

A Specialist Periodical Report

Organophosphorus Chemistry

Volume 14

A Review of the Literature published
between July 1981 and June 1982

Senior Reporters

D. W. Hutchinson

J. A. Miller

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between July 1981 and June 1982**

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Introduction

This year we welcome an occasional review on the mass spectrometry of organophosphorus compounds by Dr J. R. Chapman of Kratos Analytical Instruments, Manchester. This analytical technique is becoming increasingly useful in the organophosphorus field (particularly for the analysis of insecticides) with the development of chemical ionization and 'in beam' evaporation techniques. While mass spectrometry has been little used so far for the analysis of natural products such as oligonucleotides, mainly because of volatility problems, the mass spectra of intact vitamin B₁₂ and vitamin B₁₂-coenzyme have been obtained, which must be regarded as a minor landmark in the application of this technique. The occasional review which has been commissioned for next year is on phosphazenes, and will be written by Drs van de Grampel and de Ruiter of the University of Groningen, the Netherlands.

During the past year, Lawesson's reagent [2,4-bis-(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetan 2,4-disulphide] has become the reagent of choice for the replacement of oxygen by sulphur in synthetic reactions. There has been an increase in the number of rearrangement reactions reported which involve organophosphorus compounds and there has been considerable interest in the synthesis of esters of fluorinated phosphorus acids. The explosive expansion in studies of two-co-ordinate phosphorus has continued and, for example, frontier orbital theory has been applied to cyclo-addition reactions of these compounds.

The development of automated synthesizers employing solid-phase methods for oligonucleotide synthesis is a significant advance which has been made during the past year, and this has been accompanied by an avalanche of papers detailing improvements in 'phosphotriester' methodology. The latter route has also been used for the synthesis of phospholipids — another area in which many new syntheses have been reported recently. The synthesis of chiral phosphates and thiophosphates and their use for investigating the stereochemical course of enzyme reactions continues to spur much elegant investigation. Some novel and interesting nucleoside 5'-triphosphate analogues, containing modifications in the tripolyphosphate chain, have been described.

The identification of the exact sites of phosphorylation in phosphoproteins has been the subject of much recent research. While the sites of phosphorylation are usually histidine, serine, or tyrosine, an acyl phosphate has recently been identified as an intermediate during the enzymic hydrolysis of ATP.

The Senior Reporters are aware of, and regret, the considerable recent increases in price of this Report. However, new methods for the reproduction of formulae and cheaper typesetting methods should, hopefully, reduce the

cost of producing these volumes in the future. This is the last volume with which one of us (J.A.M.) will be associated, and we are pleased to announce that Dr B. J. Walker will become a Senior Reporter from Volume 15 onwards.

D. W. Hutchinson
J. A. Miller

Abbreviations*

AIBN	bisazoisobutyronitrile
CIDNP	Chemically Induced Dynamic Nuclear Polarization
CNDO	Complete Neglect of Differential Overlap
Cp	cyclopentadienyl
DAD	diethyl azodicarboxylate
DBN	1,5-diazabicyclo[4.3.0]non-5-ene
DBU	1,5-diazabicyclo[5.4.0]undec-5-ene
DCC	dicyclohexylcarbodi-imide
DIOP	[(2,2-dimethyl-1,3-dioxolan-4,5-diyl)bis(methylene)]-bis(diphenylphosphine)
DMF	dimethylformamide
DMSO	dimethyl sulphoxide
DMTr	4,4'-dimethoxytrityl
EDTA	ethylenediaminetetra-acetic acid
E.H.T.	Extended Hückel Treatment
ENU	<i>N</i> -ethyl- <i>N</i> -nitrosourea
FID	Free Induction Decay
g.l.c.—m.s.	gas—liquid chromatography—mass spectrometry
HMPT	hexamethylphosphortriamide
h.p.l.c.	high-performance liquid chromatography
i.r.	infrared
L.F.E.R.	Linear Free-Energy Relationship
MINDO	Modified Intermediate Neglect of Differential Overlap
MO	Molecular Orbital
MS-Cl	mesitylenesulphonyl chloride
MS-nt	mesitylenesulphonyl-3-nitro-1,2,4-triazole
MS-tet	mesitylenesulphonyltetrazole
NBS	<i>N</i> -bromosuccinimide
n.q.r.	nuclear quadrupole resonance
p.e.	photoelectron
PPA	polyphosphoric acid
SCF	Self-Consistent Field
TBDMS	<i>t</i> -butyldimethylsilyl
TDAP	tris(diethylamino)phosphine
TFAA	trifluoroacetic acid
Tf ₂ O	trifluoromethanesulphonic anhydride

*Abbreviations used in Chapters 7 and 8 are detailed in *Biochem. J.*, 1970, 120, 449 and 1978, 171, 1.

