

New insights into steric and electronic effects in a series of phosphine ligands from the perspective of local quantum similarity using the Fukui function

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Abstract The field of molecular quantum similarity (MQS) was introduced by Carbó-Dorca 30 years ago. MQS currently suffers from numerous bottlenecks, for example when studying similarities in chemical reactivity, because there is no clear guidance on the best methodology to follow. For this reason, we have revisited this topic here. Today's search tools and methodologies have made an important contribution to studying steric and electronic effects in phosphine ligands (PR_3). In this contribution, we propose a hybrid methodology joining (MQS) and chemical reactivity. Additionally, a chemical reactivity study using global and local reactivity descriptors was performed in the context of density functional theory (DFT). Phosphines are σ -donor and π -acceptor ligands, therefore reactivity descriptors allow us quantify the retrodonor process in terms of quantum similarity (QS). In this regard, new ways to characterize steric and electronic effects in phosphine ligands and their chemical bonds are presented in the QS context.

Keywords Phosphine ligand · Molecular quantum similarity · Reactivity descriptor · Density functional theory

Introduction

Phosphine ligands are an important class of ligand due to their electronic and steric properties [1–10]. Currently, the search for methodologies with which to study the effects of stereochemical and electronic behavior in phosphine ligands is very important; these effects have

been studied from the perspective of quantum similarity (QS) formalism [11–19] and chemical reactivity using density functional theory (DFT).

In an effort to find steric and electronic patterns on ligand phosphines (PR_3), in this study we used a molecular assembly studied previously by Mathew and Suresh [20]. These latter authors analyzed a series of phosphine ligands using a combination of quantum mechanics (QM) and molecular mechanics (MM)—the ONIOM method—showing that hybrid methodologies can be very useful in obtaining a possible quantitative assessment of the stereo-electronic profile. For this reason, in this study, we adopted a combined approach of molecular quantum similarity indexes (MQSI) [11–19] and chemical reactivity descriptors supported in DFT [21–24]. Due to the crucial role of the electron density in MQSI, it is natural that a close relationship exists between DFT [24, 25] and QS [26–31]; the primary aim of this research was to find patterns of QS in the chemical reactivity in phosphine ligands, taking into account the mathematical background of QS together with the excellent predictions of reactivity indexes available today.

It is expected that this hybrid methodology will lead to new insights into steric and electronic effects in the DFT context; moreover, this study agrees with many current theoretical and experimental methodologies [32–35].

Computational methods

Similarity indexes

The similarity indexes used here were introduced by Carbó and co-workers almost 30 years ago [11–19]; these latter authors defined the QS measure Z_{AB} between molecules A and

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B with electron density $\rho_A(r)$ and $\rho_B(r)$ based on the idea of minimizing the expression for Euclidean distance as:

$$D_{AB}^2 = \int |\rho_A(r) - \rho_B(r)|^2 dr = \int \rho_A^2(r) dr + \int \rho_B^2(r) dr - 2 \int \rho_A(r) \rho_B(r) dr = Z_{AA} + Z_{BB} - 2Z_{AB} \quad (1)$$

The overlap integral involves the Z_{AB} between the electron density of molecule A and B, Z_{AA} and Z_{BB} are the self-similarity of molecules A and B, respectively [16].

The most common QS index is the one generalized by the cosine, introduced by Carbó et al. [11, 12]. This index can be expressed mathematically as:

$$I_{AB} = \frac{\int \rho_A(r) \rho_B(r) dr}{\sqrt{\int \rho_A(r) \rho_A(r) dr \int \rho_B(r) \rho_B(r) dr}} \quad (2)$$

Or, as a function of the elements Z and an operator (Ω) as:

$$I_{AB} = \frac{Z_{AB}(\Omega)}{\sqrt{Z_{AA}(\Omega) Z_{BB}(\Omega)}} \quad (3)$$

Another alternative to express QS is the Hodgkin-Richards index [36, 37]; this index appears naturally when using the arithmetic mean, and can be defined mathematically as:

$$I_{AB} = \frac{2Z_{AB}(\Omega)}{Z_{AA}(\Omega) + Z_{BB}(\Omega)} \quad (4)$$

Local quantum similarity indexes

The Hirshfeld approach

Since the Hirschfeld approach was postulated [38–41], many studies have been conducted on this partitioning scheme. Consequently, a considerable background is available on this topic and we chose this scheme to obtain local contributions of the QS on the phosphorus atom (PH_3) (Fig. 1) and compared them with the studied molecular set [38].

