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Keywords:	Lewis basicity, phosphanes



Preview

Methyl Cation Affinity (MCA) Values for Phosphanes

Christoph Lindner^a, Boris Maryasin^a, Frank Richter^b and Hendrik Zipse^{a*}

Abstract

Methyl cation affinity (MCA) values have been calculated for a variety of phosphanes at the MP2(FC)/6-31+G(2d,p)//B98/6-31G(d) level of theory. The analysis of MCA values for tri-alkyl phosphanes reveals that substituent effects are additive for unbranched and cyclic alkyl substituents, and (with some modification) also for most of the branched alkyl substituents.

Key Words: Lewis basicity, phosphanes, methyl cation affinity

INTRODUCTION

Most chemists consider phosphanes almost exclusively as ligands for transition metal complexes, but their role as catalysts in, for example, acylation reactions,^[1,2] the Morita-Baylis-Hillman reaction,^[3,4] Rauhut-Currier reaction^[5,6] or Michael addition reactions^[7] should not be underestimated. The homopolymerization of isocyanates – another, rather exotic yet industrially applied, example for the direct use of organophosphanes as catalysts – is known for more than a century,^[8] but still attracts the interest of researchers today.^[9] In all these areas of application phosphane catalysts react with carbon-centered electrophiles and thus activate these substrates for subsequent steps in the catalytic cycle. The affinity of phosphanes towards a reference carbon electrophile will thus help to correlate observed catalytic reactivity with the phosphane substitution pattern. Hardly any data of this kind is available from experiment,^[10] and we have therefore established a quantum mechanical protocol for the reliable calculation of the reaction of N- and P-centered nucleophiles with the methyl cation, the smallest C-centered electrophile.^[11-14] In contrast to gas or solution phase proton affinities, methyl cation affinities (MCAs) provide a much more realistic assessment of the nucleophilic potential of

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3 phosphanes in organocatalytic processes. In an effort to
4 provide quantitative data for phosphorus-based nucleophiles
5 used in organocatalytic processes we report here MCA values
6 for a wide variety of phosphanes.
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10 11 **COMPUTATIONAL METHODS**

12 Methyl cation affinities of phosphane bases have been
13 calculated as the reaction enthalpy at 298.15 K and 1 atm
14 pressure for the methyl cation detachment reaction shown in
15 eqn. (1). This is in analogy to the mass spectrometric
16 definition of proton affinities.
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25 The geometries of all species in eqn. (1) have been optimized
26 at the B98/6-31G(d) level of theory. The conformational space
27 of flexible trialkylphosphanes and the corresponding
28 phosphonium cations has been searched using the MM3 force
29 field and the systematic search routine in the TINKER program
30 and, for selected systems, also with the MM3* force field and
31 the systematic search routine implemented in MACROMODEL
32 9.7.^[15,16] All stationary points located at force field level
33 have then been reoptimized at B98/6-31G(d) level as described
34 before. Thermochemical corrections to 298.15 K have been
35 calculated for all minima from unscaled vibrational
36 frequencies obtained at this same level. The thermochemical
37 corrections have been combined with single point energies
38 calculated at the MP2(FC)/6-31+G(2d,p)//B98/6-31G(d) level to
39 yield enthalpies H_{298} at 298.15 K. In conformationally flexible
40 systems enthalpies have been calculated as Boltzmann-averaged
41 values over all available conformers. This procedure (termed
42 "MP2-5" in recent publications) has been found to reproduce G3
43 methyl cation affinity values of selected small and medium
44 sized organocatalysts within 4.0 kJ/mol.^[11] All quantum
45 mechanical calculations have been performed with Gaussian
46 03.^[17]
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RESULTS and DISCUSSION

MCA values for a variety of substituted phosphanes are shown in a graphical manner in Figure 1 (unbranched and branched acyclic alkyl substituents) and Figure 2 (cyclic substituents). The MCA values have also been collected in Table 1. The MCA values for all trisubstituted alkyl and aryl phosphanes are significantly larger than those obtained for the parent phosphane PH_3 (MCA = +448.5 kJ/mol) and its mono- and di-methylated variants (Table 1).

