

Charged ligands for catalyst immobilisation and analysis

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Received 9th January 2008, Accepted 18th March 2008

First published as an Advance Article on the web 22nd April 2008

DOI: 10.1039/b800371h

Ligands involved in organometallic chemistry have been functionalised at locations somewhat removed from the binding site for diverse reasons, including modification of electronic and steric characteristics, improving solubility, to confer chirality, to add a spectroscopic “handle”, to facilitate electron-transfer processes or for spin-labelling. Here, the focus is specifically on catalytically active metal complexes in which a charged or highly polar group has been appended to the periphery of one or more of the ligands. For the most part, the motivation has been to alter the solubility properties of the catalytic metal complex to which it is attached, for the purposes of immobilisation in another phase (water, ionic liquids, etc.) and improvement of the green credentials of the process. However, other uses are also becoming recognised, for example to aid *in situ* analysis of catalysts by electrospray ionisation mass spectrometry.

Introduction

Great effort is expended by many researchers on ligand design and synthesis, nearly always involving direct modification of the coordination environment at the metal centre. Numerous reasons drive this research, but most importantly, powerful steric and electronic control can be exerted over the properties of the metal, and these effects are particularly significant in facilitating and enhancing catalytic behaviour. The payoffs from increasing catalyst reactivity, lifetime, chemoselectivity and enantioselectivity are enormous: cleaner, faster and cheaper reactions as well as the development of new transformations that can change the way in which chemists approach the art of making molecules.

Less work has been done on modifying ligands at sites remote from the metal centre, and with good cause: the payoff is more obscure. If the changes made fail to affect the reactivity of the metal complex, why bother? This Perspective tackles that question, and focuses on examples in which a charged

appendage (or “tag”) has been tethered to the ligand periphery. The motivation for this type of alteration was first spurred by the ability of the charged functional group to confer dramatically different solubility properties on the metal complex to which it is (indirectly) bound. In particular, water solubility is highly desirable in biphasic catalysis, whereby ease of separation of catalyst from products is added to the more general advantages of homogeneous catalysis (mild conditions, selectivity, the ability to rationally optimise the system, *etc.*). The recent rise in popularity of ionic liquids (IL) as novel reaction media has reinvigorated the strategy of functionalising ligands with charged tags, this time to facilitate the immobilisation of catalysts in ionic liquid phases. Contemporaneously, it was also illustrated by a number of groups that charged tags bestow upon ligands (and their complexes) an unusual advantage in their characterisation: they may now be analysed rapidly at extraordinarily high levels of sensitivity using electrospray ionisation mass spectrometry (ESI-MS). ESI-MS can handle complicated mixtures with ease, so a synergy was established: charged tags not only conferred desirable solubility properties on catalysts, they also enabled the catalytic system in which they were involved to be studied using a powerful approach

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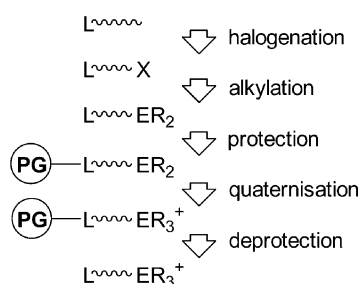
not available to their neutral predecessors. This Perspective will examine the extent to which this synergy has been realised.

Schemes have been drawn to highlight the tagged ligand; metal complexes, counterions *etc.* have been de-emphasised (greyed out). Brief details on reaction conditions and reagents are described in the captions for clarity.

Synthetic strategies

Ideally, synthesis of a functionalised ligand should involve a single step and quantitative yield, and appending a charge is no exception. Direct sulfonation with fuming sulfuric acid ("oleum", containing 20–65% SO₃ in conc. H₂SO₄) is the only strategy that comes close to attaining this challenging goal. It is an efficient way of attaching –SO₃H to the aryl group(s) of a ligand; neutralisation with sodium hydroxide provides water-soluble L–SO₃[–] Na⁺, and has been extensively used to render phosphines and, to a lesser extent, bipyridines water-soluble.

Appending other charged entities, such as ammonium or phosphonium groups, is more synthetically challenging, typically requiring a sequence of reactions such as halogenation, alkylation, protection of the ligand (in some cases), quaternisation of the attached amine or phosphine, followed by deprotection (Scheme 1). A variety of synthetic strategies have been applied to this problem, primarily associated with finding a suitable protecting group to ensure L–ER₃⁺ (E = N, P) is formed in preference to ⁺RL–ER₂; L has been protected by coordination to O, boranes and metal fragments. Ligands not susceptible to alkylation at the binding site (or that are already bound to the desired metal) are correspondingly easier to prepare.



Scheme 1 Appending a charged tag of the type –ER₃⁺ to a generic ligand L (X = halogen; R = H, alkyl or aryl; E = N or P; PG = protecting group). The protection and deprotection steps may be omitted when the ligand binding site(s) is not itself prone to quaternisation.

Carboxylates are another option for conferring water-solubility on ligands. They have been less frequently employed than sulfonates, perhaps due to the fact that they are somewhat less innocent than other options when it comes to interfering with coordination to metals (carboxylates are decent ligands for many metal centres themselves). Borates have also been employed as tethered anionic groups. Much of the work in this area has in fact been done with the intention of making zwitterionic complexes, but the synthetic strategies are of interest as the charged precursors are often of relevance. The distinction is somewhat blurred, but tris(pyrazolyl)borates are not included in this class of ligands; while the charge on the borate is remote from the metal center, such complexes are rarely formally anionic (and are hence more

akin to cyclopentadienyl complexes) and are not considered in this Perspective.

A somewhat less frequently employed strategy is to attach functionality that is not in itself charged but has a high affinity for charged species through non-covalent interactions. Examples include crown ethers, which possess a high equilibrium constant and selectivity for alkali metal ions, and proton sponges, with a high Brønsted basicity and selectivity for protons. Attaching these groups confers many of the advantages of tethering a permanent charge, with the added benefit that the addition of the charge is reversible (Fig. 1).

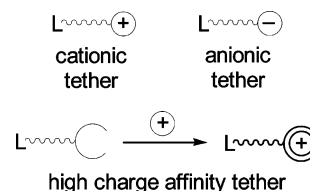


Fig. 1 The three types of charged ligand: cationic tether, anionic tether, and a tether with a very high affinity for cationic species *e.g.* crown ethers, polyethers, proton sponges.

While the conceptually related polyethylene glycol tethers provide desirable solubility characteristics for immobilization or spent catalyst removal and have been attached to dipyriddy ligands,¹ cyclopentadienyl ligands² and *N*-heterocyclic carbenes,³ they are not considered here because they do not have a uniform masses and are hence less useful in ESI-MS studies of mixtures (though single PEG oligomers would work well and are commercially available).

ESI-MS

ESI-MS was developed in the late 1980s by Fenn and co-workers⁴ and exploded in popularity in the 1990s due to its ability to analyse thermally fragile, highly polar biomolecules.⁵ Meanwhile, it was rather less widely embraced by organometallic chemists who found its inability to detect neutral molecules, preference for polar solvents and wet environment compromised its usefulness.⁶ However, its fundamental ability to transfer ions from solution to gas phase with little or no fragmentation (hence enabling the direct study of complex mixtures) coupled with the standard advantages of a mass spectrometric approach (speed, sensitivity) means that the employment of ESI-MS in the investigation of catalytic mechanisms continues to grow.^{7–13} Further broadening of the power of the technique, notably in facilitating gas-phase reactivity studies, have been developed by various groups including those of Chen¹⁴ and O'Hair.¹⁵

Classes of ligand: phosphines

Sulfonated phosphines were among the first developed for aqueous biphasic catalysis. Treatment of triphenylphosphine with fuming sulfuric acid followed by careful neutralisation with NaOH produces (depending on the conditions and stoichiometry) PPh_{3–*n*}(*m*-C₆H₄SO₃Na)_{*n*} (*n* = 1–3).¹⁶ This synthesis has been adopted for many other aryl phosphines (Fig. 2), and been improved by employing an H₂SO₄–B(OH)₃–SO₃ system that reduces unwanted formation of phosphine oxides.¹⁷

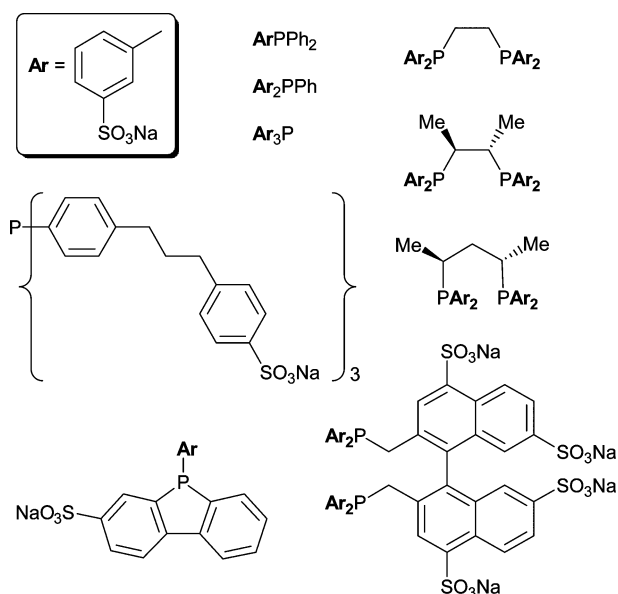


Fig. 2 Some sulfonated phosphines. Syntheses of all nine of these ligands may be found in Volume 32 of *Inorg. Synth.*^{18–21}

Sulfonated phosphines may be characterized routinely by negative ion ESI-MS; $P(m\text{-C}_6\text{H}_4\text{SO}_3\text{Na})_3$, for example, provides strong ions corresponding to $[P(m\text{-C}_6\text{H}_4\text{SO}_3)_3\text{Na}_{3-n}]^{n-}$ ($n = 1, 2, 3$). No one, however, seems to have exploited this characteristic in studying catalytic systems, almost certainly because a catalytic system composed of a mixture of species with multiple multi-anionic ligands provides a combinatorial complexity of ions that is very difficult to disentangle. This complication is in evidence even in simple systems such as $[\text{Ru}_6\text{C}(\text{CO})_{16}\{P(m\text{-C}_6\text{H}_4\text{SO}_3\text{Na})_3\}]^{3-}$, which provides strong signals for $[M]^{3-}$, $[M + \text{Na}]^{2-}$ and $[M + 2\text{Na}]^{-}$ (Fig. 3).²² Multiply-charged anions have only a limited existence in the gas phase (at low m/z values, they charge-reduce through electron evaporation),²³ and the potential for ion pairing with cations other than Na^+ (e.g. H^+ , K^+) adds to the confusion.