The Hirshfeld approach was developed for the calculation of stockholder charge partitioning. This approach is based on partitioning of the electron density $\rho(r)$ of a molecule in contributions $\rho(r)$. These contributions are proportional to the weight $w_A(r)$ of the electron density of the isolated molecule, called the promolecular density [42–45], and this weight is defined as the sum of the electron density of the isolated atom constructed from the superposition of the density of all atoms isolated in

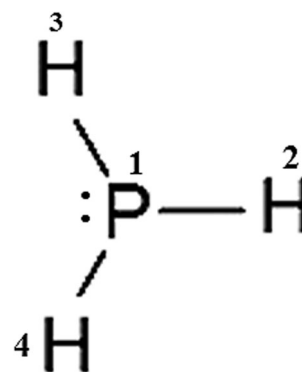


Fig. 1 Structure used in the molecular alignment (PH_3). The atoms used in molecular alignment are labeled

the same position of the molecule (i.e., the promolecular density). This is obtained as:

$$\rho_A^{\text{prom}}(r) = \sum_x \rho_x^0(r) \quad (5)$$

The contribution of atom A, $\rho_A(r)$ to the electron density $\rho(r)$ is obtained as:

$$\rho_A(r) = w_A(r) \rho(r) \quad (6)$$

Whereby the weight [$w_A(r)$] is obtained as:

$$w_A(r) = \frac{\rho_A^0(r)}{\sum_x \rho_x^0(r)} \quad (7)$$

where $\rho_A^0(r)$ is the electron density of the isolated atom A [46].

The contribution of the atomic (P^1) phosphorus atom to molecule A is given by:

$$\rho_{P^1,A}(r) = w_{P^1}(r) \rho_A(r) \quad (8)$$

with

$$w_{P^1,A} = \frac{\rho_{P^1,A}^0(r)}{\sum_x \rho_{x,A}^0(r)} \quad (9)$$

Thus the contribution of the atomic phosphorus atom (P^2) in molecule B is obtained as:

$$\rho_{P^2,B}(r) = w_{P^2}(r) \rho_B(r) \quad (10)$$

with

$$w_{P^2,B} = \frac{\rho_{P^2,B}^0(r)}{\sum_x \rho_{x,B}^0(r)} \quad (11)$$

So it is possible to write the contribution of the asymmetric phosphorus atom products $\rho_A(r)\rho_B(r)$ as:

$$\rho_{P,AB}(r) = w_{P,AB}(r)\rho_A(r)\rho_B(r) \tag{12}$$

with

$$w_{P,AB}(r) = \left(\frac{\rho_{P^1,A}^0(r)}{\sum_x \rho_{x,A}^0(r)} \right) \left(\frac{\rho_{P^2,B}^0(r)}{\sum_x \rho_{x,B}^0(r)} \right) \tag{13}$$

Where $\sum_x \rho_{x,A}^0(r)\sum_x \rho_{x,B}^0(r)$ is the total promolecular density overlay of the two molecules considered, so that we can express the Carbó index (Eq. 3) as:

$$Z_{A,B}^{Local,P} = \frac{Z_{AB}}{\sqrt{Z_{AA}Z_{BB}}} = \frac{\int \int \left(\frac{\rho_{P^1,A}^0(r)}{\sum_x \rho_{x,A}^0(r)} \right) \left(\frac{\rho_{P^2,B}^0(r)}{\sum_x \rho_{x,B}^0(r)} \right) \rho_A(r)\rho_B(r) dr}{\sqrt{\left(\int \frac{\rho_{P^1,A}^0(r)}{\sum_x \rho_{x,A}^0(r)} \rho_A(r) dr \right)^2 \left(\int \frac{\rho_{P^2,B}^0(r)}{\sum_x \rho_{x,B}^0(r)} \rho_B(r) dr \right)^2}} \tag{14}$$

where we can see the global index (Eq. 3), partitioned in atomic contributions from the atomic shell approximation (ASA) [46, 47].

Global and local reactivity descriptors

As a detailed presentation and discussion of the reactivity parameters used in this paper can be found elsewhere [21–24, 47–53], only the relevant expressions used for the evaluation of different quantities for phosphine ligands are given here.

Chemical potential, hardness and softness are calculated as follows:

$$\mu \approx \frac{\varepsilon_L + \varepsilon_H}{2} \tag{15}$$

$$\eta \approx \frac{\varepsilon_L - \varepsilon_H}{2} \tag{16}$$

$$S = \frac{1}{\eta} \tag{17}$$

where ε_L and ε_H represent the energies of the higher occupied molecular orbital (HOMO) and lowest unoccupied molecular

orbital (LUMO), respectively. These descriptors describe global properties for a system as a whole.

