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Quantitative Assessment of the Stereoelectronic Profile of Phosphine Ligands

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The stereoelectronic profile of a variety of phosphine ligands (PR_3) have been estimated using a combined approach of quantum mechanics (QM) and molecular mechanics (MM). The quantum mechanically derived molecular electrostatic potential minimum (V_{min}) of a PR_3 ligand at the phosphorus lone pair region provides a direct measure of the total electronic (E_{eff}) and steric effects (S_{eff}) of the ligand. The difference between the V_{min} of unsubstituted PH_3 ($V_{min}(PH_3)$) and the V_{min} of PR_3 is considered as $E_{eff} + S_{eff}$. It is found that a two-layer QM-MM ONIOM method comprising PH_3 in the inner QM layer and the R groups in the outer MM layer is useful to locate the structure of a PR_3 ligand in an electronic effect free environment of the substituents. The V_{min} of the ONIOM-optimized PR_3 at the phosphorus lone-pair region thus provides the quantification of the steric effect as $S_{eff} = V_{min}(PH_3) - V_{min}(ONIOM\_PR_3)$. Because $V_{min}(PR_3)$ contains both E_{eff} and S_{eff}, the E_{eff} can be easily defined as $E_{eff} = V_{min}(ONIOM\_PR_3) - V_{min}(PR_3)$. A modified form of the symmetric deformation coordinate (S4) is calculated for all of the fully optimized and ONIOM-optimized free phosphines to obtain their S4-based steric effect values.[24] Good linear correlation between S4 of ONIOM-optimized phosphines and the MESP-based S_{eff} values was obtained. Further, the determination of the stereoelectronic profile of PR_3 ligands has been achieved, leading to a general classification of the ligands into four categories, namely, ligands with (i) ($+E_{eff}$, $+S_{eff}$), (ii) ($+E_{eff}$, $-S_{eff}$), (iii) ($-E_{eff}$, $+S_{eff}$), and (iv) ($-E_{eff}$, $-S_{eff}$), where plus and minus signs indicate electron donation and electron withdrawal properties, respectively.

Introduction

Phosphine ligands (PR_3) are considered as one of the most important ligands in organometallic catalyst systems because they allow the tuning of catalysts in terms of steric and electronic effects by the appropriate use of various R groups.[1−9] They are easy to synthesize, and their ability to stabilize and solubilize transition-metal complexes in a low oxidation state[10] is advantageous for the designing of a variety of catalytic systems, such as the famous Grubbs ruthenium-based metathesis catalysts.[11] In the case of many of the existing catalytic systems, further improvement is required to achieve better efficiency, particularly for the enantioselective synthesis. So, the area of designing and synthesis of organometallic catalysts is very attractive, and to the development of this field, advanced quantum chemical simulations have given immense contributions.[12]

Rapid progress in homogeneous catalysis is expected when well-defined steric and electronic parameters of a ligand are known beforehand when one is targeting the designing of a new catalyst or targeting further improvement on an existing catalyst. In this respect, the earliest, simple, and still one of the best-known parameters for the quantification of the electronic effects of phosphines is Tolman's electronic

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parameter, which is based on the A1 ν(CO) vibration of $(R_3P)Ni(CO)_3$ in the IR spectrum.[8] Tolman reasoned that because the back-donation of electron density to the π^* orbital of CO causes the lowering of the ν(CO) vibration, a better donor power of PR_3 will lower the ν(CO) vibration.[8] Quantitative analysis of ligand effects to study the electronic effect of phosphines was discussed by Giering and co-workers.[6,13] Crabtree et al. reported a method for quantifying the electronic effect of phosphines through the ab initio calculations on $Ni(CO)_3(PR_3)$ complexes and concluded the results as computationally derived ligand electronic parameter.[14] Electronic parameters were quantified by Lever et al. using redox couples, and it can be summarized as Lever electronic parameters.[15,16] Recently, the electronic effects of substituted phosphines were quantified in terms of the molecular electrostatic potential minimum (V_{min}) by Suresh and Koga.[17] In a recent review, Kühl had compared various methods used for predicting the electronic effect of phosphine ligands and supported the use of V_{min} as a parameter for the quantification of the electronic effect of phosphine ligands.[18] The use of V_{min} as a measure of the electron-attracting tendencies of a substituent in NH_2-X systems is described in the work of Murray and Politzer.[19] Cundari et al. had done the assessment of the electronic profile of phosphines on the basis of the semiempirical electronic parameter on rhodium Vaska complexes.[20]

The steric effect of phosphines was quantified by Tolman in 1977 based on the Corey−Pauling−Koltun model of ligand−metal complexes known as the Tolman cone angle (θ).[8,21] It is defined as the apex angle of a cylindrical cone centered 2.28 Å from the center of the phosphorus atom and just touching the van der Waals radii of the outermost atoms of the molecules.[7,8] This method was very useful, even if it is a crude method and because from this work it has been considered that the steric profile of the phosphine can impart a significant degree of control over the outcome of transition-metal-mediated reactions. Subsequently, attempts were made by various groups to quantify the steric effect of phosphines and to improve the Tolman model using the geometry parameters obtained from crystallographic structure and from the quantum mechanically calculated structure of the ligand−metal complex. Brown and co-workers calculated the ligand repulsive energy parameter (E_R) on the basis of a molecular mechanics (MM) model.[22,23] Orpen et al. have used the angles at the coordinated phosphine P for measuring the steric effect of phosphines, and the quantity used is the symmetric deformation coordinate (S_4').[24] Cundari et al. focused on the S4 values of the rhodium Vaska complex using PM3(tm) calculations. They have found a good correlation between the S4 values calculated using PM3(tm) and from X-ray crystallographic data. They considered a number of cyclic, noncyclic, and heterocyclic phosphines and phosphites and had given a stereoelectronic profile for phosphine ligands.[20] Very recently, Suresh has proposed a QM-MM-based method in conjunction with molecular electrostatic potential (MESP) analysis for the study of the steric effect of phosphine ligands.[25] This method was found to be very simple and effective for the separation of the steric effect from the electronic effect of a phosphine ligand. In the present work, we further explore this MESP-based technique to unravel the stereoelectronic profile of a variety of phosphine ligands including some of the typically used phosphite systems.

