A computational study of the methanolysis of palladium–acyl bonds†

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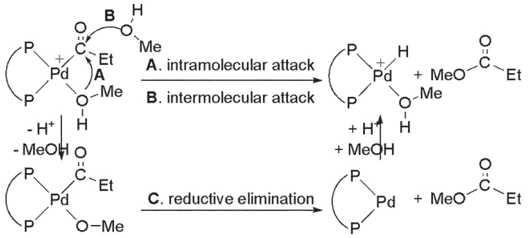
Density functional calculations suggest that intermolecular attack of methanol may be important in the methanolysis of simple Pd–acyl systems and that the energetics of this process are strongly dependent on the metal coordination environment.

The development of highly efficient Pd–diphosphine catalysts for ethene methoxycarbonylation[1] has prompted much interest in the mechanism of this process.[2] Experimental studies with the most active diphosphine, bis(di-*tert*-butylphosphinomethyl)benzene, DTBPMB, have shown the reaction is initiated by a Pd–hydride species.[3] Subsequent steps involve successive insertions of C_2H_4 and CO to generate a Pd–acyl, methanolysis of which releases methyl propanoate and regenerates the Pd–hydride catalyst. Although all of these intermediates have been characterised spectroscopically,[4] the details of the methanolysis step remain unclear. In a separate study of a range of different diphosphines, methanolysis of $[Pd(C(O)Me)(DTBPMB)(O_2CCF_3)]$ was found to be fastest and indeed too fast to measure even at −90 °C.[2b]

Formally, methanolysis involves the addition of the O–H bond of methanol across a Pd–acyl bond and a number of mechanisms can be envisaged for this process (see Scheme 1).[2,5] Starting from $[(P–P)Pd\{C(O)Et\}(MeOH)]^+$, methanolysis may proceed *via* either the intramolecular (**A**) or intermolecular (**B**) attack of methanol. van Leeuwen and co-workers have suggested that intramolecular attack is favoured on the basis of a failure to observe methanolysis in systems where the chelating phosphine imposes a *trans* geometry.[2b] This proposal is apparently supported by the observation that methanolysis of $[Pd(DIBPP)\{C(O)Me\}(MeCN)]^+$ (DIBPP = $^iBu_2P(CH_2)_3P^iBu_2$) in CH_2Cl_2 does not occur, as MeOH cannot displace MeCN from the Pd coordination sphere.[5]



Scheme 1 Possible methanolysis mechanisms.

In other work, however, methanolysis *has* been observed where a *trans* arrangement of phosphines is thought to be imposed.[6] Moreover, the binding mode of these *trans* diphosphine ligands can be ambiguous, as *cis* geometries can still sometimes be accessed[7] and because they often feature non-innocent donor atoms in the diphosphine backbone that may affect the methanolysis process.

An alternative methanolysis mechanism, **C** in Scheme 1, is based on initial deprotonation to generate a methoxide. Reductive elimination from this species is then expected to be very fast.[8] This process seems to be operative in the presence of added base,[9] but may be less relevant under the acidic conditions used for efficient ethene methoxycarbonylation. A further possibility (not shown in Scheme 1) is that the high *trans* influence acyl ligand induces dissociation of a *trans* phosphine ligand. This should then enhance the electrophilicity of the acyl carbon, making it more susceptible to either the intra- or inter-molecular attack of methanol.[2c]

We report here the results of density functional calculations[10] on the methanolysis of simple acyl complexes of the type $[Pd(DHPP)\{C(O)Et\}(L)]^+$ (DHPP = $H_2P(CH_2)_3PH_2$), L = MeOH, C_2H_4, CO and MeCN). Our aim is to define the fundamental features of methanolysis mechanisms **A** and **B** in the absence of significant steric effects. For L = MeOH we show that intermolecular attack, **B**, is in fact strongly favoured over an intramolecular process. Moreover, computed activation barriers for methanolysis *via* Pathway **B** are particularly dependent on both the identity of the coligand L and the metal coordination sphere.

