



Fluorous biphase catalysis

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Abstract

The evolution and future prospects for the fluorous biphase approach to homogeneous catalysis are discussed. © 1999 Elsevier Science S.A. All rights reserved.

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1. Introduction

In contrast to the diverse and well-documented applications of partially fluorinated organic molecules in synthetic chemistry or as solvents, the scope and applicability of their perfluorinated cousins has been much more limited. This relative neglect undoubtedly stems from their unique physical properties (apolarity, miscibility behaviour) but, as we near the end of the 20th century, scientists in a broad range of disciplines are beginning to exploit these unique properties in a series of applications (including medical, horticultural, cosmetic and heavy industry) [1–6] and it may be anticipated that these will expand and increase in the next millennium. In this article, we consider one potential new industrial avenue for perfluorinated organic solvents, *fluorous biphase catalysis*.

The concept of fluorous biphase catalysis was first introduced, publicly, in a seminal paper by Horváth and Rábai in 1994 [7], although Vogt had earlier undertaken similar studies based upon the same idea [8]. Both teams recognised independently that since only highly fluorinated moieties are soluble in perfluorinated solvents, then, after appropriate derivatisation with long perfluoroalkyl substituents, it should be possible to render conventional homogeneous catalysts preferentially soluble in the highly unreactive perfluorinated solvents. Thence, since typical organic substrates and products are essentially insoluble in these perfluorinated solvents, catalyst/product separation simplifies to the separation of two, immiscible, liquid phases. In essence, therefore, this method is very similar to the well-established, industrially-

applied, aqueous phase/organic solvent biphase approach to homogeneous catalysis exploited in the Ruhrchemie–Rhône Polenc process for the hydroformylation of C₆–C₈ alkenes using the water-soluble [RhH(CO){P(4-C₆H₄SO₃Na)₃]₃ catalyst [9]. However, the fluorous biphase approach offers one more, very important, advantage over other two-phase approaches. Not only it is compatible with hydrolytically-sensitive substrates, but also, with an appropriate choice of organic- and fluoruous-phases, on warming or under pressure the two-phase organic/fluorous system becomes a single phase (Fig. 1). Consequently, catalysis occurs under genuine homogeneous conditions (with all the associated rate and selectivity advantages), but on cooling/pressure release the two-phase system is re-established very quickly, for facile product/catalyst separation. Hence, the fluorous biphase approach offers an alternative, generic, approach to the heterogenisation of homogeneous catalysts to be compared with other methods currently attracting considerable attention; “ship-in-a-bottle”, anchoring to insoluble polymers/solid supports and supercritical solvents [9].

In this article, we describe the five year evolution of the fluorous biphase concept, including unpublished results from our own laboratory, and set out our view of the potential scope of this approach into the next millennium. For further details, the reader is directed to a number of recent review and highlights articles in this rapidly expanding area [10–15].

2. Phosphorus (III) ligands

In order to render a catalytically-active metal centre preferentially soluble in a perfluorocarbon solvent it is

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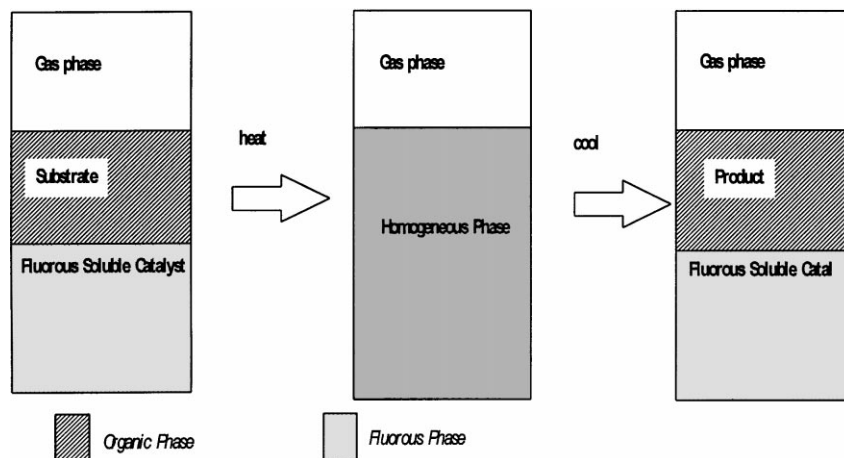


Fig. 1. Catalysis within a fluoruous biphasic system (FBS).

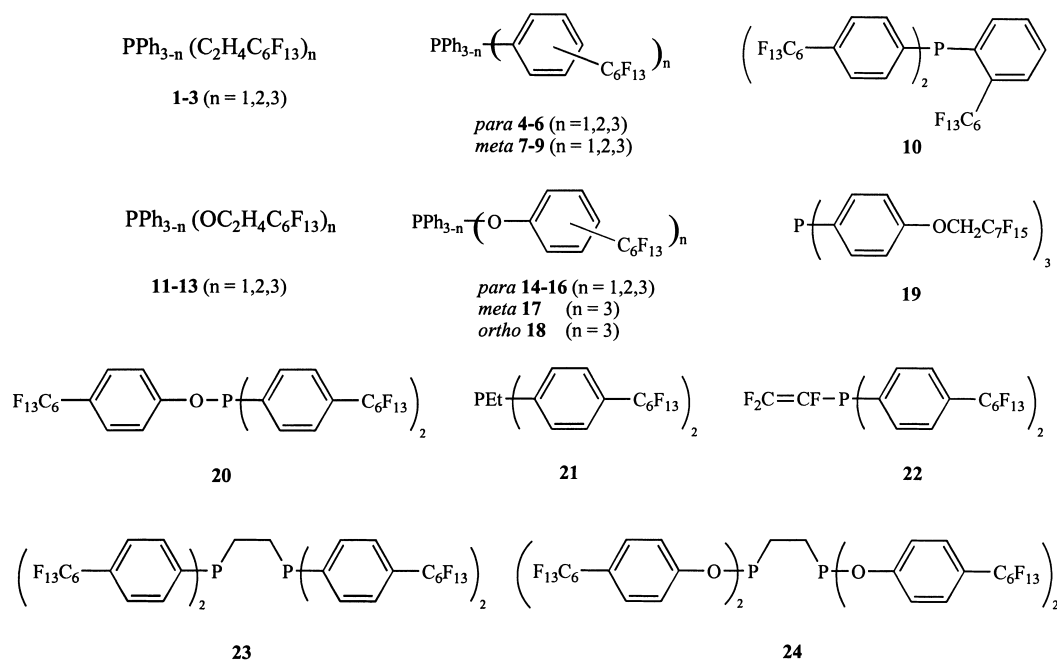


Fig. 2. Some perfluoroalkyl-substituted phosphorus(III) ligands.

