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Review

Organometallic phosphonic acids: synthesis and coordination chemistry

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Contents

Abstract

The synthesis, structure and application of highly functionalized organometallic phosphonic acids are reviewed. Phosphonic acid derivatives of phosphorus(III) and transition metals are emphasized. Coordination chemistry, homogeneous catalytic reactions and synthesis of new materials are also reviewed. This present review provides an exhaustive literature survey through to September 2004.

Keywords: Phosphonic acids; Organometallic; Phosphine

1. Introduction and scope of review

Organometallic compounds containing the phosphonic acid group, PO_3H_2 can be divided into two broad classes: (a) complexes in which the phosphonic acid group is part of a supporting ligand (e.g. a cyclopentadienyl ring or a phosphine ligand) and (b) complexes containing a formal metal–phosphorus bond (e.g. M–PO_3H_2). Such acids have potential application in aqueous phase homogeneous catalysis, crystal engineering, and in the fabrication of layered materials. Like sulfonic acids, phosphonic acids are strong acids, with the first p$K_a \approx 1$–2, and so remain ionized over a wide pH range in aqueous media. Although phosphonate-functionalized ligands may potentially coordinate to transition metals through the anionic phosphonate oxygens, late transition metals, such as rhodium and palladium show much less affinity for hard ligands, such as oxygen or fluorine, as compared to nitrogen ligands, halogens, cyanide, and Group V donor atoms. Thus, a variety of organometallic complexes containing a pendant phosphonic acid group have been prepared and characterized. The scope of this review is restricted to phosphonic acid-functionalized organometallic compounds, including phosphine derivatives and also includes anionic phosphonate derivatives. Transition metal complexes containing phosphonic acids but without metal

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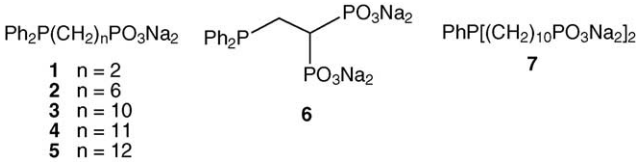
carbon bonds, and organosilicon phosphonic acids have been excluded. This present review provides an exhaustive literature survey through to September 2004.

2. Phosphonic acid-functionalized phosphines

Phosphonic acid-functionalized phosphines and their salts are important because of the high solubility in water that the phosphonate group affords. Water-soluble phosphines have received a great deal of attention due to their application in aqueous phase and biphasic homogeneous catalysis [1]. One of the first examples of a phosphonate-functionalized phosphine, 2-(diphenylphosphino)ethylphosphonate (**1**), was reported by Roundhill and co-workers in 1992 [2]. The compound was prepared by the action of $LiPPh_2$ on diethyl 2-bromoethylphosphonate in liquid NH_3/THF, followed by trans-esterification with $BrSiMe_3$ and hydrolysis of the bis-TMS ester. The disodium salt was obtained by neutralization with 6 M NaOH. The product was characterized by NMR and IR spectroscopies. The complex derived from Na_2PdCl_4 and five equivalents of **1** was found to have minor activity as a catalyst for the hydration of diethyl maleate [3]. Reaction of the sodium salt of **1** and $[\{Rh(COD)Cl\}_2]$ in methanol, followed by hydrogenolysis, gave a water-soluble phosphine stabilized cluster containing 2057 rhodium atoms [4].

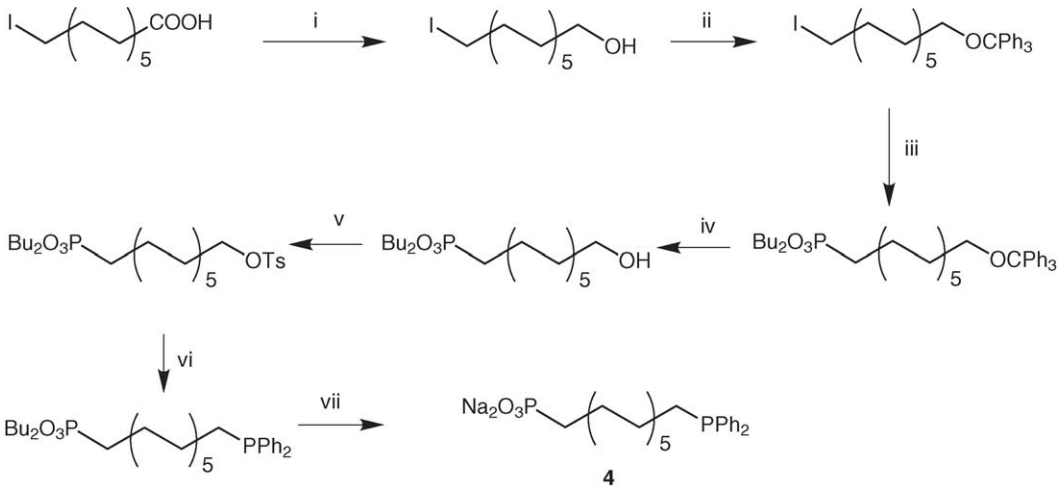


As the chain length of ω-(diphenylphosphino)alkylphosphonates increases, the potential for amphiphilic character arises. This can have a significant effect on the rate of reaction for hydrophobic substrates under aqueous or biphasic conditions. Thus, Bischoff et al. synthesized the series of compounds **2, 3, 5, 6**, and **7** to evaluate their activity as ligands in the rhodium-catalyzed hydroformylation of alkenes. Diphosphonate **6** was prepared by addition of a stoichiometric amount of Ph_2PH to $CH_2{=}C(PO_3Et_2)_2$ at room temperature, followed by acid hydrolysis. The other ligands were prepared by nucleophilic substitution of bromoalkylphosphonate esters by phosphide anion, followed by hydrolysis of the phosphonate ester by refluxing in degassed hydrochloric acid [5].

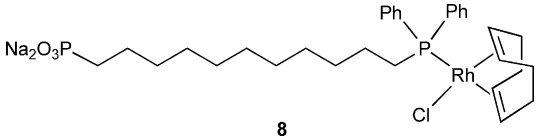
A comparison of the water solubilities of compounds **1**–**3** and **5**–**7** gave interesting results. The water solubility was greater for the six-carbon chain compound **2** (400–420 g/L) than the two-carbon chain compound **1** (340–370 g/L). Moreover, the water solubility of bis-phosphonate **6** (260–290 g/L) was less than that of **1**, and the bis-phosphonate **7**, possessing two 10-carbon alkylphosphonate arms, displayed considerably less water solubility than the single-armed 10-carbon alkylphosphonate **5** (*ca*. 100 g/L versus 320 g/L).

In contrast to these methods, Knight and co-workers, prepared ligand **4** from cyclodecanone in an eight-step sequence in 14% overall yield (Scheme 1) [6].

Addition of two equivalents of **4** to a methanolic solution of $[Rh(cod)Cl]_2$ resulted in the formation of the rhodium-phosphine species **8**, as evidenced by ^{31}P NMR spectroscopy. The ^{31}P NMR spectrum consisted of two peaks, a broad singlet at 26 ppm, attributable to the phosphonate group, and a doublet at 27 ppm (J_{RhP} = 154 Hz), consistent with proposed structure. No other peaks were present in the spectrum. Complex **8** was ineffective as a hydrogenation catalyst, suffering decomposition, however, the Rh complex derived from $[Rh(cod)_2]BF_4$ and three equivalents of **4** was active as catalyst for the room temperature hydrogenation of 1-decene in water.

