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Review

Developments in the chemistry of tris(hydroxymethyl)phosphine

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Contents

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Dedicated to Fausto Calderazzo on the occasion of his 80th birthday. The older one of us (BRJ) first met Fausto in 1968 at one of the legendary Leeds/Sheffield conferences, and then spent a part sabbatical in Pisa in 1979; FL completed his Laurea degree in 2001 at the Università di Pisa under the auspices of Professor Calderazzo.

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ABSTRACT

Tris(hydroxymethyl)phosphine, $P(CH_2OH)_3$, a water-soluble compound, has been known for about 50 years but development of its coordination chemistry has been slow and relatively recent. During some collaborative studies with a pulp and paper research institute on testing water-soluble catalysts for hydrogenation of lignin in pulp and the unsaturated functionalities in lignin model compounds, with the aim of bleaching pulps, we discovered new, *in situ*, Ru-$P(CH_2OH)_3$ hydrogenation catalysts. Interest in the coordination chemistry of this phosphine thus ensued, and this review covers this topic as well as the coordination chemistry of a diphosphine analogue, bis[bis(hydroxymethyl)phosphino]ethane, $(HOCH_2)_2P(CH_2)_2P(CH_2OH)_2$. The applications of the water-soluble metal complexes of these two phosphines in the areas of catalysis and medicinal drugs are also described. These phosphines, in the *absence* of metals, were found serendipitously to be effective bleaching agents for pulps (and also brightness stabilizing agents), and some relevant organo-phosphorus chemistry from our group is also briefly presented, particularly because of its possible significance in hydroformylation and hydrogenation processes catalyzed by metal–phosphine complexes.

1. Introduction

Tris(hydroxymethyl)phosphine, $P(CH_2OH)_3$, which will be abbreviated as THP, is a water-soluble compound that has been known for about 50 years [1], but the first report (from Chatt's group) on its coordination *via* the P-atom to a metal (Rh, Pd, Pt) did not appear until 1973 [2], and then it was not until the late 80s that Pringle's group developed further the coordination chemistry of this phosphine (to the Group 10 metals) [3]. Interest in this phosphine in our laboratory arose in the mid-90s through some collaborative work with a pulp and paper organization, with the aim of designing some water-soluble metal complexes for catalytic hydrogenation of lignin components in pulps. This led us to study the chemistry of water-soluble coordination compounds of THP, their potential for catalytic hydrogenation, and eventually reactions of THP itself with unsaturated organics

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and carbonyl-containing organics. This review covers these topics with emphasis on the new findings from our laboratories, as well as a summary of the coordination chemistry of the diphosphine analogue bis[bis(hydroxymethyl)phosphino]ethane, $(HOCH_2)_2P(CH_2)_2P(CH_2OH)_2$, which will be abbreviated as DHMPE [4]. Section 2 briefly introduces the THP and DHMPE phosphines; Section 3 describes our development of some Ru–THP hydrogenation catalysts for lignin and lignin model compounds (LMCs); Section 4 describes our efforts to develop catalytic hydrogenation processes using cheaper metal–THP species and the discovery of the bleaching activity of the free (non-coordinated) hydroxyphosphines; Section 5, the major section, describes our advances in Rh–THP chemistry; Section 6 summarizes related literature work on metal complexes containing THP or DHMPE not mentioned in Sections 4 and 5; Section 7 describes the bleaching activity of THP and DHMPE, and some relevant organo-phosphorus chemistry; Section 8 describes some chemistry of secondary phosphines, possibly relevant to THP chemistry; and finally some conclusions are given in Section 9. Also mentioned in Sections 3–6 are other associated, more general applications of water-soluble metal complexes containing these two phosphines in the areas of catalysis and development of medicinal drugs.

2. $P(CH_2OH)_3$ (THP) and $(HOCH_2)_2P(CH_2)_2P(CH_2OH)_2$ (DHMPE)

The subject of this review focuses mainly on the coordination chemistry of the title phosphine THP, although the abbreviation THMP has been used by other groups [e.g. [3,5,6]]. This monophosphine and the corresponding tetrakis(hydroxymethyl) phosphonium salts are prepared from phosphine and formaldehyde by the essential hydroformylation chemistry outlined in Eq. (1) [1,7,8]; catalysts such as $[PtCl_4]^{2-}$ [8], and $NiCl_2$ in the presence of ethylenediamine (en) [9], have been used to promote the PH_3 reaction. THP is most readily available *via* addition of base to the air-stable phosphonium salts (chloride or sulfate); these water-soluble salts are inexpensive, being available commercially in >3000 tonnes/year for use as flame-retardants, and as biocides for oil and waste-water industries [10].

$$PH_3 + 3CH_2O \rightarrow P(CH_2OH)_3 \underset{\text{base}}{\overset{CH_2O,H^+}{\rightleftarrows}} [P(CH_2OH)_4]^+ \tag{1}$$

Despite the long-known, commercial recognition of THP, and the interest in applications of water-soluble phosphines, developments in its coordination chemistry are relatively recent, perhaps because of complicated 'side effects' of the compound (e.g. Sections 3, 5, and 6). Although THP is usually described as 'moderately air-stable' in the solid state and in aqueous solution [e.g. [8,11]], our studies reveal more specifically that there is no oxidation at 25 °C over 24 h at pH 7, but at pH 10 the phosphine is oxidized ($t_{1/2} \sim 30$ min) by OH^- to the oxide (THPO) with H_2 being the coproduct [12,13]; of note, THPO has been known for about 80 years [12]! At lower pH, THP slowly decomposes with loss of CH_2O to give the secondary phosphine; see Eq. (2) [13,14], which alludes to the reverse of the stepwise formation of THP from PH_3, *via* $H_2P(CH_2OH)$ and $HP(CH_2OH)_2$.

$$P(CH_2OH)_3 \rightarrow HP(CH_2OH)_2 + CH_2O \tag{2}$$

The other hydroxyphosphine that attracted our attention during our pulp-bleaching studies (see Section 7) is DHMPE [4,15,16]. This diphosphine is synthesized by reaction of CH_2O with $H_2P(CH_2)_2PH_2$, *via* chemistry analogous to that shown in Eq. (1) for PH_3; $[PtCl_4]^{2-}$ has again been used to catalyze the reaction [15], but we [17] and others [16] have found that a metal-based catalyst is not necessary for effective conversion.

3. Ruthenium–THP systems

Our interest in THP chemistry was generated through a collaborative research project, initiated about 15 years ago, with the Pulp and Paper Research Institute of Canada (Paprican, now called FP Innovations-Paprican) on the bleaching of pulps, work that has been reviewed [18]. The goal was to catalytically hydrogenate aromatic residues or conjugated C=C–C=O moieties within lignin with the aim of decreasing conjugation and hence the yellow colouring in pulps; all that was needed was a water-soluble, recyclable catalyst, a non-trivial objective! Our studies revealed that *in situ* Rh- and Ru-based species in 1-phase aqueous/alcohol and 2-phase aqueous/organic systems under H_2 could reduce under mild conditions organics with a reactivity order: C=C > aromatic C=C ≈ C=O bonds. However, the optimum catalysts were colloidal, zero-valent metal species stabilized by long-chain tetraalkylammonium salts or polyvinylpyrrolidone (for Rh^0), or long-chain trialkylamines (for Ru^0) [19]; such colloidal catalysts are impractical for pulp-bleaching in that they eventually precipitate as inactive black metal, and any such partially hydrogenated pulps always had a greyish tinge! Arene–Ru species, including water-soluble polyhydrido-Ru_4 cluster complexes, initially reported to be effective homogeneous hydrogenation catalysts for aromatics [20], were tested but found to be colloidal [19], and later, more detailed studies by other groups [21] have confirmed this finding. With ancillary (sulfonatophenyl)phosphine ligands, arene–Ru species did maintain homogeneity in aqueous isopropanol solution, but the systems showed marginal activity for hydrogenation of lignin moieties [19]. This led us to investigate *in situ* water-soluble, transition metal systems incorporating low-cost THP for hydrogenation of pulps and LMCs, and to survey the literature on transition metal–THP complexes (see below and Sections 4–6).

A key finding was that an *in situ* Ru–THP catalyst under H_2 did effect visible bleaching of a so-called thermomechanical pulp [22,23], of which Canada is the world's largest manufacturer; such pulp is formed by the action of mechanical forces on wood. The *in situ* catalyst was prepared by a ligand exchange reaction utilizing THP in water and $[RuCl_2(PPh_3)_3]$ in CH_2Cl_2 (exemplified ideally by Eq. (3), although none of the complexes shown has been identified). The *air-stable*, yellow-brown aqueous phase containing the Ru–THP catalyst was effective in alkaline aqueous or aqueous/EtOH solution, typically at 80 °C and up to 340 psi H_2, for homogeneous hydrogenation of activated olefins, carbonyl groups and, of more interest, hydrogenolysis of some aromatic alcohols (Eq. (4), *Ar* = aromatic, R = H or Me) [23]; all these organic functionalities are present in lignin. The hydrogenolysis step, which requires the presence of a *p*-OH in the aromatic moiety, is thought to be a concerted process rather than a 2-stage process *via* dehydration to the alkene followed by hydrogenation. Although the composition of the solution Ru–THP solution changed with time at room temperature, even for a fixed THP:Ru ratio, the catalytic activity did not vary under the relatively severe conditions used, implying that the various *in situ* catalyst precursors are converted to the same active hydride species [23].

$$RuCl_2(PPh_3)_3 + n\text{THP} \rightarrow nPPh_3 + RuCl_2(\text{THP})_n(PPh_3)_{3-n} \qquad (n = 1.0\text{–}6.0) \tag{3}$$

$$Ar\text{–}C(R)\text{=}O \rightarrow Ar\text{–}CH(R)OH \rightarrow Ar\text{–}CH_2R \tag{4}$$

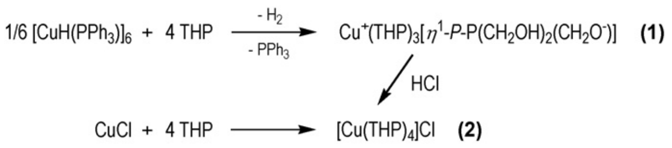
Efforts to determine the nature of the catalyst have thus far been unsuccessful, and this may be related to the fact that THP can be a non-innocent ligand when coordinated to Pt-metals, including Ru (see below).

Hydrogenolysis of an aldehyde or ketone C=O group to CH_2 (Eq. (4)) is an important transformation and, although there are procedures for doing this [24], we are unaware of any earlier reported homogeneous systems that catalyze such hydrogenolysis; this is a key process when applied to carbohydrate and fatty acid substrates in terms of renewable resources, and recently other water-soluble Ru catalysts, including (sulfonatophenyl)phosphine species, have been found effective for such substrates in 2-phase aqueous/organic or neat substrate media under conditions similar to those we reported for our THP catalyst systems [25].