Using Eqs. 15 and 16 is possible to determine the electrophilicity (ω) index, defined as:

$$\omega = \frac{\mu^2}{2\eta} \tag{18}$$

Where (ω) is another global property and represents the stabilization energy of the system when it is saturated by electrons from the external environment. The descriptors displayed in Eqs. 15–18 are also known as global descriptors; they are dependent on N and $\nu(r)$, and provide information on the reactivity and stability of a chemical system [21, 22]. Local properties are obtained taking into account the variation in energy with respect to the external potential. This variation depends on the position (r), and can be defined as selectivity indexes. It is possible to use the Fukui function [54, 55] in this context; the Fukui function explains the selectivity of a region of a molecule and is defined mathematically as:

$$\begin{aligned} \langle f(\vec{r}) \rangle &= \left(\frac{\delta \mu}{\delta \nu(\vec{r})} \right)_N = \left(\frac{\partial \rho(\vec{r})}{\partial N} \right)_{\nu(\vec{r})} \\ &= \left(\frac{\partial^2 E}{\partial N \partial \nu(\vec{r})} \right) \end{aligned} \tag{19}$$

The Fukui function is interpreted as the change in chemical potential given an external perturbation, or the variation of the electron density function when the electron number changes. To calculate the Fukui function $f^+(r)$, the condensed approach proposed by Yang and Mortier [69] was used, using the Mulliken charge at atom K, q_k , for systems with N, N + 1, and N – 1 electrons, respectively, calculated at the same geometry as defined in the following equations [54, 55]:

$$\begin{aligned} \langle f_k^+(\vec{r}) \rangle &\approx \int_k [\rho_{N+1}(\vec{r}) - \rho(\vec{r})] \\ &= [q_k(N + 1) - q_k(N)] \end{aligned} \tag{20}$$

$$\begin{aligned} \langle f_k^-(\vec{r}) \rangle &\approx \int_k [\rho_N(\vec{r}) - \rho_{N-1}(\vec{r})] \\ &= [q_k(N) - q_k(N-1)] \end{aligned} \tag{21}$$

With $q_k(N)$ denoting the electronic population of atom k of the system under study, in the atomic orbital condensate

(AOC) approximation these Fukui functions consider only the contribution of atom frontier orbitals [56, 57].

$$\langle f_k^+ \rangle \approx \int_k \rho_L(\vec{r}) d\vec{r} = q_k^L \quad (22)$$

$$\langle f_k^- \rangle \approx \int_k \rho_H(\vec{r}) d\vec{r} = q_k^H \quad (23)$$

with q_k^L and q_k^H representing the electronic populations on LUMO and HOMO, respectively, for atom k.

Connecting QS and chemical reactivity

Using the formalism of the Dirac delta distribution $\Omega(r_1, r_2) = \delta(r_1, r_2)$ [58], it is possible to define the so called overlap molecular quantum similarity measure (MQSM) and to express the volume associated with the overlap of the two densities ρ_A and ρ_B mathematically using the following equation [58]:

$$\begin{aligned} Z_{AB}(\Omega) &= \iint \rho_A(r_1) \delta(r_1 - r_2) \rho_B(r_2) dr_1 dr_2 \\ &= \int \rho_A(r) \rho_B(r) dr \end{aligned} \quad (24)$$

Equation 24 provides information about the electron concentration in the molecule and indicates the degree of overlap between the compared compounds.

When the Ω operator in Eq. 4 is the Coulomb operator $\Omega(r_1, r_2) = |r_1 - r_2|^{-1}$ it represents the electronic coulomb repulsion energy between molecular densities ρ_A and ρ_B , and can be expressed mathematically as:

$$Z_{AB}(\Omega) = \iint \rho_A(r_1) \frac{1}{|r_1 - r_2|} \rho_B(r_2) dr_1 dr_2 \quad (25)$$

The coulomb operator considers the molecular density functions as electron distributions in space and calculates the coulomb repulsion between the electron distributions (Eq. 26). Equations 24 and 25 show a way to obtain the QS measure in terms of steric and electronic effects, taking into account these considerations. In this study we propose a relationship between QS and chemical reactivity through Eqs. 26 and 27, using Fukui functions.

$$R_{PX}(f_{PX}^+) = \frac{(f_P^+)(f_X^+)}{\sqrt{(f_{PP}^+)(f_{XX}^+)}} \quad (26)$$

$$R_{PX}(f_{PX}^-) = \frac{(f_P^-)(f_X^-)}{\sqrt{(f_{PP}^-)(f_{XX}^-)}} \quad (27)$$

In Eqs. 26 and 27, P represents the phosphorus atom and X represents the molecular set. We used the Carbó index and Fukui functions to represent the MQSM with respect to the reference compound (PH₃). Equations 26 and 27 refer to the σ donor and π acceptor capacities in the phosphine ligands. In this sense, a greater value in Eq. 26 with respect to the same measurement in Eq. 27 means that the molecule has a greater π acceptor capacity and less donor σ capacity, and vice versa.

One of the important features of the similarity field in chemical reactivity is global similarity. For this reason, we used global softness to study the degree of distortion that occurs in the electron cloud when a π acceptance or σ donation takes place. For this, Eqs. 28 and 29 are used:

$$R_{PX}(Sf_{PX}^+) = S \left(\frac{(f_P^+)(f_X^+)}{\sqrt{(f_{PP}^+)(f_{XX}^+)}} \right) \quad (28)$$

$$R_{PX}(Sf_{PX}^-) = S \left(\frac{(f_P^-)(f_X^-)}{\sqrt{(f_{PP}^-)(f_{XX}^-)}} \right) \quad (29)$$

An advantage of linking the local QS with chemical reactivity is that both QS indexes and the Fukui functions used in this study are normalized to unity and therefore have convergence.