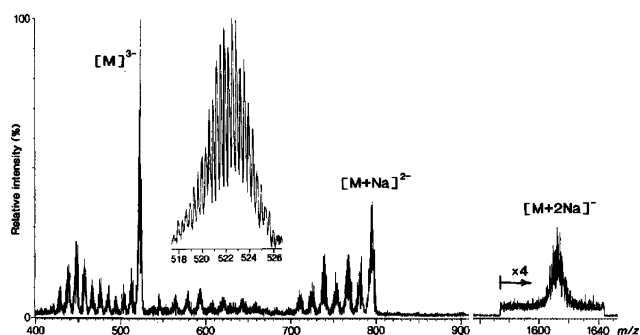
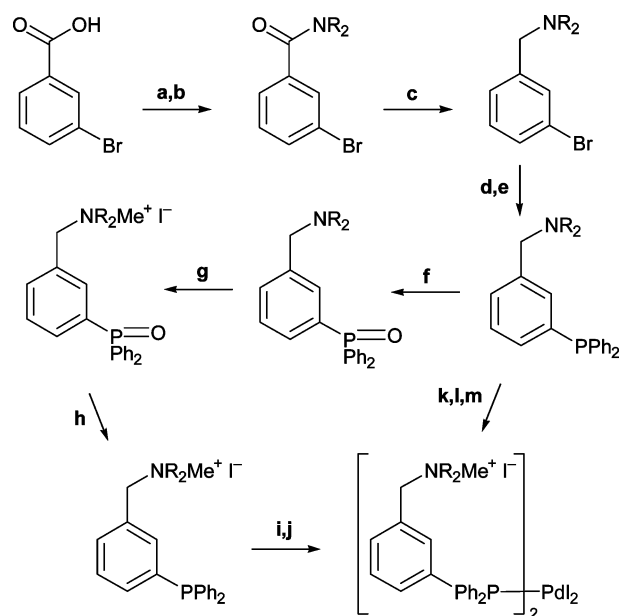


Fig. 3 Negative ion electrospray mass spectrum of $[\text{Ru}_6\text{C}(\text{CO})_{16}\{P(m\text{-C}_6\text{H}_4\text{SO}_3\text{Na})_3\}]^{3-}$ in water under conditions designed to induce some fragmentation. Inset: Expansion of the peak at $523\ m/z$, showing the mass separation of $1/3\ m/z$ between peaks in the isotope pattern. Reproduced with permission from ref. 22. Copyright 1998, Elsevier.

Sulfonated phosphines have not yet been employed as ESI-MS probes for understanding catalytic reactions in any solvent. Crucial to the success of analyzing a complex mixture is the requirement that each species present in the solution is represented by as few signals as possible, and ideally the correspondence

is one-to-one, making spectra easy to interpret and minimizing the chances of accidental overlap between species. As such, the worst candidates for ESI-MS analysis are also those that are possibly the most useful in biphasic catalysis: the tris-sulfonated phosphines. These are highly water-soluble, but the superfluity of charged groups makes for complicated spectra, especially when multiple ligands are present. A better choice for analysis are singly-sulfonated ligands, which provide just one charge per ligand.

Attaching a pendant ammonium group to a phosphine ligand can be synthetically challenging even though the preparation of mixed P/N ligands is not difficult, because the phosphine tends to be more reactive towards alkylation than a dialkylamino group. For example, *m*-bromobenzoic acid can be converted into lithiated dialkylbenzylamine in four steps, which when reacted with PPh_2Cl generates $\text{PPh}_2(m\text{-C}_6\text{H}_4\text{CH}_2\text{NR}_2)$ (Scheme 2).²⁴ However, alkylation with MeI occurs exclusively at the phosphorus atom, so the ligand must first be converted into the phosphine oxide, alkylated at nitrogen and reduced back to the phosphine using HSiCl_3 . Palladium complexes of this ligand could be generated in conventional fashion. Alternatively, the high affinity of palladium for P over N could be used to first generate the neutral bis(phosphine) complex followed by alkylation of N with MeI .

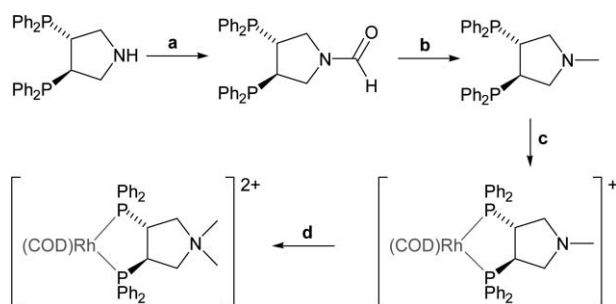


Scheme 2 Reagents and conditions: a SOCl_2 ; b HNR_2 ($\text{R} = \text{Me}, ^n\text{Bu}$); c LiAlH_4 ; d $^n\text{BuLi}$, $-78\ ^\circ\text{C}$; e PPh_2Cl ; f H_2O_2 ; g MeI , toluene; h HSiCl_3 ; i $\text{PdBr}_2(\text{cyclooctadiene})$, CH_2Cl_2 ; j NaI ; k $\text{PdBr}_2(\text{cyclooctadiene})$, CH_2Cl_2 ; l MeI ; m NaI .

A related series of ligands, 4-mono- and 3,5-bis(dimethylamino)methyl-functionalised triarylphosphines, can be accessed using a similar synthetic scheme, and complexes of the type $\text{ClAu}(\text{PR}_3)$ can be prepared.²⁵ Alkylation of these complexes with benzyl bromide proceeds efficiently, with the phosphorus effectively protected by the Au–P coordination, generating ligands with up to six ammonium groups that are soluble in polar solvents only. Similarly, protonation of the neutral complexes produces water-soluble HCl salts. Interestingly, addition of H_3PO_4 produces a very insoluble polymeric network product, allowing the facile

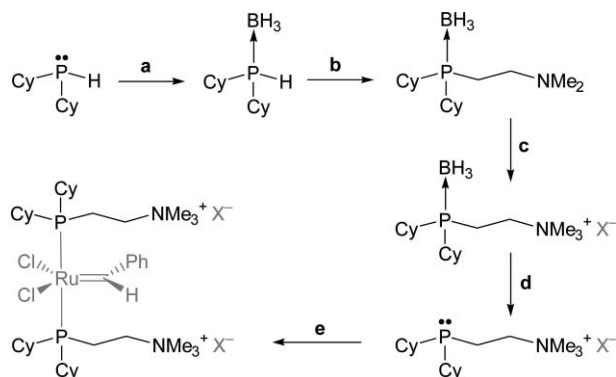
recovery of such gold(I) phosphine complexes from almost any solvent.

Other protecting groups for phosphines have been experimented with, including metal complexes, but even $W(CO)_6$, which reacts selectively with $PPh_2(p-C_6H_4NMe_2)$ at the phosphorus and is readily methylated at the nitrogen to form $[W(CO)_5PPh_2(p-C_6H_4NMe_3)] [CH_3SO_4]$, suffers from the drawback that subsequent deprotection is problematic.²⁶ The final option is to coordinate an uncharged ligand, and then quaternise it on the metal, as exemplified by Nagel's water-soluble rhodium complex with a charged chiral chelating bisphosphine ligand (Scheme 3).²⁷



Scheme 3 Synthesis of a charged ligand after binding to the metal. *Reagents and conditions:* **a** 20 atm H_2 , 120 °C, 25 h; **b** $LiAlH_4/THF$, 24 h, reflux, 1 h; **c** $Rh(COD)BF_4$, CH_2Cl_2 , 24 h; **d** $(CH_3)_3OBF_4$, CH_2Cl_2 , 24 h.