During our studies on the above Ru–THP systems, other groups reported on a structurally characterized, water-soluble complex $\{Ru(THP)_2[PH(CH_2OH)_2]_2Cl_2\}$, synthesized *via* the essential chemistry outlined in Eq. (3) [26,27]; note here that two THP groups have eliminated formaldehyde (*cf.* Eq. (2)). This complex effects catalytic hydrogenation of supercritical CO_2 to formate, while $[Cp^*RuCl(THP)_2]$ in the presence of dimethylamine catalyzes hydrogenative amidation of $scCO_2$ to give DMF; both systems operate under $scCO_2/H_2O$ multi-phase conditions at 100 °C, ∼8 atm H_2, and ∼20 atm CO_2 [27]. Other water-soluble Ru complexes with intact THP ligands are known within species containing: (a) ancillary arene ligands, e.g. $[(arene)RuCl(THP)_2]Cl$ [28,29], which catalyze in 2-phase aqueous/organic media isomerization of allylic alcohols to ketones, and in ${}^{i}PrOH/H_2O$ the hydration of terminal alkynes [28]; and (b) ancillary Cp* ligands, e.g. $[Cp^*RuCl(CO)(THP)]$ [30], while an *in situ* cationic species formed from this chloro-complex by treatment with Ag salts catalyzes in a 2-phase aqueous/*n*-heptane system, at ∼100 °C and ∼100 atm H_2, the selective hydrogenation of olefinic moieties of sorbic acid, $CH_3CH{=}CH{-}CH{=}CH{-}CO_2H$ [30]. The cluster complex $[H_4Ru_4(CO)_8(THP)_4]$ has been synthesized from a phosphine ester analogue during studies on catalyzed hydrogenolysis of carboxylic acids in the absence of solvent, again under relatively harsh conditions [31]. A structurally characterized dimer, $\{Ru(\mu\text{-}PCH_2OH)[\mu\text{-}P,O{-}P(CH_2O)(CH_2OH)_2]Cl_2\}_2$, has been isolated from a $RuCl_3$/THP reaction, and contains bridged-phosphido groups and bridged-monoalkoxides, thus revealing extensive THP decomposition during the synthesis of the complex [32]. There is no report of a Ru-DHMPE complex, but the water-soluble Ru(III) complex *trans*-$[RuCl_2(P{-}P)_2]Cl$, where P–P is the *P*,*P*-chelated $[HO(CH_2)_4]_2P(CH_2)_2P[(CH_2)_4OH]_2$, has been synthesized from $RuCl_3$ [33]; during the synthesis, there is no decomposition of the diphosphine ligand, a property that likely depends on the absence of a hydroxyl group α to the P-atom [34].

4. Tests using water-soluble cobalt, nickel, and copper systems

Our finding of the pulp-bleaching by the Ru–THP catalysts ([22,23], see Section 3) encouraged us to test for the catalytic hydrogenation activity in 1- or 2-phase systems of water-soluble species of the cheaper metals Co, Ni and Cu, either with or without ancillary THP ligands [35]. However, only marginal activity for hydrogenation of a range of LMCs (aromatic ketones and aldehydes typically containing OH or OMe substituents in the aromatic ring, styrenes, propenylbenzenes, α,β-unsaturated organics, etc. [23]) was usually observed under conditions that varied from ambient (1 atm H_2 at room temperature) to 35 atm H_2 at 80 °C. Olefinic but not carbonyl moieties were sometimes readily reduced, and thus pulp systems were not investigated. Transition metal species tested included those of known hydrogenation activity such as $[Co(CN)_5]^{3-}$ and $[Co(en)(CN)_3]^-$ [36], $NiCl_2$, which was tested also for hydrogen-transfer catalysis from ${}^{i}PrOH$ [37], and *in situ* $NiCl_2$/en/THP and $[Cu(MeCN)_4]^+$/en/THP systems; the addition of en to promote hydrogenation activity is not uncommon (see Section 5). The reported catalytic activity of $[CuH(PPh_3)]_6$ for hydrogenation of olefinic and carbonyl groups, depending on conditions [38], prompted us to try and synthesize a water-soluble THP analogue, and this led to the chemistry of Scheme 1 [35]. A phosphine ligand exchange reaction with the hexamer gives the zwitterionic tetrahedral complex **1** that contains a non-bonded CH_2O^- alkoxide moeity, which is readily protonated to give **2**, a regular tetrahedral Cu(I) complex; both water-soluble complexes were characterized crystallographically [35], while another group simultaneously synthesized **1** using $[Cu(MeCN)_4]ClO_4$ as precursor [11]. Although neither **1** nor **2** was effective for hydrogenation activity, the zwitterion was tested with a mechanical pulp at 80 °C and 340 psi H_2, and visible bleaching became evident [39]. Subsequently, control experiments revealed that neither H_2 nor the Cu complex was needed; i.e. the phosphine itself was the bleaching agent [39]! The use of THP in bleaching led us into new organo-phosphorus chemistry, a topic that is outside the scope of coordination chemistry, but will be summarized in Section 7 of this review, because of the potential relevance of organo-phosphorus chemistry to hydrogenation and hydroformylation processes catalyzed by transition metal–phosphine complexes.



Scheme 1. Outline of some Cu(I)–THP chemistry.

The $[Cu(THP)_4]PF_6$ complex (*cf.* **2** in Scheme 1) has very recently been shown to possess anti-tumour properties, and the ${}^{64}Cu$-labelled analogue has been used for positron emission tomography (PET) imaging [40,41]. Copper(I) species of the type $[Cu(THP)_2(N{-}N)]$, where N–N is a scorpionato-type ligand, have been similarly tested [40], while $[Cu(DHMPE)_2]PF_6$ also tests positive against several human tumour cell lines [40].

5. Rhodium–THP chemistry

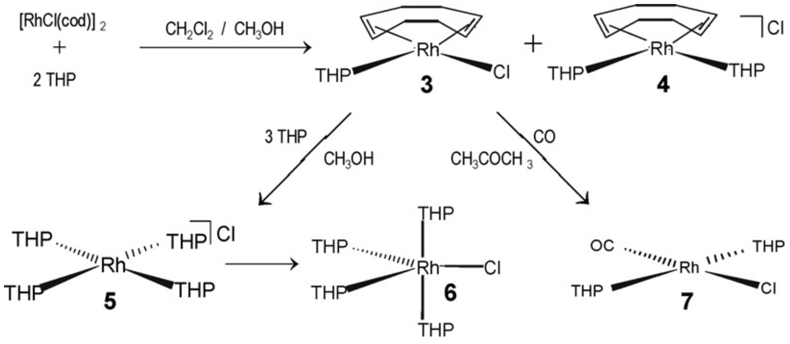
Our findings on the hydrogenation activity of the Ru–THP species (see Section 3) encouraged us to investigate such activity of THP complexes of Rh (perhaps the metal 'par excellence' for catalytic hydrogenation and hydroformylation), particularly for potential application in the areas of aqueous or 2-phase aqueous/organic catalysis—*cf.* the Rührchemie/Rhône-Poulenc propylene hydroformylation process, which employs (sulfonatophenyl)phosphine ligands to maintain aqueous solubility of the Rh catalyst [42,43]; an attractive factor for the use of THP is its low cost. Another topic of interest is the use of THP in the design of water-soluble drugs (see end of Section 4, and Section 6) and, in particular, ${}^{105}Rh$ has appropriate β-emitter properties for use as a cancer radiotherapeutic agent [44].

Some interesting chemistry of Rh–THP systems was elucidated during our attempts to devise water-soluble hydrogenation catalysts. As a follow-up to our Rh-colloid work (Section 3), we first tested hydrogenation of LMCs (e.g. crotonic acid, acetovanillone, and substituted styrenes) using *in situ* $RhCl_3{\cdot}3H_2O$ or $[RhCl(diene)]_2$ (diene = 1,5-cyclooctadiene (cod) or 1,5-hexadiene) with added THP in aqueous or aqueous/ethanol solution, and varied the THP:Rh ratio, pH, and $[Cl^-]$; active systems were evident at 80 °C and 500 psi, but Rh metal precipitated during the hydrogenation [35], implying that THP (certainly more basic than PPh_3) was not an effective phosphine for stabilizing Rh-hydride species. These findings generally agree with early data from Chatt et al. who tested *in situ* Rh(I)–THP systems in EtOH and who also isolated *fac*-$[RhCl_3(THP)_3]$ [2], a complex that has been recently "rediscovered" and characterized crystallographically [44]. We then found that addition of en to *in situ* Rh(III)– or Rh(I)–THP systems (Rh:en:THP = 1:1:2) in aqueous solutions gave active species for olefin hydrogenation at ambient conditions, and prevented precipitation of metal [35]. During the work-up procedure after a catalytic hydrogenation of 3,4-dimethoxystyrene, a serendipitously formed crystal of *trans*-$[RhCl_2(en)(THP)_2]Cl$ was isolated and characterized by X-ray analysis [35]. The complex, more readily isolated from a methanol solution containing a 1:1:2 mixture of $RhCl_3{\cdot}3H_2O$/THP/en, when dissolved in aqueous solution, regenerated under H_2 the catalytically active system that was presumed to require a Rh(I) precursor catalyst [35,45], but we were unable to elucidate details of the Rh(III)/en/H_2 chemistry involved. Of interest was whether the en was playing a role in a so-called 'bifunctional mechanism' where a proton for the hydrogenation process derives from the $-NH_2$ moiety; this process is well documented within Ru(II) systems [46], and has been invoked for some Rh–diamine systems but with no direct evidence [47]. As an alternative approach to this problem, we decided to try to synthesize Rh(I)–THP complexes for use as precursor catalysts. There were literature reports that reaction of excess THP with $[RhCl(cod)]_2$ in aqueous CH_2Cl_2 or THF generated mixtures containing *cis*-$[Rh^{III}(H)_2(THP)_4]^+$, the source of the hydrido ligands being considered as either THP or water [5,48], but at this stage of our studies (late 2006) the only reported Rh^I–THP species were the carbonyls, square-planar *trans*-$[RhCl(CO)(THP)_2]$ [2,48] and the trigonal bipyramidal $[Rh(CO)_2(THP)_3]Cl$ with *trans*-carbonyls [48], and neither had been characterized crystallographically. Further, reactions of $[RhCl(cod)]_2$ with THP at defined THP:Rh ratios had been stated to give "a complicated mixture and isolation of products was unsuccessful" [5]. This same reference notes that *cis*-$[Rh^{III}(H)_2(THP)_4]Cl$ in biphasic aqueous/benzene solution does catalyze the hydroformylation of pent-1-ene to aldehyde products at 100 °C under 20 atm of both CO and H_2 [5].