Centroid origin shift in the Fukui function sets

According to Carbó et al. [11, 12] it is possible to consider a set of specific vectors and to associate a center for this molecular basis. In this study, a molecular set represented by Fukui functions is defined as:

$$M = \{|I\rangle | I = 1, N\} \quad (30)$$

In Eq. 29, the first order densities can be constructed by a set of molecular orbital (MO) of shape function (ShF) contributions as:

$$P = \{\sigma_I = |I\rangle \langle I| | I = 1, N\} \quad (31)$$

The P elements correspond to the squared MO modulus. In this sense, we can relate the frontier orbitals (HOMO and LUMO) in the molecular set. Defining $\{w_I\}$ as the number of occupation in the MOs, we can construct a linear combination of P to the first order density functional (DF) as [12]:

$$\rho = \sum_I w_I \sigma_I \quad (32)$$

with

- (1) v is the number of electrons: $\sum w_I = v$
- (2) Where the Minkowski norms of the elements of the ShF set P are normalized to unity, belonging to the MO set normalization ($\forall I: \langle \sigma_I \rangle = 1$).

Taking into account these characteristics, we can define a centroid ShF, using an average function [12]:

$$\sigma_C = N^{-1} \sum_I \sigma_I \rightarrow \langle \sigma_C \rangle = 1 \quad (33)$$

Therefore, each element of set P can be compared with the centroid function, which can be built as:

$$\forall I: \theta_I = \sigma_I - \sigma_C \rightarrow Z = \{\theta_I | I = 1, N\} \quad (34)$$

The Minkowski pseudonorm of the centroid ShF set Z can be written as:

$$\forall I: \theta_I = \langle \sigma_I - \sigma_C \rangle = \langle \sigma_I \rangle - \langle \sigma_C \rangle = 0 \quad (35)$$

so that the shifted elements have a null Minkowski pseudonorm. Where the ShF is comprised of N linearly independent elements, the centroid ShF set is also comprised of $(N - 1)$ independent elements [12]. Therefore, the elements of the centroid ShF set Z can be written as:

$$\forall I: \theta_I = N^{-1} \left((N-1)\sigma_I - \sum_{J \neq I} \sigma_J \right) = \sigma_I + N^{-1} \sum_{J \neq I} (\sigma_I - \sigma_J) \quad (36)$$

This equation (Eq. 36) shows that each centroid ShF can be defined as a function of the differences of the ShF of P from the other elements in the studied set. In these steps, we can compare the phosphine ligands with respect to the reference molecule PH_3 .

Molecular alignment and computational details

The question of how the similarity between different molecules should be addressed is not yet completely answered [11–15]. There are also practical problems with the computation and application of QS. The first serious difficulty appears when a quantification of the notion of similarity is applied to chemical compounds, because the concept of structure is not defined uniquely in chemistry. In fact, the molecular structure of the same molecule can be represented by more than one mutually distinct and non-equivalent object (vide infra).

A uniform approach to the characterization of molecular structure is a goal of the various strategies currently used to perform MQS. Indeed, many methods have now been established to create the best conditions for an optimal overlap, including the comparative molecular field analysis

(CoMFA) and comparative molecular similarity indices analysis (CoMSIA) methodologies that have been used widely to obtain three-dimensional quantitative structure-activity relationship (3D-QSAR) models [59]. In this regard, many alignment methods have been implemented in this field, such as the maximum similarity superposition algorithm (MSSA) proposed by Constans et al. [60].

This method takes into account the fact that optimal alignment provides the maximum value of similarity measures for a given similarity operator. Another algorithm implemented in the QS field is the topo-geometrical superposition algorithm (TGSA) proposed by Girones et al. [19, 61–63]. Unlike the MSSA, this alignment technique considers the optimal alignment of overlap given the recognition of a common skeleton, taking into consideration only the kinds of atoms and bond distances.

Given that the molecular space is well defined from the local partition in the QS indexes using density function type (ASA), the TGSA alignment method was used in this study. This method can be considered as a general purpose alignment procedure, designed to superimpose rigid molecules based on atomic numbers, molecular coordinates, and connectivity. The TGSA algorithm was developed to enable handling of rotations around single bonds; in this way, common structural features that are not properly aligned due to conformational causes can be brought together, thus improving the molecular similarity alignment [19, 61–63].

The molecular set of study and molecular electrostatic potential (MESP) V_{\min} (PR_3) values were taken from reference [20] and are shown in Table 1.