necessary to connect a number of long perfluoroalkyl side-chains, called *fluorous ponytails*. This is most readily achieved by preparing ligands incorporating a large number of these ponytails; experimental studies indicate that ca. 62% w/w fluorine is necessary to confer exclusive perfluorocarbon solubility [16]. Phosphorus(III) ligands (Fig. 2) are the most extensively studied ligand system in fluoruous biphasic catalysis partly as a consequence of their ubiquitous place in homogeneous catalysis, partly because of the plethora of synthetic approaches for the incorporation of perfluoroalkyl substituents and partly because this was the ligand class chosen by Horváth and Rábai in their original work [7]. A crucial element in all studies in this area is the need to minimise the electronic (and possibly steric) consequences of incorporating many extremely electron-withdrawing fluorine atoms into the ligand, which has been

accomplished, with varying degrees of success, by the incorporation of a number of hydrocarbon spacer groups. It should be noted that there have been extensive studies of the simplest fluorinated organo-phosphorus(III) ligand $\{\text{P}(\text{CF}_3)_3\}$ which coordinates very weakly to metals and has found no industrial applications [17].

2.1. Ligand synthesis

The earliest preparation of a ligand compatible with perfluorinated solvents pre-dates Horváth and Rábai's work by nine years. The fluoruous-derivatised ligand (**3**) was initially prepared from the reaction of $\text{C}_6\text{F}_{13}\text{C}_2\text{H}_4\text{ZnI}$ with PCl_3 [18], but the potential value of this molecule in fluoruous biphasic catalysis was not recognised and no metal-based chemistry was reported. Subsequently, this

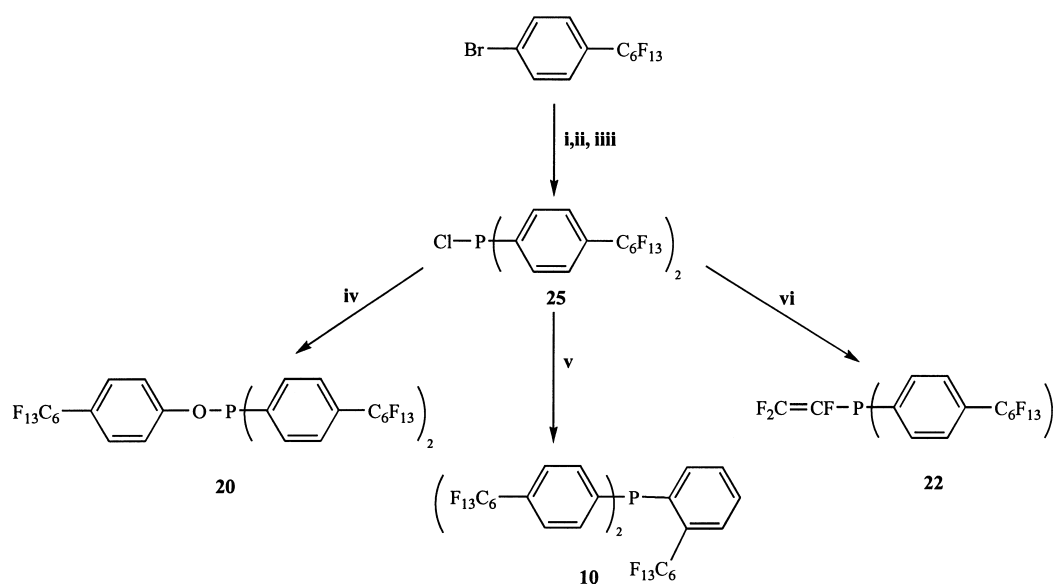
Table 1
Calculated electronic properties of $P[(CH_2)_nCF_2CF_3]_3$ molecules

	Phosphorus lone-pair level (eV)	Phosphorus Mulliken population (<i>q</i>)	Protonation energy (eV)
$P(CF_2CF_3)_3$	-11.7	0.83	-6.5
$P(CH_2CF_2CF_3)_3$	-10.6	0.62	-7.7
$P(C_2H_4CF_2CF_3)_3$	-9.9	0.48	-8.3
$P(C_3H_6CF_2CF_3)_3$	-9.5	0.40	-8.6
$P(C_4H_8CF_2CF_3)_3$	-9.3	0.38	-8.8
$P(C_5H_{10}CF_2CF_3)_3$	-9.2	0.36	-8.9

ligand (and analogues with longer perfluoroalkyl substituents, or chelating systems or mixed aryl-alkyl systems) has been prepared by the radical-induced reaction of $C_6F_{13}CH=CH_2$ with PH_3 [7,19–21], or the reactions of $RfCH_2CH_2MgI$ [22,23], $RfCH_2CH_2ZnI$ and $(RfCH_2CH_2)_2Zn$ [24] with phosphorus-chloride reagents. These molecules have been characterised by elemental analysis, mass spectrometry and multinuclear NMR studies; of interest is the minimal variation in $\delta(^{31}P)$ between these ligands and their ethyl-phosphine parents and their characteristic ^{19}F NMR spectra which show little or no changes across the series. In this work, the C_2H_4 unit has been used to minimise the electronic influence of the perfluoroalkyl substituents, and Horváth has undertaken some theoretical calculations (Table 1) [25] in an attempt to assess the effectiveness of this unit. This work concludes that even very long hydrocarbon inserts do not completely insulate the phosphorus atoms from the electronic influence of the fluorinated units, but that beyond a C_3H_6 group the variation

with additional CH_2 units is minimal. Subsequently, Gladysz [20,21] have prepared a comprehensive series of derivatised phosphine ligands with $(CH_2)_n$ ($n = 1, 2, 3, 4$) spacer units for which the spectroscopic data confirm these theoretical calculations, although coordination chemistry/catalytic studies with these ligands has not been reported to date. It should be noted that for the ligands with longer spacer groups it is necessary to incorporate longer perfluoroalkyl substituents in order to confer preferential perfluoro-carbon solubility.