THF	tetrahydrofuran
t.l.c.	thin-layer chromatography
TPS-Cl	tri-isopropylbenzenesulphonyl chloride
TPS-nt	tri-isopropylbenzenesulphonyl-3-nitro-1,2,4-triazole
TPS-tet	tri-isopropylbenzenesulphonyltetrazole
TsOH	toluene- <i>p</i> -sulphonic acid
u.v.	ultraviolet

Contents

Chapter 1	Phosphines and Phosphonium Salts	1
	<i>By D. W. Allen</i>	
1	Phosphines	1
	Preparation	1
	From Halogenophosphines and Organometallic Reagents	1
	From Metallated Phosphines	3
	By Addition of P-H to Unsaturated Compounds	6
	By Reduction	7
	Miscellaneous Methods	8
	Reactions	10
	Nucleophilic Attack at Carbon	10
	Nucleophilic Attack at Halogen	12
	Nucleophilic Attack at Other Atoms	14
	Miscellaneous Reactions	17
2	Phosphonium Salts	19
	Preparation	19
	Reactions	24
	Alkaline Hydrolysis	24
	Additions to Unsaturated Phosphonium Salts	25
	Miscellaneous Reactions	26
3	$p\pi$ -Bonded Phosphorus Compounds	28
4	Phospholes and Phosphorins	32
Chapter 2	Quinquecovalent Phosphorus Compounds	37
	<i>By C. D. Hall</i>	
1	Introduction	37
2	Structure, Bonding, and Reorganization of Ligands	38
3	Phosphoranes that contain a P-H Bond	40
4	Acyclic Phosphoranes	41
5	Four-membered-ring Phosphoranes	44
6	Five-membered-ring Phosphoranes	45
7	Six- and Seven-membered-ring Phosphoranes	56
8	Hexaco-ordinated Phosphorus Compounds	58

Chapter 3	Halogenophosphines and Related Compounds	60
	<i>By J. A. Miller</i>	
1	Introduction	60
2	Halogenophosphines	60
	Preparation	60
	Physical and Structural Aspects	61
	Reactions that lead to p_{π} Bonds to Phosphorus	62
	Reactions with Alkenes or Dienes	63
	Reactions with Carbanions	64
	Reactions with Carbonyl Compounds	65
	Reactions with Oxygen Nucleophiles	68
	Reactions with Phosphorus Nucleophiles	68
	Miscellaneous Reactions	70
3	Silylphosphines	71
4	Halogenophosphoranes	72
	Preparation	72
	Physical and Structural Aspects	72
	Reactions	73
Chapter 4	Phosphine Oxides and Related Compounds	77
	<i>By J. A. Miller</i>	
1	Introduction	77
2	Preparation of Acyclic Oxides	77
3	Preparation of Cyclic Oxides	80
4	Structural and Physical Aspects	83
5	Reactions at Phosphorus	84
6	Reactions of the Side-Chain	90
7	Phosphine Oxide Complexes and Extractants	92
Chapter 5	Tervalent Phosphorus Acids	95
	<i>By B. J. Walker</i>	
1	Introduction	95
2	Phosphorous Acid and its Derivatives	95
	Nucleophilic Reactions	95
	Attack on Saturated Carbon	95
	Attack on Unsaturated Carbon	97