Table 1 Compound studied and molecular electrostatic potential (MESP) V_{\min} (PR_3) values [20]

Notation	Compound	V_{\min} (PR_3) (kcal mol^{-1})
1	PH_3	-28.22
2	PMe_3	-43.02
3	P(Et)_3	-43.55
4	P(iPr)_3	-44.18
5	P(tBu)_3	-44.90
6	$\text{P(CF}_3)_3$	-5.95
7	PH_2Ph	-31.05
8	PEtPh_2	-37.23
9	P(tBu)Ph_2	-38.86
10	PMe_2Ph	-40.41
11	PMePh_2	-36.76
12	PCy_3	-44.99
13	PPh_3	-34.07

Table 2 Molecular quantum similarity matrix (MQSM) using the overlap operator

Compound	1	2	3	4	5	6	7	8	9	10	11	12	13
1	1.000												
2	0.623	1.000											
3	0.503	0.479	1.000										
4	0.489	0.499	0.655	1.000									
5	0.456	0.373	0.511	0.461	1.000								
6	0.436	0.759	0.514	0.453	0.584	1.000							
7	0.429	0.625	0.497	0.625	0.506	0.360	1.000						
8	0.415	0.454	0.397	0.437	0.360	0.181	0.545	1.000					
9	0.405	0.612	0.413	0.463	0.367	0.274	0.526	0.515	1.000				
10	0.395	0.567	0.710	0.323	0.605	0.494	0.410	0.358	0.426	1.000			
11	0.385	0.544	0.676	0.535	0.819	0.653	0.422	0.465	0.563	0.442	1.000		
12	0.356	0.517	0.732	0.464	0.477	0.382	0.493	0.586	0.588	0.444	0.624	1.000	
13	0.354	0.504	0.713	0.456	0.468	0.375	0.489	0.553	0.575	0.548	0.593	0.614	1.000

All calculations were carried out using Gaussian-03 [64]. All geometries were completely optimized using B3LYP [65] 6-311++G(2d,2p) [66]; Fukui functions were computed according to Eqs. 22 and 23.

Results and discussion

Molecular quantum similarity indexes analysis

This study calculated the overlap-MQSM in order to describe the steric effects in the studied compound (see Table 1) and to determine its structural correlation. These overlap-MQSM values are shown in Table 2.

The overlap values calculated with Eq. 24 are shown in Table 2, with the self-similarity located in the matrix

diagonal. The lowest similarity value using the overlap index was obtained between molecules 6 and 8 (0.181) and the corresponding Euclidean distance of overlap was 4.993, while the highest value was between molecules 5 and 11 (0.819) and their Euclidean distance was 2.698. Taking into account the range (0, 1) of the Carbó index, where $C_{AB} = 0$ means dis(similarity) and $C_{AB} = 1$ self-similarity, according to the Schwartz integral, inequality is expressed as:

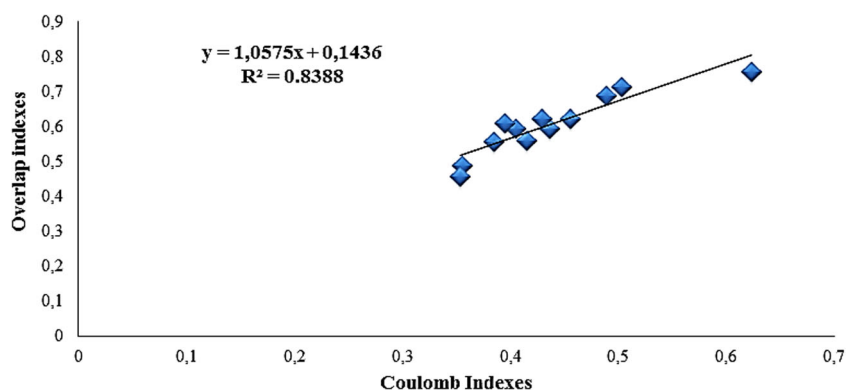
$$\left[\int \rho_A(r)\rho_B(r)dr \right]^2 \leq \int \rho_A^2(r)dr \int \rho_B^2(r)dr \quad (36)$$

where $\rho_A(r)$ and $\rho_B(r)$ are the analyzed density functions of the compound studied.

Table 3 MQSM using the Coulomb operator

Compound	1	2	3	4	5	6	7	8	9	10	11	12	13
1	1.000												
2	0.756	1.000											
3	0.714	0.873	1.000										
4	0.689	0.862	0.914	1.000									
5	0.624	0.874	0.939	0.951	1.000								
6	0.596	0.834	0.913	0.939	0.981	1.000							
7	0.621	0.956	0.890	0.899	0.919	0.878	1.000						
8	0.561	0.940	0.907	0.944	0.925	0.891	0.952	1.000					
9	0.595	0.857	0.861	0.899	0.863	0.677	0.942	0.979	1.000				
10	0.611	0.941	0.888	0.905	0.903	0.869	0.944	0.953	0.963	1.000			
11	0.558	0.909	0.870	0.786	0.825	0.806	0.784	0.793	0.849	0.764	1.000		
12	0.488	0.883	0.911	0.934	0.968	0.947	0.851	0.914	0.934	0.906	0.859	1.000	
13	0.458	0.892	0.964	0.922	0.905	0.886	0.909	0.941	0.947	0.923	0.845	0.941	1.000

Fig. 2 Correlation ($R^2=0.8388$) between the overlap and Coulomb indexes with respect to reference compound 1. See Tables 2 and 3, respectively



In order to study the phosphines ligands from an electronic point of view, coulomb-MQSI values were calculated (see Table 3).