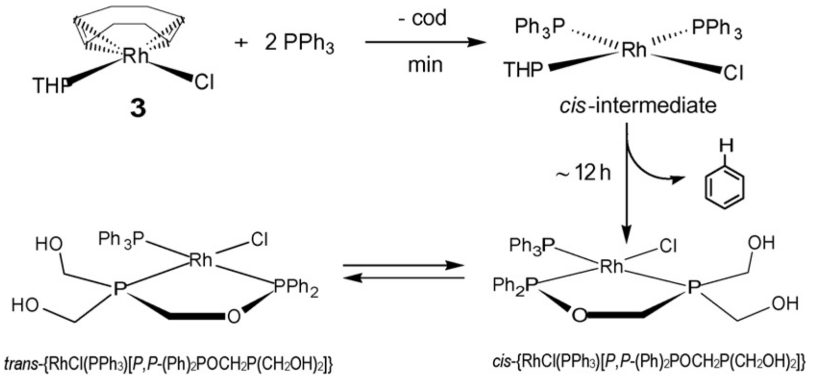
Our accomplished Rh(I)–THP chemistry, carried out under an inert atmosphere, is shown in Scheme 2, with isolation of the water-soluble complexes **3**, **4**, **6**, and **7**, and determination of crystal structures for **3** and the known carbonyl species **7**; good evidence for intermediate **5** leading to **6** was also found [45]. Although the chemistry appears simple, the isolation of the complexes was challenging, and involved a judicious choice of solvents and reagent stoichiometries. For example, **4** is best prepared *via* the 1:1 THP/Rh shown, rather than the more obvious 2:1 stoichiometry, and similarly **7**, a bis-THP complex, is optimally isolated from reaction of CO with **3**, a mono-THP species! Complexes [RhCl(cod)(THP)] (**3**) and $[Rh(cod)(THP)_2]Cl$ (**4**) are the first useful precursors into Rh(I)–THP chemistry, by direct replacement of the diene with other ancillary ligands, or under H_2 to remove the cod as cyclooctene/cyclooctane. In attempts to probe the Rh(I)/THP/en hydrogenation catalyst system (see above), addition of one equivalent of en to **3** in acetone or MeOH generated immediately *in situ* [RhCl(en)(THP)] with liberation of free cod but the species decomposes in solution and has not been isolated; further, we have not been able to simulate the catalytic hydrogenations using this *in situ* system [45]. Of note, the CH_2OH moiety of THP can undergo condensation reactions with amines [49], which represents a further non-innocent aspect of THP ligand chemistry (see Sections 3 and 6). Addition of pyridine to **3** yields $[Rh(cod)(THP)(py)_2]Cl$ [50]. Complexes **5** and **6** both readily react with H_2 in MeOH to generate the known dihydride $[Rh^{III}(H)_2(THP)_4]Cl$ [50] noted above, while complex **3** catalyzes slowly the selective hydrogenation of cod to cyclooctene (coe) in acetone at ambient conditions [50].

Some novel chemistry exemplified in Scheme 3 was unearthed during our attempts to synthesize mixed THP/PR_3 complexes of Rh *via* reaction of **3** with PR_3 (R = aryl, alkyl or mixed alkyl/aryl) in MeOH or acetone [51]. The expected, initial, rapidly formed product was $[RhCl(PR_3)_2(THP)]$, but this was followed by slow, THP-promoted P–C bond cleavage of a coordinated PR_3 to generate an equilibrium mixture of the water-insoluble species *trans*- and *cis*-$\{RhCl(PR_3)[P,P\text{-}R_2POCH_2P(CH_2OH)_2]\}$ containing a chelated *P*,*P*-phosphine–phosphinite ligand [51]. The *cis*- and *trans*-designations refer to the orientation of the PR_3 ligand and the R_2POCH_2 derived from the second PR_3 ligand; one R group has been converted to hydrocarbon co-product (RH), the hydrogen coming from a THP-hydroxyl group that becomes the alkoxy group at the residual PR_2 moiety. In CD_3OD, the THP exists as $P(CH_2OD)_3$ and the hydrocarbon product is deuterated (e.g. C_6H_5D for the PPh_3 reaction, Scheme 3). Of note, each isomer contains three different P-atoms, each of which is seen as a doublet of doublets of doublets in the $^{31}P\{^1H\}$ NMR spectrum, and so assignment of the P-signals was a challenging exercise! The generation of the equilibrium mixture was much slower for an alkyl-containing phosphine than for a $P(aryl)_3$ system, which is consistent with more general facile, metal-catalyzed cleavage of P–aryl bonds versus P–alkyl bonds, at least as substantiated under homogeneous hydrogenation and hydroformylation conditions, where such cleavage is critical in determining catalytic activity [52].

Cleavage of a P–C bond concurrent with formation of a P–O bond is rare. A related example to our work is formation of a *cis*/*trans* mixture of $\{M[P,P\text{-}(HOCH_2)_2POCH_2P(CH_2OH)_2]_2\}Cl_2$ (M = Pt, Pd) from reaction of *cis*-$[MCl_2(THP)_2]$ with excess THP, again in MeOH; the findings within this non-mixed phosphine system (in which all the substituents at each P-atom are hydroxymethyl) resulted from studies on metal complex-catalyzed addition of PH_3 to formaldehyde to give THP (see Eq. (1)) [53]. Analogous to our Rh system, a phosphine–phosphinite ligand is formed. The suggested multistep mechanism involved initial formation of a binuclear metal alkoxide derived from deprotonation of a coordinated THP, and a final ring closure by nucleophilic attack of a coordinated PCH_2O^- moiety at a second (mutually *cis*) coordinated P-atom [53]; the proton was incorporated into a phosphonium species, while in our Rh system the proton becomes a component of a hydrocarbon product. A similar proton loss from the THP and ring closure by nucleophilic attack at a *cis*-P moiety is likely the essential mechanism in the Rh system; none of the commonly proposed mechanisms



Scheme 2. Synthetic pathways for some Rh(I)–THP complexes.



Scheme 3. Synthesis of *trans*- and *cis*-$\{RhCl(PR_3)[P,P\text{-}R_2POCH_2P(CH_2OH)_2]\}$, illustrated for the PPh_3 system.

for metal-catalyzed P–C bond cleavage (oxidative insertion of a low-valent metal into a P–C bond, electrophilic substitution, and orthometallation processes [54]) seems appropriate. In contrast to the Pt/Pd systems, the corresponding reaction of [RhCl(cod)(THP)] with THP in MeOH generates $[RhCl(THP)_4]$ (**6** in Scheme 2) and no bond cleavage is seen [45]. A related example is P–C bond cleavage of a OTf–Ru^{II}–$P(OH)Ph_2$ moiety induced by external MeOH to form a species containing the Ph–Ru^{II}–P(OH)(OMe)Ph moiety with HOTf as co-product: the MeOH proton has removed coordinated triflate which is replaced by a Ph of the phosphine and methoxide replaces the phosphine phenyl [55]. There are other less germane examples of P–C bond cleavage with co-formation of a P–O bond at Ir^{III} and Pd^{II} centres, where MeOH is not involved [56].

We subsequently reacted **3** with $Ph_2P(CH_2)_2PPh_2$ (diphos) to see whether the $-PPh_2$ moiety of a chelated diphosphine (P–P) would undergo a similar cleavage process with the THP-hydroxyl proton; however, on coordination of the diphos, the water-insoluble [RhCl(P–P)(THP)] was formed, in which the diphos retained its integrity (*cf.* the *cis*-intermediate in Scheme 3) and no subsequent cleavage was observed [50]. We then tested, for the same reason, reaction of a P–N ligand with **3** using *o*-diphenylphosphino-*N*,*N*-dimethylaniline (Fig. 1). This generated [RhCl(P–N)(THP)] (**8**) that was structurally characterized, but again no subsequent THP-promoted cleavage was seen [57]; quite remarkably, crystals of **8** were best obtained by subjecting an acetone solution of the complex to an atmosphere of H_2! The observed, immediate precipitation of crystals was a completely reproducible phenomenon, and was evident *only* when using H_2. The absence of any ^1H NMR-hydride resonance in a CD_3OD solution of the crystals and in an acetone-d_6 solution from which they were obtained showed (disappointingly!) that no Rh-hydride derivatives were formed; indeed the ^1H- and $^{31}P\{^1H\}$-NMR spectra measured in CD_3OD under H_2 were identical to those seen for a CD_3OD solution of **8** under Ar. We speculate that a seeding process (presumably involving the formation of an undetectable amount of a hydride derivative) is the likely cause of the crystallization. Aerial oxidation of an acetone solution of complex **8** yielded [RhCl(*O*P–N)(THP*O*)] (**9**) containing now two O-bonded phosphine monooxide ligands. In contrast, the triphenylphosphine analogue of **8**, $[RhCl(P–N)(PPh_3)]$, readily undergoes oxidative addition of O_2 to form a stable Rh(III)–peroxide complex, although this reaction was performed in toluene solution [58]. The oxidized complex **9** showed no reactivity toward H_2 under mild conditions, and no serendipitous crystallization from its solutions was observed. An acetone solution of **8** reacted with 1 atm CO to give a mixture of products, which included the known species [RhCl(CO)(P–N)] [59]. The reactions with H_2 and with CO were carried out to investigate potential catalytic hydrogenation/hydroformylation activity of **8** and **9**, but the findings [57], coupled with the insolubility of **8** and **9** in aqueous solution, are not promising for any activity promoted by the presence of the THP or THPO ligand. There is, of course, vast literature on the use of complexes containing either P–N or P–O type ligands, or oxidized phosphine ligands in catalysis, especially carbonylation and hydroformylation systems (see Refs. within [57]).