Methodology

(a) Selection of Ligands. We have taken cyclic and heterocyclic phosphines and phosphites along with some commonly known noncyclic phosphines for this study, and they are shown in Figure 1. Also included in this study are the bowl shaped phosphine ligands TRMP and TRIP designed by Kawashima and co-workers,[26−29] which bear *m*-terphenyl-based P substituents. In many of the ligands, the phosphorus atom is connected to saturated/conjugated/partially conjugated units showing four-, five-, six-, and eight-membered ring structures. Cyclic three-membered phosphines are exempted from the study due to the lack of adequate force fields to model them. Some of the recently synthesized bulky phosphine systems are also included in the study. A compilation of many of these structures can be seen in the work of Cundari et al.[20] The X-ray structures of all of the reported ligands are known in their metal complexes, and in some cases, the X-ray structure of free forms is also available. Herein, each ligand is named with the CCDC database code,[30] which has been used to locate the X-ray structures of its metal complex. For some commonly encountered ligands, their typical names are also given.

(b) Optimization of Ligands. The X-ray structure of all of the PR_3 ligands are located from the CCDC database[30] (the name used to identify each structure in the database is given in Figure 1), and they are used as input geometries for optimization methods. Two levels of optimization procedures are used. In the first one, the full optimization of a PR_3 structure is carried out with the B3LYP/6-31G(d,p) level of the density functional theory (DFT) method.[31,32] In the second method, the hybrid QM-MM method known as ONIOM (*Our own n-layered integrated molecular orbital + molecular mechanics*), developed by Morokuma and co-workers[33,34] is used.[35−38] The attractive feature of the ONIOM method is that a

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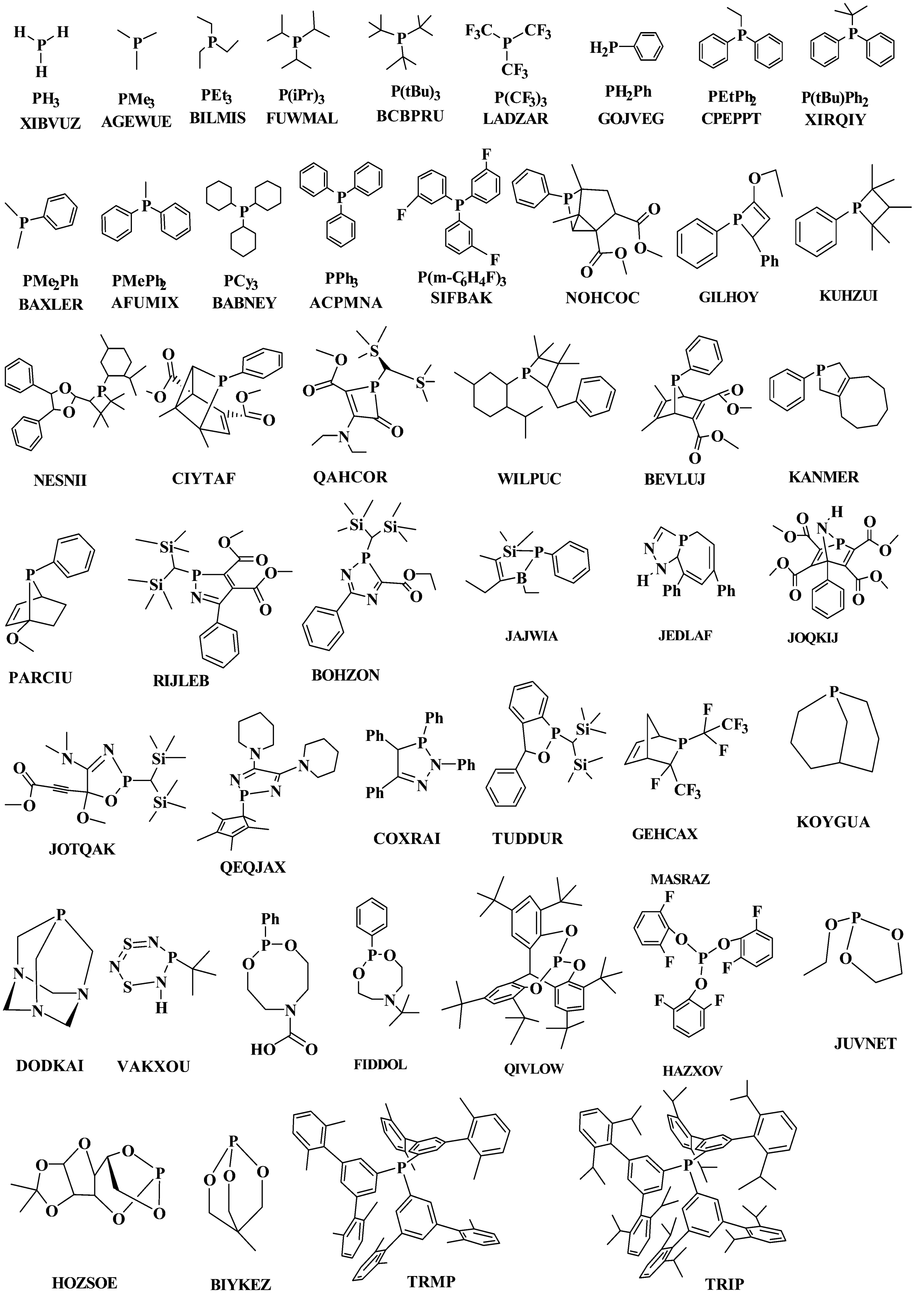


Figure 1. Ligands used in the present study. See the Supporting Information for all of the related references.

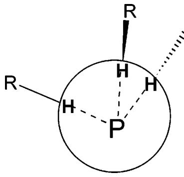


Figure 2. Two-layer ONIOM method. Hydrogen atoms are the link atoms.

chemical system can be partitioned into two or three layers so that each layer can be treated at different computational levels. Therefore, the advantage is that the most critical part of the system can be treated with a high level of QM method, whereas remaining part of the system can be calculated at a low level of theory, often an MM method. In the present work, we have adopted a two-layer ONIOM technique, which is illustrated in Figure 2. The outer layer contains the substituent R groups, and the inner layer comprises of PH_3. For the outer layer, the MM method utilizing the universal force field (UFF)[39] is selected while for the inner layer, the QM method of B3LYP/6-31G(d,p) is chosen. Because the R groups are treated with the MM force field, we consider that the optimized geometry of PR_3 is obtained in the electronic effect free environment of the R substituents. For all of the calculations, the *Gaussian 03*[40] suite of programs are used.

