



Maximum nucleophilicity principle

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Abstract

An empirical principle, viz. maximum nucleophilicity principle (MNP), is proposed based on studying the change in nucleophilicity index (ΔN) for some basic reactions. It is observed that $N_{\text{Product}} > N_{\text{Reactant}}$ and $\Delta N \geq 0$ in majority of the reactions. Based on the obtained outcomes, it is revealed that ‘a chemical reaction or any species naturally directs itself towards a state of maximum nucleophilicity and stability’ and this behaviour can be known as MNP. It is believed that MNP could act as a valuable tool in predicting reactive behaviours, tendencies and stable geometries of real as well as hypothetical species.

Keywords Chemical reactivity descriptors · Maximum hardness principle · Minimum polarizability principle · Minimum electrophilicity principle · Nucleophilicity index · Stability

Introduction

A variety of phenomenon and reactions can be well understood using fundamental principles and concepts in chemistry. Information such as the rate of reaction, favourability of reaction, stability of newly formed products is some of the important aspects of any chemical reaction. It is well known that thermodynamics offers an insight about the extent of the reaction. However, in order to understand the characteristics mentioned above and similar other behaviours, reactivity descriptors (Geerlings et al. 2003) work as a handy tool. They provide us information on the changes any species undergoes while a reaction is at play. Such data are useful to interpret the stability of any probable or hypothetical product and can help in guiding about the fate of a reaction. There are several descriptors within the framework

of density functional theory (DFT) which help in this purpose (Parr and Pearson 1983; Parr et al. 1999; Tandon et al. 2019a, 2020, 2021a, b), and nucleophilicity index is one of them (Tandon et al. 2019b). Conceptually, nucleophilicity index (N) is understood as the power of an atom, molecule or ion to donate its electrons.

In order to study chemical processes in a better way, there are some well-known principles based on various reactivity descriptors, namely hard–soft acid–base (HSAB) principle (Drago 1973) and maximum hardness principle (MHP) (Pearson 1987) for hardness, electronegativity equalization principle (EEP) (Sanderson 1951, 1955) for electronegativity, minimum polarizability principle (MPP) (Chattaraj and Sengupta 1996) for polarizability, minimum magnetizability principle (MMP) (Tanwar et al. 2006) for magnetizability, electrophilicity equalization principle (EEP) (Chattaraj et al. 2010) and minimum electrophilicity principle (MEP) (Noorizadeh 2005, 2007) for electrophilicity index. Several studies have also been done to confirm the reliability of these principles in various conditions (Chattaraj et al. 2000; Selvarengan and Kolandaivel 2004; Anandan et al. 2005; Noorizadeh 2005; Pasha et al. 2005; Zhang and Yang 2006; Tandon et al. 2021c). However, our literature search leads to the observation that a principle based on ‘nucleophilicity index’, which is an immensely important descriptor of chemical reactivity, is not proposed yet. Due to the lack of such an electronic principle for the latter, there have been limitations on its employability. There has been a necessity for a principle which could be used for predicting fate of any

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interaction, especially those which are highly controlled by nucleophilicity, solely or conjointly with other principles. Thus, to overcome this complication, we are putting forward the ‘maximum nucleophilicity principle’ (MNP) which states ‘a chemical reaction naturally directs towards a state of maximum nucleophilicity and stability’. This empirical principle is proposed for nucleophilicity index (N) by calculating change in nucleophilicity index (ΔN) for 30 basic reactions. It can explain the direction of a chemical reaction and probably assist in understanding the changes taking place during the process.

Method of computation

In the present endeavour, we have selected 30 basic reactions to examine the nature and trend of these reactions in order to rule out whether a species prefers the state of maximum nucleophilicity. For this purpose, molecular nucleophilicity index has been calculated for the chosen reactants and products, using the geometric average rule (Eq. 1).

$$N_{GM} \approx (\prod_{k=1}^P N_k)^{1/P} \quad (1)$$

The atomic nucleophilicity index values for the calculation have been taken from the work of Tandon et al. (2019b). Here N_{GM} is the molecular nucleophilicity index calculated using geometric average. P refers to the number of atoms in a molecule, and N_k denotes the nucleophilicity of the each atom in that molecule.