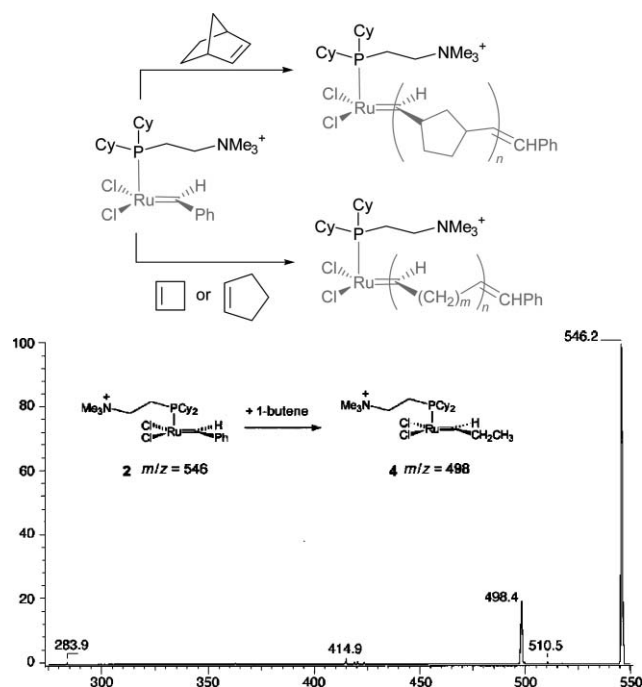
Preparation of water-soluble, *aliphatic* phosphines is complicated by increased sensitivity to oxidation and tendency to react with other electrophiles. However, protection of primary or secondary phosphines with borane generates $R_{3-n}H_nP-BH_3$ (R = alkyl, n = 1 or 2), which may be readily lithiated and treated with amine-functionalised alkyl halides to form, for example, $R_{3-n}(Me_2NCH_2CH_2)_nP-BH_3$.²⁸ Alkylation and deprotection with morpholine produces the charged phosphines $[R_n(Me_3NCH_2CH_2)_{3-n}P]^{n+}$ (Scheme 4).



Scheme 4 Synthesis of water-soluble, aliphatic phosphines (Cy = cyclohexyl). *Reagents and conditions:* **a** BH_3-THF ; **b** $n-BuLi$, THF, -78 °C, $ClCH_2CH_2NMe_2$; **c** MeX ($X = Cl, I$); **d** morpholine, 110 °C, 2 h; **e** $(Ph_3P)_2Cl_2Ru=CHPh$, CH_2Cl_2-MeOH , -78 °C.

A water-soluble version of Grubbs' first-generation catalyst may be produced using this ligand to displace two equivalents of triphenylphosphine from $(Ph_3P)_2Cl_2Ru=CHPh$. This charged complex has been imaginatively exploited by Chen and co-workers, who used it to explore its reactivity as an olefin metathesis catalyst in the gas phase using ESI-MS.^{29,30} The complex was analysed as the di-

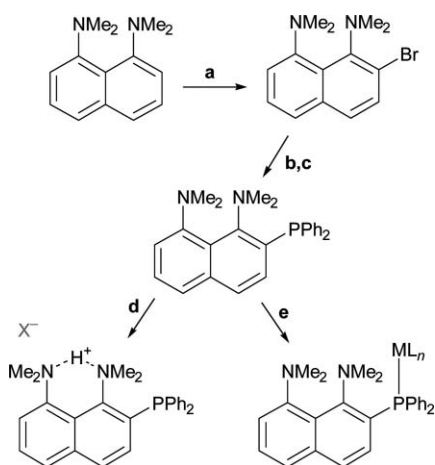
iodide salt, and the mass spectrum revealed peaks due to the dication and the monocations $[(Me_3NCH_2CH_2Cy_2P)Cl_2Ru=CHPh]^+$ ($X = Cl, I$), generated through loss of one of the charged phosphine ligands. The monocations were shown to react with 1-butene and the cyclic olefins cyclobutene, cyclopentene and norbornene in the gas phase, generating products due to ring-opening metathesis polymerization (Scheme 5). Addition of up to three cycloolefin units was observed.



Scheme 5 Top: gas-phase reactions of cyclic alkenes with $[(Me_3NCH_2CH_2Cy_2P)Cl_2Ru=CHPh]^+$ in an electrospray ionization mass spectrometer ($m = 2$ or 3 ; $n = 1, 2$ or 3). Bottom: ESI-MS product ion spectrum from the selected 546.2 m/z ion after gas-phase reaction with 1-butene. Reproduced with permission from ref. 29. Copyright 1998, Wiley-VCH Verlag GmbH & Co. KGaA.

Primary aminoalkylphosphines $R_2N(CH_2)_nPH_2$ can be selectively *N*-quaternised with alkyl iodides in a two-phase CH_2Cl_2/H_2O system to form $[R'_2N(CH_2)_nPH_2]I$, and these primary phosphines may also be protonated at nitrogen.³¹ Alkylation at phosphorus generates charged tertiary phosphines that have been used as ligands in tungsten carbonyl, Rh(I)-olefin and Pd(II) complexes.³²

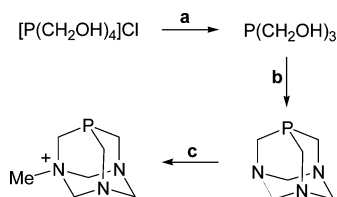
Ligands expressly designed for amenability to ESI-MS analysis have been introduced. Desirable properties for such ligands include a peripheral site capable of associating with a charged species, such as H^+ , Na^+ , etc., but that does not compete for coordination sites on the metal. The first such ligands were the phosphines $PPh_n(p-C_6H_4OMe)_{3-n}$ and $PPh_n(p-C_6H_4NMe_2)_{3-n}$ ($n = 0-3$) and the arsine $As(p-C_6H_4OMe)_3$, which when coordinated to metal carbonyl complexes all provided readily detectable $[M + H]^+$ ions, in contrast to the related PPh_3 complexes that were invisible to ESI-MS.³³ This idea has been further developed in our laboratory, where we have shown that tethering a proton sponge to a phosphine ligand (Scheme 6) renders it highly electrospray-active, providing signals almost as intense as a (permanently charged) phosphonium ion.³⁴



Scheme 6 Reagents and conditions: **a** *N*-bromosuccinimide, THF, $-78\text{ }^{\circ}\text{C}$; **b** $n\text{-BuLi}$, THF, $-78\text{ }^{\circ}\text{C}$; **c** $\text{Ph}_2\text{P}(\text{Cl})$; **d** HX ($\text{X} = \text{Br}, \text{BF}_4$); **e** $\text{Fe}_2(\text{CO})_9/\text{heat}$ or $\text{W}(\text{CO})_6/\text{ONMe}_3$ or $(\eta^5\text{-C}_5\text{H}_5)\text{Mn}(\text{CO})_3/h\nu$; $\text{ML}_n = \text{Fe}(\text{CO})_4$, $(\eta^5\text{-C}_5\text{H}_5)\text{Mn}(\text{CO})_2$, $\text{W}(\text{CO})_5$.

The high Brønsted basicity of the sponge-functionalised ligand ($\text{p}K_{\text{a}} \sim 12$) means that $[\text{M} + \text{H}]^+$ ions are produced exclusively and with high efficiency, even in the absence of an added proton source. The ligand also displays pH-dependent solubility properties, migrating from non-polar to aqueous phases upon addition of acid. Such proton sponge phosphines will probably prove most useful in conditions which are marginal for ESI-MS, *e.g.* *in situ* characterization of the complex mixtures generated in catalytic reactions, in the characterisation of complexes in ionic liquids,^{35,36} or in non-polar solvents such as toluene or hexane (in which lipophilic ionic liquids are required to assist the formation of a stable spray).³⁷

The 1,3,5-triaza-7-phosphaadamantane (PTA) ligand is neutral and hydrophilic with low steric demand (cone angle 103°), and its coordination chemistry has been extensively investigated.³⁸ It is relatively easy to prepare and to derivatise, including by *N*-methylation to produce the formally charged and still water-soluble ligand $[\text{PTAME}]^+$ (Scheme 7). The fact that the phosphorus does not need to be protected makes this an especially attractive ligand, and ESI-MS has been shown to be a suitable method of characterizing $[\text{PTAME}]^+$ complexes, such as $[\text{Ru}(p\text{-cymene})\text{Cl}_2(\text{PTAME})]^+$.³⁹



Scheme 7 Synthesis of PTA and $[\text{PTAME}]^+$. Reagents and conditions: **a** NaOH ; **b** NH_3 , HCHO (excess); **c** MeI .

An alternative route to water-soluble electron-rich phosphines has been described by Beller, who showed that the condensation of appropriate secondary amines with $\text{P}(\text{CH}_2\text{OH})_3$ produces the air-stable $\text{P}(\text{CH}_2\text{NR}^1\text{R}^2)_3$ ($\text{R}^1 = \text{CH}_3$, $\text{R}^2 = \text{CH}_2\text{CO}_2\text{Na}$, $\text{CH}_2\text{CH}_2\text{OH}$, $\text{CH}_2\text{CO}_2\text{SO}_3\text{Na}$).⁴⁰

Multiple protonation of $(\text{Me}_2\text{NCH}_2\text{CH}_2)_3\text{P}$ by $\text{Ph}_3\text{P}\cdot\text{HBr}$ or aqueous HCl affords the tricationic tertiary phosphine ligand $[(\text{HMe}_2\text{NCH}_2\text{CH}_2)_3\text{P}]^{3+}$. Reaction with PdBr_2 produced the highly water-soluble complex $[\text{PdBr}_2\{\text{P}(\text{CH}_2\text{CH}_2\text{NMe}_2\text{H})_3\}]^{6+}$.³² The same ligand could be prepared by stepwise aminoalkylation of PH_3 with $\text{Me}_2\text{NCH}_2\text{CH}_2\text{Cl}$ in the superbasic medium DMSO/KOH , followed by metalation with $n\text{-BuLi}$, further reaction with $\text{Me}_2\text{NCH}_2\text{CH}_2\text{Cl}$ and protonation with $\text{Ph}_3\text{P}\cdot\text{HBr}$ in CH_2Cl_2 .⁴¹

Deprotonation of phosphines for the purposes of providing an $[\text{M} - \text{H}]^-$ ion for ESI-MS study is unusual but not unprecedented; the observation that bis(diphenylphosphino)methane behaves in this way by deprotonation at the methylene carbon⁴² was exploited in kinetic studies on the cobalt-catalysed intermolecular Pauson–Khand reaction (Fig. 4).⁴³ This investigation provided the first observations of proposed key intermediates in this synthetically useful reaction.