(c) Calculation of Molecular Electrostatic Potential Minimum (V_{min}). For all of the ligands optimized at the B3LYP/6-31G(d,p) level, the same level of wave function is used to calculate the molecular electrostatic potential (MESP). The MESP is rigorously calculated using eq 1 where Z_A is the charge on nucleus *A*, located at R_A[41,42] and $\rho(\boldsymbol{r})$ is the electron density.

$$V(\boldsymbol{r}) = \sum_{A}^{N} \frac{Z_A}{|\boldsymbol{r} - \boldsymbol{R}_A|} - \int \frac{\rho(\boldsymbol{r}')d^3\boldsymbol{r}'}{|\boldsymbol{r} - \boldsymbol{r}'|} \tag{1}$$

In general, electron-dense π and lone-pair regions are expected to show a high negative MESP, whereas electron-deficient regions are characterized by positive MESP. In the case of phosphine ligands, a negative-valued MESP minimum (V_{min}) is expected at the lone-pair region of the phosphorus atom and it is calculated in all of the cases (cf. Figure 3).[17,25] In the case of the ONIOM-level-optimized PR_3, the V_{min} always corresponds to the MESP minimum of the inner QM layer, viz. PH_3. From the visual inspection of the calculated MESP data using a freely available graphical interface such as the *MOLEKEL* program,[43] one can easily find out the V_{min} values. If a guess point near V_{min} is used along with the Prop =-(potential, opt) keyword in *Gaussian 03*,[40] the exact location and the value of V_{min} can be obtained from a rigorous calculation. A detailed account on the determination of V_{min} values from the calculated MESP values can be seen in ref 25.

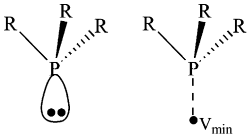
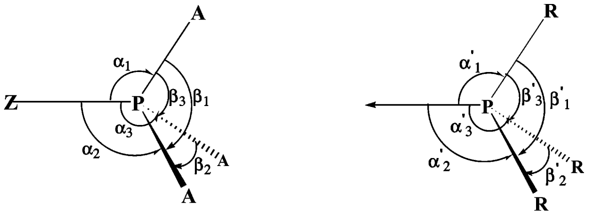


Figure 3. Phosphine ligand with its lone pair and V_{min} in the lone-pair region.



(a) (b)

Figure 4. Definition of the angles used for the calculation of S4′ by Orpen et al. and S4 in the present work.

(d) Calculation of Modified Symmetric Deformation Coordinates (S4). The quantity known as the symmetric deformation coordinate (S4′) was introduced by Orpen et al. as an alternative to the cone angle to measure the steric bulk of phosphines.[24] It is a numerical quantity derived from geometrical calculations and can be calculated from the difference between the sum of angles between the substituents and the coordinated atom (a transition metal, a main group metal, or a nonmetal) and the angles between substituents. Using the angles α1, α 2, α 3, β1, β2, and β3, as defined in part a of Figure 4, S4′ can be written as

$$S4' = (\alpha 1 + \alpha 2 + \alpha 3) - (\beta 1 + \beta 2 + \beta 3) \tag{2}$$

In part a of Figure 4, *Z* and *A* notations represent the metal center and substituent atoms, respectively.

In a recent article, Cundari et al. have calculated the S4′ values for a number of phosphines from fully optimized geometries of *trans*-$Rh(PR_3)_2(CO)Cl$ using the semiempirical PM3(tm) method and found that there is a reasonable correspondence between the S4′ calculated from X-ray structures and that calculated from optimized geometries.[20] In the present work, because we are dealing only with the PR_3 ligands, the definition of α1, α2, and α3 angles are not possible. However, angles that can closely resemble those of α1, α2, and α3 can be defined as given in part b of Figure 4.

In part b of Figure 4, to define α′ angles for a PR_3 ligand, a line passing through the phosphorus atom is drawn in such a way that it is perpendicular to a plane containing the three atoms directly connected to the phosphorus atom. In the case of phosphine−metal complexes, the metal center is expected on this line at the appropriate bonding distances from the phosphorus atom. Therefore,

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Table 1. MESP $V_{\min}(PR_3)$ Values of Fully Optimized Geometries of PR_3 Ligands (X-ray IDs Are Given for Most of the Ligands)[a]

ligand	$V_{\min}(PR_3)$	$E_{\text{eff}} + S_{\text{eff}}$	ligand	$V_{\min}(PR_3)$	$E_{\text{eff}} + S_{\text{eff}}$
PH_3	−28.22	0.00	PARCIU	−36.52	8.30
PMe_3	−43.02	14.80	RIJLEB	−17.63	−10.59
PEt_3	−43.55	15.33	BOHZON	−15.31	−12.90
$P(^{i}Pr)_3$	−44.18	15.96	JAJWIA	−33.57	5.35
$P(^{t}Bu)_3$	−44.90	16.68	JEDLAF	−30.12	1.90
$P(CF_3)_3$	−5.95	−22.27	JOQKIJ	−22.78	−5.44
PH_2Ph	−31.05	2.83	JOTQAK	−31.94	3.72
PMe_2Ph	−40.41	12.19	QEQJAX	−35.52	7.29
$PEtPh_2$	−37.23	9.01	COXRAI	−22.90	−5.31
$P(^{t}Bu)Ph_2$	−38.86	10.64	TUDDUR	−33.89	5.67
$PMePh_2$	−36.76	8.54	GEHCAX	−16.50	−11.72
PCy_3	−44.99	16.77	KOYGUA	−42.36	14.14
PPh_3	−34.07	5.85	DODKAI	−33.69	5.48
$P(m\text{-}C_6H_4F)_3$	−27.77	−0.45	VAKXOU	−26.73	−1.44
NOHCOC	−25.48	−2.74	MASRAZ	−26.48	−1.74
GILHOY	−32.07	3.84	FIDDOL	−30.12	1.90
KUHZUI	−36.77	8.55	QIVLOW	−16.30	−11.90
NESNII	−38.91	10.68	HAZXOV	−12.17	−16.04
CIYTAF	−25.48	−2.74	JUVNET	−23.16	−5.06
QAHCOR	−32.94	4.72	HOZSOE	−16.57	−11.65
WILPUC	−39.97	11.75	BIYKEZ	−23.16	−5.06
BEVLUJ	−33.07	4.85	TRMP	−31.75	3.53
KANMER	−39.53	11.31	TRIP	−33.69	5.47

[a] See Figure 1 for each structure. All values are in Kcal/mol.

for free ligands, on the basis of α′ and β′ angles, a modified symmetric deformation coordinate named S4 is defined as given in eq 3.

$$S4 = (\alpha'1 + \alpha'2 + \alpha'3) - (\beta'1 + \beta'2 + \beta'3) \quad (3)$$

In the present work, S4 values are measured for all of the fully optimized and the ONIOM-level-optimized geometries.

