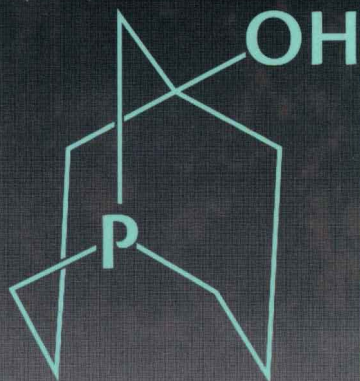


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Organophosphorus *Chemistry*

Volume 34

senior reporters D.W. ALLEN
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Organophosphorus Chemistry

Volume 34

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Volume 34

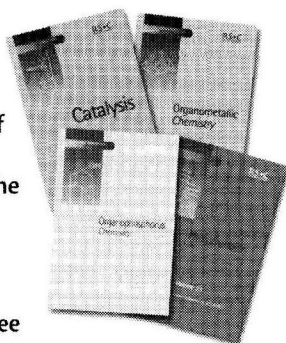
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Preface

The literature of organophosphorus chemistry remains buoyant, activity in the area continuing at a high level. As has been the case in recent years, we have again encountered problems in securing new authors for some areas, and this has inevitably led to delays in publication. For this volume, we are pleased to welcome Dr Aleksandra Skowrońska and her colleague Dr Richard Bodalski, from the Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Lodz and the Technical University in Lodz, respectively, who have provided a two-year survey of the literature relating to the chemistry of quinquevalent phosphorus acids. In this volume, the usual chapter on penta- and hexa-coordinated phosphorus compounds is missing, the reason being that the volume of literature in this area has declined significantly and the author feels that a two-year coverage would now be more appropriate. We hope that the first biennial review of this area will appear in volume 35 in due course.

July 4–9 2004 saw the first ICPC to be held in Britain. The Conference was held in the International Conference Centre in Birmingham and despite the high cost, it was well attended and attracted chemists, as usual, from all corners of the globe. Papers on synthesis and reactions were popular, ligand and medicinal chemistry were also strong and there were many good contributions in organometallic, applications and theoretical areas. An excellent presentation on the next 2007 ICPC conference, which will be held in Xiamen City, China, indicated that there will be a wide choice of cultural activities.

The drive for improved performance in transition metal ion-catalysed processes continues to stimulate the synthesis of new types of chiral phosphine and related chiral trivalent phosphorus ester and amide ligands. Activity has also remained high in the chemistry of heteroaromatic phosphorus ring systems and low-coordination number $p\pi$ -bonded systems. Also noteworthy are the developing applications of organophosphines in the Mitsunobu and Staudinger protocols in general synthetic chemistry.

As would be expected, synthetic applications of the Wittig and related reactions continue to dominate the literature relating to phosphorus-based ylides. Nevertheless, fundamental studies of the structure, bonding and reactivity of these compounds continue to appear.

In the mononucleotide area, the development of new protecting groups for the synthesis of oligoribonucleotides, particularly on solid supports, continues to be a major effort, as does interest in the synthesis of new antiviral and antitumour nucleoside analogues. The number of publications relating to oligo- and polynucleotide chemistry has continued to grow, the two most dominant research

areas being new base analogues and NMR solution structures, these being driven by advances in chemistry and NMR methodology. Other newly developing areas are the synthesis of oligonucleotides attached to metal and glass surfaces, and of oligonucleotide-conjugates.

Over the two year period covered there have been some impressive advances in many areas of quinquivalent phosphorus chemistry. New and improved synthetic procedures include the use of iodophosphates, P-nitrosophosphates, amidophosphates and a PhS^+ reagent for generating POP bonds. Amongst various isotopic labelling studies, a novel route to ^{32}P labelled compounds has been described. Mechanistic studies of reactions concerning phosphate ester hydrolysis continue to be reported and it has been shown that increased rates of phosphorylation can be achieved by facilitating an AE mechanism with the formation of phosphene intermediates. The importance of enantiomeric and asymmetric synthesis using chiral phosphorus (V) reagents is highlighted, which includes the use of a wide range of organometallic reagents and intermediates. There have been reports on enzyme enantioselective hydrolysis.