While the reaction of [RhCl(cod)(THP)] (**3**) with $PRPh_2$ [R = Me, cyclohexyl (Cy)] in MeOH or acetone solution under Ar followed the chemistry of Scheme 3, the corresponding reaction (*at phosphine:Rh = 2.1*) in a 1:1 MeOH/acetone mixture under H_2 precipitated crystals of the tris(phosphine) complex *cis-mer*-$[Rh(H)_2Cl(PRPh_2)_3]$ (**10**) in ~80% yields based on the phosphine [60]. Of note, the more obvious route to the dihydrides by reacting (under H_2) $[RhCl(cod)]_2$ with the phosphines ($PRPh_2$:Rh = 3), or by reaction of **3** (under H_2) with 3 mol equivalents of phosphine, does not precipitate a dihydride and affords a more complicated mixture of products. The THP ligand clearly plays a role and appears to promote oxidative addition of H_2 to a $[RhCl(PRPh_2)_2(THP)]$ intermediate (*cf.* Scheme 3) to give *cis*-$[Rh(H)_2Cl(PRPh_2)_2(THP)]$, which was detected by NMR spectroscopy; displacement of the THP of this species by $PRPh_2$ would generate **10**, the product, as shown in Eq. (5) [60], which in essence implies a synthetic reaction catalyzed by THP. However, free THP was not detected as co-product, and the observation of a 2-phase solvent system where the dihydride crystals formed suggests that other factors are involved. An important, unanswered question in the syntheses of the dihydrides is the fate of the THP; that it is a reducing reagent (Section 7), can lose CH_2O to give $HP(CH_2OH)_2$ (Eq. (2)), and can readily form phosphonium salts [53], makes prediction difficult.

$$3 + \underset{(R=Me,Cy)}{2PRPh_2} \xrightarrow{-cod} RhCl(PRPh_2)_2(THP) \xrightarrow{H_2} \xrightarrow[-THP]{PRPh_2} \underset{\mathbf{10}}{Rh(H)_2Cl(PRPh_2)_3} \qquad (5)$$

Formation of trace amounts of *trans*-$[RhCl(CO)(PR_3)_2]$ *via* decarbonylation of the CH_2O has been seen in systems outlined in Scheme 3 [51], as well as in the systems that generate the dihydrides [60,61]. Further, reaction of **3** with $PEtPh_2$, $P(p\text{-tolyl})_3$, $P(p\text{-F-}C_6H_4)_3$, and P^nPr_3 under the same conditions used for the reactions of Eq. (5), yielded a complicated mixture of products, and so why the fortuitous high yield syntheses are seen for **10** remains a mystery. Such dihydrides are of importance in catalyzed olefin hydrogenation using $[RhCl(PR_3)_3]$ complexes [62], and yet only $[Rh(H)_2Cl(PPh_3)_3]$ had been previously characterized crystallographically in a study where the hydride ligands were not located [63]; the hydrides were located in the structures of **10** containing either $PMePh_2$ or $PCyPh_2$ [60].

It was the above investigations into Rh–THP chemistry that first led us to realize that THP was not a 'normal' tertiary phosphine and that it appeared to play 'non innocent' roles even in its 'integral'

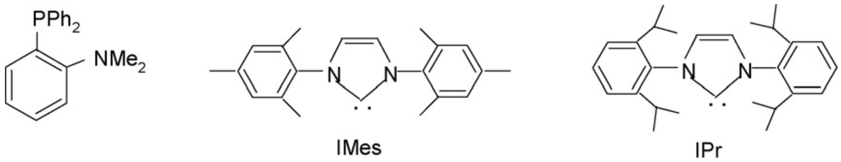


Fig. 1. The P–N and carbene ligands referred to in Section 5.

state, while the Ru–THP literature presented in Section 3 [26,27,32] and the P–C cleavage chemistry of the *cis*-[$MCl_2(THP)_2$] complexes (M = Pt, Pd) mentioned above [53] had also established processes resulting from its decomposition chemistry. The reported syntheses and reactivity of the complexes [$M(THP)_4$] (M = Ni, Pd, or Pt [[8], see Section 6]) and *cis*-[$PtR_2(THP)_2$] (R = alkyl or aryl [53,64]) appear 'normal', although the acidity of the CH_2OH alkoxide proton is suggested to lead to instability of the latter complexes by protonation of the Pt–R bond [64]. Brief general descriptions of these Ni–, Pd–, and Pt–THP complexes and other transition metal–THP complexes will be presented in Section 6.

A research project concurrent with that of the Rh–THP work in our group has been focusing on Rh–carbene complexes, both with and without ancillary phosphine ligands, and especially their reactivity toward H_2, O_2, and CO [58,65,66]. The carbene ligands employed are shown in Fig. 1. An obvious study was to synthesize Rh–carbene–THP complexes, and thus THP dissolved in CD_3OD was added to a C_6D_6 solution of [RhCl(coe)(IMes)]$_2$ (THP:Rh = 2); this immediately gave clean, quantitative conversion to the unexpected 1:1 complex [RhCl(coe)(IMes)(THP)] as evidenced by $^{31}P\{^1H\}$- and ^1H-NMR data [50]. Corresponding addition of THP to [RhCl(coe)(IPr)]$_2$ generated about a 1:1 mixture of [RhCl(coe)(IPr)(THP)] and *cis*-[RhCl(IPr)$_2$(THP)] [50]. The isolation, full characterization, and reactivity of these carbene/THP species are on-going studies within our group.

6. Other metal complexes containing THP or DHMPE

Literature data on some characterized THP complexes of Ru, Cu, and Rh have been discussed in Sections 3–5, respectively, during the presentation of recent studies from our group. This section will summarize relevant literature on other metal–THP systems, and also metal-systems containing coordinated DHMPE (see Section 1). Our interest in these two specific (hydroxymethyl)phosphines stems from the facts that these phosphines were the ones we discovered to be effective pulp-bleaching agents (Section 7), and that pulps do contain trace transition metals.

A review of metal–(hydroxymethyl)phosphine complexes focusing on their use in homogeneous catalysis, covering the literature up to 2001, appeared in 2003 [42]. The few cited publications involving Ru–, Rh–, and Ir–THP systems are also covered in this current review, respectively, in Sections 3 and 5, and this Section. As far as we are aware, the first report on a transition metal complex containing phosphorus-coordinated THP was in 1973 by Chatt's group on *fac*-[$RhCl_3(THP)_3$] [2] (see Section 5). There is, however, a 1969 report (unearthed *via* SciFinder) that mentions the oxygen-coordinated, alkoxide complex $\{Ti[OCH_2P(CH_2OH)_2]_4\}$ [67], while equally poorly characterized [$(HOCH_2)_3P{\cdot}HgX_2$] adducts (X = halide) had been noted in 1966 for use in detecting the presence of THP [68]. The number of coordination compounds containing P-bound THP ligands, including those of Ru, Cu, and Rh mentioned in Sections 3–5, is limited. Several complexes containing THP have been associated with their potential in biomedical applications, particularly development of water-soluble drugs because THP is a water-soluble, crystalline solid at room temperature (m.p. 58 °C) that is oxidatively stable in air; not often noted, however, is that its stability in aqueous media is very dependent on pH (see Section 1). Indeed, a recent report questions the usefulness of (hydroxymethyl)phosphines in general for commercial radiopharmaceutical applications because of their poor oxidative stability, with concomitant generation of closely related by-products [69] (*cf.* Section 2, and Eqs. (1) and (2)).

The prospect of using radiometals of diagnostic and therapeutic importance within nuclear medicine (e.g. ^{99m}Tc, γ-emitter; ^{188}Re, β-emitter) has thus encouraged synthesis of the Re(V) and ^{99m}Tc(V) complexes of the type *trans*-[$M(O)_2(THP)_4$]Cl, and the pyridyl derivatives *trans,cis,cis*- and *trans,trans,trans*-[$ReO_2(THP)_2(py)_2$]Cl [6,70]. A tetranuclear [Re(V)]$_4$ species containing a bridging η^2-*P,O*-[$P(CH_2OH)_2(CH_2O^-)$] ligand has also been isolated [70]; the same η^2-moiety was noted in a dinuclear [Ru(II)]$_2$ complex ([32], see Section 3), while the η^1-*P*-bound form of the ligand exists in the zwitterionic Cu(I) complex **1** shown in Scheme 1 [11,35]. The cationic Tc(I) species [$^{99m}Tc(CO)_3$(THP)(peptide)], where the peptide is an *N,N*-chelated moiety, has been shown to target specifically receptor sites, for example, within human prostate cancer cells [71]. The complexes *fac*-[$ReBr(CO)_3$(DHMPE)] and *trans*-[$Re(O)_2(DHMPE)_2$]Cl have also been made for potential use in nuclear medicine [70,72]. The DHMPE ligand is also found in: the Mo(II) complex [$H_3N^+CH_2CH_2Cp)Mo(CO)_2(DHMPE)]^{2+}$ [16] (where Cp implies a substituted cyclopentadiene ring); and the Mo(IV) cluster complex [$Mo_3S_4Cl_3(DHMPE)_3$]Cl which, on dissolution in water, forms what is thought to be [$Mo_3S_4(DHMPE)(DHMPE\text{-}H)_2(H_2O)]^{2+}$ (where DMHPE-H represents loss of a proton from a CH_2OH moiety with formation of a chelated η^3-*P,P,O*-ligand [73]). Synthesized also are the complexes: [$Ni(DHMPE)_2]Cl_2$ [16], [$M(DMHPE)_2]Cl_2$ (M = Pd, Pt) [74], and [$Au(DHMPE)_2$]Cl and [$Au_2(\mu\text{-DHMPE})_2]Cl_2$ where again potential chemotherapeutic applications were suggested [75]. The related bis(hydroxyalkyl)phosphinoethane ligands [$HO(CH_2)_n]_2P(CH_2)_2P[(CH_2)_nOH]_2$ (n = 2–4; abbreviated here as P-P) have been used to form the water-soluble complexes [$Ni(P\text{-}P)_2Cl$]Cl, [$Rh(P\text{-}P)_2$]Cl, *trans*-[$RuCl_2(P\text{-}P)_2$]Cl [33], and *trans*-[$FeCl_2(P\text{-}P)_2$] [76]. Other well characterized THP complexes of Fe include the water-soluble complexes [$FeCl(NO)_2(THP)$], [$Fe(NO)_2(THP)_2$], [$Fe(NO)_3(THP)]PF_6$ and [$Fe(NO)_2$(DHMPE)], these species being synthesized as potential NO-releasing drugs, though the published formal oxidation states for the metal [77] are incorrect. A range of ferrocenyl-derived (hydroxymethyl)phosphines, where a "$CH_2P(CH_2OH)_2$" substituent is present on the Cp ring, have also been well characterized [78], and some have been used as *in situ* added ligands in Pd-catalyzed formation of methyl propionate from C_2H_4, CO, and MeOH [79].

Pharmacokinetic studies on ^{199}Au-based agents in general reflect that most of these compounds are hydrophobic, and this has limited their use in therapeutic applications in cancer treatment; the hydrophilic [$Au(THP)_4$]Cl was thus studied and found to be active against a range of tumour cells [80]. Gold complexes formulated as [AuL(THP)]NO_3, where L is a nucleoside (adenosine, cytidine, guanosine) have been synthesized from [AuCl(THP)] [81], and the complexes [$Au(THP)_2R_2$]X and [$AuX(THP)R_2$] (R = Me, Et; X = Br, I) have also been synthesized from the corresponding [$AuXR_2]_2$ precursors [82]. Gold nanoparticles capped by THP bind effectively to DNA for use in fabrication of DNA-templated nanowires in which hydrophilic interactions between THP and DNA are thought to play a key role [83].