Results and Discussion

(a) MESP Analysis of Fully Optimized Phosphine Ligands. The $V_{\min}$ values of MESP calculated for the fully optimized PR_3 ligands are given in Table 1. As expected, all of them show a negative value for $V_{\min}$. It can be seen that the $V_{\min}$ value of the unsubstituted phosphine PH_3 is −28.22 kcal/mol, and the values for other ligands lie in the range of −44.90 to −5.95 kcal/mol. A pictorial illustration of the MESP is depicted in Figure 5, using an isosurface value of −18.83 kcal/mol for a representative set of systems. This value is chosen because even for the most electron deficient system in Figure 5 (GEHCAX); the visual inspection of the isosurface is possible. The position of the $V_{\min}$ corresponding to the lone pair region of the phosphorus atom is also depicted for each ligand in Figure 5.

There are 29 PR_3 ligands showing a higher negative value for $V_{\min}$ than for $V_{\min}(PH_3)$, and hence they may be classified as electron-donating, and the remaining 16 ligands are expected to behave as electron-withdrawing ligands. This classification is meaningful because the MESP is often used as a direct measure of electron-donating and electron-withdrawing ability of substituents, functional groups, and ligands.[44−49] It may be noted that both steric and electronic effects of the substitutent R are contributing to the electron-donating/ withdrawing effect of the PR_3 ligand. For instance, the changes in the bulkiness of R groups can alter the p character of the sp^3-hybridized lone-pair orbital of the phosphorus atom, which in turn would lead to a corresponding increase/decrease in the negative character of the $V_{\min}$ at the lone pair. Because the P−R connection is through a single bond, the electronic effect is mainly inductive in nature. Considering the $V_{\min}$ of PH_3 as a reference point, the difference of $V_{\min}(PH_3)$ and $V_{\min}(PR_3)$ can be taken as the combined effect of the electronic and steric effects of the PR_3 ligand. We propose the notations E_{eff} and S_{eff} to designate the electronic and steric effects, respectively. Therefore,

$$E_{\text{eff}} + S_{\text{eff}} = V_{\min}(PH_3) - V_{\min}(PR_3) \quad (4)$$

The values for $E_{\text{eff}} + S_{\text{eff}}$ are calculated for all of the PR_3 ligands, which are given in Table 1 along with $V_{\min}(PR_3)$ values.

It can be seen from Table 1 that the $E_{\text{eff}} + S_{\text{eff}}$ values are ranging from −22.27 to 16.77 kcal/mol. Among these, PCy_3 is the most electron-donating ($V_{\min} = -44.99$) and $P(CF_3)_3$ is the most electron-withdrawing ligand ($V_{\min} = -5.95$). Among phosphites, HAZXOV is found to be the most electron-withdrawing ligand. All of the phosphites have negative values for $E_{\text{eff}} + S_{\text{eff}}$, indicating their electron-withdrawing nature due to the presence of the electronegative oxygen attached to phosphorus. The higher electron-donating tendency observed for PMe_3, $P(^{t}Bu)_3$, PEt_3, $P(^{i}Pr)_3$, and PCy_3 can be attributed to the presence of electron-donating alkyl groups, whereas the presence of electron-withdrawing fluorine in $P(CF_3)_3$ makes it highly electron-withdrawing in nature. The $V_{\min}$ value of −42.36 kcal/mol observed for the caged ligand KOYGUA is comparable to the $V_{\min}$ value of PCy_3, as the former has cyclohexyl-type R group connections to phosphorus. But in another caged ligand with six-membered rings (DODKAI), the presence of nitrogen in the ring structure caused the formation of a less-negative $V_{\min}$ (−33.69 kcal/mol).

The lesser electron-donating tendency of PPh_3 can be observed from its low $V_{\min}$ value of −34.07 kcal/mol compared to alkyl phosphines such as PEt_3 ($V_{\min} = -43.55$ kcal/mol). This is expected because the phenyl ring is normally assigned higher group electronegativity when compared to an alkyl group. In general, the $V_{\min}$ values are more influenced by the type of R groups than the steric bulkiness of the R group. Thus, in GEHCAX, the presence of fluorine drastically reduces the negative value of $V_{\min}$ (−16.50 kcal/mol), whereas PARCIU has an appreciable amount of electron-donating ability, as its $V_{\min}$ is −36.52 kcal/mol.

(b) MESP Analysis of ONIOM Optimized Phosphine Ligands. The $V_{\min}$ values of the ONIOM-optimized PR_3 ligands are given in Table 2, which always correspond to