One of the principle problems associated with trialkylphosphines is their air-sensitivity. In contrast, triarylphosphines are significantly more air-stable and for fluorine-derivatised triarylphosphines, the C_6H_4 unit represents an alternative electronic insulator. Interestingly, the first preparation of this type of phosphine was published in a patent in 1970 [26] (for perfluorocarbon soluble phosphorus(III) antioxidant oil additives) but the potential for these molecules as ligands for catalysis in the fluorine biphasic system was overlooked. In 1997, the perfluoroalkyl-*para*-substituted triphenylphosphine (**6**) was prepared independently by two groups using copper-mediated cross-coupling reactions followed by lithiation and reaction with phosphorus chlorides [22,27]. The extension of this methodology to *ortho*- and *meta*-substituted ligands, chelating bidentate analogues of dppe and longer perfluoroalkyl substituents is straightforward [22,28]. Alternatively, following the synthesis of the perfluoroalkyl-derivatised phosphorus chloride intermediate (**25**), ligands with mixed perfluoroalkyl substituents are available (Fig. 3) [29]. Spectroscopic and catalytic studies (see below) indicate that, although the C_6H_4 spacer



Reaction Conditions: i, $nBuLi$, Et_2O ; ii, $PCl_2(NEt_2)$, Et_2O ; iii, HCl ; iv, $HO-C_6H_4-4-C_6F_{13}$, NEt_3 , Et_2O ; v, $Li-C_6H_4-2-C_6F_{13}$, Et_2O , $-78^\circ C$; vi, $LiCF=CF_2$, Et_2O , $-100^\circ C$.

Fig. 3. The synthesis of phosphorus(III) ligands with mixed spacer units.

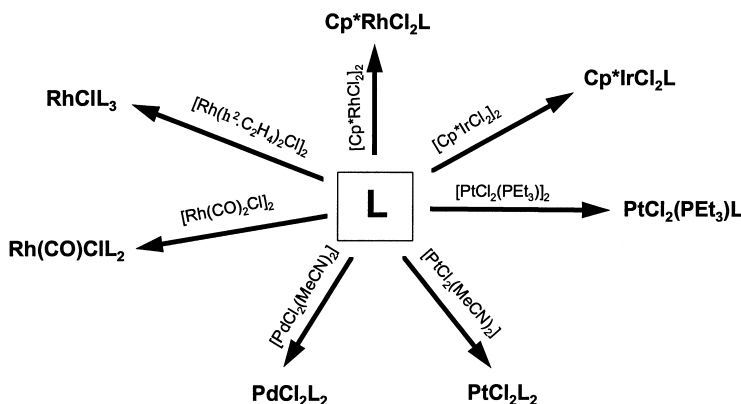


Fig. 4. Coordination chemistry of perfluoroalkyl-derivatised phosphorus(III) ligands.

is a better insulator than the C_2H_4 spacer, it does not completely insulate the donor atom(s) from the electronic influence of the fluorinated substituent(s) and the incorporation of additional spacer units has been investigated. Leitner et al. [30,31] have described mono- and bi-dentate triarylphosphines with *meta*- or *para*-substituted $\text{C}_2\text{H}_4\text{C}_6\text{F}_{13}/\text{C}_2\text{H}_4\text{C}_8\text{F}_{17}$ units whilst Gladysz [20] has given preliminary details of *para*- $\text{C}_3\text{H}_6\text{C}_n\text{F}_{2n+1}$ -aryl phosphines using a Wittig-hydrogenation sequence. We have incorporated $\text{O}(\text{CH}_2)_x\text{C}_n\text{F}_{2n+1}$ units from the reaction of $\text{Rf}(\text{CH}_2)_x\text{OTf}$ with *para*-hydroxy-arylphosphines or -arylphosphine oxides [32] whilst van Koten et al. have prepared *para*-substituted triarylphosphines with up to nine C_6F_{13} or C_8F_{17} ponytails using $\text{Si}(\text{Me})_x(\text{C}_2\text{H}_4\text{Rf})_{3-x}$ ($x = 0, 1, 2$) linkages [33]. As with the alkylphosphines, ^{19}F NMR data for all of these types of derivatised compounds are very similar and $\delta(^{31}\text{P})$ are consistent with little variation in the phosphorus environment.

The possibility for additional electronic insulation using an oxygen atom bound to the phosphorus atom was described by Horváth and Rábai in their initial publication, [7] whence the highly moisture-sensitive trialkylphosphite was obtained from the reaction of $\text{HOCH}_2\text{CH}_2\text{C}_8\text{F}_{17}$ with PCl_3 . We [22], and Nolan et al. [34], have extended this work to the related monodentate phosphites, phosphonites and phosphinites with C_6F_{13} (**11–13**), C_8F_{17} and $\text{C}_{10}\text{F}_{21}$ ponytails and potentially-chelating bis-phosphonites. Alternatively, the copper-mediated cross coupling of a perfluoroalkyl iodide with *ortho*-, *meta*- or *para*-iodophenols followed by condensation with phosphorus chlorides give triaryl-phosphite, -phosphonite and -phosphinite ligands (**14–18**, **24**) which incorporate the OC_6H_4 spacer group [22].

2.2. Coordination chemistry

At the outset of this work, the influence of the perfluoroalkyl substituents on the donor properties of these ligands and, consequently, the catalytic activity of metal complexes incorporating these molecules was unknown. Since many

active transition metal catalysts are generated in situ from free ligand and metal-containing precursors, the successful exploitation of these ligands in fluorous biphasic catalysis depended upon their reactivity patterns reflecting conventional phosphorus(III) ligands. A significant amount of work has been undertaken in this area and, throughout, direct analogues of established metal-phosphorus(III) ligand complexes have been prepared by conventional methodologies (Fig. 4) confirming that catastrophic changes in ligand properties do not arise from perfluoroalkyl substitution.

The first work on the coordination chemistry of fluorous-derivatised ligands [35–37], the synthesis and characterisation of Vaska's complex analogues *trans*- $[\text{MCl}(\text{CO})\text{L}_2]$ { $\text{M} = \text{Rh}$, $\text{L} = \text{P}(\text{C}_2\text{H}_4\text{C}_6\text{F}_{13})_3$, $\text{P}(4\text{-C}_6\text{H}_4\text{C}_6\text{F}_{13})_3$; $\text{M} = \text{Ir}$, $\text{L} = \text{P}(\text{C}_2\text{H}_4\text{C}_6\text{F}_{13})_3$ }, was undertaken by two, independent, groups. The variation in $\nu(\text{CO})$ between these complexes and the related triethyl- and triphenyl-phosphine derivatives indicates that the aryl spacer is a better electronic insulator than the alkyl spacer, but that neither completely shields the metal centre. This is supported by comparative enthalpic studies on the formation of the rhodium-trialkylphosphine complex using anaerobic solution calorimetry in THF at 30°C which suggests that the ligand is a poorer σ -donor than PEt_3 [38]. Related work on the reaction of this ligand with $[\text{Cp}^*\text{RuCl}(\text{COD})]$, where ligand sterics dominate the thermodynamics, suggests that PEt_3 and the trialkylphosphine are sterically similar. Direct evidence for this arises from single crystal structural characterisations [35–37] of the rhodium and iridium trialkylphosphine complexes, which indicate that the metal environments (bond lengths and bond angles) are not significantly different from those for related, protio-metal complexes. In fact, the perfluoroalkyl units radiate away from the metal centres and do not interact with them. The predominate structural feature in these, and many other structures of metal complexes with fluorous ponytails, is that the ponytails are aligned and include short, inter- and intra-molecular contacts (Fig. 5). These generate “fluorocarbon” and “hydrocarbon” domains within the extended lattices and if these arrangements are maintained in solution, these are likely to play an important role in catalysis in

