C–O Bond Activation | Hot Paper

Unexpected Vulnerability of DPEphos to C–O Activation in the Presence of Nucleophilic Metal Hydrides

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We dedicate this paper to the memory of friend, colleague and collaborator Professor Jonathan M. J. Williams

Abstract: C–O bond activation of DPEphos occurs upon mild heating in the presence of [Ru(NHC)$_2$(PPh$_3$)$_2$H$_2$] (NHC = N-heterocyclic carbene) to form phosphinophenol-ate products. When NHC = IE$_2$Me$_2$, C–O activation is accompanied by C–N activation of an NHC ligand to yield a coordinated N-phosphino-functionalised carbene. DFT calculations define a nucleophilic mechanism in which a hydride ligand attacks the aryl carbon of the DPEphos C–O bond. This is promoted by the strongly donating NHC ligands which render a trans dihydride intermediate featuring highly nucleophilic hydride ligands accessible. C–O bond activation also occurs upon heating cis-[Ru(DPE-phos)$_2$H$_2$]. DFT calculations suggest this reaction is promoted by the steric encumbrance associated with two bulky DPEphos ligands. Our observations that facile degradation of the DPEphos ligand via C–O bond activation is possible under relatively mild reaction conditions has potential ramifications for the use of this ligand in high-temperature catalysis.

Since their introduction ca. 20 years ago,[1] wide-angle phosphines such as xanthophs and DPEphos (Scheme 1) have become indispensable ligands for a range of catalytic reactions.[2] Their usage stems from two advantageous properties; firstly, the availability of highly flexible bite angles that allow cis- and trans-, as well as hemilabile P-O-P coordination modes, to be adopted[3] and, secondly, resistance to the types of P–C degradation reactions reported in tertiary phosphine metal complexes.[4] This latter property has promoted the use of xanthophs and DPEphos in reactions that require high temperatures.[5a,b,c]

Any suggestion that such phosphines might be susceptible to degradative reactions, particularly under relatively mild conditions, could therefore have important ramifications for their applications in catalysis. While xanthophs has been reported to be susceptible to P–C bond activation at room temperature,[6] cleavage of DPEphos appears to be restricted to a single example of high temperature C–O bond activation reported by Weller and Willis.[7] In the course of studies on [Rh(H$_2$-ortho-xylene)(DPEphos)]$^+$ catalysed carbothiation of alkynes, they reported that heating the Rh complex together with ortho-MeSC$_6$H$_4$(O)Me at 120 °C in the absence of any alkyne led to C–O cleavage of DPEphos to afford a catalytically inactive Rh complex with chelating phosphine arylxide and bidentate phosphine arylthioether ligands. Herein, we demonstrate that C–O activation of DPEphos can take place even at room temperature in the presence of ruthenium dihydride complexes. DFT calculations reveal that such processes involve attack of highly nucleophilic hydride ligands on the aryl carbon on the C–O bond.

In the course of studies to investigate the substitution chemistry of the all trans-dihydride complex [Ru-(IMe$_2$)$_2$(PPh$_3$)$_2$H$_2$] (1, Scheme 2),[8] 1 was treated with 1.1–1.5 equiv DPEphos in benzene. No immediate reaction was observed at room temperature, but upon heating to 90 °C for ca. 12 h, a single ruthenium-containing product 2 (Scheme 2) was

Scheme 1. Structures of xanthophs and DPEphos.

Scheme 2. C–O activation of DPEphos by 1 to give 2.
formed. An X-ray crystal structure (Figure 1) revealed the presence of a phosphinophenolate ligand generated upon C–O activation of DPEphos. The P,O-termini of the ligand were trans to PPh₃ and Ru–H respectively. The coordination sphere was completed by two mutually trans IMe ligands, each of which displayed an N-Me group with a short C–H–O contact to the phosphinophenolate ligand (Supporting Information). The trans H-Ru-O arrangement led to both a long Ru–O distance (2.2720(16) Å) and a low frequency (δ = −18.40 ppm) hydride resonance. The same trans H-Ru-OAr arrangement as in 1 (Ru–O = 2.265(2) Å). The phosphino moiety appended to N3 exhibited a considerable cone-tilt, with Ru-P-C₈₈ angles ranging from 102° to 132°. In support of the C–N cleavage process, the ¹H NMR spectrum showed just three NCH₃CH₃ methyl and six NCH₃CH₂ methylene resonances. The Ru–H resonance (δ = −17.7 ppm) was coupled to the two inequivalent phosphorus nuclei (δ = 59 and 55 ppm) with cis-²J(H,P) coupling constants of 20 and 15 Hz.