Within the Group 10 metals, the [M(THP)$_4$] complexes (M = Ni, Pd, Pt) are well characterized including an X-ray structure of the Pd complex, and indeed the complexes catalyze the addition of PH_3 to formaldehyde for the synthesis of THP [3,8,53]. The Ni and Pd complexes in aqueous solution catalyze the oligomerization of neat 1,3-butadiene [84]. The Pt complex can undergo a net oxidative addition of water to generate in solution [PtH(THP)$_4$]OH [3,8]. Other synthesized complexes within the Group 10 metals are *cis*-and/or *trans*-[MX$_2$(THP)$_2$] (X = halide) [2,3,53,85], [PtCl(Me)(THP)$_2$] and [PtR$_2$(THP)$_2$] (R = Me, Et, Ph) [8,64]. From solutions containing $[Pt(H_2O)_2(THP)_2]^{2+}$ (with readily replaceable aqua ligands), the hydroxy-bridged species $[Pt_2(\mu\text{-}OH)_2(THP)_4]^{2+}$ and $[Pt_3(\mu\text{-}OH)_3(THP)_6]^{3+}$ were likely formed by addition of base [86]. The Pt(II) complex [Pt(malonato)(THP)$_2$] has been shown to damage bacterial DNA and have potential for anti-cancer activity [87].

Formation of {M[*P*,*P*-(HOCH$_2$)$_2$POCH$_2$P(CH$_2$OH)$_2$]$_2$}Cl$_2$ (M = Pt, Pd), containing the phosphine–phosphinate ligand, from reaction of *cis*-[MCl$_2$(THP)$_2$] with excess THP [53], which has some similarities to our Rh chemistry illustrated in Scheme 3, was discussed in Section 5. Much of the reactivity of these Group 10 complexes presented in the references arises because of their water-solubility [3,8,53,64]. Extensive inter- and intra-molecular hydrogen-bonding involving the hydroxyl groups is observed in the solid state structure of most metal–THP complexes, as exemplified by structures of Pd(THP)$_4$ [3,8], the {Ru(THP)$_2$[PH(CH$_2$OH)$_2$]$_2$Cl$_2$} complex mentioned in Section 3 [26], the rhodium–THP complexes **3** and **7** shown in Scheme 2 [45], and the Cu–THP complexes **1** and **2** shown in Scheme 1 [11,35].

Worth noting is that addition of THP to [IrCl(cod)]$_2$, unlike the corresponding chemistry with [RhCl(cod)]$_2$ (Scheme 2), results in the formation of [Ir(cod)(THP)$_3$]Cl with no displacement of the cod [5]. This Ir complex catalyzes the hydrogenation of cinnamaldehyde in a biphasic water/benzene medium and, in the presence of excess THP, conditions were found for selective formation of cinnamyl alcohol (90 °C and 125 atm H_2); the catalyst remains in the aqueous layer that was re-used twice without loss of activity [5]. Iridium carbonyl clusters bound to THP grafted on a silica surface, and represented by [Ir$_4$(CO)$_{10}$(THP-SiO$_2$)$_2$], effect (i) catalytic hydroformylation of C_2H_4 to propanal (with C_2H_6 as by-product) at sub-atmospheric pressures of gases (CO, H_2, and C_2H_4) at ~60 °C, and (ii) catalytic O_2-oxidation of propene to acetone under conditions similar to those used for the hydroformylation [88]. Similar silica-supported dimetallic Rh/Co clusters and Rh clusters, including a supposed [Rh$_4$(CO)$_{10}$(THP)$_2$] complex, reveal impressive hydroformylation activity with high selectivity for propanal product from C_2H_4 [89].

To the best of our knowledge, no studies on Co–THP or –DHMPE systems have been reported, although Co(II) complexes of the oxide THPO are known [90].

7. Bleaching activity and organo-phosphorus chemistry of THP

We described in Section 4 our serendipitous finding, after testing many transition metal–THP systems for catalytic hydrogenation of unsaturated moieties in LMCs and of lignin itself within pulps, that THP was an effective bleaching agent for certain pulps. Indeed, the bleaching power (for spruce thermomechanical pulps) was found to be similar to that of the industrially used dithionite ($Na_2S_2O_4$, called 'hydrosulfite' in the pulp and paper industry) at similar loadings, but THP has advantages in that it can be used over a wider range of pH (~4–9, despite the sensitivity of THP to oxidation at the higher pH values), temperature (20–130 °C) and consistency (1.5–20%, i.e. the weight % of pulp in a pulp/water mixture), without the need for removal of O_2 or transition metals [39]. Whether transition metal–THP interactions are involved in any way in the bleaching process, which seems plausible, is currently an unanswered, important question. For the bleaching treatment, THP can be readily formed *in situ* from the air-stable tetrakis(hydroxymethyl)phosphonium salts by addition of base to a pulp slurry (reverse of Eq. (1)). A further benefit is that THP-bleached pulps show higher heat-, moisture- and light-stability than those bleached with $S_2O_4^{2-}$; i.e. THP is also a brightness stabilizing agent [39], a finding compatible with a report that [P(CH$_2$OH)$_4$]Cl prevents yellowing of fluorescently whitened wool in simulated sunlight [91].

Analysis of phosphorus introduced into the pulp and pulp wastewater showed that the bleaching results from organo-phosphorus moieties formed in the pulp, and the brightness gain correlates with the amount of covalently bonded-P; qualitative UV–vis data on LMCs, and lignin isolated from the bleached pulp, suggested that the phosphorus interacts with coniferaldehyde (cinnamaldehyde with *m*-OMe and *p*-OH substituents, see Fig. 2) and *p*-quinone units, both important chromophores within pulp [92]. Such interactions have been substantiated by detailed NMR and crystallographic studies on LMCs that include these chromophores, and this work in organophosphorus chemistry, although outside the scope of this journal, did increase our appetite for transition metal–THP chemistry and so is summarized below. The interaction of tertiary phosphines with unsaturated (including carbonyl-containing) organics is also highly relevant within catalytic processes homogeneously catalyzed by transition metal-phosphine complexes, a vast research area that is frequently covered by articles in this journal [93]. A relevant example is reactivity of phosphines toward α,β-unsaturated aldehydes under hydroformylation conditions [94].

We have shown that the relatively basic P-atom of THP acts toward LMCs as a reductant and, compatible with this, also as a strong nucleophile. The (hydroxypropyl)phosphine P[(CH$_2$)$_3$OH]$_3$, which is also a bleaching agent [39], is less prone to decomposition than THP, and was thus mostly used as a reactant rather than THP itself, since this resulted in cleaner reactions. Reactions were generally studied in H_2O/D_2O solutions by ^{31}P, ^{1}H, and ^{13}C NMR spectroscopies (including 2D-correlation methods), product isolation and, when possible, X-ray analysis of isolated compounds or their derivatives. There is extensive literature on nucleophilic attack by phosphines on unsaturated organics and carbonyl-containing organics, typically in non-aqueous solvents (for the relevant references see our papers [95–97]), and this includes considerable, early Russian work (1960–75) that was devoid of ^{31}P NMR data. Our studies, especially those in aqueous media, have revealed many novel findings, which are summarized below.

Aromatic aldehyde moieties present in lignin, exemplified by the LMC **3** (Fig. 2) can be reduced by (hydroxyalkyl)phosphines in water to the corresponding alcohols (**4**), with co-production of the phosphine oxide; in D_2O, the –CH(D)OD moiety is formed selectively [95]. The mechanism proceeds *via* a phosphonium species formed by initial nucleophilic attack of the P-atom at the carbonyl C-atom, i.e. *via* ArCH(OH)P$^+$R$_3$, where Ar is the aromatic residue and R is the hydroxyalkyl substituent [95]. When the aldehyde contains a *p*-OH substituent, the alcohol product subsequently reacts with the phosphine more readily than the aldehyde precursor to give a phosphobetaine; in D_2O, exchange of both benzyl protons of the phosphobetaine occurs to give **5** *via* phosphorus ylide intermediates, which can also lead to exchange of the R–CH$_2$ protons adjacent to the P-atom [95]. Treatment of species such as **5** with aqueous HCl protonates the phenolate group and gives the phosphonium chloride salt [4-OH-3,5-(OMe)$_2$-C$_6$H$_2$CH$_2$P$^+$R$_3$]Cl, which was structurally characterized in the case where R = Et. The occurrence of the novel redox reaction requires the key role of OH$^-$ in forming the

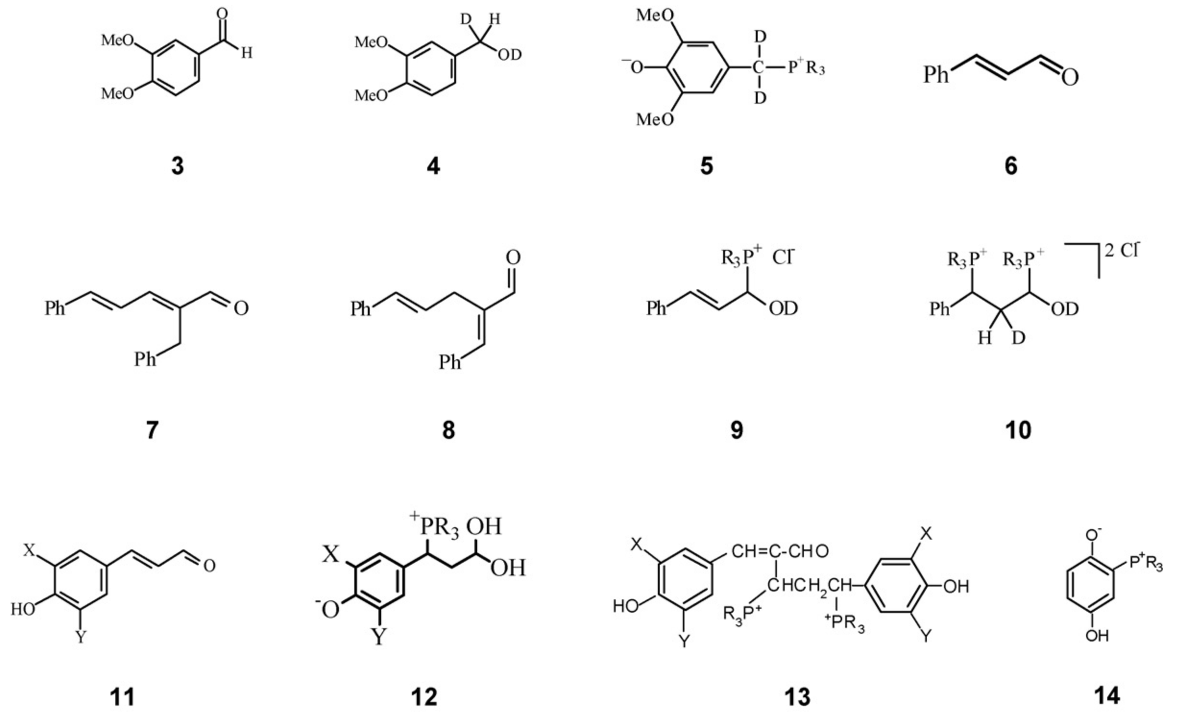


Fig. 2. Structures of typical organic substrates used by our group, and their products from reactions with tertiary phosphines.

