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Reactivity and stability of aromatic carbonyl compounds using density functional theory-based local and global reactivity descriptors

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ABSTRACT: The reactivity of acetaldehyde and some aromatic aldehydes towards acid-catalysed oxygen-18 exchange reactions with H_2O^{18} was studied using the density functional theory (DFT)-based reactivity descriptors local softness and local hardness. Local softness is used to predict the preferable reactive sites within a given molecule, whereas local hardness reproduces the experimental intermolecular reactivity trends. A new concept, intrinsic global hardness, obtained via filtering out the volume effect of the global softness, shows an excellent correlation with the degree of aromaticity of the compounds. Copyright © 1999 John Wiley & Sons, Ltd.

KEYWORDS: aromatic carbonyl compounds; density functional theory; reactivity; stability

INTRODUCTION

The prediction and interpretation of intra- and intermolecular reactivity sequences of organic molecules have been an important area of theoretical organic chemistry from the very early days. Understanding of reactivity trends has been achieved using concepts such as inductive, resonance, mesomeric and hyperconjugative effects.[1]

In recent years, a lot of effort has been devoted by some workers, including the present group, to explain intra- and intermolecular reactivity sequences using reactivity descriptors based on the local hard and soft acids and bases (HSAB) concept.[2] The key parameters used for intramolecular reactivity studies are the Fukui function[3] and the local softness.[4] Langenaeker *et al.*[5] proposed new reactivity descriptors based on local hardness and demonstrated its superiority over local softness in predicting intermolecular reactivity sequence for electrophilic aromatic substitution. Roy *et al.*[6] used the same local hardness parameters and invoked the Felkin–Anh model to predict successfully the intermolecular electrophilicity order of the carbonyl carbon of a series of aliphatic aldehydes and ketones.

The present work extends this approach to aromatic compounds using experimental data of Byrn and Calvin[7] on the rate of oxygen-18 exchange reactions of some aldehydes with oxygen-18 enriched water. By means of infrared spectroscopy, these authors showed that in acidic tetrahydrofuran (THF) the exchange times for the aldehydes increase in the order acetaldehyde <benzaldehyde <2-naphthaldehyde <1-naphthaldehyde <9-anthraldehyde <9-phenanthraldehyde. The order of reactivity (in the present case the electrophilicity of the carbonyl carbon, as the nucleophilic attack on this carbon atom by H_2O^{18} is the rate-determining step) of these compounds is the reverse of the order of exchange times.

In this paper, the verification of the reliability of these local hardness parameters in predicting experimental reactivity trends of these series of aldehydes towards the oxygen-18 exchange reaction is presented.

Another important aspect of our study was to verify and interpret whether the reactivity trend of these compounds bears any correlation with the trend of their aromaticity. A multitude of aromaticity criteria have been proposed hitherto.[8] In recent years, the link between aromaticity and hardness has been investigated under the impetus of Parr and co-workers. Zhou and Parr[9] have shown that global hardness (both absolute and relative) can explain various aspects of aromaticity for a large number of unsubstituted aromatic compounds. Hiruta *et al.*[10] obtained improved excitation energies of 38 polycyclic aromatic hydrocarbons considering the correlation of chemical softness and absolute hardness.

In the present case, the aromatic ring influences the reactivity through delocalization of the positive charge on the carbonyl carbon; increasing aromaticity (implying

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more delocalization) causes a decrease in reactivity. As the parent hydrocarbons show the aromaticity trend[11] methane (non-aromatic) $<$ benzene $<$ naphthalene $<$ anthracene $<$ phenanthrene, we expect the following aromaticity trend of the corresponding aldehydes: acetaldehyde (non-aromatic) $<$ benzaldehyde $<$ 1-naphthaldehyde $\approx$ 2-naphthaldehyde $<$ 9-anthraldehyde $<$ 9-phenanthraldehyde, which means that the rate of oxygen-18 exchange will follow the reverse order: acetaldehyde $>$ benzaldehyde $>$ 2-naphthaldehyde $\approx$ 1-naphthaldehyde $>$ 9-anthraldehyde $>$ 9-phenanthraldehyde. Hence the local hardness values on the carbonyl carbon of these aldehydes (considered as an indicator of the intermolecular reactivity trends) should correlate with their aromaticity.