Fig. 1 shows the key stationary points for the methanolysis of $[Pd(DHPP)\{C(O)Et\}(MeOH)]^+$, **1**. As expected, the computed structure of **1** shows an elongated Pd–P distance *trans* to acyl. However, intramolecular attack of MeOH (Pathway **A**) induces a major structural reorganisation such that in the methanolysis transition state, $\mathbf{TS_{1A}}$, the MeOH molecule has moved out of the metal coordination plane and a significant lengthening of the Pd–acyl bond to over 2.9 Å has occurred. The new C···O and Pd···H bonds in $\mathbf{TS_{1A}}$ are both partially formed (1.66 Å and 1.85 Å respectively) although the O···H bond is only slightly lengthened (1.12 Å) at this stage. Overall, the $\{Pd–C_{acyl}–O_{Me}–H\}$ unit is near-planar and this is consistent with a concerted addition of O–H over the Pd–acyl bond. The computed activation energy is, however, very large at 36.4 kcal mol^{-1}. The initial methanolysis product, $\mathbf{P_{1A}}$, features methyl propanoate loosely associated with a highly distorted (and high energy) $[Pd(DHPP)H]^+$ species.‡

The transition state located for intermolecular attack ($\mathbf{TS_{1B}}$, Pathway **B**) features a very similar geometry for the $\{Pd–C_{acyl}–O_{Me}–H\}$ unit to that computed in $\mathbf{TS_{1A}}$ above, although here the Pd–P bond *trans* to acyl lengthens in the transition state. In this

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† Electronic supplementary information (ESI) available: Full computational details and computed Cartesian coordinates and energies for all stationary points. See DOI: 10.1039/b617125g

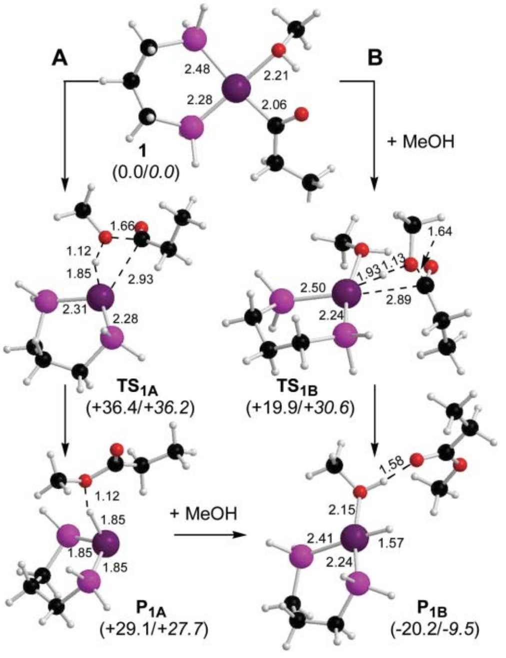

Fig. 1 Computed stationary points (Å) for methanolysis of **1** *via* pathways **A** and **B**. Energies (kcal mol^{-1}) relative to **1** plus free methanol with free energies shown in italics.

case the initial methanolysis product, $\mathbf{P_{1B}}$, exhibits a conventional square-planar geometry as well as H-bonding between methyl propanoate and the remaining MeOH ligand. Both factors make $\mathbf{P_{1B}}$ far more stable than $\mathbf{P_{1A}}$ formed along Pathway **A**. Most significant, however, is the much lower activation energy of only +19.9 kcal mol^{-1} computed for Pathway **B**, 18 kcal mol^{-1} lower than that for Pathway **A**. This preference is retained in the free energy values (italics in Fig. 1) although entropic effects reduce the difference to only 6 kcal mol^{-1}. It therefore appears that in the absence of steric effects intermolecular attack of MeOH is favoured kinetically in the [Pd(DHPP){C(O)Et}(MeOH)]$^+$ system.

Changing the nature of the coligand, L, in our model system was found to have a profound effect on both the methanolysis transition state geometry and its energy. We first considered [Pd(DHPP){C(O)Et}(C_2H_4)]$^+$, **2**, a model of a possible intermediate formed prior to chain propagation in CO–ethene copolymerisation. The methanolysis transition state, $\mathbf{TS_{2B}}$, located for this species is shown in Fig. 2 and exhibits an unusual geometry related to a trigonal bipyramid with one missing axial ligand. Thus the {Pd(DHPP)(C_2H_4)} moiety adopts a local trigonal planar arrangement, while the acyl ligand moves into an axial position. The geometry of the {Pd–C_{acyl}–O_{Me}–H} unit is again similar to those seen in $\mathbf{TS_{1A/B}}$, although the shorter O···H distance (1.05 Å) and longer Pd···H distance (2.10 Å) suggest an earlier transition state in this case. This view is consistent with the low computed activation barrier of only 7.8 kcal mol^{-1} relative to the separated reactants.§ Intermolecular attack of methanol at [Pd(DHPP){C(O)Et}(CO)]$^+$ (**3**) and [Pd(DHPP){C(O)Et}(MeCN)]$^+$ (**4**) led to similar transition state geometries to $\mathbf{TS_{2B}}$ (see Supporting Information). The computed activation energies, however, were found to be highly dependent on the nature of L with in particular strong π-acceptor coligands leading to dramatically reduced barriers (see Table 1).¶

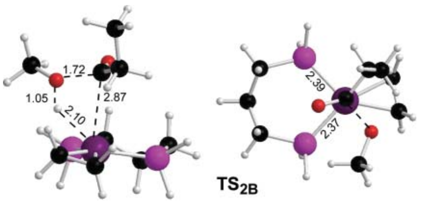

Fig. 2 Two views of $\mathbf{TS_{2B}}$ computed with [Pd(DHPP){C(O)Et}(C_2H_4)]$^+$.