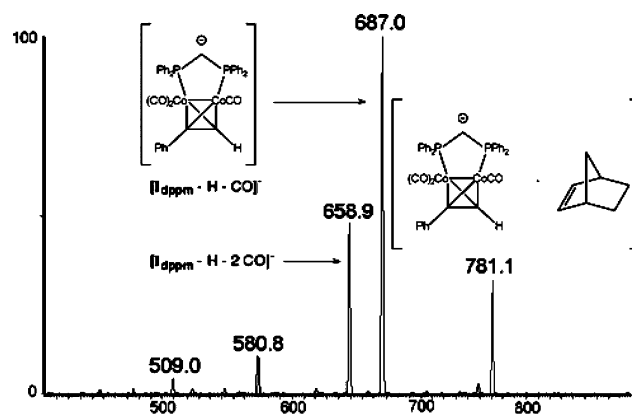


Fig. 4 Gas-phase reaction of $[\text{Co}_2(\text{CO})_3(\text{dppm} - \text{H})(\mu\text{-PhCCPh})]^-$ ($687\text{ }m/z$) with norbornene under ESI conditions. Reprinted with permission from ref. 43. Copyright 2003, American Chemical Society.

A class of water-soluble phosphine ligands that may provide $[\text{M} - \text{H}]^-$ ions are Beller's carbohydrate-substituted triarylphosphanes;^{44,45} sugars are often acidic enough to deprotonate under ESI-MS conditions.

Carbenes

An array of closely related Hoveyda-type olefin metathesis catalysts have been prepared, by three different research groups, in which the benzylidene ligand has been functionalised with an ionic tag (Fig. 5, top). The complex has an imidazolium tag to immobilise the catalyst in an ionic liquid phase during biphasic ring-closing metathesis reactions.⁴⁶ After 10 cycles, the catalyst retained 95% of its original reactivity and residual ruthenium levels in the products were found to be less than 10 ppm by ICP-MS.^{47,48} Without the ionic tag, the catalysts rapidly leached from the ionic liquid and activity dropped to zero. Reported simultaneously was a very similar complex (Fig. 5, bottom), shown to be an effective catalyst for the ring-closing metathesis of diene and enyne substrates in $1 : 9$ $[\text{bmim}][\text{PF}_6] : \text{CH}_2\text{Cl}_2$. The catalyst could be repeatedly recycled and reused, with conversion dropping only from 98 to 90% after 10 cycles.⁴⁹

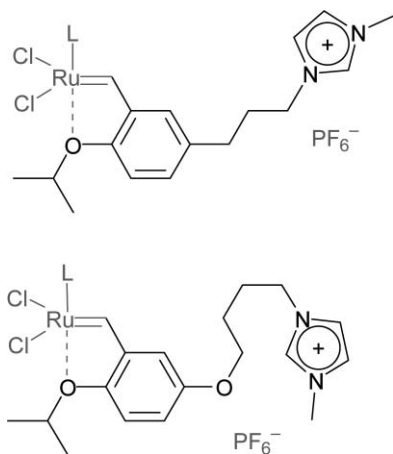
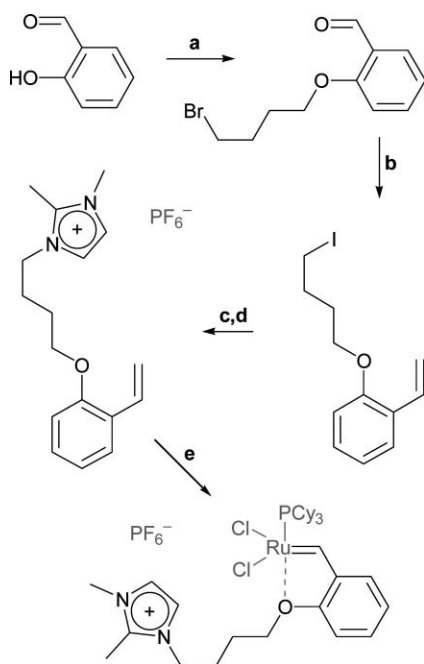


Fig. 5 Hoveyda-type catalysts with ionic tags ($L = \text{PCy}_3, \text{IMesH}_2$).

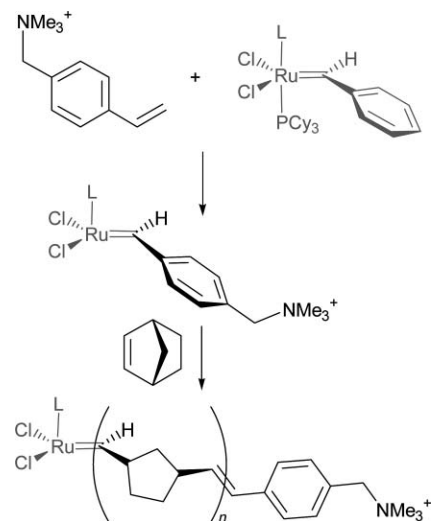
Other closely-related imidazolium-tagged carbene ligands have been since reported by Dixneuf and co-workers and said to be easier to prepare than the aforementioned examples (Scheme 8), being prepared in five steps from salicylaldehyde. However, attachment of the tag to the ortho oxygen led to slow initiation and in the ring-closing metathesis of *N,N*-diallyltosylamide in $[\text{bmim}][\text{PF}_6]$ the conversion dropped from 90 to 60% after three cycles.



Scheme 8 Reagents and conditions: **a** K_2CO_3 , 1,4-dibromobutane, DMF, 60°C , 20 h; **b** $\text{Ph}_3\text{PCH}_3^+\text{I}^-$, $n\text{-BuLi}$, Et_2O , r.t.; **c** 1,2-dimethylimidazole, toluene, 80°C , 3 days; **d** KPF_6 , H_2O , rt 1 h; **e** $(\text{Cy}_3\text{P})_2\text{Cl}_2\text{Ru}=\text{CHR}$, CuCl , CH_2Cl_2 , 40°C , 2 h.

All of the above examples were prepared with the intention of immobilizing the catalyst, without using the charge as a handle with which to extract mechanistic information. However, work in the Chen lab showed that incubation of $(\text{Cy}_3\text{P})(\text{L})\text{Cl}_2\text{Ru}=\text{CHPh}$ ($L = \text{PCy}_3$ or NHC, first- and second-generation Grubbs' catalyst) with 4-[(trimethylammonium)methyl]styrene produces complexes

in which the charge is tethered through a benzylidene ligand (Scheme 9). The complexes so formed were used to study gas-phase ring-opening metathesis polymerisation and to show that the increased solution-phase reactivity of the second-generation catalyst was due to entry of the active species into the catalytic cycle being preferred over return to the precatalyst (by rebinding the phosphine).⁵⁰ Chen's earlier work with charged phosphine ligands has obvious parallels with this follow-up work, but there is a sound argument for switching the location of the charge on the one ligand to another in this case: perturbing the phosphine ligand has up to four orders of magnitude difference on the reactivity, whereas modification of the benzylidene moiety has only a modest influence.



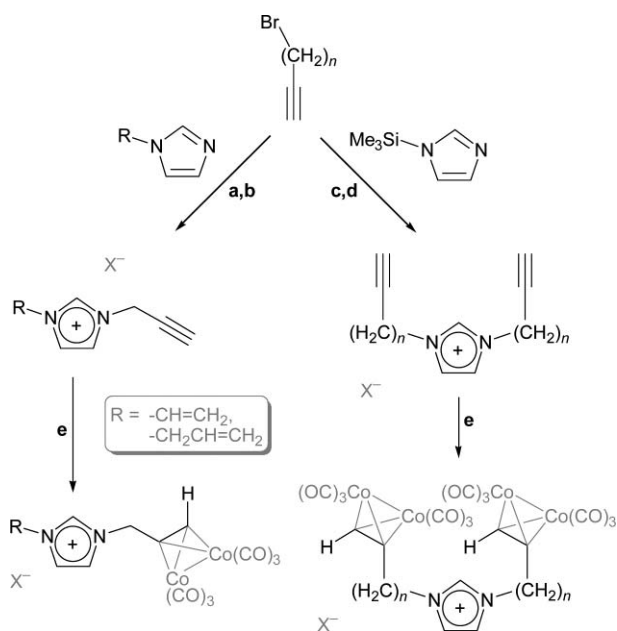
Scheme 9 Preparation of charged, 14-electron olefin metathesis catalysts ($L = \text{PCy}_3$ or NHC) and their gas-phase reactivity with norbornene ($n = 1-6$).