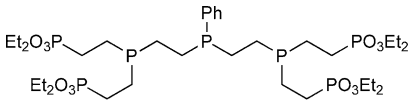


Scheme 1. Synthesis of phosphonate ligand **4**. *Reagents and Conditions:* (i) $NaBH_4$,$TiCl_4$; (ii) ph_3CCl, $Et_4N^+ClO_4^+$, 2, 4, 6-collidine; (iii) Na, HPO_3Bu_2; (iv) H_2, Pd–C, $HClO_4$; (v) TsCl, Et_3N, 0 °C; (vi) $LiPPh_2$, −78 °C; (vii) Me_3SiBr, H_2O, NaOH.



8

Poly-phosphonate *esters* **9**–**11** are themselves water-soluble and in fact are hygroscopic materials, difficult to isolate in an anhydrous state. The tris(phosphine)–phosphonate **9** (etpEPO), first reported by DuBois and co-workers in 1994, was prepared by free-radical addition of phenylphosphine to diethyl vinylphosphonate, reduction of the phosphonate groups by $LiAlH_4$, and a second free-radical addition to diethyl vinylphosphonate [7].



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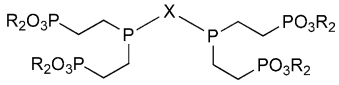
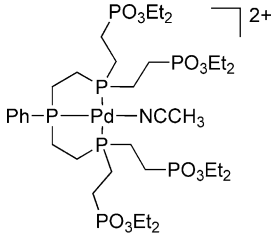


10a X = *o*-C_6H_4; R = CH_3
10b X = *o*-C_6H_4; R = CH_2CH_3
11c X = CH_2CH_2; R = CH_3
11d X = CH_2CH_2; R = CH_2CH_3

The bis(phosphines) **10** and **11** were prepared by a *t*-BuOK-catalyzed Michael addition of *o*-$C_6H_4(PH_2)_2$ or $H_2PCH_2CH_2PH_2$ to diethyl vinylphosphonate in boiling THF. The aryl derivative required a 6 h reflux, whereas the ethane derivative required 6 days. Their oily nature, coupled with residual unreacted vinylphosphonate (<5% by HPLC) precluded verification of their structure by elemental analysis. However, all compounds exhibited peaks corresponding to their parent ions $[M + H]^+$ using high-resolution FAB–MS.

The reaction of etpEPO with $[Pd(MeCN)_4](BF_4)_2$ gives water-soluble complex **12**, in which the metal is bound exclusively through the phosphines in a terdentate fashion [8]. The structurally similar bis-phosphine ligands **10** and **11** react efficiently with $[ReO_2I(PPh_3)_2]$ under biphasic conditions (H_2O/CH_2Cl_2) to give water-soluble complexes **13a**–**d** in 80–85% yield.



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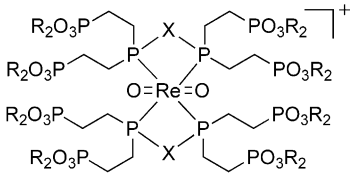
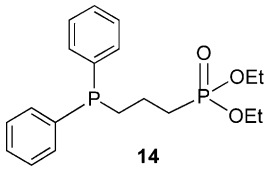


13a X = *o*-C_6H_4; R = Et
13b X = *o*-C_6H_4; R = Me
13c X = CH_2CH_2; R = Et
13d X = CH_2CH_2; R = Me

The usual mode of bonding in metal complexes with phosphonate ester-functionalized phosphines is through the phosphine only. Thus, the reaction of **14** with $PtCl_2(PhCN)_2$ gives the expected mixture of *cis*- and *trans*-$[PtCl_2L_2]$. The reaction of **14** with $PdCl_2$ was found to give *trans*-$[PdCl_2L_2]$ along with a small amount of the chloro-bridged dimer **15** [9].



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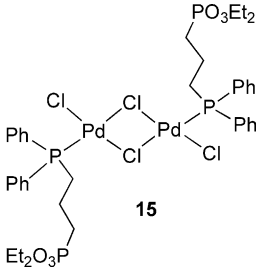
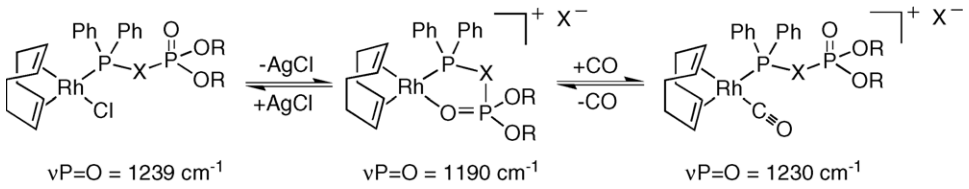


15

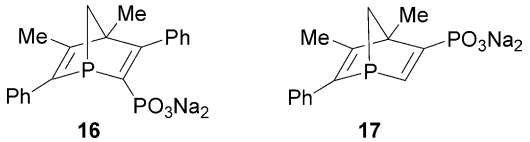
Under certain conditions, the donor properties of the P=O bond can enable phosphonate esters to act as ligands toward later transition metals [10], and phosphine–phosphonates may form *P*,*O*-chelates or open-chain phosphine complexes, depending on the ring size of the chelate [11]. For complexes derived from $[Rh(cod)Cl]_2$ and $Ph_2P(CH_2)_nPO_3Et_2$, where $n = 1$, 2, or 3, a halogen-free chelate could be obtained upon treatment with $AgBF_4$ or $AgPF_6$ (Scheme 2).

Analysis of the products by IR and ^{31}P NMR spectroscopies was consistent with the assumption of a P=O–Rh interaction, as evidenced by a pronounced shift in the P=O stretching frequency from 1239 to 1190 cm^{-1}, and a 3–7 ppm change of the chemical shift of the phosphonate phosphorus, as well as the additional splitting of the phosphonate resonance via P-Rh coupling in the NMR spectrum. The reversible nature of the phosphonate coordination was shown by coordination of CO to the complex, after which the IR spectrum again showed a P=O stretching frequency characteristic of a free phosphonate ester.

1-Phosphanorbornadienes have been shown to be excellent ligands for rhodium-catalyzed hydrogenation [12] and hydroformylation [13] of alkenes, and the sulfonated water-soluble version 3,4-dimethyl-2,5,6-tris(*p*-sulfonatophenyl)-1-phosphanorbornadiene (NORBOS) showed outstanding activity in the biphasic hydroformylation of propene. The phosphonate analogue has recently been introduced [14]. The synthesis of 1-phosphanorbornadienes involves the [4 + 2] cycloaddition of a transient 2*H*-phosphole with an alkyne [15]. The first compounds prepared were amides of 4,5-dimethyl-3,6-diphenyl-1-phosphanorbornadien-2-yl phosphonate, obtained from the reaction of diethyl- or dimorpholinophenylethynylphosphonamide and 2-phenyl-3,4-dimethyl-5*H*-phosphole, derived from the thermal isomerization of 1-phenyl-3,4-dimethylphosphole. These compounds were hydrolyzed by 3 M HCl in aqueous THF to give the corresponding phosphonic acid. Neutralization with NaOH gave the disodium salt **16**, which proved only sparingly soluble in water (20 mg/mL).



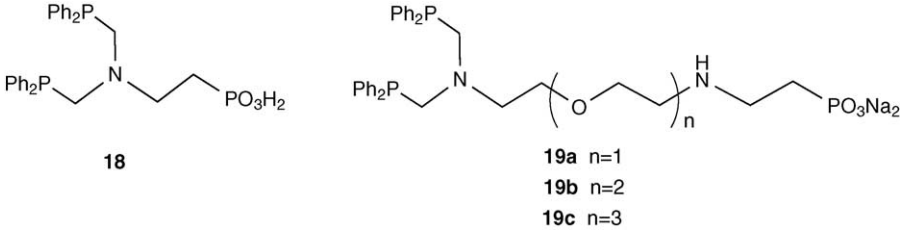
Scheme 2. Hemilabile interaction of phosphine–phosphonate ligand with Rh(I).