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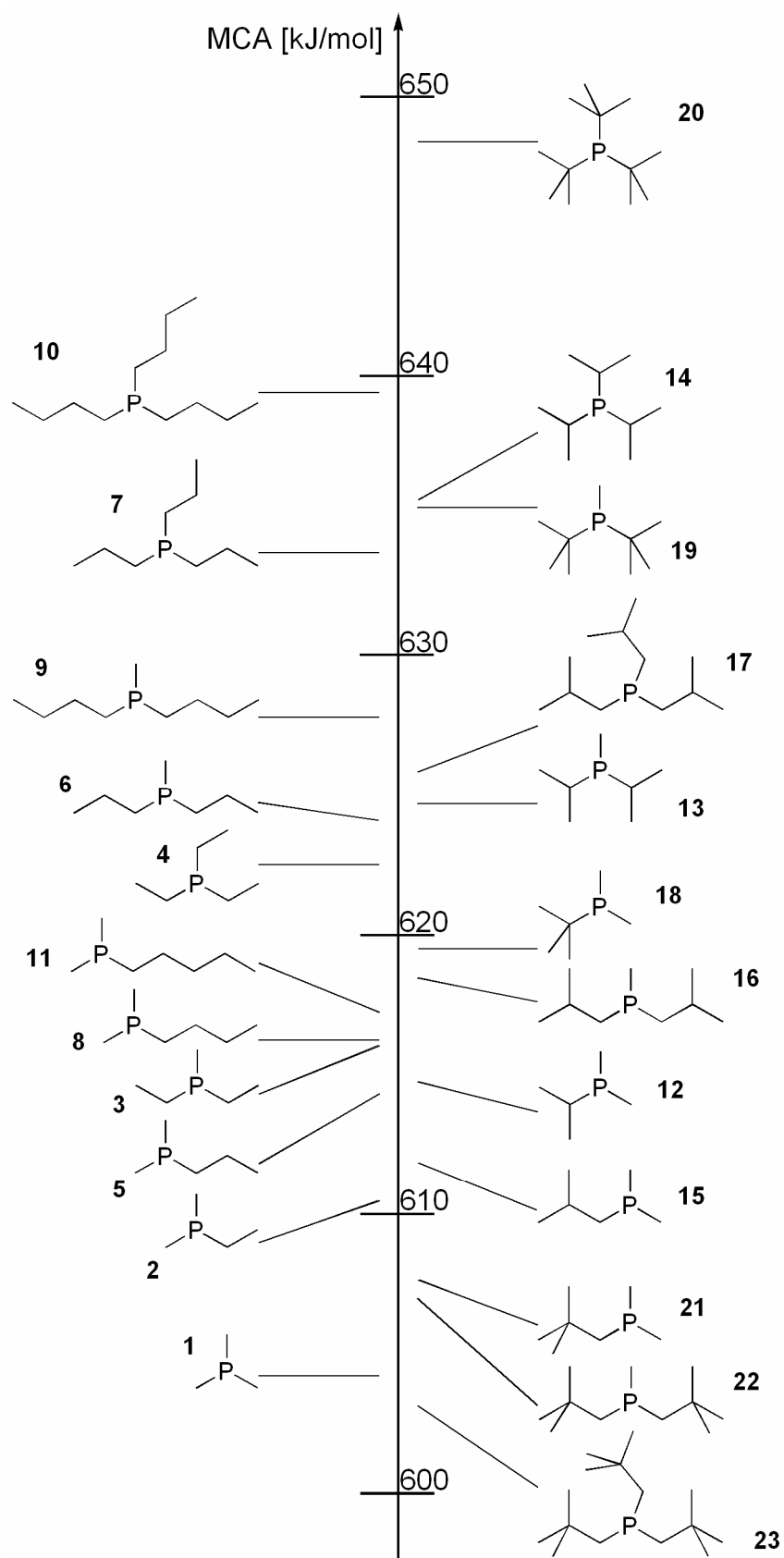


Figure 1. Structures of trisubstituted phosphanes with acyclic alkyl substituents, ordered by their respective MCA values (in kJ/mol).