C–N activation of a metal-bound NHC ligand has been described previously, including studies on Ru-NHC complexes related to those employed here. However, this process has only rarely been observed alongside the activation of another ligand, and, certainly not as a route to the formation of a phosphinocarbene. The C–O activation of DPEphos was not restricted to NHC-containing ruthenium hydride precursors. The reaction of [Ru(PPh₃)₂H₂] with DPEphos gave the isolable cis-dihydride complex [Ru(DPEphos)₂H₂] (5, Supporting Information), which upon heating to 80 °C overnight underwent C–O activation of one of the DPEphos ligands to afford [Ru(DPEphos)-Ph₃PC₆H₄O]H (6, Scheme 4). This was characterized by the presence of a quartet Ru–H resonance at δ = −14 ppm with a ²J(H,P) splitting (22 Hz) indicative of hydride cis to all three phosphorus nuclei and a ³¹P(¹H) NMR spectrum which showed a triplet at δ = 77 ppm (³¹J(P,H) = 30 Hz), together with a broad, featureless signal at δ = 50 ppm. We attribute the latter to the intact DPEphos ligand switching rapidly between κ¹⁻P,P and κ¹⁻P,O,P coordination. At −15 °C, this signal resolved into two doublets, the two ends of the DPEphos ligand becoming inequivalent as a result of the oxygen now staying bound to Ru. Although an X-ray structure of 6 proved elusive, crystals of the chloride derivative 7 were isolated from CH₂Cl₂/pentane solutions of 6, affording a structure (Figure 2) which confirmed the coordination modes at ruthenium.

DFT calculations have been used to explore the mechanism of the C–O bond cleavage reactions in 1 and 5 and the factors promoting them. For 1, no intermediates are observed experimentally and so all free energies are quoted relative to this species plus free DPEphos. PPh₃ substitution in 1 by DPEphos gives [Ru(IMe₃)₃(DPEphos)H₂]₇₈, for which the all-cis isomer, ₇₈ccc (+3.6 kcal mol⁻¹), and the cis,cis,trans-isomer, ₇₈ctt (+4.2 kcal mol⁻¹) are most stable. The accessibility of the trans dihydride isomer ₇₈ctt suggested a hydride nucleophilic attack mechanism may be involved, similar to that characterised for the hydrodefluorination of...
(hetero)aromatics at trans-[Ru(NHC)2H2] complexes.\textsuperscript{[23, 24]} Figure 3 shows the computed reaction profiles for this process in B8 and B8c. For B8 the trans hydride arrangement gives a long Ru–H\textsuperscript{+} bond (1.70 Å) and NBO calculations indicate significant hydridic character (−0.21). Nucleophilic attack proceeds via TS(8-2)\textsubscript{cc} at +25.0 kcal mol\textsuperscript{−1}, with a short H\textsuperscript{+}–C\textsuperscript{1} distance of 1.56 Å and Ru–H\textsuperscript{+} stretching to 1.84 Å. The C\textsuperscript{1}–O bond also lengthens to 1.48 Å and elongated C\textsuperscript{1}–C\textsuperscript{2} and C\textsuperscript{1}–C\textsuperscript{6} distances in the aryl ring suggest a Meisenheimer-type structure consistent with nucleophilic aromatic substitution. Hydride attack is also accompanied by a conformational change in the 8-membered Ru\textsuperscript{+}–P–C–C–O–C–C–P ring, from a distorted twist-boat conformation in B8\textsubscript{cc} to a boat conformation in the transition state,\textsuperscript{[25]} similar to the DPEphos fac-k\textsuperscript{+}-PO,P binding mode.\textsuperscript{[26]} IRC calculations confirm that TS(8-2)\textsubscript{cc} links directly to 2\textsubscript{cc} in which H\textsuperscript{+} is trans to the phosphinophenolate oxygen. The lowest energy conformation of 2\textsubscript{cc} is at −31.5 kcal mol\textsuperscript{−1}.\textsuperscript{[27]}