16 **17**

Using the same transient 2*H*-phosphole as in the previous synthesis, reaction with diethyl ethynylphosphonamide gave a 75% yield of a mixture of the two possible regioisomers with an α/β ratio of 3:1. The isomers were easily separated by column chromatography using silica gel. The ^{31}P NMR spectra of the isomers shows a characteristic AX spectrum for the α-isomer (δ −4.6, δ 26.0, $^{2}J_{PP}$ = 49 Hz), whereas the β-isomer shows two singlets at δ −22.1 and δ 26.1. Acid hydrolysis, followed by neutralization with NaOH, afforded the disodium salt **17**, which was much more readily soluble in water (230 mg/mL). Whereas **17** was demonstrated to be a good ligand for the biphasic rhodium-catalyzed hydrogenation of *Z*-α-(*N*-acetamido)cinnamic acid, ligand **16** was ineffective. This was interpreted as possibly due to the formation of a stable, *P*,*O*-chelated species $[RhL_2]^-$, which is catalytically inert.

The synthesis of a series of diphenylphosphino-functionalized alkylamine phosphonates, exemplified by structure **18**, has been reported by Fu and co-workers [16]. The compounds were readily prepared by the action of bis(hydroxymethyl) diphenylphosphonium chloride on 2-aminoethylphosphonic acid and its *N*-substituted derivatives. The water solubilities of the disodium salts of these compounds ranged from 0.13 to 0.29 g/mL. These workers have also reported the synthesis of ethoxylated derivatives **19a**–**c**. The water solubilities of these compounds were not quantified, but were stated to have higher water solubilities than $Ph_2PCH_2CH_2PO_3H_2$ or $Ph_2P(4\text{-}C_6H_4PO_3H_2)$, presumably as their disodium salts.



18

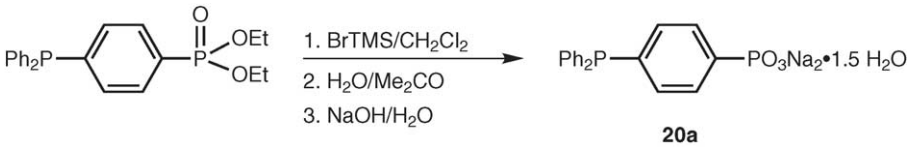
19a n=1
19b n=2
19c n=3

The reaction of phosphines **19a**–**c** with H_2PdCl_4 in refluxing *n*-butanol gave palladium complexes in which the ligands were bound to the metal through *P*-, *N*-, and *O*-coordination, as evidenced by XPS and NMR data. These complexes, although not structurally defined, were demonstrated to be active in the biphasic carbonylation of benzyl chloride.

Given the long history of success and widespread use of the archetypal water-soluble phosphine TPPTS (triphenylphosphine trisulfonate, $P(3\text{-}C_6H_4SO_3Na)_3$), it is not surprising that a number of phosphonated triarylphosphines have appeared in the literature. The first example of a phosphonate-functionalized triarylphosphine was $Ph_2P(4\text{-}C_6H_4PO_3Na_2)$ (triphenylphosphine monophosphonate, TPPMP) (**20a**) [17,18]. The three isomers can be prepared from the appropriate (diphenylphosphino)bromobenzenes via formation of the corresponding aryllithium reagent at −78 °C and reaction with diethyl chlorophosphate. The resulting phosphonate esters can then be cleaved to the free acids by known methods and neutralized with base to give the desired salts (Scheme 3).

There is a significant variation in the water solubility of the isomeric monophosphonates. The *para*-isomer is the most soluble (380–410 mg/mL), followed by the *meta*-isomer (190 mg/mL), and *ortho*-isomer (35 mg/mL). This can be compared to the monosulfonated analogue, TPPMS, $Ph_2P(3\text{-}C_6H_4SO_3Na)$, which has a water solubility of approximately 80 mg/mL at 20 °C.

Recrystallization of **20a** from aqueous methanol gave the solvated phosphonate $Na_2[(TPPMP)(H_2O)_3(CH_3OH)]\cdot CH_3OH$ and the crystal structure reveals some rather unusual features (Fig. 1). The unit cell contains two formula units bound together in a dimeric structure, which is supported by multiple anion–cation interactions and bridging water molecules. There are two discrete types of sodium coordination; in the first, two sodium cations Na(2) and Na(2′) are three-coordinate and bridge two phosphonate moieties via phosphoryl oxygen atoms, O(1) and O(2′); and O(1′) and O(2). The second type of sodium coordination involves



20a

Scheme 3. Synthesis of $Na_2[Ph_2P(4\text{-}C_6H_4PO_3)]\cdot 1.5H2O$ (**20a**).

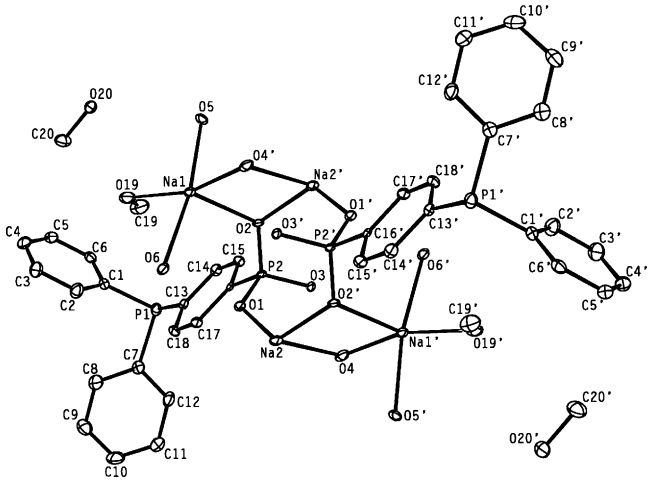
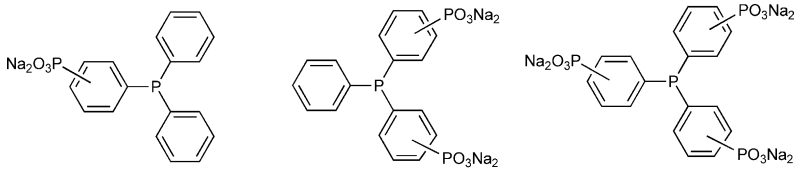


Fig. 1. ORTEP representation of $Na_2[(TPPMP)(H_2O)_3(CH_3OH)]\cdot CH_3OH$ [18].

bonding of Na(1) and Na(1′) to O(2) and O(2′), respectively giving rise to two distinct O–Na–O–Na rings and a larger P–O–Na–O–P–O–Na–O– ring via bridging water molecules. The cations Na(1) and Na(1′) are five-coordinate and stabilized by bonding to two further water molecules and a methanol molecule. The unit cell also contains two uncoordinated methanol molecules.

Variations on the preparation of TPPMP have been described. Instead of generating an aryllithium species via metal-halogen exchange, Villemin et al. introduced the diethylphosphonate group by the palladium-catalyzed phosphonylation of $4\text{-}BrC_6H_4PPh_2$ with diethyl phosphite [19].