Attack on Oxygen	104
Attack on Halogen	107
Electrophilic Reactions	109
Reactions involving Two-co-ordinate Phosphorus	112
Cyclic Esters of Phosphorous Acid	118
Miscellaneous Reactions	120
3 Phosphonous and Phosphinous Acids and their Derivatives	122
 Chapter 6 Quinquevalent Phosphorus Acids	 123
<i>By R. S. Edmundson</i>	
1 Synthesis	123
General	123
Phosphoric Acid and its Derivatives	124
Phosphonic and Phosphinic Acids and their Derivatives	129
2 Reactions	139
General	139
Phosphoric Acid and its Derivatives	142
Phosphonic and Phosphinic Acids and their Derivatives	149
 Chapter 7 Phosphates and Phosphonates of Biochemical Interest	 157
<i>By D. W. Hutchinson</i>	
1 Introduction	157
2 Coenzymes and Cofactors	158
3 Sugar Phosphates	161
4 Phospholipids	163
5 Phosphonates	166
6 Enzyme Mechanisms	167
7 Other Compounds of Biochemical Interest	169
 Chapter 8 Nucleotides and Nucleic Acids	 172
<i>By J. B. Hobbs</i>	
1 Introduction	172
2 Mononucleotides	172
Chemical Synthesis	172
Cyclic Nucleotides	180
Affinity Chromatography	183

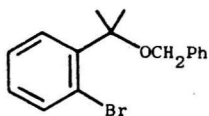
3 Nucleoside Polyphosphates	185
Chemical Synthesis	185
Affinity Labelling	195
4 Oligo- and Poly-nucleotides	200
Chemical Synthesis	200
Enzymatic Synthesis	214
Sequencing	219
Other Studies	221
5 Analytical Techniques and Physical Methods	227
Chapter 9 Ylides and Related Compounds	231
<i>By B. J. Walker</i>	
1 Introduction	231
2 Methylenephosphoranes	231
Preparation and Structure	231
Reactions	236
Aldehydes	236
Ketones	243
Miscellaneous	244
3 Reactions of Phosphonate Anions	248
4 Selected Applications in Synthesis	256
Carbohydrates	256
Carotenoids and Related Compounds	258
β -Lactam Antibiotics	261
Leucotrienes and Related Compounds	261
Pheromones	266
Prostaglandins	269
Miscellaneous Applications	271
Chapter 10 Mass Spectrometry of Organophosphorus Compounds	278
<i>By J. R. Chapman</i>	
1 Introduction	278
2 Techniques	278
Chemical Ionization and 'In-Beam' Evaporation	
Techniques	278
Negative-ion Chemical Ionization	280
Field Desorption and Ionization by Energetic Particles	281
Identification of Metastable Ions	282
Liquid Chromatography	283

3 Natural Products	283
Nucleotides	283
Phospholipids	287
Miscellaneous Natural Phosphates	289
4 Synthetic Compounds	290
Organophosphorus Ester Pesticides	290
Phosphates	292
Phosphonates	296
Phosphites	298
Phosphinates	298
Phosphines	299
Phosphonium Salts	301
Phosphazenes	302
Miscellaneous	303
Chapter 11 Physical Methods	305
<i>By J. C. Tebby</i>	
1 Nuclear Magnetic Resonance Spectroscopy	305
Biological, Analytical, and Instrumental Aspects	305
Chemical Shifts and Shielding Effects	305
Phosphorus-31	305
δ_P of n^1 compounds	306
δ_P of n^2 compounds	306
δ_P of n^3 compounds	306
δ_P of n^4 compounds	307
δ_P of n^5 compounds	308
Hydrogen-1, -2, and -3	308
Carbon-13	309
Oxygen-17	309
Fluorine-19	309
Studies of Equilibria, Hydrogen-Bonding, and Shift	
Reagents	309
Variable-Temperature Studies: Inversion	310
Restricted Rotation and Conformation	310
Pseudorotation	311
Spin-Spin Couplings	311
$J(PM)$ and $J(PP)$	311
$J(PF)$	312
$J(PN)$	312
$J(PC)$	313
$^1J(PD)$	313
$^2J(PCH)$	313
$J(PCC_nH)$ and $J(POC_nH)$	313

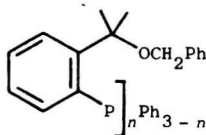
Relaxation, CIDNP, and N.Q.R.	314
Relaxation	314
CIDNP	314
N.Q.R.	314
2 Electron Spin Resonance Spectroscopy	315
3 Vibrational and Rotational Spectroscopy	316
Band Assignments and Absorptivity	316
Bonding	316
Stereochemistry	317
Rotational Data	318
4 Electronic Spectroscopy	319
Absorption Spectroscopy	319
Photoelectron Spectroscopy	319
Optical Rotation	320
5 Diffraction	320
X-Ray Diffraction	320
Electron Diffraction	325
6 Dipole Moments and Kerr Effects	325
7 Values of pK_a and Thermochemical and Kinetic Studies	326
8 Chromatography and Surface Properties	327
Gas-Liquid Chromatography	327
Thin-Layer, Paper, and Gel Chromatographies	328
High-Performance Liquid Chromatography	328
Column Chromatography	328
Surface Properties	328
Author Index	329