A large number of natural and unnatural phosphates, including carbohydrates and their phosphonate and phosphinate analogues, as well as many inositols, have been synthesized, usually with some biologically related purpose. The synthesis of phosphorus analogues of all types of amino acids, phospho- and phosphono-peptides and some glucosyl phosphates has also been developed. Several phosphorylated C_{60} fullerenes have been made and the first asymmetric PC bond formation under heterogeneous conditions has been described. Fluorinated phosphonates have also received much attention.

The phosphazide intermediate in the Staudinger synthesis of phosphazenes has been isolated by the use of sterically demanding reagents. There has been much attention to the preparation of multidentate phosphazene ligands and their complexation with a wide variety of metals. Many of the complexes are cyclic and some caged. An unusual ferrocenylboron complex consists of a planar four membered BBNB ring. Deprotonated methylene groups of bis (aminophosphorano)methanes have been used to form carbon metal bonds. There has been a range of studies on the use of phosphazenes as catalysts for polymerisations. Non-ionic phosphazene bases have been found to be excellent catalysts for Michael addition reactions. Reviews on the incorporation of phosphazenes in complexes and polymers have appeared and some interesting preferences for geminal substitution rather than 1,3 substitution in tricyclophosphazenes have been reported. Compounds which incorporate crown ether structures show an interesting variety of affinities for alkali metal ions. Recent developments in polyphosphazene chemistry have been reviewed, including thionyl phosphazenes. Polyphosphazenes have also been used in the synthesis of light-emitting polymers as well as in the synthesis of a variety of membranes.

D.W. Allen and J.C. Tebby

Abbreviations

BAD	Benzamide adenine dinucleotide
cDPG	Cyclodiphospho D-glycerate
CE	Capillary electrophoresis
CK	Creatine kinase
CPE	Controlled potential electrolysis
Cmpmp	1-(2-chlorophenyl)-4-methoxypiperidin-2-yl
CV	Cyclic voltammetry
DETPA	Di(2-ethylhexyl)thiophosphoric acid
DMAD	Dimethylacetylene dicarboxylate
DMF	Dimethylformamide
DMPC	Dimyristoylphosphatidylcholine
DRAMA	Dipolar restoration at the magic angle
DSC	Differential scanning calorimetry
DTA	Differential thermal analysis
ERMS	Energy resolved mass spectrometry
ESI-MS	Electrospray ionization mass spectrometry
EXAFS	Extended X-ray absorption fine structure
FAB	Fast atom bombardment
Fmpmp	1-(2-fluorophenyl)-4-methoxypiperidin-2-yl
HPLC	High-performance liquid chromatography
LA-FTICR	Laser ablation Fourier Transform ion cyclotron resonance
MALDI	Matrix assisted laser desorption ionization
MCE	Micellar electrokinetic chromatography
MIKE	Mass-analysed ion kinetic energy
PAH	Polycyclic aromatic hydrocarbons
QDA	Hydroquinone- <i>O,O'</i> -diacetic acid
PMEA	9-[2-(phosphonomethoxy)ethyl] adenine
SATE	S-acyl-2-thioethyl
SIMS	Secondary ion mass spectrometry
SSAT	Spermidine/spermine-N1-acetyltransferase
SSIMS	Static secondary ion mass spectrometry
TAD	Thiazole-4-carboxamide adenine dinucleotide
tBDMS	tert-Butyldimethylsilyl
TFA	Trifluoroacetic acid
TGA	Thermogravimetric analysis
TLC	Thin-layer chromatography
TOF	Time of flight
XANES	X-Ray absorption near edge spectroscopy

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Phosphines and Phosphonium Salts