Compound 5 has a higher Coulomb index value with respect to compound 6 with a value of 0.981 (Table 3); their Coulomb Euclidean distance is 12.782. The lowest value in the Coulomb index (0.458) was obtained between compounds 1 and 13, with a Euclidean distance of 33.439. These values match those obtained in the overlap similarity (see Table 2). In this regard, these calculations allow us to study the electronic effects associated with the substituent groups in the molecular set with respect to compound 1; their correlation is shown in Fig. 2.

Figure 2 shows that the use of MQS allows us study steric and electronic effects independently and in a complementary manner, therefore making it possible to quantify the stereo-electronic character in each phosphine as strong and weak, and to state their differences. As the Coulomb descriptor is the most important, the condensed Fukui function at a given

atomic site can be related directly to the molecular polarization (Coulomb hole) according to Senet et al. [47]. Thus, in this study, we calculated chemical reactivity descriptors to study electronic correlation along the serie in systematic form.

Global and local reactivity descriptors

A possible way to understand Coulomb similarity is to take into account the fact that phosphines are σ -donors and π -acceptors. To perform the analysis on the reactivity indexes was studied the stabilization of low oxidation states in coordination compounds through the global and local reactivity descriptors (Tables 4 and 5, respectively).

In Table 4, molecule 5 is the most reactive and 6 is the most stable, with chemical potentials of -1.881 and -4.750 , respectively. These values are consistent with the hardness value of compound 6 ($\eta=3.873$) and the softness value of compound 5 ($S=0.280$), and also consistent with the Coulomb values (see Table 3). In order to analyze the retro-donor character and determine the type of interactions present in this molecular set, we calculated the Fukui functions $\langle f^-(r) \rangle$ and $\langle f^+(r) \rangle$ on the central P atom (Table 5).

Table 4 Global reactivity indexes

Compound	μ^a (eV)	η^b (eV)	S^c (eV $^{-1}$)	ω^d (eV)
1	-2.3173	3.932	0.254	0.341
2	-2.116	3.869	0.259	0.289
3	-2.160	3.726	0.268	0.313
4	-2.062	3.594	0.278	0.296
5	-1.881	3.563	0.280	0.248
6	-4.750	3.873	0.258	1.456
7	-3.593	3.091	0.324	1.043
8	-3.114	2.690	0.372	0.902
9	-3.170	2.577	0.388	0.975
10	-3.232	2.867	0.349	0.911
11	-3.358	2.751	0.364	1.024
12	-2.075	3.495	0.286	0.308
13	-3.118	2.613	0.383	0.930

^a μ chemical potential

^b η chemical hardness

^c S chemical softness

^d ω electrophilicity

Table 5 Condensed local reactivity indexes to the σ -donor character $\langle f^-(r) \rangle$ and π -acceptor character $\langle f^+(r) \rangle$ on the phosphorus (P) central atom (data from [67])

Compound	$\langle f^+(r) \rangle$	$\langle f^-(r) \rangle$
1	0.944	0.750
2	0.795	0.746
3	0.660	0.737
4	0.539	0.733
5	0.591	0.736
6	0.720	0.712
7	0.096	0.311
8	0.082	0.489
9	0.106	0.588
10	0.093	0.752
11	0.095	0.685
12	0.366	0.714
13	0.103	0.440