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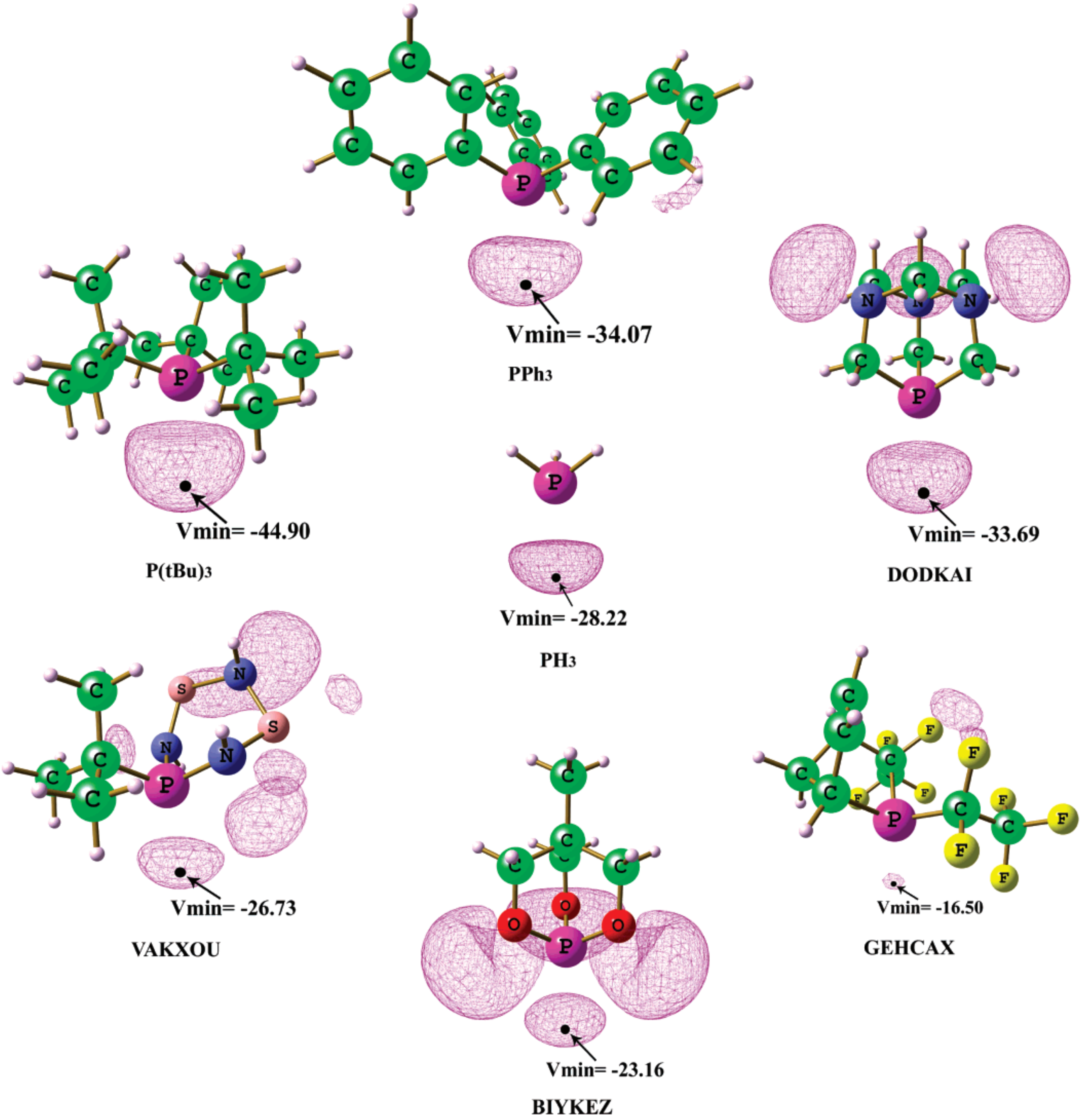

Figure 5. V_{min} points (black dots) located for a representative set of PR_3 ligands. The MESP isosurface of −18.83 kcal/mol is also plotted.

the PH_3 unit of the QM layer. In the QM layer, the H−P−H angle of the PH_3 will increase when the steric effect of the R groups in the outer layer increases.[25] In other words, the steric effect of the R groups are causing the shrinking or the expansion of the H−P−H angle, which in turn will cause a change in the electron density at the lone-pair region when compared to that of the fully optimized PH_3 ligand. Therefore, the difference between the $V_{min}(PH_3)$ and the V_{min}(ONIOM_PR_3) is considered as a measure of the steric effect provided by the substituents (cf. eq 5).[25]

$$S_{eff} = V_{min}(PH_3) - V_{min}(\text{ONIOM\_PR}_3) \qquad (5)$$

From eqs 4 and 5, the electronic effect of a PR_3 ligand (E_{eff}) can be defined as the difference between V_{min}(ONIOM_PR_3) and $V_{min}(PR_3)$

$$E_{eff} = V_{min}(\text{ONIOM\_PR}_3) - (V_{min}(PR_3)) \qquad (6)$$

The calculated values of E_{eff} and S_{eff} are summarized in Table 3.

(c) Symmetric Deformation Coordinate. The symmetric deformation coordinates S4′ as defined by Orpen et al. (cf. part a of Figure 4) are calculated for all of the ligands in their respective metal complexes, and they are presented in Table S1 of the Supporting Information. Further, the modi-

Table 2. MESP V_{min}(ONIOM_PR_3) Values of ONIOM-Level-Optimized Geometries of PR_3 Ligands[a]

ligand	V_{min}(ONIOM_PR_3)	ligand	V_{min}(ONIOM_PR_3)
PH_3	−28.22	PARCIU	−28.68
PMe_3	−30.62	RIJLEB	−29.93
PEt_3	−33.01	BOHZON	−29.12
$P(^{i}Pr)_3$	−37.46	JAJWIA	−30.99
$P(^{t}Bu)_3$	−42.90	JEDLAF	−29.30
$P(CF_3)_3$	−33.68	JOQKIJ	−22.21
PH_2Ph	−28.63	JOTQAK	−28.61
PMe_2Ph	−32.83	QEQJAX	−27.29
$PEtPh_2$	−35.12	COXRAI	−28.70
$P(^{t}Bu)Ph_2$	−36.58	TUDDUR	−27.86
$PMePh_2$	−32.47	GEHCAX	−31.50
PCy_3	−37.83	KOYGUA	−35.01
PPh_3	−34.20	DODKAI	−30.62
$P(m\text{-}C_6H_4F)_3$	−33.82	VAKXOU	−28.61
NOHCOC	−25.16	MASRAZ	−28.18
GILHOY	−22.46	FIDDOL	−28.18
KUHZUI	−28.61	QIVLOW	−31.60
NESNII	−28.18	HAZXOV	−25.10
CIYTAF	−25.92	JUVNET	−26.86
QAHCOR	−24.22	HOZSOE	−24.54
WILPUC	−27.11	BIYKEZ	−26.04
BEVLUJ	−27.36	TRMP	−32.13
KANMER	−30.99	TRIP	−35.77

[a] All values are in Kcal/mol.