Now, if in majority of the cases, the products in a reaction are found to be of higher nucleophilicity in comparison with the reactants, a maximum nucleophilicity condition may prevail. As we know, a chemical reaction (R_m) in the condensed form can be represented as $\sum r_m R_m = 0$. Here r_m refers to the stoichiometry of the m th molecule. Based on this, it can be said that Eq. (2) can present the resultant deviation in the nucleophilicity index (ΔN) in a specific reaction.

$$\Delta N = \sum_m r_m N_m \quad (2)$$

Here N_m refers to the nucleophilicity index value of the m th molecule in the given chemical reaction. The positive or negative sign of ΔN can serve as an indication of the direction of progression of a chemical reaction. Hence, ΔN has been calculated for the reactions under study using Eq. (2) empirically. For each chemical reaction, we have calculated total product nucleophilicity index value and total reactant nucleophilicity index value followed by determining the change (or difference) between these values according to Eq. (2).

Results and discussion

The present work suggests maximum nucleophilicity principle for studying the behaviour and characteristics of any chemical moiety and reaction. The reactions chosen for the study are common and simple chemical reactions including inorganic and organic (aliphatic and aromatic) molecules using the geometric average rule (Table 1). The cases considered for this study include some of the existing reactions as well as the hypothetical ones. Only exothermic reactions have been taken into account as they present thermodynamic stability. Additionally, reactions 17 and 18 comprise of same reactants, but the considered reactions and the products formed are different. The calculated nucleophilicity indices (N) for all the reactant and product molecules of the reactions in study are listed in Supplementary Table S1. Table 1 lists the computed total nucleophilicity indices for the reactants (N_{Reactant}) and products (N_{Product}) with corresponding change in nucleophilicity index (ΔN). Looking at the Table 1, it can be observed that 76.66% of the reactions under study have $N_{\text{Product}} > N_{\text{Reactant}}$ and $\Delta N \geq 0$. Hence, it is apparent that the condition of maximum nucleophilicity is achieved at the end of the reaction. Here we have evaluated the overall change in the nucleophilicity index during a reaction.

If maximum nucleophilicity principle does truly exist, then the products should be formed when the product nucleophilicity index is higher than that of the reactant. Also, the sign of ΔN should provide an idea for the reactions’ direction. On looking at Table 1, it is observed that the maximum nucleophilicity principle exists for chemical reactions since $\Delta N > 0$ for various reactions. Further, ΔN is positive in most of the cases which reveals that ΔN provides a sign for the most stable species. Hence, it can be said that the preferred direction of a chemical reaction is towards more nucleophilicity. When products to be formed are more stable than the reactants, enthalpy change is less than zero. This criterion is met by the selected reactions. Nevertheless, this principle does not follow always but in majority of the cases. It is consistent for approximately 76.66% of the selected reactions. It is noted that the presence of some hard bases, more number of lone pairs, hydrogen bonding or crowding around electronegative atoms is related to the failure of principle in some cases. For example, in reaction 3, it can be seen that the reactants O_2 and CO possess lone pairs while the product CO_2 has none. As it is well known, the presence of lone pairs increases nucleophilicity of the molecule. Hence, the change in nucleophilicity for this reaction is negative. A look at reaction 17 shows that the product has a tendency of hydrogen bond formation as one H is directly attached to the electronegative O atom and another H is

Table 1 Selected reactions with their computed reactant (N_{Reactant}) and product (N_{Product}) total nucleophilicity indices with corresponding change in nucleophilicity index (ΔN) (in au)