20a *p*-isomer
20b *m*-isomer
20c *o*-isomer

21a *p, p*-isomer
21b *m, m*-isomer

22a *p, p, p*-isomer
22b *m, m, m*-isomer

Köckritz et al. first prepared the 4-halophenylphosphonate ester by the palladium-catalyzed phosphonylation of 1,4-dibromobenzene or 1-bromo-4-fluorobenzene with a dialkyl phosphite (ethyl or isopropyl ester), followed by a nucleophilic aromatic substitution reaction with $LiPPh_2$ to introduce the diphenylphosphino moiety [20]. This methodology was unsuccessful for the preparation of **20b** or **20c**, however. Reaction of 2- or 3-halophenylphosphonates with $LiPPh_2$ or by the use of *n*-BuLi followed by $ClPPh_2$ was reported to give only dealkylation products or cleavage of the diphenylphosphino group.

The use of consecutive Pd-catalyzed P–C coupling reactions and nucleophilic aromatic phosphanylation was explored in detail by Stelzer and co-workers, a strategy used to prepare **20a** and **20b**, as well as the bisphosphonate **21a** [21]. In one approach, (diphenylphosphino)bromobenzenes were obtained in good yield (62–76%) by the Pd-catalyzed reaction of iodobromobenzene with Ph_2PH. The reaction can be carried out on a relatively large (20 g) scale, and may be considered the method of choice for the preparation of (diphenylphosphino)bromobenzenes, particularly for the *ortho*-isomer, which can be quite difficult to obtain using other methods, especially on this scale. By using phenylphosphine instead of diphenylphosphine, the same methodology can be used to prepare bis-(4-bromophenyl)phenylphosphine, the precursor to bisphosphonate **21a**.

Palladium-catalyzed phosphonylation with diethyl phosphite allowed *p*-(diphenylphosphino)bromobenzene (not, apparently, the *meta*- or *ortho*-isomers) to be converted to the corresponding phosphonate ester and thence to **20a**. Starting with *para*- or *meta*-bromofluorobenzene, the fluoroarylphosphonate esters were also prepared. These compounds underwent nucleophilic substitution of the fluoro group by $KPPh_2$ (THF, room temperature, 3 h) to give the desired triarylphosphines, although competing ester dealkylation was observed. Ester dealkylation by metal phosphides during the nucleophilic aromatic substitution reaction can be avoided by using tetraalkylphosphonodiamides instead of dialkylphosphonate esters. Thus, Kant and Bischoff were able to prepare bisphosphonates **21a** and **21b** by the reaction of $PhPLi_2$ with $4\text{-}FC_6H_4P(O)(NEt_2)_2$ and $3\text{-}FC_6H_4P(O)(NEt_2)_2$, respectively [22]. The phosphonodiamide groups are stable to the reaction conditions (THF, 55 °C), but can readily be hydrolyzed by dilute mineral acid.

Nucleophilic aromatic substitution of fluoroarylphosphonodiamides was used by Schull et al. to prepare trisphosphonates **22a** and **22b** [23,24]. The phosphide anion was generated in situ by the reduction of a suspension of red phosphorus in liquid ammonia/THF with lithium or sodium metal. The presence of a proton source, such as *t*-BuOH facilitates the reduction. Addition of the fluroarylphosphonodiamide to the reaction mixture results in the nearly exclusive conversion to the desired triarylphosphine. After allowing the liquid ammonia to evaporate overnight, work-up consists of adding ether and water, filtering, and partitioning the phases. The product is located almost exclusively in the aqueous phase. It may be isolated by sparging the solution vigorously with nitrogen gas until a precipitate develops, or the free phosphonic acid may be obtained directly by acidification of the mixture with hydrochloric acid and refluxing. The use of 4-$FC_6H_4PO_3Et_2$ as a starting material led almost exclusively to the mono-dealkylation product, although it should be noted that the diisopropyl ester is stable to the reaction conditions. The ester is, however, less reactive than the phosphonodiamide species, and the product is invariably an oil, which is laborious to separate from any unreacted starting material.

The water solubility of *p*-TPPTP (**22a**) was determined to be approximately 550 mg/mL, which is surprisingly low when compared to the bis-phosphonate phosphines **21a** and **21b**, which are reported to have water solubilities of approximately 1000 mg/mL, or the tris-sulfonate TPPTS (approximately 1100 mg/mL). The unexpectedly low value may result, in part, from the extensive degree of hydration already present in the sample. The single crystal X-ray structure of **22a** was solved and was shown to contain 27 waters of hydration in the unit cell (Fig. 2) [25].

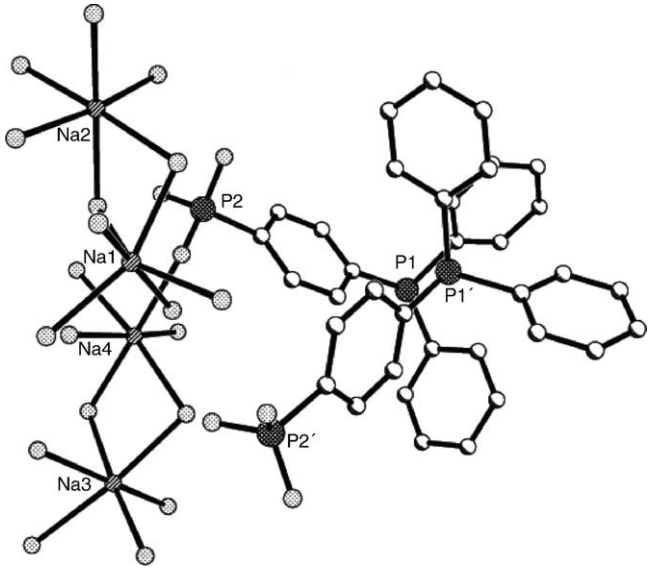


Fig. 2. ORTEP representation of *p*-TPPTP (**22a**) [25].

Phosphine ligand **22a** forms a stable complex with palladium(0), which was shown to be an active catalyst for the biphasic phosphonylation of phenyl triflate. A palladium(0) complex of **22a** was grafted onto silica gel and used as a supported catalyst for a phosphonylation reaction [26].

The reaction of 1.6 equivalents of *p*-$TPPTP(H)_6$ with K_2PtCl_4 in water gave *cis*-$[PtCl_2(p\text{-}TPPTP(H_6)_2]$, and when an aqueous solution of this complex was layered with 2-propanol, crystals of $[PtCl_2(p\text{-}TPPTP(H_7)_2]Cl_2{\cdot}4H_2O{\cdot}(CH_3CH(OH)CH_3)$ (**23**) were obtained (Fig. 3) [27]. Complex **23** contains a rare example of a protonated phospho-

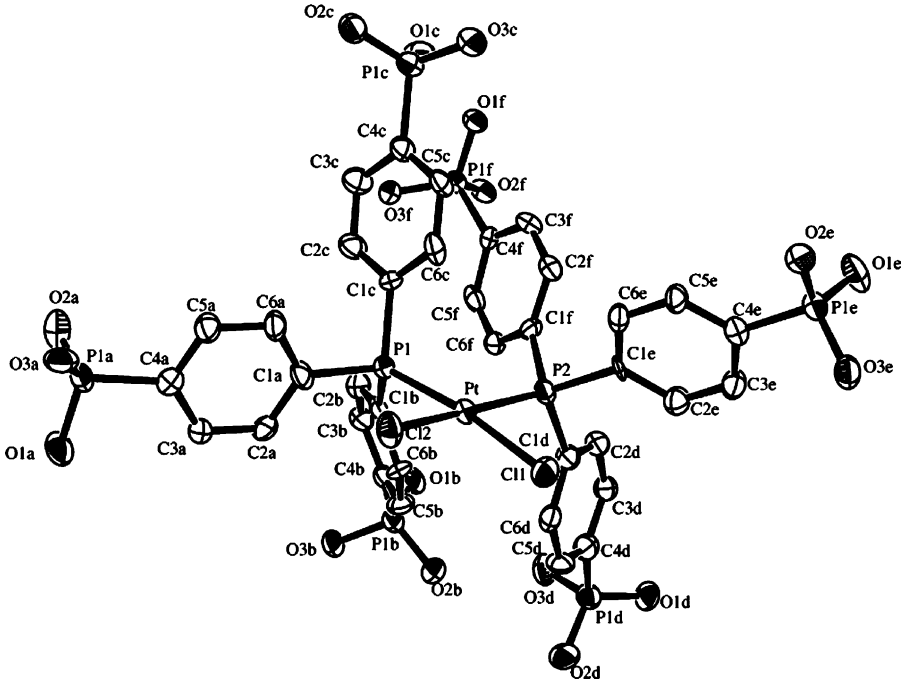


Fig. 3. ORTEP representation of platinum complex **23** [27].

nic acid moiety, which is involved in both intra- and intermolecular hydrogen bonding in the solid state. The exclusive formation of the *cis*-isomer may be due to the intra-molecular hydrogen bonding effect.