THEORETICAL BACKGROUND

The analytical definition of global hardness of a chemical species was first proposed by Parr and Pearson as[12]

$$\eta = (\partial^2 E/\partial N^2)_\nu = (\partial \mu/\partial N)_\nu \qquad (1)$$

where E is the total energy, N is the number of electrons of the chemical species, ν the external potential (i.e. the potential due to the nuclei) and μ the chemical potential, which is identified as the negative of the electronegativity[13] as defined by Iczkowski and Margrave.[14] The global softness S of the system is defined as the inverse of the global hardness.

Application of a finite difference approximation to Eqn. (1) yields the following operational definition of η:

$$\eta = IP - EA \qquad (2)$$

where IP and EA are the vertical ionization potential and electron affinity of the chemical species respectively. Consequently,

$$S = 1/IP - EA \qquad (3)$$

The analytical definition of local softness $s(\boldsymbol{r})$ was first proposed by Parr and co-workers as follows:[4]

$$s(\boldsymbol{r}) = [\partial \rho(\boldsymbol{r})/\partial \mu]_\nu \qquad (4)$$

where $\rho(\boldsymbol{r})$ is the electron density of the system. Using a chain rule, Eqn. (4) can be written as

$$s(\boldsymbol{r}) = [\partial \rho(\boldsymbol{r})/\partial N]_\nu (\partial N/\partial \mu)_\nu = f(\boldsymbol{r})S \qquad (5)$$

i.e. the local softness is the product of the global softness and a function $f(\boldsymbol{r})$, termed by Parr and Yang[3] the Fukui function, a frontier molecular orbital reactivity index.

The derivative $[\partial \rho(\boldsymbol{r})/\partial N]_\nu$ at some integral value of N will in general have one value from the right, one from the left and an average. Thus three types of $f(\boldsymbol{r})$ can be defined which, when multiplied by S, result in three different local softness functions. By applying a finite difference approximation the condensed form of these three local softness functions for any particular atom (k) can be written as[15]

$$s_k^+ = [\rho_k(N_0 + 1) - \rho_k(N_0)]S \qquad (6)$$

suited for studies of nucleophilic attack,

$$s_k^- = [\rho_k(N_0) - \rho_k(N_0 - 1)]S \qquad (7)$$

suited for studies of electrophilic attack and

$$s_k^0 = 12[\rho_k(N_0 + 1) - \rho_k(N_0 - 1)]S \qquad (8)$$

suited for studies of radical attack.

In these equations, $\rho_k(N_0 + 1)$, $\rho_k(N_0)$ and $\rho_k(N_0 - 1)$ represent the electronic population on atom k for the $N_0 + 1$, N_0 and $N_0 - 1$ electron system, respectively.

Local hardness was introduced as[16–18]

$$\eta(\boldsymbol{r}) = 1/N \int \rho(\boldsymbol{r}')\delta^2 F/\delta\rho(\boldsymbol{r})\delta\rho(\boldsymbol{r}')d\boldsymbol{r}' \qquad (9)$$

where F is the so-called Hohenberg–Kohn functional, containing the systems' kinetic and electron–electron repulsion energies. Neglecting the kinetic energy and the exchange-correlation parts in F, Berkowitz, Ghosh, Parr and their co-workers[16–18] obtained the following approximation for the local hardness:

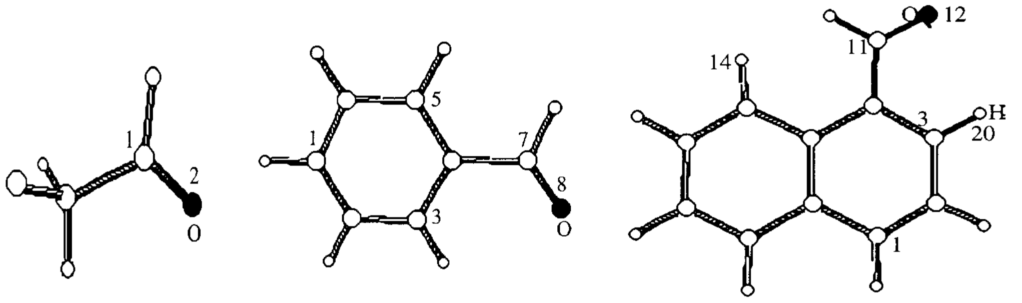
$$\eta(\boldsymbol{r}) \approx -V_{\mathrm{el}}(\boldsymbol{r})/-2N \qquad (10)$$

where V_{el} is the electronic part of the electrostatic potential[19] and N the number of electrons.