S. No.	Reaction	N_{Reactant}	N_{Product}	ΔN
1	$\text{H}_2 + \text{O}_2 \rightarrow \text{H}_2\text{O}_2$	3.5199	4.7338	1.2139
2	$2\text{NO} \rightarrow \text{O}_2 + \text{N}_2$	0.4898	0.4898	0.0000
3	$\text{O}_2 + 2\text{CO} \rightarrow 2\text{CO}_2$	0.7549	0.5033	-0.2516
4	$\text{Cl}_2 + \text{H}_2 \rightarrow 2\text{HCl}$	7.0451	7.0451	0.0000
5	$\text{I}_2 + \text{H}_2 \rightarrow 2\text{HI}$	7.1212	7.1212	0.0000
6	$\text{O}_2 + 2\text{H}_2 \rightarrow 2\text{H}_2\text{O}$	13.8360	9.2240	-4.6120
7	$2\text{NO}_2 \rightarrow \text{N}_2\text{O}_4$	0.4890	0.2445	-0.2445
8	$\text{HCN} + \text{CH}_3\text{Cl} \rightarrow \text{CH}_3\text{CN} + \text{HCl}$	6.6176	7.0508	0.4332
9	$4\text{NH}_3 + 5\text{O}_2 \rightarrow 4\text{NO} + 6\text{H}_2\text{O}$	21.8530	28.6516	6.7986
10	$2\text{NH}_3 + 3\text{Cl}_2 \rightarrow \text{N}_2 + 6\text{HCl}$	11.0642	21.3815	10.3173
11	$\text{CH}_4 + 2\text{O}_2 \rightarrow \text{CO}_2 + 2\text{H}_2\text{O}$	5.9778	9.4756	3.4978
12	$\text{CH}_4 + \text{Cl}_2 \rightarrow \text{CH}_3\text{Cl} + \text{HCl}$	5.7394	7.7035	1.9642
13	$\text{C}_2\text{H}_2 + 2\text{H}_2 \rightarrow \text{C}_2\text{H}_6$	17.1241	32.8409	15.7167
14	$\text{C}_2\text{H}_2 + \text{N}_2 \rightarrow 2\text{HCN}$	3.7780	4.8732	1.0952
15	$2\text{C}_2\text{H}_2 + 5\text{O}_2 \rightarrow 4\text{CO}_2 + 2\text{H}_2\text{O}$	8.2821	10.2305	1.9484
16	$\text{C}_2\text{H}_2 + \text{Cl}_2 \rightarrow \text{Cl}_2\text{CCH}_2$	3.7808	2.4376	-1.3433
17	$\text{C}_2\text{H}_6 + \text{O}_2 \rightarrow (\text{CH}_2\text{OH})_2$	5.4077	4.1799	-1.2277
18	$\text{C}_2\text{H}_6 + 1/2\text{O}_2 \rightarrow (\text{CH}_3)_2\text{O}$	5.2858	4.6173	-0.6685
19	$\text{C}_3\text{H}_8 + 5\text{O}_2 \rightarrow 3\text{CO}_2 + 4\text{H}_2\text{O}$	6.2340	19.2029	12.9689
20	$\text{CH}_3\text{F} + \text{CHF}_3 \rightarrow \text{CH}_4 + \text{CF}_4$	5.7254	5.7254	0.0000
21	$2\text{C}_6\text{H}_6 + 15\text{O}_2 \rightarrow 12\text{CO}_2 + 6\text{H}_2\text{O}$	10.7189	30.6916	19.9727
22	$2\text{CH}_3\text{OH} + 3\text{O}_2 \rightarrow 2\text{CO}_2 + 4\text{H}_2\text{O}$	9.9630	18.9512	8.9883
23	$\text{C}_2\text{H}_5\text{OH} + 3\text{O}_2 \rightarrow 2\text{CO}_2 + 3\text{H}_2\text{O}$	5.3483	14.3392	8.9909
24	$\text{C}_2\text{H}_5\text{OH} \rightarrow \text{CH}_2\text{CH}_2 + \text{H}_2\text{O}$	4.6173	9.2319	4.6146
25	$\text{C}_2\text{H}_5\text{Cl} + \text{KOH} \rightarrow \text{CH}_2\text{CH}_2 + \text{KCl} + \text{H}_2\text{O}$	6.8954	9.6613	2.7658
26	$\text{C}_3\text{H}_7\text{OH} + \text{HCl} \rightarrow \text{C}_3\text{H}_7\text{Cl} + \text{H}_2\text{O}$	8.1405	9.0324	0.8919
27	$\text{N}_2\text{H}_4 + \text{O}_2 \rightarrow \text{N}_2 + 2\text{H}_2\text{O}$	4.8565	9.4701	4.6136
28	$\text{C}_6\text{H}_5\text{CH}_3 + \text{H}_2 \rightarrow \text{C}_6\text{H}_6 + \text{CH}_4$	10.5456	9.0223	-1.5233
29	$\text{C}_6\text{H}_5\text{NH}_2 + \text{H}_2\text{O} \rightarrow \text{C}_6\text{H}_5\text{OH} + \text{NH}_3$	8.1423	8.4376	0.2952
30	$\text{CuO} + \text{H}_2\text{SO}_4 \rightarrow \text{CuSO}_4 + \text{H}_2\text{O}$	2.4491	4.8887	2.4396