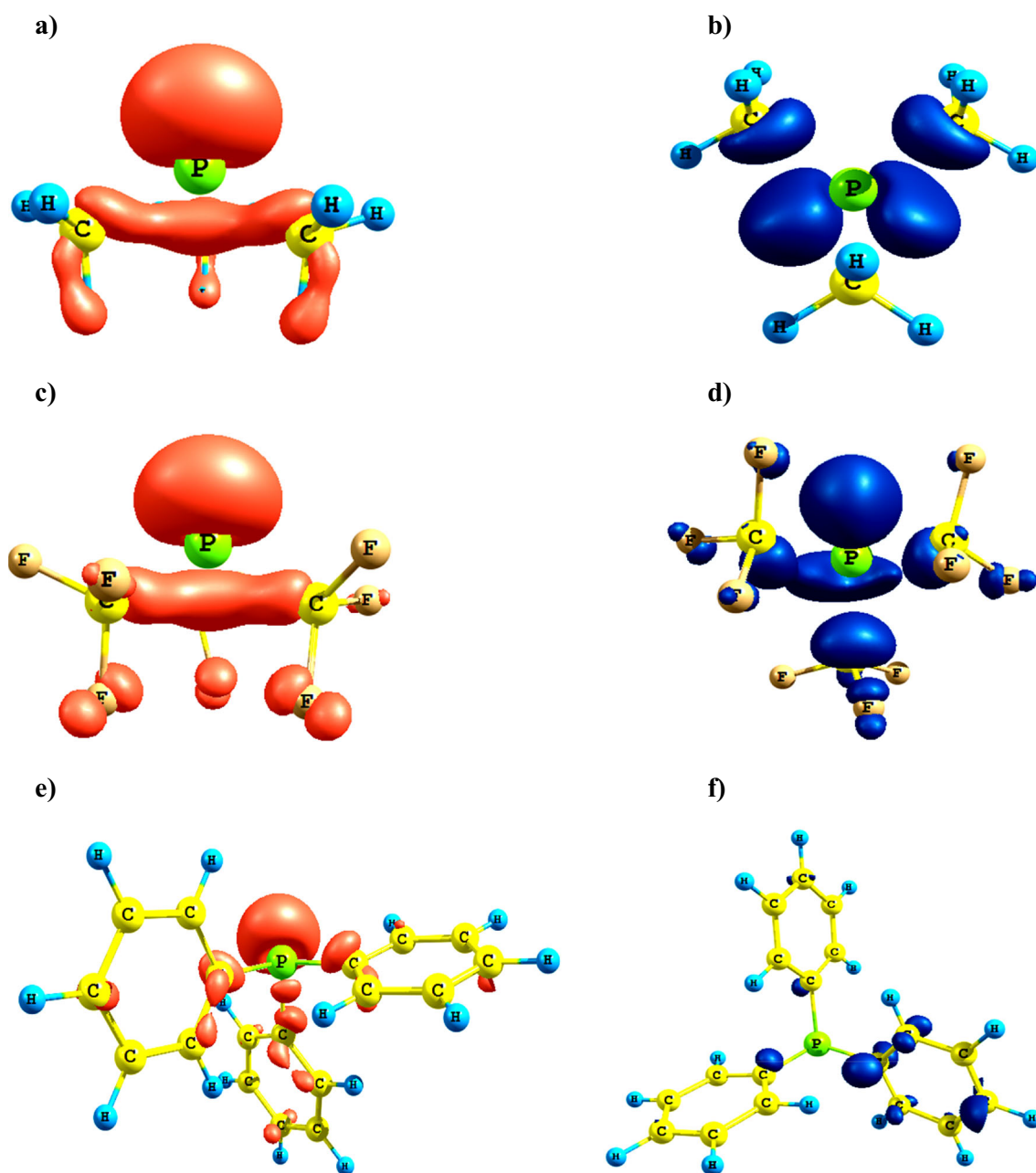


Fig. 3 a–f Surfaces (0.005) of the highest occupied molecular orbital (HOMO; orange) and the lowest unoccupied molecular orbital (LUMO; blue). **a** Charge donors (σ -regions) and **b** charge acceptors (π -

regions) for the compound 2. **c** σ -regions and **d** π -regions for compound 6. **e** σ -regions and **f** π -regions for compound 13 (see Table 1)

As seen in Table 5, $\langle f^+(r) \rangle$ is associated with a region susceptible to attack of transition metals with nucleophilic character. The coordination compounds with metals of low oxidation states are able to have a π -interaction. The Fukui function $\langle f^-(r) \rangle$ reflects the susceptibility to attack of electrophilic species, allowing the study of such ligands in coordination of inorganic compounds [67].

In Table 5, compounds 2–6 are characterized by have non-aromatic substituents. These compounds have better π -interactions than those compounds with aromatic

substituents. Additionally, these compounds have a higher capacity to donate σ electrons, showing a high retro-donor character. On the other hand, compounds 7–11 and 13 have a high ability to donate σ charge and these results are consistent with experimental data [2, 4–10]. The Fukui functions needed in order to study the most favorable retro-donor (σ - π) regions are shown in Fig. 3, which shows the charge donors (σ -regions) and charge acceptors (π -regions) for compounds 2, 6 and 13 (see Table 1) in the vicinity of the central P.

From the point of view of chemical reactivity, it is possible to relate the σ -donor character with $\langle f^-(\vec{r}) \rangle$ and the π -acceptor character with $\langle f^+(\vec{r}) \rangle$. On these topological surfaces (Fig. 3), we can see large areas associated with high retro-donor character and, in this regard, large areas of chemical reactivity. On the other hand, compounds 7–11 and 13 have aromatic rings as substituents and therefore are more nucleophilic than compounds 2–6 (see Table 1). Additionally, these results are consistent with experimental data [1–3] and reveal new insights regarding the nature of the P–C chemical bond, and on ligand–metal bonds in transition metal complexes.