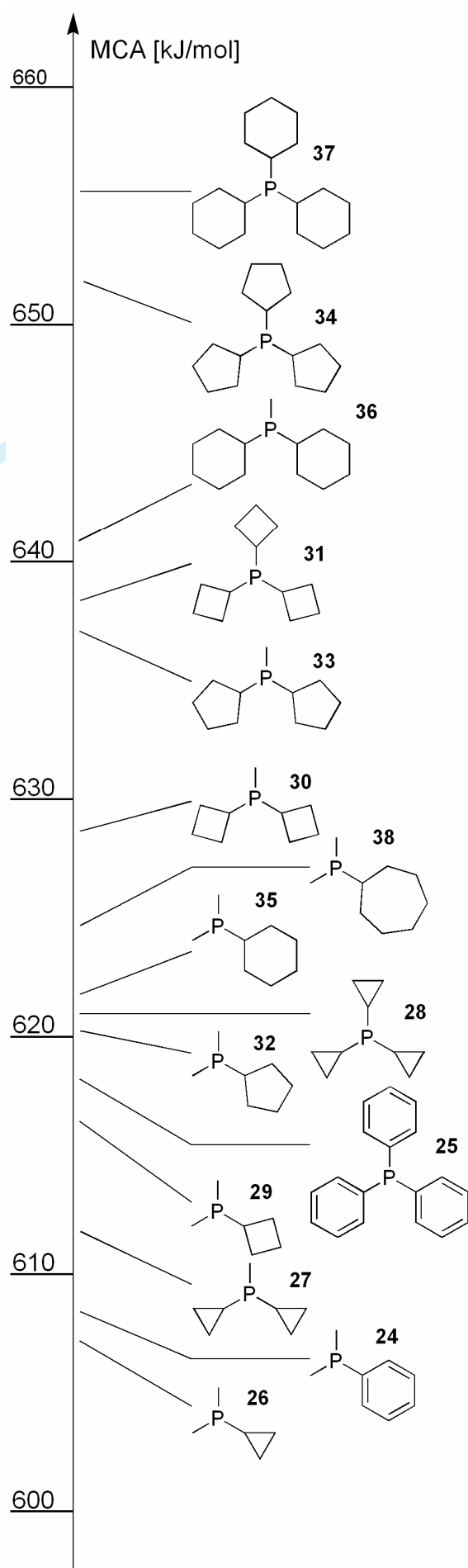


Figure 2. Structures of trisubstituted phosphanes with cyclic substituents, ordered by their respective MCA values (in kJ/mol).

Table 1. Methyl Cation Affinity (MCA) values for a variety of phosphanes calculated according to eqn. (1) at MP2(FC)/6-31+G(2d,p)//B98/6-31G(d) level (in kJ/mol).^a

System	MCA [kJ/mol]	System	MCA [kJ/mol]
PH ₃	+448.5 ^b	PH ₂ Me	+513.0
PHMe ₂	+564.2	P(CH ₂ tBu) ₃ (23)	+603.3
PMe ₃ (1)	+604.2	PMe(CH ₂ tBu) ₂ (22)	+606.9
PMe ₂ (cPr) (26)	+607.2	PMe ₂ (CH ₂ tBu) (21)	+607.9
PMe ₂ Ph (24)	+608.5	PMe ₂ Et (2)	+610.5
PMe(cPr) ₂ (27)	+611.8	PMe ₂ (iBu) (15)	+611.9
PMe ₂ (iPr) (12)	+613.5	PMe ₂ (nPr) (5)	+614.3
PMeEt ₂ (3)	+616.1	PMe ₂ (nBu) (8)	+616.3
PMe ₂ (cBu) (29)	+616.7	PMe ₂ (nPen) (11)	+617.3
PPh ₃ (25)	+618.4	PMe(iBu) ₂ (16)	+618.5
PMe ₂ (tBu) (18)	+619.4	PMe ₂ (cPen) (32)	+620.4
P(cPr) ₃ (28)	+621.8	PMe ₂ (cHex) (35)	+621.9
PEt ₃ (4)	+622.5	PMe(nPr) ₂ (6)	+624.1
PMe(iPr) ₂ (13)	+624.8	PMe ₂ (cHep) (38)	+624.9
P(iBu) ₃ (17)	+625.7	PMe(nBu) ₂ (9)	+627.8
PMe(cBu) ₂ (30)	+628.7	P(nPr) ₃ (7)	+633.6
PMe(tBu) ₂ (19)	+633.9	PMe(tBu) ₂ (19)	+635.1
P(iPr) ₃ (14)	+635.4	PMe(cPen) ₂ (33)	+637.1
P(cBu) ₃ (31)	+638.5	P(nBu) ₃ (10)	+639.5
PMe(cHex) ₂ (36)	+641.0	P(tBu) ₃ (20)	+648.3
P(cPen) ₃ (34)	+650.8	P(cHex) ₃ (37)	+655.7

^aAbbreviations: Pen stands for pentyl, Hex for hexyl, Hep for heptyl. ^bRef. [11].

A general trend towards higher MCA values for phosphanes with larger alkyl systems is readily identified in Figure 1 and 2 in a qualitative way. For unbranched alkyl substituents as well as for cyclic and for most of the branched substituents the effects are largely additive. Correlations between the number by substituents (replacing the methyl groups in PMe₃

(1)) and the respective MCA values are shown in Figures 3 - 5. The reference point in these correlations is trimethylphosphane PMe_3 (**1**) with $\text{MCA} = 604.2 \text{ kJ/mol}$.

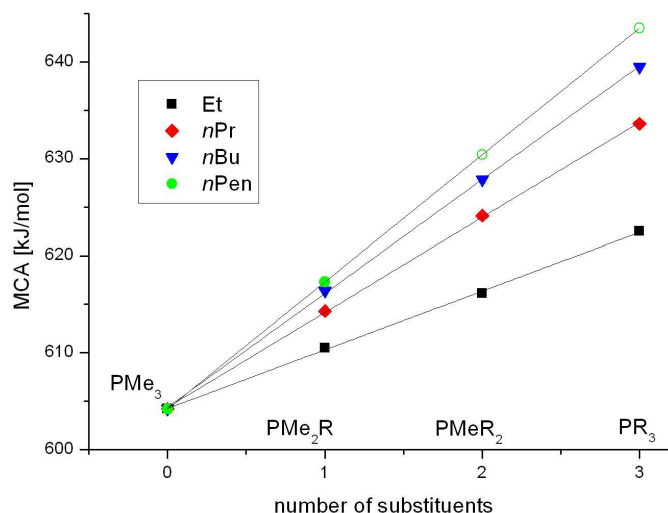


Figure 3. MCA values of trialkylphosphanes with linear alkyl substituents.