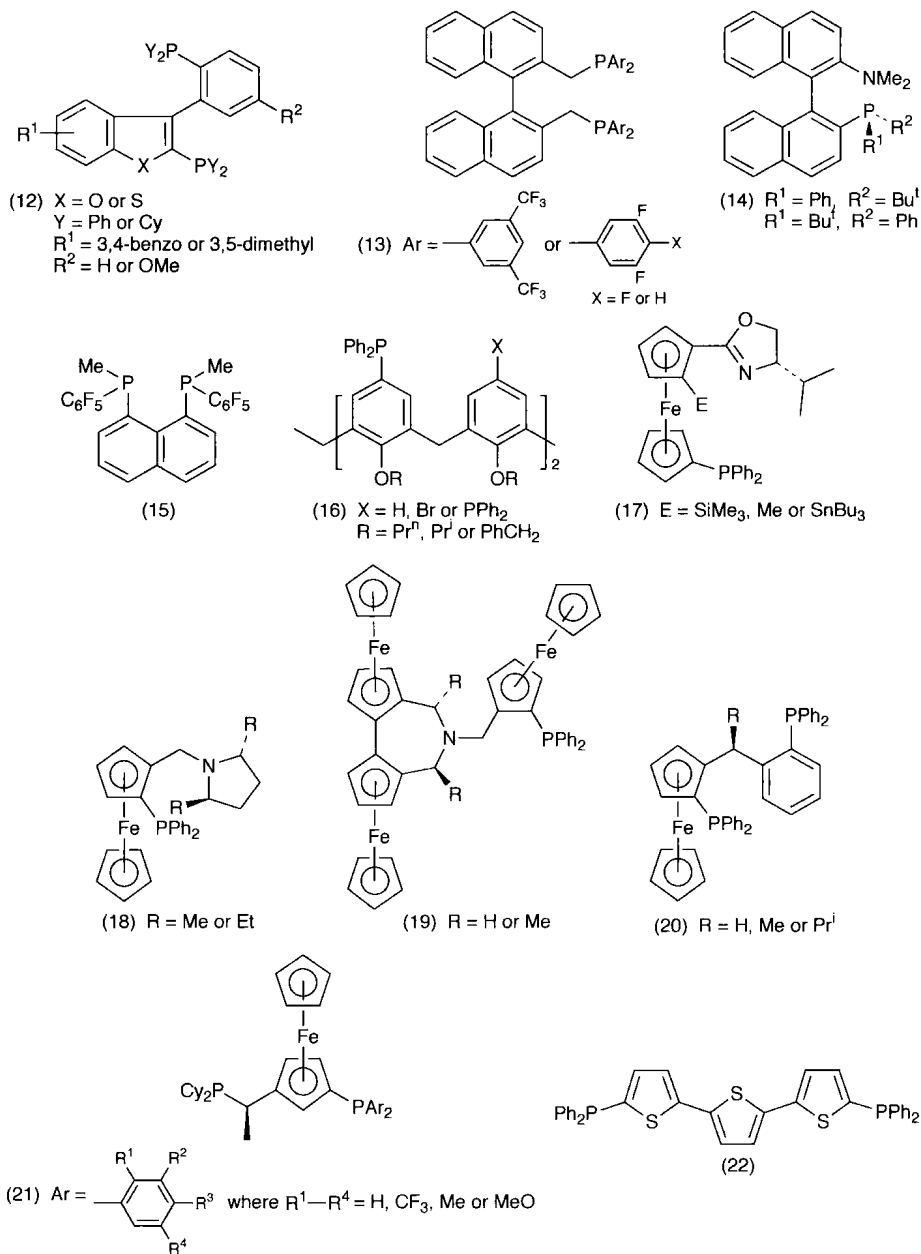
BY D. W. ALLEN

1 Introduction

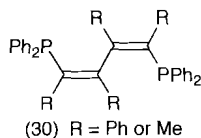
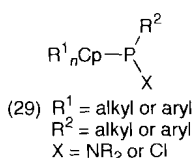
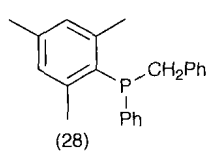
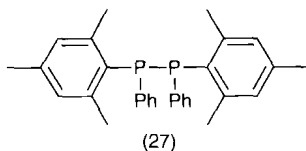
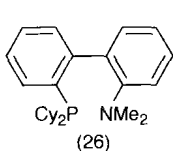
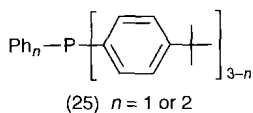
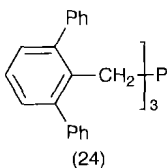
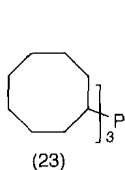
Perhaps the most noteworthy of publications relating to this chapter are the texts of the 2001 Nobel Prize lectures given by W.S. Knowles and R. Noyori, describing their work on the synthesis and applications in catalysis of chiral diphosphines,^{1,2} and the publication of three ‘*Chemical Reviews*’, concerned with the synthesis and reactivity of phosphetanes,³ the reactions of α -diketones and *o*-quinones with phosphorus compounds,⁴ and with the chemistry of annelated heterophospholes and related phospholides.⁵ A new review publication, ‘*Phosphorus-Carbon Heterocyclic Chemistry: The Rise of a New Domain*’, edited by François Mathey, has also appeared, providing a series of comprehensive reviews of the literature of the 1980’s and 1990’s, and covering many topics relevant to this chapter.⁶