In this regard, we can study retro-donor character from a qualitative point of view. The retro-donation process is usually produced by electronic transfer from the p or d orbitals of a central metal to an antibonding (σ^*) molecular orbital in phosphine ligands with π -symmetry, causing the bond order and vibrational frequency in the ligands to decrease; these effects can be measured using infrared (IR) spectroscopy [67, 68]. Such effects are more relevant in metal complexes with low oxidation number, increasing the electronic population in P–C bonds [68].

Local QS on the Fukui functions

I

The premise in QS is that “*the same molecules tend to have similar behavior*”. Based on this premise, Eqs. 26 and 27 can be used to measure QS in chemical reactivity. Table 6 lists the values associated with quantification of chemical reactivity using the Carbó index, which is used widely in the molecular QS field [14–19].

Table 6 reveals the similarity in the Fukui function values. The highest QS value (0.866) in the Fukui functions (F^-) was seen between compound 10 and the reference compound (PH_3); this value shows that the distribution of molecular space around the areas susceptible to attack by electrophilic species is similar to that of molecule 1. This QS shows the effects of the groups substituted to molecule 10 and their impact on the reactivity of this species. This same comparison revealed the lowest value when comparing their Fukui functions (F^+) (0.296); this value shows that, in terms of molecular distribution of chemistry reactivity in the molecular set studied, there is little affinity to nucleophilic species.

Table 6 Molecular quantum similarity (QS) using Fukui functions on the central phosphorus (P) atoms in the molecular set studied using Eqs. 26 and 27

Molecules	Quantum similarity ($f^-(r)$)	Quantum similarity ($f^+(r)$)
1 vs 1	1.000	1.000
vs 2	0.748	0.866
vs 3	0.743	0.789
vs 4	0.739	0.713
vs 5	0.744	0.747
vs 6	0.731	0.824
vs 7	0.483	0.301
vs 8	0.606	0.278
vs 9	0.664	0.316
vs 10	0.866	0.296
vs 11	0.717	0.299
vs 12	0.732	0.588
vs 13	0.574	0.312

On the other hand, in the Fukui functions (F^+), a higher QS value (0.866) was obtained by comparison of compounds 1 and 2, showing that the substituents on compound 2 have areas susceptible to nucleophilic attack similar to the reference compound. This QS value explains the similarity in chemical reactivity, showing how substituent effects can create electronic distributions related to electrophilic and nucleophilic species.

On the other hand, taking into account that the DF is defined in terms of shape function as:

$$\rho(r) = N\sigma(r) \quad (37)$$

Where N and $\sigma(r)$ are independent variables, this shape function [$\sigma(r)$] also was used to define the centroid ShF; this molecular set was also normalized to unity and these features were also consistent with the interval of the Carbó index (0,1). Therefore, the two normalized methodologies were combined to obtain the local QS on the Fukui function associated with the central P atom. In this sense, the Euclidean distance can be written as:

$$D_{AB}^2 = \int \left| \left(\frac{\partial \rho_A(r)}{\partial N} - \frac{\partial \rho_B(r)}{\partial N} \right)^\pm \right|^2 dr = \int \left(\frac{\partial \rho_A(r)}{\partial N} \right)_A^2 (r) dr_A + \int \left(\frac{\partial \rho_B(r)}{\partial N} \right)_B^2 (r) dr_B - 2 \int \left(\frac{\partial \rho_A(r)}{\partial N} \right)_A \left(\frac{\partial \rho_B(r)}{\partial N} \right)_B dr_A dr_B \quad (38)$$

$$= \int f_A(r)^2 dr_A + \int f_B(r)^2 dr_B - 2 \int f_A(r) f_B(r) dr_A dr_B$$

Equation 38 determines the values of QS in the Carbó indexes for Fukui functions in the molecular set with respect to PH_3 . Moreover, in this equation, the momentum-space for molecules A and B are the densities associated with the frontier orbitals and are the central property in generalized overlap measures.

Conclusions

The range and complexity of phosphine ligands has increased dramatically in recent years. For this reason, a study on steric and electronic effects on a series of phosphine ligands is presented using the MQS field together with the use of global and local reactivity descriptors in the DFT framework, with the aim of presenting new ways to understand the chemical behavior of phosphine ligands.

Upon merging of chemical reactivity and QS, we can see the distribution of chemical reactivity generated by the substituent effects. This way of understanding steric and electronic effects can be an alternative to quantifying local chemical reactivity and its impact on substituents. In general, this analysis reveals new insights into the retro-donor process in phosphine ligands using Fukui functions on the central atom P.

On the other hand, molecular alignment is crucial in QS. For this reason, we used the TGSA, which allows reliable results to be obtained. This method can be considered as a straightforward procedure to deal with the problem of relative molecular orientation when applying MQS.

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