The correlations in Figure 3 for phosphanes with linear unbranched alkyl substituents are of impressively good quality. These correlations imply that MCA values for trisubstituted phosphanes PR_3 can be estimated with good confidence on the basis of the MCA values of the corresponding monosubstituted phosphane PMe_2R and that of PMe_3 (**1**). In quantitative terms this additivity rule can be expressed using eq. (2) with n = number of substituents other than methyl.

$$\text{MCA}(\text{PMe}_{3-n}\text{R}_n) = \text{MCA}(\text{PMe}_3) + n \times (\text{MCA}(\text{PMe}_2\text{R}) - \text{MCA}(\text{PMe}_3)) \quad (2)$$

Taking $\text{R} = n\text{Bu}$ as an example, the replacement of one methyl group in PMe_3 (**1**) by $n\text{Bu}$ as in $\text{PMe}_2(n\text{Bu})$ (**8**) ($\text{MCA} = +616.3 \text{ kJ/mol}$) increases the MCA value by 12.1 kJ/mol . Using this increment value per $n\text{Bu}$ group in combination with the MCA value for PMe_3 (**1**) leads to $\text{MCA}(\text{P}(n\text{Bu})_3, \mathbf{31}) = (3 \times 12.1 + 604.2) \text{ kJ/mol} = 640.5 \text{ kJ/mol}$. The actual value calculated for $\text{P}(n\text{Bu})_3$ (**31**) is $+639.5 \text{ kJ/mol}$ (Table 2), only 1 kJ/mol less than estimated with the additivity assumption expressed through eq. (2). In a completely analogous way the results for $\text{PMe}_2(n\text{Pen})$ (**11**) with $\text{MCA} = +617.3 \text{ kJ/mol}$ can be

used to predict MCA values for the hypothetical systems $\text{PMe}(n\text{Pen})_2$ and $\text{P}(n\text{Pen})_3$ of +630.4 and +643.5 kJ/mol, respectively (indicated by the unfilled symbols in Figure 3).

Table 2. Methyl Cation Affinity (MCA) values obtained from direct calculation (MP2-5) and from the extrapolation schemes in eq. (2) and eq. (5) (in kJ/mol).

System	MCA (MP2-5)	MCA (eq. 2)	MCA (eq. 5)
PMe_3 (1)	+604.2	+604.2	+604.2
PMe_2Et (2)	+610.5	+610.5	+610.3
PMeEt_2 (3)	+616.1	+616.8	+616.4
PEt_3 (4)	+622.5	+623.1	+622.5
$\text{PMe}_2(n\text{Pr})$ (5)	+614.3	+614.3	+614.0
$\text{PMe}(n\text{Pr})_2$ (6)	+624.1	+624.4	+623.8
$\text{P}(n\text{Pr})_3$ (7)	+633.6	+634.5	+633.6
$\text{PMe}_2(n\text{Bu})$ (8)	+616.3	+616.3	+616.0
$\text{PMe}(n\text{Bu})_2$ (9)	+627.8	+628.4	+627.8
$\text{P}(n\text{Bu})_3$ (10)	+639.5	+640.5	+639.6
$\text{PMe}_2(n\text{Pen})$ (11)	+617.3	+617.3	+617.0
$\text{PMe}(n\text{Pen})_2$	n/a	+630.4	+629.8
$\text{P}(n\text{Pen})_3$	n/a	+643.5	+642.6

One additional result obtained from the linear correlations in Figure 3 is that the slope of the correlation lines increases with increasing size (or more precisely: length) of the alkyl substituents. This is readily rationalized on the basis of inductive electron-donating effects of alkyl substituents, whose size is expected to depend on the length of the alkyl substituents. The exponentially convergent nature of these effects as observed in Figure 4 can be used to derive an analytic function for the chain-length dependence of MCA values as expressed in eq. 3. This three-parameter equation describes the explicitly calculated data points with excellent fidelity ($R^2 = 0.9995$) and is somewhat better suited than other exponential formulae.

