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# A general description of phosphorus containing functional groups

Tom Leyssens *, Daniel Peeters

*Laboratoire de Chimie Quantique, Université Catholique de Louvain, Place L. Pasteur 1, 1348 Louvain-la-Neuve, Belgium*

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**Abstract**

Phosphorus containing functional groups induce an important stabilizing effect on adjacent carbanions. Such an interaction is, however, not observed for the neutral compounds. Using computational methods, we clarify the fundamental properties of these functional groups that lead to these differences. By doing so, a general description of phosphorus containing functional groups of the $–PY_2$ and $–POY_2$ type is obtained. These groups should be seen as highly ionic groups having a σ donor/π acceptor character.

*Keywords:* Computational chemistry; Phosphorus functional groups; σ Donor/π acceptor; NBO analysis; Fukui function; Isodesmic reactions

Phosphorus compounds are important species in modern chemistry. They intervene in many medicinal and biochemical processes. These compounds are often synthesized using reactants carrying phosphorus containing functional groups. The influence of the latter on reactivity strongly depends on the nature of the reactants. Phosphorus containing functional groups of the $–PY_2$ and $–POY_2$ type have been known for many years to be highly effective at stabilizing adjacent carbanion centers.[1] This has been widely exploited in organic synthesis[2] to the extent that P-stabilized carbanions now rank amongst some of the most useful reagents for a wide range of important organic transformations, such as the Horner or Horner–Wadsworth–Emmons reactions.[3] In contrast to the important influence these groups have on reactions involving carbanions, little to no effect is observed on the reactivity of reactions involving neutral compounds, such as the Diels–Alder reaction.[4]

Recently, we have shown by theoretical means that this difference can be explained by considering the bonding interactions between the phosphorus containing functional group and the organic backbone for the neutral as well as anionic compounds. $–PY_2$ and $–POY_2$ functional groups act as weak σ donors, polarizing the adjacent σ C–H, σ C–C and π C–C bonds of neutral compounds toward the functionalized carbon atom,[5] mainly due to the high electropositive character of these groups,[6] as well as the presence of a strongly positively polarized central phosphorus atom. Similar bonding interactions are observed for the anionic organophosphorus compounds. The strong stabilization observed for the latter comes from a supplementary π back-bonding interaction from the carbanion lone pair toward the empty σ* P–Y and P–O orbitals.[7] We report herein, why such a stabilizing back-bonding interaction is not observed for the neutral compounds and propose a general description of the bonding interaction with phosphorus containing functional groups.

To understand the difference between the anionic and neutral organophosphorus compounds, we consider the anionic and radical $CH_2POF_2$ compounds as well as the unsaturated $C_2H_3POF_2$ molecule. The $POF_2$ group was chosen to represent $–PY_2$ and $–POY_2$ functional groups, as the studied interactions are most pronounced for the former.[5,7] Similar trends can nevertheless be obtained for other $–PY_2$ and $–POY_2$ groups and the final conclusion can, therefore, be considered as general for this type of substituent.

In a previous application on metal–ligand bonding toward phosphine complexes,[8] we have shown how

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* Corresponding author. Tel.: +32 10 47 28 13; fax: +32 10 47 27 07.
*E-mail address:* t.leyssens@chim.ucl.ac.be (T. Leyssens).

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back-bonding can be investigated using a tool from conceptual chemistry, namely the electronic Fukui function.[9] This function was introduced in the context of density functional theory by Parr and Yang in 1984, and corresponds to the derivative of the electron density with respect to the number of electrons. In practice, this function usually needs to be approximated as a finite-difference term corresponding to removing ($f^-$) or adding ($f^+$, not considered here) a whole electron.

$$f^-(r) = \left[\frac{\partial(\rho(r))}{\partial N}\right]^-_{v(r)} \approx \frac{\rho^- - \rho^0}{N^- - N^0} = \rho^- - \rho^0 \tag{1}$$

Figure 1 shows the Fukui function for the anionic $CH_2POF_2{}^-$ as well as neutral $CH_2POF_2$ and $C_2H_3POF_2$ molecules. As expected, red zones corresponding to a loss in electron density predominate. These zones indicate that ionization formally occurs out of the carbon lone pair, the carbon singly occupied orbital, and the π orbital for the $CH_2POF_2{}^-$, $CH_2POF_2$, and $C_2H_3POF_2$ compounds, respectively. The regions of increased electron density, shown in blue, are mostly located along the inter-nuclear axis and can be attributed to the polarization along the σ bonds.