In order to characterise the intermolecular methanolysis reaction in more detail we have compared the computed natural charges on the key atoms involved in this process for model system **1** (see Fig. 3). In the reactant both the Pd centre and, in particular, the acyl carbon carry significant positive charge and this is consistent with the presence of an electrophilic acyl ligand. However, in $\mathbf{TS_{1B}}$ a significant increase in positive charge of +0.31 is computed on the acyl carbon, while at the same time the electron density increases on Pd. We interpret these results in terms of a formal reductive elimination of an acylinium cation from the Pd centre, a process that is stabilised to some extent by interaction with the incoming methanol molecule. Crucially, however, the Pd centre will be formally reduced in this process and takes on increasing Pd^0 character in the transition state. When the extent of this reduction is sufficent the Pd centre becomes a strong enough base to accept a proton from the methanol molecule, resulting in O–H bond cleavage and methanolysis product formation.

Viewed in this light, the unusual transition state geometries located with models **2**, **3** and **4** can be understood. As the {Pd(P–P)} fragment takes on more Pd^0 character in the transition state, the ability of the π-acceptor ligand to stabilise the Pd centre becomes more important. Strong π-acceptors such as C_2H_4 and CO offer significant stabilisation and this results in the much lower barriers to methanolysis for models **2** and **3**. Moreover, the particular orientation of the C_2H_4 ligand in the {PdP_2} plane over in $\mathbf{TS_{2B}}$, is indicative of preferential stabilisation through π-back donation – this arrangement has been observed in many discrete Pd(P–P)(alkene) complexes. In contrast, for **4** the ability of the weaker π-acceptor MeCN ligand to stabilise the Pd centre is much reduced and a much higher activation barrier is computed.

Further support for this interpretation can be gained by considering the behaviour of the *cis* and *trans* isomers of [Pd(PH_3)$_2${C(O)Et}(MeOH)]$^+$, **5**, featuring simple monodentate phosphines. Methanolysis transition states for both isomers exhibit very similar {Pd–C_{acyl}–O_{Me}–H} units to those seen with **1** (Fig. 4). In *trans*-**5** the linear geometry of the {PdP_2} fragment is ideal to stabilize the increased Pd^0 character in the transition state. Indeed, the MeOH ligand *trans* to acyl clearly plays a minimal role in stabilising the metal as the Pd···O distance actually lengthens by over 0.3 Å in $\mathbf{TS}_{\textit{trans}\text{-}\mathbf{5B}}$. This elongation *trans* to acyl was also noted above in $\mathbf{TS_{1B}}$ and reflects a drive to a linear two-coordinate geometry around Pd in the methanolysis transition state.

Table 1 Computed activation energies (kcal mol^{-1}) for intermolecular attack of methanol with [Pd(DHPP){C(O)Et}(L)]$^+$ species

L	Δ*H* (0 K)	Δ*G* (298 K)
C_2H_4	7.8	19.9
CO	11.3	23.1
MeCN	20.0	31.4
MeOH	19.9	30.6

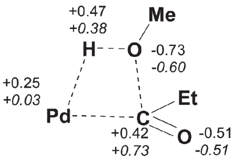

Fig. 3 Natural charges for key atoms in **1** and (in italics) $\mathbf{TS_{1B}}$. For the external MeOH plain text charges refer to the free molecule.

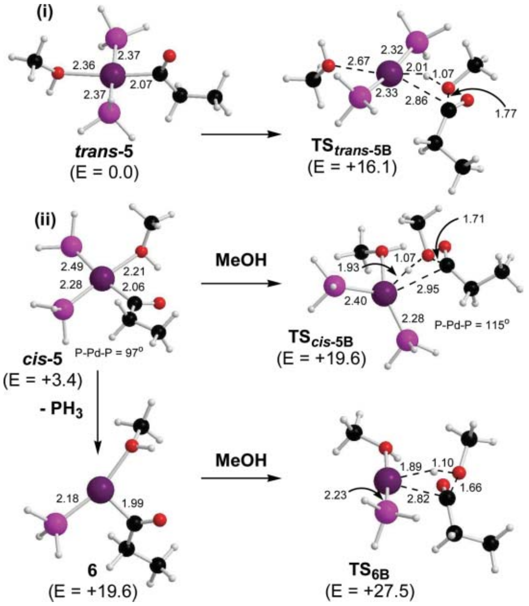

Fig. 4 Computed stationary points (Å) for Pathway **B** for (i) *trans*-**5** and (ii) *cis*-**5**. (ii) also shows methanolysis after initial PH_3 dissociation. All energies (kcal mol^{-1}) relative to *trans*-**1** plus free MeOH.