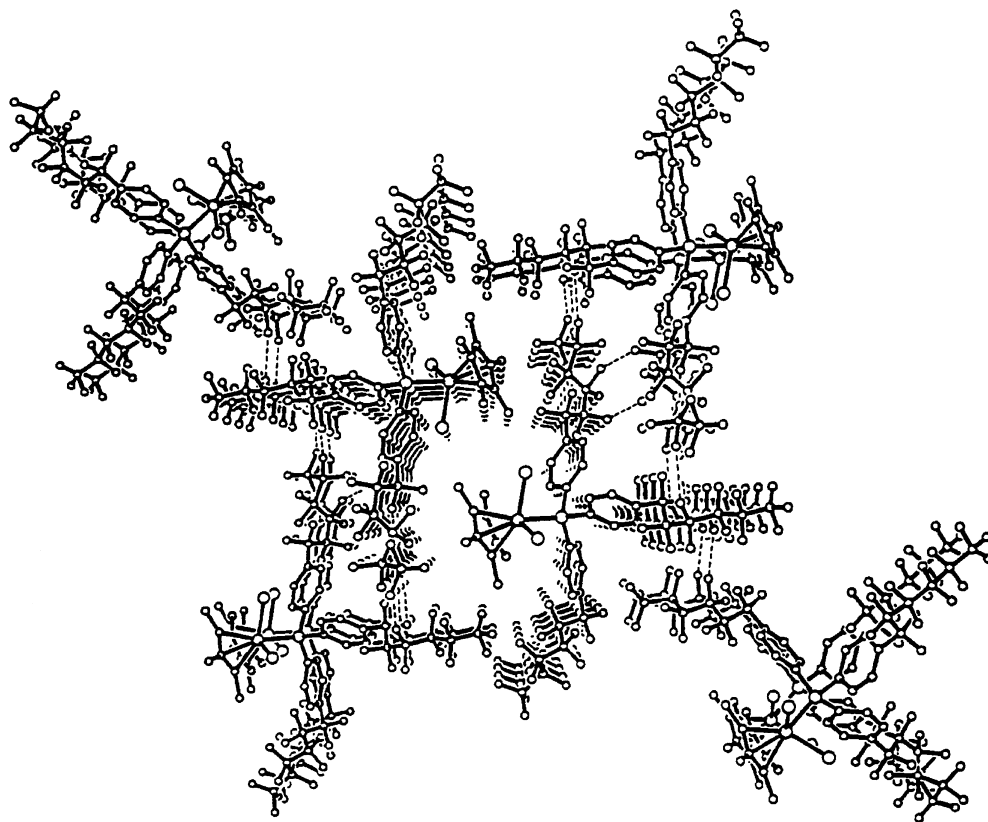


Fig. 5. Extended structure of $[\text{Cp}^*\text{RhCl}_2\{\text{P}(4\text{-C}_6\text{H}_4\text{C}_6\text{F}_{13})_3\}]$ showing short intermolecular interactions. (Reproduced with permission from [39]).

fluorous biphasic systems. Further structural studies, using Rh K-edge EXAFS in the solid state and in perfluorocarbon solution indicate that, within the accuracy of the technique, the metal first coordination sphere is unperturbed on dissolution [35].

Comparable structural and spectroscopic effects have been observed in comprehensive coordination studies using *para*-derivatised triarylphosphines (**4–6**) [39] and the derivatised-dppe analogue (**23**) [40]; spectroscopic studies indicate a stepwise increased electronic influence on the addition of each perfluoroalkyl substituent, whilst structural characterisations of $[\text{Cp}^*\text{RhCl}_2\text{L}]$ (Fig. 5) and a highly unusual mixed *cis*-/*trans*- $[\text{PtCl}_2\text{L}_2]$ co-crystal $\{\text{L} = \text{P}(4\text{-C}_6\text{H}_4\text{C}_6\text{F}_{13})_3\}$ illustrate marginal variations in the metal first coordination spheres and the formation of fluorine-rich regions within the solid state packing. Inclusion of the perfluoroalkyl substituents in the *meta*-position (**7–9**) has a greater electronic influence than that for *para*-substitution and, since we have been unable to prepare *cis*- $[\text{PtCl}_2\text{L}_2]$ $\{\text{L} = \text{P}(3\text{-C}_6\text{H}_4\text{C}_6\text{F}_{13})_3\}$ (**9**), we conclude that some steric congestion is occurring on *meta*-substitution [28]. Unfortunately, we have been unable to confirm this by a single crystal X-ray study. Even greater steric congestion is observed in the coordination chemistry of the *ortho*-derivatised ligand (**10**) [29].

Studies on the rates of oxidation/oxidative addition to *trans*- $[\text{IrCl}(\text{CO})\text{L}_2]$ $\{\text{L} = \text{P}(\text{C}_2\text{H}_4\text{C}_6\text{F}_{13})_3$ (**3**), $\text{PPh}_3 - n(4\text{-}$

$\text{C}_6\text{H}_4\text{C}_6\text{F}_{13})_n$ (**4–6**)} offer further clues to the value of fluorous-derivatised complexes as potential catalysts. For the aryl phosphines, the rate of dioxygen addition decreases with the introduction of successive ponytails [39]. However, attempts to verify the well-documented pseudo-first order kinetics, which is typically found for complexes containing perproto-phosphines, were unsuccessful indicating that the perfluoroalkyl substituents *do* physically or chemically influence the mechanism of this reaction. Further kinetic studies are in progress. For the alkyl phosphine, the rates of H_2 and O_2 addition in conventional organic solvents also show reductions between proto- and fluorous-ligands [37]. However, despite the higher molar solubilities of hydrogen and oxygen in perfluorocarbon solvents, kinetic studies indicate that these solvents can retard the rates of addition in comparison to those in conventional solvents. It is unclear whether this arises from solvent polarity considerations or from the presence of cavities within the perfluorinated solvents but, undoubtedly, the metal complex and gas molecules are stabilised more than the transition state in these cases. Furthermore, the rate and mechanism of the addition of alkyl halides to this Vaska's analogue are solvent dependent; i.e. in perfluoromethylcyclohexane there is no evidence for the typical $\text{S}_{\text{N}}2$ oxidative addition pathway and the authors advocate a free radical reaction mechanism in this solvent [37].