The *meta*-isomer **22b**, which was determined by single crystal X-ray diffraction to be a dihydrate in the crystalline state, had a water solubility of approximately 650 mg/mL [23]. The ORTEP representation of **22b** is shown in Fig. 4.

Phosphonic acids are known to form lamellar structures in the solid state. The phosphine **22b** also possesses a layered structure with the organic triphenylphosphine groups forming one layer and the phosphonic acid groups forming a second layer. A hydrogen-bonded network is formed within the phosphonic acid layer. The molecular drawing of **22b** is shown in Fig. 5.

Phosphine ligands **22a** and **22b** form stable complexes with Pt(II) and either *cis*- or *trans*-geometries were found depending on the nature of the ligand [26]. The molybdenum complex $Mo(CO)_5$(*m*-TPPTP(H_6)) was prepared via the reaction of $Mo(CO)_6$ and *m*-TPPTP in ethanol [26]. The complex was grafted onto an alumina surface and forms a single monolayer as evidenced by XPS, RBS, and AFM studies.

The applicability of the Pd-catalyzed coupling of Ph_2PH with aryl halides has been further extended to *o*- and *m*-iodobenzylhalides, which can then undergo an Arbuzov reaction to give the benzyl phosphonate [28]. Trans-esterification with $BrSiMe_3$, followed by hydrolysis and neutralization with NaOH afforded compounds **23a** and **23b**. The *meta*-isomer is considerably more water-soluble than the *ortho*-isomer (20 mg/mL versus 240 mg/mL at 20 °C).

Organophosphonic acids are known to form layered materials on reaction with metal ions. A number of reports on the use of phosphonic acid-functionalized phosphines in the formation of metal phosphonate-phosphine catalysts have recently appeared. Bischoff synthesized the hydroxyphosphonic acid **24** and prepared a mixed zirconium phosphonate with the formula $Zr(O_3PCH_3)_x(O_3PC_6H_{12}PO_3)_y$(**24**)$_z$, ($x+2y+z=2$) [29]. Rhodium was incorporated into this organic-inorganic polymer and the resulting supported catalyst used for the vapor-phase hydroformylation of propene to butanals. The catalyst showed high selectivity for aldehydes compared to other supported rhodium catalysts with a linear/branched ratio for butanals ranging from 2.7/1 to 3.5/1. The phosphonic acid **25**, originally reported by Dines and co-workers [30], was not considered a suitable ligand in these studies due to extensive formation of $H_2O_3PC_2H_4P(Me)Ph_2]^+I^-$ during ligand synthesis [29].

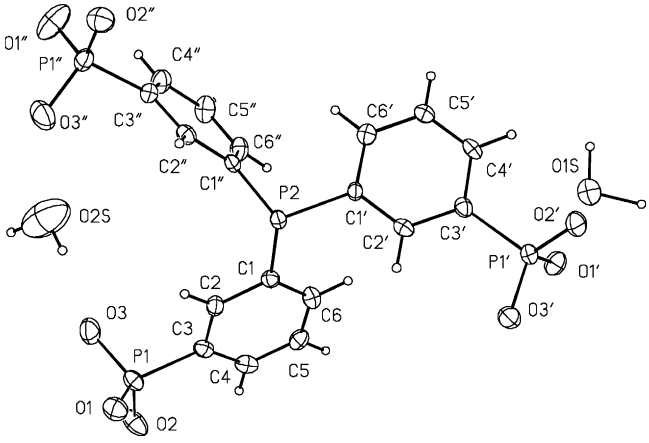


Fig. 4. ORTEP representation of *m*-TPPTP (**22b**).

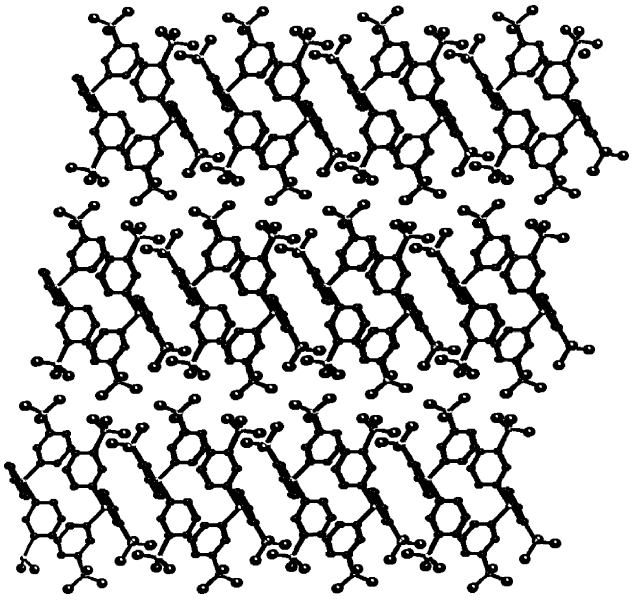
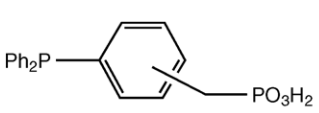
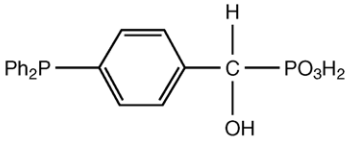


Fig. 5. Molecular drawing of **22b** showing layered structure of crystal lattice. View is approximately along the *a*-axis [26].

Villemin et al. also used the ligand *p*-TPPMP in combination with Pd(II) to prepare a zirconium phosphite-phosphonate supported catalyst for a competitive Heck coupling of iodobenzene and a number of iodobenzoates [19]. The study suggested that active palladium sites were present not only on the surface of the catalytic material, but within



23a *o*-isomer
23b *m*-isomer



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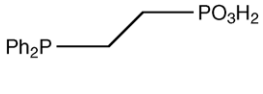

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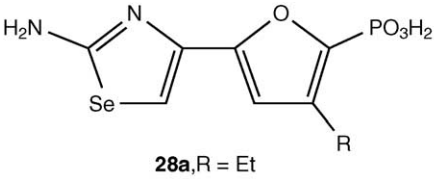
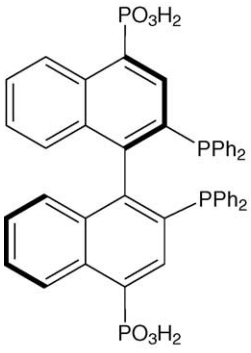
the lattice, which is shape selective. The authors proposed the structure shown in Fig. 6.

The chiral phosphine–phosphonic acid ligand **26** based on the BINAP platform was prepared by Kant et al. using established synthetic methodologies [31]. The monophosphonic acid was also reported. Ligand **26** was used in the biphasic rhodium-catalyzed asymmetric hydrogenation of dimethyl itaconate and hydroformylation of styrene. The highest enantioselectivity to date (26% ee) for biphasic rhodium-catalyzed hydroformylation of styrene was reported [32].