1 Phosphines

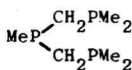
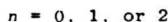
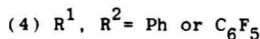
Preparation.—From Halogenophosphines and Organometallic Reagents. The reactions of the Grignard reagent derived from the bromo-ether (1) with halogenophosphines have yielded the phosphino-ethers (2), which react with bromine to give a series of stable cyclic phosphoranes.¹ Treatment of alkyl- or aryl-phosphonous dichlorides with the 'magnesium butadiene' complex gives rise to the phosphirans (3), which isomerize to phospholens above 150°C.² Acetylenic Grignard reagents have been employed in the synthesis of the phosphines (4).³ Methylmagnesium chloride converts the halogenophosphine that was extracted from the residues in the synthesis of bis(dichlorophosphino)methane into the triphospha-alkane (5),⁴ and phenylmagnesium bromide has been used to convert the cyclic halogenophosphines that are obtained from the reactions of diarylamines and phosphorus trichloride at elevated temperatures into the cyclic phosphines (6).⁵



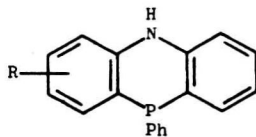
(1)

(2) $n = 1$ or 2 

(3)



(5)



(6)

¹ I. Granoth, *J. Chem. Soc., Perkin Trans. 1*, 1982, 735.

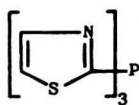
² W. J. Richter, *Angew. Chem., Int. Ed. Engl.*, 1982, 21, 292.

³ S. A. Krupoder, G. N. Dolenko, G. G. Furin, O. I. Andreevskaya, and G. G. Yakobson, *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk*, 1981, No. 6, p. 119 (*Chem. Abstr.*, 1982, 96, 104 401).

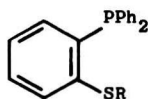
⁴ S. Hietkamp, H. Sommer, and O. Stelzer, *Angew. Chem., Int. Ed. Engl.*, 1982, 21, 376.

⁵ H. S. Freeman and L. D. Freedman, *J. Org. Chem.*, 1981, 46, 5373.

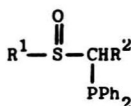
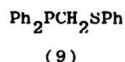
Many examples of the use of organolithium reagents have also been reported. The heteroaryl-phosphine (7) has been prepared by the reaction of 2-thiazolyl-lithium and phosphorus trichloride. Unfortunately, this route fails for the preparation of the related tris-(2-benzothiazolyl)phosphine and also for that of tris-[2-(1-methyl)imidazolyl]phosphine. However, phosphines bearing these, and other, heteroaryl groups have been successfully prepared by the reactions of halogenophosphines and the appropriate trimethylsilyl-substituted heterocycle.⁶ *ortho*-Lithiation of phenyl sulphides, followed by treatment with diphenylphosphinous chloride, affords the phosphino-thioethers (8).⁷ The reaction of lithiomethyl phenyl thioether with diphenylphosphinous chloride offers an improved route to the phosphino-thioether (9).⁸ Treatment of α -lithiomethyl sulphoxides with halogenophosphines gives the sulphoxide-phosphines (10), which are stable only at low temperatures, tending to undergo transfer of oxygen from sulphur to phosphorus.⁹ Attempts to prepare the phosphine (11) by the reaction of 2,6-bis(difluoromethyl)phenyl-lithium with phosphorus trichloride are frustrated by side-reactions of the difluoromethyl groups, the desired compound being isolated in only 2% yield.¹⁰ The vinyl carbanions that are formed in the reactions of ketone arylsulphonylhydrazones with the butyl-lithium-TMEDA complex can be trapped with halogenophosphines, giving a general method for the preparation of vinyl-phosphines (12).¹¹



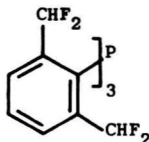
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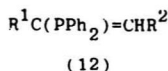
(8) R = alkyl or Ph



(10)



(11)



Dilithiated reagents have been used in the preparation of a range of potentially chelating diphosphines (13)–(15), based on the biphenyl,¹² naphthalene,¹³ and ferrocene¹⁴ systems.