The equivalent reaction of B8\textsubscript{cc} involves an initial conformational change of the Ru–P–C–C–O–C–C–P ring to form B8\textsubscript{oc} at +14.5 kcal mol\textsuperscript{−1}. C–O bond cleavage then proceeds via TS(8-2)\textsubscript{oc} at +34.1 kcal mol\textsuperscript{−1} with similar geometric changes to those described above for TS(8-2)\textsubscript{cc}. The shorter Ru–H\textsuperscript{+} distance in B8\textsubscript{oc} and B8\textsubscript{cc} (1.65 Å) and lower NBO charges (ca. −0.12) indicate that H\textsuperscript{+} is now less nucleophilic than in B8\textsubscript{cc} and this reflects the change in the trans ligand, from a hydride in B8\textsubscript{cc} to IMe in B8\textsubscript{oc}. This also correlates with C–O bond cleavage being less kinetically accessible in B8\textsubscript{cc}. TS(8-2)\textsubscript{oc} leads to 2\textsubscript{cc} at −25.2 kcal mol\textsuperscript{−1}, substantially less stable than 2\textsubscript{cc} as this structure lacks the favourable trans-H-Ru-O arrangement.\textsuperscript{[26]}

C–O bond cleavage was also modelled for [Ru(DPEphos)H\textsubscript{2}] and the most accessible pathway is shown in Figure 4. The all-\textsuperscript{cis} isomer, 5\textsubscript{cc} reacts via 5\textsubscript{oc} and TS(5-9)\textsubscript{cc} at +29.9 kcal mol\textsuperscript{−1} to give a phosphinophenolate product, 9\textsubscript{cc} at −23.0 kcal mol\textsuperscript{−1}. The short Ru–H\textsuperscript{+} distance in 5\textsubscript{oc} (1.60 Å) and low NBO charge on H\textsuperscript{+} (−0.02) indicate reduced hydride nucleophilicity compared to B8\textsubscript{cc} although the barrier in the bis-DPEphos system is actually lower (see below). In stark contrast to B8\textsubscript{cc}, the trans dihydride isomer of [Ru(DPEphos)H\textsubscript{2}] 5\textsubscript{cc} has a large barrier of +48.5 kcal mol\textsuperscript{−1}. This difference is due in part to the higher energy of 5\textsubscript{cc} (+13.8 kcal mol\textsuperscript{−1}) and the reduced charge on H\textsuperscript{+} (ca. −0.08 cf. −0.21 in B8\textsubscript{cc}). The latter result highlights how the NHC ligands also serve to enhance hydride nucleophilicity. Differential steric effects in the transition states may also be a factor, as probed by calculations on S\textsubscript{cc} and S\textsubscript{cc}, in which the PPh\textsubscript{3} groups were replaced by PH\textsubscript{3}. This model system gave a similar relative energy for S\textsubscript{cc} (+12.6 kcal mol\textsuperscript{−1}), but a reduced barrier for the subsequent nucleophilic attack (i.e. from S\textsubscript{cc} to TS(5-9)\textsubscript{cc}: 30.2 kcal mol\textsuperscript{−1} cf. 34.7 kcal mol\textsuperscript{−1} in the full system). In contrast, the computed barrier for S\textsubscript{cc} with the small model is 38.6 kcal mol\textsuperscript{−1}, 8.7 kcal mol\textsuperscript{−1} higher than the full model.
On a more constructive note, the hydride nucleophilic attack, in this case by a thiophos ligand.[7] On a more constructive note, the hydride nucleophilic attack mechanism proposed here has already been shown to operate in catalytic C–F functionalization, and so may also be an effective means of promoting C–O bond activation of the type required for the valorization of lignin and of its highly oxygenated monomers.[9]

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Conflict of interest

The authors declare no conflict of interest.

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Figure 4. Computed free energy profile (kcal mol\(^{-1}\), BP86(benzene, D3BJ)) for hydride attack in \(S_{\text{ccc}}\) with selected distances in Å and computed NBO charges at Ru and H\(^{\text{2}}\) in italics for the dihydride precursors. For clarity, phenyl substituents are truncated at the ipso carbons and DPEphos hydrogens are omitted.
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