Alkynes

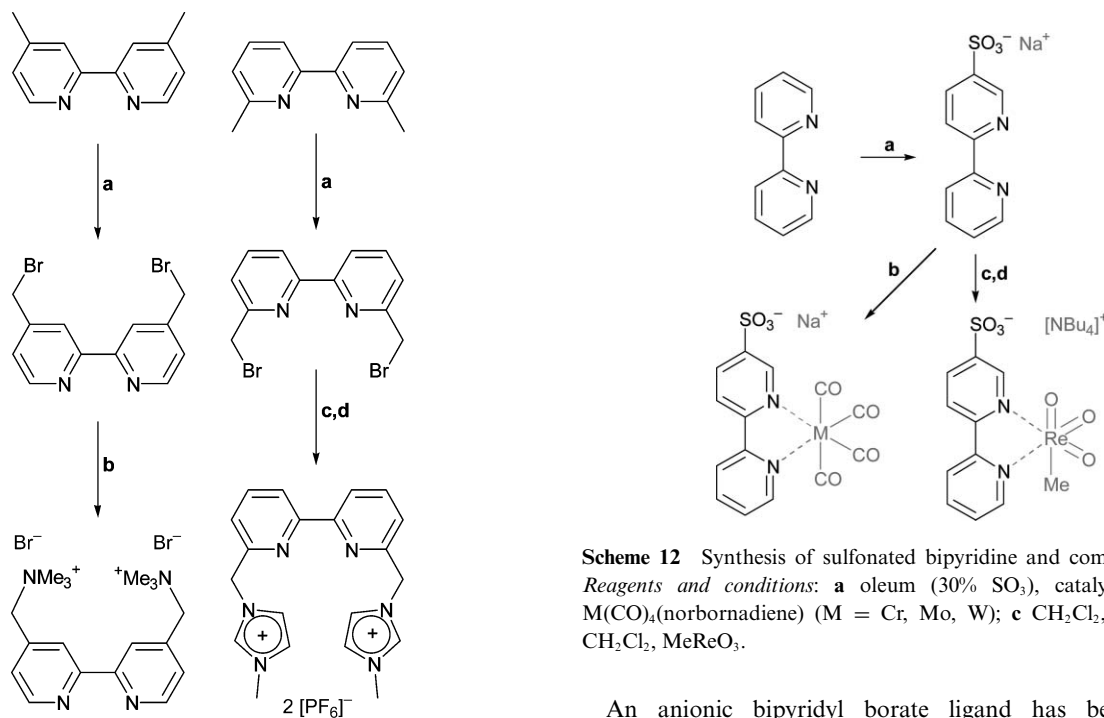
Alkynes have been appended to imidazolium ions and employed as ligands in organometallic chemistry (Scheme 10).⁵¹ Alkynes react readily with $\text{Co}_2(\text{CO})_8$ to form $(\mu, \eta^2\text{-RCCR})\text{Co}_2(\text{CO})_6$ complexes, and alkyne-functionalised imidazolium ionic liquids behave similarly. Imidazolium ions bearing two alkyne groups have also been prepared and showed to serve as ligands in reactions with $\text{Co}_2(\text{CO})_8$.⁵² The ligands themselves may be classed as ionic liquids and, perhaps surprisingly, so can one of the organometallic derivatives where $n = 3$ and $\text{X}^- = \text{BF}_4^-$, as it has a melting point of 100°C .

Nitrogen donor ligands

Bipyridines have been functionalised with imidazolium groups for the purposes of facilitating catalysis in ionic liquids.⁵³ Commercially available 6,6'-dimethyl-2,2'-bipyridine was brominated using NBS and treated with methylimidazole then KPF_6 . The ligand (Scheme 11, right) has been successfully employed in the copper-catalysed oxidation of alcohols to aldehydes (or ketones) in the IL solvent $[\text{bmim}][\text{PF}_6]$. The products could be removed from the IL by washing with diethyl ether, but degradation of catalytic activity was noted upon recycling the catalyst/IL solution. Direct



Scheme 10 Synthesis of alkyne-substituted imidazolium salts and organometallic complexes thereof. *Reagents and conditions:* **a** CH_2Cl_2 , toluene, 2.5 h, rt ($n = 1$); **b** $[\text{NH}_4]\text{X}$ ($\text{X} = \text{BF}_4, \text{BPh}_4, \text{PF}_6$); **c** toluene, 60°C , 24 h ($n = 1$ or 3); **d** NaX ($\text{X} = \text{BF}_4, \text{BPh}_4$); **e** $\text{Co}_2(\text{CO})_8$, CH_2Cl_2 , rt.



Scheme 11 Synthesis of cation-tagged bipyridine ligands. *Reagents and conditions:* **a** *N*-bromosuccinimide; **b** NMe_3 , $\text{H}_2\text{O}/\text{CH}_2\text{Cl}_2$, rt, 24 h, c methyl imidazole; **d** $\text{K}[\text{PF}_6]$.

distillation of the products was shown to be an improved strategy in terms of retaining catalyst activity.

A closely-related ligand (Scheme 11, left) was conveniently prepared by brominating 4,4'-dimethyl-2,2'-bipyridine and reacting it with trimethylamine. The ligand is water-soluble and may be reacted with an equimolar amount of $\text{Pd}(\text{NH}_3)_2\text{Cl}_2$ in

water to produce an air-stable solution capable of catalysing the Suzuki cross-coupling of aryl bromides and aryl boronic acids.⁵⁴ Catalyst loadings of 0.005% produced TOFs of up to 81000 h^{-1} , and product separation was achieved by filtration. The aqueous filtrate could be reused in subsequent catalytic runs, though activity diminished somewhat due to dilution during the workup procedure.

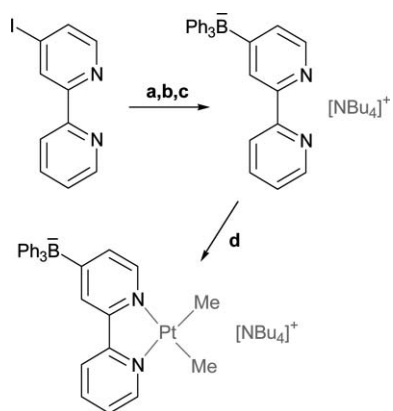
Reaction of 5,5'-di(bromomethyl)-2,2'-bipyridine with NEt_3 or N^tBu_3 produces the dicationic ligands 5,5'-di{1-(trialkylammonio)methyl}-2,2'-bipyridine (alkyl = Et or ^tBu), which have been attached to zinc⁵⁵ and copper⁵⁶ complexes. These complexes act as artificial nucleases, cleaving double-stranded DNA efficiently. The positive pendant groups in this application assist by establishment of a strong electrostatic interaction with the phosphates on DNA, drawing the active $\text{N}_4\text{M}^{\text{II}}\text{-OH}$ metal centre close to the phosphate backbone and stabilising the transition state leading to hydrolysis.

Mercury(II) catalysed sulfonation of 2,2'-bipyridine in fuming sulfuric acid generates a ligand with easily tuneable solubility properties.^{57,58} Treatment with hydroxides results in cation exchange to form ammonium and phosphonium salts, which may be reacted in conventional fashion with metal complexes in high and low oxidation states (Scheme 12). The derivatisation of the ring was found to have no influence on the complex chemistry of the chelating ligand.

Scheme 12 Synthesis of sulfonated bipyridine and complexes thereof. *Reagents and conditions:* **a** oleum (30% SO_3), catalytic HgSO_4 ; **b** $\text{M}(\text{CO})_4(\text{norbornadiene})$ ($\text{M} = \text{Cr}, \text{Mo}, \text{W}$); **c** CH_2Cl_2 , $[\text{NBu}_4]\text{OH}$; **d** CH_2Cl_2 , MeReO_3 .

An anionic bipyridyl borate ligand has been reported (Scheme 13).⁵⁹ This ligand forms a complex with platinum, $[(\text{X})\text{PtMe}_2]^-$, in an entirely analogous way to bipyridine, with negligible changes in the Pt–C bond length or $^2J_{\text{Pt-H}}$ indicating a very similar *trans* influence of the anionic ligand. The principal change observed was a blueshift of the intense metal-to-ligand charge transfer transition, indicating a destabilisation of the bipyridyl LUMO by the anionic borate appendage.

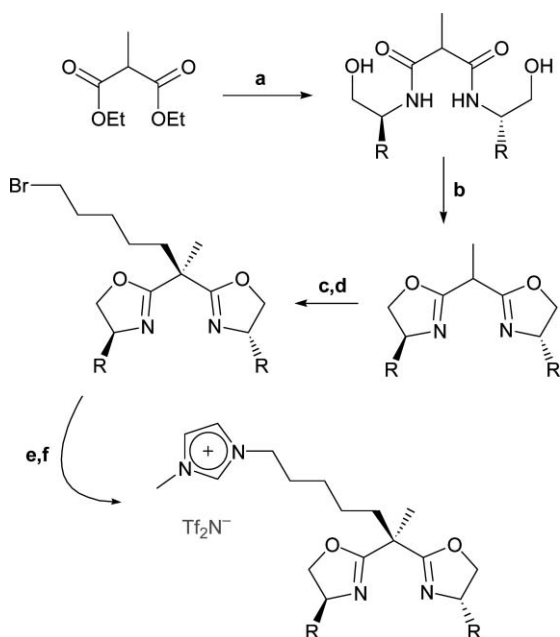
Protonolysis of $[(\text{X})\text{PtMe}_2]^-$ in acetonitrile led to elimination of CH_4 and appreciable quantities of both *cis* and *trans* isomers of $(\text{X})\text{PtMe}(\text{NCMe})$, suggesting that the *trans* effect of the pyridyl



Scheme 13 Reagents and conditions: **a** PrMgCl , Et_2O , -78°C ; **b** BPh_3 , Et_2O ; **c** $[\text{NBu}_4]\text{Br}$, 1 : 1 CH_2Cl_2 : H_2O ; **d** $[\text{Me}_2\text{Pt}(\mu\text{-SMe}_2)_2]$, THF, rt.

donor with the *p*-borate group is not dramatically different to that of the unsubstituted pyridyl donor.