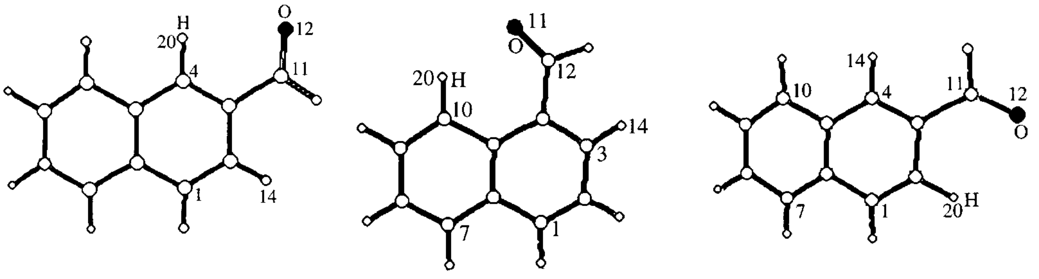
It was shown by us that this approximated form of local hardness can be used as a reliable parameter for comparison of intermolecular reactivity sequences of any particular site in a series of molecules.[5,6]

METHODOLOGY AND COMPUTATIONAL DETAILS

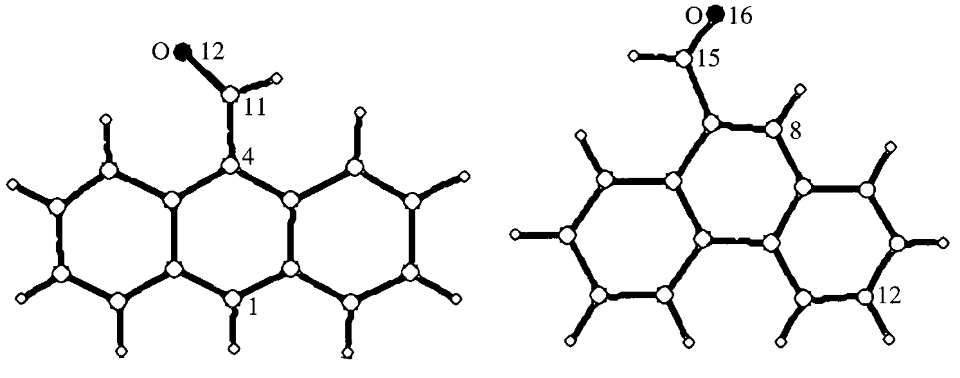
For the present study we considered the following six aldehydes: acetaldehyde, benzaldehyde, 1-naphthaldehyde, 2-naphthaldehyde, 9-anthraldehyde and 9-phenanthraldehyde. These are the aromatic aldehydes (except acetaldehyde) which Byrn and Calvin chose in their experimental study.[7] However, we excluded their remaining three aldehydes (3-indolaldehyde, chlorophyll *b* and phenophytin *b*). Two of these three systems, containing heteroatoms in the aromatic ring (chlorophyll *b* and phenophytin *b*) are still too large systems to be treated reliably by our computational techniques.



Acetaldehyde Benzaldehyde 1- Naphthaldehyde (A)



2- Naphthaldehyde (B) 1-Naphthaldehyde (A') 2- Naphthaldehyde (B')



9- Anthraldehyde 9- Phenanthraldehyde

Figure 1. Structures and numbering of the relevant atoms of the aldehydes considered

The geometries were generated using the Unichem program system[20] and are shown in Fig. 1. Subsequently these geometries were optimized at the DZP[21] level of basis set using the Gaussian 94 program[22] on the Cray J916/8-1024 computer of the Universities of Brussels. A remark should be made about 1- and 2-naphthaldehyde. Two conformations of the formyl group were studied for both of these two systems (A, A′ and B, B′ in Fig. 1). For 1-naphthaldehyde, conformer A′ is more stable than A by *ca* 1.7 kcal mol^{-1} (1 kcal = 4.184 kJ). Similarly for 2-naphthaldehyde conformer B′ is more stable than B by just less than 1 kcal mol^{-1}. An explanation for this higher stability for the conformers A′ and B′ can be given in terms of a six- and five-membered ring formation (Fig. 1) through the O and the H atoms in A′ and B′, respectively. However, we chose to work with conformers A and B since for these molecules the nucleophilicity of the oxygen appears to be much higher from local softness values (see below); it can thus be anticipated, considering the small energy differences between the conformers, that the structures A and B will be more stable in an acidic medium. For neutral systems (closed shell) RHF and for the corresponding cations and anions (open-shell) ROHF[23] methods are used.