⁶ S. S. Moore and G. M. Whitesides, *J. Org. Chem.*, 1982, 47, 1489.

⁷ L. Horner, A. J. Lawson, and G. Simons, *Phosphorus Sulfur*, 1982, 12, 353.

⁸ T. Gerdau and R. Kramolowsky, *Z. Naturforsch., Teil. B*, 1982, 37, 332.

⁹ E. Vedejs, H. Mastalerz, G. P. Meier, and D. W. Powell, *J. Org. Chem.*, 1981, 46, 5253.

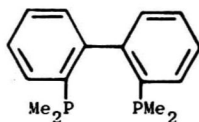
¹⁰ E. E. Wille, D. S. Stephenson, P. Capriel, and G. Binsch, *J. Am. Chem. Soc.*, 1982, 104, 405.

¹¹ D. G. Mislankar, B. Mugrage, and S. D. Darling, *Tetrahedron Lett.*, 1981, 22, 4619.

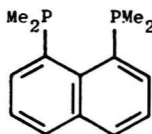
¹² T. Costa and H. Schmidbaur, *Chem. Ber.*, 1982, 115, 1367.

¹³ T. Costa and H. Schmidbaur, *Chem. Ber.*, 1982, 115, 1374.

¹⁴ J. D. Unruh and J. R. Christenson, *J. Mol. Catal.*, 1982, 14, 19.



(13)

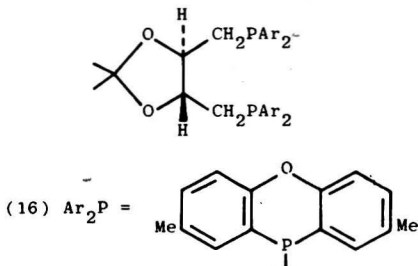


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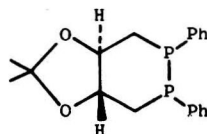


(15)

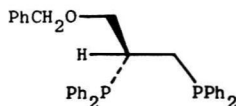
Preparation of Phosphines from Metallated Phosphines. The reactions of metallophosphide reagents with alkyl halides or tosylates (and related sulphonate esters) have found extensive application in the past year for the synthesis of a wide range of new phosphines. Once again, the driving force has been the search for new chiral phosphine ligands for use in transition-metal-complex-catalysed homogeneous hydrogenation and other reactions. A number of modifications of the DIOP structure have appeared, all involving the reactions of lithiophosphide reagents with tosylate esters.



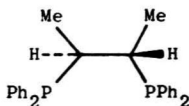
(16)



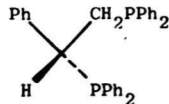
(17)



(18)



(19)



(20)

In addition to polymer-supported DIOP systems,^{15,16} the ligands (16)¹⁷ and (17)¹⁸ have been described. The latter – ‘cycloDIOP’ – is an example of a new class of chiral diphosphines, having a P–P bond. The lithiophosphide–tosylate route has also been employed in the synthesis of chiral phosphines that are derived from inexpensive, optically active, natural products,^{19–21} e.g. (18).²⁰ Some degree of steric inhibition has been noted in the reactions of lithiophosphide reagents with neopentyl tosylates.¹⁹ An

¹⁵ K. Ohkubo, M. Haga, K. Yoshinaga, and Y. Motozato, *Inorg. Nucl. Chem. Lett.*, 1981, 17, 215.

¹⁶ M. Cerny, Czech. P. 185 139 (*Chem. Abstr.*, 1981, 95, 62 412).

¹⁷ C. F. Hobbs and W. S. Knowles, *J. Org. Chem.*, 1981, 46, 4422.

¹⁸ S. Y. Zhang, S. Yemul, H. B. Kagan, R. Stern, D. Commereuc, and Y. Chauvin, *Tetrahedron Lett.*, 1981, 22, 3955.