Table 3. E_{eff} and S_{eff} Values of PR_3 Ligands[a]

ligand	E_{eff}	S_{eff}	ligand	E_{eff}	S_{eff}
PH_3	0.00	0.00	PARCIU	7.84	0.46
PMe_3	12.40	2.40	RIJLEB	−12.29	1.71
PEt_3	10.54	4.79	BOHZON	−13.81	0.89
$P(^{i}Pr)_3$	6.71	9.24	JAJWIA	2.57	2.78
$P(^{t}Bu)_3$	1.95	14.70	JEDLAF	0.82	1.08
$P(CF_3)_3$	−27.73	5.46	JOQKIJ	0.56	−6.01
PH_2Ph	2.42	0.41	JOTQAK	3.33	0.39
PMe_2Ph	7.58	4.61	QEQJAX	8.22	−0.92
$PEtPh_2$	2.11	6.90	COXRAI	−5.80	0.52
$P(^{t}Bu)Ph_2$	2.28	8.36	TUDDUR	6.02	−0.36
$PMePh_2$	4.29	4.25	GEHCAX	−14.99	3.28
PCy_3	7.16	9.61	KOYGUA	7.34	6.79
PPh_3	−0.13	5.98	DODKAI	3.07	2.40
$P(m\text{-}C_6H_4F)_3$	−6.05	5.19	VAKXOU	−1.88	0.39
NOHCOC	0.31	−3.06	MASRAZ	−1.69	−0.04
GILHOY	9.60	−5.76	FIDDOL	1.94	−0.04
KUHZUI	8.16	0.39	QIVLOW	−15.20	3.30
NESNII	10.73	−0.04	HAZXOV	−12.92	−3.12
CIYTAF	−0.44	−2.30	JUVNET	−3.70	−1.36
QAHCOR	8.72	−3.99	HOZSOE	−7.97	−3.68
WILPUC	12.86	−1.11	BIYKEZ	−2.89	−2.18
BEVLUJ	5.71	−0.86	TRMP	−0.38	3.91
KANMER	8.53	2.78	TRIP	−2.07	7.55

[a] All values are in Kcal/mol.

Table 4. S4 Values of B3LYP/6-31G(d,p)-Level-Optimized and ONIOM-Level-Optimized (in Parenthesis) of PR_3 Ligands[a]

ligand	S4	ligand	S4
PH_3	88.1 (88.1)	PARCIU	74.9 (84.7)
PMe_3	41.7 (74.3)	RIJLEB	22.2 (73.9)
PEt_3	49.3 (90.8)	BOHZON	24.7 (78.4)
$P(^{i}Pr)_3$	31.1 (35.9)	JAJWIA	36.4 (76.5)
$P(^{t}Bu)_3$	12.0 (4.2)	JEDLAF	76.0 (78.8)
$P(CF_3)_3$	64.4 (58.0)	JOQKIJ	111.0 (114.9)
PH_2Ph	72.7 (86.6)	JOTQAK	53.3 (74.3)
PMe_2Ph	50.6 (64.1)	QEQJAX	51.3 (80.4)
$PEtPh_2$	37.4 (51.8)	COXRAI	67.3 (78.9)
$P(^{t}Bu)Ph_2$	27.1 (42.5)	TUDDUR	57.1 (82.9)
$PMePh_2$	45.7 (65.9)	GEHCAX	64.8 (65.3)
PCy_3	39.2 (34.1)	KOYGUA	54.6 (51.4)
PPh_3	39.6 (56.9)	DODKAI	82.0 (71.1)
$P(m\text{-}C_6H_4F)_3$	40.3 (59.0)	VAKXOU	38.2 (73.2)
NOHCOC	60.3 (98.1)	MASRAZ	55.1 (73.4)
GILHOY	87.6 (118.4)	FIDDOL	57.1 (73.3)
KUHZUI	55.7 (82.1)	QIVLOW	45.3 (60.7)
NESNII	62.9 (80.2)	HAZXOV	68.0 (85.7)
CIYTAF	57.3 (98.1)	JUVNET	52.9 (77.9)
QAHCOR	72.0 (105.8)	HOZSOE	65.0 (85.4)
WILPUC	64.1 (82.1)	BIYKEZ	55.0 (76.0)
BEVLUJ	72.3 (90.8)	TRMP	39.3 (56.8)
KANMER	63.3 (72.6)	TRIP	27.5 (40.9)

[a] All values are in degrees.

fied symmetric deformation coordinates S4 (cf. part b of Figure 4) are calculated for all of the fully optimized geometries of PR_3 ligands at the B3LYP/6-31G(d,p) as well as at the ONIOM(B3LYP/6-31G(d,p):UFF) levels. These values are depicted in Table 4, wherein the values in parenthesis correspond to the ONIOM-level-optimized structures.

Because the S4 values represent a steric measure of phosphine, correlation between the S4 values of the DFT-level-optimized structures and the S4′ values of the X-ray structures were studied and it is presented in Figure 6. The deviation from linearity in the correlation diagram given in Figure 6 is expected because there is no metal in the optimized geometry of phosphine ligands. But it can be seen that there is an acceptable agreement between the S4′ values of the X-ray structures and the S4 values of the optimized geometries because the correlation coefficient (*r*) here is 0.889, which suggests that the S4 definition given in Figure 4 is reasonable for assessing the steric effect.

It may be noted that in a (PR_3)ML_n complex, the metal-to-PR_3 interaction can also be influenced by interactions of the other ligands L_n in it. The effect of these interactions will be different in different complexes, and so the S4′ calculated for a particular PR_3 ligand from the X-ray structure may not be the same in all of the complexes. To account for

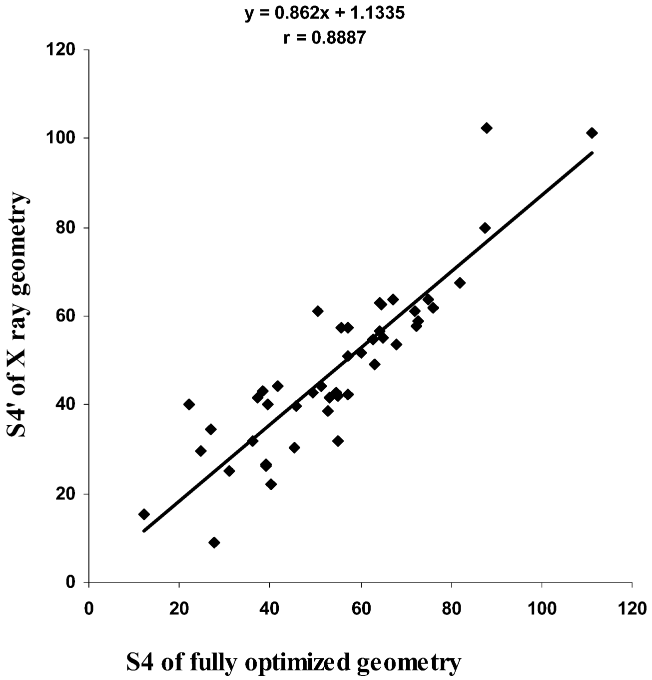

Figure 6. Correlation between S4 values of the fully optimized structures and X-ray structures of the PR_3 ligands.