Local softness values are calculated in a straightforward way from the Mulliken population of the individual atoms using Eqns (6) and (7). However, for the calculation of local hardness, the electronic part of the electrostatic potential is required. This quantity has been evaluated only for the carbonyl carbon as the intramolecular reactivity study will reveal that this atom normally is the most reactive. To choose the direction of attack by the nucleophile (i.e. H_2O^{18}) on the C=O group, we invoked the Felkin–Anh model.[24] This model was

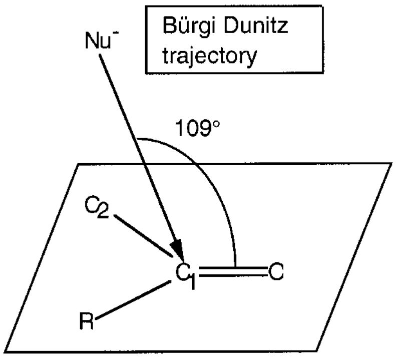


Figure 2. The Felkin–Anh model for nucleophilic addition to the carbonyl group

originally proposed to predict or rationalize the stereochemical outcome of kinetically controlled additions to the carbonyl group of chiral aldehydes and ketones having a stereogenic centre adjacent to the carbonyl group. According to this model, the bulkiest of the groups attached to the stereogenic carbon takes up a perpendicular relationship to the plane of the carbonyl group *anti* to the incoming nucleophile; the sterically next most demanding substituent (medium-sized groups) is placed *gauche* to the carbonyl function. The argument was given that the torsional strain involving the partially formed bonds in the transition state will be minimized for such a mode of attack.[24a–c] Later, Bürgi and co-workers[25] suggested that the preferred transition state can be obtained if the angle of approach of the attacking nucleophile is about 109° with respect to the plane of the carbonyl group (known as the Bürgi–Dunitz trajectory) and that it is not necessary for the medium-sized group to be *gauche* to the oxygen atom. However, none of the aldehydes we are studying here contains any stereogenic centre adjacent to the carbonyl carbon. Therefore, in a rigorous sense, the Felkin–Anh model (or its modified form by Bürgi and co-workers) cannot be applied. That is why we considered the optimized geometry at the DZP basis set and then invoked the Bürgi–Dunitz trajectory to choose the angle $\angle \mathrm{Nu}^-$—C_1—O = 109° (see Fig. 2). While applying this model we also took account of the fact that the attacking nucleophile (Nu^-) will try to avoid repulsion by the electron cloud of the aromatic rings. In most cases in the present study the situation is identical if Nu^- attacks from either of the sides of the plane containing the CHO group as it is coplanar with the rest of the molecule. In the case of 9-anthraldehyde, however, the optimized geometry shows that the CHO group is not coplanar with the rest of the molecule (avoiding the repulsive interaction between the H-atom of the CHO group and that of the adjacent ring). Therefore, we had to choose that side of attack which is less repulsive to the Nu^-, i.e. the side in which the incoming Nu^- and the Ph ring are at a larger distance.

The dihedral angle $\angle$Nu—C_1—O—C_2 is taken as 90°. The Nu—C_1 distance is 4 a.u. as Langenaeker *et al.*[5] have shown that at a distance of 4 a.u. the approximation to the local hardness used in the present work is justified.

RESULTS AND DISCUSSION

Local softness: indicator of the preferable reactive site

In Fig. 1, we have indicated the atomic centres which show high s_k^+ and s_k^- values in our calculation. The corresponding atoms with their s_k^+, s_k^-, s_k^+/s_k^- and s_k^-/s_k^+ values are listed in Table 1. For 1-naphthaldehyde two types of geometries are possible depending on the orientation of the CHO group. Our study reveals that these two geometries (denoted by A and A′ in Fig. 1) differ very slightly in energy. The case with 2-naphthaldehyde is similar (denoted by B and B′ in Fig. 1).