Of most interest in the present context are the losses in electron density due to a decrease in back-bonding. These losses can be clearly observed for the anionic compound in the region corresponding to the π-accepting σ* P–F orbitals. The Fukui function of the radical $CH_2POF_2$ species shows less important back-donation from the singly occupied carbon orbital, whereas this interaction seems to be undetectable for the unsaturated $C_2H_3POF_2$ compound.

| Isodesmic Reaction | | ΔE |
|---|---|---|
| $CH_3POF_2$ + $CH_3^-$ | → $CH_2POF_2^-$ + $CH_4$ | -60.30 / -61.08 |
| $CH_3POF_2$ + $CH_3^{\circ}$ | → $CH_2POF_2^{\circ}$ + $CH_4$ | -1.80 / 0.21 |
| $CH_3POF_2$ + $C_2H_4$ | → $C_2H_3POF_2$ + $CH_4$ | -1.11 / -1.41 |

Scheme 1. Isodesmic reactions and reaction energies (B3LYP/MP2) (kcal/mol).

The impact these differences in back-bonding interaction have on the energetic stabilization by the phosphorus containing functional groups can be evaluated using isodesmic reaction energies as presented in Scheme 1. These reactions show little to no stabilization for the α radical carbon as well as the π C–C bond by the $-POF_2$ functional group. The high stabilization observed for the anionic compounds clearly requires the presence of a pair of electrons on the α carbon atom. Based on the data from the Fukui functions, this difference is expected to be linked to the importance of the back-bonding interaction.

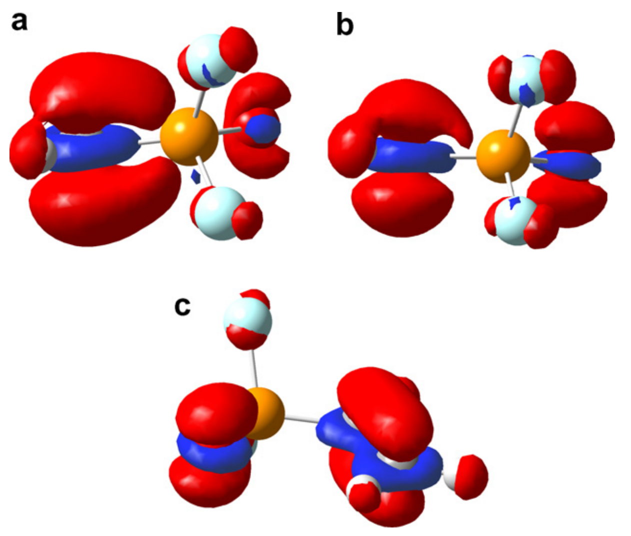

Fig. 1. B3LYP Fukui function of the anionic $CH_2POF_2{}^-$, radical $CH_2POF_2$, and neutral $C_2H_3POF_2$ molecules (taken at isodensity value of 0.005 e bohr$^{-3}$).