Chiral bisoxazolines have been tagged with an imidazolium group in an effort to render this class of ligand amenable to catalysis in ionic liquids (Scheme 14).⁶⁰ A marked improvement in rate and enantioselectivity of copper-catalysed Diels–Alder reactions was noted in $[\text{emim}][\text{Tf}_2\text{N}]$ (complete conversion in 2 min, 95% ee) compared to dichloromethane (60 min for complete conversion, 16% ee) and the catalyst mixture could be recycled 10 times without loss of activity or enantioselectivity. Compared to the uncharged ligand, the imidazolium-tagged catalyst demonstrated much higher affinity for the IL in the recycling process.



Scheme 14 Reagents and conditions: **a** amino alcohol; **b** DAST; **c** BuLi ; **d** 1,5-dibromopentane; **e** methyl imidazole; **f** $[\text{Li}][\text{Tf}_2\text{N}]$.

Synthesis of functionalized pyridine-imine ligands (Fig. 6) was motivated by a desire to increase the applicability to aqueous catalysis through stabilization of the imine towards hydrolysis.⁶¹ Benzoic and benzenesulfonic acid derivatives of pyridinylimine ligands (substituted in the 3- and 4-positions) were obtained as

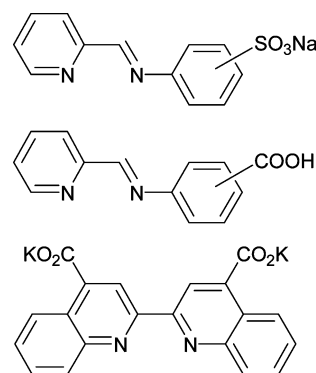


Fig. 6 Hydrophilic pyridinylimine- (top, middle) and biquinoline- (bottom) based ligands.

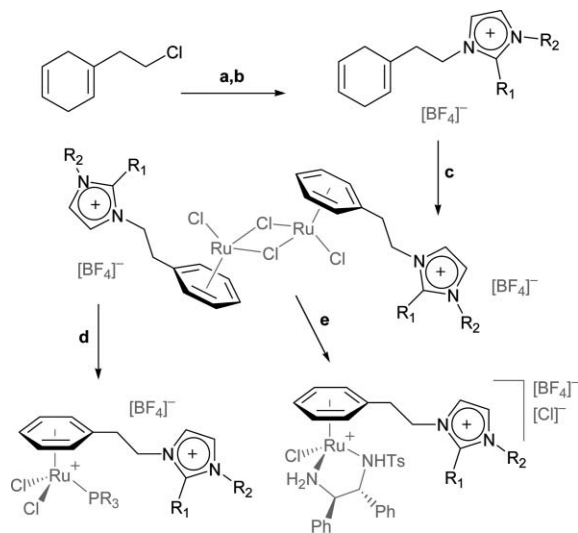
air-stable solids from the addition of the appropriate pyridinecarbaldehyde to a refluxing solution of benzoic or benzenesulfonic acid in ethanol or methanol.

All metal complexes of these ligands are soluble in polar organic solvents (including methanol, ethanol and DMF) but insoluble in non-polar hydrocarbon solvents. At neutral pH the benzenesulfonic acid complexes are also water-soluble. Under alkaline conditions the complexes can be drawn into aqueous solution but decomposition of $\text{Pd}(\text{II})$ and $\text{Pt}(\text{II})$ complexes occurs within minutes.⁶² However, a $\text{W}(\text{O})$ complex is stable under alkaline conditions, and pH-controlled cycling between CH_2Cl_2 and water was repeated over 20 times with no sign of decomposition.⁶³ The commercially available dipotassium salt of 2,2'-biquinoline-4,4'-dicarboxylic acid trihydrate was also found to be a useful ligand in aqueous catalysis, allowing palladium-catalysed aerobic oxidation of primary, secondary and benzylic alcohols to be conducted in water at pH 11.⁶⁴ Separation of catalyst was accomplished by washing the aqueous reaction with diethyl ether or dichloromethane to extract the products.

Arenes

Arene ligands, $\eta^6\text{-C}_6\text{R}_6$, are good candidates for peripheral functionalisation. They are usually strongly bound to the metal, occupying three adjacent coordination sites and typically behaving in a spectator role only. Arenes are not necessarily preformed; the 1,3-cyclohexadiene in Scheme 15 is transformed into an arene ligand upon reaction with RuCl_3 .⁶⁵ Subsequent treatment with a chiral diamine ligand generates an asymmetric transfer hydrogenation catalyst which, due to the tethered charge, can be successfully immobilised in $[\text{C}_4\text{C}_1\text{C}_1\text{Im}][\text{PF}_6]$. Conversion rates and enantioselectivity of this catalyst in the biphasic asymmetric hydrogenation of acetophenone with isopropanol are comparable to the neutral catalyst, but leaching of the catalyst from the IL phase was greatly reduced.

The tagged dimer is a useful precursor for a wide range of tagged ruthenium arene complexes; treatment with a neutral two-electron donor ligand such as a phosphine (PR_3) generates mononuclear complexes in high yield.⁶⁶ The same route is open to any number of other ligands (carbenes, chiral bisphosphines, *etc.*) with the tagged arene endowing the complex with potential for biphasic chemistry and the new ligand providing the catalytic performance. The phosphine complexes were found in this instance to be catalysts, albeit rather slow, for CO_2 hydrogenation.



Scheme 15 Synthesis of tagged arene ligands. *Reagents and conditions:* **a** substituted imidazole, toluene, 110 °C; **b** Na[BF₄], CH₂Cl₂; **c** RuCl₃, MeOH, 80 °C; **d** PR₃, MeOH–CH₂Cl₂, rt; **e** (1*R*,2*R*)-*N*-tosyl-1,2-diphenylethylenediamine, DMF, rt.

Benzo-crown ethers can act as arene ligands to a range of different metal complexes, and this chemistry has been studied by several groups with different motivations (Fig. 7). Like benzene and its derivatives, benzo-crown ethers react with Cr(CO)₆ under UV irradiation to afford Cr(CO)₃(η⁶-benzo-crown) complexes. The CO stretching frequencies of the Cr(CO)₃ group are not influenced when an alkali metal ion is complexed to the dibenzo-18-crown-6,⁶⁷ but the benzo-18-crown-6 can act as an IR-readable sensor for alkali-metal ions⁶⁸ and 2-phenylethyl ammonium ions.⁶⁹ Both benzo- and dibenzo-18-crown-6 may be attached to a hexanuclear ruthenium cluster by simply refluxing the crown ether with Ru₆C(CO)₁₇ in dibutyl ether. The product, (η⁶-{di}benzo-18-crown-6)Ru₆C(CO)₁₄, displays host–guest chemistry with alkali-metal ions and ammonium ions.^{70,71} The crown ether can also be used to anchor the cluster to polymers or mesoporous silica

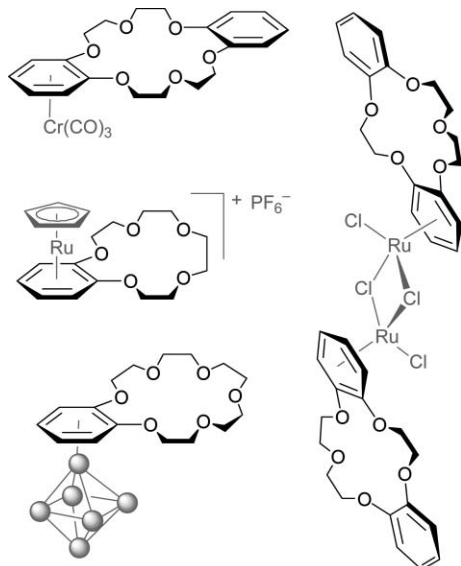


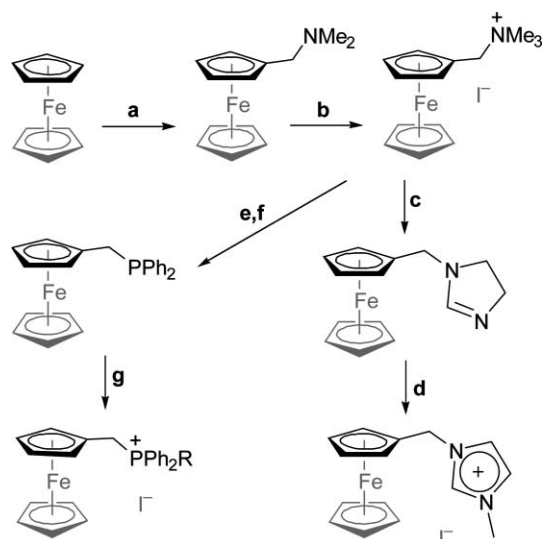
Fig. 7 Some organometallic complexes of benzo crown ethers.

functionalised with ammonium groups, and the resulting heterogenised clusters have been shown to act as efficient hydrogenation catalysts.^{72,73} The sandwich compound [(η⁵-C₅H₅)Ru(η⁶-benzo-15-crown-5)][PF₆] was prepared by heating [CpRu(NCMe)₃][PF₆], benzo-15-crown-5 and 1,2-dichloroethane in a sealed ampoule at 80 °C for 16 h,⁷⁴ and used for studying intercalation of metallocenes in layered MPS₃ (M = Mn, Cd, Zn) structures.