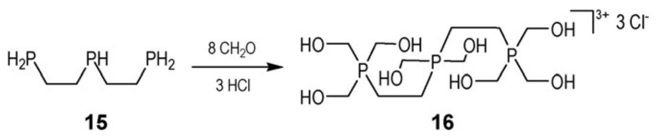
phosphonium intermediate and the phosphine oxide co-product [95]. Any such aldehyde reduction or phosphobetaine formation decreases the extent of conjugation, and could thus contribute to the bleaching of pulp.

Reaction in water of $P[(CH_2)_3OH]_3$ with cinnamaldehyde (**6**), which has the phenyl-unsaturated propanoid backbone similar to that found in lignin [98], revealed self-condensation of **6** to the isomers **7** and **8**. The reaction occurs *via* initial nucleophilic attack of the phosphine at the α-carbon (the one adjacent to the Ph); in D_2O, all but the Ph and –CHO protons in the products are exchanged by D [96]. NMR data are consistent with formation of a carbanion and subsequent condensation of two phosphonium-containing aldehydes to generate the products with concomitant elimination of phosphine oxide, in which OH^- provides the O-atom [96]. In aqueous DCl, phosphine attacks at the aldehyde C-atom first forming **9**, and then the bis(phosphonium) salt **10**; species **9** and **10**, although having up to three chiral carbon centres, are formed with high stereoselectivity in just enantiomeric forms, which is attributed to electrostatic interactions between a phosphonium centre and a carbanion lone-pair [96]. When the phenyl group of **6** has a *p*-OH substituent, quite different chemistry is seen because of deprotonation of the OH-substituent; substrates studied were the lignin components: coumaraldehyde (**11**, X = Y = H), coniferaldehyde (**11**, X = OMe, Y = H), and sinapaldehyde (**11**, X = Y = OMe) [97]. Initial phosphine attack is now at the γ-carbon, but the product is now the zwitterionic **12**, and this undergoes self-condensation to give a zwitterionic di(phosphonium) diphenolate that can react with aqueous HCl to give the dichloride of **13**. All the intermediates were well characterized, and X-ray structures were obtained for the PEt_3 and PMe_3 derivatives of **13**; elucidation of this chemistry involved addition of a range of neat tertiary phosphines (not necessarily water-soluble) to aqueous suspensions of **11**. The P-atoms of **13**, being adjacent to chiral C-centers, are prochiral and thus contain magnetically inequivalent, diastereotopic Et/Me groups; this results in 'exotic' NMR spectra that were successfully interpreted [97]. Again, there is extensive literature describing reactivity of phosphines with α,β-unsaturated carbonyl compounds, but the aqueous medium leads to novel chemistry seen with phosphines including $P[(CH_2)_3OH]_3$, and the chemistry again realizes decreased conjugation [96,97]. A phosphobetaine of type **14** is formed from *p*-quinones with OMe and/or Me substituents [13], the essential chemistry of which has long been known [96].

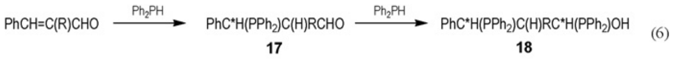
The above organo-phosphorus chemistry exemplifies how bleaching activity likely occurs by loss of conjugation, and the less conclusive data on lignin itself lead to the same conclusion. The hydrogenations of C=C and C=O functionalities of the LMCs in the Ru–THP/H_2 catalytic system (Section 3) similarly lead to decreased conjugation; whether the pulp-bleaching by these systems involves any catalytic hydrogenation process is an interesting question that requires further study, particularly using ^1H and ^{31}P NMR data from experiments with isolated lignin. It should be noted that THP in conjunction with dithionite has led to commercial use within a pulp mill [99,100].

The presence of a hydroxymethyl substituent within a tertiary phosphine was shown to be essential for optimum bleaching activity for mechanical pulps [39], and the diphosphine DHMPE [4,16] was shown to have a bleaching power greater than that of THP at the same phosphorus loading and reaction conditions [39,101]. This diphosphine has good oxidative stability and excellent metal complexation ability ([4,11,12,73], see Section 6) but, unlike THP, is currently not available commercially. Syntheses of the diphosphine and the diphosphonium salts correspond to those shown in Eq. (1) for THP, but the required precursor is now $H_2P(CH_2)_2PH_2$.

Our studies on the pulp-bleaching, and a report that THP had been used to remove trace Ru species from polymers synthesized by Grubbs-type Ru–carbene catalysts [102], led us to extend the (hydroxymethyl)phosphine theme by synthesizing the new oligophosphine **15** and the corresponding tetra- and hexaphosphines, and the corresponding phosphonium salts such as **16** (Scheme 4; [103]). Treatment of the salts with base (*cf.* Eq. (1)) should yield 'poly-THP' compounds, which are expected to be powerful metal sequestering agents. More generally there is considerable literature on the syntheses of (hydroxymethyl)phosphorus



Scheme 4. An example of conversion of an oligophosphine to its phosphonium salt.



$$\mathrm{PhCH{=}C(R)CHO} \xrightarrow{\mathrm{Ph_2PH}} \underset{\mathbf{17}}{\mathrm{PhC^{*}H(PPh_2)C(H)RCHO}} \xrightarrow{\mathrm{Ph_2PH}} \underset{\mathbf{18}}{\mathrm{PhC^{*}H(PPh_2)C(H)RC^{*}H(PPh_2)OH}} \quad (6)$$

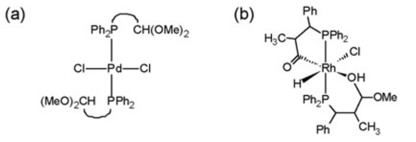


Fig. 3. (a and b) Structural diagrams of unpublished studies on two crystallographically characterized complexes synthesized in our group (see Section 8).

compounds, and relevant references are listed in our publication [103] and in an earlier review [104].

8. Secondary phosphine systems

As mentioned in Section 3 dealing with Ru systems, and illustrated in Eq. (1) of Section 2, $HP(CH_2OH)_2$ can be generated in solutions of THP, and indeed this secondary phosphine was also detected during our studies on the use of THP in the bleaching of pulps ([17,99], Section 7). This enforced us to investigate reactions of secondary phosphines with LMCs such as cinnamaldehyde, a study that led to isolation of new tertiary-phosphines and -diphosphines of type **17** and **18**, respectively (Eq. (6), R = H, Me; * = chiral centre). For example, a 1:1 reaction of Ph_2PH with cinnamaldehyde itself (R = H) using neat reagents gives, *via* hydrophosphination of the olefinic bond, the new tertiary phosphine **17** (R = H) as a racemic mixture, while a 2:1 reaction shows hydrophosphination of both the C=C and C=O bonds to give the new diphosphine **18** as a diastereomeric mixture with a diastereomeric ratio of ∼2.3 [105]. Both reactions lead to loss of conjugation in α,β-unsaturated carbonyl compounds, and could play a role in lignin bleaching. The new phosphines **17** and **18** promise to show rich coordination chemistry, including insight into stereochemical aspects. Structurally characterized thus far are: *trans*-$[PdCl_2L_2]$ where L is the acetal derivative of **17** formed in MeOH (R = Me; Fig. 3a; [106]), the $[PdCl_2(P-P)]$ complex, where P–P represents chelated **18** (R = H; [105]), and hydrido-acyl complexes of Rh(III) and Ir(III), formed by oxidative addition of the aldehyde group of **17** (R = Me) to Rh(I) and Ir(I) precursors. This last mentioned type is exemplified by the product made from $[RhCl(cod)]_2$ and the phosphino-aldehyde in MeOH [106]; the oxidative addition is observed within one (presumably initially chelated) **17** ligand, while a second **17**, converted in the MeOH to the hemi-acetal, chelates *via* the P-atom and the O-atom of the hemi-acetal-OH (Fig. 3b; [106]).

9. Conclusions

The review describes how our group at UBC, through collaboration with a pulp and paper research group, became involved in studies on the use of transition metal–water-soluble phosphine systems to effect bleaching/brightness stabilization of pulps *via* catalytic hydrogenation of aromatic moieties in lignin. Such studies revealed that stabilized colloidal Ru and Rh were effective catalysts for such hydrogenation, while Ru–THP species proved useful for hydrogenation of olefinic and carbonyl groups, and for hydrogenolysis of certain alcohol groups. Subsequent control/blank experiments led to the serendipitous finding that THP itself (in the absence of metals) was an effective bleaching and brightness stabilization agent for certain pulps, indeed to the extent that THP has been used commercially in a pulp-mill. This discovery forced us to study the interaction of hydroxyphosphines with a wide range of lignin model compounds and lignin itself, and this has led to significant advances in the area of organo-phosphorus chemistry. The related (hydroxymethyl)diphosphine DHMPE was also found effective as a bleaching agent. That pulps can contain trace metals led us to study the literature on, and extend the chemistry of, transition metal complexes of THP and DHMPE; such (hydroxymethyl)phosphine ligands are not 'innocent' because of pH-dependent decomposition pathways under anaerobic or aerobic conditions. The review attempts to cover principally our work on metal–THP chemistry, with incorporation of literature findings on such systems and the related DHMPE studies, and the organo-phosphorus chemistry. It remains to be seen whether such metal complexes become commercially useful in (a) aqueous or 2-phase aqueous/organic catalytic systems, or (b) as water-soluble medicinal drugs.

On a philosophical point, the research described all evolved from a short application, about 15 years ago, for funding from the pulp and paper industry to study hydrogenation of aromatics. On-going findings subsequently and slowly led to significant broadening of the research topic(s), and much fundamental and novel chemistry has evolved from the initial collaborative, more applied work with Paprican—seemingly the reverse of the more typical scenario. A retrospective look at the compulsory 'milestones' required for the initial commercial application now makes for amusing reading!

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References

[1] M. Reuter, L. Orthner, Ger. Patent 1,035,135 (1958).
[2] J. Chatt, G.J. Leigh, R.M. Slade, J. Chem. Soc., Dalton Trans. (1973) 2021.
[3] (a) K.N. Harrison, P.A.T. Hoye, A.G. Orpen, P.G. Pringle, M.B. Smith, J. Chem. Soc. Chem. Commun. (1989) 1096;
(b) P.G. Pringle, D. Brewin, M.B. Smith, K. Worboys, in: T. Horváth, F. Joó (Eds.), Aqueous Organometallic Chemistry and Catalysis, NATO, 1995, p. 111.
[4] D. Klötzer, P. Mäding, R.Z. Münze, Z. Chem. 24 (1984) 224.
[5] A. Fukuoka, W. Kosugi, F. Morishita, M. Hirano, L. McCaffrey, W. Henderson, S. Komiya, Chem. Commun. (1999) 489.
[6] D.E. Berning, K.V. Katti, P.R. Singh, C. Higgenbotham, V.S. Reddy, W.A. Volkert, Nucl. Med. Biol. 23 (1996) 617.
[7] K.A. Petrov, V.A. Parshina, M.B. Luzanova, Zh. Obshch. Khim. 32 (1962) 553.
[8] J.W. Ellis, K.N. Harrison, P.A.T. Hoye, A.G. Orpen, P.G. Pringle, M.B. Smith, Inorg. Chem. 31 (1992) 3026.
[9] L.I. Grekov, I.A. Novakov, Kinetics Catal. 47 (2006) 358.