28a,R = Et
28b,R = SMe
28c,R = ^{i}Bu



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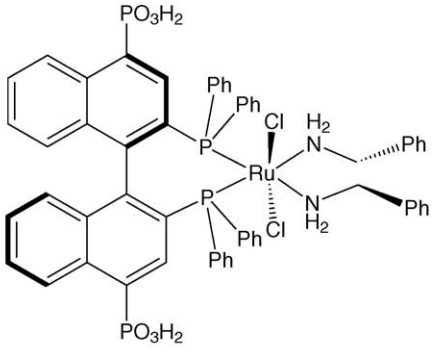

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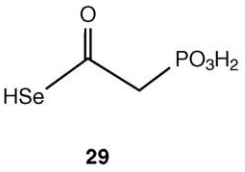
In 2003, Lin and co-workers described the use of ruthenium complex **27** in the formation of a chiral porous hybrid solid via the reaction of the phosphonic acid with $Zr(O^{t}Bu)_4$ in methanol. The resulting heterogeneous catalyst was used for the asymmetric hydrogenation of aromatic ketones with high enantioselectivity [33].

3. Phosphonic acid-functionalized organoselenium complexes

The chemistry of phosphonic acid derivatives of selenium is poorly developed, but a few examples of such compounds exist in the literature. Selenium-based phosphonic acids have been prepared as precursors or intermediates to a number of biologically active molecules and have been reported in the patent literature. The selenium-containing heteroaromatics **28a–c** were shown to be inhibitors for fructose-1, 6-bisphosphatase and were used in combination with insulin for the treatment of diabetes [34].



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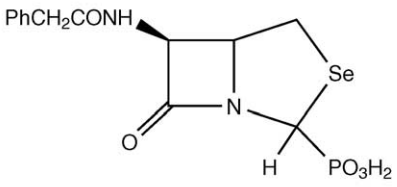

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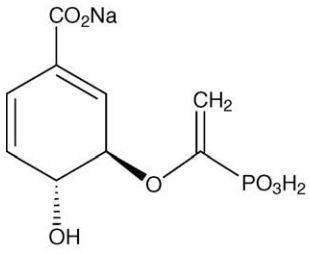
Phosphonic acid **29** is a precursor to a phosphonoformate with anti-viral properties [35] and the selenium-containing β-lactam **30** is a precursor to a potent anti-microbial agent [36]. The phosphonochorismic acid **31** is a mechanism-based mutase inactivator which was prepared from the selenium phosphonic acid **32** using hydrogen peroxide as an oxidant [37], and the unusual benoselenophene **33** was synthesized via the cyclization reaction of 2-phenylethynylphosphonic acid with selenium dioxide and HBr in ethereal solvent [38].



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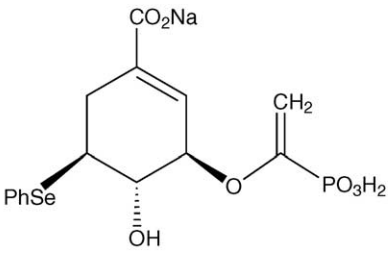

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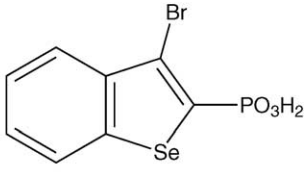

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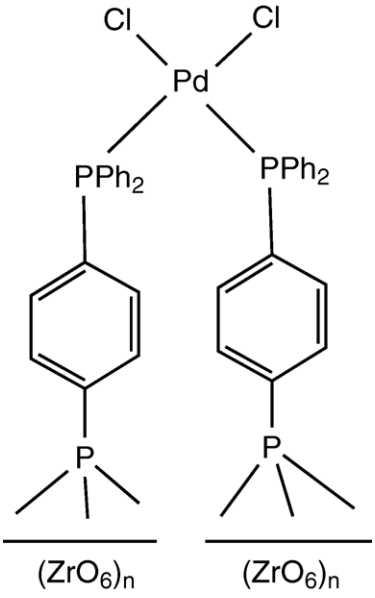
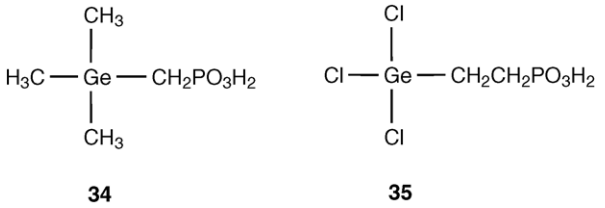


Fig. 6. Proposed structure of Zr-phosphite-phosphonate supported Pd(II)–*p*-TPPTP complex.

4. Phosphonic acid-functionalized organogermanium complexes

The Arbuzov reaction is frequently employed for the synthesis of organophosphonates which in turn are useful precursors to mono and diphosphonic acids via hydrolysis. The reaction of triethylphosphite with $ClCH_2Ge(CH_3)_3$, followed by acid hydrolysis yielded the phosphonic acid-functionalized organogermanium complex **34** [39]. No further reaction chemistry of this unusual phosphonic acid was reported. The related trichlorogermanium complex **35** reacts with ammonia in methanol at 0 °C to a give a oxygermylalkanephosphonate polymer [40].

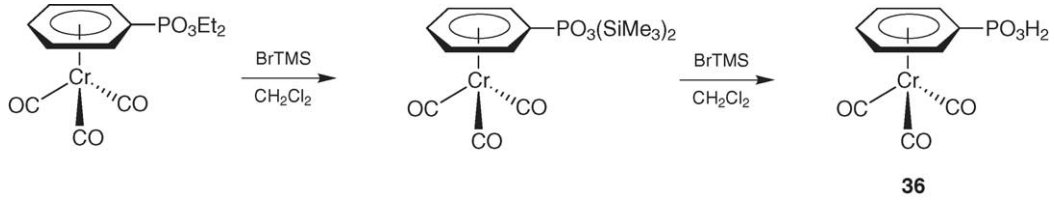


5. Phosphonic acid-functionalized organomercury complexes

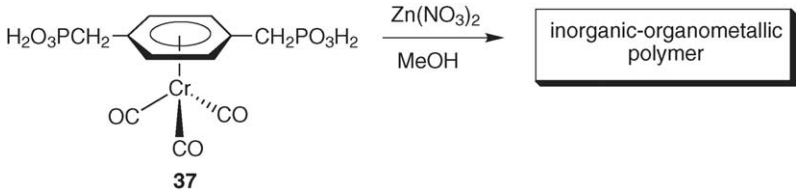
Only one example of a phosphonic acid containing a mercury–carbon bond has been described. Reaction of the mercury acetate complex $H_2NOCH_2CH(OCH_3)CH_2HgAc$, with the thiol, $HSCH_2CH_2PO_3H_2$ gave the phosphonic acid $H_2NOCH_2CH(OCH_3)CH_2HgS\ CH_2CH_2PO_3H_2$. This mercury phosphonic acid reacts with the enzyme aspartate aminotransferase to give a stable enzyme complex, which was analyzed using absorption spectroscopy [41].

6. Phosphonic acid-functionalized arene complexes of chromium

Phosphonic acids derivatives of arene chromium tricarbonyl complexes were first reported by Deemie and Knight in 1997 [42]. The classical synthetic procedure for arene chromium tricarbonyl involving displacement of carbon monoxide with the appropriate arene could not be used for phosphonic acid-functionalized arenes, and an alternative synthesis involving formation of aryl phosphonic acid diethyl ester complexes followed by trans-esterification using bromotrimethylsilane and hydrolysis with water, was described. Scheme 4 shows a representative synthesis of $[\eta^6\text{-}C_6H_5(PO_3H_2)]Cr(CO)_3$ (**36**). The phosphonic acid



Scheme 4. Synthesis of chromium phenylphosphonic acid tricarbonyl complex **36**.