A benzo-crown ether melt was found to be a convenient way to displace PhCOOEt from [RuCl(μ-Cl)(η⁶-C₆H₅COOEt)₂] and form [RuCl(μ-Cl)(η⁶-benzo-crown ether)₂].⁷⁵ Four different benzo-crown ethers were explored in this study. The resulting chloro-bridged ruthenium dimers are useful precursors for a range of catalytically active mononuclear complexes, whose solubility could be tuned depending on the choice of cation and hence have potential for biphasic catalysis (*cf.* Scheme 15 (tagged arenes), above). Their high affinity for Na⁺ renders them ideal for ESI-MS analysis, though somewhat surprisingly, all complexes in this case were observed as the [M – Cl]⁺ ion, rather than the [M + Na]⁺. Halide loss is frequently observed as an ionization pathway for metal complexes,⁷⁶ but the best spectrometric handles should compete effectively against other pathways: crowns may not be the best solution for halide-containing complexes due to their propensity to eliminate NaX.

Cyclopentadienyl ligands

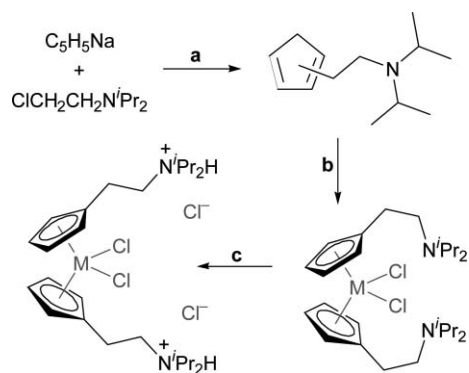
A wide range of ferrocene-derived compounds are known in which a charge is appended to one or both of the cyclopentadienyl rings. Perhaps the most well-known is [FcCH₂NMe₃]⁺,⁷⁷ which is widely used in electrochemistry and is itself a useful synthon for further chemistry (Scheme 16). A range of ferrocene-substituted (benz)imidazolium and 1,2,4-triazolium ions have been made in this fashion, and by salt metathesis with KPF₆ these may be converted into room-temperature, organometallic-containing ionic liquids.⁷⁸ Direct reaction of [FcCH₂NMe₃]⁺ with PPh₂H yields [(FcCH₂)₂PPh₂]⁺ as a minor product.⁷⁹ Treatment of



Scheme 16 Synthesis of charged ferrocenes. *Reagents and conditions:* **a** Me₂NCH₂NMe₂, H₃PO₄, HOAc, heat; **b** MeI, MeOH, heat; **c** imidazole, DMF, reflux; **d** MeI, reflux; **e** Ph₂PCH₂OH, reflux; **f** NEt₃; **g** RI (R = Me, Et).

$[\text{FcCH}_2\text{NMe}_3]\text{I}$ with $\text{Ph}_2\text{PCH}_2\text{OH}$ results in $\text{FcCH}_2\text{PPh}_2$, which may be easily quaternised with alkyl iodides.⁸⁰

A large number of aminoethyl-functionalised cyclopentadienyl complexes have been reported. The precursor ligand, $\text{R}_2\text{NCH}_2\text{CH}_2\text{C}_5\text{H}_5$ is made by reacting an excess of sodium cyclopentadienylide with 2-dimethylaminoethyl chloride hydrochloride in THF.⁸¹ Other research groups have adopted this useful synthesis and applied it to a wide range of metal complexes which exploit the pendant amino group (which is easily transformed to ammonium *via* protonation or alkylation, Scheme 17) as a hemilabile ligand, as a means to form bimetallic complexes, to tether the complex to a surface, to alter the steric and electronic effects of the ligand or to render the complex water-soluble.⁸² For example, McGowan has reported a range of functionalized titanocene dichlorides in which one or both cyclopentadienyl rings are substituted with an ammonium pendant arm, and has shown these complexes to be both water-soluble and to display potent antitumor activity.^{83,84}

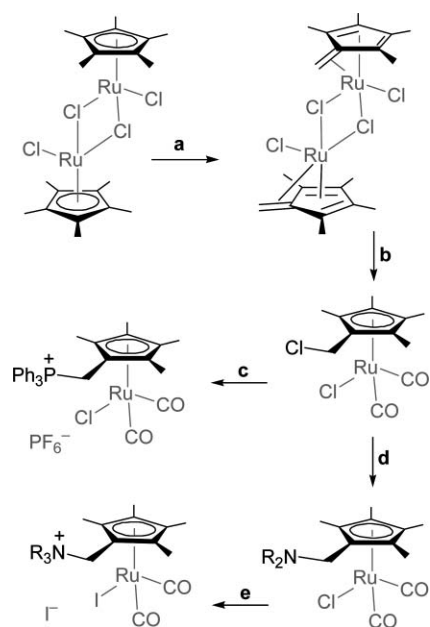


Scheme 17 Synthesis of aminoethyl cyclopentadienyl ligands and their complexes. *Reagents and conditions:* **a** THF, 0 °C; **b** MCl_4 ($\text{M} = \text{Ti}, \text{Zr}$), toluene, -40 °C; **c** HCl, MeOH.

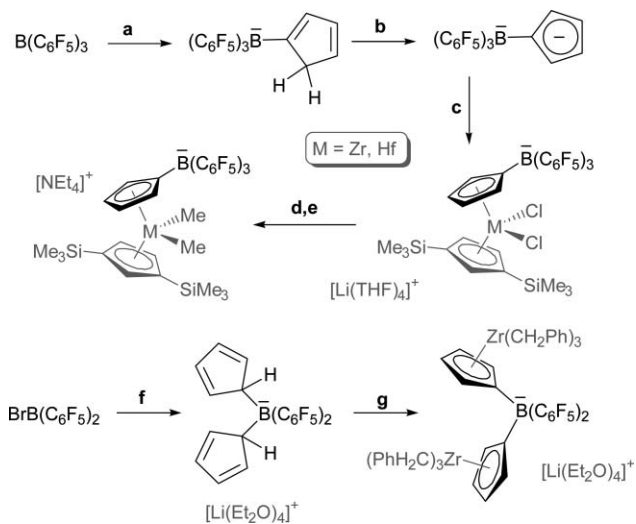
Other cyclopentadienyl ligands with tethered charges have been prepared rather more adventitiously. The methyl groups of the pentamethylcyclopentadienyl (Cp^*) ligand can be readily activated through the formation of fulvene complexes (Scheme 18).⁸⁵ Carbonylation leads to a chloromethyl group on the cyclopentadienyl ring, which may be transformed in straightforward fashion to a charged ammonium or phosphonium group.

$[(\eta^5\text{-C}_5\text{Me}_5)\text{Ir}(\text{NCMe}_2)_3]^{2+}$ reacts with PPh_3 to form $[(\eta^5\text{-C}_5\text{Me}_4\text{CH}_2\text{PPh}_3)\text{Ir}(\text{PPh}_3)_2\text{H}]^{2+}$, which possesses a tethered $(\eta^5\text{-C}_5\text{Me}_4\text{CH}_2\text{PPh}_3)$ ligand *via* activation of a C–H bond of the bound Cp^* ligand.⁸⁶ In chlorinated solvents, the hydride ligand is readily exchanged with a chloride to form $[(\eta^5\text{-C}_5\text{Me}_4\text{CH}_2\text{PPh}_3)\text{Ir}(\text{PPh}_3)_2\text{Cl}]^{2+}$.

Cyclopentadienyl ligands have also been prepared with peripheral anionic groups (Scheme 19), and attached to Zr and Hf complexes.⁸⁷ These borates react with cyclopentadienyl Group 4 trichlorides to form monoanionic complexes, which upon treatment with LiMe produce precursors for zwitterionic single-component alkene polymerisation catalysts (the active catalyst being the demethylated compound). In addition to $[(\text{F}_5\text{C}_6)_3\text{B}(\text{C}_5\text{H}_5)_2]^{2-}$, the formally trianionic ligand $[(\text{F}_5\text{C}_6)_2\text{B}(\text{C}_5\text{H}_5)_2]^{3-}$ appears in a borate-bridged, anionic dinuclear



Scheme 18 Synthesis of charged pentamethylcyclopentadienyl derivatives. *Reagents and conditions:* **a** O_2 , CHCl_3 , $-\text{H}_2\text{O}$; **b** CO; **c** PPh_3 , PF_6^- , MeOH; **d** $2\text{NR}_2\text{H}$, Et_2O ; **e** MeI.