2.3. Catalysis

Homogeneous catalysts can provide very high activity and selectivity towards industrially-desirable products, but their commercialisation can be hampered by their separation from products and solvents and, hence, there are difficulties associated with recycling. As indicated above, the fluororous biphasic approach offers a number of potential advantages.

Horváth and Rábai [7,19] describe the hydroformylation of 1-octene in a toluene/perfluoromethylcyclohexane solvent system at 100 °C under 10 atm syngas using a catalyst generated in situ from [Rh(CO)₂(acac)] and P(C₂H₄C₆F₁₃)₃ (**3**) (1:40) affording 85% conversion to aldehydes with an *nli* ratio of 2.9. Subsequently, Horváth and co-workers have extended this initial study to an in-depth analysis of the hydroformylation of 1-decene and ethylene using the same catalyst under batch and semi-continuous fluororous biphasic system (FBS) conditions {100 °C, 1.1 MPa syngas, toluene/CF₃C₆F₁₁ (1:1)} [25]. Here, the long-term stability of the catalyst has been shown to be greater than the catalyst based on PPh₃, the selectivity is similar but the activity is an order of magnitude lower. Furthermore, selectivity increases with phosphine concentration to a peak of 7.84 (*nli*) at a P:Rh ratio of *ca.* 100 (total ligand concentration 0.3 mol dm⁻³) but the activity is decreased drastically. During nine cycles of the semi-continuous experiments, total turnovers of up to 35 000 were reported with only 1.18 ppm loss of rhodium per mole of product; the catalyst loss is ascribed to the slight solubility of the catalyst in the organic phase. Using the catalyst generated in situ from the tris-*para*-derivatised triarylphosphine (**6**), in the hydroformylation of 1-hexene under 20 atm syngas at a 3:1 ligand:Rh ratio, we observe better selectivity and reactivity than that obtained using PPh₃, although the reaction kinetics are no longer first order (Table 2) [41,42]. Further improvements are obtained for the catalyst prepared, in situ, using the tris-*para*-derivatised triarylphosphite (**16**) (*nli* ratio up to 6.6 at a 3:1 P:Rh ratio) (Table 2) which is also active for the hydroformylation of internal alkenes [42].

Using a perfluorocarbon soluble analogue of Wilkinson's catalyst, [RhCl{P(C₂H₄C₆F₁₃)₃}₃], the hydroboration of alkenes has been carried out in toluene or THF/CF₃C₆F₁₁ FBS systems [43]. However, reaction rates can be improved by not using an organic solvent (i.e. using the substrate/product as a second phase) wherein high catalyst recovery, with minimal reductions in yields or turnover frequencies, was established by recycling the fluororous phase. Nevertheless, the rates of hydroboration using this fluororous-derivatised catalyst were lower than those obtained using Wilkinson's catalyst under homogeneous conditions. This pre-catalyst has also been used to evaluate the hydrogenation of alkenes (2-cyclohexen-1-one, 1-dodecene, cyclododecene and 4-bromostyrene) in a toluene/CF₃C₆F₁₁ biphasic system under 1 atm hydrogen at 45 °C [44]. Although direct comparisons with catalysts incorporating protio-phosphines under identical conditions were not made, the relatively poor reactivity in this system (with reference to established hydrogenation catalysts) was noted. There was no significant loss in catalytic activity over three cycles, but the subsequent formation of insoluble black residues substantially reduced hydrogenation rates during further cycles. In related work, the rates of hydrogenation of styrene, in a series of FBS solvent systems, using Wilkinson's catalyst analogues incorporating either perfluoroalkyl-derivatised trialkyl- or triaryl-phosphines are all lower than those for the catalysts incorporating the related protio-phosphines, (Table 3); the least reduction in rate is observed using the C₆H₄OCH₂ spacer unit illustrating the size of the spacer unit necessary to minimise the electronic influence of the fluororous ponytails [41,45]. It should be noted, however, that just the inclusion of the fluororous phase appears to have a pronounced effect upon the rate of hydrogenation using Wilkinson's catalyst itself. The low conversions obtained in the hydrogenation of 1-hexene, using a catalyst generated from [Rh(COD)Cl]₂ and P(OC₂H₄C₆F₁₃)₃ (**13**), in a substrate/CF₃C₆F₁₁ solvent system under 1 atm hydrogen at 40 °C can be directly ascribed to the relatively poor σ -donor properties of this derivatised phosphite [34].

The palladium catalysed cross-coupling reactions of organozinc bromides and aryl iodides in a toluene/

Table 2
Hydroformylation of 1-hexene catalysed by rhodium complexes^a

Ligand	Conversion (%)	Selectivity (%)	<i>nli</i>	Rate constant (s ⁻¹)	Initial rate (mol dm ⁻³ s ⁻¹)
PPh ₃ ^b	99.6	96.1	2.5	^c	2.3 × 10 ⁻³
PPh ₃	99.0	98.2	3.1	^c	3.2 × 10 ⁻³
P(4-C ₆ H ₄ C ₆ F ₁₃) ₃	98.3	89.2	3.8	6.3 × 10 ⁻³	1.3 × 10 ⁻²
P(OPh) ₃	99.6	92.0	2.9	^c	4.75 × 10 ⁻²
P(OC ₆ H ₄ -4-C ₆ F ₁₃) ₃	99.7	82.3	6.4	6.2 × 10 ⁻³	1.2 × 10 ⁻²
P(OC ₆ H ₄ -4-C ₆ F ₁₃) ₃ ^d	99.7	89.3	6.6	3.2 × 10 ⁻³	6.4 × 10 ⁻³

^a Reaction conditions: [Rh(acac)(CO)₂] = 0.01 mol dm⁻³, ligand = 0.03 mol dm⁻³, 1-hexene = 1 cm³ in a mixture of toluene (2 cm³) and perfluoro-1,3-dimethylcyclohexane (PP3) (2 cm³), 70 °C, 20 bar, 1 h, (unless otherwise stated), product analysis by GC.

^b In toluene (4 cm³).

^c Zero order throughout most of the reaction.

