationship between these values does not present a good linear, R = 0.79, they follow the same trend (see Fig. 3). Note that the experimental nucleophilicities of amines in water are strongly dependent of the formation of the hydrogen-bonds, which are not considered by the PCM model. The effect of alkyl substituents in solution phase is similar to the intrinsic gas phase discussed above for alkenes and amines. This group of nucleophiles shows a trend consistent with the ER effect attributed to alkyl group.

Table 2
Experimental IPs, and nucleophilicity values in gas and solution phases ($CHCl_3$ and DMSO) calculated at B3LYP/6-31G(d) and PCM model

Nucleophiles	IP_{exp} (eV)	$HOMO_{GP}$ (au)	N_{GP} (eV)	$HOMO_{CHCl_3}$ (au)	N_{CHCl_3} (eV)	$HOMO_{DMSO}$ (au)	N_{DMSO} (eV)
C_4H_5N (pyrrole)	8.21	−0.2015	3.64	−0.2022	3.31	−0.2032	3.16
$NH_2CH_2CH_2NH_2$	8.60	−0.2017	3.63	−0.1976	3.44	−0.1964	3.34
$N(CH_3)_3$	7.82	−0.2072	3.48	−0.2089	3.13	−0.2099	2.98
$CH_3CH_2NH_2$	8.01	−0.2107	3.39	−0.2110	3.08	−0.2112	2.94
Cp	8.56	−0.2116	3.36	−0.2116	3.06	−0.2122	2.92
C_5H_6O (2-methylfuran)	8.35	−0.2125	3.34	−0.2140	2.99	−0.2150	2.84
CH_3SCH_3	8.69	−0.2150	3.27	−0.2225	2.76	−0.2260	2.54
$NH(CH_3)_2$	8.24	−0.2152	3.27	−0.2159	2.94	−0.2162	2.80
$C_6H_5(OH)$	8.47	−0.2189	3.16	−0.2176	2.90	−0.2177	2.77
C_8H_8 (styrene)	8.43	−0.2217	3.09	−0.2216	2.79	−0.2222	2.64
C_4H_4O (furan)	8.83	−0.2245	3.01	−0.2241	2.72	−0.2244	2.58
$CH_2{=}CHOCH_3$	8.93	−0.2249	3.00	−0.2267	2.65	−0.2275	2.50
$CH_2CH{=}CHCH_2NH_2$	9.07	−0.2274	2.93	−0.2270	2.64	−0.2272	2.51
NH_2CH_3	8.97	−0.2286	2.90	−0.2283	2.60	−0.2283	2.48
$CH_3CH_2NH_2$	8.86	−0.2295	2.88	−0.2293	2.58	−0.2292	2.45
$CH_2{=}CHCH_2NH_2$	8.79	−0.2324	2.80	−0.2298	2.56	−0.2292	2.45
C_4H_8O (tetrahydrofuran)	9.41	−0.2342	2.75	−0.2375	2.35	−0.2392	2.18
$HOCH_2CH_2NH_2$	8.96	−0.2403	2.58	−0.2346	2.43	−0.2326	2.36
CH_3CONH_2	9.65	−0.2439	2.48	−0.2516	1.97	−0.2549	1.75
CH_3OCH_3	9.98	−0.2452	2.45	−0.2480	2.07	−0.2494	1.90
$CH_3CH{=}CHOH$	9.67	−0.2452	2.45	−0.2453	2.14	−0.2457	2.00
$CH_3CO_2CH{=}CH_2$	9.19	−0.2495	2.33	−0.2508	1.99	−0.2512	1.85
$CH_3CH{=}CH_2$	9.73	−0.2498	2.32	−0.2500	2.01	−0.2502	1.88
NH_3	10.17	−0.2525	2.25	−0.2516	1.97	−0.2515	1.85
CH_3CH_2OH	10.49	−0.2543	2.20	−0.2556	1.86	−0.2559	1.72
$CH_3CHOHCH_3$	10.10	−0.2607	2.03	−0.2590	1.77	−0.2583	1.66
$CH_3CH_2CH_2CH_2OH$	10.04	−0.2612	2.01	−0.2582	1.79	−0.2573	1.69
$CH_3CH_2CH_2OH$	10.22	−0.2614	2.01	−0.2597	1.75	−0.2591	1.64
CH_3OH	10.84	−0.2620	1.99	−0.2612	1.71	−0.2609	1.59
CH_3CH_2OH	10.51	−0.2667	1.86	−0.2666	1.56	−0.2667	1.43
$HC{\equiv}CH$	11.40	−0.2819	1.45	−0.2831	1.11	−0.2838	0.96
H_2O	12.62	−0.2912	1.20	−0.2856	1.05	−0.2837	0.97
$(CN)_2C{=}C(CN)_2$		−0.3352	0.00	−0.3240	0.00	−0.3193	0.00