From Table 1 it is clearly seen that the s_k^- value of the O atom is the highest in all four systems (i.e. acetaldehyde, benzaldehyde, 9-anthraldehyde and 9-phenanthraldehyde). This indicates why the O atom is the most preferable towards protonation in acidic medium. As the carbonyl carbon ($\mathrm{C}_{\mathrm{carb}}$) is directly bonded to the O atom it experiences the maximum electron-withdrawing effect of the latter. Hence C_{carb} should show the highest electrophilicity (i.e. the highest s_k^+ value), indicating it to be the most preferable site towards nucleophilic attack on it. However, the results in Table 1 show that this is only true for acetaldehyde. Roy *et al.*[6] have argued that the probable reason for the unexpected trend of intramolecular s_k^+ or s_k^- values, which arises in some cases, is the neglect of correlation or relaxation effects in evaluating them. It was suggested that their ratios s_k^+/s_k^- and s_k^-/s_k^+ are expected to cancel this error and make the trend as expected. In the present case also we see that the $\mathrm{C}_{\mathrm{carb}}$ has the highest s_k^+/s_k^- value, except in 9-anthraldehyde. However, Byrn and Calvin[7] argued that the extensive aromatic system would try to diminish the electrophilicity of $\mathrm{C}_{\mathrm{carb}}$ through delocalization of the positive charge on it. Interestingly, our study also shows some other sites in the aromatic ring having high electrophilicity, as indicated by their high s_k^+ values. Perhaps this delocalization effect is very high in the case of 9-anthraldehyde as the s_k^+ value of the $\mathrm{C}_{\mathrm{carb}}$ in this molecule is very low. This is evident from the very high s_k^+ value of the tenth position (i.e. carbon 1 in Fig. 1). However, we may expect that the s_k^+ value of the $\mathrm{C}_{\mathrm{carb}}$ in acidic medium will be enhanced owing to the protonation of the O atom, thus justifying nucleophilic attack on the $\mathrm{C}_{\mathrm{carb}}$.

Table 1. s_k^+, s_k^-, s_k^+/s_k^- and s_k^-/s_k^+ values at the relevant atomic centres. (all values in au)[a]

Aldehyde	Atom	s_k^+	s_k^-	s_k^+/s_k^-	s_k^-/s_k^+
Acetaldehyde	1 (C_{carb})	0.9833	0.1469	6.6951	0.1494
	2 (O)	0.5284	1.0739	0.4920	2.0324
Benzaldehyde	1	0.4555	0.1957	2.3272	0.4297
	3	0.3631	0.1618	2.2445	0.4455
	5	0.2558	0.2031	1.2596	0.7939
	7 (C_{carb})	0.4444	0.0937	4.7448	0.2108
	8 (O)	0.4246	1.2031	0.3529	2.8338
1-Naphthaldehyde	1	0.5063	0.2430	2.0837	0.4799
	3	0.3959	0.2218	1.7850	0.5602
	11 (C_{carb})	0.2030	0.0812	2.4984	0.4003
	12 (O)	0.3467	1.2550	0.2763	3.6198
	14	0.0525	−0.0751	−0.6996	−1.4295
	20	0.0862	−0.0619	−1.3937	−0.7175
2-Naphthaldehyde	1	0.2639	0.0396	6.6732	0.1498
	4	0.5182	0.2464	2.1035	0.4754
	11 (C_{carb})	0.2735	0.0520	5.2554	0.1903
	12 (O)	0.3515	1.2515	0.2809	3.5600
	14	0.1113	0.0481	2.3150	0.4320
	20	0.0702	−0.0481	−1.6560	−0.6039
9-Anthraldehyde	1	0.5611	0.3355	1.6723	0.5980
	4	0.3322	−0.0756	−4.3935	−0.2276
	11 (C_{carb})	0.0956	−0.0221	−4.3213	−0.2314
	12 (O)	0.3099	1.4071	0.2203	4.5400
9-Phenanthraldehyde	8	0.5072	0.2993	1.6943	0.5902
	12	0.2752	0.1425	1.9319	0.5176
	15 (C_{carb})	0.2102	0.0639	3.2898	0.3040
	16 (O)	0.3355	1.2681	0.2646	3.7801

[a] The s^- value of the oxygen atom in conformer A′ of 1-naphthaldehyde and in conformer B′ in 2-naphthaldehyde are 0.1318 and 0.1803, respectively.