This hypothesis is confirmed by a NBO second-order perturbative energy analysis, allowing to quantify the effect of a specific perturbative bonding interaction. NBO analysis is based on a method for optimally expressing a given wavefunction into a Lewis-like form. The overall density matrix is transformed to give localized natural bonding orbitals (or NBOs), that are either centered on one atom (‘core’ or ‘lone pair’), two atoms (‘bond’ orbitals), or three atoms (‘delocalised bond over three centres’ orbitals). The density matrix is first used to define a minimum basis of atomic orbitals, the natural atomic orbitals (or NAOs), and the NBOs are expressed as an expansion of these orbitals. The NBO orbitals are chosen in such a way as to maximize occupancy, so that delocalization effects appear as weak departures from the idealized localized Lewis structure in which all NBOs have occupancies of exactly 2, 1 or 0. The Natural Bond Orbital (NBO)[10] method developed by Weinhold and co-workers provides an estimate of the energy impact of secondary bonding interactions which act as small perturbations to the total bonding. The energy contribution is derived from interactions between donor and acceptor orbitals.[11] Back-bonding energy contributions are obtained from the NBO estimates of the stabilization interactions associated with partial electron donation from the localized NBOs (carbanion lone pair) of the idealized Lewis structure into the empty non-Lewis orbitals (σ* P–Y and P–O orbitals), that is, with partial departure from the idealized Lewis structure description. As these interactions are only small departures from the idealized Lewis structure they can be estimated within the NBO method using perturbation theory. The stabilization energy $E(2)$ associated with delocalization from a donor orbital $i$ to an acceptor orbital $j$ is given as $E(2) = \Delta E_{ij} = q_i \times F(i,j)^2/(\varepsilon_j - \varepsilon_i)$. In this expression, $q_i$ is the donor orbital occupancy, $\varepsilon_i$ and $\varepsilon_j$ are the respective

Table 1
Total second-order perturbative interaction $\Delta E_{bb}$ between the two acceptor $\sigma^*$ P–F and donor lone pair, singly occupied orbital, and $\pi$ C–C orbital for $CH_2POF_2^-$, $CH_2POF_2$, and $C_2H_3POF_2$ molecules, respectively

| | $\Delta E_{bb}$ | $\Delta\varepsilon$ | $F$ |
|---|---|---|---|
| $CH_2POF_2^-$ | 47.48 | 194.4 | 47.0 |
| $CH_2POF_2$ | 11.21 | 263.3 | 40.1 |
| $C_2H_3POF_2$ | 8.14 | 294.7 | 25.7 |

Energy gap ($\Delta\varepsilon$) between the donor/acceptor orbitals, as well as the corresponding Fock matrix element $F$ (kcal/mol/B3LYP).

orbital energies and $F(i,j)$ is the off-diagonal Fock matrix element expressed in the NBO basis.

This approach has been applied to a number of chemical problems, yielding chemically satisfying models accounting for effects such as the small energy difference between cis and trans difluoroethene,[12] the torsional barrier to rotation in ethane,[13] the relative stability of the isomers of the HOI–$H_2O$ complexes,[14] the properties of X–H bonds in X–H...Y hydrogen bonds[15] for a wide range of X and Y groups, as well as the impact of negative hyperconjugation on the reactivity of complex heterocyclic systems.[16]

Table 1 shows the total second-order perturbative interaction between the two $\sigma^*$ P–F orbitals and the lone pair, singly occupied carbon orbital and $\pi$ C–C orbital for the $CH_2POF_2^-$, $CH_2POF_2$, and $C_2H_3POF_2$ molecules, respectively, as well as the two factors affecting the magnitude of the back-bonding interaction, namely, the energy difference between the donor and acceptor orbitals, and the off-diagonal Fock matrix element $F(i,j)$. This latter is a resonance integral, measuring how much energy is gained by sharing electrons between orbitals $i$ and $j$. In practice, this term can be interpreted as measuring the extent of overlap between these orbitals in physically important regions.

As can be seen from this table, the back-bonding interaction from the carbanion lone pair toward the $\sigma^*$ orbitals explains the large stabilization observed for the anionic compounds. Although present, the back-bonding interaction from the $\pi$ C–C orbital to the $\sigma^*$ P–F orbitals is too small to be observed, smaller even than the interaction of the singly occupied orbital of the $CH_2POF_2$ radical with the $\sigma^*$ orbitals. The decrease in back-bonding interaction observed for the neutral compounds is not only due to the larger energy gap between interacting orbitals but also to a less favorable overlap as shown by the decreasing $F$ values. The $\pi$ acceptor capabilities of the phosphorus containing functional group therefore remain present, but the neutral compounds lack the presence of an effective donating orbital.