^d Pressure = 8 bar.

Table 3
Hydrogenation of styrene catalysed by rhodium complexes^a

Ligand	Rate (mmol dm ⁻³ h ⁻¹)	Ligand	Rate (mmol dm ⁻³ h ⁻¹)	Ligand	Rate (mmol dm ⁻³ h ⁻¹)
PPh ₃	155	P(4-C ₆ H ₄ CF ₃) ₃	139	P(4-C ₆ H ₄ C ₆ F ₁₃) ₃	128
PPh ₃ ^b	211	P(3-C ₆ H ₄ CF ₃) ₃	100	P(3-C ₆ H ₄ C ₆ F ₁₃) ₃	117
PPh ₃ ^c	160			P(4-C ₆ H ₄ C ₆ F ₁₃) ₃ ^c	146
PPh ₃ ^d	276			P(4-C ₆ H ₄ C ₆ F ₁₃) ₃ ^d	86
PEt ₃	177	P(C ₂ H ₄ C ₆ F ₁₃) ₃	79	P(4-C ₆ H ₄ C ₆ F ₁₃) ₃ ^e	115
PEtPh ₂	105	PE((4-C ₆ H ₄ C ₆ F ₁₃) ₂	62		
P(4-C ₆ H ₄ OCH ₃) ₃	218	P(4-C ₆ H ₄ OCH ₂ C ₇ F ₁₅) ₃	201		

^a Conditions: The ligand (1.257×10^{-4} mol dm⁻³) (except where stated) was dissolved in a degassed mixture of hexane (6 cm³), perfluoro-1,3-dimethylcyclohexane(PP3)(10 cm³) and styrene (1.8 cm³; 15.7 mmol), pressurised to 1 bar with H₂ and equilibrated with stirring at 63.5 °C (unless otherwise stated). A solution of [RhCl(C₂H₄)₂]₂ (6.1 mg, 1.571×10^{-5} mol) in toluene (2 cm³) was added and the mixture was stirred for 1 h. Analyses by glc. Rates \pm 4 mmol dm⁻³ h⁻¹.

^b Solvent system toluene (18 cm³).

^c Catalytic runs at 75 °C and solvent system fluorobenzene (8 cm³)/PP3 (10 cm³).

^d Solvent system toluene (8 cm³)/PP3 (10 cm³).

^e Solvent system PP3 (18 cm³) (product extracted at the end of the catalytic runs with toluene).

C₈F₁₇Br biphasic system has been investigated using the tris-*para*-substituted triarylphosphine (**6**) [27]. Catalyst activity is higher than that for the related Pd(0)–PPh₃ system which has been ascribed to the residual electronic influence of the perfluoroalkyl substituents. Palladium(0) catalysed allylic substitution reactions have recently been performed under fluoruous biphasic conditions using the related triarylphosphine with a *para*-C₆H₄C₂H₄ spacer unit [46]. Using cinnamyl methyl carbonate and palladium loadings of either 1 or 5 mol% essentially quantitative conversions were

observed with (up to) five quantitative recycles of the catalyst.

3. Macrocyclic ligands

Following Horváth and Rábai's derivatisation [7] of phthalocyaninato-iron(II), -nickel(II) and -cobalt(II) with perfluorooctyl sidechains (the intense blue colour of the cobalt complex lends itself to a very useful demonstration of

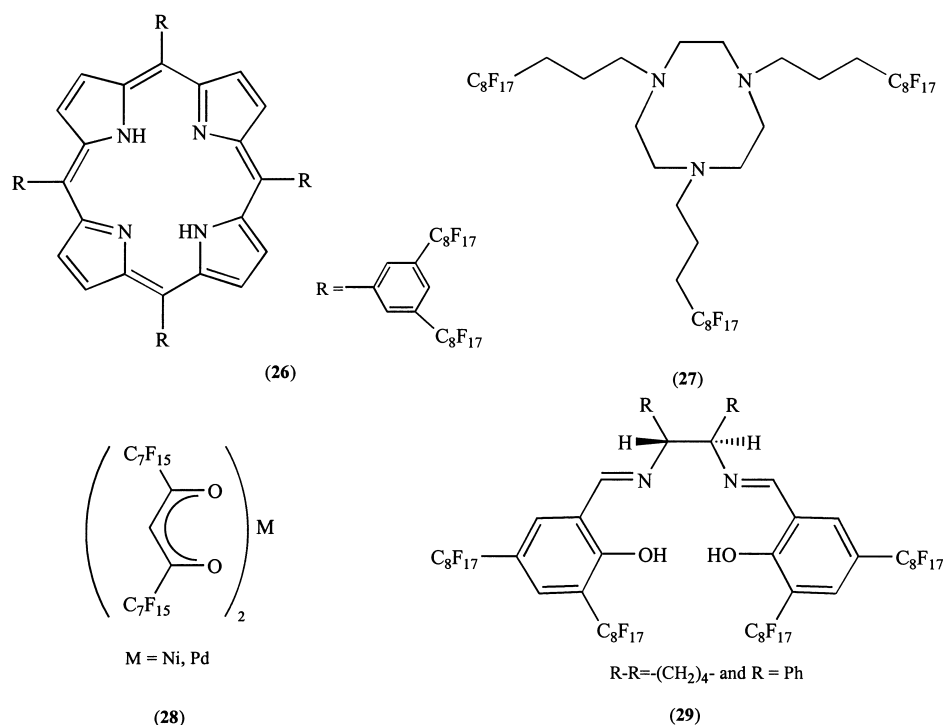


Fig. 6. Other perfluoroalkyl-substituted ligands.

the phase transitions in fluorous systems), three groups have investigated the synthesis and applications of perfluoroalkyl-derivatised macrocyclic ligands in fluorous biphasic catalysis. Eight C_8F_{17} chains are necessary to confer preferential perfluorocarbon solubility for derivatised tetra-*meso*-aryl porphyrins [47]. The cobalt complex of (**26**, see Fig. 6) is an active catalyst for the two-phase (in a rapidly stirred perfluorocarbon–acetonitrile mixture) aerobic epoxidation of alkenes with 2-methylpropanol. Conversions, selectivities and catalyst recoveries were all high using this system, but, more importantly, much higher substrate–catalyst ratios (1000:1 vs 20:1) than those typically used for oxidations with underderivatised cobalt-*meso*-tetraarylporphyrins could be tolerated. In closely related work, manganese and cobalt complexes of the tri-substituted triazacyclononane (**27**) show good activity for the *t*-BuOOH/O₂ oxidation of alkenes (particularly those with allylic hydrogens) in a substrate/perfluoroheptane two-phase system [48]. Catalyst recovery and recycle were established and the product ratios support the autooxidation mechanism involving alkoxy or alkylperoxy radicals.