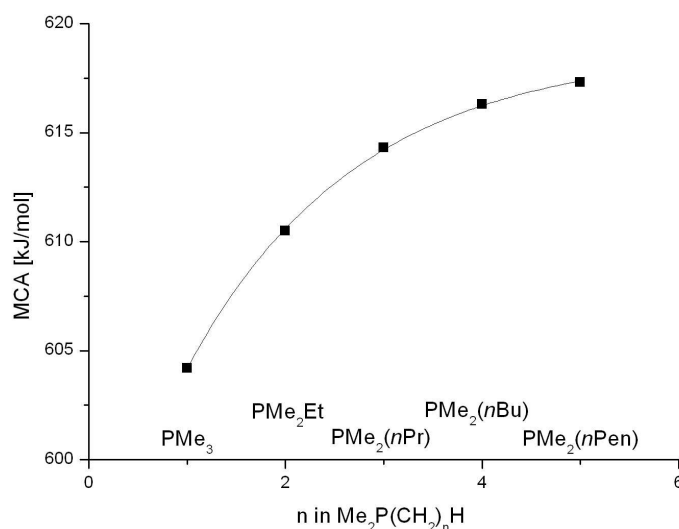


Figure 4. MCA values of monosubstituted phosphanes of general formula $\text{Me}_2\text{P}(\text{CH}_2)_n\text{H}$ ($n = 1 - 5$, in kJ/mol).

$$\text{MCA}(\text{Me}_2\text{P}(\text{CH}_2)_n\text{H}, \text{kJ/mol}) = 618.8 - 26.1 \times 0.56^n \quad (3)$$

The description of the systematically convergent nature of a single alkyl substituted phosphane can be extended to systems containing an alkyl substituent with infinite length. The limit of infinity of MCA values for monosubstituted phosphanes with linear alkyl chains corresponds to the first parameter in eq. (3) (618.8 kJ/mol). On the basis of the additivity assumption a phosphane with three linear alkyl substituents with infinite length provides a MCA value of 648.0 kJ/mol. MCA values beyond this limit thus appear to be out of reach for phosphanes with linear alkyl substituents.

The same observations on the additivity and size-dependence of substituent effects as for linear alkyl substituents can also be made for systems with simple cycloalkyl substituents (Figure 5).

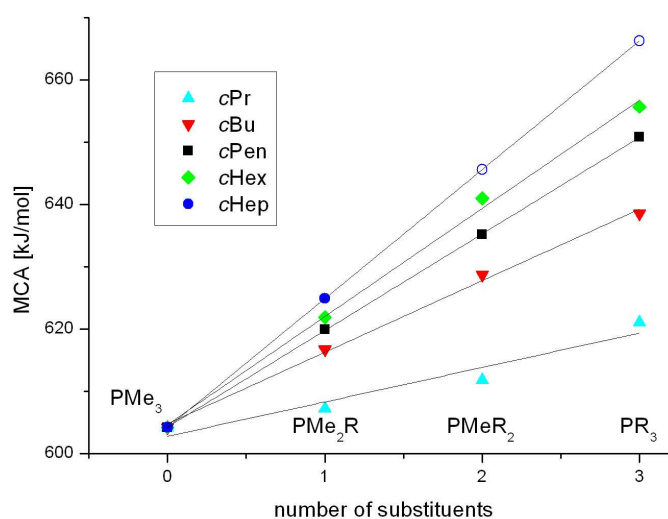


Figure 5. MCA values of trialkylphosphanes with cycloalkyl substituents.

More specifically, the MCA values again depend linearly on the number of substituents. The correlations in Figure 5 for phosphanes with cyclic alkyl substituents are of good quality in analogy with the linear unbranched alkyl substituted phosphanes. It is noticeable that the correlation is worst for systems containing highly strained cyclopropyl substituents, with particularly large deviations from the correlation line being observed for tricyclopropylphosphane (**28**). In order to test whether this is due to problems of the B98 functional with strained cyclopropane ring structures, the MCA value for **28** was recalculated with geometries obtained at MP2(FC)/6-31+G(2d,p) level. The value of $MCA(\mathbf{28}) = +623.5$ kJ/mol obtained in this way is, however, hardly different from that obtained using the B98/6-31G(d) structures with $MCA(\mathbf{28}) = +621.8$ kJ/mol. We thus conclude that the non-perfect additivity behaviour of the cyclopropyl-substituted phosphanes represents an intrinsic property of this class of systems.

For all other systems, however, the observed correlations allow for the prediction of MCA values for trisubstituted phosphanes PR_3 with high reliability on the basis of the MCA values of the corresponding monosubstituted phosphane PMe_2R and that of PMe_3 (**1**) (Table 3). In quantitative terms this

additivity rule can again be expressed using eq. (2) given before. Taking R = cHep as an example, the replacement of one methyl group in PMe_3 (**1**) by cHep as in $\text{PMe}_2(\text{cHep})$ (**38**) (MCA = +624.9 kJ/mol) leads to an increase in MCA value of 20.7 kJ/mol. With the use of this increment value per cHep group in combination with the MCA value for PMe_3 (**1**) it is possible to estimate the MCA values of $(2 \times 20.7 + 604.2)$ kJ/mol = 645.6 kJ/mol for $\text{PMe}(\text{cHep})_2$ and $(3 \times 20.7 + 604.2)$ kJ/mol = 666.3 kJ/mol for $\text{P}(\text{cHep})_3$ (indicated by the unfilled symbols in Figure 5).

Table 3. Methyl Cation Affinity (MCA) values obtained from direct calculation (MP2-5) and from the extrapolation schemes in eq. (2) and eq. (5) for phosphanes with cycloalkyl substituents (in kJ/mol).