Rate of oxygen-18 exchange reactions: use of local hardness as a measure of intermolecular reactivity order

The mechanism of the acid-catalysed oxygen-18 exchange reaction suggests that the rate-determining step is the attack of the nucleophile (in this case H_2O^{18}) on the C_{carb}. Our study on the site selectivity (previous section) also shows that C_{carb} is the most preferable site to be attacked by a nucleophile. The earlier studies by Langenaeker *et al.*[5] and also by Roy *et al.*[6] clearly established that local hardness values provide more reliable intermolecular reactivity trends than their softness counterparts. It was argued that the rate-determining step, which involves the attack of the nucleophile on the C_{carb}, is mainly charge controlled (i.e. hard–hard interaction) and not necessarily orbital controlled (i.e. soft–soft interaction).[6] Therefore, in the present study we evaluated local hardness values on the C_{carb} in the way discussed under Methodology. The corresponding results are given in Table 2.

The experimental study of Byrn and Calvin[7] indicated that the time to reach equilibrium for oxygen-18 exchange reaction increases in the order acetaldehyde < benzaldehyde < 2-naphthaldehyde < 1-naphthaldehyde < 9-anthraldehyde < 9-phenanthraldehyde. Hence, in principle, the rate of the exchange reaction should decrease in the order acetaldehyde > benzaldehyde > 2-

Table 2. Local hardness values for the carbonyl carbon [$\eta_C(r)$], molecular volumes (V), global and intrinsic softness (S and S^{int}) and hardnesses (η and η^{int}) for the six aldehydes (all values in au), and the empirical resonance energies (*ERE*) of the unsubstituted hydrocarbons (kcal mol^{-1})

Aldehyde	$\eta_C(\boldsymbol{r})$	V	S	S^{int}	η	η^{int}	*ERE*
Acetaldehyde	0.1089	442.87	2.252	0.00508	0.444	196.7	0.0
Benzaldehyde	0.0869	938.93	2.722	0.00290	0.367	344.9	36.0
1-Naphthaldehyde (A)	0.0788	1356.12	2.911	0.00215	0.344	465.9	61.0
2-Naphthaldehyde (B)	0.0731	1330.40	2.890	0.00217	0.346	460.3	61.0
9-Anthraldehyde	0.0729	1791.09	3.352	0.00187	0.289	534.3	83.5
9-Phenanthraldehyde	0.0702	1766.00	2.982	0.00169	0.335	592.3	91.3

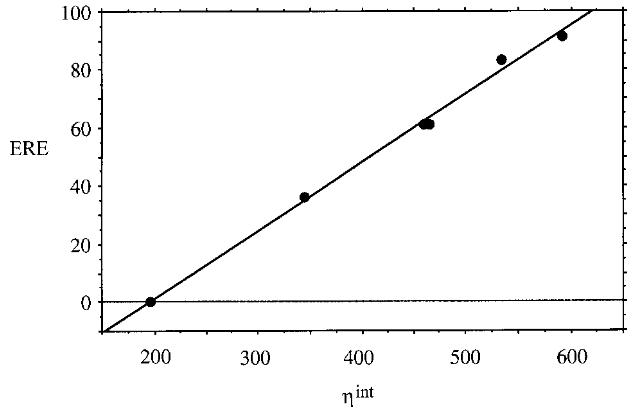


Figure 3. Correlation of the 'intrinsic global hardness' η^{int}, of the aldehydes with the empirical resonance energies (*ERE*) of the parent hydrocarbons

naphthaldehyde > 1-naphthaldehyde > 9-anthraldehyde > 9-phenanthraldehyde, which implies that the values of local hardness, being an indicator of the intermolecular reactivity trend, should decrease in the same order. Table 2 shows the same trend of local hardness with a single exception. The local hardness value of 1-naphthaldehyde is higher than that of 2-naphthaldehyde, although experimental oxygen-18 exchange times suggest that it should be the reverse. Bearing this single exception in mind, our study on local hardness is seen to explain the experimental reactivity trends for this series of aromatic aldehydes, in line with the previous results on their aliphatic counterparts.[6]

Relationship between aromaticity and local and global hardness parameters

In the present context it may be worthwhile to check whether there is any correlation between aromaticity and local and/or global hardness. Byrn and Calvin[7] argued that the reactivity (i.e. electrophilicity) of the C_{carb} would be decreased by delocalization of its positive charge through extended resonance. Hence the more aromatic the system, the higher is the delocalization (i.e. resonance stabilization) of the positive charge on the C_{carb}, causing it to be less reactive towards a nucleophile. This is also found in the present work, the difference between 1- and 2-naphthaldehyde being the single exception. Although the aromaticity of both 1- and 2-naphthaldehyde is nearly the the same, the local hardness value of the former is higher than that of the latter. As expected, 9-phenanthraldehyde, being the most aromatic in the present series, has the lowest local hardness value.