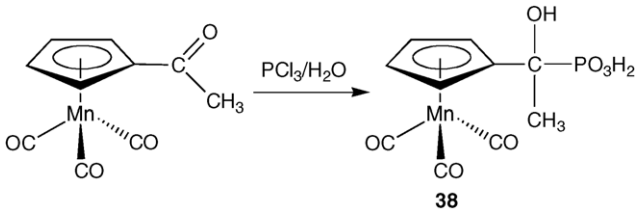
Scheme 5. Formation of phosphonate supported chromium arene tricarbonyl complex **37**.

complexes are highly unstable to oxygen and light, yielding chromium oxide on decomposition.

The crystal structure of the xylenyl bisphosphonic acid complex $[\eta^6\text{-}C_6H_4(CH_2PO_3H_2)_2]Cr(CO)_3$ (**37**) was reported [43] and shows that the phosphonic acid groups are *syn* to one another and directed away from the chromium-coordinated carbonyl ligands. The substituted arene ring is also *syn*-eclipsed (*EE*) with respect to the CO ligands. The organometallic phosphonic acid **37** forms a stable hybrid inorganic–organometallic material on reaction with Zn(II) (Scheme 5). The hybrid material contains intact arene chromium tricarbonyl moieties, is amorphous as shown by powder X-ray diffraction, and acts as a catalyst for the oligomerization of phenylacetylene [44].

7. Phosphonic acid-functionalized organomanganese complexes

Only a single organomanganese phosphonic acid has been reported in the literature. The reaction of acetylcyclopentadienylmanganese tricarbonyl with PCl_3, followed by hydrolysis, gave the hydroxyphosphonic acid complex **38** in 46% yield (Scheme 6) [45].



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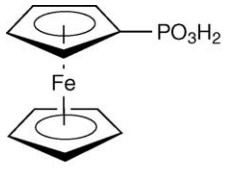
Scheme 6. Synthesis of α-hydroxyphosphonic acid manganese complex **38**.

8. Phosphonic acid-functionalized organometallic complexes of iron, ruthenium, and osmium

Ferrocene complexes are well known for their rich electrochemistry and application in materials chemistry and catalysis. Not surprisingly, phosphonic acid derivatives of ferrocene have received attention. The first phosphonic acid derivative of ferrocene, $FcP(O)(OH)_2$ (**39**) is described in *Chemical Abstracts* [46], although the cited US Patent describes only the ferrocenyl *phosphinic* acid FcP(O)(OH) [47]. Compounds **39** and **40** were prepared by Henderson and co-workers via the reaction of lithioferrocene or dilithioferrocene and chlorodiethylphosphate in THF or petroleum spirits [48]. An alternative phosphonation of ferrocene using H_3PO_4 was reported by Mu, although no experimental details or yields were recorded [49]. While the X-ray crystal structures of **39** and **40** have not yet been reported, those of related ferrocene derivatives **41** and **42** ($n = 1$) have been solved [48]. As expected, the X-ray crystal structures reveal extensive hydrogen bonding in the solid state. Electrospray mass spectroscopy was also used to characterize the phosphonic acids. Compounds **41** and **42** were prepared using hydrolytic cleavage of the corresponding alkyl esters. In contrast to the behavior of the phosphonic acid **22**, the ferrocene phosphonic acids form Pt(II) complexes in which the phosphonate coordinates in a bidentate chelating fashion to the platinum ion, e.g. $[FcPO_3Pt(PPh_3)_2]$. Complexes $[FcCH_2PO_3Pt(PPh_3)_2]$ and $[FcCH_2CH_2PO_3Pt(PPh_3)_2]$ exhibited moderate anticancer activity. Interestingly, the ferrocene phosphonic acid **41** ($n = 2$) can be reduced to a rare example of an air-stable primary phosphine using diazomethane followed by Me_3SiCl–$LiAlH_4$ [50].



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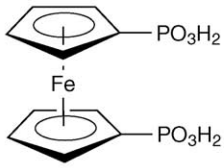

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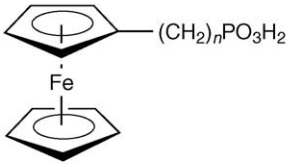
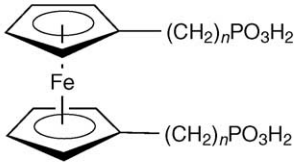
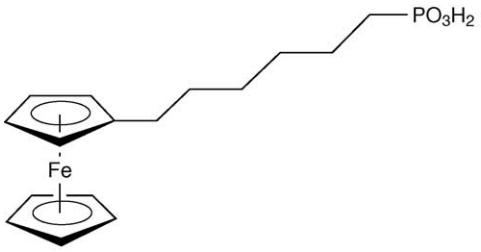


41 ($n = 1, 2$)



42 ($n = 1, 2$)

Hexylferrocene phosphonic acid **43** was synthesized from corresponding diethyl ester again using trans-esterification with Br–TMS and hydrolysis in methanol [51]. Zotti and co-workers studied the absorption of **43** onto ITO surfaces and amino-primed ITO electrodes. The resulting monolayers were shown to be stable in acetonitrile, and that domains of self-interacting and free ferrocenes were formed [52]. The electroactive probe molecules **44**, were prepared using a similar protocol by Mallouk [53] and Hong, respectively [54]. The surface adsorption and electrochemistry of the longer chain phosphonic acid, 11-ferrocenylundecanephosphonic acid, was also studied [55]. The π-conjugated ferrocenyl molecules **45** and **46** have recently been prepared using a palladium-catalyzed Heck reaction of the diethyl ester precursor [56,57]. Compounds **45** and **46** were studied using cyclic voltametry, absorption spectroscopy and ^{13}C NMR spectroscopy to probe the electronic effects of the phosphonate group [58]. The phosphonic acid **45** can be bound to metal oxide colloids, such as SnO_2 and TiO_2 [59].



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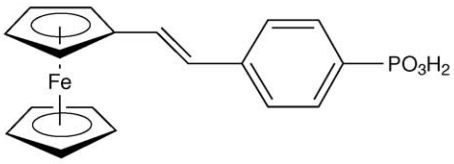

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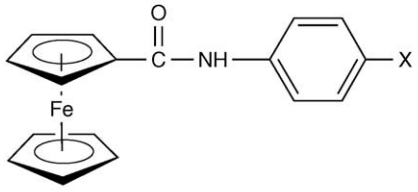
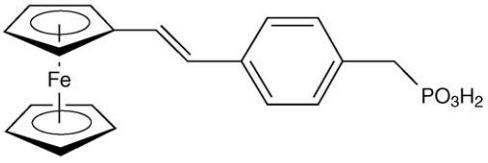


44a X = PO_3H_2
44b X = $CH_2PO_3H_2$



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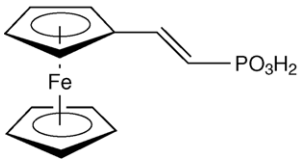
The vinylphosphonic acid **47** was prepared from the phosphonate ester using standard de-alkylation procedures [60] with the (*E*)-isomer being formed exclusively. The β-nitrophosphonic acid **48** was synthesized using a Michael addition reaction [61] and the arylphosphonic acid **49** was prepared using a palladium-catalyzed phosphonylation of an aryl iodide using the secondary phosphite $HP(O)(OSiMe_3)_2$ followed by hydrolysis [62]. To the best of our knowledge, this is the first report of a metal-catalyzed addition of a secondary silylphosphite to an aryl halide.