System	MCA (MP2-5)	MCA (eq. 2)	MCA (eq. 5)
$\text{PMe}_2(\text{cPr})$ (26)	+607.2	+607.2	+612.8
$\text{PMe}(\text{cPr})_2$ (27)	+611.8	+610.2	+621.9
$\text{P}(\text{cPr})_3$ (28)	+621.1	+613.2	+627.2
$\text{PMe}_2(\text{cBu})$ (29)	+616.7	+616.7	+616.5
$\text{PMe}(\text{cBu})_2$ (30)	+628.7	+628.8	+629.3
$\text{P}(\text{cBu})_3$ (31)	+638.5	+641.1	+638.3
$\text{PMe}_2(\text{cPen})$ (32)	+620.4	+620.4	+620.2
$\text{PMe}(\text{cPen})_2$ (33)	+637.1	+636.6	+636.7
$\text{P}(\text{cPen})_3$ (34)	+649.0	+652.8	+649.4
$\text{PMe}_2(\text{cHex})$ (35)	+621.9	+621.9	+622.2
$\text{PMe}(\text{cHex})_2$ (36)	+641.0	+639.6	+640.7
$\text{P}(\text{cHex})_3$ (37)	+655.7	+657.3	+655.4
$\text{PMe}_2(\text{cHep})$ (38)	+624.9	+624.9	+624.2
$\text{PMe}(\text{cHep})_2$	n/a	+645.6	+644.7
$\text{P}(\text{cHep})_3$	n/a	+666.3	+661.4

As already observed for phosphanes with linear alkyl substituents, the slopes of the correlation lines in Figure 5 increase with increasing size of the substituents. This is readily rationalized on the basis of inductive electron-donating effects of the cycloalkyl substituents, whose size depends on the dimension of the substituents. The exponentially convergent nature of these effects as observed

in Figure 6 can be used to derive an analytic function for the ring-size dependence of MCA values as expressed in eq. (4).

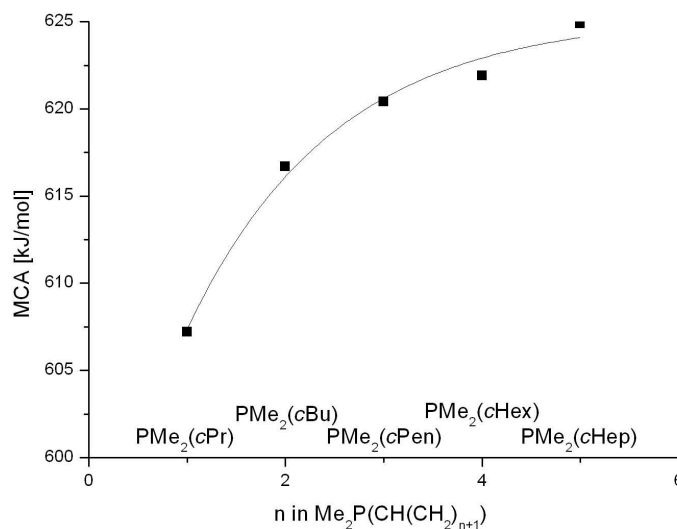


Figure 6. MCA values of monosubstituted phosphanes of general formula Me₂P(CH(CH₂)_{n+1}) (n = 1 – 5, in kJ/mol).

$$\text{MCA}(\text{Me}_2\text{P}(\text{CH}(\text{CH}_2)_{n+1}), \text{kJ/mol}) = 625.3 - 35.5 \times 0.51^n \quad (4)$$

The description of the systematically convergent nature of a single cycloalkyl substituted phosphane can be extended to systems containing cycloalkyl substituents with infinite ring size. For phosphanes carrying one cyclic substituent the limit of infinite ring size corresponds to a MCA value of 625.3 kJ/mol (the first parameter in eq. (4)). Based on the additivity assumption a phosphane with three cycloalkyl substituents with infinite ring size provides a MCA value of 667.5 kJ/mol, defining the upper limit for phosphanes with cyclic alkyl substituents.

Phosphanes including branched acyclic substituents follow the additivity and saturation rules established before in some, but not all cases (Figure 7).

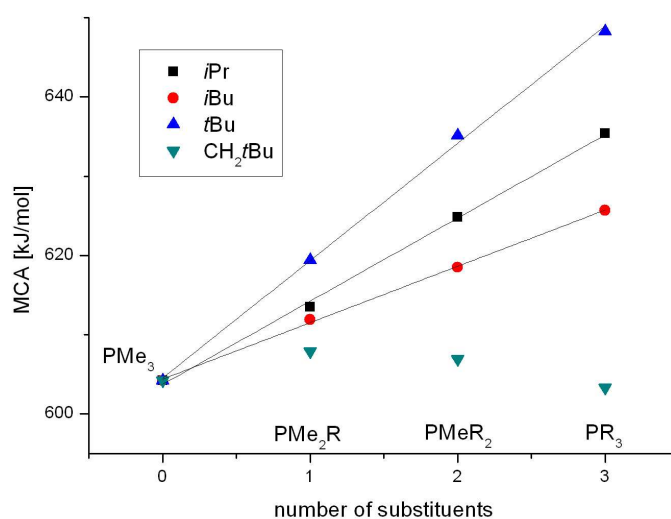


Figure 7. Trends for the MCA values of branched alkyl substituted phosphanes.