This observation points to the fact that local hardness can be correlated with the aromaticity, whereas previous studies[8,9] concentrated only in establishing a correlation between global hardness and aromaticity.

In this context, the global softnesses for the set of aromatic aldehydes were also calculated and are given in Table 2. As can be seen, the softness increases on going from acetaldehyde to 9-phenanthraldehyde, an apparently conflicting situation with the fact that global hardness should be positively correlated with aromaticity. However, it is generally known that softness is proportional to the volume of the molecule.[26] In order to account for the 'volume effect' on the global softness, an 'intrinsic global softness', S^{int} is introduced as

$$S^{\mathrm{int}} = SV \tag{11}$$

where V is the volume of the corresponding molecule. It should be noted that this intrinsic global softness is nothing else than the local softness of the corresponding homogeneous system with the same global softness, i.e. with $\rho(\mathbf{r}) = N/V$ for all $\mathbf{r}$, N again being the number of electrons. Demanding that the intrinsic global softness and intrinsic global hardness should give a value of one upon multiplication, the corresponding 'intrinsic global hardness' is given as

$$\eta^{\mathrm{int}} = \eta V \tag{12}$$

Again, it should be noted that this intrinsic global hardness is nothing else than the exact local hardness of the corresponding homogeneous system with the same global hardness. In Table 2, we have listed the volumes of the molecules studied, together with their corresponding intrinsic global softnesses and hardnesses. These volumes were obtained by integrating the volume enclosed by the 0.001 au contour of the electron density using the Gaussian 94 program. A correlation was then set up between the intrinsic global hardness of the aldehydes and the empirical resonance energies of the corresponding hydrocarbons. As can be seen in Fig. 3, a very good correlation exists, much better than, e.g., the correlation of the global softness and this measure of aromaticity. By filtering out the volume effect on the global softness, quantities arise, the intrinsic global softness and hardness, that directly reflect aromaticity. In terms of wavefunction quantum chemistry, these quantities can be thought of as being a measure of the specific valence orbital structure of the chemical species. This double aspect of molecular hardness (local and global) and its application to reactivity and stability of organic molecules merits further investigation. Moreover, future work will involve the testing of these new concepts in predicting aromaticity of other molecules.

From these findings, it can be said that the local hardness yields information about the intermolecular reactivity sequences, whereas the intrinsic global hardness measures the stability of the molecule.

CONCLUSION

This study clearly shows that the intra- and intermolecular reactivity sequence of a series of aromatic aldehydes (except acetaldehyde) towards acid-catalysed oxygen-18 exchange reactions can be explained using DFT-based local reactivity descriptors. While local softness values reproduce intramolecular reactivity (i.e. site selectivity) trends, the intermolecular O-18 exchange sequence is explained via local hardness.

Finally, the concepts of 'intrinsic' global softness and hardness were introduced. The intrinsic global hardness of the aldehydes was shown to yield an excellent and positive correlation with the empirical resonance energies of the corresponding hydrocarbons, being a measure of aromaticity.

From this work, it can be concluded that local softness and hardness are important in measuring intramolecular and intermolecular reactivity, respectively; the corresponding global properties, however, are a measure of the system's stability, as probed in this case by the empirical resonance energies.