2 Phosphines

2.1 Preparation. – *2.1.1 From Halogenophosphines and Organometallic Reagents.* As in previous years, the use of organolithium reagents has dominated the field, with relatively few examples of the use of Grignard or other organometallic reagents. Among unusual monotertiary phosphines prepared using organolithium reagents are the blue, phosphorescent triarylphosphine (1)⁷, the cationic phosphine ligand (2), (in the form of a light-harvesting ruthenium complex),⁸ the imidazolium phosphines (3)⁹, and the norbornadiene-derived phosphine (4), which undergoes a ruthenium-catalysed ring-opening metathesis gel-forming reaction to give the polymer-supported system (5).¹⁰ Interest has continued in the synthesis of arylphosphines bearing fluorosubstituents, and the organolithium route has been employed in the preparation of (6),¹¹ and (7).¹² Organolithium reagents have been widely utilised in the synthesis of phosphine ligands bearing other donor atoms, *e.g.*, the bis(alkylaminoaryl)phosphines (8),¹³ new chiral iminoarylphosphines, *e.g.*, (9)¹⁴ and (10),¹⁵ and the non-biaryl atropisomeric P,O-ligands (11).¹⁶ Further examples of biaryl atropisomeric diphosphines, *e.g.*, (12),^{17,18} based on 3-arylbenzo-(and naphtho-) furan and thiophene systems, the new family of atropisomeric diphosphines (13),¹⁹ and



undergo sulfonation in the phenyl rings to form amphiphilic phosphines.³³ Biphenyl-based phosphine ligands can be prepared on a significantly larger scale than has been possible as a result of some fundamental work on the key reactions. Thus, *e.g.*, it has been found that copper(I) chloride catalyses the coupling of bulky dialkylchlorophosphines such as chlorodicyclohexylphosphine with Grignard reagents, enabling the synthesis of (26).³⁴ The synthesis of the P,P-diphosphine (27), from the reaction of the mesityl Grignard reagent with



phenyldichlorophosphine, is a key step in the synthesis of benzyl(mesityl)phenylphosphine (28), a new P-chiral bulky ligand, which is obtained from the diphosphine by lithium cleavage and subsequent reaction with benzyl chloride.³⁵

The reactions of organosodium reagents with chlorophosphines have been employed in the synthesis of two new triphosphacarboranes.³⁶ A range of phosphino-substituted cyclopentadienes, (29), has been obtained from the reactions of alkali-metal cyclopentadienides with chlorophosphines, and then used to prepare new phosphino-functional half-sandwich metallocene derivatives of titanium and zirconium.³⁷

The reactions of zirconacyclopentadienes with chlorodiphenylphosphine in the presence of copper(I) chloride, followed by decomplexation, have provided a route to the diphosphadiene ligands (30).³⁸

2.1.2 Preparation of Phosphines from Metallated Phosphines. Treatment of red phosphorus with lithium metal in liquid ammonia affords a lithiophosphide reagent which displaces the fluorine atom from fluoroarenes bearing an electron-withdrawing group in the *m*- or *p*- position, to give the substituted triarylphosphine. The reaction fails with nitro- and bromo-substituents, and also if substituents *ortho* to the fluorine are present.³⁹ Problems in Appel's synthesis of diphenyl(trimethylsilyl)phosphine, using lithium diphenylphosphide generated by lithium cleavage of triphenylphosphine, have been attributed to the presence of phenyllithium in the reaction mixture, which has been overcome by quenching the lithium cleavage products with water, and isolating the diphenylphosphine, prior to its conversion to lithium diphenylphosphide.⁴⁰ Treatment of lithium diphenylphosphide with an excess of selenium gives the lithium salt (31), and lithiation of cyclohexylphosphine, followed by selenation, has given the salt (32).⁴¹ The borane-protected chiral lithiophosphide reagent (33) has been applied to the synthesis of a range of new chiral chelating diphosphines, including the