4. Cyclopentadienyl ligands

Although delocalised organic ligands, such as $\eta^5-C_5H_5$ (Cp), are extensively studied in academia and find considerable application in industry, there have been few reports of attempts to derivatise compounds in this class to investigate their fluorous phase compatibility. Hughes et al. have prepared Cp-manganese, -rhenium, -iron and -cobalt complexes containing one $C_2H_4C_nF_{2n+1}$ ($n = 6, 8, 10$) substituent per Cp ring and have shown, from spectroscopic and electrochemical measurements, that the metal centres are completely insulated from the perfluoroalkyl-substituents [49]. However, none of these complexes are preferentially soluble in perfluorocarbon solvents, although in a collaboration with Horváth, preferential solubility is achieved with the mixed ligand complex, $[(CpRf)Rh(CO)\{P(C_2H_4C_6F_{13})_3\}]$ [16].

5. Other ligand systems

In the earliest attempt to utilise the fluorous biphasic approach to catalysis, Vogt [8] prepared a series of carboxylate ligands incorporating hexafluoropropylene oligomers. Coordination afforded oxidation catalysts (based upon manganese and cobalt) and nickel-based butadiene polymerisation catalysts which were preferentially soluble in highly fluorinated fluids. However, although the catalytic results were reasonable, complex stability and catalyst recovery were poor. More recently, it has been shown that linear perfluoro-*n*-alkyl cobalt(II) and manganese(II) carboxylate complexes are only slightly soluble in perfluorocarbon solvents [48,50] implying that either the oxygen spacers

or the lengths of the perfluoroether units in Vogt's ligands are necessary to convey preferential perfluorocarbon solubility.

Vogt [8] also prepared nickel–cyclooctadienyl ethene polymerisation catalysts functionalised with a β -diketonate ligand containing one perfluoroalkylether substituent but, again, although the complex was catalytically active, catalytic decomposition was observed. The related nickel and palladium complexes incorporating two β -diketonate ligands each incorporating two C_7F_{15} ponytails (**28**, see Fig. 6) which are compatible with the fluorous biphasic approach have subsequently been described [51,52]. The nickel complex is an active catalyst for the oxidation of aldehydes with O₂/isobutyraldehyde in a vigorously stirred toluene/perfluorodecalin two-phase system, whilst the palladium complex has been used for the Wacker oxidation of alkenes using *t*-BuOOH in a benzene/ $C_8F_{17}Br$ solvent system. In both systems, no leaching of the catalyst was observed and the catalysts were re-used with modest reductions in yields.

The possibility of asymmetric induction in a fluorous biphasic system was first speculated upon by Horváth and Rábai [7]. Manganese(II) complexes of the perfluoroalkyl-substituted C₂-symmetric salen ligands (**29**) have been evaluated as chiral catalysts for the aerobic oxidation of alkenes under FBS-modified Mukaiyama conditions [53]. Although the catalysts are active and catalyst recovery is good, unfortunately low enantioselectivities were observed in most cases. This is obviously an area which commands further investigations, but the influence of the apolar perfluorocarbon solvents should not be ignored.

6. The future

The fluorous biphasic approach to homogeneous catalysis appears to polarise the catalysis community; people are either firmly in favour or have staunch objections. Undoubtedly, if fluorous biphasic catalysis is going to find widespread application in the next millennium then a number of crucial issues still need to be addressed. On the positive side, the successes to date in the facile derivatisation of a range of classes of metal complexes for perfluorocarbon solubility offers significant hope for the future. However, the long term stability of these metal complexes and even the solvents themselves under process conditions has still to be verified. From a negative point of view, the apolarity of these solvents will preclude their application in many processes whilst many have questioned their expense and global warming potential. However, in view of the drive towards environmentally-friendly processes with zero emissions, any new and many existing processes will have to consider solvent issues and, since the fluorous biphasic approach demands total recycling of the metal catalyst, recycling and zero emission of the solvent should be a parallel aim. At this point, the price of the solvent becomes an inventory/plant

cost which will be significantly less than the price of a distillation column for conventional catalyst/product separation. If this is allied to reducing heating/energy costs, then the application of these solvents will represent a net *reduction* in global warming from the burning of fossil fuels.

From the fluorine chemist's point of view, we look forward to the resolution of many of these issues and hope for the widespread adoption of perfluorinated solvents in academic and industrial laboratories.