[10] (a) A.W. Frank, D.D. Daigle, S.L. Vail, Textile Res. J. 52 (1982) 738;
(b) A.W. Haack, D. Downward, D. Talbot, Proc. 1997 TAPPI Engin. Papermakers Conf., 1997, p. 1115;
(c) T.A. Calamari, R.J. Harper, Flame-Retardants for Textiles, Kirk-Othmer Encyclopedia of Chemical Technology, vol. 10, 4th ed., 2000, p. 998.

[11] D.S. Bharathi, M.A. Sridhar, J.S. Prasad, A.G. Samuelson, Inorg. Chem. Commun. 4 (2001) 490.

[12] (a) A. Hoffman, J. Am. Chem. Soc. 52 (1930) 2995;
(b) S.M. Bloom, S.A. Buckler, R.F. Lambert, E.V. Merry, J. Chem. Soc. D, Chem. Commun. (1970) 870.

[13] D.V. Moiseev, B.R. James, T.Q. Hu, unpublished data.

[14] (a) W.J. Vullo, Ind. Eng. Chem. Prod. Res. Dev. 5 (1966) 346;
(b) L. Maier, Helv. Chim. Acta 54 (1971) 1434.

[15] V.S. Reddy, K.V. Katti, C.L. Barnes, Inorg. Chim. Acta 240 (1995) 367.

[16] G.F. Nieckarz, T.J.R. Weakley, W.K. Miller, B.E. Miller, D.K. Lyon, D.R. Tyler, Inorg. Chem. 35 (1996) 1721.

[17] P. Marcazzan, B.R. James, T.Q. Hu, unpublished data.

[18] B.R. James, Chem. Ind., vol. 123, (Catal. Org. React., CRC Press), 2008, p. 1.

[19] (a) T.Q. Hu, B.R. James, S.J. Rettig, C.-L. Lee, Can. J. Chem. 75 (1997) 1234;
(b) T.Y.H. Wong, R. Pratt, C.G. Leong, B.R. James, T.Q. Hu, Chem. Ind., vol. 82, (Catal. Org. React., Dekker), 2001, p. 255.

[20] (a) M.A. Bennett, T.-N. Huang, T.W. Turney, J. Chem. Soc., Chem. Commun. (1979) 312;
(b) L. Plasseraud, G. Süss-Fink, J. Organomet. Chem. 539 (1997) 163;
(c) G. Süss-Fink, M. Faure, T.R. Ward, Angew. Chem. Int. Ed. 41 (2002) 99.

[21] (a) J.A. Widegren, M.A. Bennett, R.G. Finke, J. Am. Chem. Soc. 125 (2003) 10301;
(b) L. Vieille-Petit, G. Süss-Fink, B. Therrien, T.R. Ward, H. Stœckly-Evans, G. Labat, L. Karmazin-Brelot, A. Neels, T. Bürgi, R.G. Finke, C.M. Hagen, Organometallics 24 (2005) 6104.

[22] T.Q. Hu, B.R. James, in: T.Q. Hu (Ed.), Chemical Modification, Properties and Usage of Lignin, Kluwer Academic/Plenum, New York, 2002, p. 247 (and Refs. therein).

[23] M.B. Ezhova, A.Z. Lu, B.R. James, T.Q. Hu, Chem. Ind., vol. 104, (Catal. Org. React., Dekker), 2001, p. 135.

[24] (a) J. March, Advanced Organic Chemistry, 2nd ed., McGraw-Hill, New York, 1977, p. 1119;
(b) W.F. Maier, K. Bergmann, W. Bleicher, P.v.R. Schleyer, Tetrahedron Lett. 22 (1981) 4227;
(c) H.A. Zahalka, H. Alper, Organometallics 5 (1986) 1909.

[25] H. Mehdi, V. Fábos, R. Tuba, A. Bodor, L.T. Mika, I.T. Horváth, Top. Catal. 48 (2008) 49.

[26] L. Higham, A.K. Powell, M.K. Whittlesey, S. Wocadlo, P.T. Wood, J. Chem. Soc., Chem. Commun. (1998) 1107.

[27] (a) Y. Kayaki, T. Suzuki, T. Ikariya, Chem. Lett. 30 (2001) 1016;
(b) Y. Kayaki, Y. Shimokawatoko, T. Ikariya, Inorg. Chem. 46 (2007) 5791.

[28] V. Cadierno, P. Crochet, S.E. García-Garrido, J. Gimeno, J. Chem. Soc., Dalton Trans. (2004) 3635.

[29] J. Čubrilo, I. Hartenbach, T. Schleid, R.F. Winter, Z. Anorg. Allg. Chem. 632 (2006) 400.

[30] B. Drießen-Hölscher, J. Heinen, J. Organomet. Chem. 570 (1998) 141.

[31] (a) M. Bianchi, P. Frediani, A. Salvini, L. Rosi, L. Pistolesi, F. Piacenti, S. Ianelli, M. Nardelli, Organometallics 16 (1997) 482;
(b) A. Salvini, P. Frediani, M. Bianchi, F. Piacenti, L. Pistolesi, L. Rosi, J. Organomet. Chem. 582 (1999) 218.

[32] A. Romeroso, T. Campos-Malpartida, M. Serrano-Ruiz, M. Peruzzini, Proc. Dalton Discuss. 6, Organomet. Chem. and Catal., York, UK, 2003, Poster 15.

[33] G.T. Baxley, W.K. Miller, D.K. Lyon, B.E. Miller, G.F. Nieckarz, T.J.R. Weakley, D.R. Tyler, Inorg. Chem. 35 (1996) 6688.

[34] D.V. Moiseev, P. Marcazzan, B.R. James, Can. J. Chem. 87 (2009) 582.

[35] (a) B.R. James, T.Q. Hu, Pacifichem Conf., Honolulu, 2005, Abstract INORG 937;
(b) G. Ma, B.R. James, T.Q. Hu, unpublished results.

[36] B.R. James, Homogeneous Hydrogenation, Wiley, New York, 1973 (Ch. X).

[37] (a) M.D. Le Page, B.R. James, Chem. Commun. (2000) 1647;
(b) M.D. Le Page, D. Poon, B.R. James, Chem. Ind., vol. 89, (Catal. Org. React., Dekker), 2003, p. 61.

[38] (a) J.-X. Chen, J.F. Daeuble, D.M. Brestensky, J.M. Stryker, Tetrahedron 56 (2000) 2153;
(b) J.-X. Chen, J.F. Daeuble, J.M. Stryker, Tetrahedron 56 (2000) 2789.

[39] (a) T.Q. Hu, B.R. James, D. Yawalata, M.B. Ezhova, J. Pulp Pap. Sci. 30 (2004) 233;
(b) T.Q. Hu, B.R. James, D. Yawalata, M.B. Ezhova, PCT/WO 2004/070110 A1 (August 2004); European Patent EP 1,590,525 B1 (October 2006); US Patent 7,285,181 B2 (October 2007).

[40] C. Marzano, V. Gandin, M. Pellei, D. Colavito, G. Papini, G.G. Lobbia, E. Del Giudice, M. Porchia, F. Tisato, C. Santini, J. Med. Chem. 51 (2008) 798.

[41] S. Alidori, G.G. Lobbia, G. Papini, M. Pellei, M. Porchia, F. Refosco, F. Tisato, J.S. Lewis, C. Santini, J. Biol. Inorg. Chem. 13 (2008) 307.

[42] N. Pinault, D.W. Bruce, Coord. Chem. Rev. 241 (2003) 1.

[43] E. Wiebus, B. Cornils, in: D.J. Cole-Hamilton, R. Tooze (Eds.), Catalyst Separation, Recovery and Recycling, Springer, Dordrecht, The Netherlands, 2006 (Chapter 5 and Refs. therein).

[44] K. Raghuraman, N. Pillarsetty, W.A. Volkert, C. Barnes, S. Jurisson, K.V. Katti, J. Am. Chem. Soc. 124 (2002) 7276.

[45] F. Lorenzini, B.O. Patrick, B.R. James, J. Chem. Soc., Dalton Trans. (2007) 3224.

[46] G. Ma, R. McDonald, M. Ferguson, R.G. Cavell, B.O. Patrick, B.R. James, T.Q. Hu, Organometallics 26 (2007) 846 (and refs. therein).

[47] D.G. Blackmond, M. Ropic, M. Stefinovic, Org. Process Res. Dev. 10 (2006) 457.

[48] L.J. Higham, M.K. Whittlesey, P.T. Wood, J. Chem. Soc., Dalton Trans. (2004) 4202.

[49] (a) A.W. Frank, G.L. Drake Jr., J. Org. Chem. 37 (1972) 2752;
(b) J.A. Hatnean, R. Raturi, J. Lefebvre, D.B. Leznoff, G. Lawes, S.A. Johnson, J. Am. Chem. Soc. 128 (2006) 14992 (and Refs. therein).

[50] F. Lorenzini, B.R. James, unpublished results.

[51] F. Lorenzini, B.O. Patrick, B.R. James, Inorg. Chem. 46 (2007) 8998.

[52] (a) A. Ceriotti, L. Garlaschelli, G. Longoni, M.C. Malatesta, D. Strumolo, A. Fumagalli, S. Martinengo, J. Mol. Catal. 24 (1984) 309;
(b) T. Sakakura, T.-A. Kobayashi, T. Hayashi, Y. Kawabata, M. Tanaka, I. Ogata, J. Organomet. Chem. 267 (1984) 171;
(c) P.E. Garrou, Chem. Rev. 85 (1985) 171.

[53] (a) P.G. Pringle, M.B. Smith, Plat. Met. Rev. 34 (1990) 74;
(b) P.A.T. Hoye, P.G. Pringle, M.B. Smith, K. Worboys, J. Chem. Soc., Dalton Trans. (1993) 269.

[54] (a) P.S. Braterman, R.J. Cross, G.B. Young, J. Chem. Soc., Dalton Trans. (1976) 1310;
(b) K. Kikukawa, T. Yamane, Y. Ohbe, M. Takagi, T. Matsuda, Bull. Chem. Soc. Jpn. 52 (1979) 1187;
(c) R.A. Dubois, P.E. Garrou, K.D. Lavin, H.R. Allcock, Organometallics 3 (1984) 649;
(d) A.B. Goel, Inorg. Chim. Acta 84 (1984) L25.