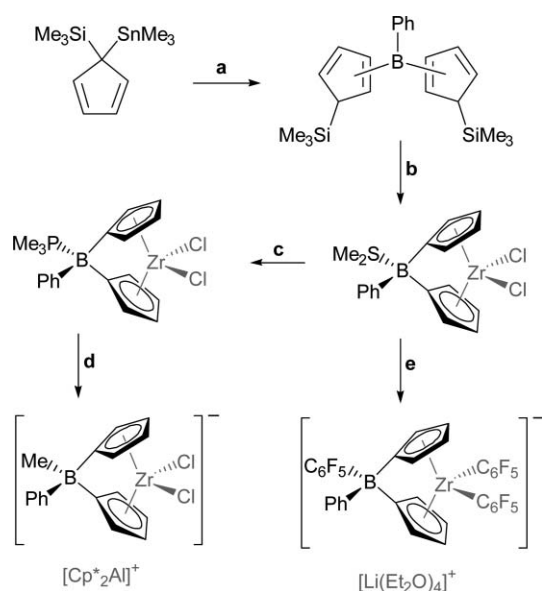
Scheme 19 Synthesis of anionic metallocenes. *Reagents and conditions:* **a** $\text{Li}(\text{C}_5\text{H}_5)$, thf, rt; **b** Li^+Bu , thf, -78 °C; **c** MLCl_3 [$\text{L} = \text{C}_5\text{H}_5$ or $\text{C}_5\text{H}_3(\text{SiMe}_3)_2$], thf, -78 °C to rt; **d** $[\text{NEt}_4]^+\text{BF}_4^-$, CH_2Cl_2 ; **e** LiMe , Et_2O -thf, -78 °C to rt; **f** $2\text{Li}(\text{C}_5\text{H}_5)$, Et_2O , -78 °C to rt; **g** $\text{Zr}(\text{CH}_2\text{Ph})_4$, toluene, rt.

complex upon reaction of $[(\text{F}_5\text{C}_6)_2\text{B}(\text{C}_5\text{H}_5)_2]^{3-}$ with two equivalents of $\text{Zr}(\text{CH}_2\text{Ph})_4$.

The motivation for the above work was principally the desire to make neutral complexes of the type $[\text{MR}(\text{L})(\eta^5\text{-C}_5\text{H}_5)]$ whose Lewis acidity is impaired as little as possible, achieved by a ligand already possessing an anionic group and hence obviating the need for a counterion that may coordinate to the metal and compromise its reactivity.⁸⁸ Such zwitterionic complexes continue to be actively studied,⁸⁹ but are beyond the scope of this review.

Ansa metallocenes in which an anionic borate links the two cyclopentadienyl rings have been prepared by Shapiro

and co-workers (Scheme 20).^{90,91} Treatment of $\{\text{Ph}(\text{Me}_3\text{P})\text{B}(\eta^5\text{-C}_5\text{H}_4)_2\}\text{ZrCl}_2$ with Cp^*AlMe or $[\text{PPN}]\text{Cl}$ results in the anionic complexes $[\{\text{Ph}(\text{Me})\text{B}(\eta^5\text{-C}_5\text{H}_4)_2\}\text{ZrCl}_2]^-$ and $[\{\text{Ph}(\text{Cl})\text{B}(\eta^5\text{-C}_5\text{H}_4)_2\}\text{ZrCl}_2]^-$, respectively.⁹² Lancaster and Bochmann found that Shapiro's precursor complex $[\text{Ph}(\text{Me}_2\text{S})\text{B}(\eta^5\text{-C}_5\text{H}_4)_2]\text{ZrCl}_2$ reacted directly with three equivalents of LiC_6F_5 to form $[\{\text{Ph}(\text{C}_6\text{F}_5)\text{B}(\eta^5\text{-C}_5\text{H}_4)_2\}\text{Zr}(\text{C}_6\text{F}_5)_2]^-$, which could be selectively methylated with AlMe_3 to provide $[\{\text{Ph}(\text{C}_6\text{F}_5)\text{B}(\eta^5\text{-C}_5\text{H}_4)_2\}\text{ZrMe}_2]^-$, a useful ethene polymerisation catalyst when activated by methylaluminoxane.⁹³

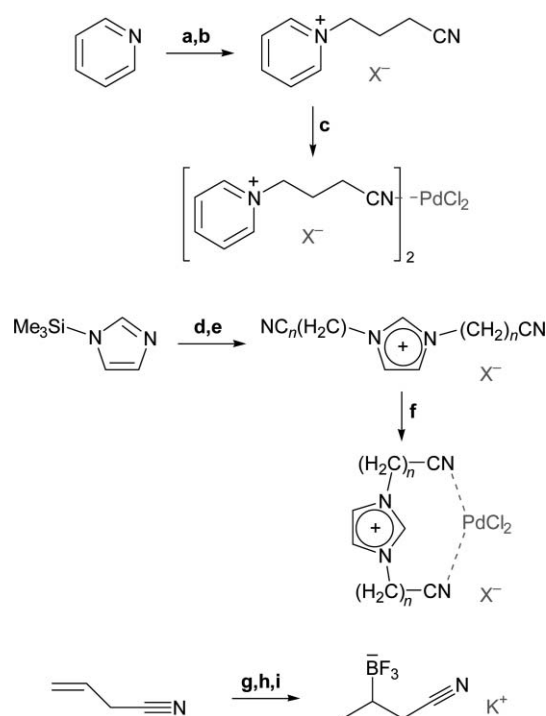


Scheme 20 Synthesis of borate-bridged *ansa*-metalloenes. *Reagents and conditions:* **a** toluene, PhBCl_2 , rt, $-\text{Me}_3\text{SnCl}$; **b** $\text{ZrCl}_4(\text{SMe}_2)_2$, toluene, 70°C , $-\text{SMe}_2$, $-2\text{Me}_3\text{SiCl}$; **c** PMe_3 , CH_2Cl_2 , -78°C ; **d** $2\text{Cp}^*\text{AlMe}$, $-\text{PMe}_3$, CH_2Cl_2 , rt; **e** LiC_6F_5 , Et_2O , -78°C .

Isonitriles

Isonitrile-functionalised ionic liquids have been used for the stabilisation of palladium-based catalysts for cross-coupling reactions.⁹⁴ The ionic liquids are inexpensive and easily prepared by reaction of chloroalkylnitriles with pyridine or imidazole precursors, followed by salt metathesis with HPF_6 , $\text{Li}[\text{Tf}_2\text{N}]$ or NaBF_4 (Scheme 21). Reaction of the monofunctional pyridinium ionic liquids with PdCl_2 generated a series of complexes $[\text{PdCl}_2(\text{C}_3\text{CNpy})_2]^{2+}$, with nitrile coordination being established by means of IR spectroscopy. The palladium complexes are active precatalysts for Suzuki cross-coupling reactions, and show remarkable recyclability properties compared to PdCl_2 in the unfunctionalised IL. $\text{PdCl}_2/[\text{C}_3\text{CNpy}][\text{Tf}_2\text{N}]$ could be recycled 9 times without loss of activity, and Pd leaching into the organic phase was <5 ppm. In comparison, the activity of $\text{PdCl}_2/[\text{C}_4\text{py}][\text{Tf}_2\text{N}]$ dropped to zero after five cycles.

Similar results were obtained for nitrile-functionalised imidazolium ionic liquids in the Pd-catalysed Stille cross-coupling reaction.⁹⁵ For both classes of ligand, the nitrile is thought to stabilise the palladium nanoparticles formed in the catalytic reaction by discouraging aggregation of colloids, so the role of the nanoparticles as active catalyst reservoirs is retained. The difunctional imidazolium salt further increases the retention



Scheme 21 Synthesis of nitrile-functionalised ionic liquids and their use as ligands. *Reagents and conditions:* **a** $\text{Cl}(\text{CH}_2)_3\text{CN}$, 80°C ; **b** HPF_6 or $\text{Li}[\text{NTf}_2]$ or NaBF_4 ; **c** PdCl_2 , CH_2Cl_2 ; **d** $\text{Cl}(\text{CH}_2)_n\text{CN}$ ($n = 1, 2$ or 3); **e** HPF_6 or $\text{Li}[\text{NTf}_2]$ or NaBF_4 ; **f** PdCl_2 , CH_2Cl_2 ; **g** BCl_3 , HSiEt_3 , -78°C ; **h** 0°C , H_2O ; **i** KHF_2 .

ability, and in this case nanoparticles are not observed, so chelation of the bis(nitrile) to palladium efficiently stabilises a mononuclear catalyst.⁹⁶ Borate anions may also be nitrile-functionalised (Scheme 21, bottom) with the same goals in mind. Salt metathesis with nitrile-functionalised cations result in novel materials in which both anion and cation have coordinating abilities.⁹⁷

Conclusions

Considerable synthetic effort has been expended on the synthesis of ligands with a charged tag appended, for diverse reasons but primarily for the immobilisation of homogeneous catalysts in aqueous or ionic liquid phases. This development in turn has been driven by the increasing prominence of green chemistry and the importance of catalysis as a cornerstone of this technology. This growth has coincided with the development of ESI-MS as a rapid means of analysing complex mixtures, but the extent to which the two fields have overlapped has been limited. Relatively few researchers have taken advantage of the fact that in making complexes with a charged tag, the system is primed for direct and rapid investigation by ESI-MS. This Perspective has identified a representative sampling of systems ripe for further study. Particularly appropriate systems would appear to include those using functionalised nitrogen donor ligands, for which ESI-MS has been utilised as little more than an additional means of characterisation, if at all. Many examples are not difficult to prepare, chelating (hence are likely to be tenacious binders and be retained throughout the catalytic cycle), carry a single charge and only one ligand is found per metal center (hence simple

spectra). Additionally, the coordinating properties of the ligands often changes little upon modification, a key requirement if subsequent study by ESI-MS is to be relevant and revealing of the chemistry of the uncharged complex. The functionalisation of cyclopentadienyl ligands is also well established but little-exploited as a spectroscopic probe. Greater recognition of the dual advantages of tethering a charged tag to a ligand can only lead to better understanding of catalytic processes, especially in alternative media such as water and ionic liquids.

Acknowledgements

J. S. M. thanks Natural Sciences and Engineering Research Council (NSERC) of Canada, the Canada Foundation for Innovation (CFI) and the British Columbia Knowledge Development Fund (BCKDF), and the University of Victoria for instrumentation and operational funding. D. M. C. thanks the University of Victoria for a graduate fellowship.

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