available for hydrogen bond formation. This bond formation accounts for the decrease in the nucleophilicity of ethylene glycol in this reaction in comparison with the reactants leading to violation of the principle. Similarly, steric crowding is also responsible for decrease in the nucleophilicity as can be seen from reactions 16–18.

Table 2 presents a comparison of proposed maximum nucleophilicity principle (MNP) with some of the important existing principles such as maximum hardness principle (MHP), minimum polarizability principle (MPP), minimum electrophilicity principle (MEP) and minimum magnetizability principle (MMP). For the purpose of this comparison, we have selected all those reactions from reference (Tandon et al. 2021c) which have also been studied in the present work. It is noted that both MEP and MMP are valid for 87.50% of the total selected reactions. MNP follows the order and is found to be valid for 75% of the reactions used for the comparison. As expected, MPP is valid for 62.50% reactions and only 56.25% reactions are

in accordance with MHP. Hence, it can be appropriately put forward that MNP exists in case of molecule formation or chemical reaction. MNP is nearly as useful as MEP in anticipating the direction of any reaction. As with other descriptors, the sign of ΔN can also be helpful in giving information about the higher thermodynamic stability of products.

Considering the results of previous studies on different principles, and looking at the results of the present study, it can be assumed that MNP is also just as useful as other principles. We included several types of molecules in the analysis, to create diversity, so that study of chemical effects could be done in the best way. It is to be noted that the variation in nucleophilicity index values along the reaction path was not taken into account here. However, further studies on this matter can be valuable and assist the present outcomes. The future prospect of this work could be the evaluation of this principle in terms of different levels of theory and larger molecules.

Table 2 Change in the hardness ($\Delta\eta$) (in au), polarizability ($\Delta\alpha$) (in au), electrophilicity index ($\Delta\omega$) (in au), magnetizability ($\Delta\xi$) (in au) and nucleophilicity index (ΔN) (in au) values, along with MHP, MPP, MEP, MMP and MNP validity (V) or invalidity (I) for some reactions