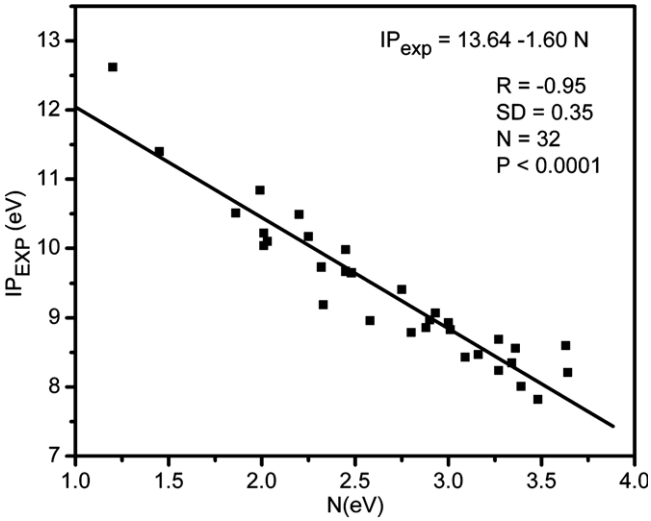

Fig. 1. Relationship between experimental ionization potential (in eV) and calculated gas-phase nucleophilicity index (in eV). *R* is the regression coefficient, SD is the standard deviation, *N* is the number of points and *P* is the probability that the observed correlation is randomly obtained.

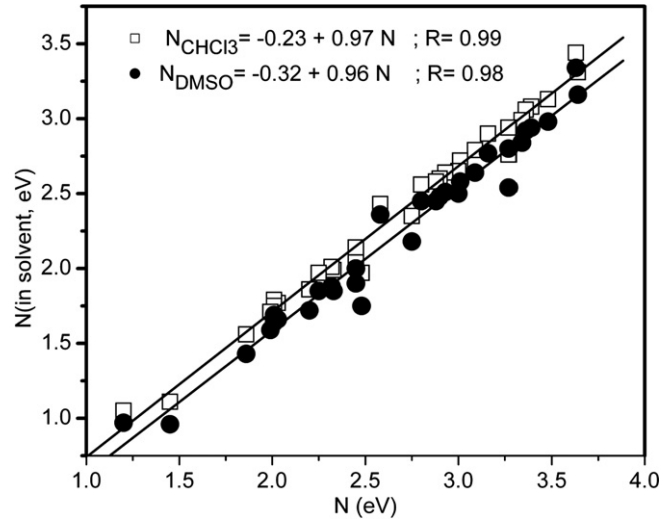

Fig. 2. Relationship between nucleophilicity values obtained from DMSO and $CHCl_3$ as solvents and gas-phase nucleophilicity index. See the text for details.