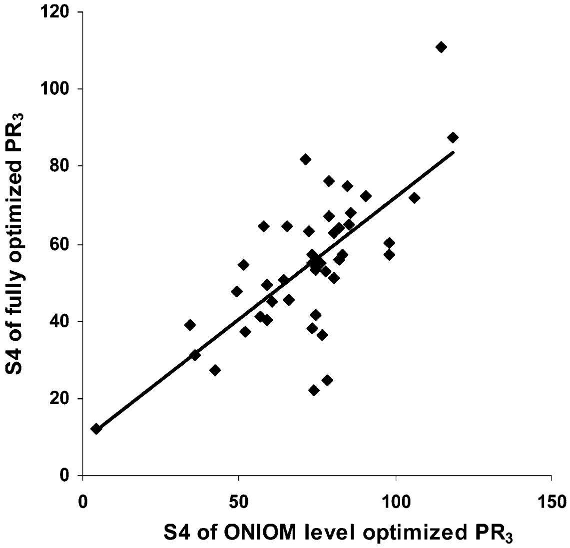

Figure 7. Correlation between the S4 values of fully optimized and ONIOM-level-optimized PR$_3$ ligands.

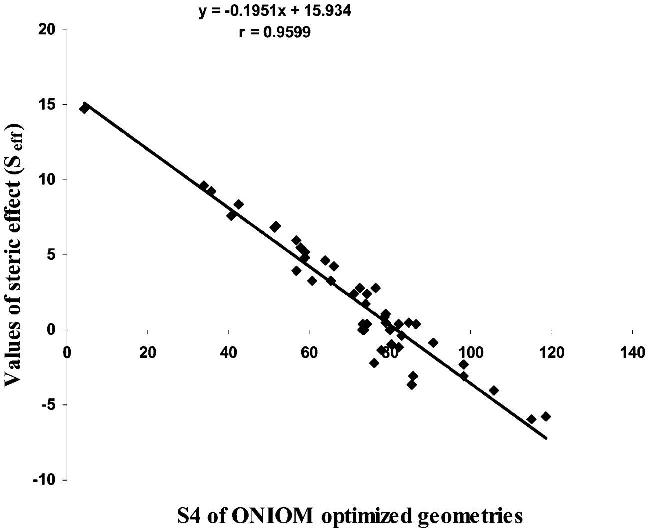

Figure 8. Correlation between S4 values of ONIOM-optimized geometries and calculated S_{eff}.

this, Orpen et al. have calculated S4′ for a particular ligand in various complexes and calculated the mean S4′.[24] Since then, a large number of X-ray structures were added to Cambridge Structural Database,[30] and the mean S4′ calculated by Orpen et al. has been found to vary when more structures were included.[20] Thus, S4′ of a phosphine calculated from a single structure may not produce an actual steric effect defined by Orpen et al. but can be considered as a measure of the steric effect only within that complex. However, S4′ values can provide a general trend in the steric effect when considering a series of phosphine ligands, and Cundari et al. have successfully used S4′ values from PM3 calculations as a measure of steric effect.[20] Compared to the S4′ values, the modified S4 values calculated in the present work can be considered as a measure of the steric effect of only the isolated PR$_3$ ligand in the *electronic effect included* atmosphere of the R moieties. The usage *electronic effect included* means that the optimization of PR$_3$ is carried out using a full QM approach, and therefore, the R−P−R angles in the definition of S4 are determined by both the electronic and steric effects of the R moieties. In this spirit, even the S4′ values obtained from the X-ray geometries are also not truly representing the steric effect because the electronic effect is not separated out.

The S4 values of the ONIOM-level-optimized structures may be considered as a measure of the steric effect of the PR$_3$ ligand in an *electronic effect free* environment of the R moieties. The correlation between the S4 values of the QM-level-optimized structures and ONIOM-level-optimized structures of the PR$_3$ ligands are depicted in Figure 7. There is apparently no correlation between the two quantities, which is expected because the electronic effects provided by the substituents in phosphines were absent in the ONIOM-level calculation, whereas both steric and electronic effects were present in the QM-level-optimized structures.

(d) Comparison of Steric Effect Calculated from MESP and S4. The S4 values calculated for ONIOM-level-optimized geometries may be considered as a geometric parameter for the quantification of the steric effect in the *electronic effect free* atmosphere of R moieties. Therefore, it can be compared with the steric effect (S_{eff}) calculated using the MESP approach. There is in fact good agreement between the S4 and the corresponding MESP-based S_{eff} values because they show a good linear dependency (correlation coefficient = 0.921) (cf. Figure 8).

It may be noted that a positive value of S_{eff} represents a higher steric effect, and a negative value shows a lesser steric effect provided by that ligand when compared to the reference point of PH$_3$. Cundari et al. have reported that phosphites cannot be treated along with phosphines while measuring S4′ values because of its conformational flexibility.[20] But from the above correlation, which includes phosphites, it is clear that the MESP-based approach to the steric effect can incorporate a wider range of ligands. Further, the correlation confirms that the present approach is advantageous because the steric effect based on the S4′ value depends on various other electronic factors in a complex. In other words, the combination of the QM and QM-MM methods augmented with the MESP-based analysis of the electronic variations around the phosphorus lone pair makes it possible to separate the electronic and steric effects from one another.

(f) Stereoelectronic Profile of Ligands. Because the steric and electronic effects of phosphines can be separated using MESP, it is possible to construct a stereoelectronic plot of the ligands using the values in Table 3, and such a plot is depicted in Figure 9.

The stereoelectronic correlations plotted above provide both steric and electronic measures of various types of phosphine ligands, which include cyclic, noncyclic, and heterocyclic structures, and the method adopted for their determination is simple and less expensive in terms of computational cost. Such a stereoelectronic profile could be highly useful in the designing of catalysts because phosphine ligands constitute the major class of co-ligands in inorganic and organometallic chemistry. Positive values of both E_{eff} and S_{eff} indicate electron-donating ability, whereas their