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References

- [1] D.S.L. Slinn, S.W. Green, in: R.E. Banks (Ed.), Preparation, Properties and Industrial Applications of Organofluorine Compounds, Ellis Horwood, Chichester, 1982, Chapter 2.
- [2] S.W. Green, D.S.L. Slinn, R.N.F. Simpson, A.J. Woytek, in: R.E. Banks, B.E. Smart, J.C. Tatlow (Eds.), Organofluorine Chemistry. Principles and Commercial Applications, Plenum, New York, 1994, Chapter 4.
- [3] D. Sianesi, G. Marchionni, R.J. De Pasquale, in: R.E. Banks, B.E. Smart, J.C. Tatlow (Eds.), Organofluorine Chemistry. Principles and Commercial Applications, Plenum, New York, 1994, Chapter 20.
- [4] Y. Ohsaka, in: R.E. Banks, B.E. Smart, J.C. Tatlow (Eds.), Organofluorine Chemistry. Principles and Commercial Applications, Plenum, New York, 1994, Chapter 21.
- [5] G. May, Chem. Br. 33 (1997) 34.
- [6] K.C. Lowe, in: R.E. Banks, B.E. Smart, J.C. Tatlow (Eds.), Organofluorine Chemistry. Principles and Commercial Applications, Plenum, New York, 1994, Chapter 26.
- [7] I.T. Horváth, J. Rábai, Science 266 (1994) 72.
- [8] M. Vogt, Dissertation, Technische Hochschule Aachen, 26 August 1991.
- [9] B. Cornils, W.A. Herrmann (Eds.), Applied Homogeneous Catalysis with Organometallic Compounds, vol. 1. VCH, Weinheim, 1996.
- [10] J.A. Gladysz, Science 266 (1994) 55.
- [11] B. Cornils, Angew. Chem. Int. Ed. Engl. 34 (1995) 1575.
- [12] B. Cornils, Angew. Chem. Int. Ed. Engl. 36 (1997) 2057.
- [13] D.E. Bergbreiter, Chemtracts Org. Chem. 8 (1995) 108.
- [14] I.T. Horváth, Acc. Chem. Res. 31 (1998) 641.
- [15] E.G. Hope, A.M. Stuart, in: T. Nakajima, A. Tressaud, B. Zemva (Eds.), Advanced Inorganic Fluorides: Synthesis, Characterisation and Applications, Chapter 14, in press.
- [16] V. Herrera, P.J.F. de Rege, I.T. Horváth, T. Le Husebo, R.P. Hughes, Inorg. Chem. Commun. 1 (1998) 197.
- [17] D.M. Roddick, R.C. Schnabel, in: J.S. Thrasher, S.H. Strauss (Eds.), Inorganic Fluorine Chemistry. Toward the 21st Century, ACS, Washington, 1994, Chapter 27.
- [18] S. Benefice-Malouet, H. Blancou, A. Commeyras, J. Fluorine Chem. 30 (1985) 171.
- [19] I.T. Horváth, J. Rábai, US Patent 5 463 082, 1995.
- [20] J.A. Gladysz, Abstracts of Papers of the American Chemical Society vol. 216, 1998, Pt. 1, p. 20-FLUO.
- [21] L.J. Alvey, D. Rutherford, J.J.J. Juliette, J.A. Gladysz, J. Org. Chem. 63 (1998) 6302.
- [22] P. Bhattacharyya, D. Gudmunsen, E.G. Hope, R.D.W. Kemmitt, D.R. Paige, A.M. Stuart, J. Chem. Soc. Perkin Trans. 1 (1997) 3609.
- [23] M.A. Carroll, A.B. Holmes, Chem. Commun. (1998) 1395.
- [24] F. Langer, K. Püntener, R. Stürmer, P. Knochel, Tetrahedron: Asymmetry 8 (1997) 715.
- [25] I.T. Horváth, G. Kiss, R.A. Cook, J.E. Bond, P.A. Stevens, J. Rábai, E.J. Mozeleski, J. Am. Chem. Soc. 120 (1998) 3133.
- [26] C. Tamborski, US Patent, 3 499 041, 1970, C. Tamborski, C.E. Synder, Jr., US Patent 4 011 267 1977, C. Tamborski, C.E. Synder, Jr., J.B. Christian, US Patent, 4 454 349, P. Gavezotti, E. Strepparola, US Patent, 4 681 693, 1987.
- [27] B. Betzemeier, P. Knochel, Angew. Chem. Int. Ed. Engl. 36 (1997) 2623.
- [28] D.R. Paige, Ph.D. Thesis, University of Leicester, 1998.
- [29] E.G. Hope, A.M. Stuart, Unpublished observations.
- [30] S. Kainz, D. Koch, W. Baumann, W. Leitner, Angew. Chem. Int. Ed. Engl. 36 (1997) 1628.
- [31] D. Koch, W. Leitner, J. Am. Chem. Soc. 120 (1998) 13398.
- [32] D. Sinuo, G. Pozzi, E.G. Hope, A.M. Stuart, Tetrahedron Lett. 40 (1999) 849.
- [33] B.-J. Deelman, B. Richter, G. van Koten, Abstracts of the CERC3 Young Chemists Workshop on Homogeneous Catalysis, Rostock, Germany, 1999, p. 11.
- [34] C.M. Haar, J. Huang, S.P. Nolan, J.L. Petersen, Organometallics 17 (1998) 5019.
- [35] J. Fawcett, E.G. Hope, R.D.W. Kemmitt, D.R. Paige, D.R. Russell, A.M. Stuart, D.J. Cole-Hamilton, M.J. Payne, Chem. Commun. (1997) 1127.
- [36] M.-A. Guillevic, A.M. Arif, I.T. Horváth, J.A. Gladysz, Angew. Chem. Int. Ed. Engl. 36 (1997) 1612.
- [37] M.-A. Guillevic, C. Rocaboy, A.M. Arif, I.T. Horváth, J.A. Gladysz, Organometallics 17 (1998) 707.
- [38] C. Li, S.P. Nolan, I.T. Horváth, Organometallics 17 (1998) 452.
- [39] J. Fawcett, E.G. Hope, R.D.W. Kemmitt, D.R. Paige, D.R. Russell, A.M. Stuart, J. Chem. Soc. Dalton Trans. (1998) 3751.
- [40] E.G. Hope, R.D.W. Kemmitt, A.M. Stuart, J. Chem. Soc. Dalton Trans. (1998) 3765.
- [41] E.G. Hope, R.D.W. Kemmitt, D.R. Paige, A.M. Stuart, Abstracts of the 11th International Symposium on Homogeneous Catalysis, St. Andrews, Scotland, 1998, p. C7.
- [42] A.M. Stuart, D. Gudmunsen, E.G. Hope, G.P. Schwarz, D.F. Foster, D.J. Cole-Hamilton, Br. Patent Appl., 1999, (1998) 26619.
- [43] J.J.J. Juliette, I.T. Horváth, J.A. Gladysz, Angew. Chem. Int. Ed. Engl. 36 (1997) 1610.
- [44] D. Rutherford, J.J.J. Juliette, C. Rocaboy, I.T. Horváth, J.A. Gladysz, Catalysis Today 42 (1998) 381.
- [45] E.G. Hope, D. Gudmunsen, R.D.W. Kemmitt, D.R. Paige, A.M. Stuart, Abstracts of Papers of the American Chemical Society, vol. 216, 1998, Pt. 1, p. 21-FLUO.
- [46] R. Kling, D. Sinuo, G. Pozzi, A. Choplin, F. Quignard, S. Busch, S. Kainz, D. Koch, W. Leitner, Tetrahedron Lett. 39 (1998) 9439.
- [47] G. Pozzi, F. Montanari, S. Quici, Chem. Commun. (1997) 69.
- [48] J.-M. Vincent, A. Rabion, V.K. Yachandra, R.H. Fish, Angew. Chem. Int. Ed. Engl. 36 (1997) 2346.
- [49] R.P. Hughes, J.A. Trujillo, Organometallics 15 (1996) 286.
- [50] G. Pozzi, M. Cavazzini, S. Quici, S. Fontana, Tetrahedron Lett. 38 (1997) 7605.
- [51] I. Klement, J. Lütjens, P. Knochel, Angew. Chem. Int. Ed. Engl. 36 (1997) 1454.
- [52] B. Betzemeier, F. Lhermitte, P. Knochel, Tetrahedron Lett. 39 (1998) 6667.
- [53] G. Pozzi, F. Cinato, F. Montanari, S. Quici, Chem. Commun. (1998) 877.