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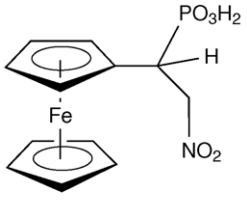

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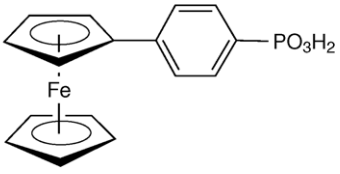

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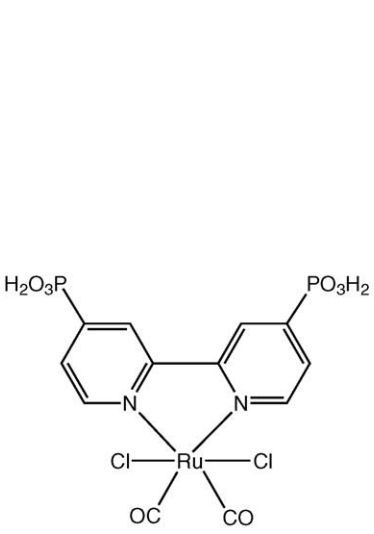
Phosphonic acid-functionalized complexes of ruthenium have been studied for their photochemical and electrochemical properties. Haukka and co-workers prepared a series of octahedral monobipyridine dicarbonyl complexes of ruthenium(II) and studied the electronic effects of substituents in the 4 and 4′ positions of the bipyridine ligand [63]. The electronic characters of the substituents were correlated with the carbonyl absorption bands in the infra-red spectra. It was shown that the electron withdrawing phosphonic acid groups in **50** shifted the CO stretching bands to higher wavenumbers compared to the unsubstituted complex. The electrochemical properties of **50** were also reported [64].

Only one phosphonic acid-functionalized organo–osmium complex have been reported. The water-soluble osmium(II) porphyrinate carbonyl **51**, with phosphonic acid groups in the *para*-position of the phenyl rings, was synthesized via an Arbuzov reaction followed by saponification of the resulting phosphonate ester using TMS–Br/KOH. The complex in the deprotonated anionic phosphonate form represents a rare example of a water-soluble porphyrin system with anionic functional groups.



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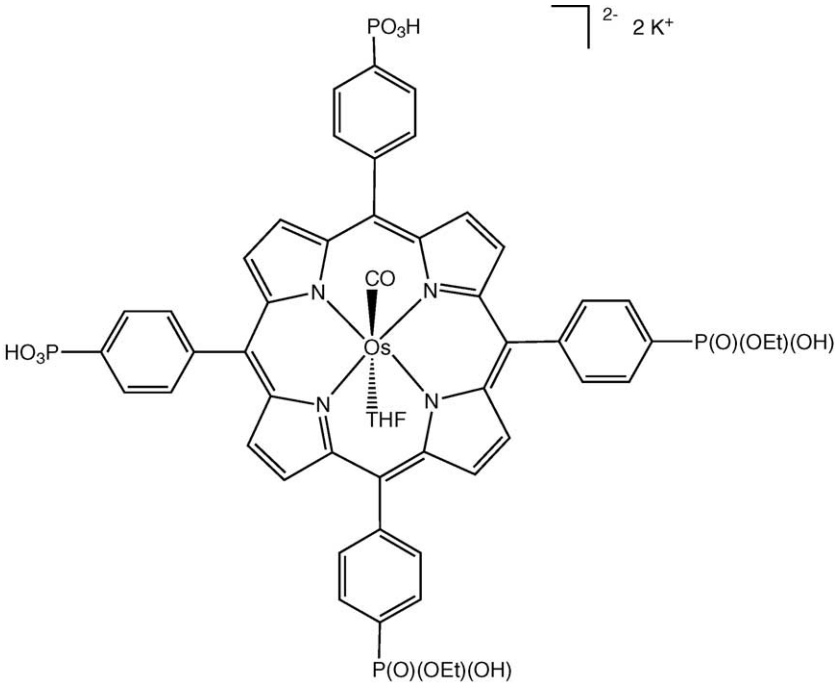

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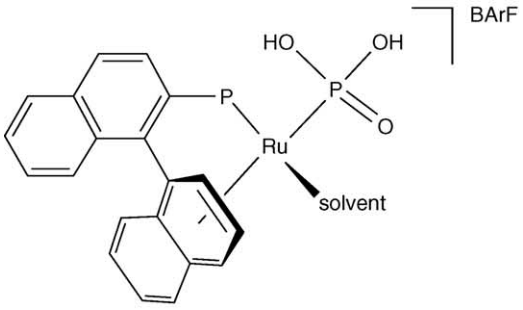
9. Metallo-phosphonic acids

Very few examples of metallo-phosphonic acids, M–P(O)(OH)$_2$ have been reported in the literature. Pregosin and co-workers recently described the synthesis and ^{31}P NMR characterization of a new mononuclear ruthenium(II) complex **52** containing a coordinated phosphonic acid ligand [65]. Complex **52** is solvent stabilized and converts to the dimer **53** on solvent removal and work-up. The crystal structure of **53** was solved and shows the presence of P=O and P–OH bonds. Extensive hydrogen bonding to solvent THF molecules is present. The triflate salt analog of **52** was also reported.

The novel organometallic tripodal tris-phosphonic acid **53** was formed from the corresponding methyl ester via hydrolysis in boiling water [66]. This acid is unusually strong (pK_{a_1}, 2.0; pK_{a_2}, 4.0; pK_{a_3}, 6.3; pK_{a_4}, 9.6) and reacts with glass to give the water-soluble six-coordinate silicon complex **54**. The crystal structure of the related potassium salt K[(η^6-C_5H_5)Co{P(O)(OH)$_2$}$_3$] was also reported.



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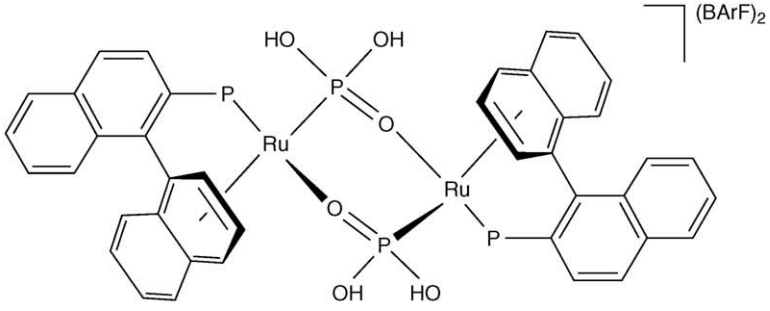

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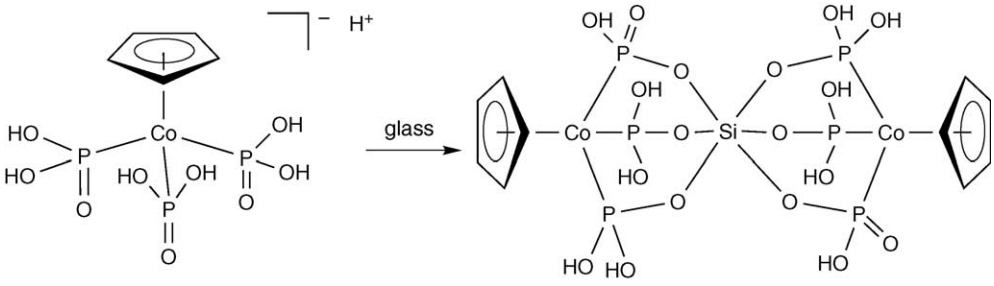

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