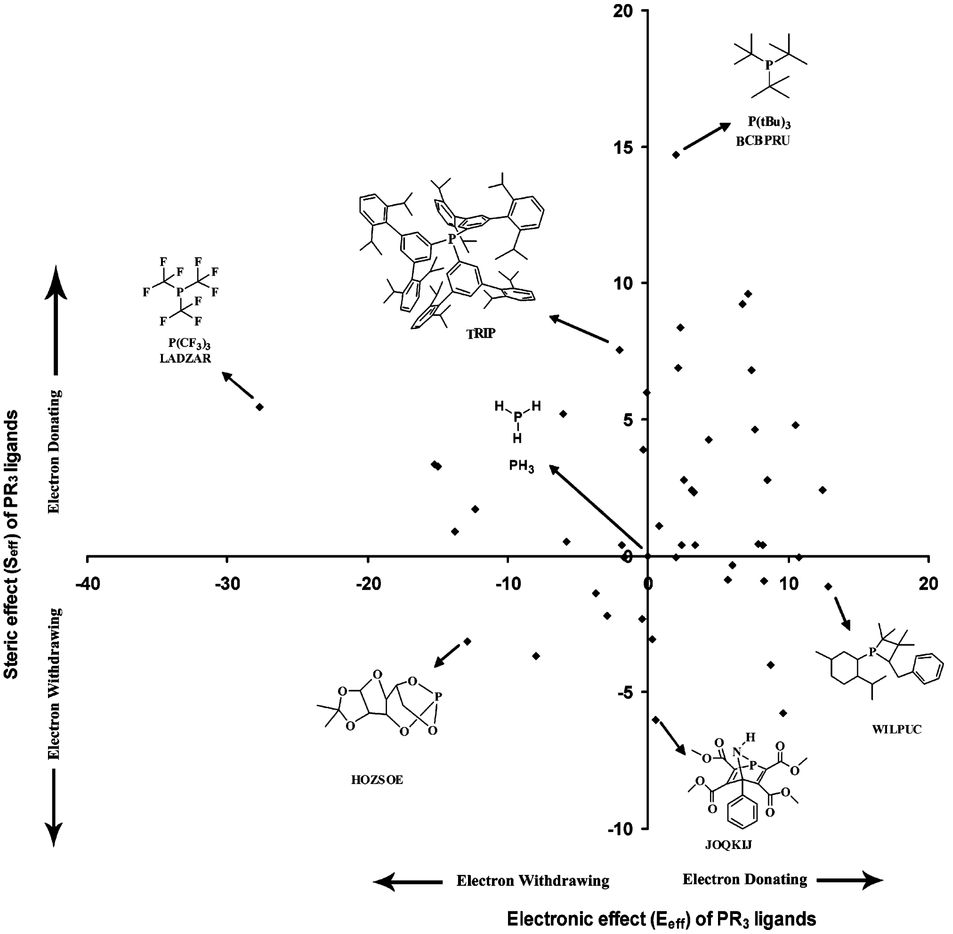

Figure 9. Stereoelectronic plot of PR_3 ligands.

negative values suggest an electron-withdrawing tendency of the ligands. Therefore, the ligands can be classified into four categories, namely, ligands with (i) ($+E_{\mathrm{eff}}$, $+S_{\mathrm{eff}}$), (ii) ($+E_{\mathrm{eff}}$, $-S_{\mathrm{eff}}$), (iii) ($-E_{\mathrm{eff}}$, $+S_{\mathrm{eff}}$), and (iv) ($-E_{\mathrm{eff}}$, $-S_{\mathrm{eff}}$), where plus and minus signs indicate electron-donation and electron-withdrawal properties, respectively. It can be seen that PR_3 ligands are distributed in all of the four quadrants of the coordinate system, and the number of ligands in first quadrant is the highest where both S_{eff} and E_{eff} are positive. Among all of the ligands, $P(CF_3)_3$ has the highest negative E_{eff} value (−27.73 kcal/mol), meaning that it has the maximum electron-withdrawing effect, and among phosphites, QIVLOW ($E_{\mathrm{eff}} = -15.20$ kcal/mol) is the most electron-withdrawing. All of the other phosphites fall in the third quadrant, where both S_{eff} and E_{eff} are negative. WILPUC has the maximum positive value for E_{eff} (12.86 kcal/mol), and so it is the most electron-donating. The ligand that has the maximum steric effect is $P(^t\mathrm{Bu})_3$ ($S_{\mathrm{eff}} = 14.70$ kcal/mol), and the ligand that has the minimum steric effect is JOQKIJ ($S_{\mathrm{eff}} = -6.01$). The bowl-shaped ligand TRIP possesses a large positive steric effect of 7.55 kcal/mol, whereas its electronic effect has a moderate negative value of −2.07 kcal/mol. It can also be noted that there are ligands in which the steric bulkiness of the substituents makes it electron-donating, though the electronic effect of it is electron-withdrawing in nature and vice versa. Thus, in JOQKIJ the electronic effect of the substituents favors the donation of electrons, but a higher negative value for S_{eff} makes the ligand electron-withdrawing in nature. In $P(CF_3)_3$ (LADZAR), the steric effect favors the electron-donating nature, but it remains the most electron-withdrawing because of the high negative value for $E_{\mathrm{eff.}}$ The S_{eff} value for FIDDOL, MASRAZ, and NESNII is near to zero, and so the nature of the ligand is decided by the electronic effect of the substituents. Similarly in PPh_3, the value for E_{eff} is close to zero, but the ligand is electron-donating because of the positive value for S_{eff}.

Conclusions

The work presented here describes a method for the separation of the steric effect of a PR_3 ligand from its electronic effect. It may be noted that the steric and electronic effects are intermingled and nearly inseparable in every system, and therefore only the combined effect is always observed in their associated electronic properties. The present approach combining both the QM and QM/MM methods is attractive because it gives a simple and effective way to assess the amount of steric-effect-induced electronic variations of the PR_3 ligand. The variation in the electron-donating ability with bulkiness in substituents of phosphines is quantified from the MESP minimum (V_{min}) values in the lone-pair region of the phosphorus atom. A method for the calculation of symmetric deformation coordinates (S4) of free phosphines was introduced, and the steric effect of phosphines was measured using a two-layer ONIOM-level QM/

MM method. A good linear correlation between MESP-based S_{eff} values and the S4-based steric parameters provided direct support for the relevance of this method. A stereoelectronic plot was made using the calculated E_{eff} and S_{eff} values, and from this plot it is very easy to find the ligands with desired amounts of electronic and steric effects. Such a stereoelectronic plot will be useful in selecting the ligands in the designing of catalyst systems in organometallic chemistry. We also hope that the stereoelectronic plots for other popular ligand families such as *N*-heterocyclic carbenes, amines, etc., can be estimated by following the combined approach of QM and MM methods described in this work.

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Supporting Information Available: Complete references of all of the ligands and geometric parameters used for the calculation of S4 values for all of the optimized ligands. This material is available free of charge via the Internet at http://pubs.acs.org.

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