The MCA values again depend linearly on the number of substituents for three of the four systems. A linear correlation is possible for the *iPr*, *iBu* and *tBu* systems. No simple correlation is found, however, for the *neo*-pentyl (CH_2tBu) substituted systems in which the MCA values decrease irregularly with an increasing number of *neo*-pentyl groups. This is undoubtedly a consequence of unfavourable interactions in the methyl cation adducts of these phosphanes.

Using the results obtained for all systems exhibiting additive substituent effects shows that the systematic size-dependence of inductive effects can be cast into a general equation (5) describing the dependence of MCA values on the size of the alkyl groups attached to the phosphorous center.

$$\text{MCA [kJ/mol]} = 604.2 + 6.1b + 3.7c + 2.0d + 1.0e + x \quad (5)$$

The MCA value of trimethylphosphane PMe_3 (**1**) (604.2 kJ/mol) is again chosen as the reference point. The characters *b*, *c*, *d* and *e* stand for the number of methyl- and methylene-groups, respectively, in α -, β -, γ - and δ -position. Character *x* represents a correction factor whose size depends on the particular class of compounds. The correction factor for

unbranched alkyl groups is zero, as the deviations are quite small, e.g. the MCA ($P(nBu)_3$, (10)) is 639.5 kJ/mol (MP2-5) and 639.6 kJ/mol (eq. 5). For cyclic alkyl groups x depends on the number of substituents and is listed in Table 4. For the $P(cHex)_3$ system the MCA value is 655.7 kJ/mol (MP2-5), while the predicted value including the correction is 655.4 kJ/mol (eq. (5)). Results for the branched alkyl substituents are, unfortunately, not fully consistent, and a scheme using a single correction factor for all branched substituents could not be derived in a satisfactory manner. The correction factors for *iPr* and *tBu* groups are therefore listed in Table 4 separately from those for the *iBu* group. The irregular nature of MCAs for *iBu*-substituted systems are caused by 1,5-*syn*-pentane interactions in the cationic adducts as shown in Figure 8. The number of these repulsive interactions is larger in the methyl cation adducts as compared to the neutral phosphane, thus leading to a reduction of MCA values.

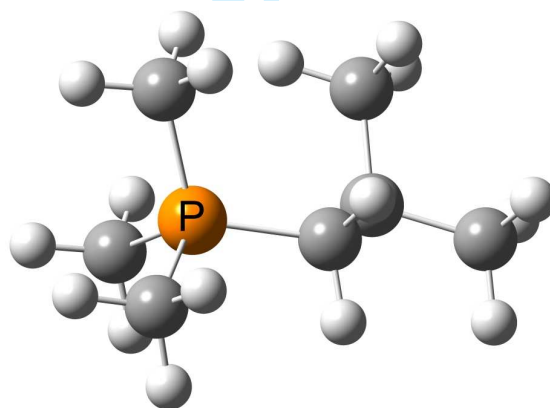


Figure 8. Structure of the methyl cation adduct $PMe_3(iBu)^+$.

Table 4. Averaged correction factors x .

cyclic systems:			
number of substituents	1	2	3
correction factor x	-3.6	-6.7	-13.6
branched systems (<i>iPr</i> and <i>tBu</i>):			
number of substituents	1	2	3
correction factor x	-3.0	-4.7	-8.1
branched systems (<i>iBu</i>):			
number of substituents	1	2	3

correction factor x	-6.3	-12.6	-18.9
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Pictorial representations of the correlation of MCA values calculated quantum mechanically at MP2-5 level with those derived from eq. (5) are shown in Figure 9.