In contrast, the bent $\{PdP_2\}$ fragment of *cis*-**5** is not so well set up to stabilize Pd^0 character and to compensate for this the P–Pd–P angle increases from 97° in *cis*-**5** to 115° in $\mathbf{TS}_{\mathbf{\mathit{cis}\text{-}5B}}$. The incomplete opening of the P–Pd–P angle means that the transition state is somewhat higher for *cis*-**5** (19.6 kcal mol^{-1}) compared to *trans*-**5** (16.1 kcal mol^{-1}). However, the ability of the monodentate system to adjust the P–Pd–P angle means a reduced barrier to methanolysis compared to that computed for **1**, where the DHPP chelate is relatively inflexible and P–Pd–P angles between 90° and 100° are maintained throughout.

We have also investigated the effect of initial phosphine loss on methanolysis. PH_3 dissociation *trans* to acyl ligand in *cis*-**5** produces the 3-coordinate species, **6**, which then undergoes an intermolecular methanolysis reaction *via* $\mathbf{TS_{6B}}$. The overall barrier for this process is 27.5 kcal mol^{-1}, however, the majority of this barrier is associated with PH_3 loss while the barrier for the methanolysis step is only 7.9 kcal mol^{-1}. Thus, in circumstances where phosphine loss is facile, the subsequent methanolysis of the unsaturated acyl species is expected to be greatly facilitated.

In summary, we have used DF calculations to define the key features of the methanolysis of Pd–acyl bonds *via* both internal and external methanol attack and have shown external attack, Pathway **B**, to be favoured. The coordination environment of the metal greatly affects the energetics of this methanolysis process. In particular, strong π-acceptor coligands significantly lower the activation energy. A flexible $\{PdP_2\}$ unit will also facilitate methanolysis by widening the P–Pd–P angle, while intermolecular attack of methanol is particularly favoured from 3-coordinate species with a vacant site *trans* to acyl.

Our results are at odds with the idea that methanolysis is restricted to intramolecular attack by MeOH within species containing *cis*-PdP_2 units. Moreover, the strong effect of the coligand, L, in determining the computed activation energy for methanolysis in $[Pd(P\text{–}P)\{C(O)Me\}(L)]^+$ species indicates that an external attack mechanism can also be consistent with the experimental trends observed in the $[Pd(DIBPP)\{C(O)Me\}(L)]^+$ system.[5] There, methanolysis was observed for L = CO and MeOH, but not for L = MeCN. Our computed barriers for the DHPP analogue indicate a much lower barrier for L = CO (**3**) although the barriers when L = MeOH (**1**) or MeCN (**4**) are very similar. However, the transition state geometries for **1** and **4** vary significantly, as the π-acceptor MeCN ligand induces movement of the acyl moiety into an axial position (*cf.* Fig. 2 for L = C_2H_4) and this arrangement may be more susceptible to steric effects than the 'in-plane' arrangement seen in $\mathbf{TS_{1B}}$ where L = MeOH. As such, each diphosphine–L coligand combination may introduce specific properties that may influence the energetics of the methanolysis process. Indeed, it has been suggested that steric effects may be crucial in making this facile for DTBMPB complexes.[2b] In future studies we intend to consider the full steric bulk of the diphosphine ligands to see how this, in combination with the ligand electronic effects identified here, will affect the methanolysis process.

Notes and references

‡ The distorted geometry of $[Pd(DHPP)H]^+$ is retained in the absence of methyl propanoate and so seems to be a result of the constraints imposed by the chelate ligand; with $[Pd(PH_3)_2H]^+$ a more usual T_H shape is located.
§ Ethene insertion in **2** proceeds *via* a transition state at +14 kcal mol^{-1}. Insertion becomes favoured, however, upon including entropic effects.
¶ Methanolysis products formed with **2–6** generally feature a short contact between the ester OMe group and the newly-formed Pd–H bond.

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10 Calculations employed Gaussian 03 and used the BP86 functional. Pd and P were described with Stuttgart RECPs and basis sets with added polarization on P atoms. 6-31 G** basis sets were used for C, O, and H atoms. Zero-point energy corrections are included. See Supplementary Information for full details.