[55] T.J. Geldbach, D. Drago, P.S. Pregosin, Chem. Commun. (2000) 1629.

[56] (a) K. Kikukawa, T. Matsuda, J. Organomet. Chem. 235 (1982) 243;
(b) M. Cowie, M.D. Gauthier, S.J. Loeb, I.R. McKeer, Organometallics 2 (1983) 1057.

[57] F. Lorenzini, B.O. Patrick, B.R. James, Inorg. Chim. Acta 361 (2008) 3199.

[58] X.-Y. Yu, B.O. Patrick, B.R. James, Organometallics 25 (2006) 4870.

[59] P. Suomalainen, S. Jääskeläinen, M. Haukka, R.H. Laitinen, J. Pursiainen, T.A. Pakkanen, Eur. J. Inorg. Chem. (2000) 2607.

[60] F. Lorenzini, B.O. Patrick, B.R. James, Inorg. Chim. Acta 361 (2008) 2123.

[61] (a) F. Lorenzini, B.O. Patrick, B.R. James, Acta Crystallogr. E64 (2008) m179;
(b) F. Lorenzini, B.O. Patrick, B.R. James, Acta Crystallogr. E64 (2008) m464.

[62] L.A. Oro, D. Carmona, in: J.G. de Vries, C.J. Elsevier (Eds.), Handbook of Homogeneous Hydrogenation, vol. 1, Wiley-VCH, Weinheim, Germany, 2007 (Chapter 1 and Refs. therein).

[63] (a) K. Burgess, W.A. Van der Donk, S.A. Westcott, T.B. Marder, R.T. Baker, J.C. Calabrese, J. Am. Chem. Soc. 114 (1992) 9350;
(b) W. Clegg, M.R.J. Elsegood, N.C. Norman, N.L. Pickett, Acta Crystallogr. E 58 (2002) m406.

[64] (a) S. Komiya, M. Ikuine, N. Komine, M. Hirano, Chem. Lett. 31 (2002) 72;
(b) S. Komiya, M. Ikuine, N. Komine, M. Hirano, Bull. Chem. Soc. Jpn. 76 (2003) 183.

[65] X.-Y. Yu, B.O. Patrick, B.R. James, Organometallics 25 (2006) 2359.

[66] (a) X.-Y. Yu, H. Sun, B.O. Patrick, B.R. James, Eur. J. Inorg. Chem. (2009) 1752;
(b) H. Sun, X-Y. Yu, P. Marcazzan, B.O. Patrick, B.R. James, Can. J. Chem. (in press).

[67] E.V. Kuznetsov, E.K. Ignat'eva, Trudy Kazans. Khim. -Tekhnol. Inst. 40 (1969) 196 (through SciFinder Scholar).

[68] (a) I. Gordon, G.M. Wagner, US Patent 3,257,460 (1966);
(b) E.I. Grinshtein, A.B. Bruker, L.Z. Soborovskii, Zh. Obshch. Khim. 36 (1966) 302;
(c) A.W. Frank, G.L. Drake Jr., J. Org. Chem. 36 (1971) 549.

[69] D.V. Griffiths, H.J. Groombridge, M.C. Salt, Phosphorus, Sulfur Silicon Relat. Elem. 183 (2008) 473.

[70] (a) V.S. Reddy, D.E. Berning, K.V. Katti, C.L. Barnes, W.A. Volkert, A.R. Ketring, Inorg. Chem. 35 (1996) 1753;
(b) D.E. Berning, K.V. Katti, L.J. Barbour, W.A. Volkert, Inorg. Chem. 37 (1998) 334.

[71] C.J. Smith, G.L. Sieckman, N.K. Owen, D.L. Hayes, D.G. Mazuru, R. Kannan, W.A. Volkert, T.J. Hoffman, Cancer Res. 63 (2003) 4082.

[72] R. Schibli, K.V. Katti, W.A. Volkert, C.L. Barnes, Inorg. Chem. 40 (2001) 2358.

[73] A.G. Algarra, M.G. Basallote, M.J. Fernández-Trujillo, E. Guillamón, R. Llusar, M.D. Segarra, C. Vicent, Inorg. Chem. 46 (2007) 7668 (and Refs. therein).

[74] V.S. Reddy, K.V. Katti, C.L. Barnes, J. Chem. Soc., Dalton Trans. (1996) 1301.

[75] D.E. Berning, K.V. Katti, C.L. Barnes, W.A. Volkert, A.R. Ketring, Inorg. Chem. 36 (1997) 2765.

[76] W.K. Miller, J.D. Gilbertson, C. Leiva-Paredes, P.R. Bernatis, T.J.R. Weakley, D.K. Lyon, D.R. Tyler, Inorg. Chem. 41 (2002) 5453.

[77] S.A.T. Dillinger, H.W. Schmalle, T. Fox, H. Berke, Dalton Trans. (2007) 3562.

[78] (a) N.J. Goodwin, W. Henderson, J.K. Sarfo, Chem. Commun. (1996) 1551;
(b) W. Henderson, S.R. Alley, J. Organomet. Chem. 658 (2002) 181 (and Refs. therein).

[79] I.R. Butler, P.K. Baker, G.R. Eastham, K.M. Fortune, P.N. Horton, M.B. Hursthouse, Inorg. Chem. Commun. 7 (2004) 1049.

[80] (a) D.E. Berning, K.V. Katti, C.L. Barnes, W.A. Volkert, Chem. Ber. 130 (1997) 907;
(b) D.E. Berning, K.V. Katti, W.A. Volkert, C.J. Higginbotham, A.R. Ketring, Nucl. Med. Biol. 25 (1998) 577;
(c) N. Pillarsetty, K.K. Katti, T.J. Hoffman, W.A. Volkert, K.V. Katti, H. Kamei, T. Koide, J. Med. Chem. 46 (2003) 1130.

[81] S. Komiya, H. Awata, S. Ishimatsu, A. Fukuoka, Inorg. Chim. Acta 217 (1994) 201.

[82] N. Komine, K. Ichikawa, A. Mori, M. Hirano, S. Komiya, Chem. Lett. 34 (2005) 1704.

[83] O. Harnack, W.E. Ford, A. Yasuda, J.M. Wessels, Nano Lett. 2 (2002) 919.
[84] J. Cermak, M. Kvicalova, V. Blechta, Collect. Czech. Chem. C 62 (1997) 355.
[85] R. Foguet Ambros, F. Sampedro Camarena, J.A. Ortiz Hernández, S. Cayuela Giménez, J.M. Castello Barenys, L. De Andres Basauri, J. Bonal de Falgas, 10 p addition to Span. Patent 547,481 (1986).
[86] E. Costa, M. Murray, P.G. Pringle, M.B. Smith, Inorg. Chim. Acta 213 (1993) 25.
[87] F. Sampedro, A.M. Molins-Pujol, J.I. Ruiz, P. Santaló, J. Bonal, M. Pueyo, M. Llagostera, F. Sánchez-Ferrando, Eur. J. Med. Chem. 27 (1992) 611.
[88] T. Shido, T. Okazaki, M. Ichikawa, J. Mol. Catal. A: Chem. 120 (1997) 33.
[89] (a) T. Shido, T. Okazaki, M.A. Ulla, T. Fujimoto, M. Ichikawa, Catal. Lett. 17 (1993) 97;
(b) T. Shido, T. Okazaki, M. Ichikawa, Catal. Lett. 20 (1993) 37.
[90] (a) M.W.G. De Bolster, C. Boutkan, T.A. Van der Knaap, L. Van Zweeden, I.E. Kortram, W.L. Groeneveld, Z. Anorg. Allg. Chem. 443 (1978) 269;
(b) C.M. Mikulski, J.S. Skryantz, N.M. Karayannis, L.L. Pytlewski, L.S. Gelfand, Inorg. Chim. Acta 27 (1978) 69.
[91] L.A. Holt, B. Milligan, L.J. Wolfram, Textile Res. J. 44 (1974) 846.
[92] (a) R. Chandra, T.Q. Hu, B.R. James, M.B. Ezhova, D.V. Moiseev, J. Pulp Pap. Sci. 33 (2007), 15;
(b) T.Q. Hu, E. Yu, B.R. James, P. Marcazzan, Holzforschung 62 (2008) 389.
[93] For example: Coord. Chem. Rev. 248 (21–24) (2004).
[94] D.R. Bryant, in: D.J. Cole-Hamilton, R. Tooze (Eds.), Catalyst Separation, Recovery and Recycling, Springer, Dordrecht, The Netherlands, 2006 (Chapter 2 and Refs. therein).
[95] (a) D.V. Moiseev, B.R. James, T.Q. Hu, Inorg. Chem. 45 (2006) 10338;
(b) D.V. Moiseev, B.O. Patrick, B.R. James, Inorg. Chem. 48 (2009) 239.
[96] D.V. Moiseev, B.R. James, T.Q. Hu, Inorg. Chem. 46 (2007) 4704.
[97] D.V. Moiseev, B.O. Patrick, B.R. James, T.Q. Hu, Inorg. Chem. 46 (2007) 9389.
[98] K. Morreel, J. Ralph, F. Lu, G. Goeminne, R. Busson, P. Herdewijn, J.L. Goeman, J. Van der Eycken, W. Boerjan, E. Messens, Plant Physiol. 136 (2004) 4023.
[99] T.Q. Hu, B.R. James, T. Williams, J.A. Schmidt, D.V. Moiseev, PCT/WO 2007/016769 A1, Feb. 2007.
[100] T.Q. Hu, T. Williams, J. Schmidt, B.R. James, R. Cavasin, D. Lewing, Pulp Pap-Canada (in press).
[101] (a) T.Q. Hu, B.R. James, D. Yawalata, M.B. Ezhova, R.P. Chandra, J. Pulp Pap. Sci. 31 (2005) 69;
(b) T.Q. Hu, B.R. James, D. Yawalata, M.B. Ezhova, J. Pulp Pap. Sci. 32 (2006) 131.
[102] (a) H.D. Maynard, R.H. Grubbs, Tetrahedron Lett. 40 (1999) 4137;
(b) M.L. Ferguson, D.J. O'Leary, R.H. Grubbs, Org. Synth. 80 (2003) 85.
[103] D.V. Moiseev, B.R. James, B.O. Patrick, T.Q. Hu, Inorg. Chem. 45 (2006) 2917.
[104] K.V. Katti, H. Gali, C.J. Smith, D.E. Berning, Acc. Chem. Res. 32 (1999) 9.
[105] D.V. Moiseev, B.O. Patrick, B.R. James, Inorg. Chem. 46 (2007) 11467.
[106] D.V. Moiseev, F. Lorenzini, B.R. James, unpublished data.