4. Concluding remarks

This work reports further evidence supporting of the usefulness of the intrinsic ionization potentials defining a simple model for a nucleophilicity index, *N*, namely Eq. (1). Such *N* scale is the negative of the ionization potential calculated within the Koopmans' theorem approach with an arbitrary shifting of the origin. This model has been found to be useful to qualitatively categorizing a large series of substituted alkenes, substituted aromatic compounds and simple nucleophilic molecules, extending its applicability beyond the captodative ethylenes series recently characterized. Good correlations between the calculated *N* values and the experimental available results have been obtained. Solvent effects on the nucleophilicity index have been also studied. An excellent linear correlation between gas and solution phase nucleophilicity values for a common series of nucleophiles is also obtained. Qualitative comparisons of the calculated *N* values and the experimental nucleophilicity of amines in water further validate the model Eq. (1) as a suitable tool to predict the nucleophilic

Table 3
Gas-phase nucleophilicity (N), nucleophilicity values in water (N_{H_2O}) and experimental data (in water) for primary amines [37]

Amines	$HOMO_{GP}$ (au)	N_{GP} (eV)	$HOMO_{H_2O}$ (au)	N_{H_2O} (eV)	N_{exp} [37] (in H_2O)
Me_2NH (**1**)	−0.2153	3.26	−0.2182	2.72	17.12
CH_3NH_2 (**2**)	−0.2286	2.90	−0.2283	2.45	13.85
$CH_2CHCH_2NH_2$ (**3**)	−0.2324	2.80	−0.2405	2.12	13.21
$CH_3CH_2NH_2$ (**4**)	−0.2295	2.88	−0.2405	2.12	12.87
$HOCH_2CH_2NH_2$ (**5**)	−0.2340	2.75	−0.2312	2.37	12.61
$HC{=}CNH_2$ (**6**)	−0.2440	2.48	−0.2431	2.04	12.29
$NCCH_2NH_2$ (**7**)	−0.2719	1.72	−0.2598	1.59	10.8
NH_3 (**8**)	−0.2525	2.25	−0.2515	1.82	9.48
$(CN)_2C{=}C(CN)_2$	−0.3352		−0.3181		

See the text for details.

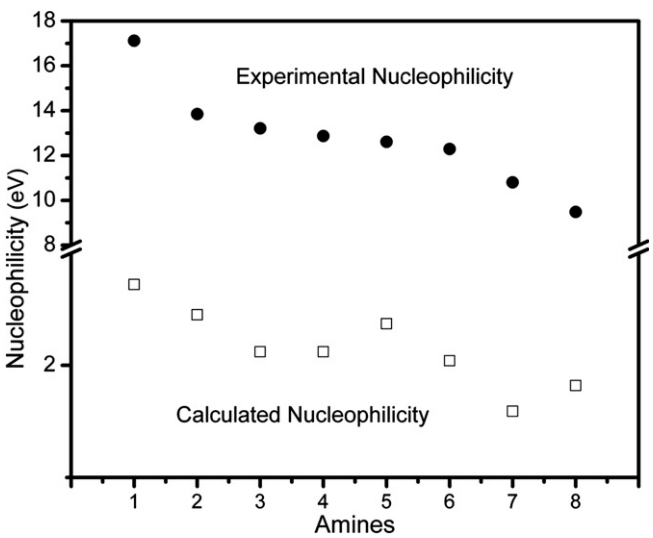

Fig. 3. Comparison between the experimental and the calculated nucleophilicity index using Eq. (1) for a series of amines in water.

behavior, feasibly asserting the qualitative nucleophilicity trends of a wider range of these species.

Acknowledgments

This work was supported by research funds provided by Fondecyt Projects No. 1060961 (P.P.) and 1070378 (E.Ch.) and the Ministerio de Educación y Ciencia of the Spanish Government (project CTQ2006-14297/BQU). E.Ch. and P.P. also thank the Universidad Andrés Bello (UNAB) by support through project DI 21-06/R and 45-08/R, respectively. P.P. acknowledges to the Generalidad Valenciana (AINV/2007/016). L.R.D. also thanks to the Fondecyt Grant No. 7070051 (International Cooperation) for financial support and the Universidad Andrés Bello for the warm hospitality. P.J. thanks to FAPESP for the postdoctoral fellowship.

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