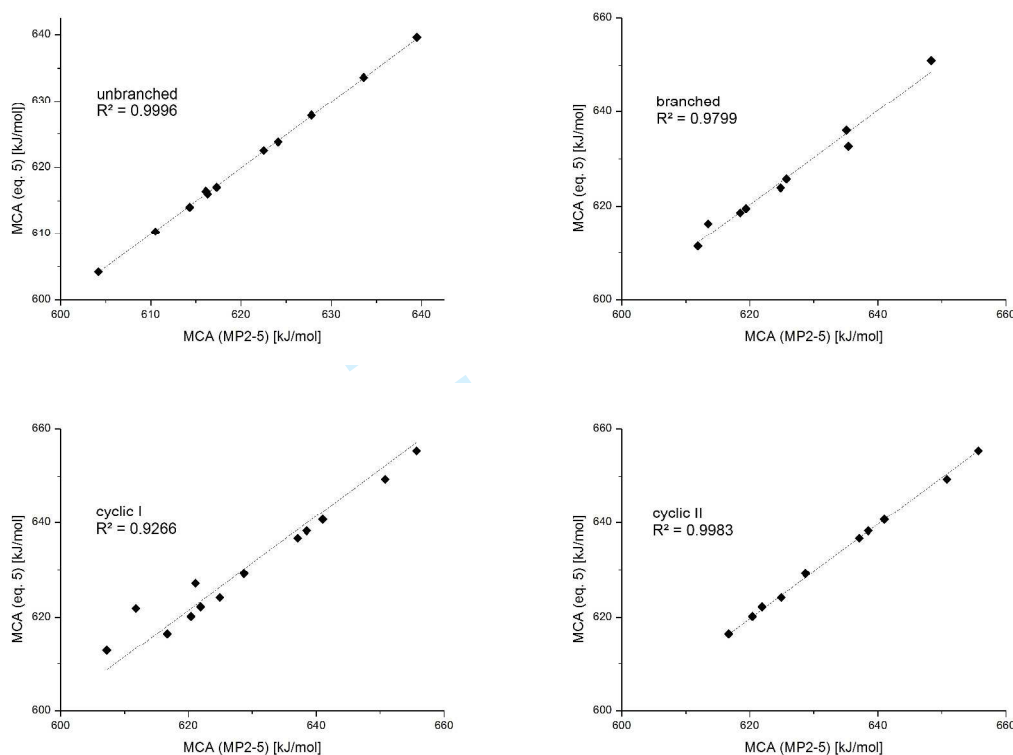


Figure 9. Correlation of MCA values calculated with eq. (5) with those obtained at MP2-5 level. "Unbranched" includes all phosphanes with linear alkyl substituents; "branched" includes all phosphanes with branched, acyclic alkyl substituents; "cyclic I" includes all cyclic substituents; "cyclic II" includes all cyclic substituents except cyclopropyl.

The largest deviations from the diagonal occur for cyclopropyl substituted phosphanes. This is likely due to the earlier observation of the non-additivity of substituent effects in this class of phosphanes. Systems with unbranched alkyl substituents, in contrast, fit the correlation line very well despite the absence of any correction factors. The general formulation of substituent effects in eq. (5) also opens the opportunity to predict MCA values for unsymmetrically

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3 substituted systems. This can be exemplified using
4 $\text{PEt}(\text{cPen})(i\text{Pr})$ as an example, whose MCA value amounts to
5 636.4 kJ/mol at MP2-5 level. Using the additivity assumptions
6 (eq. (2)) predicts a MCA value of 636.2 kJ/mol, while using
7 eq. (5) yields a MCA value of 635.5 kJ/mol. Both of the
8 predicted values are thus within 1 kJ/mol, illustrating the
9 usefulness of these approaches for unsymmetrically
10 substituted phosphanes.
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16 17 CONCLUSIONS

18 In conclusion we have shown that MCA values calculated for
19 trisubstituted phosphanes can be rationalized readily using a
20 number of additivity assumptions. Knowing the variation of one
21 substituent on the MCA is sufficient to predict the MCA of the
22 system with two or three substituents. In general the MCA
23 values increase with increasing chain length or ring size of
24 the alkyl substituents. Furthermore, an empirical equation (5)
25 for the calculation of MCA values can be established depending
26 on the number and position of methyl and methylene groups. The
27 increment system as well as the empirical equation is capable
28 of providing accurate predictions for MCA values for
29 substituents which come from the same or from different
30 classes. In particular these latter results will aid the
31 development of new phosphanes with enhanced affinity towards
32 carbon electrophiles (and possibly also higher activity in
33 organocatalytic processes). It should also not go unnoticed
34 that the two phosphines of highest MCA value in Figure 1
35 ($\text{P}(\text{tBu})_3$, $\text{MCA}(\mathbf{20}) = +648.3$ kJ/mol) and in Figure 2 ($\text{P}(\text{cHex})_3$,
36 $\text{MCA}(\mathbf{37}) = +655.7$ kJ/mol) count among the most active ligands
37 in Pd-mediated cross coupling reactions.^[18] The computed MCA
38 numbers reported here may, in combination with empirical
39 equation (5), thus also be useful for the development of new
40 ligands in this area of application.
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REFERENCES

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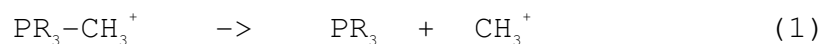
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3 **Methyl cation affinity (MCA)** values have been calculated for a
4 variety of trialkylphosphanes according to eq. (1).
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11 Analysis of these values shows that substituent effects are
12 largely additive. This allows the derivation of an empirical
13 formula for the calculation of mca values as a function of the
14 number and the size of alkyl substituents.
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