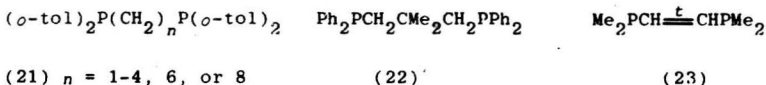
¹⁹ G. Comisso, A. Segal, and V. Šunjić, *Croat. Chem. Acta*, 1981, 54, 375.

²⁰ D. Lafont, D. Sinou, and G. Descotes, *J. Chem. Res.*, 1982, (S), 117; (M), 1401.

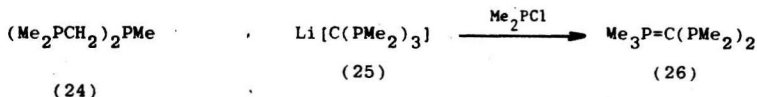
²¹ D. P. Riley, Eur. Pat. Appl. 36 741 (*Chem. Abstr.*, 1982, 96, 69 221).

improved yield of (*S,S*)-chiraphos (19) results from the use of the mesylate ester, rather than the tosylate of the precursor diol, with lithium diphenylphosphide.²² Mesylates have also been used in the synthesis of a range of chiral bis(diphenylphosphino)- α -phenyl-alkanes, e.g. (20),²³ and of chiral alkyl-diphenylphosphines.²⁴

The reactions of lithium organophosphide reagents with alkyl halides have been used to prepare a range of chelating diphosphine ligands, e.g. (21)²⁵ and (22).²⁶ Chloromethyldimethylphosphine is converted into bis(dimethylphosphino)methane on treatment with lithium dimethylphosphide.²⁷ The reactions of 1,2-dichloroethene with lithium dimethylphosphide appear to involve an addition-elimination mechanism. Whereas the *trans*-alkene yields the *trans*-diphosphine (23), the *cis*-alkene yields only a small amount of the *trans*-diphosphine and none of the *cis*-diphosphine.²⁸ Full details of the synthesis of phosphino-macrocycles have now appeared.^{29,30}



Further applications of reagents obtained by lithiation at a carbon atom alpha to phosphorus have been described and a review of such reagents as synthons has appeared.³¹ The reaction of (lithiomethyl)dimethylphosphine with methylphosphonous dichloride affords the triphosphine (24),³² and that of the reagent (25) with dimethylphosphinous chloride gives the unusual ligand (26).³³ Full details of the reactions of (lithiomethyl)diphenylphosphine with dimethylfulvene in various solvents have now appeared.³⁴



A number of examples of the use of sodium or potassium organophosphides have also appeared. The hitherto unknown phosphine (27) is formed

²² N. C. Payne and D. W. Stephan, *J. Organomet. Chem.*, 1981, 221, 203.

²³ J. M. Brown and B. A. Murrer, *J. Chem. Soc., Perkin Trans. 2*, 1982, 489.

²⁴ P. Salvadori, R. Lazzaroni, A. Raffaelli, S. Pucci, S. Bertozzi, D. Pini, and G. Fatti, *Chim. Ind. (Milan)*, 1981, 63, 492.

²⁵ P. W. Clark and B. J. Mulroney, *J. Organomet. Chem.*, 1981, 217, 51.

²⁶ C. S. Kraihanzel, J. M. Ressler, and G. M. Gray, *Inorg. Chem.*, 1982, 21, 879.

²⁷ H. H. Karsch, *Chem. Ber.*, 1982, 115, 823.

²⁸ D. J. Gulliver and W. Levason, *Inorg. Chim. Acta, Lett.*, 1981, 54, L15.

²⁹ E. P. Kyba, R. E. Davis, C. W. Hudson, A. M. John, S. B. Brown, M. J. McPhaul, L.-K. Liu, and A. C. Glover, *J. Am. Chem. Soc.*, 1981, 103, 3868.

³⁰ M. Ciampolini, P. Dapporto, A. Dei, N. Nardi, and F. Zanobini, *Inorg. Chem.*, 1982, 21, 489.

³¹ H.-P. Abicht and K. Issleib, *Z. Chem.*, 1981, 21, 341.

³² H. H. Karsch, *Z. Naturforsch., Teil. B*, 1982, 37, 284.

³³ H. H. Karsch, *Chem. Ber.*, 1982, 115, 1956.

³⁴ N. E. Schore and B. E. La Belle, *J. Org. Chem.*, 1981, 46, 2306.