In conclusion, the phosphorus containing functional groups of the $-PY_2$ and $-POY_2$ type can be characterized as highly ionic groups having a $\sigma$ donor/$\pi$ acceptor character. The importance of the acceptor interaction will nevertheless depend on the availability of an appropriate acceptor orbital, in other words on the nature of the organic molecule the functional group is linked to.

*Computational details*: All structures were optimized at B3LYP and MP2 level of theory using a 6-31++G(d,p) basis set and the Gaussian series of programs.[17] All possible conformations have been investigated and the most stable conformer is retained. Second-order perturbative NBO analysis is used to estimate the back-bonding interaction energy ($\Delta E_{bb}$).

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## References and notes

1. Izod, K. *Coord. Chem. Rev.* **2002**, *227*, 153–173.
2. (a) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863–927; (b) Katritzky, A. R.; Piffl, M.; Lang, H.; Anders, E. *Chem. Rev.* **1999**, *99*, 665–722.
3. (a) Horner, L.; Hoffmann, H.; Wippel, H. G.; Klahre, G. *Chem. Ber.* **1958**, *91*, 61–63; (b) Horner, L.; Hoffmann, H.; Wippel, H. G.; Klahre, G. *Chem. Ber.* **1959**, *92*, 2499–2505; (c) Wadsworth, W. S.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 1733–1738.
4. (a) McClure, C. K.; Hansen, K. B. *Tetrahedron Lett.* **1996**, *37*, 2149–2152; (b) Daniewski, W. M.; Griffin, C. E. *J. Org. Chem.* **1966**, *31*, 3236–3241; (c) Robiette, R.; Marchand-Brynaert, J.; Peeters, D. *J. Mol. Struct. (Theochem)* **2002**, *587*, 159–169.
5. Leyssens, T.; Peeters, D. *J. Mol. Struct. (Theochem)* **2004**, *686*, 71–82.
6. (a) Leyssens, T.; Geerlings, P.; Peeters, D. *J. Phys. Chem. A* **2005**, *109*, 9882–9889; (b) Leyssens, T.; Geerlings, P.; Peeters, D. *J. Phys. Chem. A* **2006**, *110*, 8872–8879.
7. Leyssens, T.; Peeters D. *J. Org. Chem.*, submitted for publication.
8. Leyssens, T.; Peeters, D.; Orpen, A. G.; Harvey, J. N. *New J. Chem.* **2005**, *29*, 1424–1430.
9. Parr, R. G.; Yang, W. *J. Am. Chem. Soc.* **1984**, *106*, 4049–4050.
10. (a) Weinhold, F.; Landis, C. R. *Valency and Bonding: A Natural Bond Orbital Donor–Acceptor Perspective*; Cambridge University Press, 2005; (b) Reed, A. E.; Weinstock, R. B.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 735–746; (c) Reed, A. E.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 1736–1740; (d) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899–926.
11. (a) Kwon, O.; Sevin, F.; Mckee, M. L. *J. Phys. Chem. A* **2001**, *105*, 913–922; (b) Can, H.; Zhan, D.; Balci, M.; Brickmann, J. *Eur. J. Org. Chem.* **2003**, 1111–1117; (c) Monajjemi, M.; Chahkandi, B. *J. Mol. Struct. (Theochem)* **2005**, *714*, 43–60.
12. Be found under http://www.chem.wisc.edu/~nbo5/tut_del.htm.
13. Weinhold, F. *Angew. Chem., Int. Ed.* **2003**, *42*, 4188–4194.
14. Sun, Q.; Li, Z.; Zeng, X.; Ge, M.; Wang, D. *J. Mol. Struct. (Theochem)* **2005**, *724*, 155–161.
15. Sosa, G. L.; Peruchena, M.; Contreras, R. H.; Castro, E. A. *J. Mol. Struct. (Theochem)* **2002**, *577*, 219–228.
16. Lill, S. O. N.; Rauhut, G.; Anders, E. *Chem. Eur. J.* **2003**, *9*, 3143–3153.
17. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J., Barone,

V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. GAUSSIAN 98, *Revision A.7*, Gaussian: Pittsburgh, PA, 1998.