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REFERENCES

1. J. March, *Advanced Organic Chemistry*. Wiley, New York (1992).
2. (a) F. De Proft, W. Langenaeker and P. Geerlings, *J. Phys. Chem.* **97**, 1826–1831 (1993); (b) W. Langenaeker, N. Coussement, F. De Proft and P. Geerlings, *J. Phys. Chem.* **98**, 3010–3014 (1994); (c) F. De Proft, S. Amira, K. Choho and P. Geerlings, *J. Phys. Chem.* **98**, 5227–5233 (1994); (d) F. De Proft, W. Langenaeker and P. Geerlings, *Int. J. Quantum Chem.* **55**, 459–468 (1995); (e) F. De Proft, W. Langenaeker and P. Geerlings, *Tetrahedron* **51**, 4021–4032 (1995); (f) A. Baeten, F. De Proft and P. Geerlings, *Chem. Phys. Lett.* **235**, 17–21 (1995); (g) S. M. Krishnamurti, R. K. Roy, R. Vetrivel, S. Iwata and S. Pal, *J. Phys. Chem. A* **101**, 7253–7257 (1997); (h) A. K. Chandra, P. Geerlings and M. T. Nguyen, *J. Org. Chem.* **62**, 6417–6419 (1997).
3. R. G. Parr and W. Yang, *J. Am. Chem. Soc.* **106**, 4049–4050 (1984).
4. (a) W. Yang and R. G. Parr, *Proc. Natl. Acad. Sci. USA* **82**, 6723–6726 (1985); (b) M. Berkowitz and R. G. Parr, *J. Chem. Phys.* **88**, 2554–2557 (1988).
5. W. Langenaeker, F. De Proft and P. Geerlings, *J. Phys. Chem.* **99**, 6424–6431 (1995).
6. R. K. Roy, S. Krishnamurti, P. Geerlings and S. Pal, *J. Phys. Chem. A* **102**, 3746–3755 (1998).
7. M. Byrn and M. J. Calvin, *J. Am. Chem. Soc.* **88**, 1916–1922 (1966).
8. P. v. R. Schleyer and H. Jiao, *Pure Appl. Chem.* **68**, 209–218 (1996).
9. Z. Zhou and R. G. Parr, *J. Am. Chem. Soc.* **111**, 7372–7379 (1989).
10. K. Hiruta, S. Tokita and K. Nishimoto, *J. Chem. Soc., Perkin Trans. 2*, 1443–1448 (1995).
11. G. W. Wheland, *Resonance in Organic Chemistry*. Wiley, New York (1955).
12. R. G. Parr and R. G. Pearson, *J. Am. Chem. Soc.* **105**, 7512–7516 (1983).
13. R. G. Parr, R. A. Donnelly, M. Levy and W. E. Palke, *J. Chem. Phys.* **68**, 3801–3807 (1978).
14. R. P. Iczkowski and J. L. Margrave, *J. Am. Chem. Soc.* **83**, 3547–3551 (1961).
15. W. Yang and W. J. Mortier, *J. Am. Chem. Soc.* **108**, 5708–5711 (1986).
16. S. K. Ghosh and M. Berkowitz, *J. Chem. Phys.* **83**, 2976–2983 (1985).
17. R. G. Parr and W. Yang, *Density Functional Theory of Atoms and Molecules*. Oxford University Press, New York and Clarendon Press, Oxford (1989).
18. (a) S. K. Ghosh, *Chem. Phys. Lett.* **172**, 77–82 (1990); (b) M. K. Harbola, P. K. Chattaraj and R. G. Parr, *Isr. J. Chem.* **31**, 395–402 (1991).
19. R. Bonaccorsi, E. Scrocco and J. Tomasi, *J. Chem. Phys.* **52**, 5270–5284 (1970).
20. Unichem 4.0. Oxford Molecular Group, Oxford.
21. T. H. Dunning, *J. Chem. Phys.* **53**, 2823–2833 (1970).
22. M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez and J. A. Pople, Gaussian 94, Revision B.3. Gaussian, Pittsburgh, PA (1995).
23. W. J. Hehre, L. Radom, P. v. R. Schleyer and J. A. Pople, *Ab Initio Molecular Orbital Theory*. Wiley, New York (1986).
24. (a) M. Cherest and H. Felkin, *Tetrahedron Lett.* 2205–2208 (1968); (b) M. Cherest, H. Felkin and N. Prudent, *Tetrahedron Lett.* 2199–2204 (1968); (c) M. Cherest, H. Felkin, P. Tacheau, J. Jacques and D. Varech, *J. Chem. Soc., Chem. Commum.*, 372–373 (1977); (d) N. T. Anh, *Top. Curr. Chem.* **88**, 145 (1980).
25. (a) H. B. Bürgi, J. D. Dunitz, J. M. Lehn and G. Wipff, *Tetrahedron* **30**, 1563–1572 (1974); (b) H. B. Bürgi, J. D. Dunitz and E. J. Shefter, *J. Am. Chem. Soc.* **95**, 5065–5067 (1973); (c) H. B. Bürgi, J. M. Lehn and G. Wipff, *J. Am. Chem. Soc.* **96**, 1956–1957 (1974).
26. T. Brinck, J. S. Murray and P. Politzer, *J. Chem. Phys.* **98**, 4305–4306 (1993).