S. No	Reaction	$\Delta\eta^a$	V/I	$\Delta\alpha^a$	V/I	$\Delta\omega^a$	V/I	$\Delta\xi^a$	V/I	ΔN	V/I
1	$2\text{NO} \rightarrow \text{O}_2 + \text{N}_2$	0.110	V	-0.487	V	0.352	I	118.256	I	0.000	V
2	$\text{Cl}_2 + \text{H}_2 \rightarrow 2\text{HCl}$	-0.004	I	6.223	I	-0.414	V	-0.111	V	0.000	V
3	$2\text{NO}_2 \rightarrow \text{N}_2\text{O}_4$	-0.070	I	-5.228	V	-0.287	V	-49.046	V	-0.245	I
4	$4\text{NH}_3 + 5\text{O}_2 \rightarrow 4\text{NO} + 6\text{H}_2\text{O}$	0.469	V	-0.187	V	-2.868	V	-2403.099	V	6.799	V
5	$\text{CH}_4 + 2\text{O}_2 \rightarrow \text{CO}_2 + 2\text{H}_2\text{O}$	0.333	V	-0.308	V	-1.625	V	-1439.901	V	3.498	V
6	$\text{C}_2\text{H}_2 + 2\text{H}_2 \rightarrow \text{C}_2\text{H}_6$	-0.473	I	0.314	I	-0.074	V	-2.132	V	15.717	V
7	$2\text{C}_2\text{H}_2 + 5\text{O}_2 \rightarrow 4\text{CO}_2 + 2\text{H}_2\text{O}$	0.318	V	-12.235	V	-3.771	V	-3598.660	V	1.948	V
8	$\text{C}_2\text{H}_2 + \text{Cl}_2 \rightarrow \text{Cl}_2\text{CCH}_2$	-0.104	I	-2.685	V	-0.440	V	0.085	I	-1.343	I
9	$\text{C}_2\text{H}_6 + \text{O}_2 \rightarrow (\text{CH}_2\text{OH})_2$	-0.123	I	8.306	I	-0.892	V	-718.916	V	-1.228	I
10	$\text{C}_2\text{H}_6 + 1/2\text{O}_2 \rightarrow (\text{CH}_3)_2\text{O}$	-0.084	I	-0.001	V	-0.446	V	-358.325	V	-0.669	I
11	$\text{C}_3\text{H}_8 + 5\text{O}_2 \rightarrow 3\text{CO}_2 + 4\text{H}_2\text{O}$	0.787	V	8.727	I	-4.078	V	-3601.992	V	12.969	V
12	$\text{CH}_3\text{F} + \text{CHF}_3 \rightarrow \text{CH}_4 + \text{CF}_4$	-0.270	I	-8.218	V	0.394	I	-2.221	V	0.000	V
13	$2\text{C}_6\text{H}_6 + 15\text{O}_2 \rightarrow 12\text{CO}_2 + 6\text{H}_2\text{O}$	1.679	V	-37.574	V	-11.406	V	-10,794.771	V	19.973	V
14	$2\text{CH}_3\text{OH} + 3\text{O}_2 \rightarrow 2\text{CO}_2 + 4\text{H}_2\text{O}$	0.507	V	6.158	I	-2.262	V	-2161.648	V	8.988	V
15	$\text{C}_2\text{H}_5\text{OH} + 3\text{O}_2 \rightarrow 2\text{CO}_2 + 3\text{H}_2\text{O}$	0.496	V	-5.966	V	-2.262	V	-2161.202	V	8.991	V
16	$\text{N}_2\text{H}_4 + \text{O}_2 \rightarrow \text{N}_2 + 2\text{H}_2\text{O}$	0.391	V	0.128	I	-0.655	V	-722.808	V	4.614	V

^aValues taken from Tandon et al. (2021c)

Conclusion

Information based on the direction of reaction is very crucial when predicting reactive behaviours and tendencies. Availability of such knowledge can be highly beneficial in understanding any known, potent as well as hypothetical reaction. ‘Maximum nucleophilicity principle’ (MNP) is a key which aids in providing such information. Numerous chemical and biological reactions along with activities such as corrosion, inhibition, and formation of magma, rocks and other materials present in earth’s crust can be understood based on this principle. The fate of a reaction, formation of products as well as the stability of the reactants and products can be satisfactorily deduced with the help of this principle. As apparent, a great deal of information can be understood and explained using MNP. Apart from explicating reaction direction and behaviours, this principle also helps in exploring and describing the connections with other properties such as electrophilicity and polarizability. Overall, the principle can be used in an infinite number of realms to analyse various dynamic systems.

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Author contributions HT was involved in conceptualization, methodology, formal analysis, validation, investigation, writing—original draft

and visualization. RB was responsible for resources. TC took part in conceptualization, supervision, writing—reviewing and editing.

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Declarations

Conflict of interest The authors have no competing interests.

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